

Appendix 3 (as supplied by the authors): Subgroup credibility

Sun et al. Criteria(23)	Duration of Symptoms			Severity of Symptoms		
	Age (children vs. adults)	Ionic Zinc Dose	Zinc formulation	Age (children vs. adults)	Ionic Zinc Dose	Zinc formulation
DESIGN						
Variable measured at baseline	Y	Y	Y	Y	Y	Y
Comparison within study	N	N	N	N	N	N
<i>A priori</i> hypothesis	Y	Y	Y	Y	Y	Y
Direction specified <i>a priori</i>	Y	Y	Y	Y	Y	Y
Small number subgroups	N	N	N	N	N	N
ANALYSIS						
Interaction test significant	Y	Y	Y	Y	Y	Y
Is effect independent	Y	N [#]	N [§]	N	N	N
CONTEXT						
Large size of subgroup effect	Y	Y	Y	N	N	N
Interaction consistent across studies	N/A	N/A	N*	N/A	N/A	N*
Interaction consistent across closely related outcomes within study	Y**	Y	Y	Y	Y	Y
Biologic rationale	Y	Y	Y	Y	Y	Y
Total Number	8	7	7	6	6	6
Conclusion	Plausible	Plausible	Likely related to iZn	Possible	Possible	Likely related to iZn

Zinc formulations release varying amounts of ionic zinc (zinc acetate releases 100% ionized zinc)

§ Zinc sulfate was used exclusively in children (syrup formulation) and zinc acetate (tablets/lozenges) used exclusively in adults.

*Turner et al.(24) had three zinc arms (zinc acetate, two doses zinc gluconate); zinc gluconate arm had reduction in duration of symptoms but zinc acetate did not (opposite of observed subgroup effect). No difference in severity of symptoms in those on zinc gluconate or zinc acetate.

** Subgroup effect could not be assessed for presence of symptoms at 3 and 7 days because of only 1 pediatric trial reporting these outcomes. But, reduction in severity of symptoms was seen in adults but not children.