

# The effects of nutrition and supplementation for children and adolescents with sickle cell disease: a systematic review and meta-analyses

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## INTRODUCTION

Sickle Cell Disease (SCD), a neglected chronic genetic blood disorder, is marked by severe health complications that often lead to premature death - with mortality rates reaching up to 50% in children under five. Due to its impact on nutritional status, supplementation is paramount to reduce the risk of these complications [1-3].

## OBJECTIVE

This study aimed to evaluate the effect of nutritional supplementation in SCD-related complications in children and adolescents.

## METHOD

PubMed, Scopus and Web of Science were searched for this systematic review. Randomized controlled trials (RCT) including nutrition and supplementation interventions used as complementary therapy for children and adolescents with SCD were included (PROSPERO CRD42024532369). The data for the outcomes of interest (efficacy, safety) were pooled by means of pairwise and network meta-analyses with surface under the cumulative rating curve analysis (ranking analyses based on p-score). The results were presented as odds ratio (OR) or standardized mean differences (SMD) with 95% credibility intervals (p-values <0.05 considered significant) (NMAstudio2.0).

## RESULTS

Twenty RCTs were included (2002-2023) (n=2,058), analyzing 9 dietary supplements on different regimens (Figure 1). All patients were in use of hydroxyurea as active treatment. Supplementation with fatty acids (n=3) and L-arginine (n=4) presented higher efficacy and safety, significantly improving pain intensity, vaso-occlusive crises (VOC) and inflammation when compared to usual care or placebo (p<0.05). Vitamin D3 (n=6) at different dosages may reduce respiratory complications, pain intensity and length of hospital stay. While citrulline (n=1), vitamin A (n=2), and lime juice (n=1) (p<0.001) may offer some improvement for SCD-related complications, the available evidence is limited and of poor quality. Similarly, data on the effects of add-on zin (n=4) in this population are also scarce (Figures 2 and 3).

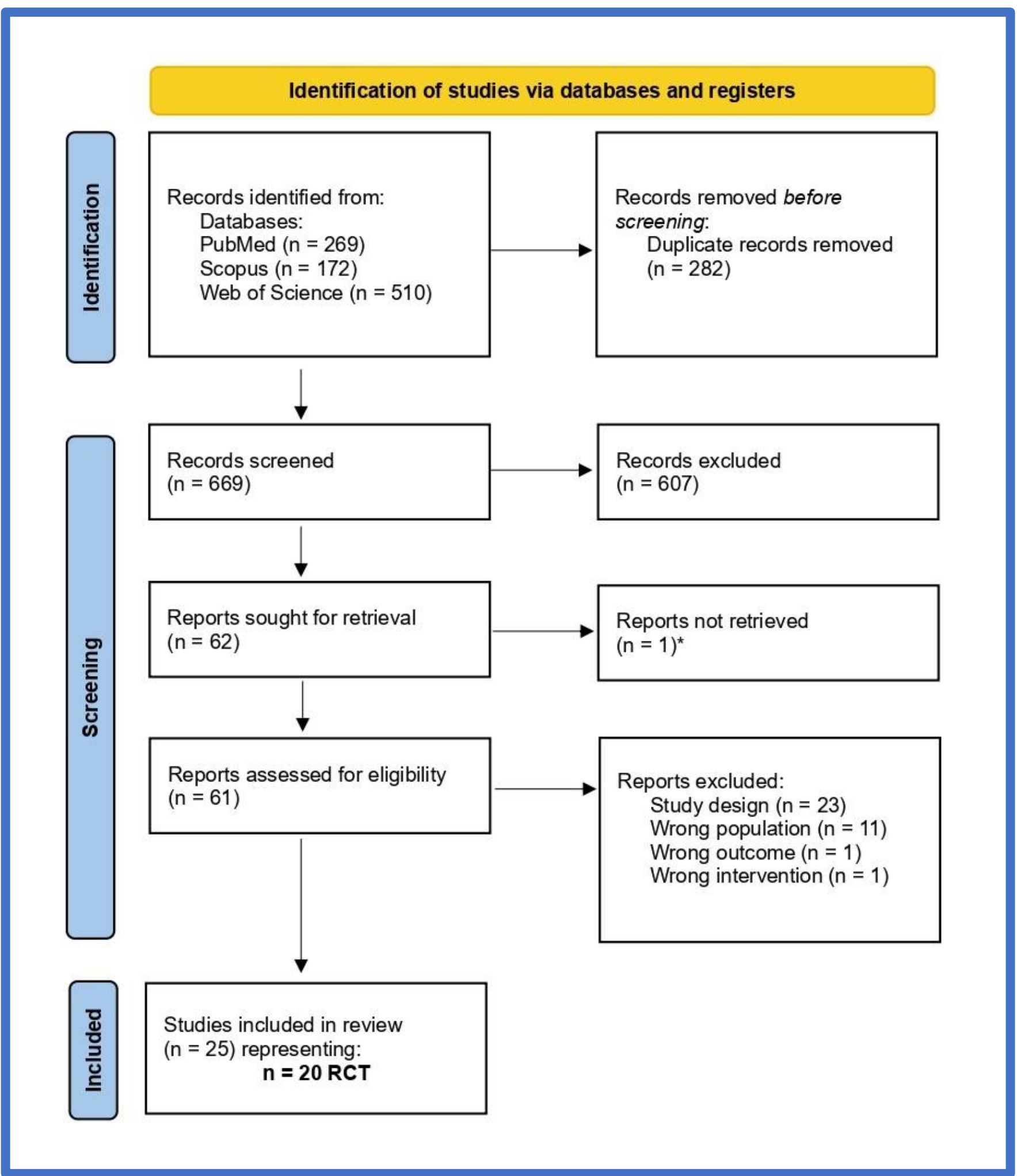


Figure 1. PRISMA flowchart



Figure 2. Network meta-analyses for the outcomes of interest

Intervention	Change in pain score	Impact on LOS	VOC	Mild AE
Arginine + Citrulline	-	-	-	49%
EPA + DHA or DHA	53%	-	27%	49%
L-arginine 100mg	86%	72%	46%	40%
L-arginine 200mg	55%	62%	65%	-
MgSO <sub>4</sub>	-	53%	-	77%
Vitamin A	-	33%	-	-
Vitamin A + Zinc	-	7%	-	-
Vitamin D3	40%	71%	20%	-
Placebo	30%	40%	67%	32%

Figure 3. Ranking analysis

AE: adverse events; DHA: docosahexaenoic acid; EPA: eicosapentaenoic acid; LOS: length of hospital stay; MgSO<sub>4</sub>: magnesium sulfate; VOC: vaso-occlusive crisis

## CONCLUSIONS

The statistical analyses indicates that the complementary use of some supplements – especially fatty acids, L-arginine (low doses) and vitamin D3 can enhance the management of VOC and improve patients’ physiological functions and health-related quality of life. These supplements are often affordable and can contribute towards the reduction of opioid use and shorten patients’ hospital stays - especially in low/middle-income countries where resources are scarce. Although further studies are needed to refine these findings (e.g., appropriate doses/regimens), practical guidelines and decision-makers may benefit from updated evidence.

## REFERENCES

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