CORA Cork Open Research Archive
Cartlann Taighde Oscailte Chorcaí

Title	Ethnic disparities in the dietary requirement for vitamin D during pregnancy: considerations for nutrition policy and research
Authors	O'Callaghan, Karen M.;Kiely, Mairead E.
Publication date	2017-11-28
Original Citation	O'Callaghan, K. M. and Kiely, M. E. (2017) 'Ethnic disparities in the dietary requirement for vitamin D during pregnancy: considerations for nutrition policy and research', Proceedings of the Nutrition Society, In Press. doi:10.1017/S0029665117004116
Type of publication	Article (peer-reviewed)
Link to publisher's version	https://www.cambridge.org/core/article/ethnic-disparities-in-the-dietary-requirement-for-vitamin-d-during-pregnancy-considerations-for-nutrition-policy-and-research/35D1FB455715DF38133B24AB7B8852BB - 10.1017/S0029665117004116
Rights	© The Authors 2017. Published by Cambridge University Press (CUP) on behalf of The Nutrition Society
Download date	2026-11-07 10:14:07
Item downloaded from	https://hdl.handle.net/10468/5247

UCC
University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

Proceedings of the Nutrition Society, Page 1 of 10 doi:10.1017/S0029665117004116
© The Authors 2017

The Nutrition Society Irish Section Meeting held at the Queens University, Belfast on 21–23 June 2017

Conference on 'What governs what we eat?'

Ethnic disparities in the dietary requirement for vitamin D during pregnancy: considerations for nutrition policy and research

Karen M. O'Callaghan[1,2]* and Mairead E. Kiely[1,2]
[1]*Cork Centre for Vitamin D and Nutrition Research, School of Food and Nutritional Sciences, University College Cork, Cork, Ireland*
[2]*Irish Centre for Fetal and Neonatal Translational Research, University College Cork, Cork, Ireland*

Despite the inverse association between skin colour and efficiency of cutaneous vitamin D synthesis, in addition to the widely accepted racial disparity in vitamin D status, populations of ethnic minority are understudied in terms of setting target serum 25-hydroxyvitamin D concentrations and corresponding dietary requirements for vitamin D. In minority groups, prevention of vitamin D deficiency on a population basis is challenging due to the lack of clarity surrounding the metabolism and transport of vitamin D. Authoritative agencies have been unable to define pregnancy-specific dietary recommendations for vitamin D, owing to an absence of sufficient evidence to confirm whether nutritional requirements for vitamin D are altered during pregnancy. While the question of setting race- and pregnancy-specific dietary reference values for vitamin D has not been addressed to date, endemic vitamin D deficiency has been reported among gravidae worldwide, specifically among ethnic minorities and white women resident at high latitude. In light of the increased risk of nutritional rickets among infants of ethnic minority, coupled with growing evidence for potential non-skeletal roles of vitamin D in perinatal health, determination of the dietary vitamin D requirement that will prevent deficiency during pregnancy is a research priority. However, systematic approaches to establishing dietary requirements are limited by the quality of the available evidence and the under-representation of minority groups in clinical research. This review considers the evidence for racial differences in vitamin D status and response to vitamin D supplementation, with particular application to pregnancy-specific requirements among ethnic minorities resident at high latitudes.

Ethnicity: Minority groups: Pregnancy: Vitamin D requirements

Owing to the inverse association between skin colour and the efficiency of cutaneous vitamin D synthesis[1], populations of ethnic minority are considered an at-risk group for vitamin D deficiency, whereby the observed racial disparity in vitamin D status has created a widely held impression that dietary vitamin D requirements are higher compared with native white populations. However, this concept is based upon a paucity of experimental evidence and individuals of ethnic minority remain understudied in terms of setting target serum 25-hydroxyvitamin D (25(OH)D) concentrations and corresponding dietary requirements for vitamin D[2,3]. In pregnancy, the absence of sufficient evidence from appropriately designed, randomised controlled trials limits the understanding of a probable increased metabolic demand for vitamin D throughout gestation, regardless of ethnicity. As such, authoritative agencies to date have been unable to define race-specific or pregnancy-specific dietary recommendations for vitamin D, due to a lack of experimental evidence to confirm whether nutritional requirements for vitamin D differ by ethnicity or during pregnancy[4]. By necessity, dietary reference

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; BMD, bone mineral density; DRV, dietary reference values; EAR, estimated average requirement; PTH, parathyroid hormone; VDBP, vitamin D-binding protein.

***Corresponding author:** K. M. O'Callaghan, email karen.ocallaghan@ucc.ie

Downloaded from https://www.cambridge.org/core. University College Cork, on 09 Jan 2018 at 10:27:22, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665117004116

Table 1. Summary of the current dietary recommendations for vitamin D in pregnant women

Agency	Countries	25(OH)D threshold (nmol/l)			Vitamin D intake (μg/d)		
		Deficiency	Population average	Individual target	EAR	RI	AI
IOM (2011)[4]	USA/Canada	<30	40	≥50	10	15	
NORDEN (2012)[5]	Nordic	<30	–	≥50	7·5	10	
SACN (2016)[6]	UK	<25	–	≥25	–	10	
EFSA (2016)[7]	EU	–	–	≥50	–	–	15

25(OH)D, 25-hydroxyvitamin D; EAR, estimated average requirement; RI, recommended (individual) intake; AI, adequate intake; IOM, Institute of Medicine; NORDEN, Nordic Council of Ministers; SACN, Scientific Advisory Committee on Nutrition; EFSA, European Food Safety Authority. Table adapted from Kiely *et al.*[13].

values (DRV) for vitamin D in non-pregnant adults have therefore been extended to pregnancy and lactation, assuming equivalent recommendations for all racial and ethnic groups[4–7].

Endemic vitamin D deficiency has been reported among gravidae worldwide, particularly among ethnic minorities[8], and nutritional rickets secondary to vitamin D deficiency is most prevalent among neonates born to women with dark or black skin[9]. The most recent national report from Ireland and the UK has estimated the overall annual incidence rate of hypocalcaemic seizures due to vitamin D deficiency as 3·49 per million children aged 0–15 years. When stratified by ethnicity, the incidence rate rises from 0·46 per million white children to as high as 20·70 and 26·04 per million children among those of black and South Asian origin, respectively[10]. Similarly in Australia, 98 % of 398 children identified with rickets had dark skin and 75 % were refugees, highlighting minority populations as a particularly at-risk group[11]. As neonatal circulating 25(OH)D concentrations are dependent on maternal vitamin D status, at minimum, vitamin D deficiency during pregnancy should be prevented to ensure adequate development of the fetal skeleton[9,12]. While neonatal requirements are unknown, avoidance of umbilical cord 25(OH)D concentrations below 25–30 nmol/l is prudent[13,14] and consistent with the prevention of nutritional rickets[9]. Considering cord serum 25(OH)D concentrations are typically 60–80 % of maternal values collected at delivery[15,16], prevention of maternal vitamin D deficiency at the lower threshold of 25–30 nmol/l will not ensure fetal protection at the same threshold. Evidence now suggests that aiming to prevent both maternal and neonatal deficiency requires achievement of a maternal cut-off of at least 50 nmol/l[17,18].

In terms of public health, DRV are useful to evaluate nutrient intakes and prevent nutritional deficiencies at a population level[19]. Determination of pregnancy-specific dietary vitamin D recommendations could therefore fundamentally help to tackle the high prevalence of global vitamin D deficiency in this life-stage group[8]. The lack of both race- and pregnancy-specific dietary recommendations places pregnant women of ethnic minority among the most vulnerable and underinvestigated population groups with regards to vitamin D. This review explores the evidence for racial differences in response to vitamin D supplementation, with particular application to pregnancy-specific requirements among ethnic minorities resident at high latitude.

Current dietary requirements for vitamin D during pregnancy

The relationship between circulating serum 25(OH)D and markers of bone health has been well established and provides the most robust evidence upon which DRV can be set[4]. Nonetheless, accumulating evidence of a role for vitamin D in non-skeletal health outcomes, including immune function, cancer prevention and cardiovascular health, complicates the establishment of deficiency thresholds. In pregnancy specifically, evidence for an association of low vitamin D status with adverse perinatal outcomes is growing[13], which has implications for pregnancy-specific requirements for vitamin D. It is plausible that a greater vitamin D intake may be required during pregnancy to improve perinatal outcomes than that necessary to support skeletal growth and development of the fetus. Though evidence to date has been insufficient to justify setting target serum 25(OH)D concentrations based on non-skeletal health outcomes, it is likely that future studies will merit consideration of pregnancy-specific 25(OH)D thresholds. In the interim, it is reasonable to apply equivalent thresholds of vitamin D deficiency and sufficiency to both pregnant and non-pregnant adults.

Notwithstanding the controversies regarding 25(OH)D thresholds and the knowledge gaps surrounding the putative extra-skeletal role of vitamin D, several authoritative agencies have defined DRV for vitamin D in recent years, all of which have been determined based on a predominantly white population. Using a risk assessment framework, the Institute of Medicine established DRV for vitamin D by way of systematic evidence-based reviews to answer *a priori* defined questions regarding vitamin D and health, resulting in a landmark report with global application[4]. In line with the Institute of Medicine, this approach has since been adopted by other agencies, as it allows for transparent evaluation of the data and alleviates decision-making[19]. As shown in Table 1, variations in the data analysed led to the establishment of more conservative recommendations among health authorities in Northern Europe[5] and the UK[6]. Despite adopting a similar risk assessment approach to other agencies, and being the only expert body to include pregnancy-related outcomes, the latest scientific opinion published by the European Food Safety Authority[7] cites insufficient data to define average or individual dietary requirements for vitamin D. We have recently expressed our regret for the decision by the European Food Safety Authority to advise

Downloaded from https://www.cambridge.org/core. University College Cork, on 09 Jan 2018 at 10:27:22, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665117004116

an adequate intake in lieu of an estimated average requirement (EAR intake level of a nutrient that meets the needs of 50 % of the population) or RDA (intake level of a nutrient sufficient to meet the needs of almost all (97·5 %) healthy people in a population) value. In terms of public policy and health practice, an adequate intake offers little clinical utility, specifically during pregnancy where implementation of a risk management approach to prevent vitamin D deficiency is likely required. An additional consideration is that application of an EAR value to pregnancy may not be appropriate; a more cautionary approach would be to set an RDA target for pregnant women. Seeing as this population is under medical supervision, application of an RDA is justifiable. Furthermore, we stress that DRV estimates for pregnancy should be established with the aim of achieving the 25(OH)D target that will ensure protection against both maternal and neonatal deficiency. Should requirements be determined based on maintaining maternal status >25–30 nmol/l, neonatal deficiency will not be prevented. As an alternative, application of an RDA value to maintain circulating 25(OH)D concentrations ≥50 nmol/l in 97·5 % of gravidae would likely guarantee prevention of neonatal vitamin D deficiency while simultaneously improving maternal vitamin D status[17,18].

Ethnic variations in vitamin D status

According to the recent systematic review by Saraf *et al.*[8], the global prevalence of 25(OH)D concentrations <50 nmol/l is 54 % among pregnant women and 75 % among newborns, denoting a worldwide public health concern. Almost one in five pregnant women and one in three newborns had concentrations <25 nmol/l, the widely acknowledged threshold at which there is increased risk of developing rickets and osteomalacia[4]. With the exception of fish and fish liver oils, few foods are naturally rich in vitamin D, meaning the predominant source of vitamin D is sunlight[20]. In cases of limited sun exposure, careful dietary planning is required to ensure adequate vitamin D intake for deficiency prevention. In the Western world, deficiency is therefore most often observed among gravidae and neonates from ethnic minorities[8,21], whereas white populations are most at risk when resident at high latitude[8]. As such, case reports of rickets are found predominantly in immigrant children and those with darker skin pigmentation[11,22–25]. Risk is highest among breastfed children without vitamin D supplementation, whose mothers had low vitamin D status during pregnancy and lactation due to inadequate dietary intakes and insufficient cutaneous vitamin D production because of darker skin and veiled clothing[9].

Ethnic disparities in vitamin D status within the UK were brought to light in the latter half of the 20th century, whereby a series of comparative prospective and cross-sectional studies described a high frequency of deficiency among pregnant Asian and African minorities[26–28]. In addition, an accumulation of case reports documented an increase in the number of children diagnosed with vitamin D-dependent rickets, the majority of whom were born to mothers from outside of the UK[23,29–31]. Despite efforts from health authorities to increase the awareness of the importance of dietary vitamin D intake among immigrant populations[6], more recent data suggest that the observed racial disparity in 25(OH)D status throughout pregnancy has not changed, with women of ethnic minority consistently presenting with lower vitamin D status during pregnancy than their native white counterparts[21,32–34].

Outside of pregnancy, lower 25(OH)D concentrations are consistently reported among racial and ethnic minorities, regardless of sex and age[35–37]. Of note is the decline in circulating 25(OH)D among immigrants that often follows relocation to areas of more Northern latitude, provided the vitamin D content of the diet is not improved[38]. Conversely, dietary transition from a traditional vitamin D-rich diet (e.g. native Inuit) to a more Western style diet parallels a reduction in vitamin D status[39]. Recent data from the European Commission-funded collaborative ODIN project (Food-based solutions for Optimal vitamin D Nutrition and health throughout the lifecycle; http://www.odin-vitd.eu)[3] revealed that the annual prevalence of vitamin D deficiency (25(OH)D < 30 nmol/l) among non-white subgroups in the UK, Norway and Finland is 3- to 71-fold higher compared with white populations. In the UK, deficiency is greatest among the Asian ethnic group (59·6 %, *n* 52), compared with the black (35·7 %, *n* 28) and white (19·6 %, *n* 1359) population, and South Asian immigrants in Norway show a remarkably higher prevalence of deficiency (64·8 %, *n* 176) than that observed in native white adults (1·3 %, *n* 866). Similarly, results from the Finnish Maamu study stress that inter-ethnic variations in vitamin D status are not limited to native and immigrant populations but are also evident within non-white ethnic groups residing in the same country. Based on standardised 25(OH)D data, 4·5, 28·0 and 50·4 % of white Russian-speaking (*n* 446), Somali (*n* 364) and Kurdish (*n* 50) adults, respectively, were classified as vitamin D deficient[3]. In the USA, year-round 25(OH)D concentrations <30 and 50 nmol/l are more apparent in non-Hispanic black (24 and 62 %, respectively) than Hispanic (6·4 and 36·0 %, respectively) populations, and least evident in those of white ethnicity (2·3 and 13·0 %, respectively)[40], while non-white ethnicity was recognised as a primary predictor of reduced 25(OH)D status among adult Canadians[41] and Australian adolescents[42] (mean concentrations not specified). In their audit of over 850 refugees, Wishart *et al.*[43] described a high prevalence of low vitamin D status (54 % <50 nmol/l) among this population in New Zealand. Moreover, women of child-bearing age were identified as a particular at-risk group (78 % <50 nmol/l), alluding to the circle of low vitamin D status among mother–infant pairs, which leads to increased risk of vitamin D-deficiency rickets in immigrant children[43].

Ethnic considerations for 25-hydroxyvitamin D thresholds

Skeletal health and calcium metabolism

In their dietary reference intake report, the Institute of Medicine highlighted uncertainty around the effect of

Downloaded from https://www.cambridge.org/core. University College Cork, on 09 Jan 2018 at 10:27:22, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665117004116

genetic variation among racial and ethnic groups, which may have implications for nutrient requirements. Polymorphisms in the vitamin D-binding protein (VDBP), vitamin D receptor and both 25- and 24-hydroxylases have been identified, and the Institute of Medicine has stressed the need to elucidate to what extent such polymorphisms will affect the epigenetic regulation of vitamin D during pregnancy and subsequent developmental outcomes in the offspring[4]. Despite the recognised knowledge gaps, the possibility that vitamin D requirements will differ based on race or ethnicity is both inclusive and exclusive of genetic variation in vitamin D metabolism. Several other factors should therefore be considered in addition to genetic determinants. The limited experimental evidence led to the establishment of mutual DRV estimates for vitamin D that are inclusive of all population groups. However, whether it is appropriate to assign DRV to all ethnic groups using data extrapolated from dose–response curves in predominantly white populations is questionable. First, 25(OH)D will likely have a greater impact on calcium metabolism and skeletal health at different thresholds depending on the populations studied. The inverse relationship between the parathyroid hormone (PTH) and 25(OH)D has been well established; low circulating 25(OH)D concentrations result in increased PTH expression, which triggers the subsequent production of 1,25-dihydroxyvitamin D, the active metabolite. The negative feedback loops involved in the calcium metabolic system therefore function to maintain calcium homeostasis[44]. The fact that black men and women have lower 25(OH)D concentrations but increased bone mineral density (BMD), coupled with increased 1,25-dihydroxyvitamin D, hence suggests a skeletal resistance to the effect of PTH in this population[45].

Racial differences in bone mass[46–48] and calcium metabolism[48,49] are apparent from a young age. Across a defined range of calcium intakes, black adolescent females were found to have higher rates of net calcium absorption and retention, and lower urinary calcium excretion than white females of the same age[48], which is consistent with findings from single-dose studies[49,50]. Similarly, black men were shown to have the greatest levels of BMD and bone mineral content at various skeletal sites when compared with Hispanic and white males[51]. Data from the National Health and Nutrition Examination Survey (2003–2004 cycle and 2005–2006 cycle) showed reduced dietary calcium intake, higher PTH and lower 25(OH)D concentrations among blacks. Differences in mean BMD, however, were not found between Mexican and white Americans (2003–2004 cycle only)[52]. Within-group comparisons confirmed the inverse relationship of dietary calcium intake and/or circulating 25(OH)D with PTH is retained across all ethnic groups, albeit only in white and Mexican Americans did a decrease in BMD parallel a decrease in calcium intake and/or 25(OH)D status[52]. More recently, the higher levels of BMD with lower 25(OH)D in blacks were verified in the multi-ethnic study of atherosclerosis, which also showed that the low 25(OH)D/low BMD relationship observed for both white and Asian adults was not present in Hispanic participants[53].

Cosman *et al.*[54] provided direct evidence for lower rates of bone resorption in response to PTH infusion in black compared with white women. Higher PTH concentrations have been reported among African American women compared with Caucasians, both in the pregnant[55] and non-pregnant[56] state, a trend only partially explained by the higher BMI and lower 25(OH)D status often seen among African Americans[56]. PTH levels have been shown to both rise and plateau at a lower 25(OH)D concentration in black adults[52,57,58], which in turn questions the use of mutual 25(OH)D thresholds to define deficiency in all racial groups. While the inverse PTH/25(OH)D relationship was maintained both above and below the 50 nmol/l threshold in white and Mexican Americans participating in the National Health and Nutrition Examination Survey, PTH levels reached a plateau in blacks at a 25(OH)D concentration below this cut-off, suggesting maximum suppression of PTH may occur at lower 25(OH)D concentrations in blacks than other ethnic groups. Thus, the evaluation of vitamin D sufficiency among black populations is hindered by a literature as yet insufficient to justify the establishment of population-specific deficiency thresholds based on race or ethnicity.

Application of standardised thresholds is further complicated in pregnancy, whereby the inverse PTH/25(OH)D relationship is slightly weakened[55,59], likely resulting from increased placental production of 1,25-dihydroxyvitamin D and/or the pregnancy-specific independent increase in calcium absorption[55]. The actions of PTH-related protein that regulate mineral metabolism, independent of PTH, challenge our understanding of the PTH–vitamin D–calcium axis in pregnancy and fetal metabolism[59]. Hence, the threshold relationship between 25(OH)D and PTH during pregnancy is somewhat controversial, as the low PTH/25(OH)D correlation hampers the estimation of the 25(OH)D threshold above which PTH begins to plateau[55].

Vitamin D binding protein and free 25-hydroxyvitamin D

The presence of superior skeletal health in tandem with a lower vitamin D status among black men and women has been termed a paradox[60]. However, because nutritional rickets is observed among black children in the presence of severe vitamin D deficiency[11,24], the association between low 25(OH)D status and poor bone health cannot be race-specific. Powe *et al.*[37] were the first to describe African American women as genetically predisposed to lower levels of the VDBP. Theoretically, free 25(OH)D concentrations are increased at lower levels of VDBP, resulting in a greater proportion of 25(OH)D available to cells. Through indirect measures, Powe *et al.*[37] found the levels of free 25(OH)D did not differ by race, despite a lower total 25(OH)D status among African American women. Notwithstanding criticism[61,62] of the methodology used by Powe *et al.*[37] to analyse VDBP and thus calculate free 25(OH)D concentrations, these results were later confirmed by Aloia *et al.*[63] using a direct method for the quantification of free 25(OH)D, but contrast with the more recent data from Alzaman *et al.*[64] and Nielson *et al.*[62]. Both studies[62,64] argue that monoclonal antibody assays do not show equal affinity for all VDBP genotypes and that racial

Downloaded from https://www.cambridge.org/core. University College Cork, on 09 Jan 2018 at 10:27:22, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665117004116

Proceedings of the Nutrition Society

differences in VDBP concentrations are not observed when measured using polyclonal assay methods. Monoclonal antibody assays will thus always underestimate VDBP concentrations in blacks, resulting in higher free circulating 25(OH)D.

While the concept of racial similarities in free 25(OH)D concentrations offers some insight towards the paradox of lower vitamin D status but improved bone health among black populations, this hypothesis is largely unproven and future research in this area is warranted. Regarding pregnancy specifically, whether free 25(OH)D concentrations remain similar among black and white pregnant women is disputed[65,66], and the clinical contribution of free 25(OH)D to perinatal health is unknown. Nonetheless, as free 25(OH)D correlates with total 25(OH)D[62], and given the unresolved debate regarding ethnic differences in VDBP, the lower total 25(OH)D status in ethnic minorities[36,38,42] remains a concern, particularly during pregnancy when neonatal 25(OH)D availability must be considered. To paraphrase Quraishi *et al.*[67], we advocate that until the physiological significance of bioavailable 25(OH)D is fully understood and the contributions of vitamin D-related gene polymorphisms to human health have been established, a reasonable objective is to aim for the achievement of targeted internationally applied 25(OH)D thresholds to prevent deficiency among the general population, including during pregnancy.

Ethnic differences in the response to vitamin D supplementation

Children

Comparative studies investigating the response to vitamin D supplementation between populations are limited, despite uncertainty that the metabolism and transport of consumed vitamin D is identical across all ethnic groups. Delineating the racial disparities in response to supplementation is necessary to ensure the efficacy and safety of supplemental vitamin D, specifically for pregnant women and their neonates[8]. Even within the available literature, however, incomplete subject characterisation is often a limiting factor when extrapolating the findings. In a comparative study of black and white children, the effect of supplementation with 25 μg/d varied by race; an increase in 25(OH)D concentrations following 2 months of supplementation was significant only for black children, which may be a result of their lower mean baseline 25(OH)D concentrations. At the end of the 6-month supplementation period, the change in 25(OH)D concentrations was similar for both groups, and the lower mean 25(OH)D and higher PTH concentrations among black children persisted from baseline to completion of the intervention[68]. Most recently, a winter-based randomised trial in Sweden (55–63°N) reported variations in the dietary requirement for vitamin D according to the skin colour among children aged 5–7 years. Based on the achievement of a 25(OH)D concentration of 30 nmol/l, an RDA of 6 and 14 μg was estimated for fair- and dark-skinned children, respectively, whereas 20 and 28 μg was estimated at the 50 nmol/l threshold, respectively. Baseline vitamin D status was shown to predict the response to vitamin D supplementation; despite a greater magnitude of increase among dark-skinned children, total serum 25(OH)D concentrations remained higher in fair-skinned children at the end of the trial[69].

Adults

Following a 1-year intervention period at various vitamin D doses from 10 to 60 μg/d, supplementation with 10 μg/d achieved a 25(OH)D concentration of 50 nmol/l in 50 % of young non-pregnant white and African American women, suggesting the EAR for vitamin D does not differ by race[70]. In terms of an RDA, a value of 10 μg/d was estimated among white women, whereas 30 μg/d was required for 97·5 % of African American women to achieve 50 nmol/l. While a linear response to the dosing regimen was observed for both ethnic groups, the difference in the dose–response curves is worth noting. As 25(OH)D concentrations were lower in black than white women prior to supplementation, the absolute increase in 25(OH)D was greater in blacks and final concentrations were similar for both ethnicities at the higher doses[70]. In contrast, no interaction effect by race was observed among older adults. Gallagher *et al.* showed that the achieved 25(OH)D concentrations in response to supplementation did not differ between white and African American women, for which a mutual RDA of 20 μg/d was suggested[71,72]. The combined analysis of two large vitamin D intervention trials of black and white prediabetic and diabetic adults in the USA suggests the response to supplementation is similar for both populations and that supplementation will increase free 25(OH)D concentrations in direct proportion to changes in total 25(OH)D, independent of race[64]. Taken collectively, the metabolism and transport of vitamin D therefore seems equivalent in blacks and whites[64,72]. Hence, the higher magnitude of change in 25(OH)D concentrations observed in blacks compared with whites following equimolar doses of vitamin D may be a corollary of lower 25(OH)D levels in this population prior to the intervention, whereby a wide inter-individual variation in the dose–response is likely to increase requirements at the individual level (i.e. at the 97·5th percentile)[73]. Therefore, it is plausible that, at a given mean 25(OH)D concentration, vitamin D requirements do not differ by race, but that additional vitamin D may be required among black populations to meet the requirement at the 97·5th percentile (i.e. the RDA).

Moving beyond the comparative studies, results from a large, four-arm (placebo and 25, 50 and 100 μg/d) randomised trial in African American adults reported a vitamin D intake of 41 μg/d was needed to reach the RDA-associated 25(OH)D threshold of 50 nmol/l[74], but this study has been criticised in terms of its design and interpretation. Firstly, Brannon *et al.*[2] have disputed the need for such high doses of vitamin D, stating the aim should not be to achieve a population intake equivalent to the RDA, as to do so would result in

Downloaded from https://www.cambridge.org/core. University College Cork, on 09 Jan 2018 at 10:27:22, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665117004116

a shift in the population distribution of 25(OH)D to values that exceed the upper limit where the risk of hypercalcaemia increases sharply. Brannon *et al.* claim that dose–response trials should focus on the estimations of the EAR, for which dietary requirements refer to the needs of the population rather than the individual[2]. However, unlike many nutrients, estimation of both an EAR and RDA is possible through dose–response trials with vitamin D, as 25(OH)D is a valid biomarker of exposure and conditions of minimal UVB availability are achieved at high latitude in winter. Therefore, reporting the vitamin D intake required to maintain 25(OH)D concentrations across a range of thresholds, including the dose needed to meet both the EAR and RDA values, would be most beneficial in terms of establishing public health policy. As discussed earlier, reporting of both individual and population requirements would have particular application in pregnancy, where an RDA value may be the prudent target. In response to the comments provided by Brannon *et al.*[2], the authors published supplementary data corresponding to an intake level of 30 μg/d to reach the EAR-associated threshold of 40 nmol/l in 97·5 % of the study population[75]. The major drawback of this study[2] is that the dose–response modelling used in the DRV estimation does not consider background dietary vitamin D intakes as the authors felt this was negligible at <5 μg/d. Hence, the intake values reported in this study[75] can only be interpreted as the supplementation dose needed to achieve specific 25(OH)D thresholds, in addition to that obtained from diet.

Further considerations

An additional concern underpinning ethnic-specific dietary requirements for vitamin D is that DRV estimates are based on the assumption that calcium intakes are adequate, and that calcium requirements do not differ by ethnic group. In reality, however, calcium intakes tend to be lower in black adults[76–78], despite the aforementioned increase in BMD compared with white populations. If dietary vitamin D requirements differ by ethnicity, it is plausible that calcium requirements follow a similar trend. Heaney[79] estimated that the calcium requirements of African American women are up to 300 mg/d less than white women, likely due to a more efficient calcium economy[60]. Thus, the question as to whether dietary vitamin D (and calcium) recommendations should differ by race is again complicated by the fact that current DRV for vitamin D have been established based on markers of bone health. While black populations may require less calcium for skeletal health, a similar or potentially greater dietary requirement for vitamin D may co-exist for skeletal and non-skeletal health benefits[80]. Acknowledging the lack of evidence to support safe long-term high vitamin D intakes[4], high-dose vitamin D diet regimes should be avoided until clear target 25(OH)D thresholds have been established.

Further to the uncertainty regarding the response to supplementation, is the limited understanding of whether the catabolism and storage of vitamin D is similar across all ethnic groups. Should the half-life of 25(OH)D vary by ethnicity, this would also have implications for vitamin D requirements and would, to some extent, contradict the clinical significance of the free hormone hypothesis proposed by Powe *et al.*[37]. Binding to the VDBP facilitates avoidance of a rapid decline in vitamin D status by stabilising the levels of circulating vitamin D metabolites and modulating conversion to the active metabolite, thereby prolonging the half-life of 25(OH)D. When fed vitamin D replete diets, VDBP knock-out mice have low levels of circulating 25(OH)D but do not display the physiological symptoms of deficiency until introduced to a vitamin D deplete diet, suggesting a continuous supply of vitamin D intake will offset the consequences of deficiency in the absence of sufficient VDBP[81]. In populations that express genetic polymorphisms in the VDBP, including that commonly observed in blacks, the associated low VDBP levels may predispose to vitamin D deficiency, provided adequate dietary and/or UV sources are not available[37]. Considering the widely acknowledged seasonal variation in vitamin D status, such observations imply that populations with a high prevalence of VDBP polymorphisms may be susceptible to a more rapid winter-dependent decline in 25(OH)D concentrations. In a comparative study of white and South Asian men and women in the UK, Kift *et al.*[36] suggested that South Asians would need to achieve a higher 25(OH)D concentration than white populations during the summer months in order to maintain sufficiency throughout winter. Nonetheless, the lower vitamin D intake and reduced efficacy of cutaneous vitamin D production in pigmented skin among South Asians[1] also contributes to the increased dependence on peak summer concentrations to maintain sufficiency throughout the winter months and this is independent of any polymorphism in VDBP. Thus, while genetic determinants of vitamin D status may partially explain ethnic variations in deficiency prevalence, this area requires further detailed exploration. In the interim, public health policy must consider the modifiable ethnocultural risk factors of deficiency, whereby supplement use may be the only feasible method to ensure adequate 25(OH)D status in populations characterised by low dietary vitamin D intakes and limited sun exposure.

Challenges for research and policy

Research and recruitment

Following introduction of the 1993 National Institutes of Health Revitalisation Act[82], considerable efforts have been made to include ethnic diversity in funded research within the USA. This, however, is seldom an easy task and populations of ethnic minority remain underrepresented in clinical and health research[83,84]. Across Europe, the importance of integrating minority groups in research is well known but strategic approaches to recruitment and retention of ethnic minorities to clinical or dietary intervention trials are rarely implemented. Meaningful comparisons across ethnic groups are therefore hindered by small and unequal sample sizes, which often lack statistical power, and the likelihood of

Downloaded from https://www.cambridge.org/core. University College Cork, on 09 Jan 2018 at 10:27:22, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665117004116

self-selection bias limits extrapolation of the findings to the wider population. Barriers to the implementation of health research mirror barriers to the provision of health care; mainly communication difficulties, religious or cultural conservativeness and modesty, delay in seeking clinical advice and poor attendance to scheduled appointments[84,85]. While a number of qualitative and narrative reviews have provided guidance on how best to engage minority populations in research[83,85–87], barriers to recruitment will not be mutually exclusive for all ethnic groups, research areas or study designs, and it is likely that regionally tailored recruitment strategies are required. With reference to vitamin D specifically, subgroup analysis by ethnicity is preferable owing to the disparities in vitamin D status and the possibility that ethnic origin could modify the primary outcome (e.g. vitamin D requirements). The literature depicts a lack of dose–response trials with vitamin D among Hispanic and Mexican Americans within the USA, and while the number of published studies in Asian subgroups continues to grow, there is a compelling demand for a specifically designed, culturally sensitive, randomised trial that will assess the explicit needs of the South Asian population who represent the largest minority group within the UK[88].

Policy implementation

A higher skin pigmentation coupled with minimum skin exposure to sunlight leads to an increased dependence on food sources of vitamin D among minority populations[89–93]. However, comparative studies highlight variations in the vitamin D content of the diet between ethnic groups, with total vitamin D intake typically lowest among Asian populations[94,95]. Both vitamin D supplementation and fortification represent effective strategies for the improvement of nutritional intake and corresponding vitamin D status[96]. In particular during pregnancy, inclusion of supplemental vitamin D to the antenatal routine could significantly improve vitamin D status, provided women are compliant with supplement use. Similar to dietary intake, antenatal supplement use has been shown to vary by ethnicity, at least from an Irish perspective, with prevalence highest among the white population (52 %) and lowest among the Middle Eastern and North African populations (17 %)[97]. Moreover, many commercially available vitamin D supplements are not suitable for those following a vegan, kosher or halal diet, meaning affordable supplements are not readily accessible to the particular subgroups that need them most. If not strategically executed, fortification of food staples has the potential to neglect vulnerable groups with dietary preferences and specific food intolerances. In the USA, where fluid milk and ready-to-eat breakfast cereals are the major contributors to vitamin D intake, significant ethnic differences are observed in the intake level from these foods on account of the higher prevalence of lactose intolerance and reduced milk consumption among African American populations[78,94,95,98]. Failure to address the specific needs of minority populations will therefore result in an unsuccessful national public health policy, which may only magnify existent disparities in health inequalities.

Conclusions

While present data indicate a black–white disparity in the 25(OH)D threshold that should define vitamin D deficiency, at least in terms of bone health, data in Asian and Hispanic populations are limited and contradicting, and data in perinatal populations are almost entirely unavailable. Considering the growing evidence in support of a non-skeletal role for vitamin D, assessing the health outcomes at various 25(OH)D threshold levels across ethnic groups should be made a priority in future studies. Health authorities must now readdress vitamin D requirements among both pregnant women and individuals of ethnic minority in order to overcome the global inequities in vitamin D status and subsequent perinatal outcomes. Understanding ethnic disparities in the metabolism and tissue-specific function of vitamin D is critical to safely establish targeted public health campaigns, but we stress that identifying ethnic and racial differences in the association of vitamin D status with health outcomes is independent to identifying the response to dietary intake. In order to facilitate the establishment of race-specific DRV, future studies must therefore follow a two-step process: first to determine the appropriate threshold for 25(OH)D across diverse populations, and secondly to estimate the amount of vitamin D needed to maintain this threshold across ethnic groups.

Dietary composition represents a modifiable factor for the improvement of vitamin D status in at-risk ethnic groups, provided relevant dietary advice and supplementation regimens are established. Public health campaigns need to target ethnic groups specifically and move away from the one-guideline-suits-all approach. Outreach strategies must be culturally tailored and population-focused, while avoiding marginalisation. Efforts should be made to educate minority groups on the value of dietary vitamin D, specifically in pregnancy and throughout infancy. Finally, it is important to acknowledge that ethnic minorities represent a heterogeneous group in our society, whose cultural values and norms vary widely. Understanding the diverse sociocultural needs of ethnic minorities is therefore central to the encouragement of diversity in health research, and will be a crucial first step to underpinning strategies to tackle the observed high prevalence of vitamin D deficiency among pregnant women and their neonates at high latitude.

Acknowledgements

Karen M. O'Callaghan's PhD programme, upon which this review focused, was supported by funding to M. E. K. from the European Commission under grant agreement 732 613977 for the ODIN Integrated Project (Food-based solutions for optimal vitamin D nutrition and health throughout the life cycle http://www.odin-vitd.eu/).

Downloaded from https://www.cambridge.org/core. University College Cork, on 09 Jan 2018 at 10:27:22, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665117004116

Proceedings of the Nutrition Society

Financial Support

None.

Conflicts of Interest

None.

Authorship

K. M. O'C. drafted the manuscript; M. E. K. was her PhD supervisor and guarantor; both K. M. O'C. and M. E. K. co-authored and approved the final version.

References

1. Farrar MD, Kift R, Felton SJ *et al.* (2011) Recommended summer sunlight exposure amounts fail to produce sufficient vitamin D status in UK adults of South Asian origin. *Am J Clin Nutr* **94**, 1219–1224.
2. Brannon PM, Mayne ST, Murphy SP *et al.* (2014) Vitamin D supplementation in African Americans: dose-response. *Am J Clin Nutr* **100**, 982–984.
3. Cashman KD, Dowling KG, Skrabakova Z *et al.* (2016) Vitamin D deficiency in Europe – pandemic? *Am J Clin Nutr* **103**, 1033–1044.
4. Institute of Medicine. Food and Nutrition Board (2011) *Dietary Reference Intakes for Calcium and Vitamin D*. Washington, DC: National Academy Press.
5. Nordic Nutrition Recommendations (2012) *Integrating Nutrition and Physical Activity*. Copenhagen: Nordic Council of Ministers.
6. Scientific Advisory Committee on Nutrition Report on Vitamin D and Health (2016) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/537616/SACN_Vitamin_D_and_Health_report.pdf (accessed July 2016).
7. European Food Safety Authority Panel on Dietetic Products, Nutrition and Allergies (2016) Scientific opinion on dietary reference values for vitamin D. *EFSA J* **14**, e04547.
8. Saraf R, Morton SM, Camargo CA Jr *et al.* (2016) Global summary of maternal and newborn vitamin D status – a systematic review. *Matern Child Nutr* **12**, 647–668.
9. Munns CF, Shaw N, Kiely M *et al.* (2016) Global consensus recommendations on prevention and management of nutritional rickets. *J Clin Endocrinol Metab* **101**, 394–415.
10. Basatemur E & Sutcliffe A (2015) Incidence of hypocalcemic seizures due to vitamin D deficiency in children in the United Kingdom and Ireland. *J Clin Endocrinol Metab* **100**, e91–e95.
11. Munns CF, Simm PJ, Rodda CP *et al.* (2012) Incidence of vitamin D deficiency rickets among Australian children: an Australian Paediatric Surveillance Unit study. *Med J Aust* **196**, 466–468.
12. Brannon PM & Picciano MF (2011) Vitamin D in pregnancy and lactation in humans. *Annu Rev Nutr* **31**, 89–115.
13. Kiely M, Hemmingway A & O'Callaghan KM (2017) Vitamin D in pregnancy: current perspectives and future directions. *Ther Adv Musculoskelet Dis* **9**, 145–154.
14. Kiely ME, O'Donovan SM, Kenny LC *et al.* (2017) Vitamin D metabolite concentrations in umbilical cord blood serum and associations with clinical characteristics in a large prospective mother-infant cohort in Ireland. *J Steroid Biochem Mol Biol* **167**, 162–168.
15. Hollis BW & Pittard WB III (1984) Evaluation of the total fetomaternal vitamin D relationships at term: evidence for racial differences. *J Clin Endocrinol Metab* **59**, 652–657.
16. Við Streym S, Kristine Moller U, Rejnmark L *et al.* (2013) Maternal and infant vitamin D status during the first 9 months of infant life-a cohort study. *Eur J Clin Nutr* **67**, 1022–1028.
17. Grant CC, Stewart AW, Scragg R *et al.* (2014) Vitamin D during pregnancy and infancy and infant serum 25-hydroxyvitamin D concentration. *Pediatrics* **133**, e143–e153.
18. March KM, Chen NN, Karakochuk CD *et al.* (2015) Maternal vitamin D(3) supplementation at 50 mug/d protects against low serum 25-hydroxyvitamin D in infants at 8 wk of age: a randomized controlled trial of 3 doses of vitamin D beginning in gestation and continued in lactation. *Am J Clin Nutr* **102**, 402–410.
19. Cashman KD & Kiely M (2014) Recommended dietary intakes for vitamin D: where do they come from, what do they achieve and how can we meet them? *J Hum Nutr Diet* **27**, 434–442.
20. Kiely M & Black LJ (2012) Dietary strategies to maintain adequacy of circulating 25-hydroxyvitamin D concentrations. *Scand J Clin Lab Invest Suppl* **243**, 14–23.
21. Kiely ME, Zhang JY, Kinsella M *et al.* (2016) Vitamin D status is associated with uteroplacental dysfunction indicated by pre-eclampsia and small-for-gestational-age birth in a large prospective pregnancy cohort in Ireland with low vitamin D status. *Am J Clin Nutr* **104**, 354–361.
22. Weisberg P, Scanlon KS, Li R *et al.* (2004) Nutritional rickets among children in the United States: review of cases reported between 1986 and 2003. *Am J Clin Nutr* **80**, 1697s–1705s.
23. Callaghan AL, Moy RJ, Booth IW *et al.* (2006) Incidence of symptomatic vitamin D deficiency. *Arch Dis Child* **91**, 606–607.
24. Ward LM, Gaboury I, Ladhani M *et al.* (2007) Vitamin D-deficiency rickets among children in Canada. *CMAJ* **177**, 161–166.
25. Wheeler BJ, Dickson NP, Houghton LA *et al.* (2015) 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* **39**, 380–383.
26. Holmes AEB, Taylor JL & Jones ME (1973) Occult rickets and osteomalacia amongst the Asian immigrant population. *Q J Med* **42**, 125–149.
27. Alfaham M, Woodhead S, Pask G *et al.* (1995) Vitamin D deficiency: a concern in pregnant Asian women. *Br J Nutr* **73**, 881–887.
28. Okonofua F, Menon RK, Houlder S *et al.* (1987) Calcium, vitamin D and parathyroid hormone relationships in pregnant Caucasian and Asian women and their neonates. *Ann Clin Biochem* **24**, 22–28.
29. Dunnigan MG, Paton JP, Haase S *et al.* (1962) Late rickets and osteomalacia in the Pakistani community in Glasgow. *Scott Med J* **7**, 159–167.
30. Arneil GC (1975) Nutritional rickets in children in Glasgow. *Proc Nutr Soc* **34**, 101–109.
31. Henderson JB, Dunnigan MG, McIntosh WB *et al.* (1987) The importance of limited exposure to ultraviolet radiation and dietary factors in the aetiology of Asian rickets: a risk-factor model. *Q J Med* **63**, 413–425.

Proceedings of the Nutrition Society

Downloaded from https://www.cambridge.org/core. University College Cork, on 09 Jan 2018 at 10:27:22, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665117004116

32. van der Meer IM, Karamali NS, Boeke AJ *et al.* (2006) High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. *Am J Clin Nutr* **84**, 350–353; quiz 468–359.
33. Ginde AA, Sullivan AF, Mansbach JM *et al.* (2010) Vitamin D insufficiency in pregnant and nonpregnant women of childbearing age in the United States. *Am J Obstet Gynecol* **202**, e431–438.
34. Whitelaw DC, Scally AJ, Tuffnell DJ *et al.* (2014) Associations of circulating calcium and 25-hydroxyvitamin D with glucose metabolism in pregnancy: a cross-sectional study in European and South Asian women. *J Clin Endocrinol Metab* **99**, 938–946.
35. Mithal A, Wahl DA, Bonjour JP *et al.* (2009) Global vitamin D status and determinants of hypovitaminosis D. *Osteoporos Int* **20**, 1807–1820.
36. Kift R, Berry JL, Vail A *et al.* (2013) Lifestyle factors including less cutaneous sun exposure contribute to starkly lower vitamin D levels in U.K. South Asians compared with the white population. *Br J Dermatol* **169**, 1272–1278.
37. Powe CE, Evans MK, Wenger J *et al.* (2013) Vitamin D-binding protein and vitamin D status of black Americans and white Americans. *N Engl J Med* **369**, 1991–2000.
38. Madar AA, Stene LC & Meyer HE (2009) Vitamin D status among immigrant mothers from Pakistan, Turkey and Somalia and their infants attending child health clinics in Norway. *Br J Nutr* **101**, 1052–1058.
39. Rejnmark L, Jorgensen ME, Pedersen MB *et al.* (2004) Vitamin D insufficiency in Greenlanders on a westernized fare: ethnic differences in calcitropic hormones between Greenlanders and Danes. *Calcif Tissue Int* **74**, 255–263.
40. Schleicher RL, Sternberg MR, Looker AC *et al.* (2016) National estimates of serum total 25-hydroxyvitamin D and metabolite concentrations measured by liquid chromatography-tandem mass spectrometry in the US population during 2007–2010. *J Nutr* **146**, 1051–1061.
41. Greene-Finestone LS, Berger C, de Groh M *et al.* (2011) 25-Hydroxyvitamin D in Canadian adults: biological, environmental, and behavioral correlates. *Osteoporos Int* **22**, 1389–1399.
42. Black LJ, Burrows SA, Jacoby P *et al.* (2014) Vitamin D status and predictors of serum 25-hydroxyvitamin D concentrations in Western Australian adolescents. *Br J Nutr* **112**, 1154–1162.
43. Wishart HD, Reeve AM & Grant CC (2007) Vitamin D deficiency in a multinational refugee population. *Intern Med J* **37**, 792–797.
44. Christakos S, Dhawan P, Verstuyf A *et al.* (2016) Vitamin D: metabolism, molecular mechanism of action, and pleiotropic effects. *Physiol Rev* **96**, 365–408.
45. Freedman BI & Register TC (2012) Effect of race and genetics on vitamin D metabolism, bone and vascular health. *Nat Rev Nephrol* **8**, 459–466.
46. Li JY, Specker BL, Ho ML *et al.* (1989) Bone mineral content in black and white children 1 to 6 years of age. Early appearance of race and sex differences. *Am J Dis Child* **143**, 1346–1349.
47. Rupich RC, Specker BL, Lieuw AFM *et al.* (1996) Gender and race differences in bone mass during infancy. *Calcif Tissue Int* **58**, 395–397.
48. Braun M, Palacios C, Wigertz K *et al.* (2007) Racial differences in skeletal calcium retention in adolescent girls with varied controlled calcium intakes. *Am J Clin Nutr* **85**, 1657–1663.
49. Abrams SA, O'Brien KO, Liang LK *et al.* (1995) Differences in calcium absorption and kinetics between black and white girls aged 5–16 years. *J Bone Miner Res* **10**, 829–833.
50. Bryant RJ, Wastney ME, Martin BR *et al.* (2003) Racial differences in bone turnover and calcium metabolism in adolescent females. *J Clin Endocrinol Metab* **88**, 1043–1047.
51. Araujo AB, Travison TG, Harris SS *et al.* (2007) Race/ethnic differences in bone mineral density in men. *Osteoporos Int* **18**, 943–953.
52. Gutierrez OM, Farwell WR, Kermah D *et al.* (2011) Racial differences in the relationship between vitamin D, bone mineral density, and parathyroid hormone in the National Health and Nutrition Examination Survey. *Osteoporos Int* **22**, 1745–1753.
53. van Ballegooijen AJ, Robinson-Cohen C, Katz R *et al.* (2015) Vitamin D metabolites and bone mineral density: the multi-ethnic study of atherosclerosis. *Bone* **78**, 186–193.
54. Cosman F, Morgan DC, Nieves JW *et al.* (1997) Resistance to bone resorbing effects of PTH in black women. *J Bone Miner Res* **12**, 958–966.
55. Haddow JE, Neveux LM, Palomaki GE *et al.* (2011) The relationship between PTH and 25-hydroxy vitamin D early in pregnancy. *Clin Endocrinol* (*Oxf*) **75**, 309–314.
56. Aloia JF, Feuerman M & Yeh JK (2006) Reference range for serum parathyroid hormone. *Endocr Pract* **12**, 137–144.
57. Wright NC, Chen L, Niu J *et al.* (2012) Defining physiologically "normal" vitamin D in African Americans. *Osteoporos Int* **23**, 2283–2291.
58. Aloia JF, Chen DG & Chen H (2010) The 25(OH)D/PTH threshold in black women. *J Clin Endocrinol Metab* **95**, 5069–5073.
59. Simmonds CS & Kovacs CS (2010) Role of parathyroid hormone (PTH) and PTH-related protein (PTHrP) in regulating mineral homeostasis during fetal development. *Crit Rev Eukaryot Gene Expr* **20**, 235–273.
60. Aloia JF (2008) African Americans, 25-hydroxyvitamin D, and osteoporosis: a paradox. *Am J Clin Nutr* **88**, 545s–550s.
61. Bouillon R, Jones K & Schoenmakers I (2014) Vitamin D-binding protein and vitamin D in blacks and whites. *N Engl J Med* **370**, 879.
62. Nielson CM, Jones KS, Chun RF *et al.* (2016) Free 25-hydroxyvitamin D: impact of vitamin D binding protein assays on racial-genotypic associations. *J Clin Endocrinol Metab* **101**, 2226–2234.
63. Aloia J, Mikhail M, Dhaliwal R *et al.* (2015) Free 25(OH) D and the vitamin D paradox in African Americans. *J Clin Endocrinol Metab* **100**, 3356–3363.
64. Alzaman NS, Dawson-Hughes B, Nelson J *et al.* (2016) Vitamin D status of black and white Americans and changes in vitamin D metabolites after varied doses of vitamin D supplementation. *Am J Clin Nutr* **104**, 205–214.
65. Powe CE, Seely EW, Rana S *et al.* (2010) First trimester vitamin D, vitamin D binding protein, and subsequent preeclampsia. *Hypertension* **56**, 758–763.
66. Schwartz JB, Lai J, Lizaola B *et al.* (2014) A comparison of measured and calculated free 25(OH) vitamin D levels in clinical populations. *J Clin Endocrinol Metab* **99**, 1631–1637.
67. Quraishi SA, Camargo CA Jr & Manson JE (2016) Low vitamin D status in Europe: moving from evidence to sound public health policies. *Am J Clin Nutr* **103**, 957–958.
68. Rajakumar K, Moore CG, Yabes J *et al.* (2015) Effect of vitamin D3 supplementation in black and in white children: a randomized, placebo-controlled trial. *J Clin Endocrinol Metab* **100**, 3183–3192.
69. Ohlund I, Lind T, Hernell O *et al.* (2017) Increased vitamin D intake differentiated according to skin color is needed to meet requirements in young Swedish children during

Downloaded from https://www.cambridge.org/core. University College Cork, on 09 Jan 2018 at 10:27:22, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665117004116

Proceedings of the Nutrition Society

winter: a double-blind randomized clinical trial. *Am J Clin Nutr* **106**, 105–112.
70. Gallagher JC, Jindal PS & Smith LM (2014) Vitamin D supplementation in young white and African American women. *J Bone Miner Res* **29**, 173–181.
71. Gallagher JC, Sai A, Templin T II *et al.* (2012) Dose response to vitamin D supplementation in postmenopausal women: a randomized trial. *Ann Intern Med* **156**, 425–437.
72. Gallagher JC, Peacock M, Yalamanchili V *et al.* (2013) Effects of vitamin D supplementation in older African American women. *J Clin Endocrinol Metab* **98**, 1137–1146.
73. Cashman KD (2014) The vitamin D RDA for African American adults: higher than that for white persons? *Am J Clin Nutr* **99**, 427–428.
74. Ng K, Scott JB, Drake BF *et al.* (2014) Dose response to vitamin D supplementation in African Americans: results of a 4-arm, randomized, placebo-controlled trial. *Am J Clin Nutr* **99**, 587–598.
75. Ng K, Hollis BW, Giovannucci EL *et al.* (2014) Reply to PM Brannon *et al. Am J Clin Nutr* **100**, 984–986.
76. Bell RA, Quandt SA, Spangler JG *et al.* (2002) Dietary calcium intake and supplement use among older African American, white, and Native American women in a rural southeastern community. *J Am Diet Assoc* **102**, 844–847.
77. Fulgoni V III, Nicholls J, Reed A *et al.* (2007) Dairy consumption and related nutrient intake in African-American adults and children in the United States: continuing survey of food intakes by individuals 1994–1996, 1998, and the National Health and Nutrition Examination Survey 1999–2000. *J Am Diet Assoc* **107**, 256–264.
78. de Hoog ML, Kleinman KP, Gillman MW *et al.* (2014) Racial/ethnic and immigrant differences in early childhood diet quality. *Public Health Nutr* **17**, 1308–1317.
79. Heaney RP (2002) The importance of calcium intake for lifelong skeletal health. *Calcif Tissue Int* **70**, 70–73.
80. Aloia JF, Talwar SA, Pollack S *et al.* (2006) Optimal vitamin D status and serum parathyroid hormone concentrations in African American women. *Am J Clin Nutr* **84**, 602–609.
81. Safadi FF, Thornton P, Magiera H *et al.* (1999) Osteopathy and resistance to vitamin D toxicity in mice null for vitamin D binding protein. *J Clin Invest* **103**, 239–251.
82. National Institutes of Health (2001) *NIH guidelines on the inclusion of women and minorities as subjects in clinical research*. https://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm.
83. Nicholson LM, Schwirian PM & Groner JA (2015) Recruitment and retention strategies in clinical studies with low-income and minority populations: progress from 2004–2014. *Contemp Clin Trials* **45**, 34–40.
84. Yancey AK, Ortega AN & Kumanyika SK (2006) Effective recruitment and retention of minority research participants. *Annu Rev Public Health* **27**, 1–28.
85. Quay TA, Frimer L, Janssen PA *et al.* (2017) Barriers and facilitators to recruitment of South Asians to health research: a scoping review. *BMJ Open* **7**, e014889.
86. Waheed W, Hughes-Morley A, Woodham A *et al.* (2015) Overcoming barriers to recruiting ethnic minorities to mental health research: a typology of recruitment strategies. *BMC Psychiatry* **15**, 101.
87. Neelotpol S, Hay AW, Jolly AJ *et al.* (2016) Challenges in collecting clinical samples for research from pregnant women of South Asian origin: evidence from a UK study. *BMJ Open* **6**, e010554.
88. Office for National Statistics (2011) *Ethnicity and National Identity in England and Wales*. National Records of Scotland; Northern Ireland Statistics and Research Agency. Available at https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration (accessed August 2017).
89. Parisaei M, Govind A, Clements J *et al.* (2011) Prevalence of vitamin D deficiency in a North London antenatal population. *Obstet Med* **4**, 113–116.
90. Alagol F, Shihadeh Y, Boztepe H *et al.* (2000) Sunlight exposure and vitamin D deficiency in Turkish women. *J Endocrinol Invest* **23**, 173–177.
91. Bugrul F, Devecioglu E, Ozden T *et al.* (2013) Effect of maternal and infant vitamin D supplementation on vitamin D levels of breastfed infants. *Turk J Pediatr* **55**, 158–163.
92. Dijkstra SH, van Beek A, Janssen JW *et al.* (2007) High prevalence of vitamin D deficiency in newborn infants of high-risk mothers. *Arch Dis Child* **92**, 750–753.
93. Vercruyssen J, Martin M & Jacquemyn Y (2010) A pilot study on 25-hydroxyvitamin D status according to sun exposure in pregnant women in Antwerp, Belgium. *Facts Views Vis Obgyn* **2**, 127–130.
94. Rees GA, Doyle W, Srivastava A *et al.* (2005) The nutrient intakes of mothers of low birth weight babies – a comparison of ethnic groups in East London, UK. *Matern Child Nutr* **1**, 91–99.
95. Donin AS, Nightingale CM, Owen CG *et al.* (2010) Nutritional composition of the diets of South Asian, black African-Caribbean and white European children in the United Kingdom: the Child Heart and Health Study in England (CHASE). *Br J Nutr* **104**, 276–285.
96. Black LJ, Walton J, Flynn A *et al.* (2015) Small increments in vitamin D intake by Irish adults over a decade show that strategic initiatives to fortify the food supply are needed. *J Nutr* **145**, 969–976.
97. Toher C, Lindsay K, McKenna M *et al.* (2014) Relationship between vitamin D knowledge and 25-hydroxyvitamin D levels amongst pregnant women. *J Hum Nutr Diet* **27**, 261–269.
98. Calvo MS & Whiting SJ (2006) Public health strategies to overcome barriers to optimal vitamin D status in populations with special needs. *J Nutr* **136**, 1135–1139.

Downloaded from https://www.cambridge.org/core. University College Cork, on 09 Jan 2018 at 10:27:22, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1017/S0029665117004116