

Hypovitaminosis D in Pregnancy: Can the Mediterranean Paradox Be Explained? A Systematic Review

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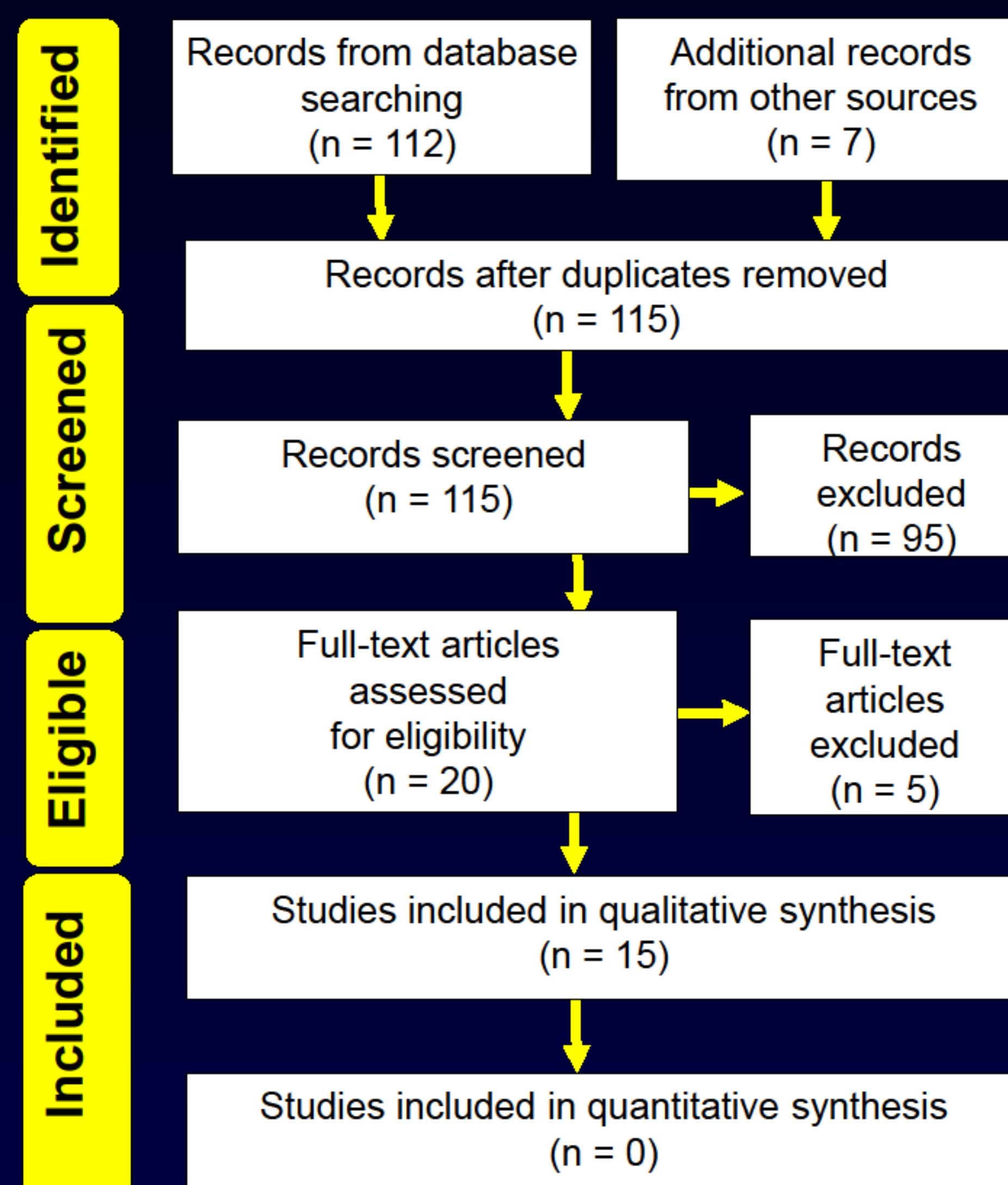
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Introduction: Despite high levels of sunshine maternal hypovitaminosis D during pregnancy is prevalent in the Mediterranean region, consisting a paradox. The aim of the study was to systematically review trials that investigated vitamin D concentrations during pregnancy in this region, in order to determine predictors of hypovitaminosis D and explain the paradox.

Methods: After applying inclusion and exclusion criteria 15 studies were entered into the systematic review, involving 2,649 pregnant women and 1,820 neonates. The main outcome was maternal vitamin D concentration. Possible predictors of the outcome included maternal and neonatal characteristics (age, body mass index, race, socioeconomic status, skin type, gestational age, sun exposure, calcium and vitamin D intake and supplementation, smoking status, parity, season of delivery, pregnancy complications).

Parameter associated with maternal 25(OH)D	Type of association	Reference(s)
Maternal vitamin B ₁₂	None	Ustuner
Maternal PTH	None	Ustuner
Skin color (light)	Positive	Nikolaidou, Perez
Race (white)	Positive	Fernandez-Alonso
Dressing pattern (uncovered)	Positive	Parildar, Pehlivan
Smoking	Controversial	Perez-Lopez, Fernandez-Alonso, Diaz-Gomez
Maternal vitamin D intake	None	Perez, Karras, Pehlivan
Maternal vitamin D supplementation	Positive	Ustuner, Pehlivan
Maternal calcium intake	Positive	Karras
Socioeconomic status (poor)	Controversial	Ustuner, Pehlivan
Rural evidence	None	Perez-Lopez, Fernandez
Season of gestation (spring / summer)	Positive	Perez-Lopez, Fernandez
Maternal BMI	Negative	Fernandez, Perez
Maternal age	None	Ustuner, Fernandez, Perez, Pehlivan, Karras
Parity	None	Ustuner, Fernandez, Perez, Pehlivan, Karras, Parildar
Gestational age	Inverse U-shaped	Perez-Lopez, Haliloglu, Fernandez-Alonso
Weight gain during pregnancy	None	Halicioglu, Ustuner
Birth weight	None	Perez, Halicioglu, Fernandez



Results: Studies differed widely in vitamin D deficiency criteria, methods of measurement and outcomes. However, prevalence of maternal and neonatal hypovitaminosis D was up to 90%. Predictors of maternal hypovitaminosis D were dark skin phototype, race and sartorial habits. Only a few pregnant women met the recommended dietary daily intake of calcium and vitamin D. Vitamin D supplementation was not a common practice.

Study	Supplementation	25(OH)D Maternal	25(OH)D Neonatal
Pehlivan (TUR) 2003	None	25(OH)D ₃ (nmol/l): 17.5 ± 10.3	n/a
Nicolaidou (GRE) 2006	On vit D supl: None On Ca supl 87%	25(OH)D (ng/ml): 16.4 (11-21.1)	20.4 (13.9-30.4) ng/ml
Diaz-Gomez (ESP) 2007	On vit D supl: None On Ca supl (mg/d): Sm 54.8%: 482 ± 101 NSm 55.2%: 484 ± 89 (p=0.95)	25(OH)D (ng/ml): 30-32 gw: NSm 30.9 ± 14.1; Sm 27.1 ± 7.6 38-40 gw: NSm 29.9 ± 11.6; Sm 23.9 ± 8.7 NSm vs Sm p=0.23; gw groups p=0.58	NSm: 22.3 ± 11.3 Sm: 14.2 ± 6.2 p=0.009
Gaggero (ITA) 2010	None	25(OH)D ₃ (ng/ml): mdn (IQR) De: 3.25(2.21-5.75) Bk; 5.75(4.8-10.5)Wh	De: 2.5 (1.5-3.88) Bk; 4.0 (2.5-9.75) Wh
Fernandez-Alonso (SPN) 2011	None	25(OH)D (ng/ml): mdn 27.4 (IQR12.1) 36.3% Suf, 40.6% inSuf, 23.2% Def	n/a
Halicioglu (TUR) 2011	During 3 rd 3er: On Mvit: 146; No Mvit: 109	25(OH)D ₃ (ng/ml): 11.5 ± 5.4, 0.4% Suf, 9.3% inSuf, 90.3% Def	11.5 ± 6.8 ng/ml 2.3% Suf, 7.4% inSuf, 90.3% def
Haliloglu (TUR) 2011	400 IU/d vitD	25(OH)D ₃ (ng/ml): 1 st 3er: 19.11 ± 7.35; 2 nd 3er: 15.69 ± 7.18; 3 rd 3er: 11.10 ± 8.96; pp: 6.97 ± 4.52; NPrg Cnt: 10.75 ± 7.0;	n/a
Perez-Lopez (ESP) 2011	None	25(OH)D (ng/ml): 27.4 (20.9-32.8), 35.9% Suf, 41.4% inSuf, 22.7% Def	n/a
Ustuner (TUR) 2011	500 IU vit D + 125 mg Ca/d (17.7% of Prg)	25(OH)D (ng/ml): 12.0 ± 7.2, < 32: 97.5%, >32: 2.5%	n/a
Fernandez-Alonso (ESP) 2012	None	25(OH)D ₃ (ng/ml): mdn (IQR) 1 st 3er: 27.6 (9.9), 3 rd 3er: 18.2(8.8) 35.6% Suf, 41.0% inSuf, 23.4% Def	n/a
Perez-Ferre (ESP) 2012	200 IU/d	25(OH)D (ng/ml): 18.9 (11.5-24.7), 157 def (59%); [<10: 44 (16.5%), 10-20: 84 (31.6%), 20-30: 84 (31.6%), >30: 25(9.4%)]	n/a
Cadario (ITA) 2013	< 400 IU vit D/d	n/a	21.4 ± 11 ng/ml, 33.3% Mi def, 22.2% Se Def
Fares (TUN) 2013	None	n/a	VLBW: 21.9 ± 15.3nmol/l; Def 65.2% f-t: 29.8 ± 15.2nmol/l; Def 40.4%
Karras (GRE) 2013	On Ca: 36, On vit D: None	25(OH)D (ng/ml): 17.9 ± 13.2	15.9 ± 13.6 ng/ml
Parildar (TUR) 2013	None	25(OH)D (ng/ml): 19.5 ± 9.3 (n=25) Def (Prg) vs 22.9 ± 10.0 (n=28) def (NPrg Cnt)	n/a

Suf: sufficiency; InSuf: insufficiency; Def: deficiency; mdn: median; gw: gestational week; Prg: pregnant; NPrg: non-pregnant; Sm: Smokers; NSm: Non Smokers; Prg: pregnant; NPrg: non-pregnant; cnt: controls; VLBW: very low birth weight; n/a: not available

Conclusions: Hypovitaminosis D during pregnancy is prevalent in the Mediterranean region. Racial, social and cultural habits as well as the absence of preventive strategies seem to negate the benefits of sun exposure.

