New Zealand College of Midwives
TE KĀRETI O NGA KAIWHAKAWHANAU KI AOTEAROA

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists
Excellence in Women's Health

Te Kāhui Oranga ō Nuku

The Paediatric Society of New Zealand
Te Kāhui Mātai Arotamariki o Aotearoa

2 June 2021

Nicky Smith
Manager: Maternity team
Ministry of Health
By email: NickySmith@health.govt.nz

Tēnā koe Nicky,

The New Zealand College of Midwives - Te Kāreti o ngā Kaiwhakawhānau ki Aotearoa, Te Kāhui Mātai Arotamariki o Aotearoa - the Paediatric Society of New Zealand, and Te Kāhui Oranga ō Nuku – the New Zealand committee of the RANZCOG, would like to raise with the Ministry the need for the Companion Statement on Vitamin D and Sun Exposure in Pregnancy and Infancy in New Zealand (2020) [1] to be:

1. updated with a full evidence review; and
2. reformatted for clarity; and
3. accompanied by a clear plan for implementation, along with appropriate resourcing.

Details and rationale for each of these requests are provided in the discussion paper that follows. We look forward to hearing from you.

Ngā mihi,

Alison Eddy
Chief Executive
Te Kāreti o ngā Kaiwhakawhānau ki Aotearoa
New Zealand College of Midwives

Celia Devenish
Chair, Te Kāhui Oranga ō Nuku
RANZCOG

Nicola Austin
President
Te Kāhui Mātai Arotamiriki o Aotearoa, **PSNZ**

Vitamin D supplementation in pregnancy, during breastfeeding and in infancy: joint discussion document

1. Evidence update needed

Although a review of the 2013 Companion Statement was undertaken and published in December 2020,[2] this review only updated the recommended and available medications and did not involve an evidence review.[1] As such, the statement remains out of date with 2013 being the most recent publication date of the literature cited in the document.

Pregnancy

Since the publication of the Companion Statement, the Cochrane Review,[3] cited in that document has been updated twice, with new and strengthened findings on the benefit of vitamin D supplementation during pregnancy. The aim of vitamin D supplementation during pregnancy as stated in the Companion Statement was primarily *to ensure that the fetus has sufficient vitamin D and is not born vitamin D deficient*, and thus prevent downstream child health problems including rickets. The Companion Statement indicates:

> *While vitamin D deficiency during pregnancy has been associated with adverse pregnancy and neonatal outcomes such as being small for gestational age, there is no convincing evidence yet that there is a causal relationship.[3] Supplementation during pregnancy has been shown to increase vitamin D levels at the end of pregnancy which is positively correlated to infant vitamin D levels but there is no strong evidence for other outcomes.[3]*

However, the latest Cochrane review[4] has amended findings and it points to reduced risks of adverse pregnancy and possibly childbirth outcomes. Because vitamin D deficiency is more likely to affect populations with darker skin pigmentation, this is an equity issue. This is magnified by the fact that a number of conditions which appear to be improved by vitamin D supplementation during pregnancy – gestational diabetes, pre-eclampsia, low birthweight, fetal/neonatal mortality and infant respiratory infections – disproportionately affect those populations that have higher rates of vitamin D deficiency. A number of individual studies and two meta-analyses have found vitamin D supplementation to be of benefit across a range of outcomes, however a systematic review is needed to fully assess the evidence for the New Zealand context. Appendix I outlines some of the research published since 2013.

Infancy

In 2015 the New Zealand Paediatric Surveillance Unit (NZPSU) published a study of New Zealand rates of vitamin D deficiency rickets and hypocalcaemia in 2015,[5] which identified rates of rickets of >10/100,000 in children under the age of 3 years (the peak period for symptomatic rickets).[5] Evidence of asymptomatic rickets in “low risk” breastfed South Island infants has also recently been published.[6] Since those publications, emergency departments have reported further presentations of infants with hypocalcaemic seizures who met the criteria for vitamin D supplementation but were not receiving it. This issue has been raised with the College of Midwives and the Paediatric Society, and discussed with the Ministry of Health. Ministry-led research is underway to assess the rate of vitamin D supplementation for infants with risk factors in Aotearoa.

The current NZ consensus statement does not align with the findings and recommendations of the "Global Consensus Recommendations on Prevention and Management of Nutritional Rickets" published in 2016[7] which recommends universal supplementation for all infants.[7] A full evidence review is required to assess the applicability of this recommendation for the New Zealand context, particularly given this country's current unacceptable rates of rickets, in addition to having emerging benefits for other aspects of health and wellbeing related to vitamin D status. New Zealand research indicates that vitamin D deficiency at birth is associated with an increased likelihood of hospitalisation for acute respiratory infection during infancy,[8] whereas daily vitamin D supplementation during pregnancy and infancy prevented acute respiratory infection primary care visits up to age 18 months,[9] a finding that is consistent with a recent systematic review and meta-analysis.[10] Vitamin D supplementation during pregnancy and infancy also prevented sensitisation to the house dust mites at 18 months.[11] Details of these studies are in Appendix I.

Recommendation

We recommend that a systematic review of the evidence since 2013 is undertaken and the current recommendations reviewed by a multidisciplinary work group.

2. Format of guidance

The format of the guidance, particularly with relation to the new medication recommendations for pregnant women needs to be amended for clarity. Dosage information for pregnant women is not quickly identifiable, appearing only as part of a page of text on p. 20, without any headings indicating dosage information.

Recommendations for supplementation appear on p. 3, but the information on dosing is vague, difficult to follow.

> *Pregnant women at high risk of vitamin D deficiency (as identified above) are recommended to consider vitamin D supplementation with colecalciferol oral liquid (188 µg per ml/7,500 international units IU/ml) which is available and subsidised for use in both the community and the hospital. Each drop provides approximately 10 µg (400 IU).*

This paragraph does not explain what dose (how many drops) women at high risk of vitamin D deficiency should take. It may be assumed that these women should take one drop per day, however this is confused by the subsequent paragraph about pregnant women at lower risk:

> *Pregnant women at lower risk of vitamin D deficiency may benefit (and are unlikely to suffer harm) from vitamin D supplementation of between 10 µg/day (400 IU) and 15 µg/day (600 IU) throughout their pregnancy but especially in the third trimester.*

As well as lacking clarity, this information is impractical given that 600 IU would be 1.5 drops of Puria® oral cholecalciferol.

Recommendation
We recommend making an unequivocal recommendation on supplementation, including both dosage and which women and infants should be recommended supplementation.

Visual aids should be included to support the recommendation, according to the outcome of the evidence review and updated recommendations. For example, if a risk-based and seasonal approach continues, it will need to be supported by an algorithm and/or checklist. If a universal approach is adopted, decision-support tools will be simpler.

Such an approach would support maternity care providers to raise the issue of vitamin D with pregnant women who have risk factors for deficiency, or, provide accurate information to all women if universal supplementation is recommended.

3. Implementation

There are a number of issues relating to the implementation of the Companion Statement's recommendations which are both long-standing (since 2013) and more recent (since the 2020 update).

1. The New Zealand Formulary has not been updated to include information about daily supplementation with cholecalciferol (Puria®) oral drops for pregnant women as recommended in the Companion Statement 2020. The College of Midwives has heard from midwives who are uncertain about prescribing, and from community and DHB pharmacy services that have received no information about dispensing the new medication regimen.

2. No national publicity has been produced by the Ministry of Health to advise practitioners or women about the guidance in the Companion Statement, either in 2013 or in 2020. As a result, uptake in practice has been compromised. We draw your attention to the contrasting implementation process for the introduction of routine iodine supplementation for pregnant and breastfeeding women in 2009. Practice updates were rolled out to maternity care providers and patient information leaflets were provided to all pregnant women.

HE4147 Folic Acid and Iodine.pdf

3. Criticism has been directed at some midwives for not prescribing vitamin D to women and/or babies who have risk factors for vitamin D deficiency. This is both unwarranted and unreasonable because:

    a) There has not been any education provided to the sector about the recommendations in the Companion Statement since either 2013 or 2020, including assessing risk with the Fitzpatrick skin type model.

    b) The recommendations are vague and open to different interpretation, for example (underline added): "*Where infants are exclusively or partially breastfed (who receive less than 500 ml of formula a day (based on current recommended dietary intakes (RDIs)*

(NHMRC 2006)) and have one or more of the risk factors above, they may benefit from vitamin D supplementation (p. 3).

c) The dosage regimen is not described, for example one drop per day, or for what length of time, for example:

"*The standard subsidised preparation in New Zealand is Puria® vitamin D drops listed on the Pharmaceutical Schedule. This preparation contains vitamin D only (this is about 10 µg or 400 IU of cholecalciferol per drop or 188 µg/7,500 IU cholecalciferol per ml). Higher doses can be given but only after consultation with a specialist* (p. 3)."

d) The Ministry document states: *"It would be reasonable to wait until breastfeeding is well established in full-term, high-risk infants, such as until six weeks of age, before introducing vitamin D supplementation* (p. 3)*."*

Midwifery care finishes by 6 weeks postpartum, therefore midwives are following the guidance exactly when they refer for the GP to consider prescribing vitamin D at the 6 week check.

The guidance to wait until 6 weeks before commencing vitamin D supplementation for full-term, high-risk infants is contrary to current paediatric expert opinion and recommended practice in a number of DHBs. This misalignment is causing confusion and further supports the need for an evidence review and update of the recommendations.

The 2020 update of the consensus statement was an opportunity to review and strengthen these recommendations or bring the commencement of infant supplementation forward if the evidence supported it, however this did not occur and variable practice continues as a result.

Recommendation

Once the recommendations have been reviewed and confirmed, a clear implementation plan is developed and resourced to include information for maternity care providers, maternity service users and the Well Child Tamariki Ora programme.

Conclusion

The evidence content of the 2020 Companion Statement on Vitamin D and Sun Exposure in Pregnancy and Infancy in New Zealand requires updating. The published literature that has been produced since the 2013 evidence review and not currently cited in the 2020 companion statement confirms maternal and infant health benefits of vitamin D supplementation during pregnancy and infancy. It also documents the persisting high prevalence of vitamin D deficiency in New Zealand during pregnancy and infancy. This is an equity issue as vitamin D deficiency and related health and obstetric issues are more commonly experienced by people with darker skin pigmentation or full body covering, including Māori, Pasifika, refugee and migrant populations. A systematic review of the literature may justify a recommendation for vitamin D supplementation of all pregnant women and infants in New Zealand. Whichever recommendations are adopted need to be articulated in a clear format and supported with an adequately resourced implementation plan.

References

1. Ministry of Health. Companion Statement on Vitamin D and Sun Exposure in Pregnancy and Infancy in New Zealand: A supplement to the Consensus Statement on Vitamin D and Sun Exposure in New Zealand. Updated 2020. . Wellington: Ministry of Health, 2020.
2. Ministry of Health. Companion Statement on Vitamin D and Sun Exposure in Pregnancy and Infancy in New Zealand. Wellington: Ministry of Health, 2013.
3. DeRegil ML, Palacios C, Ansary A, et al. Vitamin D supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2012(2)
4. Palacios C, Kostiuk LK, Pena-Rosas JP. Vitamin D supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2019;1:Cd008873.
5. Wheeler BJ, Dickson NP, Houghton LA, et al. Incidence and characteristics of vitamin D deficiency rickets in New Zealand children: a New Zealand Paediatric Surveillance Unit study. *Aust N Z J Public Health* 2015;39(4):380-3. doi: https://dx.doi.org/10.1111/1753-6405.12390
6. Wheeler BJ, Taylor BJ, de Lange M, et al. A Longitudinal Study of 25-Hydroxy Vitamin D and Parathyroid Hormone Status throughout Pregnancy and Exclusive Lactation in New Zealand Mothers and Their Infants at 45degree S. *Nutrients* 2018;10(1):13. doi: https://dx.doi.org/10.3390/nu10010086
7. Munns CF, Shaw N, Kiely M, et al. Global Consensus Recommendations on Prevention and Management of Nutritional Rickets. *J Clin Endocrinol Metab* 2016;101(2):394-415. doi: https://dx.doi.org/10.1210/jc.2015-2175
8. Saraf R, Jensen BP, Camargo CA, Jr., et al. Vitamin D status at birth and acute respiratory infection hospitalisation during infancy. *Paediatr Perinat Epidemiol* 2021;01:01. doi: https://dx.doi.org/10.1111/ppe.12755
9. Grant CC, Kaur S, Waymouth E, et al. Reduced primary care respiratory infection visits following pregnancy and infancy vitamin D supplementation: a randomised controlled trial. *Acta Paediatr* 2015;104(4):396-404. doi: http://dx.doi.org/10.1111/apa.12819
10. Jolliffe DA, Camargo CA, Jr., Sluyter JD, et al. Vitamin D supplementation to prevent acute respiratory infections: a systematic review and meta-analysis of aggregate data from randomised controlled trials. *Lancet Diabetes Endocrinol* 2021;30:30. doi: https://dx.doi.org/10.1016/S2213-8587(21)00051-6
11. Grant CC, Crane J, Mitchell EA, et al. Vitamin D supplementation during pregnancy and infancy reduces aeroallergen sensitization: a randomized controlled trial. *Allergy* 2016;71(9):1325-34. doi: https://dx.doi.org/10.1111/all.12909

Appendix I

Randomised controlled trial data reported since 2012 on vitamin D supplementation during pregnancy

Paper	Findings
Palacios C, Kostiuk L, Peña-Ross J. 2019. Vitamin D supplementation for women during pregnancy. *Cochrane Database of Systematic Reviews* 2019, Issue 7. Art. No.: CD008873. DOI:	Meta-analysis of 22 trials, almost 4000 women. Vitamin D supplementation during pregnancy associated with a reduced the risk of: • Preeclampsia (RR = 0.48, 95% CI 0.30 to 0.79) • Gestational diabetes (RR = 0.51, 95% CI 0.27 to 0.97) • Low birthweight <2500g (RR = 0.55, 95% CI 0.35 to 0.87) • Severe postpartum hemorrhage (RR = 0.68, 95% CI 0.51 to

10.1002/14651858.CD008873.pub4.	0.91) Authors conclude: *Supplementing pregnant women with vitamin D alone probably reduces the risk of pre-eclampsia, gestational diabetes, low birthweight and may reduce the risk of severe postpartum haemorrhage.* *Supplementing pregnant women with vitamin D and calcium probably reduces the risk of pre-eclampsia but may increase the risk of preterm births < 37 weeks (these findings warrant further research).*
Bi W, Nuyt A, Weiler H, Leduc L, Santamaria C, Wei S. 2018. Association Between Vitamin D Supplementation During Pregnancy and Offspring Growth, Morbidity, and Mortality: A Systematic Review and Meta-analysis. *JAMA Pediatr*; 172(7): 635–645. doi:10.1001/jamapediatrics.2018.0302	Meta-analysis of 24 RCT trials, 5405 participants. Vitamin D supplementation during pregnancy associated with a reduced the risk of: • Small for gestational age (RR = 0.72; 95% CI 0.52 to 0.99) without risk of fetal or neonatal mortality or congenital abnormality • Neonates with prenatal vitamin D supplementation had higher: ▪ 25(OH)D levels (MD, 33.75 umol/L; 95% CI 25.30 to 42.18 umol/L) ▪ calcium levels (MD, 0.04 mmol/L; 95% CI 0.00 to 0.08 mmol/L) ▪ weight at birth, 3 months, 6 months, 9 months, and 12 months Low-dose daily vitamin D supplementation during pregnancy (≤2000 IU/d) was associated with a reduced risk of fetal or neonatal mortality (RR = 0.35; 95% CI 0.15 to 0.80), but higher doses (>2000 IU/d) did not reduce this risk (RR = 0.95; 95% CI 0.59 to 1.54). Authors conclude: *Vitamin D supplementation during pregnancy is associated with a reduced risk of SGA and improved infant growth without risk of fetal or neonatal mortality or congenital abnormality. Vitamin D supplementation with doses of 2000 IU/d or lower during pregnancy may reduce the risk of fetal or neonatal mortality.*
O'Callaghan K, Taghivand M, Zuchniak A, et al. 2020. Vitamin D in Breastfed Infants: Systematic Review of Alternatives to Daily Supplementation. *Adv Nutr* . *11*(1):144-159. doi: 10.1093/advances/nmz098.	This systematic review and meta-analysis aimed to estimate the effects of maternal postpartum or infant intermittent vitamin D supplementation on infant 25-hydroxyvitamin D concentrations in comparison to routine direct infant daily oral supplementation (400 IU). Meta-analysis of 28 RCT trials, 5908 participants. However, only 5 RCTs were incorporated in meta-analyses examining infant 25-hydroxyvitamin D concentration. *Maternal postpartum or infant intermittent vitamin D supplementation are plausible substitutes to daily infant supplementation. However, note should be made of other meta-analyses which indicate that daily vitamin D supplementation is preferable.*[10]
Anderson C, Gillespie S, Thiele	RCT. Assessed DNA methylation in relation to vitamin D

D, Ralph J, Ohm J. 2018. Effects of Maternal Vitamin D Supplementation on the Maternal and Infant Epigenome. *Breastfeeding Medicine; 13*(5): 371-380.	supplementation during pregnancy at two separate doses and placebo. Results: *At birth, intervention group mothers showed DNA methylation gain and loss at 76 and 89 cytosine– guanine (CpG) dinucleotides, respectively, compared to controls. Postpartum, methylation gain was noted at 200 and loss at 102 CpGs. Associated gene clusters showed strongest biologic relevance for cell migration/motility and cellular membrane function at birth and cadherin signalling and immune function at postpartum. Breastfed 4–6-week-old infants of intervention mothers showed DNA methylation gain and loss in 217 and 213 CpGs, respectively, compared to controls. Genes showing differential methylation mapped most strongly to collagen metabolic processes and regulation of apoptosis.*
Trivedi M, Faridi M, Aggarwal A, Madhu S, Malhotra R. 2020. Oral Vitamin D Supplementation to Mothers During Lactation—Effect of 25(OH)D Concentration on Exclusively Breastfed Infants at 6 Months of Age: A Randomized Double-Blind Placebo-Controlled Trial. *Breastfeeding medicine; 15*(4): 237-245.	RCT. Assessed vitamin D status of exclusively breastfed infants whose mothers took vitamin D supplements at different doses compared with placebo during lactation. Results: *At 6 months of age, serum 25(OH)D concentration in infants was 47.33 (12.80) nmol/L in the intervention group and 16.08 (9.40) nmol/L in the control group (mean difference = 31.25; 95% CI = 27.00–34.43; p < 0.001) and vitamin D deficiency and insufficiency was corrected in 93.1% and 38% infants, respectively, in the intervention group. There was no change in the vitamin D status of infants in the control group. In 60.3% infants (RR = 0.52 95% CI = 0.49 to 0.74) of the intervention group 25(OH)D concentration was <5 nmol/L at 6 months of age. Six infants in the control group suffered from biochemical rickets. Radiological rickets developed in one infant in the intervention group and two infants in the control group.*
Grant CC, Stewart AW, Scragg R, et al. Vitamin D during pregnancy and infancy and infant serum 25-hydroxyvitamin D concentration. *Pediatrics* 2014;133(1):e143-53. doi: http://dx.doi.org/10.1542/peds.2013-2602	NZ RCT which enrolled an ethnically diverse sample of 260 pregnant women in South Auckland. Daily vitamin D supplementation during pregnancy and then infancy prevented vitamin D deficiency during infancy.
Grant C, Kaur S, Waymouth E et al. 2015. Reduced primary care respiratory infection visits following pregnancy and infancy vitamin D supplementation: a randomised controlled trial. *Acta Paediatrica; 104*(4); 396-404.	New Zealand RCT. Assessed the effect of vitamin D supplementation during pregnancy and infancy on primary care respiratory infection visits up to age 18 months. Results: *Two hundred and sixty pregnant women were randomised to placebo (n = 87), lower-dose (n = 87) or higher-dose (n = 86) vitamin D_3. In comparison with the placebo group (99%), the proportion of children making any ARI visits was smaller in the higher dose (87%, p = 0.004), but not the lower-dose vitamin D_3 group (95%, p = 0.17). The median number of ARI visits/child was less in the higher-dose vitamin D_3 group from age 6–18 months (placebo 4.0, lower dose 3.0, higher dose 2.5; p = 0.048 for higher-*

	dose vitamin D_3 vs. placebo). Conclusion: *Vitamin D_3 supplementation during pregnancy and infancy reduces primary care visits for ARI during early childhood.*
Grant CC, Crane J, Mitchell EA, et al. Vitamin D supplementation during pregnancy and infancy reduces aeroallergen sensitization: a randomized controlled trial. Allergy 2016;71(9):1325-34. doi: https://dx.doi.org/10.1111/all.12909 12.	NZ RCT. Vitamin D supplementation during pregnancy and infancy reduced the proportion of children sensitized to mites at age 18 months. Preliminary data indicate a possible effect on primary care visits where asthma is diagnosed.
Wheeler BJ, Dickson NP, Houghton LA, et al. Incidence and characteristics of vitamin D deficiency rickets in New Zealand children: a New Zealand Paediatric Surveillance Unit study. *Aust N Z J Public Health* 2015;39(4):380-3. doi: https://dx.doi.org/10.1111/1753-6405.12390	Prospective surveillance. 58 children with confirmed vitamin D deficiency rickets were identified. Median age was 1.4 (range 0.3–11) years, 47% were male, and 95% of the children were born in NZ; however, the majority of the mothers (68%) were born outside NZ. Overall annual incidence of rickets in children aged <15 years was 2.2/100,000 (95%CI 1.4–3.5); with incidence in those <3 years being 10.5/100,000 (95%CI 6.7–16.6). Skeletal abnormalities, poor growth and motor delay were the most common presenting features, with hypocalcaemic convulsion in 16% of children. Key risk factors identfied were: darker skin pigment, Indian and African ethnicity, age <3 years, exclusive breast feeding, and southern latitude, particularly when combined with season (winter/spring). Of the patients reported, none had received appropriate vitamin D supplementation.
Wheeler BJ, Taylor BJ, de Lange M, et al. A Longitudinal Study of 25-Hydroxy Vitamin D and Parathyroid Hormone Status throughout Pregnancy and Exclusive Lactation in New Zealand Mothers and Their Infants at 45degree S. Nutrients 2018;10(1):13. doi: https://dx.doi.org/10.3390/nu10010086	Descriptive study of maternal and infant longitudinal 25-hydroxy vitamin D (25OHD) and parathyroid hormone (PTH) status during pregnancy and up to 5 months postnatal age, in 126 NZ women and babies living at 45° S latitude. Vitamin D deficiency (25OHD < 50 nmol/L) was common, found at one or more time-points in 65% and 76% of mothers and their infants, respectively. Mean cord 25OHD was 41 nmol/L, and three infants exhibited secondary hyperparathyroidism by postnatal week 20. Maternal late pregnancy 25OHD (gestation 32–38 weeks) was closely correlated with infant cord 25OHD, $r^2 = 0.87$ (95% CI (Confidence interval) 0.8–0.91), while no correlation was seen between early pregnancy (<20 weeks gestation) maternal and cord 25OHD, $r^2 = 0.06$ (95% CI −0.16–0.28). Among other variables, pregnancy 25OHD status, and therefore infant status at birth, were influenced by season of conception.
Munns CF, Shaw N, Kiely M, et al. Global Consensus Recommendations on Prevention and Management of Nutritional Rickets. *J Clin Endocrinol Metab*	This global position statement recommends: • 400 IU/d (10 µg) is adequate to prevent rickets and is recommended for all infants from birth to 12 months of age, independent of their mode of feeding. • Maternal vitamin D deficiency should be avoided by ensuring that women of childbearing age meet intakes of

2016;101(2):394-415. doi: https://dx.doi.org/10.1210/jc.2015-2175	600 IU/d recommended by the Institute of Medicine.
Saraf R, Jensen BP, Camargo CA, Jr., et al. Vitamin D status at birth and acute respiratory infection hospitalisation during infancy. *Paediatr Perinat Epidemiol* 2021;01:01. doi: https://dx.doi.org/10.1111/pp.12755	Longitudinal cohort study *Growing Up in New Zealand*. The odds of being hospitalised with an acute respiratory infection during infancy were increased for infants who were vitamin D deficient at birth (OR 2.20, 95% CI 1.48 to 2.91) after adjustment for season of birth and covariates (demographic, antenatal, perinatal, and infant characteristics). Infants with the lowest levels of vitamin D at birth were more likely to be hospitalised with an acute respiratory infection more than once during infancy and to have longer stays in hospital.
Jolliffe DA, Camargo CA, Jr., Sluyter JD, et al. Vitamin D supplementation to prevent acute respiratory infections: a systematic review and meta-analysis of aggregate data from randomised controlled trials. *Lancet Diabetes Endocrinol* 2021;30:30. doi: https://dx.doi.org/10.1016/S2213-8587(21)00051-6	Systematic review and meta-analysis which included data from 48,488 participants (aged 0-95 years) enrolled in 43 randomised controlled trials of vitamin D supplementation. Despite evidence of significant heterogeneity across trials, vitamin D supplementation was safe and overall reduced the risk of acute respiratory infections compared with placebo, although the risk reduction was small. Protection was associated with administration of daily doses of 400–1000 IU for up to 12 months, and age at enrolment of 1·00–15·99 years.