# Demographic and clinical predictors of vitamin D status in pregnant women tested for deficiency in Western Australia

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## Abstract

**Objective**: This study aimed to describe the vitamin D status of pregnant women in Western Australia and identify predictors of deficiency in pregnancy.

**Methods**: A cross-sectional study was conducted using linked data from statewide administrative data collections. Participants included pregnant women aged 18–44 years who gave birth between 2012 and 2014.

**Results**: The mean 25-hydroxyvitamin D (25[OH]D) concentration was 70.7 nmol $L^{-1}$ (SD 25.7; range 5–255 nmol $L^{-1}$). Approximately one-fifth of the pregnant women were vitamin D deficient (<50 nmol $L^{-1}$). Maternal age (under 25 years) was identified as an independent risk factor of vitamin D deficiency in addition to known predictors. Only 20% of women were screened within the first 10 weeks of their pregnancy.

**Conclusions**: In addition to the existing risk factors for deficiency, maternal age was an independent predictor of vitamin D deficiency. There was a large discrepancy between the time of first antenatal visit and screening for vitamin D deficiency.

**Implications for public health**: Our findings support the addition of maternal age (under 25 years) to the current clinical guidelines for targeted screening of 25(OH)D levels in pregnancy and the practical application of screening for vitamin D deficiency at the first antenatal visit.

**Key words**: pregnancy, vitamin D status, screening, antenatal care, vitamin D deficiency

Vitamin D deficiency during pregnancy has been associated with increased risks of pre-eclampsia, gestational diabetes, caesarean section, low birthweight and preterm birth (for review[1]). Supplementation trials have shown some promising results;[2] however, the evidence does not yet support the inclusion of vitamin D supplementation as a component of routine care for all pregnant women to minimise adverse maternal and perinatal health outcomes.[3] Furthermore, there is no agreement in the literature regarding what supplemental doses should be recommended during pregnancy or what levels of 25-hydroxyvitamin D (25[OH]D) during pregnancy should be considered sufficient or indeed optimal.[4]

In Australia, the Australian Health Survey 2011–2012[5] provided population-based data on vitamin D status for women of childbearing age (16–44 years) across Australia, indicating that 24.9% are vitamin D deficient (25[OH]D<50 nmol $L^{-1}$).[6] Similar representative data for pregnant women in Australia do not exist, although primary care-based studies[4,7-10] have described rates of vitamin D deficiency of pregnant women in various subpopulations as defined by ethnicity, location and gestational age, with rates ranging from 13.9%[8] in Perth, Western Australia (WA), to 97% among veiled women within a population-based study in south-eastern Sydney, New South Wales.[10]

The current Australian and New Zealand (ANZ) position statement related to vitamin D and health in pregnancy recommends measurement of 25(OH)D levels at the first antenatal visit only of pregnant women with at least one risk factor for vitamin D deficiency.[11] These risk factors include lack of skin exposure to sunlight, more southerly latitude, darker skin phototype (Fitzpatrick types V and VI) and medical conditions that affect vitamin D metabolism and storage.[11] Routine testing in the absence of a specific indication is not supported.

The aims of the present study were to describe the vitamin D status of all pregnant women in Western Australia who had their 25(OH)D concentration measured by the state public pathology service and to examine whether there were additional indications to those currently recommended that were important predictors of vitamin D deficiency among those women.

## Methods

### *Study setting, design and population*

Western Australia covers approximately 2.5 million $km^2$ spanning a latitude range of 10.5–35.5° South latitude. The distribution of the population is highly centralised, with the majority (79%) residing in the capital city, Perth, in the state's south-west. The remaining

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population is sparsely distributed throughout the rural and remote areas of the state (average 0.2 people per km$^2$).[12] The Western Australian population is predominately Caucasian, and almost two-thirds are Australian-born.[13] This was a retrospective cross-sectional study of women who had their 25(OH)D levels tested by PathWest Laboratory Medicine WA (PathWest) between 2012–2014 during pregnancy and whose pregnancy resulted in a birth (delivery after 20 weeks or later or when the gestation was unknown and the birthweight was at least 400 grams, including all live births and stillbirths) in Western Australia. We used individually linked data from the Midwives' Notification System (MNS) and PathWest to identify the study cohort.

### Datasets

The MNS contains perinatal data from the Notification of Case Attended form as regulated by the Health (Notification by Midwives) Regulations 1994 on >99% of all births in Western Australia.[14] The PathWest database is a statewide database containing routinely collected laboratory data from PathWest, the only public pathology service in Western Australia. This represents 80% of all pathology testing in Western Australia[15] and does not include private laboratories. The data linkage methodology has been described previously.[16]

### 25(OH)D concentration assay

All 25(OH)D samples were measured by PathWest, a pathology laboratory accredited by the National Association of Testing Authorities, Australia. A minimum assay volume of 250 mL was spun at 3,500 rpm for 10 minutes at room temperature. All serum samples during the study period were measured for 25(OH)D with the ARCHITECT *i*2000SR immunoassay analyser (Abbott Diagnostics, Abbott Park, IL, USA). Only the first sample recorded for each pregnancy was included in this study.

### Covariates

Demographic and obstetric information on the mother was obtained from the MNS, while the 25(OH)D concentration, date of sample collection, date of birth and residential postcode at time of testing were obtained from the PathWest database. The mother's gestation at the time of venesection was deduced from the date of venesection and the baby's birth date and gestational age at birth. Trimesters were categorised as: first trimester (0–90 days), second trimester (91–181 days) and third trimester (≥182 days). Mother's age was calculated from the date of venesection and mother's date of birth and categorised into seven age groups (<20, 20–24, 25–29, 30–34, 35–39, 40–44 and 45+ years). Other categorisation of potential predictors included: self-reported ethnic origin (Caucasian/non-Caucasian), cigarette smoking (yes/no), parity (0, 1, 2, 3 and 4+), maternal pre-existing medical condition (yes/no) and pregnancy complications (yes/no). A list of medical conditions and pregnancy complications has been provided in Supplementary Table 1. The season of blood draw was defined as: summer (December–February), autumn (March–May), winter (June–August) and spring (September–November). Socioeconomic status was described by the Socio-Economic Indexes for Areas (SEIFA) 2011 Index of Relative Socio-Economic Disadvantage (IRSD) and the Index of Education and Occupation (IEO)[17]. IRSD and IEO scores were applied to the postcode of residence recorded at the time of venesection and categorised into five quantiles (0–10%, 11–25%, 26–75%, 76–90% and 91–100%), with higher scores indicating greater advantage and higher education.[18] The Remoteness Index of Australia was used as a measure of access to services.[18] This index divides the population into five categories of remoteness (major cities, inner regional, outer regional, remote, very remote). The mother's pregravid body mass index (BMI) was calculated from the weight (kg) and height (m): (weight/height$^2$). Vitamin D deficiency was defined as serum 25(OH)D concentration <50 nmol L$^{-1}$.

### Statistical analysis

We described the participant characteristics (including maternal age, ethnicity, parity, smoking status, medical conditions, pregnancy complications, SES and location) of women who had their blood 25(OH)D concentration measured during pregnancy and women from the original MNS cohort who did not have their 25(OH)D concentration measured by PathWest during pregnancy using numbers and percentages (%). Demographic and clinical characteristics of those screened (for vitamin D concentration) and those not screened were compared using generalised linear models with the Stata command *binreg* to estimate prevalence ratios (PR) and 95% confidence intervals (adjusted where appropriate).

For women with a 25(OH)D measure available during pregnancy, we reported the median and interquartile range of 25(OH)D levels by maternal characteristics, gestational age at the time of venesection (trimester) and season of sample collection. We also estimated the prevalence of vitamin D deficiency in each of these categories.

Logistic regression analyses were used to: a) determine the predictive ability of a model limited to the existing risk factors for vitamin D deficiency listed in the current ANZ position statement (including latitude, month of venesection, ethnicity, medical conditions and BMI); and b) identify additional predictors of vitamin D deficiency (testing also maternal age, gestational age, parity, smoking status, complications during pregnancy, IRSD, IEO and Remoteness Index). Likelihood ratio tests and the Akaike's information criterion and Bayesian information criterion were used to assess model fit. Receiver operating characteristic (ROC) curves and the area under the curves (AUC) were estimated to assess and compare diagnostic ability.

Analyses were performed using StataCorp 2017 Stata Statistical Software, Release 15 (Statacorp LLC).[19] Statistical significance was defined as two-tailed *p*-values <0.05.

## Results

In total, 14,404 25(OH)D measurements were available from 11,515 participants. This represented 14.9% of all live births in Western Australia between 2012 and 2014. Compared with all women who gave birth over the study period, women who had their 25(OH)D levels measured during pregnancy by PathWest, the state public pathology service, were significantly more likely to be non-Caucasian, have at least one pre-existing medical condition or pregnancy complication, live in remote areas of Australia and at a more northerly latitude, be of younger maternal age (≤30 years), a current smoker and in their first pregnancy. There was a clear gradient with the two socioeconomic status variables (IRSD and IEO), with the likelihood of screening using the public pathology service decreasing with advantage and education level (Table 1).

Of the 14,404 pregnancies for which a 25(OH)D measurement was available, the mean maternal age was 29 years (SD 5.1; range 18–

42 years); 60% of women were Caucasian (the common ancestries of non-Caucasian women were Asian, Indian or African American). The location of women at the time of venesection ranged from 10.5 to 34.5° South latitude (median 31.5° S) and 96.5 to 128.5° East longitude (median 115.5°E). The majority of women resided in metropolitan areas (78%) compared with 12% and 10% in rural and remote areas, respectively. Women were more often sampled during their second (PR 1.08, 95%CI [1.07, 1.10]; $p<0.001$) or third (PR 1.12, 95%CI [1.10, 1.13]; $p<0.001$) trimester than their first trimester. The mean age of gestation at the time of sample collection was 24 weeks compared with the gestational age at the first antenatal clinic of 13.5 weeks. Approximately one-fifth of women were screened within the first 10 weeks of pregnancy. Women with pre-existing medical conditions (PR 0.95, 95%CI [0.92, 0.98]; $p=0.001$), and pregnancy complications (PR 0.88, 95%CI [0.85, 0.97]; $p=0.001$) were more likely to be screened in their first trimester. Women who were screened after their first trimester were significantly more likely to be vitamin D deficient (PR 1.06, 95%CI [1.02, 1.10]; $p=0.004$), a current smoker (PR 1.17, 95%CI [1.11, 1.22]; $p<0.001$), of younger maternal age (≤ 30 years), of lower socioeconomic status as measured by SEIFA IRSD (q5 vs. q1, PR 1.11; 95%CI [1.03, 1.20]; $p<0.01$), have one or more children and reside in metropolitan Perth.

The mean 25(OH)D concentration was 70.7 nmol $L^{-1}$ (*SD* 25.7; range 5–255 nmol $L^{-1}$). Approximately one-fifth of the women (19.3%, $n=2,786$) had 25(OH)D levels consistent with deficiency (<50 nmol $L^{-1}$) at the time of sampling (Table 2), of which 14% ($n=379$) had levels below 25 nmol $L^{-1}$. In bivariate analysis, vitamin D deficiency was most common among women sampled in their third trimester (vs. tri1, PR 1.56, 95%CI [1.40, 1.73]; $p<0.001$) and during August (vs. January, PR 2.24, 95%CI [1.91, 2.62]; $p<0.001$) and September (vs. January, PR 2.00, 95%CI [1.70, 2.35]; $p<0.001$) (Figure 1). Non-Caucasian women were more than twice as likely to be deficient as Caucasian women (PR 2.25, 95%CI [2.10, 2.41]; $p<0.001$). The proportion of women who were deficient was highest among those aged <20 years (24%) and lowest among those aged 40–44 years (16%; PR 1.50, 95%CI [1.12, 2.01]; $p=0.01$) (Figure 2). Women with four or more existing children were more likely to be vitamin D deficient compared with those with 0, 1, 2 or 3 children ($p \leq 0.01$), see Table 3.

**Table 1: Participant characteristics of all women who gave birth in Western Australia between 2012–2014.**

| Participant characteristics | | Not screened | Screened for Vitamin D deficiency[a] | PR, *p* [95%CI][b] |
|---|---|---|---|---|
| Total | 82,449 (85.13%) | 14,404 (14.87%) | | |
| Age, n (%) | < 20 years | 3,417 (4.14%) | 657 (4.56%) | 1.19, < 0.001 [1.10, 1.28] |
| | 20–24 years | 8,880 (10.77%) | 2,106 (14.62%) | 1.41, < 0.001 [1.35, 1.48] |
| | 25–29 years | 23,009 (27.91%) | 4,768 (33.10%) | 1.27, < 0.001 [1.22, 1.31] |
| | 30–34 years | 28,618 (34.71%) | 4,487 (31.15%) | Reference |
| | 35–39 years | 14,907 (18.08%) | 2,095 (14.54%) | 0.91, < 0.001 [0.87, 0.95] |
| | 40–44 years | 3,425 (4.15%) | 291 (2.02%) | 0.58, < 0.001 [0.52, 0.65] |
| | 45+ | 193 (0.23%) | NIL | - |
| Ethnicity, n (%) | Caucasian | 63,849 (77.44%) | 8,645 (60.02%) | Reference |
| | Non-Caucasian | 18,600 (22.56%) | 5,759 (39.98%) | 1.98, < 0.001 [1.92, 2.04] |
| Existing children | 0 | 35,855 (43.49%) | 6,949 (48.24%) | Reference |
| | 1 | 29,276 (35.51%) | 4,511 (31.32%) | 0.82, < 0.001 [0.79, 0.85] |
| | 2 | 11,734 (14.23%) | 1,904 (13.22%) | 0.86, < 0.001 [0.82, 0.90] |
| | 3 | 3,582 (4.34%) | 662 (4.60%) | 0.96, 0.28 [0.89, 1.03] |
| | 4+ | 2,002 (2.43%) | 378 (2.62%) | 0.98, 0.65 [0.89, 1.08] |
| Cigarette smoking | Non-smoker | 75,636 (91.74%) | 12,872 (89.36%) | Reference |
| | Current smoker | 6,813 (8.26%) | 1,532 (10.64%) | 1.26, < 0.001 [1.20, 1.32] |
| BMI | < 18.5 | 1,241 (83.68%) | 242 (16.32%) | Reference |
| | 18.5–24.9 | 38,075 (85.36%) | 6,530 (14.64%) | 0.90, 0.70 [0.80, 1.00] |
| | 25–29.9 | 22,084 (84.66%) | 4,001 (15.34%) | 0.94, 0.31 [0.83, 1.05] |
| | > 30 | 21,049 (85.29%) | 3,631 (14.71%) | 0.90, 0.09 [0.80, 1.01] |
| Medical conditions | No | 50,386 (61.11%) | 6,432 (44.65%) | Reference |
| | Yes | 32,063 (38.89%) | 7,972 (55.35%) | 1.76, < 0.001 [1.71, 1.81] |
| Pregnancy complications | No | 56,476 (68.50%) | 10,046 (69.74%) | Reference |
| | Yes | 25,973 (31.50%) | 4,358 (30.26%) | 0.95, 0.003 [0.92, 0.98] |
| Social disadvantage (IRSD) | 0–10% | 7,337 (8.90%) | 2,088 (14.50%) | Reference |
| | 11–25% | 11,447 (13.88%) | 2,714 (18.84%) | 0.86, < 0.01 [0.82, 0.91] |
| | 26–75% | 40,300 (48.88%) | 6,845 (47.52%) | 0.66, < 0.01 [0.63, 0.68] |
| | 76–90% | 12,735 (15.45%) | 1,425 (9.89%) | 0.45, < 0.01 [0.43, 0.48] |
| | 91–100% | 8,592 (10.42%) | 840 (5.83%) | 0.40, < 0.01 [0.37, 0.43] |
| | Missing | 2,038 (2.47%) | 492 (3.42%) | |
| Education and occupation (IEO) | 0–10% | 7,701 (9.34%) | 1,714 (11.90%) | Reference |
| | 11–25% | 11,653 (14.13%) | 2,513 (17.45%) | 0.97, 0.36 [0.92, 1.03] |
| | 26–75% | 40,332 (48.92%) | 6,837 (47.47%) | 0.80, < 0.001 [0.76, 0.84] |
| | 76–90% | 12,212 (14.81%) | 1,923 (13.35%) | 0.75, < 0.001 [0.70, 0.79] |
| | 91–100% | 8,515 (10.33%) | 928 (6.44%) | 0.54, < 0.001 [0.50, 0.58] |
| | Missing | 2,036 (2.47%) | 489 (3.39%) | |
| Remoteness, n (%) | Metropolitan | 66,733 (80.94%) | 11,261 (78.18%) | Reference |
| | Rural | 12,330 (14.95%) | 1,690 (11.73%) | 0.83, < 0.01 [0.80, 0.88] |
| | Remote | 3,304 (4.01%) | 1,443 (10.02%) | 2.10, < 0.01 [2.01, 2.20] |
| | Missing | 82 (0.10%) | 10 (0.07%) | |
| Latitude | 10.5–14.5° S | 38 (0.05%) | 26 (0.18%) | 0.95, 0.90 [0.43, 2.09] |
| | 15.5–19.5° S | 414 (0.50%) | 387 (2.69%) | 0.46, < 0.001 [0.34, 0.63] |
| | 20.5–24.5° S | 1,741 (2.11%) | 618 (4.29 %) | 0.44, < 0.001 [0.34, 0.57] |
| | 25.5–29.5° S | 1,882 (2.28%) | 189 (1.31%) | 0.58, 0.01 [0.39, 0.85] |
| | 30.5–34.5° S | 78,374 (94.96%) | 13,184 (91.46%) | Reference |
| | Missing | 82 (0.01%) | 10 (0.07%) | |

*Note:*

*a: Vitamin D deficiency < 50 nmol L−1;*

*b: p-values from binreg comparing women screened and women not screened for vitamin D deficiency during pregnancy.*

A similar proportion of women in the 30.5 to 35.5° South latitude category were vitamin D deficient (20%) compared with women residing in the 10.5 to 15.5° S category (19%). This was likely due to the higher proportion of non-Caucasian women tested in the 10.5 to 15.5° S category than the 30.5 to 35.5° S category (61.54% vs. 41.70%, respectively).

The risk of deficiency decreased with both the SEIFA IRSD (q5 vs. q1, PR 0.56; 95%CI [0.47, 0.68]; $p$ 0.001) and IEO (q5 vs. q1, PR 0.63; 95%CI [0.53, 0.76]; $p<0.001$).

We ran logistic regression using a baseline model ($n=13,394$) limited to the risk factors for vitamin D deficiency listed in the ANZ position statement (latitude, month of

**Table 2: Characteristics of pregnant women in relation to serum 25(OH)D levels and vitamin D status.**

| | | | Median (IQR) nmol L−1 | Vit D deficient 25(OH)D < 50 nmol L−1 n (%) |
|---|---|---|---|---|
| All | | n | 68 (52, 84) | 2,786 (19.34%) |
| Age, n (%) | < 20 years | 657 | 66 (51, 81) | 159 (24.20%) |
| | 20–24 years | 2,106 | 67 (51, 83) | 483 (22.93%) |
| | 25–29 years | 4,768 | 69 (54, 85) | 941 (19.74%) |
| | 30–34 years | 4,487 | 71 (56, 87) | 795 (17.72%) |
| | 35–39 years | 2,095 | 71 (56, 86) | 361 (17.23%) |
| | 40–44 years | 291 | 73 (56, 88) | 47 (16.15%) |
| Ethnicity, n (%) | Caucasian | 8,645 | 73 (59, 89) | 1,115 (12.90%) |
| | Non-Caucasian | 5,759 | 63 (46, 80) | 1,671 (29.02%) |
| Trimester | First trimester | 2,380 | 70 (57, 85) | 363 (15.25%) |
| | Second trimester | 7,636 | 70 (55, 85) | 1,382 (18.10%) |
| | Third trimester | 4,388 | 68 (50, 85) | 1,041 (23.72%) |
| Existing children | 0 | 6,949 | 69 (54, 84) | 1,342 (19.31%) |
| | 1 | 4,511 | 71 (55, 87) | 843 (18.69%) |
| | 2 | 1,904 | 70 (54, 86) | 367 (19.28%) |
| | 3 | 662 | 71 (54, 87) | 131 (19.79%) |
| | 4+ | 378 | 64 (48, 83) | 103 (27.25%) |
| BMI | < 18.5 | 242 | 70 (52, 89) | 51 (21.07%) |
| | 18.5–24.9 | 6,530 | 72 (56, 88) | 1,103 (16.89%) |
| | 25–29.9 | 4,001 | 69 (54, 84) | 804 (20.09%) |
| | > 30 | 3,631 | 65 (51, 81) | 828 (22.80%) |
| Cigarette smoking | Non-smoker | 12,872 | 68 (52, 84) | 2,510 (19.50%) |
| | Current smoker | 1,532 | 68 (53, 85) | 276 (18.02%) |
| Medical conditions | No | 6,432 | 69 (55, 85) | 1,049 (16.31%) |
| | Yes | 7,972 | 67 (50, 84) | 1,737 (21.79%) |
| Pregnancy complications | No | 10,046 | 69 (53, 85) | 1,908 (18.99%) |
| | Yes | 4,358 | 67 (51, 83) | 878 (20.15%) |
| Season of blood sampling | Summer | 3,491 | 73 (58, 89) | 461 (13.20%) |
| | Autumn | 3,779 | 73 (57, 89) | 559 (14.79%) |
| | Winter | 3,833 | 62 (47, 77) | 1,067 (27.84%) |
| | Spring | 3,301 | 65 (50, 81) | 699 (21.18%) |
| Social disadvantage (IRSD) | 0–10% | 2,088 | 65 (49, 82) | 492 (23.56%) |
| | 11–25% | 2,714 | 67 (51, 82) | 623 (22.96%) |
| | 26–75% | 6,845 | 69 (53, 85) | 1,257 (18.36%) |
| | 76–90% | 1,425 | 69 (54, 86) | 214 (15.02%) |
| | 91–100% | 840 | 73 (57, 87) | 112 (13.33%) |
| Education and occupation (IEO) | 0–10% | 1,714 | 65 (49, 83) | 391 (22.81%) |
| | 11–25% | 2,513 | 65 (49, 82) | 518 (20.61%) |
| | 26–75% | 6,837 | 69 (53, 85) | 1,307 (19.12%) |
| | 76–90% | 1,923 | 71 (57, 86) | 348 (18.10%) |
| | 91–100% | 928 | 73 (59, 88) | 134 (14.44%) |
| Remoteness, n (%) | Metropolitan | 11,261 | 67 (51, 83) | 2,387 (21.20%) |
| | Rural | 1,690 | 69 (55, 85) | 243 (14.38%) |
| | Remote | 1,443 | 75 (61, 90) | 151 (10.46%) |
| Latitude | 10.5–14.5° S | 26 | 56 (45, 79) | 5 (19.23%) |
| | 15.5–19.5° S | 387 | 80 (65, 97) | 36 (9.30%) |
| | 20.5–24.5° S | 618 | 75 (63, 90) | 55 (8.90%) |
| | 25.5–29.5° S | 189 | 72 (56, 84) | 22 (11.64%) |
| | 30.5–34.5° S | 13,184 | 67 (52, 84) | 2,663 (20.20%) |

*Note:*

*Data presented for 2012-2014;*

*Vitamin D sufficient = (25(OH)D ≥ 50 nmol L−1); vitamin D deficient = (25(OH)D < 50 nmol L−1);*

*BMI: body mass index; IEO: Index for Education and Occupation; IRSD: Index for Relative Socio-Economic Disadvantage*

venesection, ethnicity, medical conditions and BMI) and found that each of the risk factors was an independent predictor of vitamin D deficiency.

A second logistic regression model ($n$=13,394) using all available covariates showed that the additional independent contributions of maternal age, parity, Remoteness Index and IEO to the baseline model were statistically significant (Table 3). We found no association between smoking, IRSD and pregnancy complications and vitamin D status. Of the independent predictors, only maternal age, added to the baseline model, significantly improved the model fit in the likelihood ratio test ($p$<0.001). Following ROC curve analysis, adding maternal age to the model increased the AUC significantly ($p$=0.002), although the two AUCs were not greatly different (AUC 0.71; 95%CI [0.70, 0.72] vs. 0.72; 95%CI [0.71, 0.73]).

## Discussion

In Western Australia, 19% of women who had their 25(OH)D levels tested during pregnancy between 2012 and 2014 were vitamin D deficient (<50 nmol $L^{-1}$). Of those, 14% had levels below 25 nmol $L^{-1}$ (severe deficiency). The rate of deficiency in Western Australia is comparable to that reported in Canada (24%)[20] and Slovenia (14%)[21] and lower than that for New Zealand (42–55%),[22-24] Sweden (33–65%),[25,26] Germany (78%),[27] the United States (48%),[28] Asia (77–95%)[29,30] and Africa (97%).[31] Surveys from other regions in Australia have reported rates of deficiency (25[OH]D<50 nmol $L^{-1}$) of 48% among a population-based study of pregnant women in New South Wales ($n$=971),[10] and from specific subgroups: 56% in South Australia ($n$=68),[32] 35% in Canberra ($n$=100),[9] 26% in rural Victoria ($n$=330)[33] and 9% in Queensland ($n$=75).[34] A Western Australian study of 209 pregnant women at 36–40 weeks gestation found that 14% were vitamin D deficient.[8] The percentage of pregnant women who were vitamin D deficient was more than twofold higher in an earlier study (1989–1991) of a Western Australian community-based cohort ($n$=901). The study sampled women at 18 weeks' gestation and found that 36% were vitamin D deficient.[4] Assays and seasonal distribution of sampling varied between the two studies, making it difficult to make useful comparisons.

Antenatal care is a usual part of pregnancy for most women who give birth in Australia.

The Pregnancy Care Guidelines recommend that the first antenatal visit should occur within the first 10 weeks of pregnancy and that there is a total of 7–10 visits over the course of the pregnancy. Women can opt to attend public or private services. It is recommended that screening for vitamin D deficiency should occur at the time of the first antenatal clinic.[35] However, we observed a large discrepancy between the median gestation at the first antenatal visit (13.5 weeks) and the median gestation at the time of venesection (24 weeks). Investigations into the discrepancy are required, including confirmation that testing is recommended at the first antenatal visit. It is likely that the delay is due, in part, to the sample not being taken during the antenatal visit itself, and women are required to attend a pathology collection centre at a time that is convenient to them.

There is some evidence to suggest that childhood outcomes may be differential by the timing of exposure to low vitamin D levels.[36-39] Failure to detect and treat deficiency until 24 weeks will likely have implications for those pregnancy and foetal health outcomes that have been found to be improved by higher 25(OH)D levels in early pregnancy. In addition, there will be a lag in improving levels from the time of intervention (i.e. supplementation), the delay being dependent on the source of the vitamin D (UVR vs. dietary intake vs. supplementation), dosage, baseline 25(OH)D levels,[40-42] genetics[40,43] and weight status.[40] Vitamin D sufficiency, therefore, needs to be identified earlier than is currently occurring to reduce, through intervention, the amount of time that women are deficient during pregnancy.

For most people in Australia, the majority of vitamin D is gained through endogenous generation following sun exposure.[44] Anything that interferes with the production of vitamin D3 in the skin (either the amount of UVB radiation reaching the epidermis or the availability of the vitamin D precursor, 7-DHC), the intake of dietary vitamin D or the metabolism and/or storage of vitamin D are determinants of 25(OH)D levels. Our findings support the risk factors for vitamin D deficiency listed in the ANZ position statement (Figure 3), namely lack of skin exposure to sunlight (more southerly latitude), dark skin and obesity,[11] as independent predictors of vitamin D deficiency for pregnant women in Western Australia.

**Figure 1: Proportion of pregnant women aged 18–44 years, tested for vitamin D status in pregnancy with vitamin D deficiency by month of venesection, Western Australia, 2012–2014.**

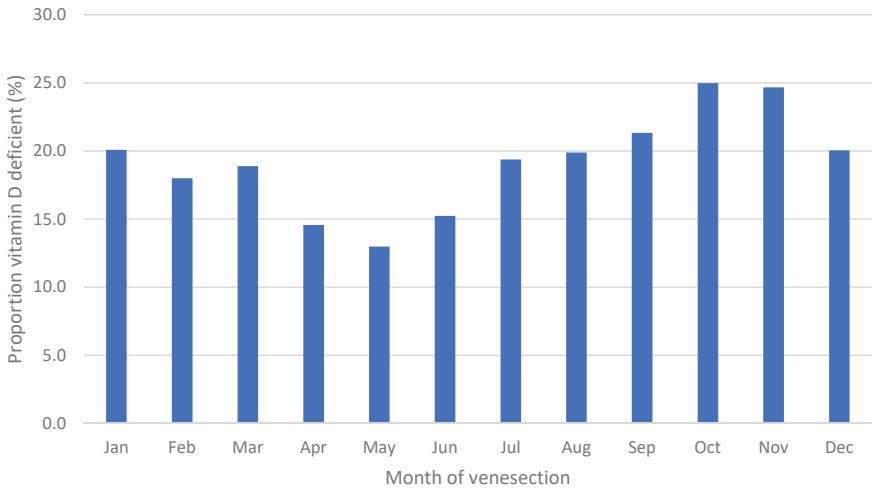


**Figure 2: Proportion of pregnant women aged 18–44 years, tested for vitamin D status in pregnancy with vitamin D deficiency by maternal age at time of venesection, Western Australia, 2012–2014.**

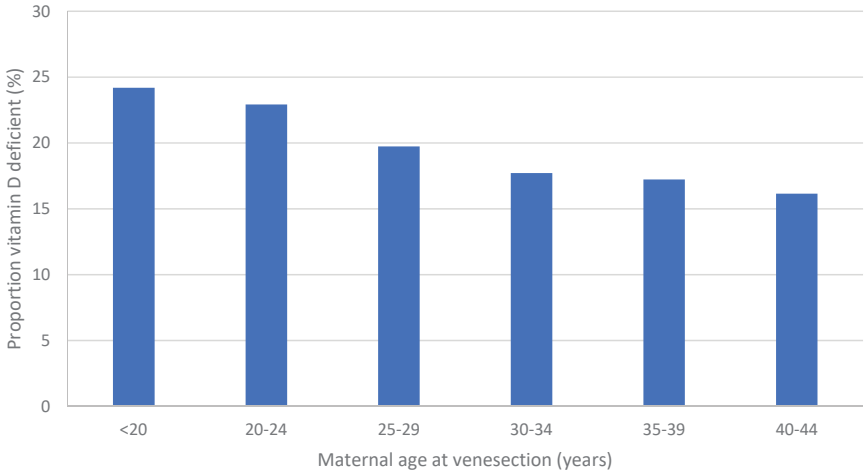


**Figure 3: Risk factors for low vitamin D.[11]**

- Lack of skin exposure to ultraviolet B radiation from sunlight (due to lifestyle factors, chronic illness or hospitalisation, complex disability, covering clothing for religious or cultural reasons or southerly latitude)
- Dark skin (Fitzpatrick types V and VI)*
- Medical conditions or medications affecting vitamin D metabolism and storage (obesity, end-stage liver disease, renal disease, drugs that increase vitamin D degradation such as rifampicin and anticonvulsants or fat malabsorption (e.g. in cystic fibrosis, coeliac disease and inflammatory bowel disease))

*Dark skin is less likely to be a significant risk factor in people with regular sun exposure in climates with high incident ultraviolet radiation (e.g. northern parts of Australia), but there is a lack of prevalence data for these populations

**Table 3: Predictors of vitamin D deficiency in pregnant women aged 18–44 years, Western Australia.**

| Variable | | Multivariate analysis | | |
|---|---|---|---|---|
| | | PR[a] | [95%CI] | *p*-value |
| Ethnicity | Caucasian | Reference | | |
| | Non-Caucasian | 2.84 | [2.57, 3.13] | < 0.001 |
| Trimester | First trimester | Reference | | |
| | Second trimester | 0.67 | [0.57, 0.78] | < 0.001 |
| | Third trimester | 0.82 | [0.69, 0.96] | 0.02 |
| Age group | < 20 years | 1.96 | [1.30, 2.94] | 0.001 |
| | 20–24 | 1.59 | [1.09, 2.28] | 0.02 |
| | 25–29 | 1.26 | [0.88, 1.82] | 0.20 |
| | 30–34 | 1.07 | [0.74, 1.54] | 0.72 |
| | 35–39 | 1.05 | [0.72, 1.52] | 0.81 |
| | 40–44 | Reference | | |
| Body mass index | | 1.04 | [1.03, 1.04] | < 0.001 |
| Year | | 0.76 | [0.72, 0.80] | < 0.001 |
| Collection month | Jan | Reference | | |
| | Feb | 0.92 | [0.72, 1.18] | 0.52 |
| | Mar | 0.73 | [0.57, 0.95] | 0.02 |
| | Apr | 1.08 | [0.86, 1.38] | 0.50 |
| | May | 1.42 | [1.13, 1.78] | 0.002 |
| | Jun | 2.07 | [1.65, 2.58] | < 0.001 |
| | July | 2.57 | [2.08, 3.19] | < 0.001 |
| | Aug | 2.98 | [2.40, 3.64] | < 0.001 |
| | Sep | 2.56 | [2.06, 3.18] | < 0.001 |
| | Oct | 1.63 | [1.30, 2.05] | < 0.001 |
| | Nov | 1.01 | [0.78, 1.31] | 0.94 |
| | Dec | 1.02 | [0.78, 1.32] | 0.90 |
| Existing children | 0 | 0.66 | [0.50, 0.86] | 0.002 |
| | 1 | 0.66 | [0.51, 0.87] | 0.004 |
| | 2 | 0.73 | [0.54, 0.96] | 0.03 |
| | 3 | 0.70 | [0.50, 0.98] | 0.04 |
| | 4+ | Reference | | |
| Cigarette smoking | Non-smoker | Reference | | |
| | Current smoker | 0.94 | [0.80, 1.10] | 0.42 |
| Latitude | 1.04 | (1.02, 1.07) | 0.002 | |
| Social disadvantage (IRSD) | 0–10% | Reference | | |
| | 11–25% | 1.08 | [0.92, 1.26] | 0.36 |
| | 26–75% | 0.92 | [0.78, 1.08] | 0.31 |
| | 76–90% | 0.88 | [0.70, 1.10] | 0.26 |
| | 91–100% | 0.81 | [0.61, 1.06] | 0.13 |
| Education and occupation (IEO) | 0–10% | Reference | | |
| | 11–25% | 0.88 | [0.75, 1.05] | 0.16 |
| | 26–75% | 0.91 | [0.778, 1.09] | 0.31 |
| | 76–90% | 0.93 | [0.75, 1.16] | 0.55 |
| | 91–100% | 0.73 | [0.55, 0.97] | 0.03 |
| Remoteness | Metropolitan | Reference | | |
| | Rural | 0.70 | [0.59, 0.84] | < 0.001 |
| | Remote | 0.68 | [0.51, 0.93] | 0.02 |
| Medical conditions | No | Reference | | |
| | Yes | 1.29 | [1.17, 1.41] | < 0.001 |
| Pregnancy complications | No | Reference | | |
| | Yes | 1.00 | [0.90, 1.10] | 0.96 |

*Notes:*

*a: PR Prevalence Ratio*

*Data presented for 2012-2014; Prevalence ratios obtained from generalised linear models (binreg)*

In addition to these risk factors, we found that maternal age (under 25 years), being in the lowest percentile for IEO and residing in the Perth metropolitan area (compared with rural and remote areas) were also independent predictors of vitamin D deficiency. Of these, only maternal age improved the predictive performance and diagnostic efficacy of the baseline model. Importantly, maternal age was an independent predictor of vitamin D deficiency after adjustment for all covariates (including ethnicity and socioeconomic status), with pregnant women aged <20 years and 20–24 years at significantly increased risk of deficiency compared with all other age groups. This is consistent with data from adults aged 18–75+ years from the Australian Health Survey, which also showed that deficiency was most common among those aged 18–24 years.[5] In the same study, among women of childbearing age, the proportion of women vitamin D deficient decreased linearly with increasing age, e.g. from 31.1% among those aged 18–24 years to 22.9% among those aged 35–44 years. Maternal age has been positively associated with higher 25(OH)D levels in some[7,10,45-47] although not all studies.[21,48] While it has been suggested by some that the association is due to greater uptake of supplements among older pregnant women,[7] one study found that 25(OH)D levels of younger women were lower, despite supplement use.[45]

Although supplement use in Australia is generally low (19%),[49] uptake of supplements is reportedly higher among pregnant women (ranging from 41–84%).[9,49] Our finding that younger maternal age and lower educational and occupational status were significant predictors of vitamin D deficiency is consistent with previous reports of lower supplement use in these groups.[49] Our finding that those residing within the Perth metropolitan area are at greater risk of vitamin D deficiency may reflect reduced sun exposure in those living in higher population density and urban environments, where the ratio of ambient erythemal UVR to personal dose is lower than that observed in rural and remote environments.[50]

This is the largest study of vitamin D status of pregnant women in Australia and, to our knowledge, worldwide, comprising all pregnant women screened for vitamin D deficiency in Western Australia by the state public pathology service. We used linked data from the population-based MNS and a statewide public pathology laboratory to

assess the characteristics of pregnant women who had their 25(OH)D levels tested, as well as characterising their vitamin D status and the predictors of vitamin D deficiency. Additional strengths of this study included the large sample size, a single-site testing sera for 25(OH)D using a consistent immunoassay method with quality assurance through a recognised provider, and the availability of comprehensive sociodemographic and clinical data from a statutory data collection for all women who gave birth in Western Australia.

The main limitations of the study were the lack of data on supplement use and personal sun exposure. Another limitation was that data were collected only from the state's public pathology service. The findings may not be generalisable to women whose 25(OH)D levels were not tested during pregnancy or were tested by private pathology services. With respect to the covariates used in the models, ethnic origin was used to predict skin colour, and we only had data on pregravid BMI. BMI at the time of venesection would have been preferred, although pregravid BMI is commonly a predictor of vitamin D deficiency during pregnancy.[51]

## Conclusion

Our data suggest that maternal age ≤24 years may be a worthwhile additional risk factor for vitamin D deficiency in addition to the existing risk factors outlined in the ANZ position statement for vitamin D and health in pregnancy. Although the Remoteness Index did not improve the AUC, living in the metropolitan area did significantly increase the risk of being vitamin D deficient. We recommend that practitioners encourage women residing in metropolitan areas to take regular vitamin D supplements or seek regular safe sun exposure[52] during pregnancy when indicated. There is evidence of widespread vitamin D deficiency in some population groups (e.g. veiled women in some locations in Australia; populations living at high latitudes) and routine supplementation may be a cost-effective way to manage these specific situations.[53] Further, we support the reinforcement of guidelines for screening for vitamin D deficiency at the first antenatal clinic to potentially at-risk women to optimise the benefits of vitamin D sufficiency throughout pregnancy on both maternal and foetal health outcomes.

## References


1. Dutra LV, Souza FISd, Konstantyner T. Effects of vitamin D supplementation during pregnancy on newborns and infants: An integrative review. *Rev Paul de Pediatr*. 2021;39:e2020087.
2. Palacios C, Kostiuk LK, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. *Cochrane Database Syst Rev. 2019;7(7):CD008873.*.
3. De-Regil LM, Palacios C, Lombardo LK, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. *Cochrane Database Syst Rev*. 2016;(1):CD008873
4. Hart PH, Lucas RM, Walsh JP, Zosky GR, Whitehouse AJ, Zhu K, et al. Vitamin D in fetal development: findings from a birth cohort study. *Pediatr*. 2015;135(1):e167-73.
5. Australian Bureau of Statistics. *4364.0.55.006 - Australian Health Survey: Biomedical Results for Nutrients, 2011-2012*. Canberra (AUST): ABS; 2013.
6. Nowson C, McGrath J, Ebeling P, Haikerwal A, Daly R, Sanders K, et al. Working Group of Australian and New Zealand Bone and Mineral Society, Endocrine Society of Australia and Osteoporosis Australia. Vitamin D and health in adults in Australia and New Zealand: A position statement. *Med J Aust*. 2012;196(11):686-7.
7. Davies-Tuck M, Yim C, Knight M, Hodges R, Doery JC, Wallace E. Vitamin D testing in pregnancy: Does one size fit all? *Aust N Z J Obstet Gynaecol*. 2015;55(2):149-55.
8. Jones A, Rueter K, Siafarikas A, Lim E, Prescott S, Palmer D. 25-hydroxyvitamin D status of pregnant women is associated with the use of antenatal vitamin supplements and ambient ultraviolet radiation. *J Dev Orig Health Dis*. 2016;7(4):350-6.
9. Perampalam S, Ganda K, Chow KA, Opie N, Hickman PE, Shadbolt B, et al. Vitamin D status and its predictive factors in pregnancy in 2 Australian populations. *Aust N Z J Obstet Gynaecol*. 2011;51(4):353-9.
10. Bowyer L, Catling-Paull C, Diamond T, Homer C, Davis G, Craig ME. Vitamin D, PTH and calcium levels in pregnant women and their neonates. *Clin Endocrinol*. 2009;70(3):372-7.
11. Paxton GA, Teale GR, Nowson CA, Mason RS, McGrath JJ, Thompson MJ, et al. Vitamin D and health in pregnancy, infants, children and adolescents in Australia and New Zealand: A position statement. *Med J Aust*. 2013;198(3):142-3.
12. Australian Bureau of Statistics. *Regional Population Growth, Australia, 2014-15*. Canberra (AUST): ABS; 2016.
13. Australian Bureau of Statistics. *2016 Census*. Canberra (AUST): ABS; 2017.
14. Western Australia Department of Health. *Guidelines for Midwives Notification of Case Attended*. Perth (AUST) State Government of Western Australia; 2016.
15. Moore HC. *Epidemiological Perspectives of Acute Lower Respiratory Infections in Young Western Australian Aboriginal and Non-Aboriginal Children*. Perth (AUST): University of Western Australia; 2011.
16. Miller KM, Lucas RM, Davis EA; Hart PH, de Klerk NH. Use of linked administrative and laboratory data to confirm that serum 25(OH)D levels in pregnant women can be predicted from satellite estimates of ultraviolet radiation. *Int J Epidemiol*. 2021;50(1):303-13.
17. Pink B. *An Introduction to Socio-Economic Indexes for Areas (SEIFA) – Information Paper*. Canberra (AUST): Australian Bureau of Statistics; 2006.
18. Australian Bureau of Statistics. *Australian Statistical Geography Standard: Volume 5 - Remotenss Structure*. Canberra (AUST): ABS; 2016.
19. *STATA*: Statistical Software. Release 15. College Station (TX): Stata Corporation; 2017.
20. Li W, Green TJ, Innis SM, Barr SI, Whiting SJ, Shand A, et al. Suboptimal vitamin D levels in pregnant women despite supplement use. *Can J Public Health*. 2011:308-12.
21. Salamon AS, Benedik E, Bratanič B, Velkavrh M, Rogelj I, Mis NF, et al. Vitamin D status and its determinants in healthy Slovenian pregnant women. *Ann Nutr Metab*. 2015;67(2):96-103.
22. Wheeler BJ, Taylor BJ, de Lange M, Harper MJ, Jones S, Mekhail A, 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 45°S. *Nutrients*. 2018;10(1):86.
23. Ekeroma AJ, Camargo C, Scragg R, Wall C, Stewart A, Mitchell E, et al. Predictors of vitamin D status in pregnant women in New Zealand. *N Z Med J*. 2015;128(1422):24-34.
24. Grant CC, Stewart AW, Scragg R, Milne T, Rowden J, Ekeroma A, et al. Vitamin D during pregnancy and infancy and infant serum 25-hydroxyvitamin D concentration. *Pediatrics*. 2014;133(1):e143-53.
25. Brembeck P, Winkvist A, Olausson H. Determinants of vitamin D status in pregnant fair-skinned women in Sweden. *Br J Nutr*. 2013;110(5):856-64.
26. Lundqvist A, Sandstrom H, Stenlund H, Johansson I, Hultdin J. Vitamin D status during pregnancy: A longitudinal study in Swedish women from early pregnancy to seven months postpartum. *PLoS One*. 2016;11(3):e0150385.
27. Gellert S, Ströhle A, Bitterlich N, Hahn A. Higher prevalence of vitamin D deficiency in German pregnant women compared to non-pregnant women. *Arch Gynecol Obstet*. 2017;296(1):43-51.
28. Hamilton SA, McNeil R, Hollis BW, Davis DJ, Winkler J, Cook C, et al. Profound vitamin D deficiency in a diverse group of women during pregnancy living in a sun-rich environment at latitude 32°N. *Int J Endocrinol*. 2010;2010:917428.
29. Choi R, Kim S, Yoo H, Cho YY, Kim SW, Chung JH, et al. High prevalence of vitamin D deficiency in pregnant Korean women: The first trimester and the winter season as risk factors for vitamin D deficiency. *Nutrients*. 2015;7(5):3427-48.
30. Shiraishi M, Haruna M, Matsuzaki M, Murayama R. Demographic and lifestyle factors associated with vitamin D status in pregnant Japanese women. *J Nutr Sci Vitaminol (Tokyo)*. 2014;60(6):420-8.
31. Ayadi ID, Nouaili EB, Talbi E, Ghdemssi A, Rached C, Bahlous A, et al. Prevalence of vitamin D deficiency in mothers and their newborns in a Tunisian population. *Int J Gynaecol Obstet*. 2016;133(2):192-5.
32. Thomas SDC, Fudge AN, Whiting M, Coates PS. The correlation between third-trimester maternal and newborn-serum 25-hydroxy-vitamin D in a selected South Australian group of newborn samples. *BMJ*. 2011;1(2):e000236.
33. Teale GR, Cunningham CE. Vitamin D deficiency is common among pregnant women in rural Victoria. *Aust N Z J Obstet Gynaecol*. 2010;50(3):259-61.
34. McLeod DS, Scott KA, Lust K, McIntyre HD. Routine screening for vitamin D deficiency in early pregnancy. *Med J Aust*. 2011;195(7):384-5.
35. Australian Department of Health. *Clinical Practice Guidelines: Pregnancy Care*. Canberra (AUST): Government of Australia; 2018.
36. Hyde NK, Brennan-Olsen SL, Wark JD, Hosking SM, Vuillermin PJ, Williams LJ, et al. The Vitamin D in Pregnancy Study: A prospective prebirth cohort in southern Australia. *BMJ*. 2020;10(8):e036003.
37. Mosavat M, Arabiat D, Smyth A, Newnham J, Whitehead L. Second-trimester maternal serum vitamin D and pregnancy outcome: The Western Australian Raine cohort study. *Diabetes Res Clin Pract*. 2021;175:108779.
38. Wei S, Audibert F, Hidiroglou N, Sarafin K, Julien P, Wu Y, et al. Longitudinal vitamin D status in pregnancy and the risk of pre-eclampsia. *Int J Gynaecol Obstet*. 2012;119(7):832-9.
39. Tian Y, Holzman C, Siega-Riz AM, Williams MA, Dole N, Enquobahrie DA, et al. Maternal serum 25-hydroxyvitamin D concentrations during pregnancy and infant birthweight for gestational age: A three-cohort study. *Paediatr Perinat Epidemiol*. 2016;30(2):124-33.
40. Weinhold A, Obeid R, Vogt T, Reichrath J. Prospective investigation of 25 (OH) D3 serum concentration following UVB narrow band phototherapy in patients with psoriasis and atopic dermatitis. *Anticancer Res*. 2016;36(3):1439-44.
41. Bogh MK, Schmedes AV, Philipsen PA, Thieden E, Wulf HC. Vitamin D production after UVB exposure depends on baseline vitamin D and total cholesterol but not on skin pigmentation. *J Invest Dermatol*. 2010;130(2):546-53.
42. Brustad M, Edvardsen K, Wilsgaard T, Engelsen O, Aksnes L, Lund E. Seasonality of UV-radiation and vitamin D status at 69 degrees north. *Photochem Photobiol Sci*. 2007;6(8):903-8.

43. Fu L, Yun F, Oczak M, Wong BY, Vieth R, Cole DE. Common genetic variants of the vitamin D binding protein (DBP) predict differences in response of serum 25-hydroxyvitamin D [25 (OH) D] to vitamin D supplementation. *Clin Biochem*. 2009;42(10):1174-7.
44. O'Sullivan F, Raftery T, van Weele M, van Geffen J, McNamara D, O'Morain C, et al. Sunshine is an important determinant of vitamin D status even among high-dose supplement users: Secondary analysis of a randomised controlled trial in Crohn's disease patients. *J Photochem Photobiol*. 2019;95(4):1060-7.
45. Moon RJ, Crozier SR, Dennison EM, Davies JH, Robinson SM, Inskip HM, et al. Tracking of 25-hydroxyvitamin D status during pregnancy: The importance of vitamin D supplementation. *Am J Clin Nutr*. 2015;102(5):1081-7.
46. Xiao J-P, Zang J, Pei J-J, Xu F, Zhu Y, Liao X-P. Low maternal vitamin D status during the second trimester of pregnancy: A cross-sectional study in Wuxi, China. *PLoS One*. 2015;10(2):e0117748.
47. Rodriguez A, Santa Marina L, Jimenez AM, Esplugues A, Ballester F, Espada M, et al. Vitamin D status in pregnancy and determinants in a southern european cohort study. *Paediatr Perinat Epidemiol*. 2016;30(3):217-28.
48. Barebring L, Schoenmakers I, Glantz A, Hulthen L, Jagner A, Ellis J, et al. Vitamin D status during pregnancy in a multi-ethnic population-representative Swedish cohort. *Nutrients*. 2016;8(10):655.
49. Black LJ, Jacoby P, Nowson CA, Daly RM, Lucas RM. Predictors of vitamin D-containing supplement use in the Australian population and associations between dose and serum 25-hydroxyvitamin D concentrations. *Nutrients*. 2016;8(6):356.
50. Elliott JC, Lucas RM, Clements MS, Bambrick HJ. Population density determines the direction of the association between ambient ultraviolet radiation and type 1 diabetes incidence. *Pediatr Diabetes*. 2010;11(6):394-402.
51. Bodnar LM, Catov JM, Roberts JM, Simhan HN. Prepregnancy obesity predicts poor vitamin D status in mothers and their neonates. *J Nutr*. 2007;137(11):2437-42.
52. Cancer Council Australia. *Preventing Skin Cancer*. Sydney (AUST): CC Australia; 2021.
53. Floreskul V, Juma FZ, Daniel AB, Zamir I, Rawdin A, Stevenson M, et al. Cost-effectiveness of vitamin D supplementation in pregnant woman and young children in preventing rickets: A modeling study. *Front Public Health*. 2020;8:439.


## Supporting Information

Additional supporting information may be found in the online version of this article:

**Supplementary Table 1**: Medical conditions and pregnancy complications recorded for pregnant women in Western Australia (2012-2014).