



臺北市立萬芳醫院 - 委託財團法人臺北醫學大學辦理
Taipei Municipal Wanfang Hospital (Managed by Taipei Medical University)

Vitamin D deficiency in patients with urticarial: a systematic review and meta-analysis

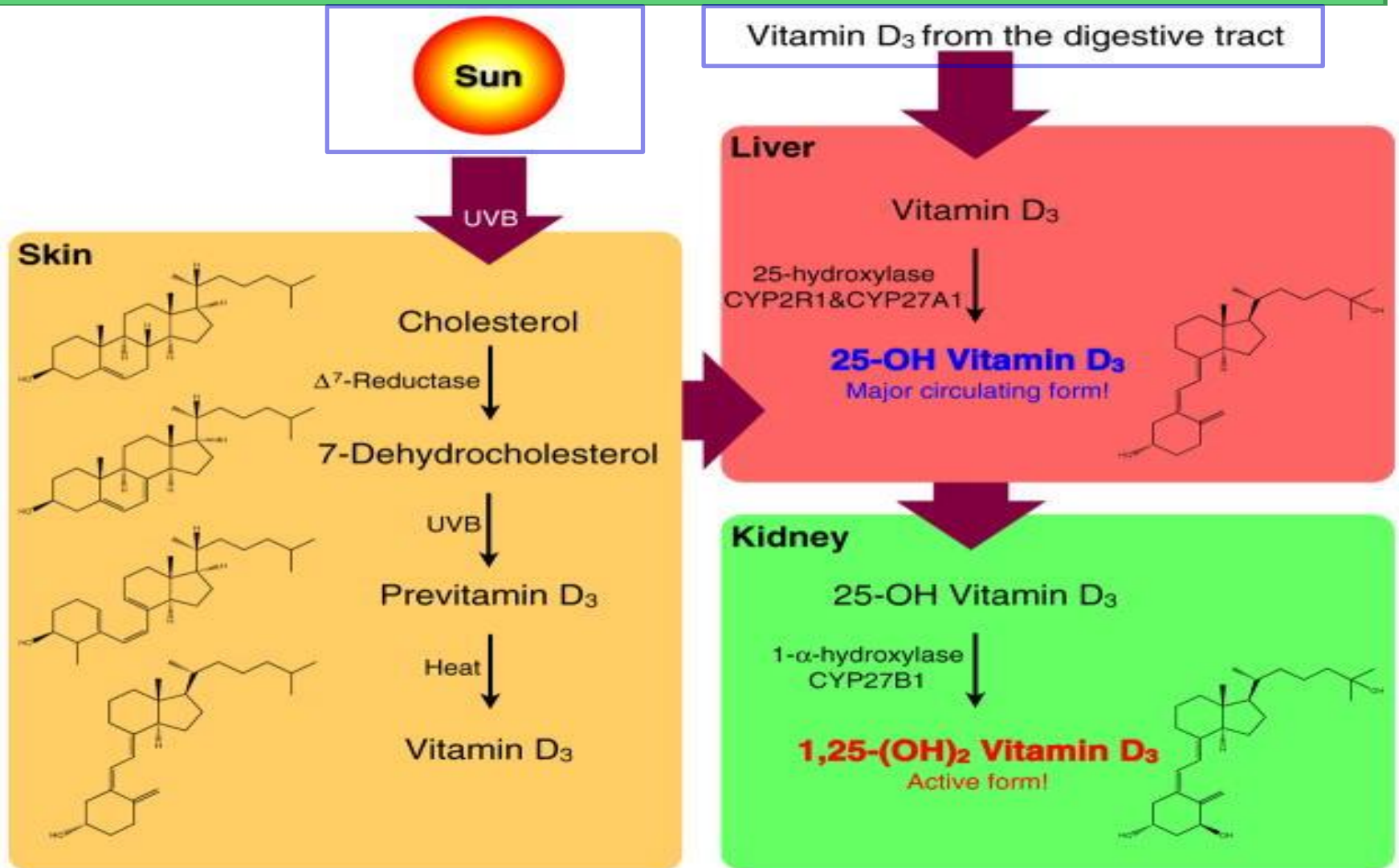
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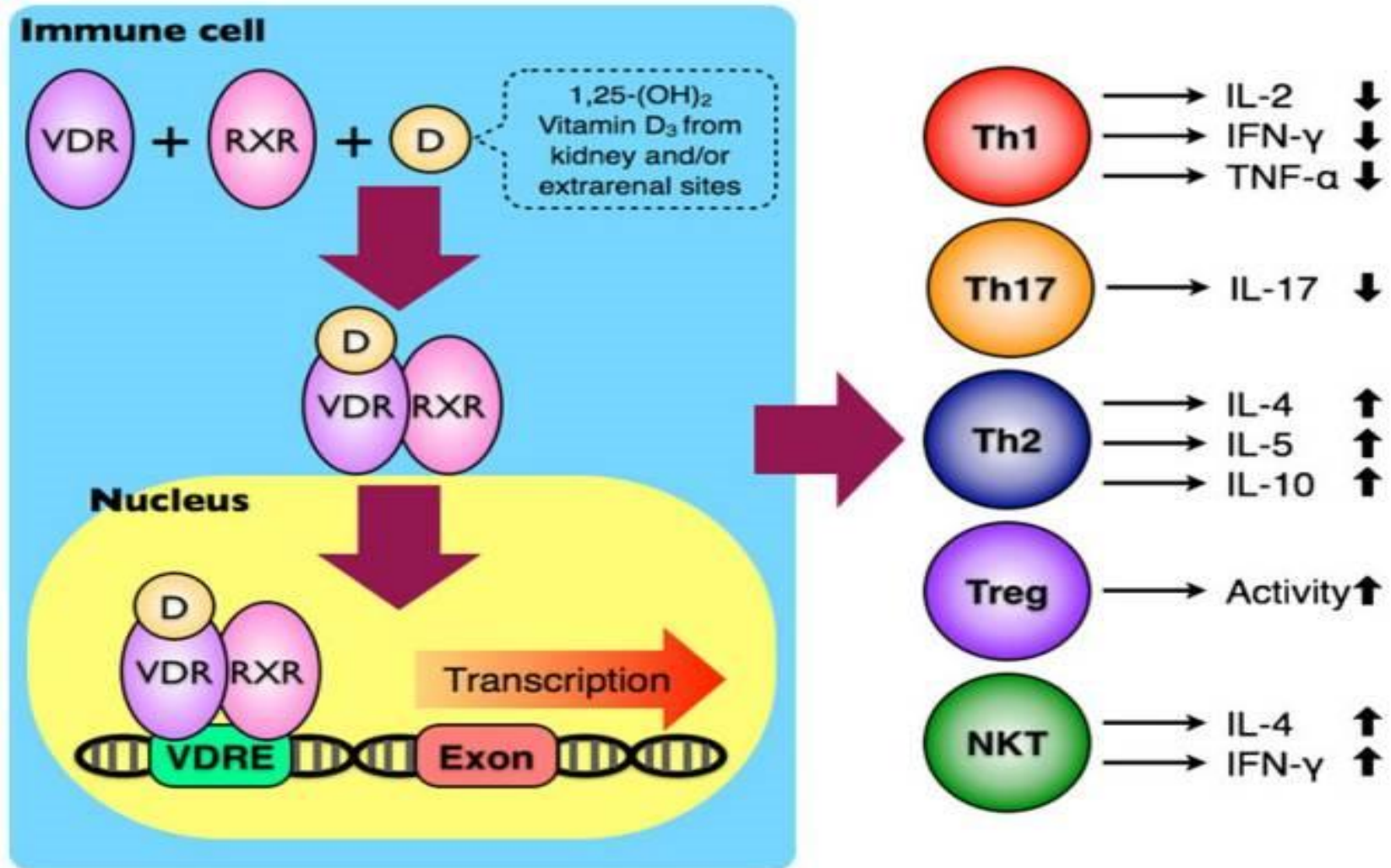
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Vitamin D metabolism



Immunomodulatory functions of vitamin D



Vitamin D

Vitamin D deficiency

25(OH)D3

- < 20 deficiency
- 20-29 insufficiency
- > 30 sufficiency

Association disease

Atopic dermatitis

[Kim et al., 2017](#)

Vitiligo

[Upala et al., 2016](#)

Alopecia areata

[Tsai et al., 2017](#)

Psoriasis

[Lee et al., 2018](#)



Urticaria

Acute

< 6 weeks

Allergy

Chronic

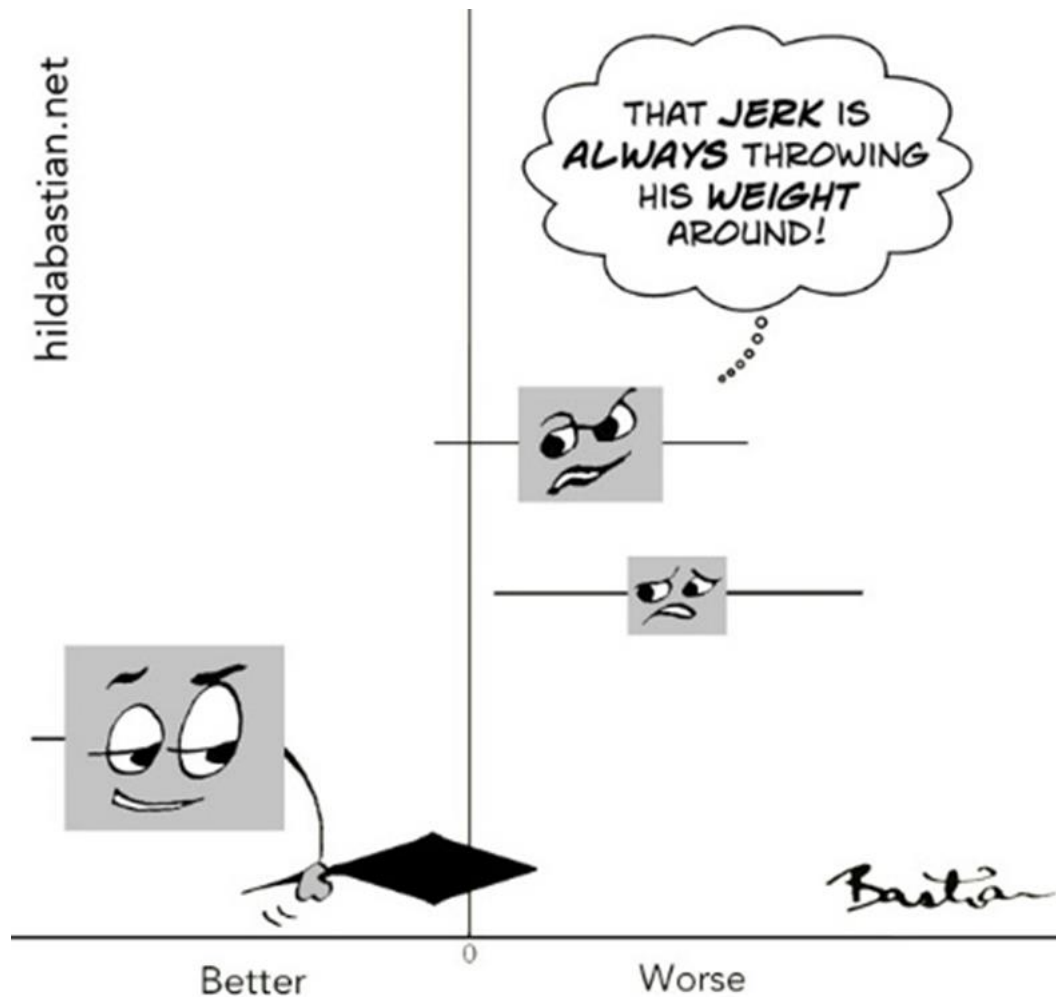
> 6 weeks

Autoimmune

Kolkhir et al., 2017



Controversy





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Meta-analysis

METHOD



Search

- PubMed, Cochrane Library, and Embase
- “Vitamin D” and “Urticaria”
- Before Nov 30, 2017
- English

Criteria

- Case-control studies
- Providing level of vitamin D or prevalence of vitamin D deficiency

Outcome

- Urticaria vs control
- Comparing prevalence of vitamin D deficiency
- Comparing level of vitamin D



Quality assessment

- Newcastle–Ottawa Scale for case-control studies
- Maximum 9 points

Data extraction

- Definition of vitamin D deficiency
- Prevalence of vitamin D deficiency
- Level of vitamin D

Data analysis

- Odds ratio or standardized mean difference
- Subgroup analysis
- CMA 3.0





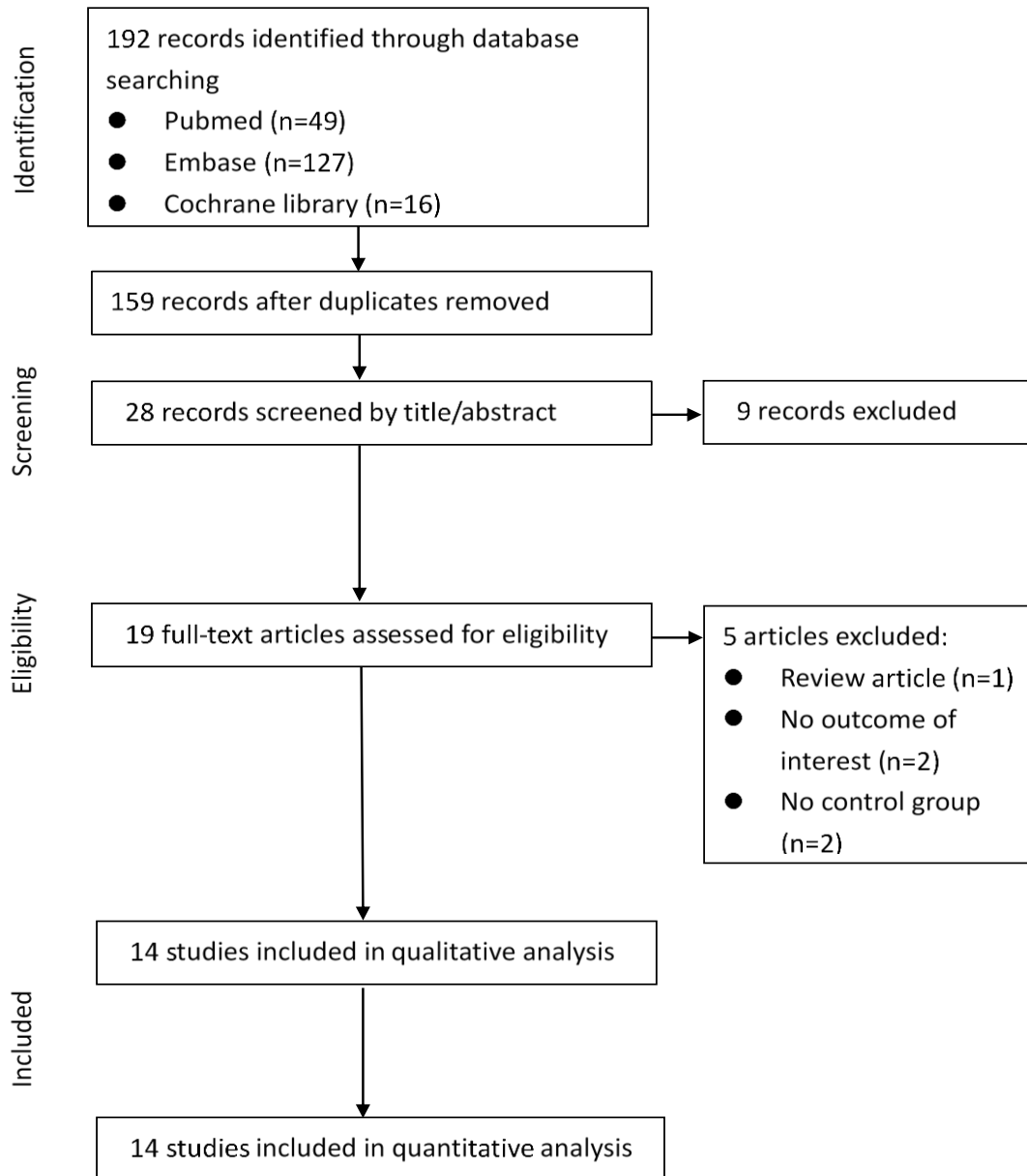
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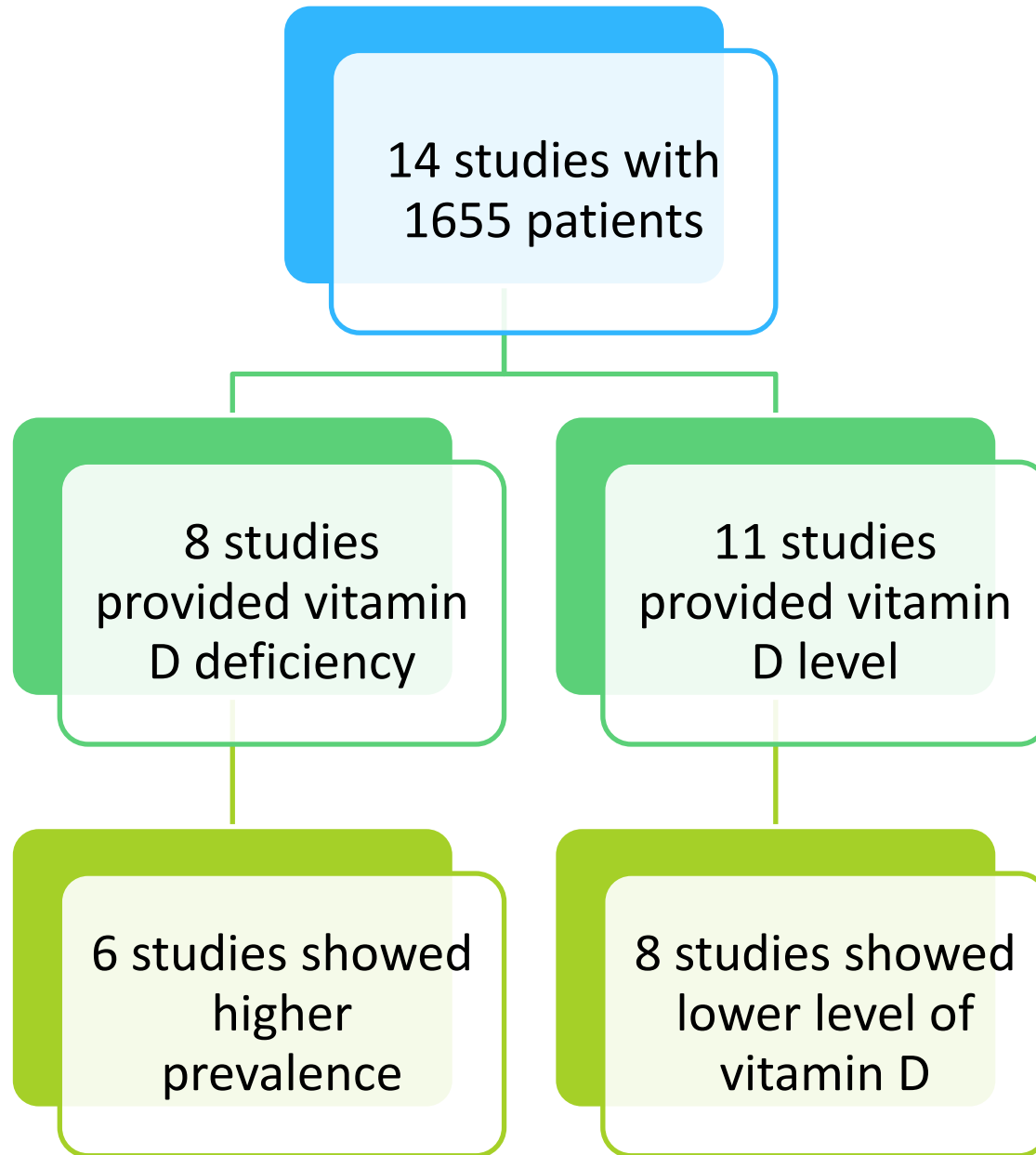
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Meta-analysis

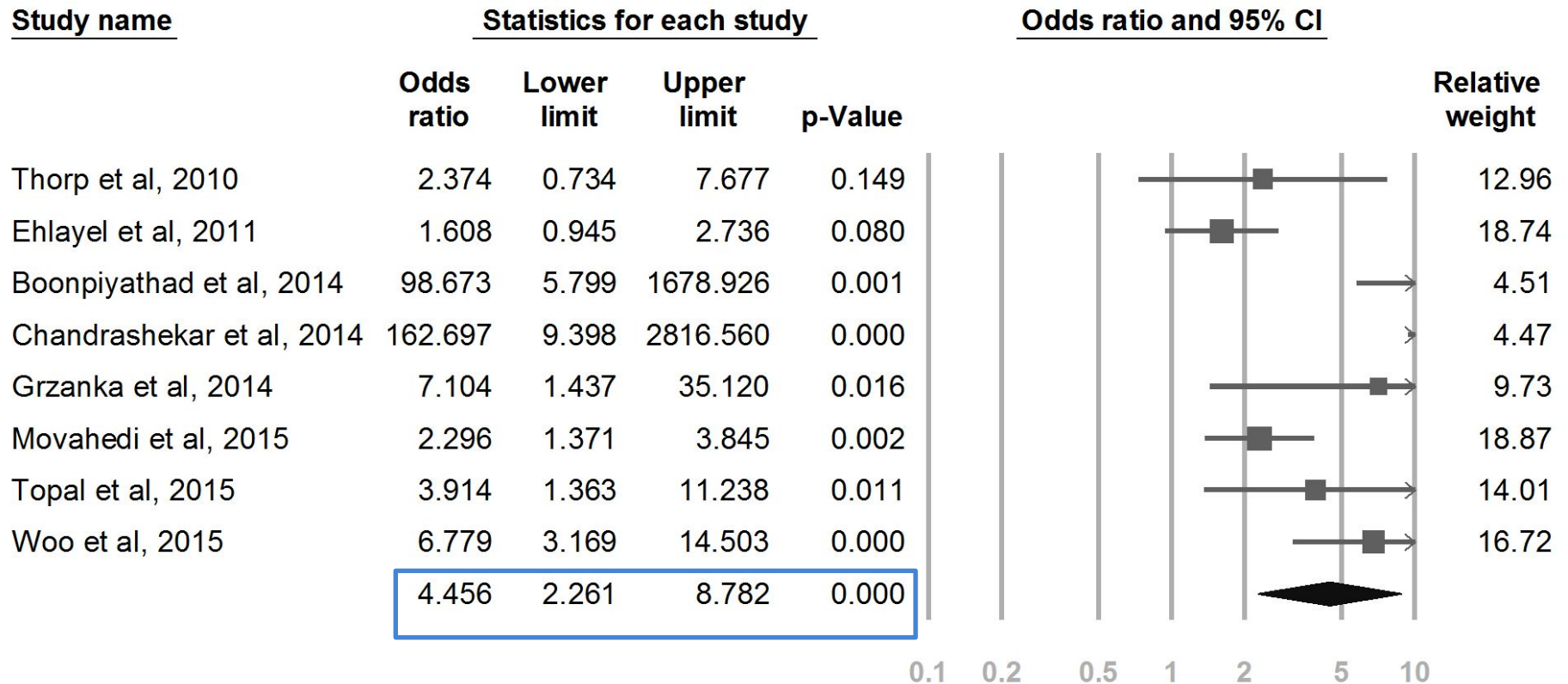
RESULTS







Vitamin D deficiency prevalence



OR: 4.456, 95%CI:2.261—8.782, p<0.001

Control

Urticaria

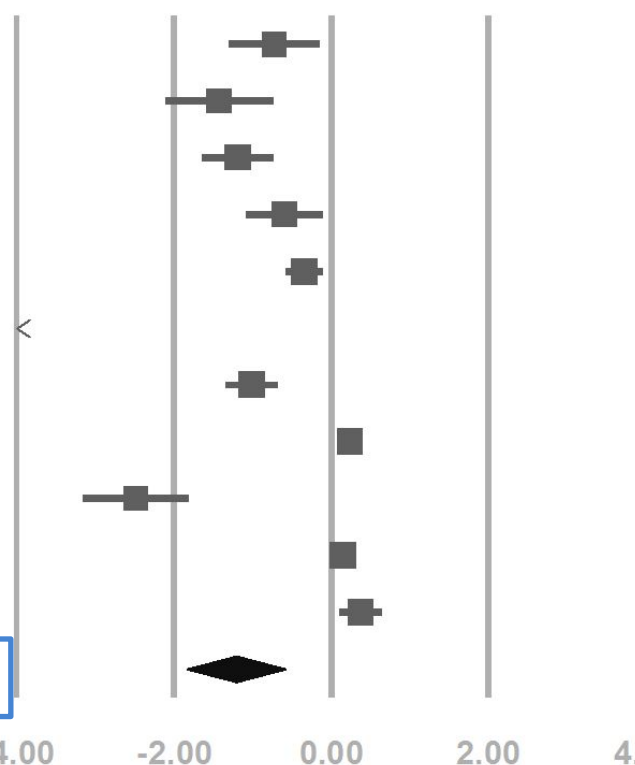


Level of vitamin D

Study name

Statistics for each study

Std diff in means and 95% CI

	Std diff in means	Lower limit	Upper limit	p-Value		Relative weight
Thorp et al, 2010	-0.725	-1.297	-0.153	0.013		8.83
Abdel-Rehim et al, 2014	-1.426	-2.104	-0.748	0.000		8.57
Chandrashekar et al, 2014	-1.192	-1.640	-0.743	0.000		9.10
Grzanka et al, 2014	-0.594	-1.080	-0.108	0.017		9.02
Movahedi et al, 2015	-0.342	-0.577	-0.108	0.004		9.42
Rasool et al, 2015	-6.802	-7.416	-6.188	0.000		8.73
Woo et al, 2015	-1.014	-1.337	-0.691	0.000		9.31
Wu et al, 2015	0.238	0.097	0.380	0.001		9.50
Ozdemir et al, 2016	-2.486	-3.160	-1.813	0.000		8.58
Lee et al, 2017	0.141	0.055	0.227	0.001		9.53
Nasiri-Kalmarzi et al, 2017	0.372	0.106	0.639	0.006		9.39
	-1.211	-1.832	-0.591	0.000		

SMD: -1.211, 95%CI:-1.832— -0.591, p<0.001

Urticaria

Control

Subgroup analysis (I)

Acute urticaria

- **Prevalence (2 studies)**
- OR = 3.031, 95% CI = 0.706 to 13.022
- **Level (3 studies)**
- SMD = -1.009, 95% CI = -2.314 to 0.296

Chronic urticaria

- **Prevalence (7 studies)**
- OR = 5.723, 95% CI = 2.617 to 12.516
- **Level (9 studies)**
- SMD = -1.067, 95% CI = -1.865 to -0.268



Subgroup analysis (II)

Pediatric

- **Level (3 studies)**
- SMD = -1.151, 95% CI = -3.725 to 1.424

Adult

- **Prevalence (4 studies)**
- OR = 15.717, 95% CI = 2.392-103.252
- **Level (6 studies)**
- SMD = -1.741, 95% CI = -3.472 to -0.010



Chronic urticaria

Adult urticaria

Lower level of Vitamin D
Higher prevalence of
vitamin D deficiency

Acute urticaria

Pediatric urticaria





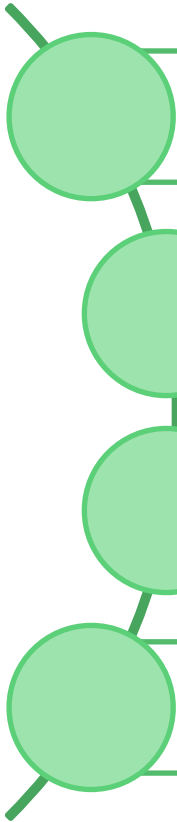
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DISCUSSION



Immunomodulatory functions of vitamin D



Repress IgE-mediated mast cell activation

Yip et al., 2014

Enhances T regulatory cells → Suppression of pro-allergic and autoimmune responses

Vassallo et al., 2010; Hewison et al., 2012

Suppress TH 1 cytokine secretion and enhances TH2 cytokine secretion → Inhibiting Th1-mediated autoimmune diseases

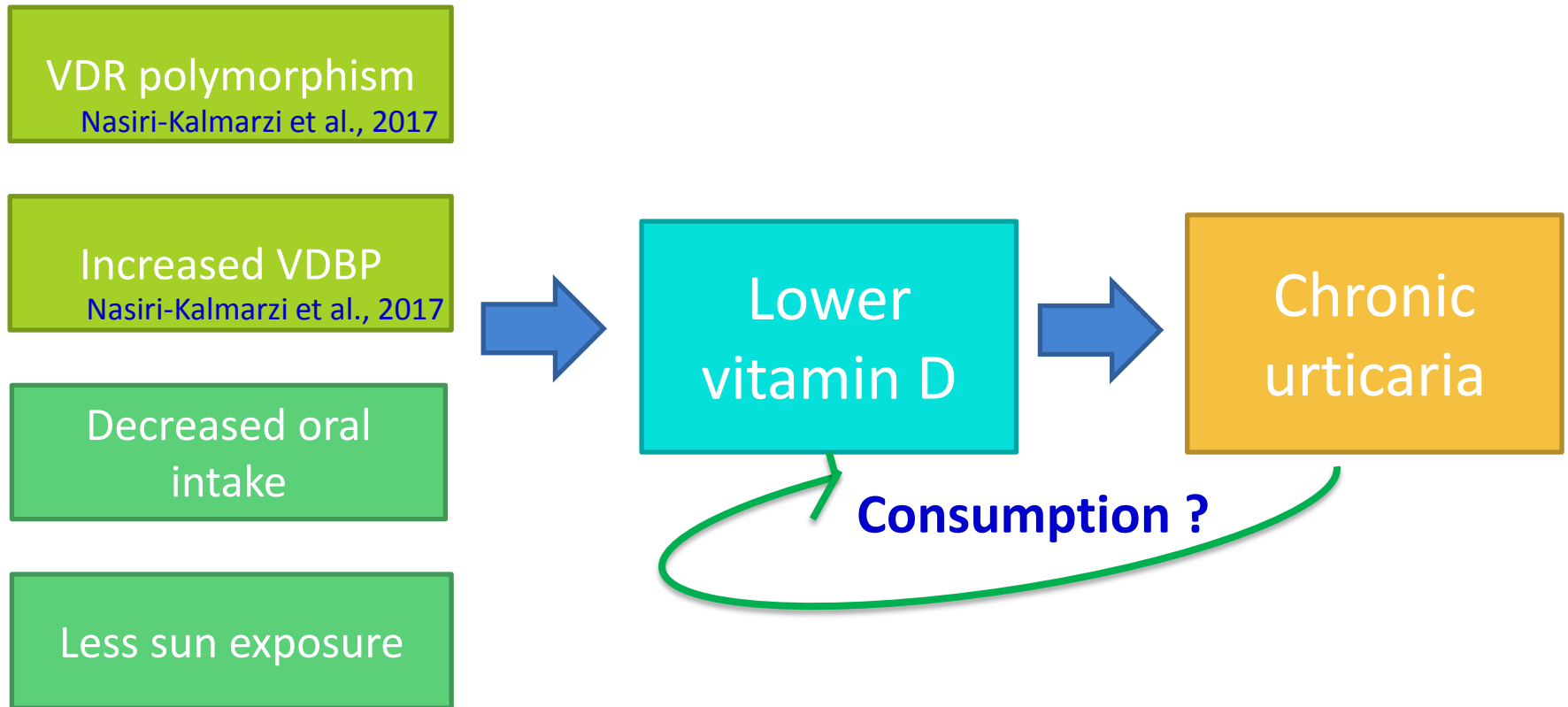
Hewison et al., 2012

Suppresses TH17 cells → Decrease triggering autoimmune diseases

Hewison et al., 2012



Lower vitamin D, The cause or consequence of chronic urticaria?



Limitation

Study heterogeneity

- Different definition
- Serum 25-hydroxyvitamin D is subject to many factors
 - Ethnicity, latitude, comorbidity, sun exposure level, and diet





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HOW ABOUT SUPPLEMENTATION OF VITAMIN D?



Case series

Goetz et al., 2011

- 63 patients, 57 vitamin D <32ng/ml
- 50000 IU/W for 8-12 weeks
- 40/75 (70%) complete resolution

Topal et al., 2015

- 58 patients, 56 vitamin D < 30 ng/ml
- 75000 IU/W for 12 weeks
- Significant improvements in UAS4 and CU-Q2oL scores

Ariaee et al., 2017

- 20 patients with vitamin D < 10ng/ml
- 50000 IU/W for 8 weeks
- USS significantly improved



Comparative studies

Boonpiyathad
et al., 2011

- 46 (< 30ng /ml) vs 14 (>30ng/ml)
- 140000IU/W for 6 weeks
- More improvement UAS7 and DLQI in supplement group

Rorie et al.,
2014

- 21 vs 21 patients RCT
- All with cetirizine, ranitidine, and montelukast. Add on 4000 IU/D vs 600 IU/D for 12 weeks
- USS with a trend of improvement

Rasool et al.,
2015

- 42 patients (H+S) vs 57 (D+H+S) RCT
- 60000 IU/W for 6 weeks
- Significantly more improvements in 5D score and VAS in supplement group



Take home message

Vitamin D deficiency in urticaria

- In chronic urticaria and adult urticaria
- Need more studies for acute or pediatric urticaria

Vitamin D supplementation for urticaria

- RCT for the therapeutic effect and optimal dosage





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Thanks for your listening

