Table 1. Characteristics of the available evidence on cardiometabolic risk factors and outcomes among LBW infants who received fortified human milk

	Methods	Population			Concept			Context	Conclusions
First Author, Year, Citation	Design	Sample Size	GA at Birth (weeks)	BW (grams)	PNA	Fortification Details	Examined Cardiometabolic Risk Factors or Outcomes		
Peila, 2020 [38]	sdRCT	122	Intervention: 52 (83.9%) <32 weeks Control: 42 (70.0%) <32 weeks	Intervention: 1,129 (321) Control: 1,196 (304)	18 (3) months CGA	Adjustable Fortification: Variable protein intake through titration to each infant's BUN level, using either a donkey milk-based or bovine milk-based fortifier added to mother' own or donor HM	Weight	Outpatient Premature Infant Developmental Evaluation Program	Both adjustable fortification donkey milk-based and bovine milk-based fortifier added to HM had adequate effects on growth, yielding target weight at 18 months of age among LBW infants.
McGee, 2019 [39]	RCT	158	27.9 (2.5)	1,013 (264)	5.7 (0.2) years	Mother's own milk supplemented by nutrient-enriched donor milk or preterm formula	Weight, BMI, Waist Circumference, Systolic BP, Diastolic BP	N/R	The long-term growth and body composition of VLBW infants who received mother's own milk supplemented with either nutrient-

									enriched donor milk or preterm formula did not differ. Studied children demonstrated body composition that is similar to those reported in term 5-year old's.
Toftlund, 2018 [12]	RCT	239	30 {24-32}	1,285 {535-2,255}	6 years CGA	HM supplemented with Enfamil HM Fortifier (17.5 kcal, 1.375 g protein per 5 packets)	Weight	N/R	Preterm infants who received HM supplemented with HM Fortifier had faster growth compared to those with unfortified HM up to 6 years of age. Rapid weight growth from 34 weeks CGA to 2 months was less common among those

									who received fortified HM compared preterm formula.
Toftlund, 2018 [36]	RCT	239	30.2 [N/R, N/R]	1,320 [535, 2,024]	6 years CGA	HM supplemented with Enfamil HM Fortifier (17.5 kcal, 1.375 g protein per 5 packets)	Weight, BMI BP Plasma Glucose, A1C, Insulin, Total Cholesterol, HDL Cholesterol, LDL Cholesterol, Triglycerides		Preterm infants who received HM supplemented with HM Fortifier were less pre-disposed to obesity. Rapid weight growth from 34 weeks CGA to 2 months occurred in 53% of children and was significantly associated with signs of metabolic syndrome at 6 years of age.
Biasini, 2018 [35]	RCT	61	Range: 23-32	Range: 580-1,250	3-24 months CGA	Mother's own milk or donor HM supplemented with protein,	Weight	Outpatient Clinic	There was no difference in the speed of growth

						either titrated up or down unchanged based infant's BUN level or kept fixed around BUN values			(weight gain) among VLBW infants who received adjustable fortification with protein supplementation compared to those who received standard fortification.
Henriksen, 2016 [37]	RCT	98	28.6 (2.7)	1,051 (297)	8.6 (0.3) years	Mother's own milk or donor HM fortified with proteins and micronutrients and supplemented with soy and medium-chain triglyceride oil and docosahexaenoic acid and arachidonic acid.	Weight, BMI, Cholesterol, A1C	N/R	VLBW infants who received HM supplemented with triglyceride oil and acids did not have differing growth outcomes compared to those without acid supplementation. Rapid growth after the first year of life was associated with high BMI and

									unfavourable metabolic markers at 8 years of age.
Zachariassen, 2011 [25]	RCT	320	Range: 23-32	Range: 535-2,225	2, 4, 6 and 12 months CGA	HM fortified with Human Milk Fortifier (17.5 kcal and 1.375 g protein per 5 packets)	Weight	Outpatient Clinic	Fortification of mother's milk after hospital discharge of very preterm infants did not improve growth at 1 year of age compared to no fortification.
Aimone, 2009 [28]	RCT	39	Intervention: 28.9 (1.2) Control: 29.8 (1.7)	Intervention: 1,253 (242) Control: 1,322 (332)	4, 6, 12, and 18 months CGA	HM fortified with a powdered multi-nutrient HM fortifier	Weight	Outpatient Clinic	The addition of a multi-nutrient fortifier to HM resulted in improved weight in the first year of life.
O'Conner, 2008 [27]	RCT	34	Intervention: 28.9 (1.2) Control: 29.8 (1.7)	Intervention: 1,253 (242) Control: 1,322 (332)	Intervention: 37.8 (3.3) weeks CGA Control: 38.4 (2.4) weeks	HM nutrient enriched with powdered fortifier (80 kcal, 2.2 grams protein)	Weight	Post-Discharge Home Visit	There was a trend of heavier weight 12 weeks after hospital discharge among infants who received nutrient

					CGA				enriched HM compared to unfortified HM
Wuaben, 1999 [23]	RCT	25	29.9 (1.7) weeks	1,211 (239)	Term, 3, 6, and 12 months CGA	HM fortified with protein, calcium, phosphorus and zinc.	Weight	Outpatient Clinic	Mean weight values among infants who received multi-nutrient fortification of HM with protein, calcium, phosphorus and zinc were between the 3rd and 97th percentiles derived from WHO reference growth standards for mother's milk-fed term infants at 1 year of age.
Backstrom, 1999 [24]	RCT	35	<37 weeks	< 2,000	3 months; 9 to 11 years	HM supplemented with calcium and phosphorus.	Weight	N/R	Supplementation with minerals was not associated

									with increased weight gain.
Wauben, 1998 [22]	RCT	37	Intervention: 29.9 (1.9) Control: 30.1 (1.5)	Intervention: 1,400 (0.2) Control: 1,300 (0.2)	Term, 3, 6, and 12 months CGA	HM with multi-nutrient fortifier	Weight	Outpatient Clinic	Mean weight among all infants who received multi-nutrient fortification of HM with protein, calcium, phosphorus and zinc were within normal ranges according to the WHO reference growth standards for mother's milk-fed term infants at 1 year of age.
Lucas, 1996 [33]	RCT	275	29.8 (2.7)	1,284 (314)	9 and 18 months CGA	HM fortified with a multi-nutrient fortifier (preterm formula used when breast milk was not available)	Weight	N/R	There was no significant growth advantage with fortification of HM compared to

									no fortification, except when breast milk exceeded 50% of intake (preterm formula was used when sufficient breast milk was not available), fortification led to faster weight gain.
Gross, 1987 [32]	RCT	50	Group 1: 30.3 (0.5) Group 2: 29.8 (0.4) Group 3: 30.0 (0.5) Group 4: 31.2 (0.5) Group 5: 30.8 (0.3)	Group 1: 1,255 (67) Group 2: 1,291 (59) Group 3: 1,218 (69) Group 4: 1,407 (58) Group 5: 1,365 (61)	44 weeks CGA	HM fortified with a high mineral containing formula (including calcium and phosphorus)	Weight	N/R	Infants fed HM with fortifier showed greater rapid weight gain compared to those fed unfortified milk or formula.

Biasini, 2012 [26]	Quasi-RCT	61	23-32	580-1,250	3 and 9 months CGA	Adjustable fortification of mother's own milk or donor HM based on BUN levels plus protein supplementation	Weight	N/R	LBW infants who received adjustable fortification had lower weight gain in hospital but higher catch-up growth following hospital discharge compared to infants who received standard fortification.
Schanler, 1992 [30]	Quasi-RCT	21	Intervention: 28 (0.7) Control: 29 (1.1)	Intervention: 1,100 (0.1) Control: 1,100 (0.2)	24.4 months	HM fortified with calcium and phosphorus.	Weight	N/R	Body weight was similar between infants fed fortified HM or formula, with average growth measurements in the 20 to 30 percentile ranges at 1 year of age.
Abrams, 1989 [29]	Quasi-RCT	17	N/R	VLBW, GA at birth N/R	1 year (52 weeks)	Fortified HM (fortification details N/R) from postnatal	Weight	Outpatient Clinic	Growth measurements, including body weight,

						weeks 10 to 25 plus solid foods and commercial formula after 25 weeks			did not differ between infants who received fortified HM compared to those who received formula.
Bergner, 2020 [34]	Prospective Cohort	51	27.8 (2.6)	893 (204)	12-15 months, 18-22 months, 2 years CGA	Mother's own milk or donor HM fortified with a pasteurized donor HM-based fortifier	Weight	Outpatient Clinic	Anthropometric z-scores of weights returned to birth levels by 18-22 months CGA and body composition at 2 years was similar to term-matched controls among preterm infants fed an exclusive HM diet during hospitalization.
Lin, 2020 [31]	Retrospective Cohort	73	Cohort 1: 27,3 (2) Cohort 2:	Cohort 1: 783.1 (131.2) Cohort 2:	Term; 24 months	HM fortified with powdered fortifier or concentrated preterm formula	Weight	N/R	Infants who received HM fortified with powdered

			26.4 (2.1)	773.9 (143.7)					HM fortifier had steadily significantly higher z-scores at week 5, week 6, week 7 and week 8, compared to infants who received HM fortified with concentrated preterm formula.

Mean (SD); Median [IQR]; Median {range}; RCT, randomised control trial; VLBW, very low birth weight; LBW, low birth weight; BUN, blood urea nitrogen; HM, human milk; BMI, body mass index; BP, blood pressure; N/R, not reported; A1c, Hemoglobin A1c; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CGA, corrected gestational age;