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e Table 1: Study Outcomes

Study ID	Results	Covariates adjusted for	Author's conclusion
Villamizar 2020	HG for ≥5 days was negatively associated with fat mass and fat free mass z scores at discharge, and fat free mass z score at 4 months' PMA. Hyperglycaemia for ≥5 days was negatively associated with cognition, language, and motor scores on the BSDI-III at 12months. Associations with body composition and BSID-III were diminished when models included first week nutrition yet remained unchanged when illness severity was included.	Gender, GA, CRIB score	HG is associated with decreased lean mass at 4 months' PMA and poorer neurodevelopmental outcome at 12 months' PMA.
Vannadil 2019	Group with higher maximum glucose (Mean 10.15 ± 0.89 mmol/L vs mean 8.71 ± 0.59		A high average blood glucose level in neonates during the

	mmol/L) had a higher incidence of ROP. p=0.179.		first week of life is an indicator for developing ROP at a later date
Bochkova 2019	9 babies from the insulin group and 7 from the no insulin group developed grade II and III IVH.		In preterm infants with VLBW, HG can be considered a transitional state. The appointment of insulin inappropriate
Jagla 2019	Univariate analysis revealed that HG was not associated with mortality before term-equivalent age (p=0.664). Higher GV was associated with grade 3 or 4 IVH (CV p=0.025; MAGE p=0.032) and ROP requiring treatment (SD p=0.019; CV p=0.026; MAGE=0.029). However, logistic regression models did not show a significant association between GV and grade 3 or 4 IVH (MAGE OR 1.31; 95% CI 0.16-10.67) or ROP requiring treatment (MAGE OR 1.74; 95% CI 0.57-5.32).	GA, O2 exposure	Logistic regression model did not show any association between glucose variability and severe IVH or ROP. No association was found between HG and IVH or PVL or mortality.
Zamir 2019	HG and its duration during postnatal weeks 1–4 were associated primarily with higher diastolic BP z-scores at 6.5 years of age. Duration of hyperglycaemia >14 mmol/L was significantly positively associated with both SBP and DBP z-scores. Each additional day with hyperglycaemia >14mmol/L was associated with an increase of ~0.05 SD in both SBP and DBP (P=0.047 and 0.014, respectively).		HG and its duration during postnatal weeks 1–4 were associated primarily with higher diastolic BP z-scores.
Goldner Perez 2019	No deaths either in HG or NG group. Incidence of NEC and PDA was more in HG group compared to NG group and is statistically significant (p= 0.039 and 0.001 respectively), whereas the incidence of CLD and IVH was not statistically significant. Moderate HG in the first week (p=0.002) and month (p=0.026) of life was associated with motor deficits. Composite BSID score was significantly lower (1SD) in infants with HG greater than 10mmol/L in the first week of life (p=0.02), but not in the first month.		HG had minimal effect on neurodevelopment. Moderate HG in the 1st week of life is associated with motor and language deficits, including after adjusting for GA and BW.
Turai 2019	No significant difference in terms of mortality (p=0.093). The GA and BW of the hyperglycaemic infants were significantly lower (p<0.001). The incidence of severe ROP and CLD was significantly higher in HG group (p= 0.012 and 0.002). Among survivors (n = 155), HG was a risk factor for severe retinopathy (p<0.001) in logistic regression analysis. Out of 17 patients with high creatinine 10 had HG.	GA, BW	HG is common in preterm infants. Monitoring of these infants for ROP, kidney dysfunction, and hypertension is recommended.
Zamir 2018	Higher 28-day mortality by a multiplicative factor of 2.45, adjusted for GA and BW (Beta 0.897; *P* = .006). HG for 2 consecutive days-multiplicative factor of 2.55, adjusted GA and BW (B 0.935; *P* = .005). No differences were noted with regards to sex, NEC, IVH grades 3-4 or number of confirmed sepsis events between HG and NG group.	GA, BW	HG during the first 28 days is associated with increased mortality. Insulin treatment during this period was associated with lower mortality.
Slidsborg	After adjustment for known risk factors,	GA, SGA,	An independent association

2018	hyperglycaemic index remained a statistically independent risk factor for development of treatment demanding ROP (OR: 1.022; 95%CI 1.002 to 1.042; p 0.031)	Gender	was found between HG events and treatment demanding ROP, when adjusted for known risk factors.
Naseh 2017	Days with glucose >8.3 mmol/l correlated independently with reduced white matter volume (p = 0.045). When BW was included in the analysis, days with glucose >8.3 mmol/l reached borderline significance (p = 0.068). In the 45 infants with follow up, only days with glucose >8.3 mmol/l was independently associated with a lower motor index on BSID-III.		Prolonged duration of high blood glucose >8.3 mmol/l during the first week of life is associated with reduced white matter volume and may also be associated with poorer motor performance at 2.5 years
Tottman 2017	Death in NG group 6/287 (2%) vs HG group 6/73 (8%) before discharge. Infants in the NG category had shorter neonatal stays and were less likely to have severe ROP, NEC, LOS, or CLD. HG and unstable infants were less likely to survive without neonatal morbidity and less likely to survive without neurodevelopmental impairment at 2 years of age. Higher mean blood glucose concentration was seen in the HG and unstable groups, and was associated with worse neonatal and 2-year outcomes. No associations between measures of neonatal glycemia and neonatal or 2-year outcomes remained after correction for gestation, birth weight z-score, and socioeconomic status.	GA, BW, ethnicity, CRIB II score Socioeconomic quantile, type of assessment at 2 years	In very preterm infants, measures of neonatal glycemia are markers of GA and intrauterine growth, and are not independent predictors of neonatal illness or outcomes at 2 years of age
Akmal 2017	Mortality- HG- 18 out of 40 neonates, NG-3 out of 20 neonates, p= 0.022. Mild/moderate HG vs Severe HG 7 /20 neonates vs 11 /20 neonates, P=0.2. There was statistically significant relation between HG and LOS and IVH. (p = 0.001, 0.003 respectively). There was statistically significant relation between severity of HG and infection in 1st week and IVH (p = 0.025 & 0.05 respectively). A significant negative correlation was found with GA and BW (p = 0.019, 0.002 respectively).		There was a statistically significant relation between HG and complications (LOS, IVH, death).
Kim 2017	In glycaemic characteristics, HG duration, average and maximum glucose level for 3 weeks after birth showed statistical significance in relation to ROP. But, in a multivariate analysis glycaemic characteristic were not. In comparisons based on ROP severity, HG duration, average blood glucose level of 3rd week after birth, and insulin use showed significant difference, but they were not independent factors.		Glycaemic characteristics were statistically significantly associated with ROP, but they were not independent factors associated with ROP development.
Reyes 2017	HG was significantly associated with ROP with a p value of 0.031.		HG is an important risk factor for ROP.
Bermick 2016	IVH developed more frequently in infants with HG (P = 0.006, odds ratio (OR) 2.3, 95% confidence interval (CI) 1.3 to 4.1), in infants with hypernatremia (P = 0.018, OR 2.0, 95% CI 1.2 to 3.5) and in infants with hypernatremia plus HG (P = 0.001, OR 3.2, 95% CI 1.6 to 6.4). Multivariate regression analysis confirmed the independent association of		HG increases the risk of IVH in hypernatremic preterm infants

	higher risk of IVH with the presence of hypernatremia plus HG (P = 0.015, OR 2.6, 95% CI 1.2 to 5.5) but not with hypernatremia or HG alone.		
Lee 2016	HG alone was not associated with severe ROP (OR=0.88 (95% CI 0.66-1.17)).	GA, SGA status, year of discharge, sex, APGAR score at 5 minutes, need for mechanical ventilation, O2 supplementation, steroid use, insulin use, bacteraemia	HG alone was not associated with severe ROP in ELBW infants.
Manzoni 2016	After controlling for all variables significantly associated with infections (i.e., LF exposure, birth weight, gestational age), occurrence of at least one episode of early HG spell retained a significant and independent association with the occurrence of infections only by Gram-positives (OR: 5.45; 95% CI: 1.92–15.42; $p < 0.001$) and fungal agents (OR: 3.37; 95% CI: 1.01–11.97; $p = 0.04$), but not by gram negatives. The day of onset of infections occurred significantly earlier in HG infants compared with NG: 13.9 versus 20.1 mean days ($p = 0.03$), regardless of the pathogen.	Lactoferrin exposure, BW, GA	Early HG spells are significantly predictive of development of LOS by gram-positives and fungal microorganisms in preterm infants
Scheurer 2016	Inpatient days, IVH and ROP was significantly higher in HG group compared to NG group. (p= <0.0001, 0.004 and 0.0001 respectively). Infants with >5 days of HG were lighter (5345 vs 6455 g, P≤ 0.001), shorter (57.9 vs 60.9 cm, P≤ 0.01), had smaller occipital-frontal head circumference (39.4 vs 42.0 cm, P≤ 0.05) and were leaner (percent body fat 15.0 vs 23.8, P ≤0.01) at 4 months CA		HG is associated with decreased body size and lower adiposity at 4 months CA independent of nutritional deficit, insulin use and illness. These changes may influence long-term growth and cognitive development.
De Carolis 2015	Mortality in NG group 18/79 (22.7) vs HG group 18/53 (33.9). Any IVH rate was higher in HG group and Hypo & HG group respect to NG Group (p=0.002) as well as IVH grade3. The rate of both any ROP and ROP ≥ stage 2 in survived neonates was higher in HG group respect to N-Group (p=0.008 and p=0.002, respectively)		All forms of IVH, ROP and sepsis was higher in the HG group.
Nicolaeva 2015	There were no significant differences in the blood glucose levels between children with and without ROP, and also between children with spontaneously regressing ROP and progressive ROP (p>0.05).		The blood glucose level is not related to the development of ROP nor with its progression or regression.
Stensvold 2015	After the introduction of early enhanced TPN, the prevalence of mortality was higher (10.9% [14 of 129] vs 24.3% [52 of 214], P = .003). Multivariate analysis- Severe HG is an independent risk factor for death (OR, 4.68; 95%CI, 1.82-12.03).	Early enhanced parenteral nutrition, GA, CRIB score, any vasopressor use	In the multivariable analysis early, severe HG is a strong predictor of death

Szymońska 2015	The tendency to increased mortality by the 28th day of life (p=0.09 for X^2 test) was observed. Moreover, a significant positive association with the severity of HG (p=0.02 for Cochran–Armitage test) was revealed. A higher incidence of IVH (p=0.09) in groups with mild and moderate/severe HG was noted. Other outcomes like CLD, PVL, NEC, ROP and hospital stay did not significantly differ between the groups.		A significantly higher mortality rate on the 28th day of life noted.
Cardona 2014	Rate of ROP increased with hyperglycaemia at 1 week and 1 month (p=0.003 and p=0.05, respectively). As the hours of HG increased, so did the probability of increase in the stage of ROP (p= 0.003). There was a trend for increase in ROP with HG >10mmol/L when corrected for BW and GA (p=0.1)		A significantly higher incidence of ROP were seen with HG in the 1st week and month of life.
Ahmadpour-Kacho 2014	The severity of ROP showed no significant differences between the2 groups (P = 0.35). The logistic regression for GA and BW showed a significant correlation between HG and ROP (P = 0.0001).	GA, BW	HG is an important risk factor for ROP that can be prevented along with other risk factors by accurate supervision
Mohsen 2014	Mortality- NG vs HG 0 vs 4 (13%), p 0.031. There were more cases of ROP in the HG group compared with the NG group (45% vs 15%, P = 0.007). Patients who developed ROP had significantly higher maximum and average glucose concentrations when compared with non-ROP patients. In a logistic regression model including all significant variables, average blood glucose in the first week of life was the factor independently associated with ROP with an OR of: 1.77 (95% confidence interval: 1.08 to 2.86), p = 0.024.CLD and IVH was not significantly different between 2 groups.		Elevated average blood glucose concentrations in the first week of life is independently associated with the development of ROP
Sabzehei 2014	91 out of 179 in HG group and 73 out of 385 in the NG group expired. (OR-4.2, 95% CI- 3-6.5, p<0.001). Higher incidence of IVH>Gr2 (OR-2.88, 95%CI-1.28-6.49, p=0.01), hospital stay>28 days in survivors (OR-3.56, 95%CI- 2.02-6.25, p=<0.001) and more ≥stage 2 ROP (OR-2.05, 95%CI-1.11-3.78, p=0.02)		HG is associated with IVH, ROP in survived neonates, prolonged hospitalization and risk of mortality. These findings underscore the need for prompt diagnosis and appropriate management.
Auerbach 2013	Increase in HG duration was most prominently increasing the adjusted OR for severe IVH (OR = 10.33, 95% CI = 10.0-10.6, P = .033). 35 out of 154 neonates with HG compared to 2 out of 24 neonates with NG died.	Semi-quantitative severity index score based on death , days of ventilation, BPD, need for dopamine treatment, and day of enteral feeds commencement	Longer duration of HG in the first 96 hours of life was most strongly associated with severe IVH in preterm infants
Mohamed 2013	HG days (mean) 2.3 ± 3.2 (No ROP group) vs 7.1 ± 6.6(ROP group) p= < 0.0001. Multiple	GA, sepsis, IVH, PDA,	HG is associated with the development of ROP in

	regression analysis for any ROP = HG days – Beta coefficient= 0.07, OR (95%CI) = 1.073 (1.004, 1.146), p value=0.04. Multiple regression analysis for stage 3 ROP= HG days- Beta coefficient= 0.0003, OR (95% CI) = 1.000 (0.938, 1.066), p = 0.99	ventilation days, neonatal steroids	premature infants
Ramel 2013	Controlling for BW, HG was a statistically significant predictor of ROP >stage 2, z=2.39, P=0.02. HG was also a significant predictor of number of episodes of sepsis, z=5.90, P=0.001. HG was not a significant predictor of IVH, z=0.64, P=0.53. By 24 months, infants with 5+ days of HG were predicted to be 2 kg lighter and 5cm shorter than infants with 0 days of HG. Statistically significant for prediction of Bayley scale scores at 12 months (initial status), but not significant for prediction of Bayley scale score at 24 months. (All infants were followed to 1-year CA and 62 (78%) were followed to 2 years CA)		Neonatal HG was associated with poor physical growth until at least 2 years CA in this cohort of VLBW preterm infants.
van der Merwe 2013	Though HG is a significant risk factor for development of ROP in univariate analysis(p=0.0267), in multiple regression analysis it was not found to be significantly associated with ROP		HG is not a risk factor for ROP
Yoo 2013	Discharge mortality: N=4/38(10.5%), P= 11/101 (10.9%), T= 38/121 (31.4%) Adjusted odds ratio- P to N odds ratio (95% CI) = 0.9 (0.2-4.8), p value- 0.89, T to N odds ratio (95% CI) = 0.8 (0.1-5.2), p= 0.84. In multivariate analysis adjusted for GA, BW, RDS, and ventilator support/major surgery/antibiotic use in 14 days, there was no significant differences in CLD, severe IVH, PVL, NEC and ROP requiring treatment between groups. Growth rate was highest in group P and lowest in group T. Although the birth weight of P was significantly smaller than N, P infants gained weight faster than N infants. Long term development found no significant difference between group N and P in terms of cerebral palsy, hearing loss or developmental delay in Bayley scale.	GA, BW, RDS, Ventilator support/ major surgery/ any antibiotics use in the first 14 days	Permissive HG up to < 16.66 mmol/L without insulin treatment during the first 14 days of life is not associated with osmotic diuresis or increased mortality or morbidities, suggesting that it is not detrimental in ELBW infants.
Bozdag 2012	Multivariate analysis for ROP- duration of HG (days; OR 3.26; 95% CI 1.09–9.80; p= 0.035) was significantly associated with ROP.	BW, Gram positive sepsis, IVH (grade 3 or more), RDS and days on CPAP, Oxygen	Duration of HG may contribute to the development of ROP
Kaempf 2011	Higher cumulative mean glucose, more episodes of HG, and more insulin exposure were associated with an increased incidence and severity of ROP. Ordinal logistic regression identified higher glucose as predictors for severity of ROP.		After adjusting for important risk factors, HG and especially Insulin use in premature infants may increase the risk of ROP.
Chavez-Valdez	The frequency of levels of blood sugar >8.3mmol/L was equal among neonates those		High overall glycaemic status is associated with the

2011	who had ROP and those who did not. Multivariate regression confirmed 30 days' time weighted glucose level of ≥6.5mmol/L (OR 9.4 to 10) was significantly associated with development of ROP. (p=<0.05)		development of severe ROP.
Van der Lugt 2010	27 out of 66 infants with HG died during admission versus 62/793 infants without HG. A multivariable regression analysis - A significant increase in mortality in the exposed cohort (p = 0.001). Sepsis was more prominent in infants with HG and a BW of >1,000 gram (p = 0.002) and/or GA of 29-32 weeks (p = 0.009) than in infants without HG. Growth at 2 years of age was similar, but neurological and behavioural development was more frequently abnormal among those with neonatal HG (p = 0.036and 0.021 respectively).		Mortality was higher in VLBW infants with HG treated with insulin during the neonatal period. At 2 years of age survivors showed normal growth, but a higher incidence of neurological and behavioural problems.
Alexandrou 2010	The proportion with HG was significantly greater among infants who subsequently died (10 [53%] of 19 infants), compared with survivors (20 [21%] of 94 infants; *P*= 0.03). Multiple regression- For mortality in the first 24 hours-1.3 ± 0.54 (B±SE), 6.0 (Wald $X^{2)}$, p-0.01, OR (95%CI) - 3.7 (1.3-10.6). Multivariate logistic regression analysis revealed that hyperglycaemia during the first 24 hours of life remained a risk factor for WM reduction= 1.1 ± 0.58 (B±SE), 4.1 (Wald $X^{2)}$ p- 0.04, OR (95%CI) - 3.1 (1.0-9.2). No statistically significant association between HG and IVH was found after adjusting gender and CRIB scores, (OR: 1.7 [95% CI: 0.58 –5.01]; *P* = .33).	GA, gender, CRIB score	HG on the first day of life was associated with increased mortality rates and brain damage, as reflected by WM reduction at term age
Heimann 2007	11 infants out of 82 in Gr1, 9 out of 125 in Gr II and 10 out of 45 in Gr III died. A significant increase in mortality (P-0.0001) with increasing median blood glucose level and repeated (≥4) incidents of blood glucose levels ≥8.3mmol/ and in infants with low GA (<27 weeks).Neonates who developed IVH, sepsis or ROP did not have an increased number of elevated blood glucose levels		Premature infants with low gestational age (<27 weeks), elevated median blood glucose levels and/or repeatedly elevated blood glucose levels have a significantly increased mortality.
Blanco 2006; USA	3 out of 19 in euglycemic group and 43 out of 150 in hyperglycaemic group died. The adjusted OR (95%CI) for death before discharge was 1.2(0.3-4.2). Threshold ROP did not reach statistical significance, although laser treatment was required in 15 of 66 patients with ROP in the hyperglycaemic group and in none of the three patients with ROP in the euglycemic group (P = 0.21). Adjusted OR (95%CI) for ROP was 4.6(1.1-18.9). Hyperglycaemia was not found to be associated incidence of CLD or IVH (Adjusted OR (95%)-1.8(0.4-7.4) and 2.3 (0.4-11.3). OR (95%CI) for length of hospital stay of >90 days was 2.5(0.6-11).	GA, BW, Postnatal steroid use	Hyperglycaemia was associated with increased incidence of ROP.
Ertl 2006	ROP occurred more frequently in HG infants.	GA, BW,	The logistic regression model

	Logistic regression model for ROP: HG OR (CI) - 3.15(1.12-8.84), p value- <0.05.	APGAR score, CRIB score	revealed that HG may influence ROP development in VLBW
Hays 2006	Early adverse outcomes (death or the occurrence of grade 3 or 4 IVH before day 10 of life) were associated with the average highest daily blood glucose concentration. (OR1.012). The length of hospital stay was associated with the time ratio for blood glucose concentrations of ≥8.3mmol/L through interaction with birth weight and the average highest daily percentage of inspired oxygen.		High blood glucose concentrations increase the risk of early death and grade 3 or 4 IVH and the length of hospital stay among survivors without IVH, which suggests that prevention and treatment of HG may improve the outcomes ELBW infants.
Kao 2006	Multivariate analysis (Mortality)- Severe HG (≥10mmol/L) but not mild to moderate HG (6.66-9.9mmol/L) was significantly associated with mortality when assessed after 7 days of life (OR (95%CI)- 30.4(3.37-274)). Multivariate analysis- HG ((≥10mmol/L) was not significantly associated with late onset sepsis when assessed after 3 or 7 days of life. (OR -0.92 and 0.56 respectively). Persistent severe HG was associated with the development of Stage II/III NEC, after adjusting for age and male gender (OR: 9.49, 95% CI: 1.52 to 59.3). There was no correlation between mean glucose category and number of days of mechanical ventilation or length of stay in the hospital on univariate or multivariate analyses	GA	Severe HG in the first few days after birth is associated with increased odds of death and sepsis in ELBW infants.
Manzoni 2006	HG occurred significantly more often in group A (21/45, 46.6%) than in group B neonates (11/46, 23.9%) (OR 1.95, 95% CI 1.235-4.432, p =0.008)		HG is significantly more frequent in neonates who subsequently develop fungal rather than bacterial late-onset sepsis, with a typical 3-d interval.
Sutija 2004	Proportion of neonates in whom HG could not be controlled was higher in the ROP group (36.8% vs 0.5%; p<0.0001)		HG presents a major risk for ROP in VLBW neonates
Garg 2003	The patients in the ROP group had higher glucose maximums (p = 0.017), averages (p = 0.043) and medians (p = 0.048) for the first month of life. On more days than controls, ROP patients had at least one glucose value exceeding 8.3mmol/L (ROP 8.4 days, controls 5.3 days, p = 0.028). A simple logistic regression analysis suggested an increased risk for the development of ROP for each 0.55mmol/L increase of mean serum glucose (OR 1.96; 95% CI 1.13 to 3.42). In a multiple regression model: An increased ROP risk for each 0.55mmol/L increase of mean serum glucose (OR 2.7; 95% CI 1.044 to 8.62)	BW, Vitamin E and FiO2	The glucose levels in the first month of life are associated with development of ROP.
Chen 2001	10 of 39 HG infants died compared to 15 of the 88 infants in the NG group. (25% vs. 17%, p<0.05). Persistent periventricular hyperechogenicity (> 2 weeks), cystic PVL and parenchymal lesions were more common in HG infants (33% vs. 11%, p<0.05)		The neonatal mortality rate was higher in the HG group. HG in VLBW neonates was associated with abnormal brain ultrasound.
Lilien 1979	11 out of 14 infants in the HG group and 5 out of 16 in the NG group died.		There was no difference in mortality between stressed HG

	9 out of 14 infants in the HG group and 2 out of 16 in the NG group had brain haemorrhage.		and stressed NG infants; stress, rather than HG, was related to mortality.

GA: Gestational age, BW: Birth weight, PMA: Post menstrual age, CA: Corrected age, VLBW: Very low birth weight infant, ELBW: Extremely low birth weight infant, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, NA: Not available, RDS: Respiratory distress syndrome, IVH: Intra ventricular haemorrhage, NEC: Necrotising enterocolitis, CLD: Chronic lung disease, LOS: Late onset sepsis, ROP: Retinopathy of prematurity, PVL: Periventricular leucomalacia, GV: Glycaemic variability, CV: Coefficient of variation, MAGE: Mean amplitude glucose excursion, OR: Odds ratio, CI: Confidence interval, SD: Standard deviation, IQR- Inter quartile range, SEM: Standard error of mean, LF: Lactoferrin, TPN: Total parenteral nutrition, WM: White matter, BSID: Bayley scale of infant development, DA: Developmental assessment, SGA: Small for gestational age, FiO2: Fraction of inspired oxygen, CRIB: Clinical risk index for babies, NG: Normoglycaemia, HG: Hyperglycaemia, RC: Retrospective cohort study, PC: Prospective cohort study, CC: Case control study.

e Table 2: Sensitivity analysis after including multiple results from the same study

Outcome		**Number of studies in the meta-analysis**	**OR (95% CI)**	**P value**	**I^2 in %**
Cohort studies					
Mortality	Unadjusted	23	3.37 (2.27-5.00)	<0.00001	69
	Adjusted	12	2.41 (1.39-4.17)	0.002	57
IVH (Undefined)	Unadjusted	13	2.81 (1.85-4.28)	<0.00001	47
	Adjusted	3	2.20 (1.12-4.32)	0.02	0
IVH (Severe)	Unadjusted	11	1.98 (1.36-2.89)	0.0004	28
	Adjusted	2	1.07 (0.36-3.17)	0.90	0
ROP (Any)	Unadjusted	8	1.66 (1.06-2.61)	0.03	41
	Adjusted	2	3.7 (1.55-8.84)	0.003	0
ROP (Severe)	Unadjusted	12	3.32 (1.84-5.99)	<0.0001	65
	Adjusted	4	1.74 (0.67-4.54)	0.26	86
LOS	Unadjusted	14	1.63 (1.03-2.57)	0.04	70
	Adjusted	6	1.09 (0.59-1.99)	0.79	58
NEC (Undefined)	Unadjusted	5	1.25 (0.73-2.15)	0.42	0
	Adjusted	No study available			
NEC (Severe)	Unadjusted	8	1.43 (0.63-3.22)	0.39	46
	Adjusted	4	1.34 (0.34-5.21)	0.67	54
CLD	Unadjusted	10	2.46 (1.92-3.15)	<0.00001	0
	Adjusted	4	1.37 (0.85-2.21)	0.19	0
PVL	Unadjusted	6	0.77 (0.37-1.60)	0.48	0
	Adjusted	2	0.56 (0.27-1.18)	0.13	0
Disability	Unadjusted	4	1.99 (1.24-3.19)	0.004	16
	Adjusted	1	1.27 (0.56-2.86)	0.57	NA (1 study only)
Case control studies					
Mortality	Unadjusted	1	3.24 (0.72-14.44)	0.12	NA (1 study only)
	Adjusted	No study available			
IVH (Undefined)	Unadjusted	3	2.06 (1.34-3.18)	0.001	0
	Adjusted	No study available			
IVH (Severe)	Unadjusted	2	2.58 (1.48-4.48)	0.0008	0
	Adjusted	1	10.33 (10-10.67)	<0.00001	NA (1 study only)
ROP (Any)	Unadjusted	3	6.49 (1.97-21.39)	0.002	82
	Adjusted	3	1.26 (0.79-2.00)	0.33	52
ROP (Severe)	Unadjusted	3	2.15 (1.98-2.34)	<0.00001	0
	Adjusted	4	1.01 (0.96-1.07)	0.67	42
LOS	Unadjusted	No study available			
	Adjusted	No study available			
NEC (Undefined)	Unadjusted	No study available			
	Adjusted	No study available			

NEC (Severe)	Unadjusted	No study available			
	Adjusted	No study available			
CLD	Unadjusted	1	3.07 (0.87-10.81)	0.08	NA (1 study only)
	Adjusted	No study available			
PVL	Unadjusted	No study available			
	Adjusted	No study available			
Disability	Unadjusted	No study available			
	Adjusted	No study available			

CLD: Chronic Lung Disease, LOS: Late onset sepsis, IVH: Intraventricular haemorrhage, ROP: Retinopathy of prematurity, NEC: Necrotising enterocolitis, PVL: Periventricular leukomalacia, NA: Not applicable, OR: Odds ratio, CI: Confidence interval, I^2: Heterogeneity

e table 3: Grade of evidence for association of neonatal hyperglycaemia with adverse outcome

Certainty assessment							**Effect**	
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Pooled OR (95% CI)**	**Certainty**
Unadjusted Odds Ratios for Mortality from Cohort Studies								
15	observational studies	not serious	serious [a]	not serious	not serious	all plausible residual confounding would suggest spurious effect, while no effect was observed	**3.25** (2.10 to 5.03)	⊕⊕◯◯ LOW
Unadjusted Odds Ratios for Mortality from Case Control studies								
1	observational studies	not serious	serious [b]	not serious	very serious [c]	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**3.24** (0.72 to 14.44)	⊕◯◯◯ VERY LOW
Adjusted Odds Ratios for Mortality from Cohort studies								
6	observational studies	not serious	serious [e]	not serious	not serious	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect [d]	**2.37** (1.40 to 4.01)	⊕◯◯◯ VERY LOW

Adjusted Odds Ratios for Mortality from Case Control studies								
0	observational studies							
Unadjusted Odds Ratios for "Any IVH" from Cohort studies								
10	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**2.30** (1.55 to 3.40)	⊕⊕◯◯ LOW
Unadjusted Odds Ratios for "Any IVH" from Case Control studies								
1	observational studies	not serious	serious [b]	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**2.30** (1.30 to 4.07)	⊕◯◯◯ VERY LOW
Adjusted Odd Ratios for "Any IVH" from Cohort studies								
2	observational studies	not serious	not serious	not serious	serious [c]	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect [d]	**2.60** (1.09 to 6.20)	⊕◯◯◯ VERY LOW
Adjusted Odds Ratios for "Any IVH" from Case Control studies								
0	observational studies							
Unadjusted Odds Ratios for "Severe IVH" from Cohort studies								
9	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**1.85** (1.37 to 2.51)	⊕⊕◯◯ LOW
Unadjusted Odds Ratios for "Severe IVH" from Case Control studies								
2	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected	**2.58** (1.48 to	⊕⊕◯◯

						all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	4.48)	LOW
Adjusted Odds Ratios for "Severe IVH" from Cohort studies								
1	observational studies	not serious	serious [b]	not serious	serious [c]	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect [d]	**0.8** (0.2 to 3.2)	⊕◯◯◯ VERY LOW
Adjusted Odds Ratios for "Severe IVH" from Case Control studies								
1	observational studies	not serious	serious [b]	not serious	not serious	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect [d]	**10.33** (10.00 to 10.67)	⊕◯◯◯ VERY LOW
Unadjusted Odds Ratios for "Any stage ROP" from Cohort studies								
7	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**1.78** (1.12 to 2.83)	⊕⊕◯◯ LOW
Unadjusted Odds Ratios for "Any stage ROP" from Case Control studies								
3	observational studies	not serious	very serious [a]	not serious	serious [c]	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**6.49** (1.97 to 21.39)	⊕◯◯◯ VERY LOW
Adjusted Odds Ratios for "Any stage ROP" from Cohort studies								
2	observational studies	not seriou	not serious	not serious	serious [c]	publication bias strongly	**3.70** (1.55	⊕◯◯

		s				suspected all plausible residual confounding would reduce the demonstrated effect [d]	to 8.84)	◯ VERY LOW
Adjusted Odds Ratios for "Any stage ROP" from Case Control studies								
3	observational studies	not serious	serious [e]	not serious	not serious	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect [d]	**1.26** (0.79 to 2.00)	⊕◯◯◯ VERY LOW
Unadjusted Odds Ratios for "Severe ROP" from Cohort studies								
9	observational studies	not serious	serious [e]	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**3.42** (1.82 to 6.40)	⊕◯◯◯ VERY LOW
Unadjusted Odds Ratios for "Severe ROP" from Case Control studies								
3	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**2.15** (1.98 to 2.34)	⊕⊕◯◯ LOW
Adjusted Odds Ratios for "Severe ROP" from Cohort studies								
3	observational studies	not serious	very serious [a]	not serious	serious [c]	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect [d]	**1.97** (0.56 to 6.93)	⊕◯◯◯ VERY LOW
Adjusted Odds Ratios for " Severe ROP" from Case Control studies								
4	observational studies	not serious	serious [e]	not serious	not serious	publication bias strongly suspected	**1.01** (0.96 to	⊕◯◯◯

						all plausible residual confounding would reduce the demonstrated effect [d]	1.07)	VERY LOW
Unadjusted Odds Ratios for "Late onset sepsis" from Cohort studies								
9	observational studies	not serious	serious [e]	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**1.97** (1.18 to 3.28)	⊕◯◯◯ VERY LOW
Unadjusted Odds Ratios for "Late onset sepsis" from Case Control studies								
0	observational studies							
Adjusted Odds Ratios for "Late onset sepsis" from Cohort studies								
3	observational studies	not serious	very serious [a]	not serious	not serious	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect [d]	**1.38** (0.41 to 4.72)	⊕◯◯◯ VERY LOW
Adjusted Odds Ratios for "Late onset sepsis" from Case Control studies								
0	observational studies							
Unadjusted Odds Ratios for "Undefined NEC" from Cohort studies								
4	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**1.29** (0.72 to 2.30)	⊕⊕◯◯ LOW
Unadjusted Odds Ratios for "Undefined NEC" from Case Control studies								
0	observational studies							
Adjusted Odds Ratios for "Undefined NEC" from Cohort studies								
0	observational studies							
Adjusted Odds Ratios for "Undefined NEC" from Case Control studies								
0	observational studies							

Unadjusted Odds Ratios for "Severe NEC" from Cohort studies								
6	observational studies	not serious	serious [e]	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**1.91** (0.74 to 4.89)	⊕◯◯◯ VERY LOW
Unadjusted Odds Ratios for "Severe NEC" from Case Control studies								
0	observational studies							
Adjusted Odds Ratios for "Severe NEC" from Cohort studies								
3	observational studies	not serious	serious [e]	not serious	serious [c]	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect [d]	**1.78** (0.29 to 10.78)	⊕◯◯◯ VERY LOW
Adjusted Odds Ratios for "Severe NEC" from Case Control studies								
0	observational studies							
Unadjusted Odds Ratios for CLD from Cohort studies								
8	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**2.55** (1.96 to 3.30)	⊕⊕◯◯ LOW
Unadjusted Odds Ratios for CLD from Case Control studies								
1	observational studies	not serious	very serious [b]	not serious	serious [c]	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**3.07** (0.87 to 10.81)	⊕◯◯◯ VERY LOW
Adjusted Odds Ratios for CLD from Cohort studies								
3	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected	**1.42** (0.85 to	⊕⊕◯◯

						all plausible residual confounding would reduce the demonstrated effect [d]	2.37)	LOW
Adjusted Odds Ratios for CLD from Case Control studies								
0	observational studies							
Unadjusted Odds Ratios for PVL from Cohort studies								
4	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**1.01** (0.40 to 2.56)	⊕⊕◯◯ LOW
Unadjusted Odds Ratios for PVL from Case Control studies								
0	observational studies							
Adjusted Odds Ratios for PVL from Cohort studies								
1	observational studies	not serious	very serious [b]	not serious	not serious	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect [d]	**0.50** (0.20 to 1.25)	⊕◯◯◯ VERY LOW
Adjusted Odds Ratios for PVL from Case Control studies								
0	observational studies							
Unadjusted Odds Ratios for Disability from Cohort studies								
3	observational studies	not serious	not serious	not serious	not serious	publication bias strongly suspected all plausible residual confounding would suggest spurious effect, while no effect was observed [d]	**2.35** (1.47 to 3.73)	⊕⊕◯◯ LOW
Unadjusted Odds Ratios for Disability from Case Control studies								
0	observational studies							
Adjusted Odds Ratios for Disability from Cohort studies								
1	observational studies	not serious	very serious [b]	not serious	not serious	publication bias strongly	**1.27** (0.56	⊕◯◯◯

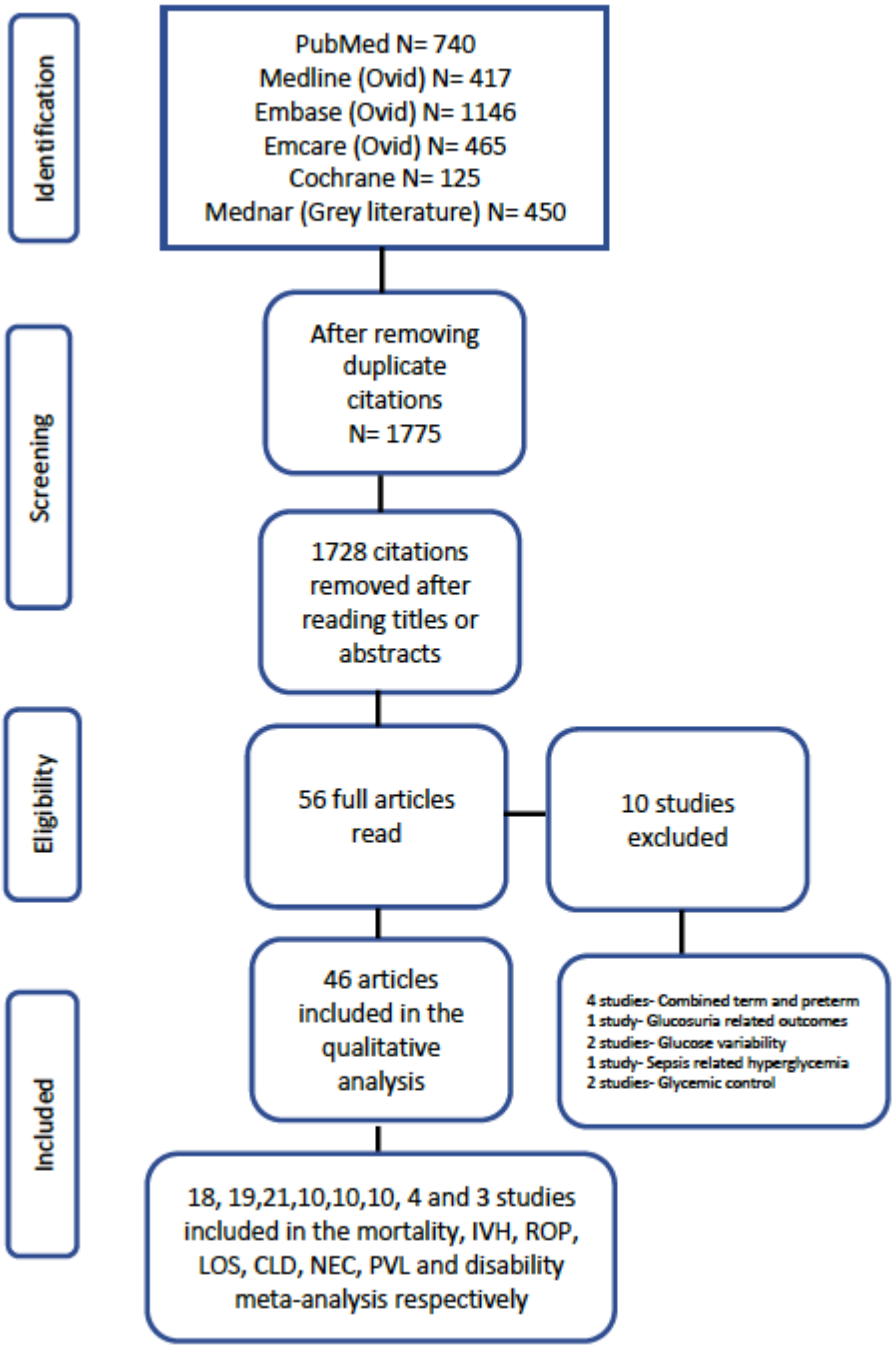
		s				suspected all plausible residual confounding would reduce the demonstrated effect [d]	to 2.86)	VERY LOW
Adjusted Odds Ratios for Disability from Case Control studies								
0	observational studies							

CI: Confidence interval; OR: Odds ratio; IVH: Intraventricular Hemorrhage; ROP: Retinopathy of Prematurity; NEC: Necrotising Enterocolitis; CLD: Chronic Lung Disease; PVL: Periventricular Leukomalacia

Explanations

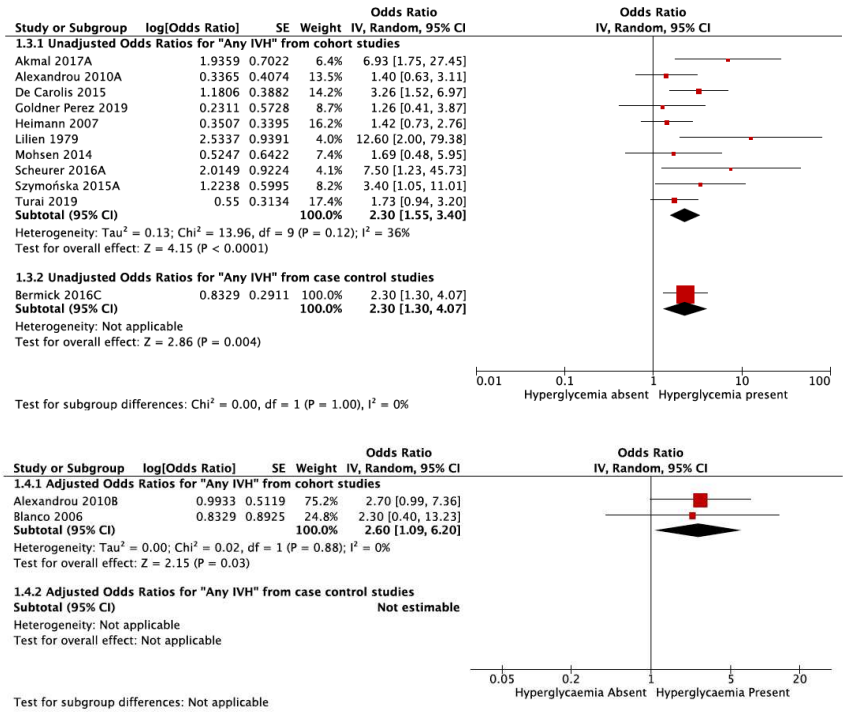
a. High statistical heterogeneity
b. Only 1 study available
c. Wide Confidence intervals
d. Publication Bias could not be assessed since less than 10 studies
e. Moderate statistical heterogeneity

E Figure 1:



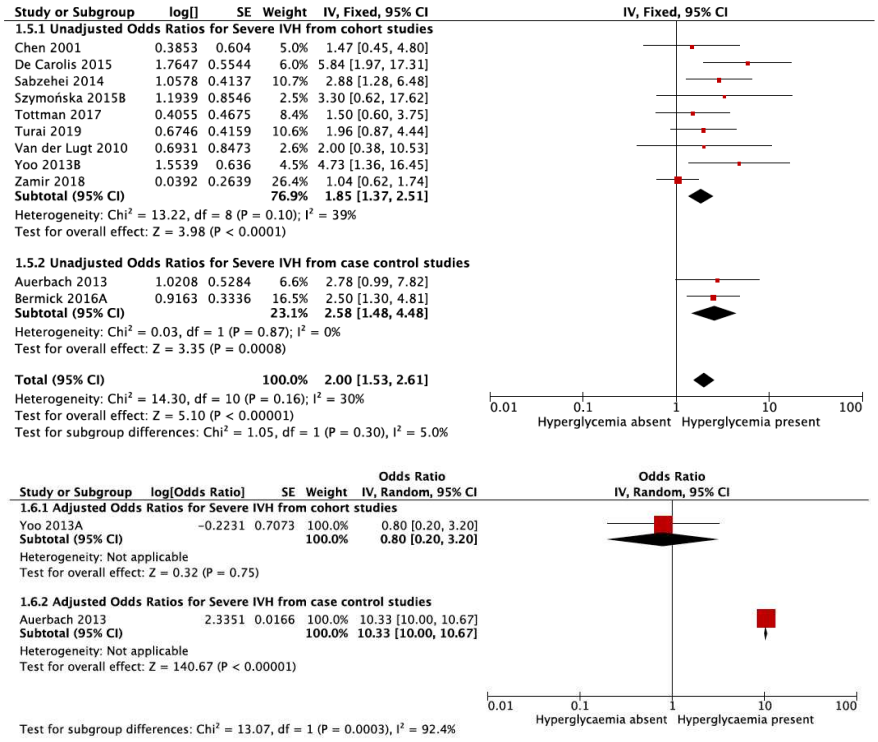
e Figure 1: Flow chart for study selection (IVH- Intraventricular hemorrhage, ROP- Retinopathy of prematurity, LOS- Late inset sepsis, CLD- Chronic lung disease, NEC- Necrotizing enterocolitis, PVL- Periventricular leukomalacia)

e Figure 2:



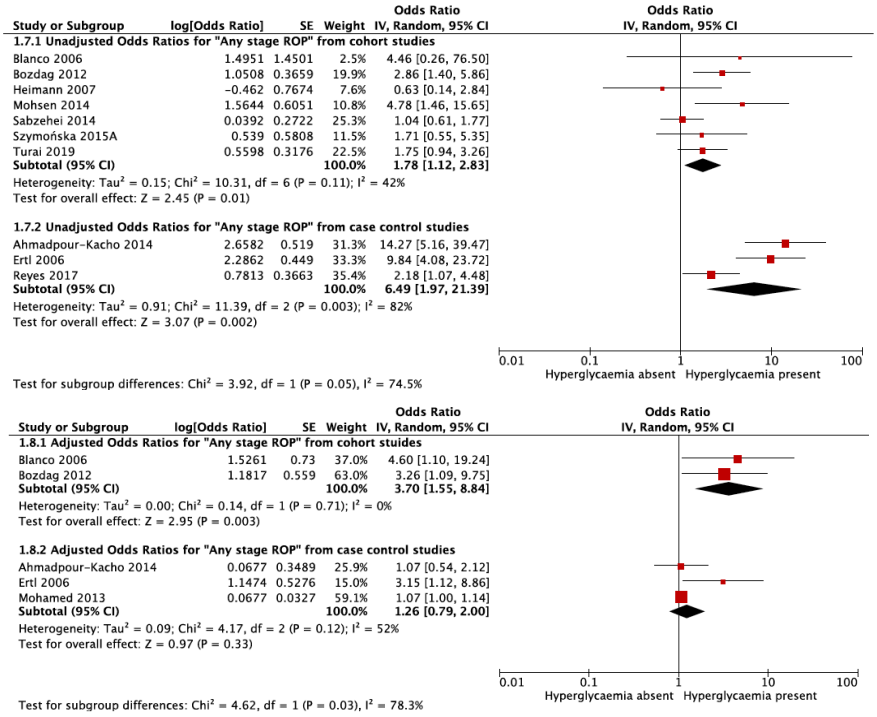
Forest plot showing the association between hyperglycemia and any grade intraventricular hemorrhage. (SE- Standard error, CI- Confidence interval, IV- Inverse variance)

e Figure 3:



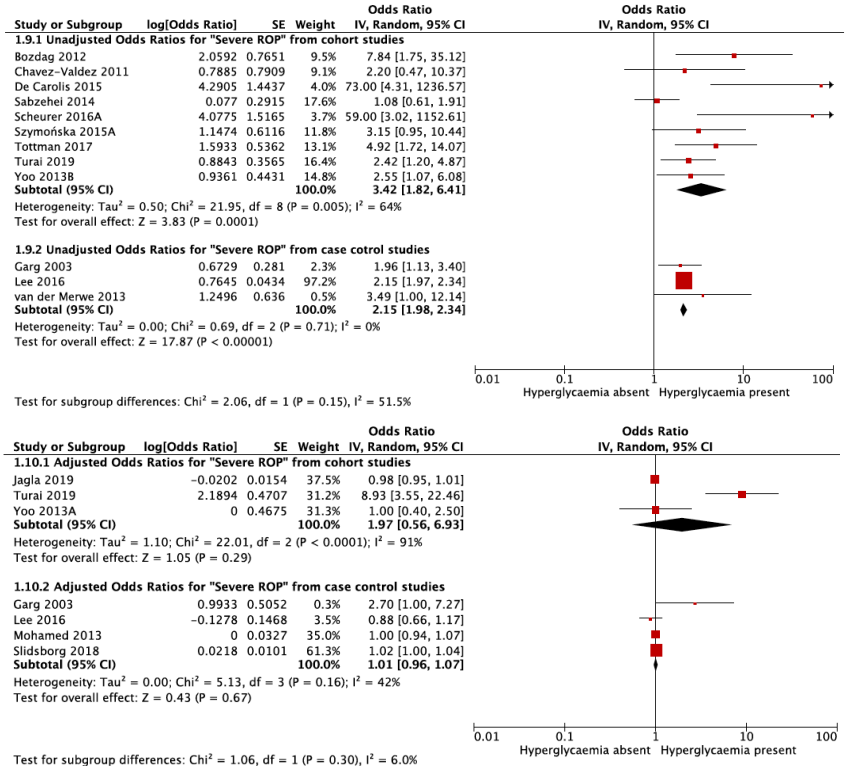
Forest plot showing the association between hyperglycaemia and severe intraventricular haemorrhage (SE- Standard error, CI- Confidence interval, IV- Inverse variance)

e Figure 4:



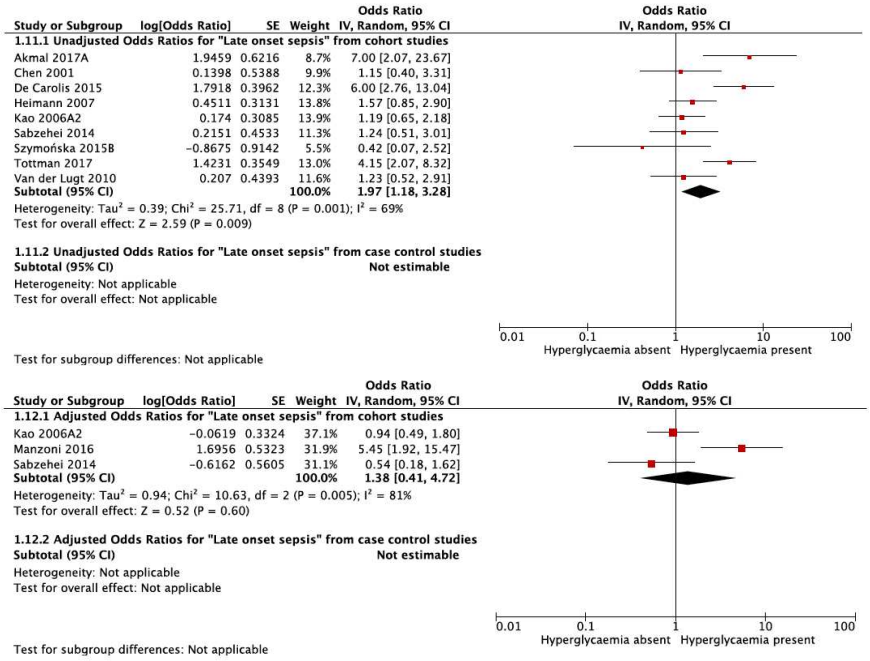
Forest plot showing the association between hyperglycemia and any stage retinopathy of prematurity. (SE- Standard error, CI- Confidence interval, IV- Inverse variance)

e Figure 5:



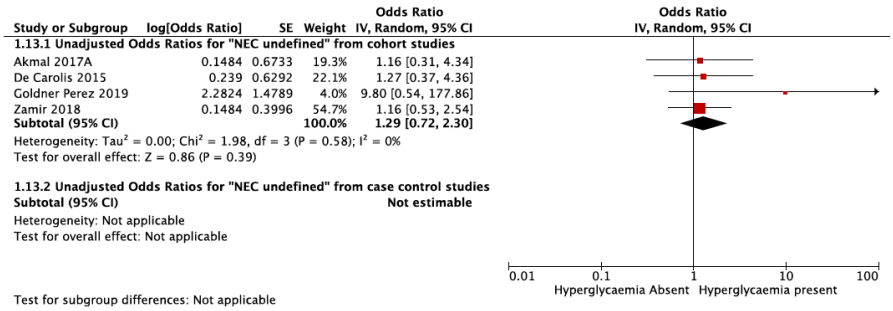
Forest plot showing the association between hyperglycemia and severe retinopathy of prematurity. (SE- Standard error, CI- Confidence interval, IV- Inverse variance)

e Figure 6:



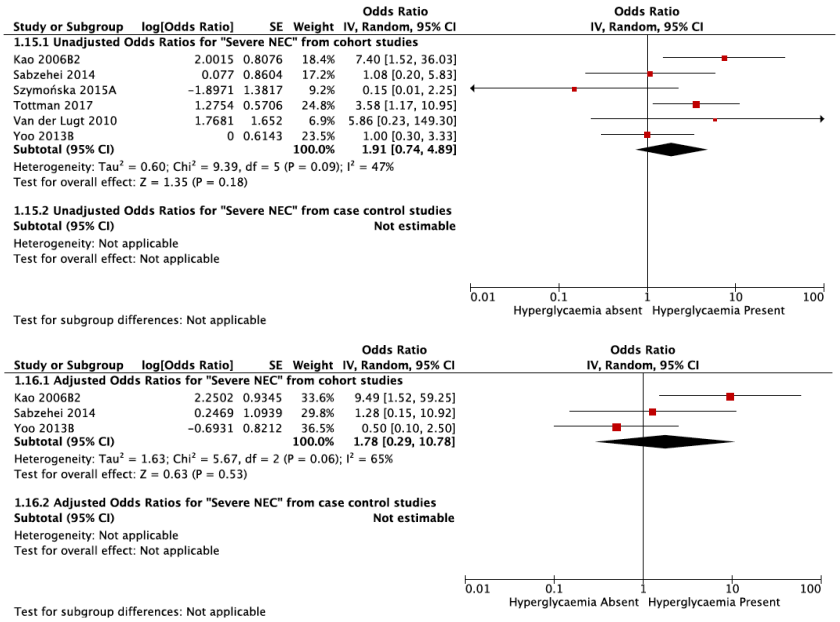
Forest plot showing the association between hyperglycemia and late onset sepsis. (SE- Standard error, CI- Confidence interval, IV- Inverse variance)

e Figure 7:



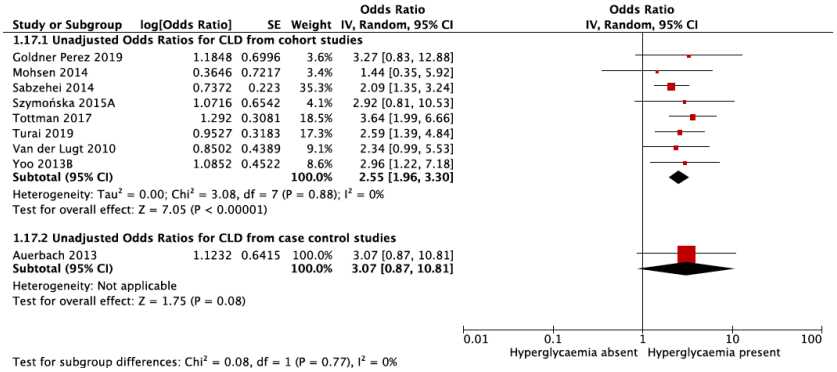
Forest plot showing the association between hyperglycemia and undefined necrotizing enterocolitis. (SE- Standard error, CI- Confidence interval, IV- Inverse variance)

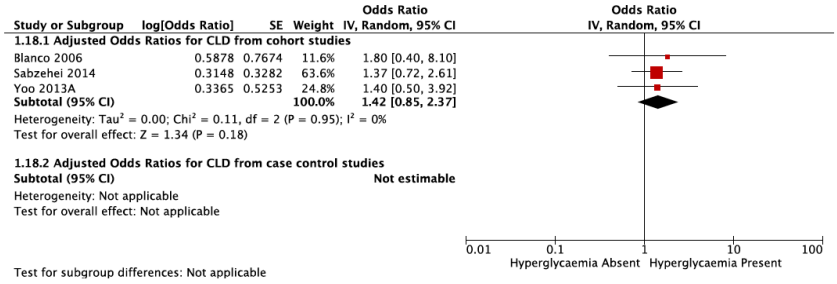
e Figure 8:



Forest plot showing the association between hyperglycemia and severe necrotizing enterocolitis. (SE- Standard error, CI- Confidence interval, IV- Inverse variance)

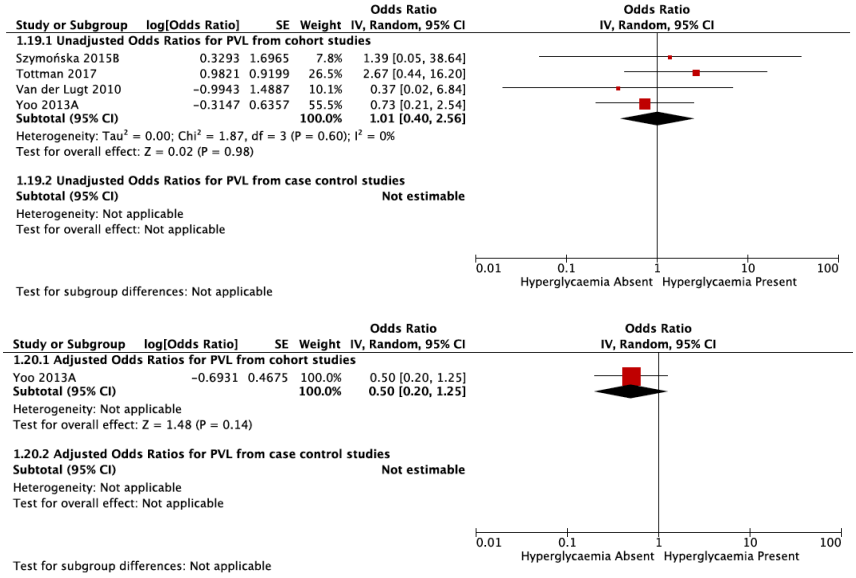
e figure 9:





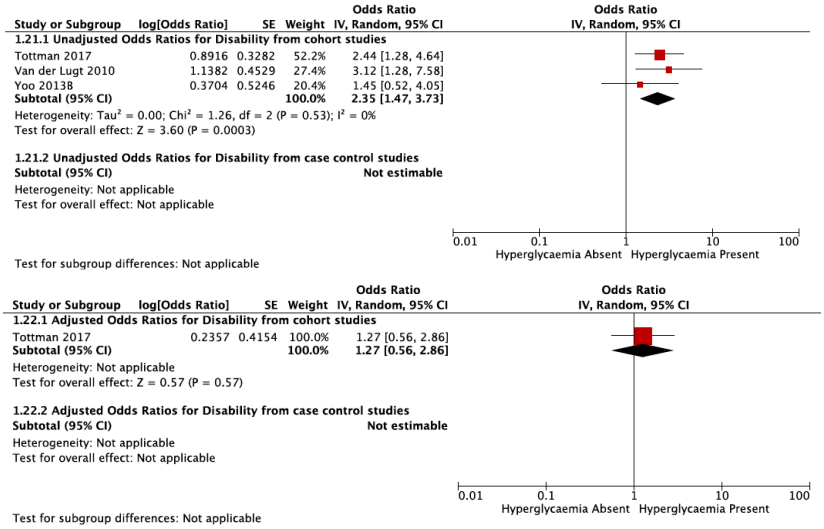
Forest plot showing the association between hyperglycemia and chronic lung disease. (SE- Standard error, CI- Confidence interval, IV- Inverse variance)

e Figure 10:



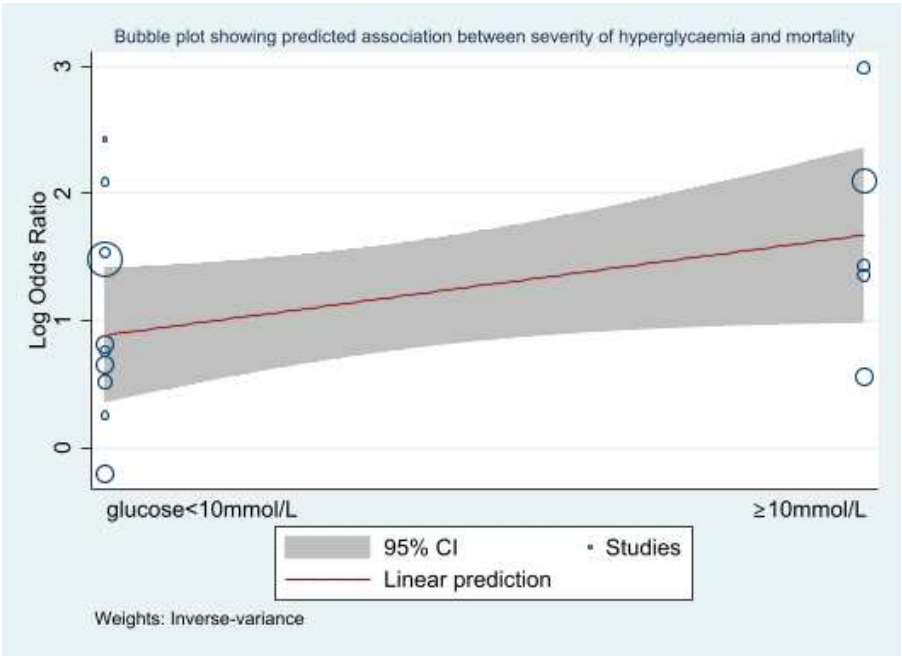
Forest plot showing the association between hyperglycemia and periventricular leucomalacia. (SE- Standard error, CI- Confidence interval, IV- Inverse variance)

\e Figure 11:



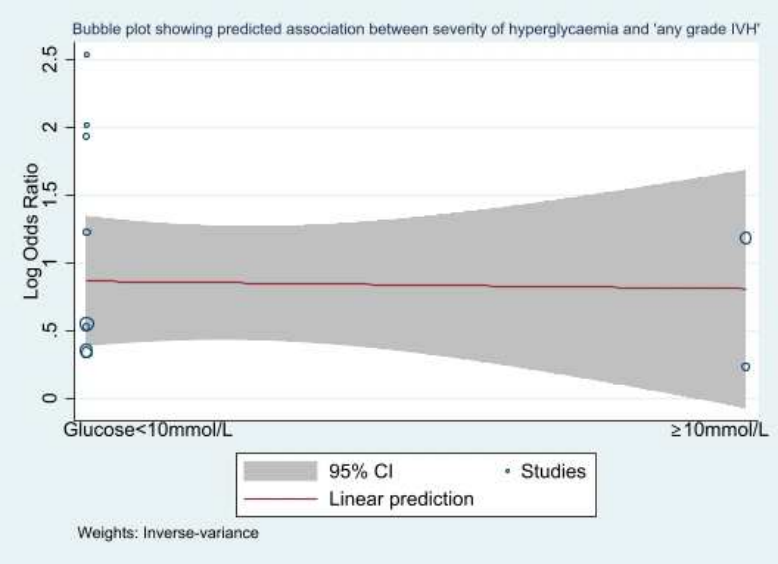
Forest plot showing the association between hyperglycemia and disability. (SE- Standard error, CI- Confidence interval, IV- Inverse variance)

e Figure 12:



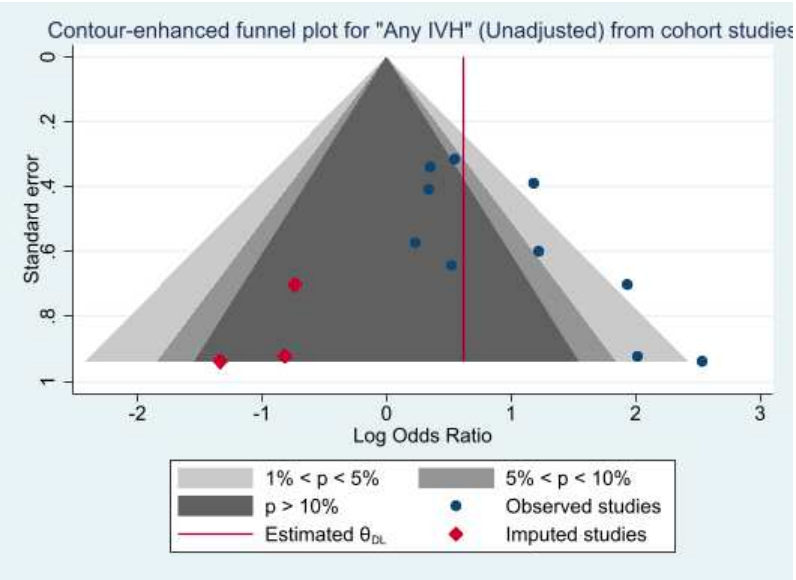
Bubble plot showing relationship between blood glucose level and unadjusted mortality

e Figure 13



Bubble plot showing relationship between blood glucose level and unadjusted any grade intraventricular hemorrhage

e Figure 14:



Funnel plot shows presence of publication bias probably due to 3 missing studies.