

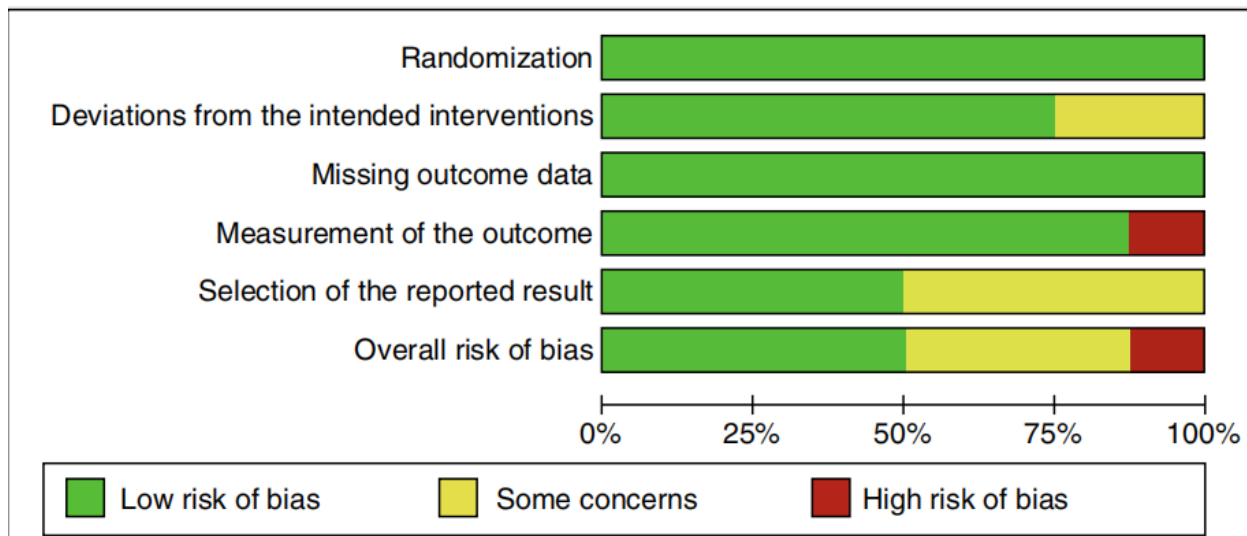
1 Supplementary Data

The search strategy for MEDLINE, Embase, and CENTRAL was performed on 10/7/2022 (n=380)

1. exp premature birth/or exp Infant, Premature, Diseases/ or exp Infant, Premature/ or exp Obstetric Labor, Premature/ or exp Infant, Extremely Premature/
2. Exp Infant, Extremely Low Birth Weight/ or Exp Infant, Low Birth Weight/ or Exp Infant, Newborn/ or Exp Infant, Small for Gestational Age/ or Exp Infant, Very Low Birth Weight/ or Exp Infant, Extremely Premature/ or Exp Infant/ or Exp Infant, Premature Diseases
3. Premature\$.mp.
4. Infant\$.mp.
5. Newborn\$.mp.
6. Low Birth Weight\$.mp.
7. 1 or 2 or 3 or 4 or 5 or 6
8. Exp < "> <" > Retinopathy of Prematurity
9. exp retrolental fibroplasia/
10. Retinopathy of Prematurity mp.
11. Retrolental fibroplasia\$.mp.
12. 8 or 9 or 10 or 11

13. exp Vitamin A/
14. Vitamin A\$.mp.
15. Retinol\$.mp.
16. Fat\$.mp.
17. exp Fatty Acids/
18. Fatty acid\$.mp.
19. exp Fatty Acids, Omega-3/
20. Omega-3\$.mp.
21. exp Fatty Acids, Omega-6/
22. Omega-6\$.mp.
23. exp Propranolol/
24. Propranolol\$.mp.
25. Inderal\$.mp.
26. Anaprilin\$.mp.
27. Obsidan\$.mp.
28. Obzidan\$.mp.

- 29. Beta blocker\$.mp.
- 30. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
- 31. exp Randomized controlled trial/exp Clinical trials/
- 32. Trial\$.mp.
- 33. 31 or 32
- 34. 7 and 12 and 30 and 33

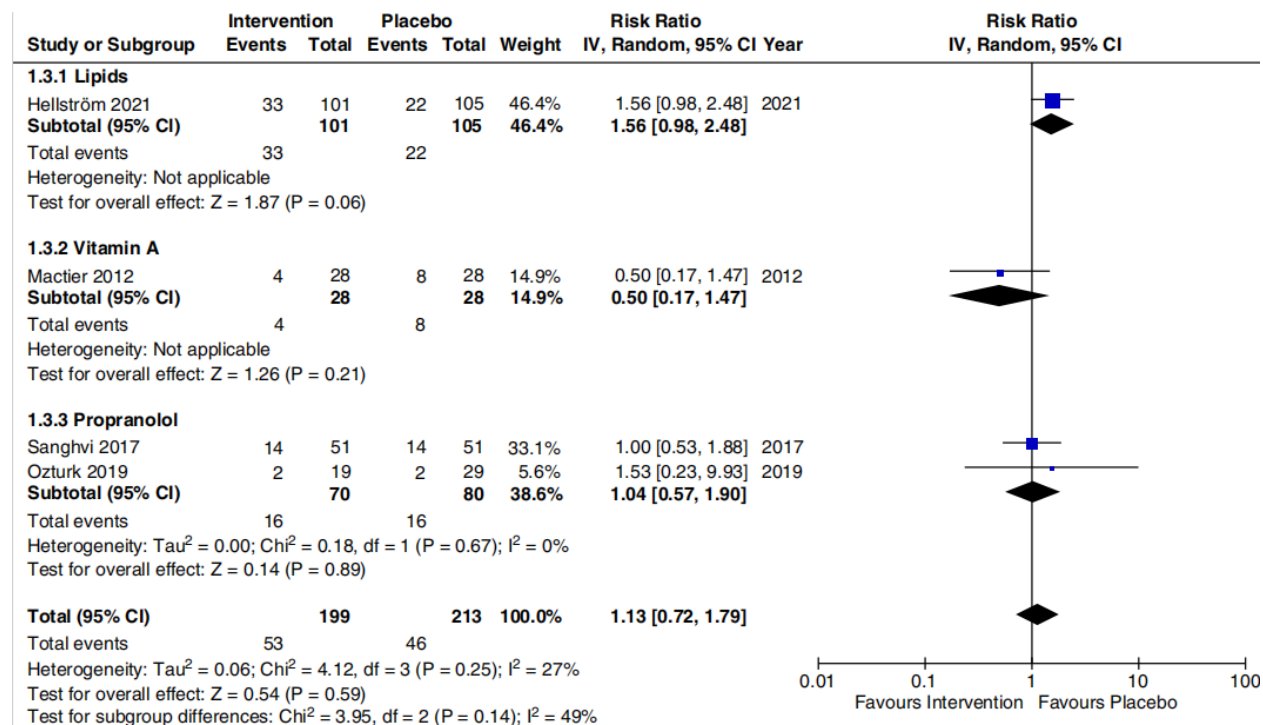


Supplementary Figure 1:

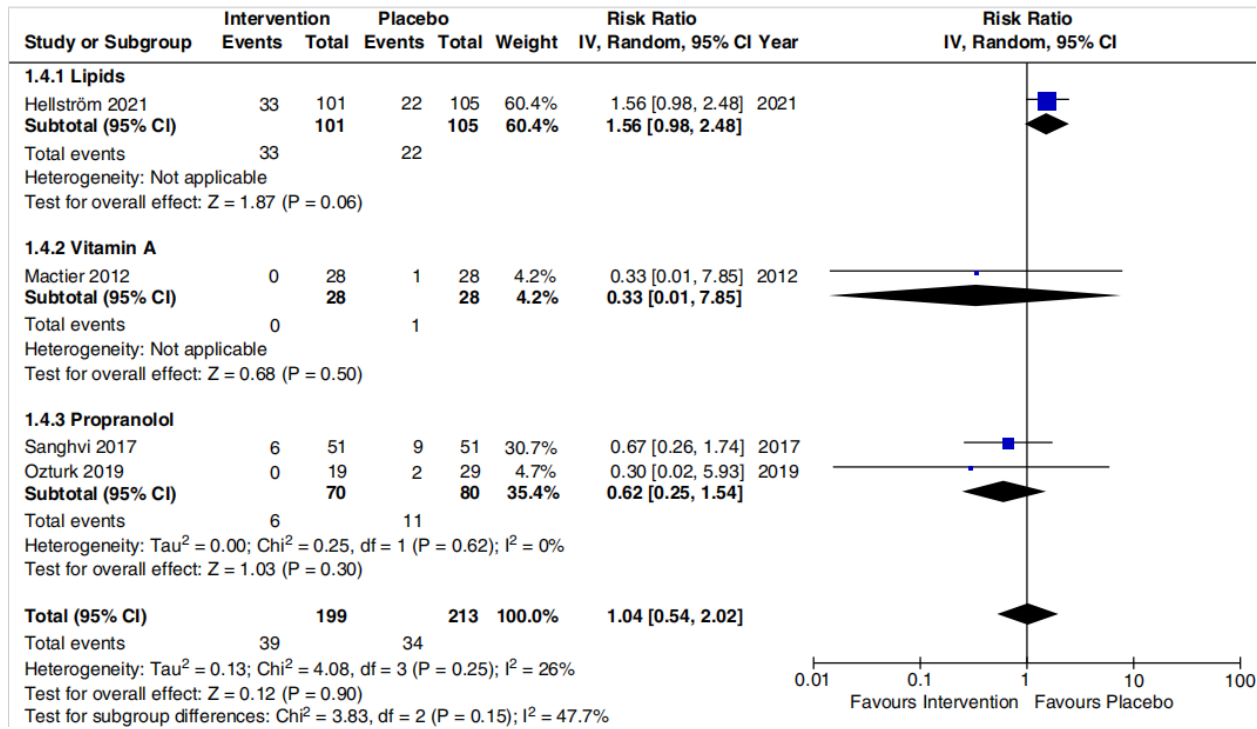
ROB results

	Randomization	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Basu 2019	+	+	+	+	+	+
Hellström 2021	+	+	+	+	+	+
Korkmaz 2016	+	?	+	+	?	?
Mactier 2012	+	+	+	+	+	+
Ozturk 2019	+	+	+	+	?	?
Sanghvi 2017	+	+	+	+	+	+
Shenai 1987	+	?	+	+	?	?
Wardle 2001	+	+	+	-	?	-

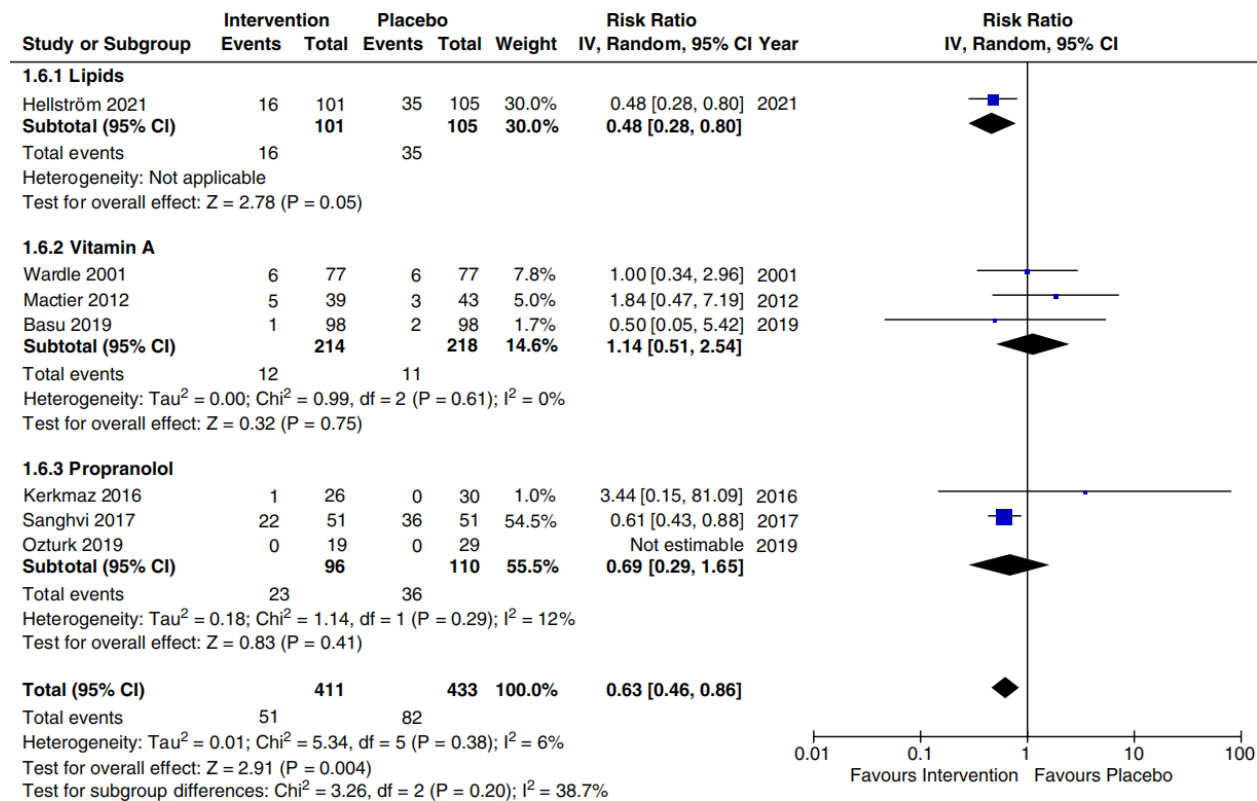
Supplementary Figure 2: ROB results



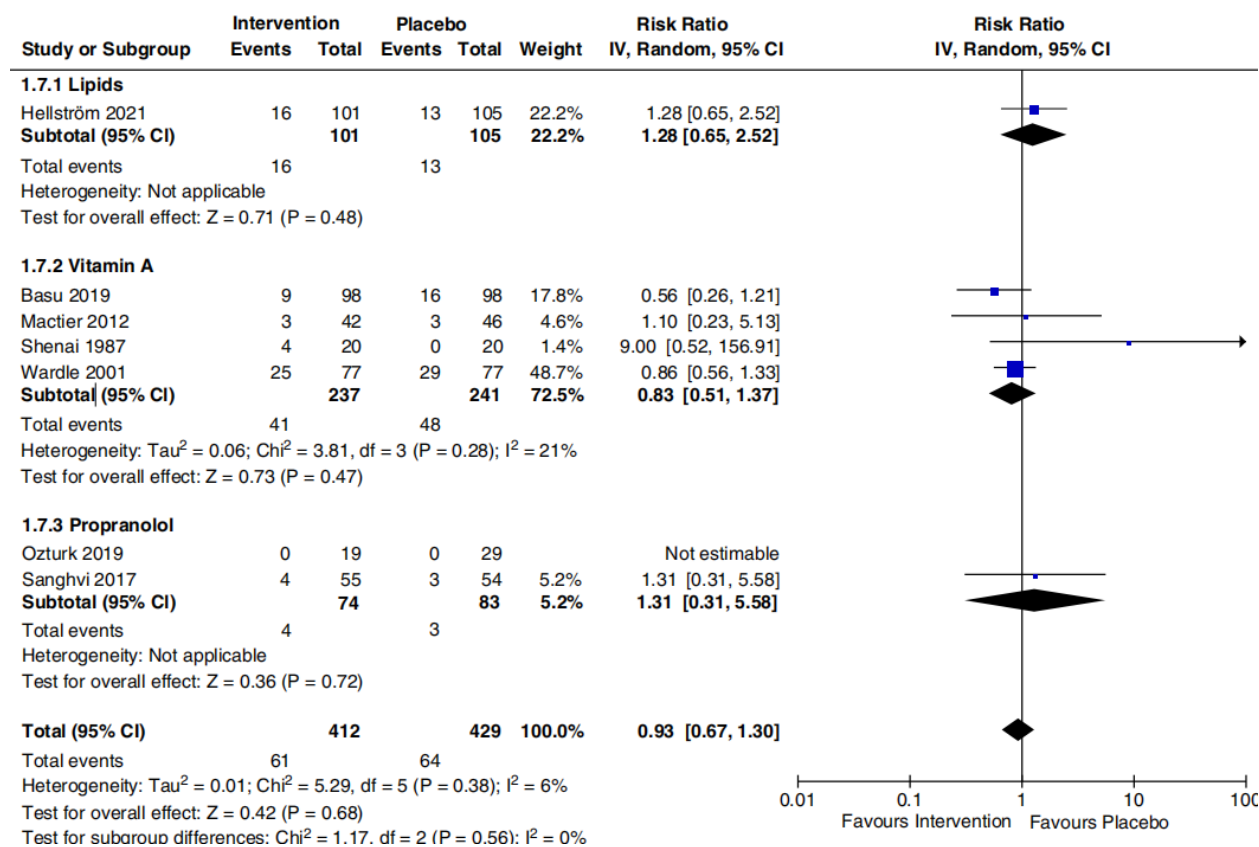
Supplementary Figure 3: Meta-analysis of ROP stage 1



Supplementary Figure 4: Meta-analysis of ROP stage 2



Supplementary Figure 5: Meta-analysis of ROP stage 3



Supplementary Figure 6: meta-analysis of mortality rate

Supplementary table: Characteristics of the Included Studies

Author, year	Intervention	Intervention specifics				Number of Participants		Gestational Age (weeks)		Mean birth weight (grams)		Gender		Measured outcomes
		Dose	Route	Time of initiation/duration	Serum concentration	Intervention	Placebo	Intervention	Placebo	Intervention	Placebo	Male	Female	

Shenai 1987	Vitamin A	2000 IU	IM injection	Postnatal day 4 and every other day thereafter for a total of 14 injections over 28 days	Day 4 of life (before) = 20 µg/dL, Day 10 = 40 µg/dL, Day 17 = 30 µg/dL, Day 24 = 25 µg/dL, Day 31 = 35 µg/dL	20	20	27.9 ± 1.3	28.0 ± 1.3	1006 ± 163	976 ± 162	Intervention: 10 (50%) Control: 10 (50%)	Intervention: 10 (50%) Control: 10 (50%)	Occurrence of BPD, pulmonary air dissection, symptomatic patent ductus arteriosus, sepsis, airway infection, intraventricular hemorrhage, and retinopathy of prematurity
Mactier 2012	Vitamin A	10000 IU	IM injection	3 times weekly from day 2, continued until commencement of oral supplementation on day 14, or for a maximum of 12 doses	Day 1 = 0.5 (0.28) µmol/L, Day 7 = 1.0 (0.60) µmol/L, Day 28 = 0.7 (0.35) µmol/L,	42	47	29.3 (24.0-33.0)	29.3 (24.3 - 32.6)	1102.5 (630-1800)	1150 (580-1770)	NR	NR	The primary outcome was cone-corrected, dark-adapted, retinal sensitivity at 36 weeks; associations were also sought between total vitamin A intake, and plasma retinol

														levels and ROP.
Wardle 2001	Vitamin A	5000 IU/day	Oral	Postnatal day 1 starting immediately until day 28	Intervention median (IQR): 0.13 (0.08–0.26) at baseline Control median (IQR): 0.13 (0.08–0.22) at baseline	77	77	Median (IQR): 26 (25–27)	Median (IQR): 26 (25–27)	Median (IQR): 806 (710–890)	Median (IQR): 782 (662–880)	Intervention: 37 (48%) Control: 30 (39%)	Intervention: 40 (52%) Control: 47 (61%)	Number of participants who had ROP requiring treatment, adverse events, and death

Basu 2019	Vitamin A	10,000 IU	Enterally	Starting at 24 h of life (total 14 doses) for 28 days	Intervention: 17.6 ± 7.0 at baseline Control: 17.5 ± 6.7 at baseline	98	98	30.9 ± 2.9	30.7 ± 2.7	1185 ± 194	1163 ± 181	Intervention: 54 (55.1%), placebo: 56 (57.1%)	Intervention: 44 (44.9%), placebo: 42 (42.9%)	Number of participants who had ROP requiring treatment, adverse events, and deaths
Korkmaz 2016	Propranolol	0.5 mg/kg/6 hours at 30 minutes before feeding	Oral	Propranolol was administered to stage 0 ROP patients at the end of phase 1 (i.e. the obliteration phase when VEGF levels were low) and at the beginning of phase 2 (i.e. neovascularization phase when VEGF levels were elevated).	NR	Stage 0 ROP= 26, Stage 1 ROP= 30, Stage 2 ROP=27 (TOTAL=83)	Stage 0 ROP= 30, Stage 1 ROP=32, Stage 2 ROP= 26 (TOTAL=88)	Stage 0 ROP= Median ± SD= 29.0 ± 2.1	Stage 0 ROP = 29.0 ± 1.5	Stage 0 ROP= 1099 ± 319	Stage 0 ROP = 1054 ± 233	NR	NR	Incidence of BPD, RDS, IVH, PDA, NEC, ROP, platelet count, platelet mass index (PMI)

Ozturk 2019	Propranolol	2 mg/kg/day 30 minutes before feeding	Oral	Propranolol treatment was given in the second phase of the disease (this phase is the neovasculari- zation phase and is also known as the essential phase	NR	Stage 0 ROP= 19, Stage 1 ROP= 19, Stage 2 ROP= 20 (TOTAL =68)	Stage 0 ROP= 29, Stage 1 ROP= 21, Stage 2 ROP= 18(TOTAL L=68)	Stage 0 ROP= 29.0 ± 1.1	Stage 0 ROP = 29.0 ± 1.3	Stage 0 ROP= 1089 ± 219	Stage 0 ROP = 1064 ± 203	Stage 0 ROP= Control: 11/29, Interven- tion: 9/19	Stage 0 ROP= Control: 18/29, Interven- tion: 10/19	Plus disease detection in retinal exam increase in ROP stage, use of laser
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Sanghvi 2017	Propranolol	0.5 mg/kg/dose every 12 hours	Oral	7 days until after 37 week or complete vascularization of retina whichever was later	NR	55	54	29.54 (±1.69)	29.12 (±1.74)	1235 (±280)	1155 (±284)	Intervention: 24 (43.6%) Control: 29 (53.7%)	Intervention: 31 (56.4%) Control: 25 (46.3%)	Number of participants who had ROP of any stage, Number of participants who had ROP requiring treatment, Number of participants who had ROP stage 1, Number of participants who had ROP stage 2, Number of participants who had ROP stage 3, Adverse events, and death
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Hellström 2021	Arachidonic acid and docosahexaenoic acid	Arachidonic acid (100 mg/kg/d) and docosahexaenoic acid (50 mg/kg/d)	Oral	3 days after birth until 40 weeks' postmenstrual age.	Arachidonic acid: 12.6 (±2.4) mol% in the intervention group vs 12.6 (±2.6) mol% in the control group Docosahexaenoic acid: 2.28 (±0.68) mol% in the intervention group vs 2.37 (±0.82) mol% in the control group	101	105	25.5 (±1.5)	25.5 (±1.4)	797 (±197)	777 (±197)	Intervention: 58 (57.4%) Control: 59 (56.2%)	Intervention: 43 (42.6%) Control: 46 (43.8%)	Number of participants who had ROP of any stage, Number of participants who had ROP requiring treatment, Number of participants who had ROP stage 1, Number of participants who had ROP stage 2, Number of participants who had ROP stage 3, Number of participants who had prethreshold ROP type 1, Adverse events, and death
IM, intramuscular; IU, international unit; ROP, retinopathy of prematurity; BPD, bronchopulmonary dysplasia; PDA, patent ductus arteriosus; IVH, intraventricular hemorrhage; RDS, respiratory distress syndrome; NEC, necrotizing enterocolitis; NR, not reported														

