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**Treatment of osteopenia in premature infants**

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**Citation** Garrubba M. & Ko H. 2009. Treatment of osteopenia in premature infants: Evidence Review. Centre for Clinical Effectiveness, Southern Health. Melbourne, Australia.

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Registrar, Monash Newborn  
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**Abstract**

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**Background** The Monash Newborn Unit at Monash Medical Centre, Clayton is developing evidence-based guidelines on treatment for infants in the care of the neonatal intensive care unit. One issue to be included in the guidelines is the effects treatment has on biochemical markers and catch-up growth on length before discharge and at term (40 weeks).  
The Centre for Clinical Effectiveness (CCE) was asked to find out if there was any evidence to suggest that treatment with a combination of additional vitamin D (in the form of calcitriol), calcium and phosphate is more effective than calcium plus phosphate at improving catch-up growth in length and biochemical markers.

**Question** In neonatal patients diagnosed with osteopenia, who are <32 weeks gestational age at birth or <1000g birth weight, how does treatment by a combination of additional vitamin D (in the form of calcitriol), calcium and phosphate compared with calcium plus phosphate effect catch-up growth in length and the following biochemical markers before discharge and at term (40 weeks): tubular reabsorption of phosphate (TRP); calcium; phosphate; albumen; alkaline phosphatase; electrolytes, urea, creatinine (EUC); and parathyroid hormone (PTH)?

**Methods** We included all trials published in English.  
We searched Medline, CINAHL, All EBM and EMBASE in April 2009.  
Studies were selected and appraised by two reviewers in consultation with colleagues, using inclusion, exclusion and appraisal criteria established a priori.

**Results** The search of medical databases (Medline, CINAHL, All EBM and EMBASE) databases returned 142 articles which were reviewed by title and abstract. A total of 61 full text articles were retrieved for review with no articles meeting the study selection criteria.

**Conclusion** CCE was unable to identify any high-quality, studies which compared treatment with a combination of additional vitamin D (in the form of calcitriol), calcium and phosphate for treatment with calcium plus phosphate of neonatal patients who are <32 weeks gestational age at birth or <1000g birth weight and diagnosed with osteopenia.

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## Background

The Monash Newborn Unit at Monash Medical Centre, Clayton is developing evidence-based guidelines on treatment for infants in the care of the neonatal intensive care unit. One issue to be included in the guidelines is the effects treatment has on biochemical markers and catch-up growth on length before discharge and at term (40 weeks).

The Centre for Clinical Effectiveness (CCE) was asked to find out if there was any evidence to suggest that treatment with a combination of additional vitamin D (in the form of calcitriol), calcium and phosphate is more effective than calcium plus phosphate at improving catch-up growth in length and biochemical markers.

## Question

In neonatal patients diagnosed with osteopenia, who are <32 weeks gestational age at birth or <1000g birth weight, how does treatment by a combination of additional vitamin D (in the form of calcitriol), calcium and phosphate compared with calcium plus phosphate effect catch-up growth in length and the following biochemical markers before discharge and at term (40 weeks): tubular reabsorption of phosphate (TRP); calcium; phosphate; albumen; alkaline phosphatase; electrolytes, urea, creatinine (EUC); and parathyroid hormone (PTH)?

## Methods

### Study selection criteria

<b>Patient</b>	Neonatal patients (<32 weeks gestational age at birth or <1000g birth weight) diagnosed with osteopenia		
<b>Intervention</b>	Additional vitamin D (in the form of calcitriol), calcium and phosphate		
<b>Comparison</b>	Calcium plus phosphate		
<b>Outcomes</b>	<ul style="list-style-type: none"><li>▪ Catch-up growth in length</li><li>▪ Biochemical markers<ul style="list-style-type: none"><li>- TRP</li><li>- Calcium</li><li>- PTH</li><li>- Phosphate</li><li>- Albumen</li><li>- Alkaline phosphatase</li><li>- EUC</li></ul></li></ul>		
<b>Study type</b>	For the specified outcomes, systematic reviews and RCTs addressing the outcomes are sought. If there are outcomes not addressed by RCTs, then evidence from lower quality comparative studies are sought.	<b>Publication Date</b>	1980 onwards
		<b>Language</b>	English

### Search strategy

Evidence source	Date of search or issue searched
Medline (Ovid)	21 April 2009
All EBM (Ovid)*	21 April 2009
CINAHL (Ebscohost)	21 April 2009
EMBASE (Ovid)	21 April 2009

\*(including The Cochrane Database of Systematic Reviews, DARE, CENTRAL and ACP Journal Club)

### Search terms in Medline\*

<b>Patient</b>	Pre-term and infant MeSH terms and keywords AND Osteopenia and related MeSH terms and keywords
<b>Intervention</b>	Vitamin D MeSH terms and keywords AND Calcium MeSH terms and keywords AND Phosphate MeSH terms and keywords
<b>Comparison</b>	-
<b>Outcomes</b>	-

\* Similar terms (appropriately translated) were used in other databases. Details of all searches are available in Appendix 1.

## Data collection and analysis

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Studies were selected and appraised by two reviewers in consultation with colleagues using study selection and appraisal criteria established a priori. All articles were reviewed by title and abstract. When a decision could not be made based on title and abstract alone, full text was retrieved.

## Results

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The search of medical databases (Medline, CINAHL, All EBM and EMBASE) databases returned 142 articles which were reviewed by title and abstract. A total of 61 full text articles were retrieved for review with no articles meeting the study selection criteria.

## Conclusion

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CCE was unable to identify any high-quality, evidence-based studies which compared treatment by a combination of additional vitamin D (in the form of calcitriol), calcium and phosphate to treatment with calcium plus phosphate of neonatal patients who are <32 weeks gestational age at birth or <1000g birth weight and diagnosed with osteopenia.

## Disclaimer

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## APPENDIX 1 – Search Strategy: Medline

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1	(preterm or pre-term or premature or low birth weight).mp. [mp=title, original title, abstract, name of substance word, subject heading word]	130427
2	exp Infant, Newborn/	417078
3	exp Infant/	781154
4	(neonat\$ or newborn\$ or infant\$ or infancy or baby or babies).mp. [mp=title, original title, abstract, name of substance word, subject heading word]	1004042
5	or/2-4	1004042
6	1 and 5	78716
7	exp Infant, Extremely Low Birth Weight/	285
8	exp Infant, Low Birth Weight/	20152
9	exp Infant, Premature/	32595
10	or/6-9	80653
11	exp Bone Diseases/	321411
12	exp Bone Diseases, Metabolic/	48717
13	Osteopenia.mp.	5102
14	exp Osteomalacia/	3976
15	osteomalacia.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	5255
16	exp Rickets/	7399
17	Rickets.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	6526
18	phosphate depletion syndrome.mp.	20
19	or/11-18	324851
20	10 and 19	1311
21	exp Vitamin D/	31836
22	Vitamin D.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	34439
23	exp Calcitriol/	11200
24	Calcitriol.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	14336
25	exp Cholecalciferol/	18825
26	Cholecalciferol.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	4706
27	(Alphacalcidol or Alfacalcidol).mp. [mp=title, original title, abstract, name of substance word, subject heading word]	354
28	(Pentavite or Penta-vite).mp. [mp=title, original title, abstract, name of substance word, subject heading word]	0
29	(Multivitamin\$ or Multi-vitamin\$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]	2089
30	or/21-29	48201
31	exp Calcium/	212306
32	exp Calcium, Dietary/	7395
33	exp Calcium Compounds/	42647
34	Calcium.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	400700
35	exp Phosphates/	70610
36	Phosphate\$.mp.	209585
37	or/31-36	585996
38	30 and 37	24434
39	20 and 38	113
40	limit 39 to (english language and humans and yr="1980 -Current")	76

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