

Kent Surrey and Sussex Neonatal Operational Delivery Network

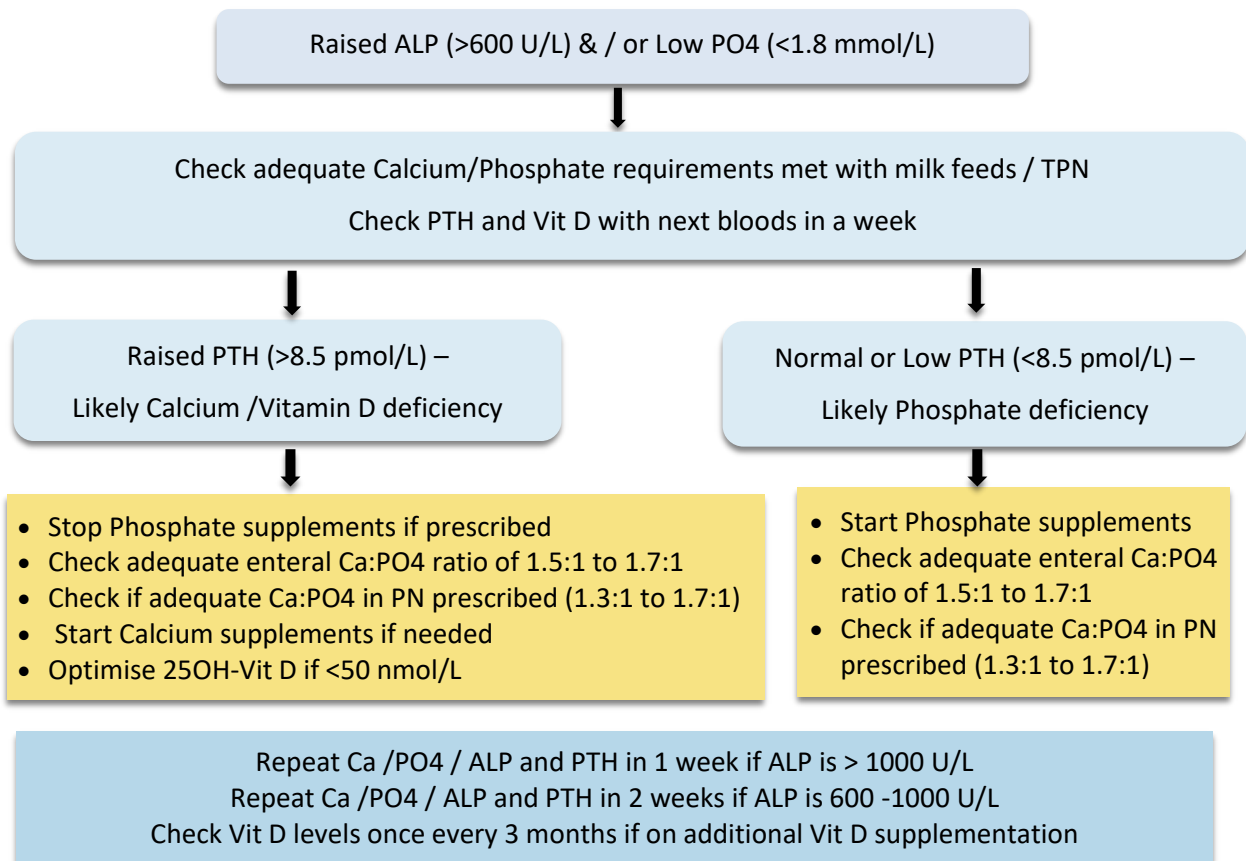
Neonatal Metabolic Bone Disease: Principles of Practice

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Presented for approval to/on	
Last Reviewed	A new document
Review date (<i>Max 3 years</i>)	
Distribution	Neonatal Units in KSS
Implications of race, equality & other diversity duties for this document	

Prevention and Management of Metabolic Bone Disease

1. Some infants are at higher risk of developing metabolic bone disease, this includes;
 - a. All extremely preterm infants <28 weeks and those with birth weight of <1000 grams and any other infant with the following risk factors:
 - b. Those with ongoing evidence of sub-optimal /poor postnatal growth
 - c. Preterm babies fed on unfortified breast milk
 - d. Infants on PN for > 2 weeks
 - e. Evidence of chronic lung disease (e.g. BPD)
 - f. Confirmed NEC – medical /surgical treatment
 - g. Prolonged use of (i.e. > 2 weeks) demineralising drugs like steroids, loop diuretics, antacids or high dose methylxanthines
2. Prevention for at-risk Infants is achieved through
 - a. Routine fortification of breast milk
 - b. Use of preterm formulas when needed
 - c. Routine Vit D supplementation (Abidec)
 - d. Regular 1 -2 weekly review of bone chemistry
3. Screen all preterm infants < 32 weeks and < 1800 grams and any other infant at higher risk of developing MBD to check bone chemistry using blood levels of Alkaline Phosphatase, Phosphate, Calcium and Parathyroid Hormone once fully enterally fed¹.
4. Do not routinely prescribe phosphate supplementation if serum phosphate is low ^(1,2), as it could worsen MDB due to secondary hyperparathyroidism.
5. To meet recommended calcium and phosphate intakes⁴, routine fortification of MEBM with at least half strength breast milk fortifier is needed (see Appendix 1a for nutritional content of a variety of feeds compared with ESPGHAN guidelines). Ideally, increasing this to full strength breast milk fortifier as tolerated should be achieved to optimise the calcium/phosphate intake in line with updated ESPGHAN guidelines (see Appendix 1b).
6. For all infants <36 weeks and <1.8kgs who are unable to receive MEBM, consider using pre-term formulas instead of term formula, following shared discussion with parents, medical team, and Dietitian.
7. Prescribe regular multivitamins as discussed within this guideline.
8. Review bone chemistry as per point 2 every 1-2 weeks based on the severity of the alkaline phosphatase and clinical risks.

Flow chart for Management of Metabolic Bone Disease



To Note:

- No risk of nephrocalcinosis if PTH levels are high
- Elevated PTH causes depletion of 25-OH Vit D - So continue supplementation of Vit D until PTH and Vit D levels are both normalised
- If both Calcium and Phosphate supplements are prescribed to a baby - Ensure they are not given together, as they precipitate in the feeds
- Aim to normalise biochemistry and stop supplements by 34 weeks.
- If needs longer supplementation, check biochemistry in 1-2 weeks after stopping. If baby is discharged prior to blood tests, book in phlebotomy clinic within 2 weeks after discharge.
- If needs to continue supplements after discharge, inform Neonatal community outreach team (NCOT) and do TTO for 4 weeks supply. NCOT team to plan blood tests after stopping supplements.

Appendices

Appendix 1 – Nutritional Composition of a Variety of Feeds

(The red boxes denote nutrients not meeting nutritional requirements)

Nutritional Content of Preterm Breast milk and Nutriprem BMF

Nutrient	Preterm Breast milk				100mls pre term milk and FS BMF	100		120		150		165		180		ESPGHAN Guidelines 2022
	100	Per 1g sachets	Per 2 scoops / 2 sachets	Per 4 scoops / 4 Sachets		100	100	120	120	150	150	165	165	180	180	
Energy (kcal)	67.0	4.3	8.5	17.0	84.0	75.5	84.0	90.6	100.8	113.3	126.0	124.6	138.6	135.9	151.2	110-140kcal/kg/day
Protein (g)	1.6	0.3	0.7	1.3	2.9	2.3	2.9	2.7	3.5	3.4	4.4	3.7	4.8	4.1	5.2	3.5-4.5g/kg/day
CHO (g)	7.3	0.4	0.8	1.5	8.8	8.1	8.8	9.7	10.9	12.1	13.2	13.3	14.5	14.5	15.8	11-15g/kg/day
Fat (g)	3.5	0.2	0.4	0.7	4.2	3.9	4.2	4.6	5.0	5.8	6.3	6.4	6.9	6.9	7.6	4.8 to 8.1 g/kg/d
Vitamin A (ug)	15.0	58.0	116.0	232.0	247.0	131.0	247.0	157.2	296.4	196.5	370.5	216.2	407.6	235.8	444.6	1.333-3.300 IU/kg (400-1000µg/kg/d)
Vitamin D (ug)	0.2	1.4	2.8	5.5	5.7	3.0	5.7	3.5	6.8	4.4	8.55	4.9	9.4	5.3	10.3	10-25 ug per day
Vitamin D IU	8.0	56.0	112.0	224.0	232.0	120.0	232.0	144.0	279.4	180.0	348	198.0	382.8	216.0	417.6	400-1000IU per day
Folic acid	3.1	7.5	15.0	30.0	33.1	18.1	33.1	21.7	39.7	27.2	49.7	29.9	54.6	32.6	59.6	35-100ug/kg/day
Iron (mg)	0.1	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.2	0.15	0.2	0.2	0.2	0.2	2-3mg/kg/day
Sodium (mg)	28.0	8.3	16.5	33.0	61.0	44.5	61.0	53.4	73.2	66.8	91.5	73.4	100.7	80.1	109.8	54-144mg/kg/day (3-8mmols/kg/day)
Potassium (mg)	50.0	5.8	11.5	23.0	73.0	61.5	73.0	73.8	87.6	92.3	109.5	101.5	120.5	110.7	131.4	41-83mg/kg/day (2.3 to 4.6 mmol/kg/d)
Calcium (mg)	25.0	17.5	35.0	70.0	95.0	60.0	95.0	72.0	114.0	90.0	142.5	99.0	156.8	108.0	171.0	3.0-5.0 mmol (120-200 mg)/kg/d
Phosphorus (mg)	14.5	9.5	19.0	38.0	52.5	33.5	52.5	40.2	63.0	50.3	78.8	55.3	86.6	60.3	94.5	2.2-3.7 mmol (70-115 mg P)/kg/d
Ca:Phos	1.7	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	

Nutritional Composition of Preterm Breast milk and SMA BMF

Nutrient	Preterm Breast milk				100mls pre term milk and FS BMF	100		120		150		165		180		ESPGHAN Guidelines 2022
	100	Per 1 sachet	Per 2 sachets	Per 4 sachets		100	100	120	120	150	150	165	165	180	180	
Energy (kcal)	67.0	4.3	8.6	17.2	84.2	75.6	84.2	90.7	101.0	113.4	126.3	124.7	138.9	136.1	151.6	110-140kcal/kg/day
Protein (g)	1.6	0.4	0.7	1.4	3.0	2.3	3.0	2.8	3.6	3.5	4.6	3.8	5.0	4.2	5.5	3.5-4.5g/kg/day
CHO (g)	7.3	0.3	0.6	1.3	8.6	7.9	8.6	9.5	10.3	11.9	12.9	13.1	14.2	14.3	15.4	11-15g/kg/day
Fat (g)	3.5	0.2	0.4	0.7	4.2	3.9	4.2	4.6	5.1	5.8	6.3	6.4	7.0	6.9	7.6	4.8 to 8.1 g/kg/d
Vitamin A (ug)	15.0	95.0	190.0	380.0	395.0	205.0	395.0	246.0	474.0	307.5	592.5	338.3	651.8	369.0	711.0	1.333-3.300 IU/kg (400-1000µg/kg/d)
Vitamin D (ug)	0.2	1.0	2.0	4.0	4.2	2.2	4.2	2.6	5.0	3.3	6.3	3.6	6.9	4.0	7.6	10-25 ug per day
Vitamin D IU	8.0	17.0	34.0	68.0	71.1	37.1	71.1	44.5	85.3	55.7	106.7	61.2	117.3	66.8	128.0	400-1000IU per day
Folic acid	3.1	0.5	0.9	1.8	1.9	1.0	1.9	1.2	2.3	1.5	2.85	1.7	3.1	1.8	3.4	35-100ug/kg/day
Iron (mg)	0.1	0.5	0.9	1.8	1.9	1.0	1.9	1.2	2.3	1.5	2.85	1.7	3.1	1.8	3.4	2-3mg/kg/day
Sodium (mg)	28.0	9.2	18.4	36.8	64.8	46.4	64.8	55.7	77.8	69.6	97.2	76.6	106.9	83.5	116.6	54-144mg/kg/day (3-8mmols/kg/day)
Potassium (mg)	50.0	12.0	24.0	48.0	98.0	74.0	98.0	88.8	117.6	111.0	147.0	122.1	161.7	133.2	176.4	41-83mg/kg/day (2.3 to 4.6 mmol/kg/d)
Calcium (mg)	25.0	19.0	38.0	76.0	101.0	63.0	101.0	75.6	121.2	94.5	151.5	104.0	166.7	113.4	181.8	3.0-5.0 mmol (120-200 mg)/kg/d
Phosphorus (mg)	14.5	11.0	22.0	44.0	58.5	36.5	58.5	43.8	70.2	54.8	87.8	60.2	96.5	65.7	105.3	2.2-3.7 mmol (70-115 mg P)/kg/d
Ca:Phos	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	

Nutritional Composition of Pre Term Formulas

Nutrient	NP1		NP2		SMA Gold Prem 1		SMA Gold Prem 2		ESPGHAN Guidelines	
	(per 100mls)	(per 150mls)	(per 100mls)	(per 150mls)	(100mls)	(150mls)	(100mls)	(150mls)		
Energy (kcal)	80.0	120.0	72.0	108.0	80.0	120.0	73.0	109.5	110-140kcal/kg/day	
Protein (g)	2.7	4.1	2.0	3.0	2.9	4.4	2.0	3.0	3.5-4.5g/kg/day	
CHO (g)	8.4	12.6	7.2	10.8	8.1	12.2	7.7	11.6	11-15g/kg/day	
Fat (g)	3.9	5.9	3.8	5.7	4.0	6.0	3.8	5.7	4.8 to 8.1 g/kg/d	
Vitamin A (ug)	366.0	549.0	100.0	150.0	330.0	495.0	68.0	102.0	1.333-3.300 IU/kg (400-1000µg/kg/d)	
Vitamin D (ug)	3.1	4.7	1.8	2.7	3.4	5.1	1.8	2.7	10-25 ug per day	
Vitamin D IU	124.0	186.0	68.0	102.0	124.0	186.0	72.0	108.0	400-1000IU per day	
Folic acid	58.0	87.0	52.8	79.2	65.5	98.3	26.0	39.0	35-100ug/kg/day	
Iron (mg)	1.6	2.4	1.2	1.8	1.6	2.4	0.8	1.1	2-3mg/kg/day	
Sodium (mg)	70.0	105.0	26.5	39.8	56.0	84.0	36.0	54.0	54-144mg/kg/day (3-8mmols/kg/day)	
Potassium (mg)	81.0	121.5	75.0	112.5	115.0	172.5	84.0	126.0	41-83mg/kg/day (2.3 to 4.6 mmol/kg/d)	
Calcium (mg)	101.0	151.5	83.0	124.5	119.0	178.5	82.0	123.0	3.0-5.0 mmol (120-200 mg)/kg/d	
Phosphorus (mg)	63.0	94.5			78.0	117.0	50.0	75.0	2.2-3.7 mmol (70-115 mg P)/kg/d	
Ca:Phos	1.6	1.6			1.5	1.5	1.6	1.6		

Nutritional Composition of Specialist Formulas

Nutrient	Peptjunior				Aptamil Pepti				Neocate LCP				Hydrolyzed Nutriprem				ESPGHAN Guidelines
	100	150	165	180	100	150	165	180	100	150	165	180	100	150	165	180	
Energy (kcal)	66.0	99.0	108.9	118.8	66.0	99.0	108.9	118.8	67.0	100.5	110.6	120.6	80.0	120.0	132.0	144.0	110-140kcal/kg/day
Protein (g)	1.8	2.7	3.0	3.2	1.6	2.4	2.6	2.9	1.8	2.7	3.0	3.2	2.6	3.9	4.3	4.7	3.5-4.5g/kg/day
CHO (g)	7.2	10.8	11.9	13.0	7.1	10.7	11.7	12.8	7.1	10.7	11.7	12.8	8.4	12.6	13.9	15.1	11-15g/kg/day
Fat (g)	3.4	5.1	5.6	6.1	3.4	5.1	5.6	6.1	3.5	5.3	5.8	6.3	4.0	6.0	6.6	7.2	4.8 to 8.1g/kg/d
Vitamin A (ug)	59.0	88.5	97.4	106.2	58.0	87.0	95.7	104.4	58.2	87.3	96.0	104.8	366.0	549.0	603.9	658.8	1.333-3.300 IU/kg (400-1000µg/kg/d)
Vitamin D (ug)	1.7	2.6	2.8	3.1	1.7	2.6	2.8	3.1	1.6	2.4	2.6	2.9	3.1	4.7	5.1	5.6	20-25 ug per day
Vitamin D IU																	400-1000IU per day
Folic acid	14.0	21.0	23.1	25.2	15.0	22.5	24.8	27.0	9.2	13.9	15.2	16.6	58.0	87.0	95.7	104.4	35-100ug/kg/day
Iron (mg)	0.7	1.1	1.2	1.3	0.5	0.8	0.9	1.0	1.0	1.5	1.7	1.8	1.6	2.4	2.6	2.9	2-3mg/kg/day
Sodium (mg)	21.7	32.6	35.8	39.1	20.8	31.2	34.3	37.4	29.3	44.0	48.3	52.7	77.0	115.5	127.1	138.6	54-144mg/kg/day (3-8mmols/kg/day)
Potassium (mg)	75.0	112.5	123.8	135.0	87.0	130.5	143.6	156.6	72.9	109.4	120.3	131.2	87.0	130.5	143.6	156.6	41-83mg/kg/day (2.3 to 4.6 mmol/kg/d)
Calcium (mg)	76.0	114.0	125.4	136.8	61.0	91.5	100.7	109.8	77.1	115.7	127.2	138.8	97.0	145.5	160.1	174.6	3.0-5.0 mmol (120-200 mg)/kg/d
Phosphorus (mg)	47.0	70.5	77.6	84.6	35.0	52.5	57.8	63.0	50.2	75.3	82.8	90.4	54.0	81.0	89.1	97.2	2.2-3.7 mmol (70-115 mg P)/kg/d

Appendix 1b - Calcium:Phosphorus Ratios for a Variety of Feeding Regimens

	Feed Type	Calcium mg	Phosphorus mg/ Phosphate mg	Ratio
Per 150mls	Breast Milk	37.5	21.75 Phosphorus	1.72
HS (2%)	Nutriprem Breast Milk Fortifier (per 2g)	35.0	19mg Phosphorus	1.84
FS (4%)	Nutriprem Breast Milk Fortifier (per 4g)	70.0	38mg Phosphorus	1.84
HS (2%)	SMA Breast Milk Fortifier (per 2g)	38	22mg Phosphorus	1.72
FS (4%)	SMA Breast Milk Fortifier (per 4g)	76	44 Phosphorus	1.72
Per 150 mls	NP1	151.5	94.5 (Phosphorus) 93mg (Phosphate) 3mmols (Phosphate)	1.60 1.6
Per 150 mls	NP2	124.5	70mg Phosphorus 314mg Phosphate 2.25mmols Phosphate	1.78 0.4
Per 150 mls	SMA Gold Prem 1	178.5	117.0 Phosphorus 361mg Phosphate 3.8mmols Phosphate	1.52 0.5
Per 150 mls	SMA Gold Prem 2	123.0	75.0 Phosphorus 230mg Phosphate 2.4mmols Phosphate	1.64 0.5

Notes:

- MEBM fortified with 2% (HS), 3% (3/4 strength) and 4% (FS) BMF will provide calcium and phosphate ratio of 1.72 to 1.73.
- ESPGHAN 2022 recommends a calcium intake of 3.0-5.0 mmol (120-200 mg/kg/d)
- ESPGHAN 2022 recommends a phosphorus intake of 2.1-2.9 mmol/kg/day (approximate ratio of 1:4) or Phosphorus intake of 65-90mg/kg/day (approximate ratio of 1:8)
- This is the equivalent of a **phosphate** intake of **200-276mg/kg/day** (approximate ratio of 0.4-0.5)
- Full fortification will provide higher amounts of calcium and phosphate to meet the updated ESPGHAN guidelines
- If on additional calcium or phosphate supplements, please add them to calculate the ratio.
- 1 mmol of Calcium provides 40 mg
- 1 mmol of Phosphate provides 95 mg of phosphate and 31mg phosphorus

Appendix 2: Calcium and Phosphate concentrations in KSS PN

	Calcium (mmol/mL)	Phosphate (mmol/mL)
SCAMP Electrolyte-free	0	0
SCAMP maintenance	0.015	0.02
SMOF 20% with vitamins	0	0.015

Note:

1 – Please calculate the Calcium:Phosphate ratio in SCAMP according to the amount of PN and SMOF given

Appendix 3: IV preparations of calcium and Phosphate

IV CALCIUM			
Formulation	Indication	Dose	Administration
Calcium Gluconate 10% solution for injection (0.22mmol/mL)	Hypocalcaemia: Maintenance infusion	0.11-0.44mmol/kg (0.5-1mL/kg)	Dilute and administer by IV infusion over 30 minutes. Follow Medusa IV guidelines for dilution.
IV PHOSPHATE			
Phosphates Polyfusor 50mmol/500mL solution for infusion	Hypophosphaemia	1mmol/kg/day May increase to 2mmol/kg from day 2 if required.	Solution is ready to infuse, no dilution required. Administer by IV infusion over 12 hours, using a dedicated IV access device. In emergency situations the rate of infusion may be increased up to 0.5mmol/kg/hour if in intensive care, with ECG monitoring and given via a central access device.
Sodium glycerophosphate 21.6% (1mmol/mL) solution for infusion			Dilute and administer by IV infusion at 0.05mmol/kg/hour. Follow Medusa IV guidelines for dilution.

Note: IV Phosphate preparations will also provide additional sodium:

- Phosphate Polyfusor: 1.62mmol of sodium for every 1mmol of phosphate
- Sodium Glycerophosphate: 2mmol of sodium for every 1mmol of phosphate

Appendix 4: Vitamin D

- If serum levels of Vitamin D (25(OH)D) is < 25 nmol/L, the baby is vitamin D deficient, supplement with 3000 units Cholecalciferol daily for 3 months. Monitor biochemistry regularly. After 3 months treatment recheck serum Vit D levels along with alkaline phosphatase, PTH, calcium and phosphate. Ensure supplementation with a daily dose of at least 400 units vitamin D is undertaken after treatment.
- If serum levels are between 25-50 nmol/L, the baby's vitamin D status is insufficient, provide dietary advice and ensure maintenance supplementation with a daily dose of at least 400 units vitamin D is continued. Recheck Vit D levels in 3 months' time.
- In babies with significant metabolic bone disease and fractures, aim for a higher level of Vit D of 75 nmol/L. Please discuss with paediatric endocrine team for further advice.

Preparations for Vitamin D:

- 0.6 mls of Abidec and 0.6 mls of Dalivit provide 400 units of Vit D
- 0.3 mls of Dalivit provides 200 units of Vit D
- Fultium D3 drops: <https://www.medicines.org.uk/emc/product/6861/smpc>
3 drops of Fultium D3 = 200 units
1 ml of Fultium D3 = 2740 units.
- Colecalciferol (Thorens®) 10,000 units/mL oral solution

Appendix 5: Contributors of KSS Neonatal Nutrition Group

Name	Position	Neonatal Unit
Dr Vennila Ponnusamy	Consultant	St Peters Hospital
Dr Ramon Fernandez	Consultant	UHSussex
Dr Vimal Vasu	Consultant	William Harvey Hospital
Dr Toria Klutse	Consultant	East Surrey NHS Trust
Duha Alsaadi	Pharmacist	RSCH
Christian Chadwick	Pharmacist	UHSussex
Anthony Evans	Pharmacist	William Harvey Hospital
Catherine Casewell	Dietitian	St Peters Hospital
Sukvinder Kaur	Dietitian	Dartford and Gravesham NHS Trust
Chantelle Hearfield	Dietitian	Surrey and Sussex
Carole Davidson	Dietitian	UHSussex
Sarah Sabey	Dietitian	East Surrey NHS Trust
Ruth Cousins	Advanced Neonatal Nurse Practitioner	Maidstone and Tunbridge Wells
Kate Jones	SLT	UHSussex

Scope of Guideline Framework

The guideline applies to all Neonatal Units covered by Kent Surrey and Sussex Neonatal ODN. This includes the following hospitals:

Kent, Surrey and Sussex	
Medway Hospital NHSFT	- Medway Maritime Hospital, Gillingham
East Kent Hospitals University NHSFT	William Harvey Hospital, Ashford Queen Elizabeth the Queen Mother, Margate
Ashford and St Peter's NHSFT	- St Peter's Hospital, Chertsey
Brighton and Sussex University Hospitals NHST	- Royal Sussex County Hospital, Brighton - Princess Royal Hospital, Haywards Heath
Frimley Health NHSFT	- Frimley Park Hospital
Surrey and Sussex Healthcare NHST	- East Surrey Hospital, Redhill
Maidstone and Tunbridge Wells NHST	- Tunbridge Wells Hospital, Pembury
Dartford and Gravesham NHST	- Darent Valley Hospital, Dartford
Western Sussex Hospitals NHSFT	- Worthing Hospital, Worthing
East Sussex Healthcare NHST	- Conquest Hospital, Hastings
Royal Surrey NHSFT	- Royal Surrey County Hospital, Guildford

Key Points:

- The DoH recommend all children to have Multivitamins containing Vit D from 6 months if breastfed or when taking <500 mls when formula fed till 4-5yrs
- Breast milk alone is not adequate in calories, protein, calcium and phosphorus to meet nutritional requirements at 150mls/kg/day in preterm babies. Breast milk fortifier should be given routinely to all infants <35weeks receiving breast milk to prevent MBD.
- Prevention is better than cure for MBD, so aim to optimise calcium /phosphate content in milk/PN and monitor for signs of MBD in high risk infants.

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