



Ruprecht-Karls-Universität Heidelberg



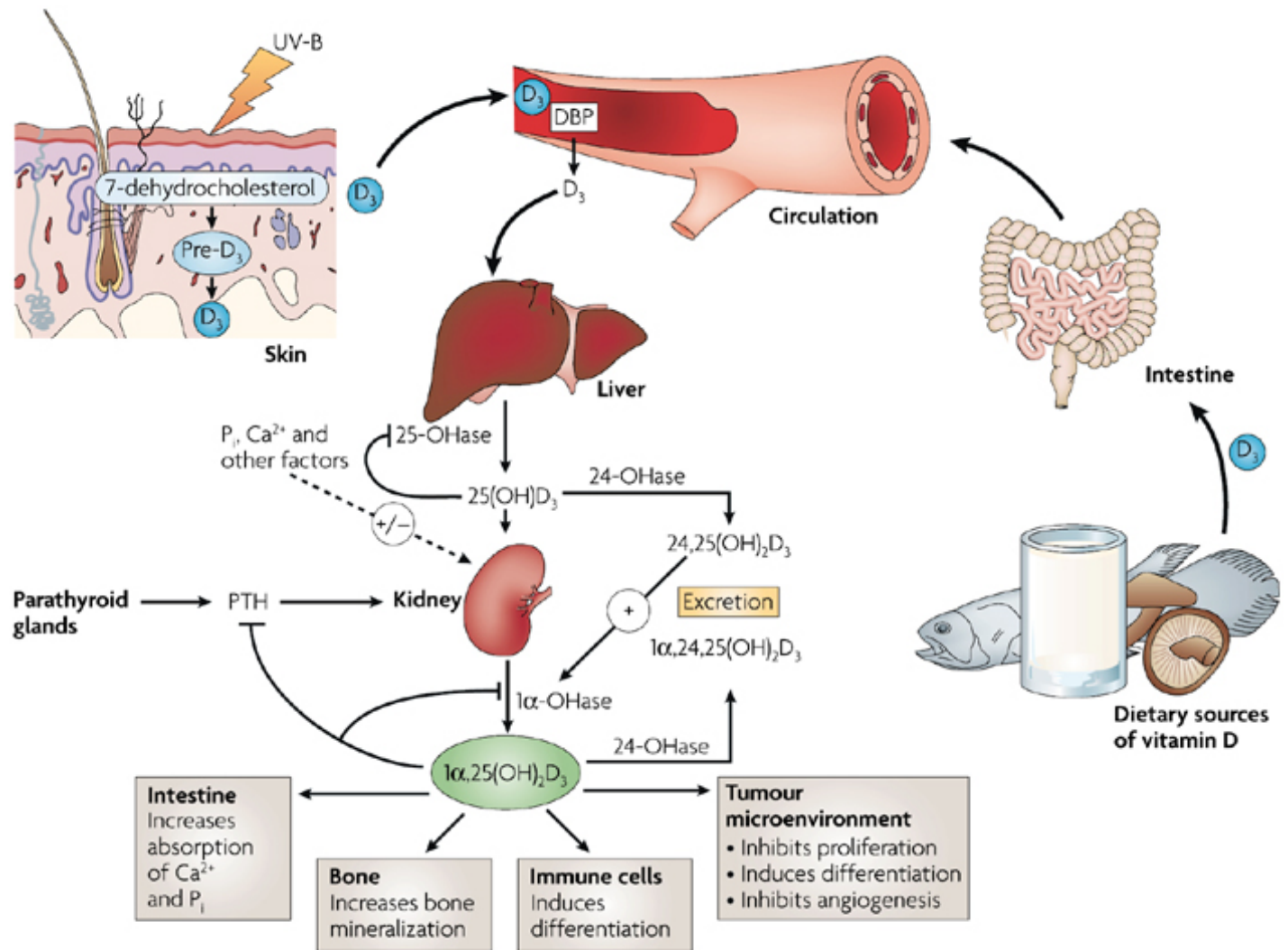
# Vitamin D in der Schwangerschaft

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*Central South University, Changsha, China*

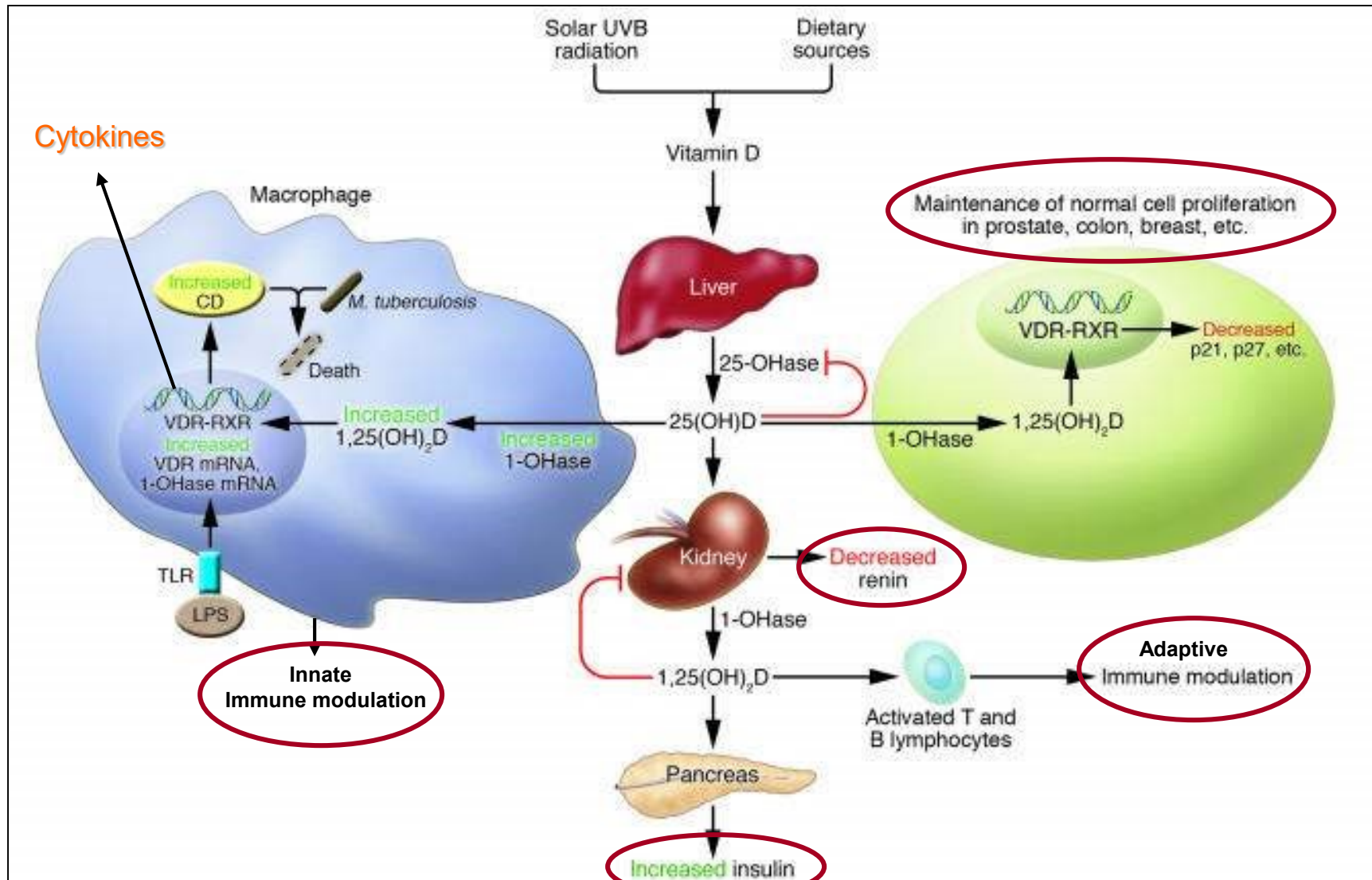




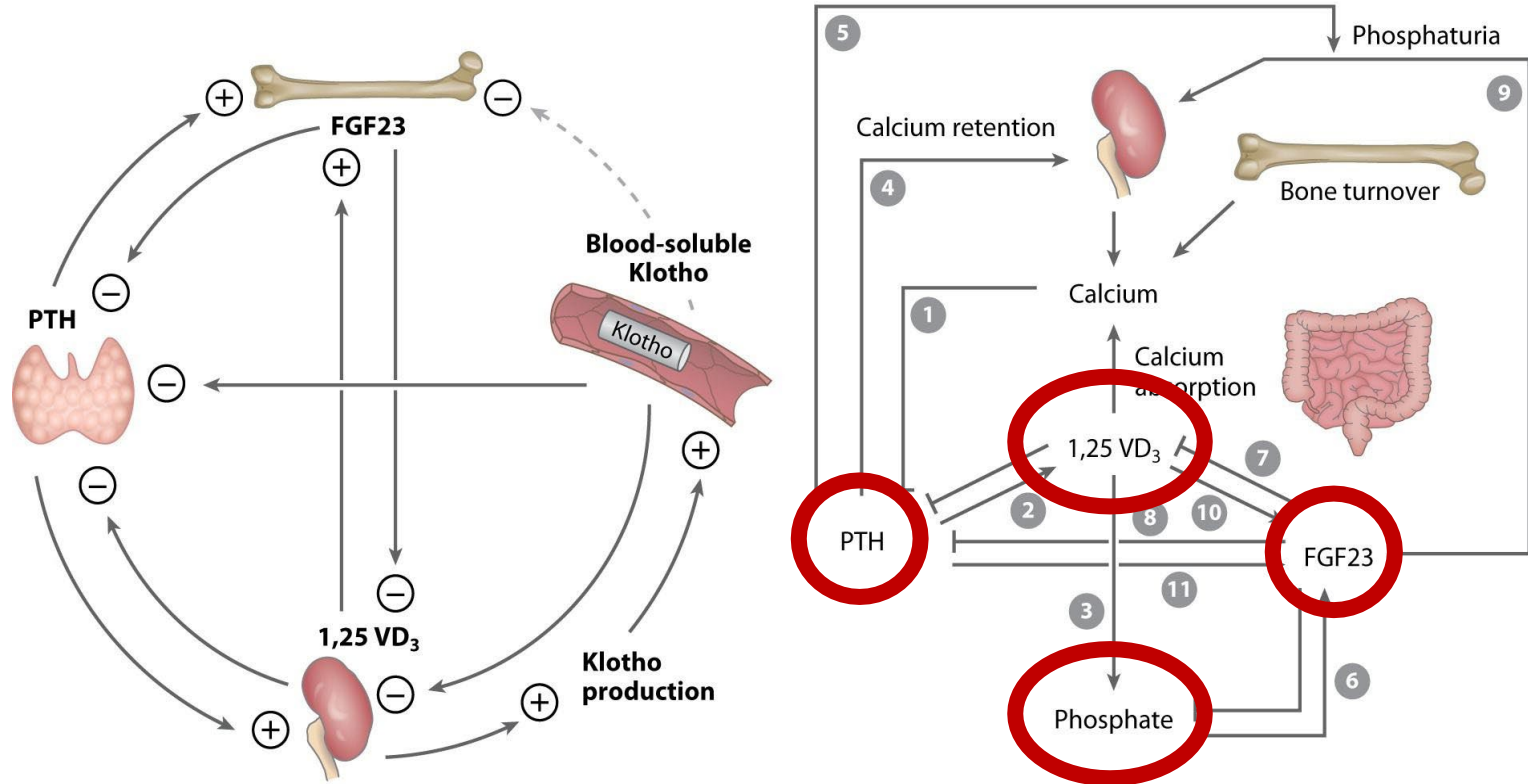
Nature Reviews | Cancer

Deeb, K. K., Trump, D. L., & Johnson, C. S. (2007). *Nature Reviews Cancer*, 7(9), 684–700. doi:10.1038/nrc2196

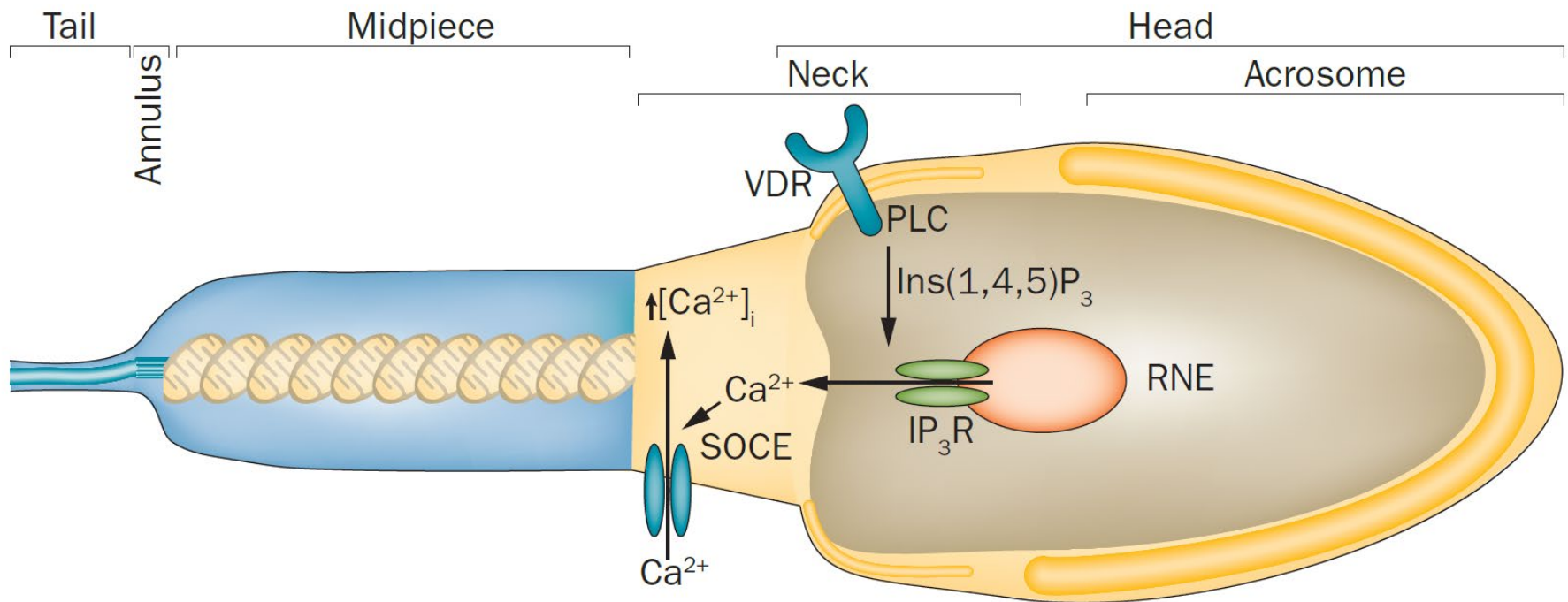
# Noncalcemic Functions of 1,25-dihydroxyvitamin D



# Vitamin D System und Ca/P- Stoffwechsel



Hu MC et al. *Ann Rev Physiol* 2013  
 Hu MC et al. *Ann Rev Physiol* 2013

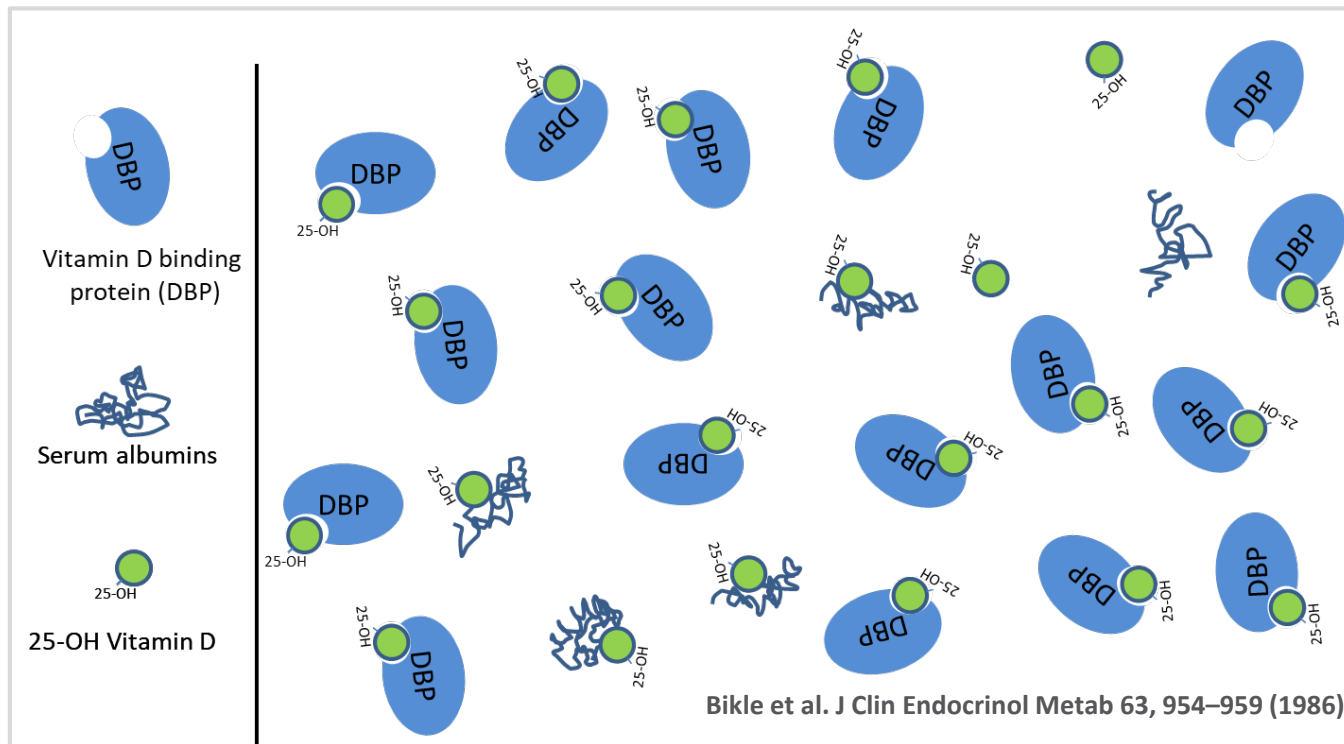


Möglicher Mechanismus für die **nichtgenomische** Wirkung von VDR in menschlichen Spermatozoen.

**1 $\alpha$ ,25-Dihydroxyvitamin D3** aktiviert membranständige VDR in der Halsregion, was eine PLC-Aktivierung und die Erzeugung von IP<sub>3</sub>-Produktion auslöst, die anschließend IP<sub>3</sub>R-gesteuerte Kalziumkanäle in der RNE öffnet und die intrazelluläre Ca<sup>2+</sup>-Konzentration erhöht. Die anfängliche Ca<sup>2+</sup>-Freisetzung aus RNE könnte durch SOCE unterstützt werden, doch scheint dies nicht über Kanäle vom Typ I- zu erfolgen, da Nifedipin nicht in der Lage ist, den durch 1 $\alpha$ ,25-Dihydroxyvitamin D3 vermittelten Anstieg von [Ca<sup>2+</sup>]<sub>i</sub> zu beeinflussen.

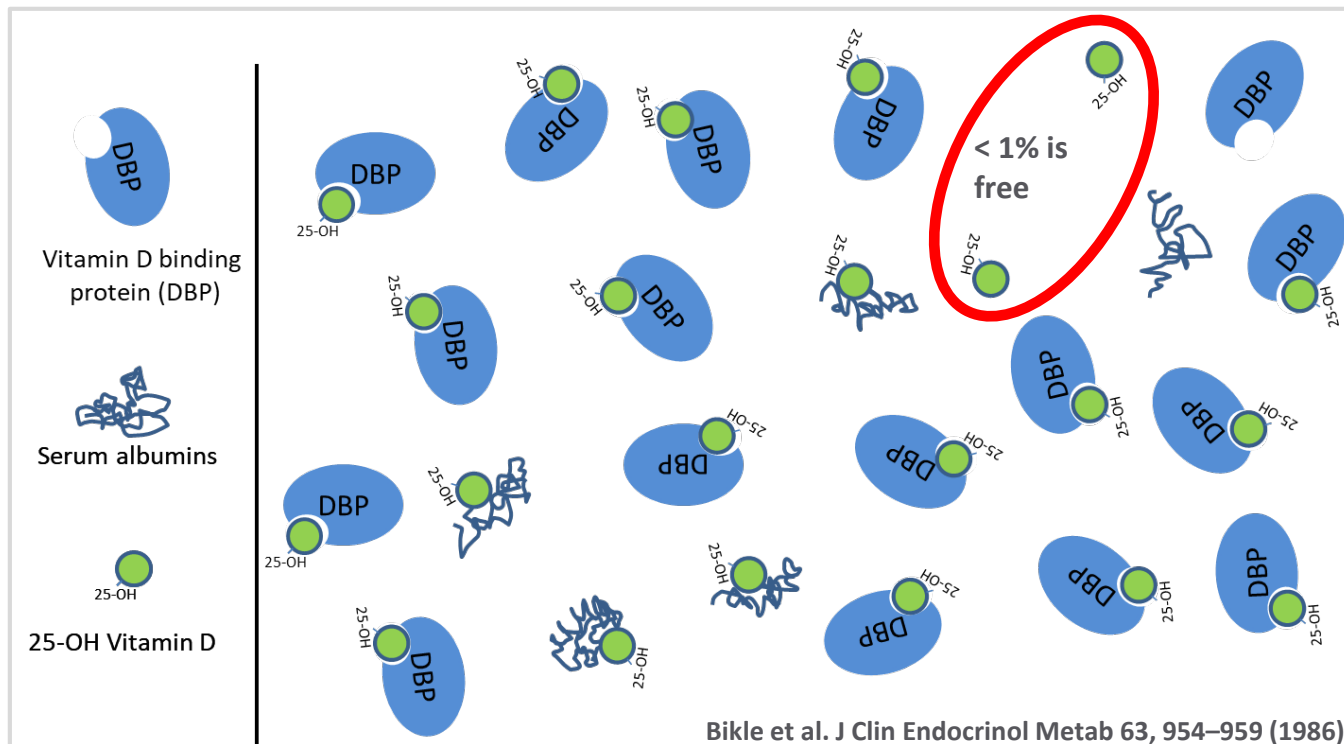
# Vitamin D Serum Isoforms

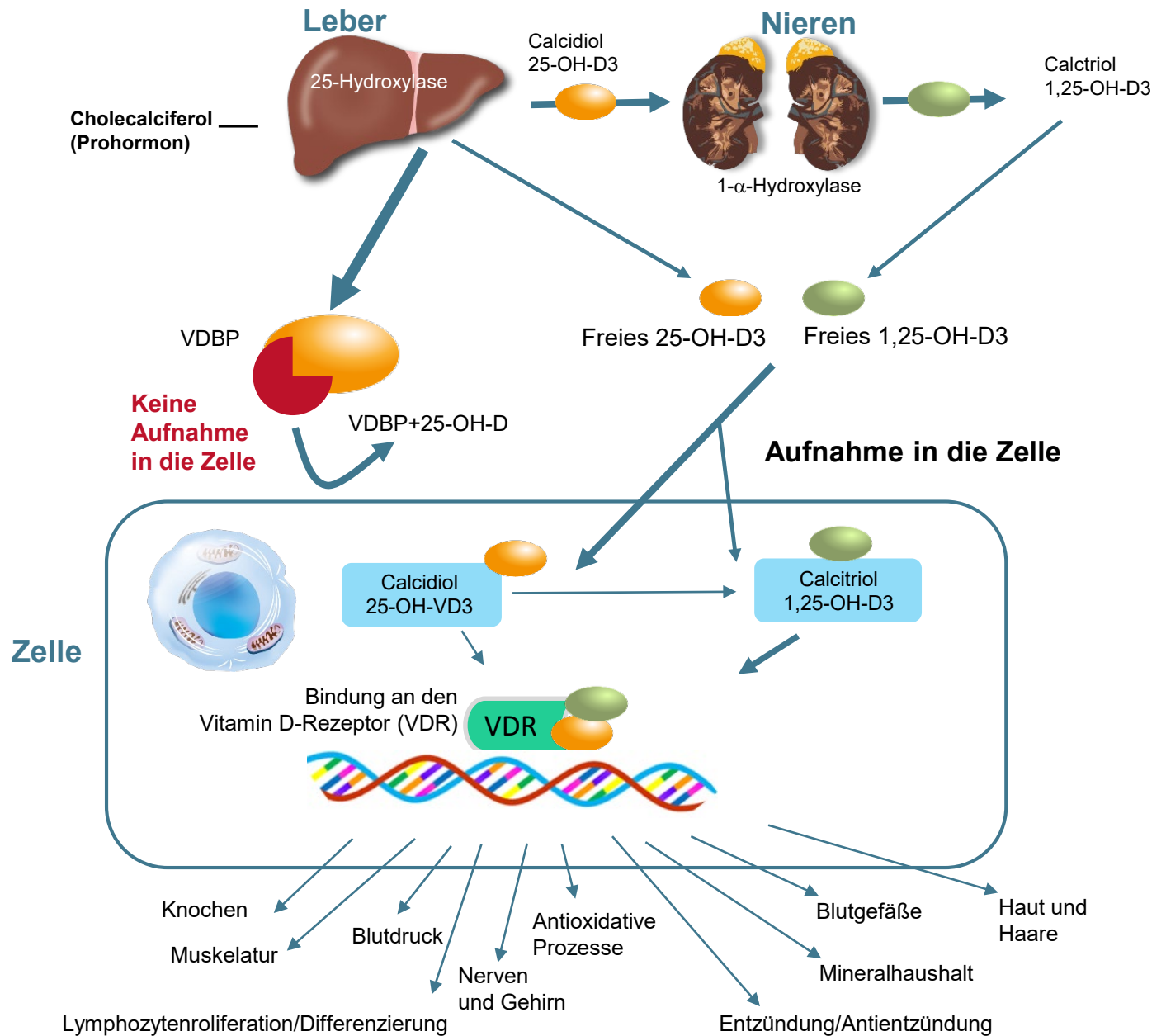
Der größte Anteil (ca. 85-90%) von 25 (OH)Vitamin D ist an VDBP gebunden, ungefähr 10–15% an Serumalbumine, während freies 25 (OH) Vitamin D nur weniger als 1% ausmacht.



# Vitamin D Serum Isoforms

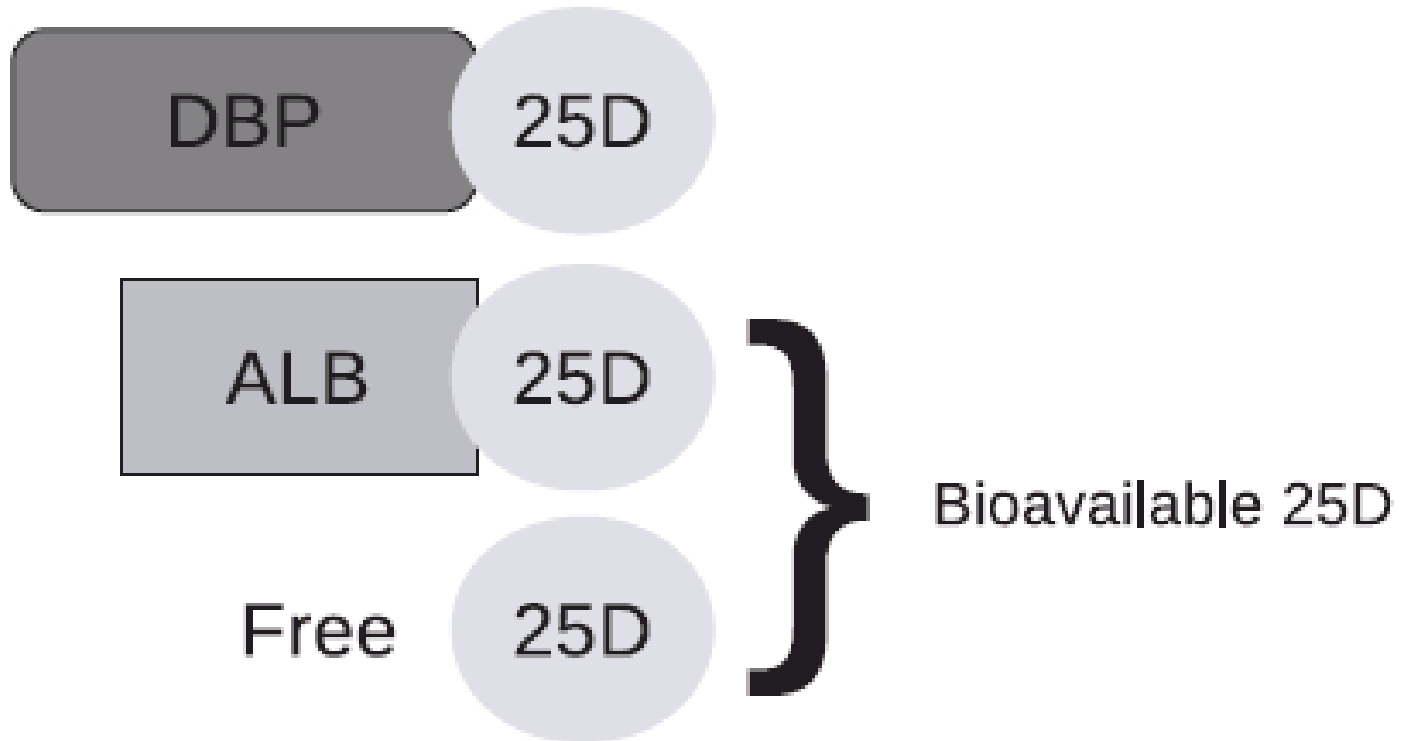
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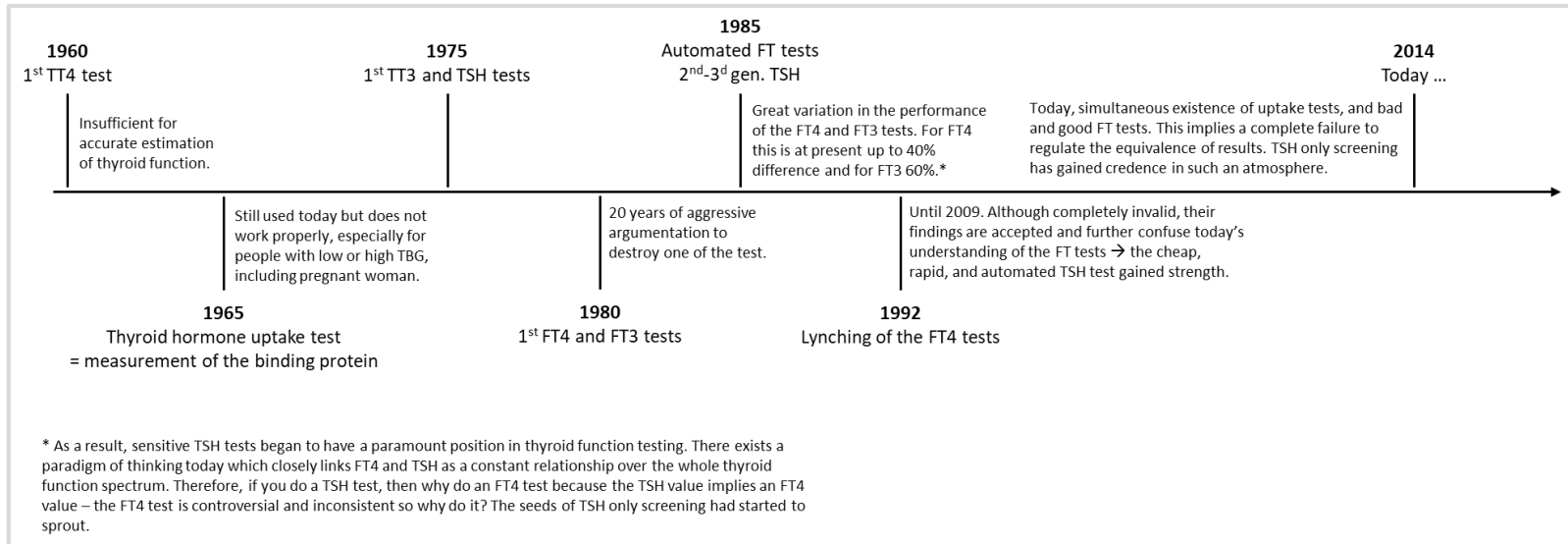




**Total 25D =**

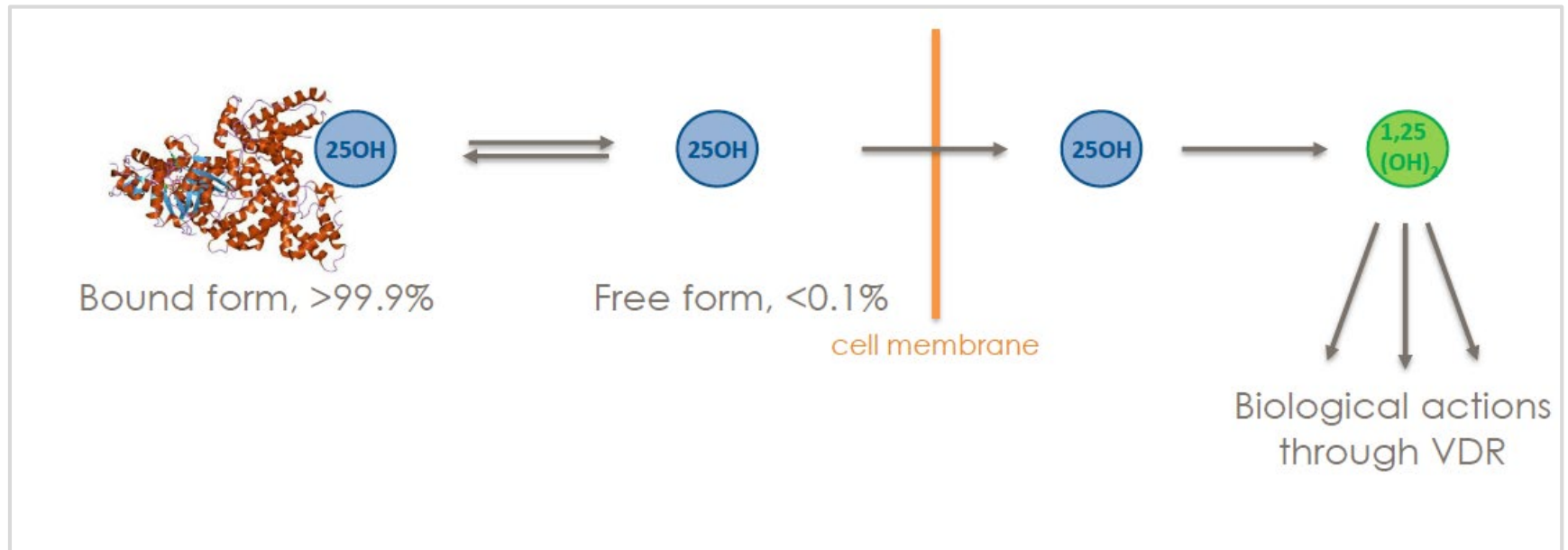


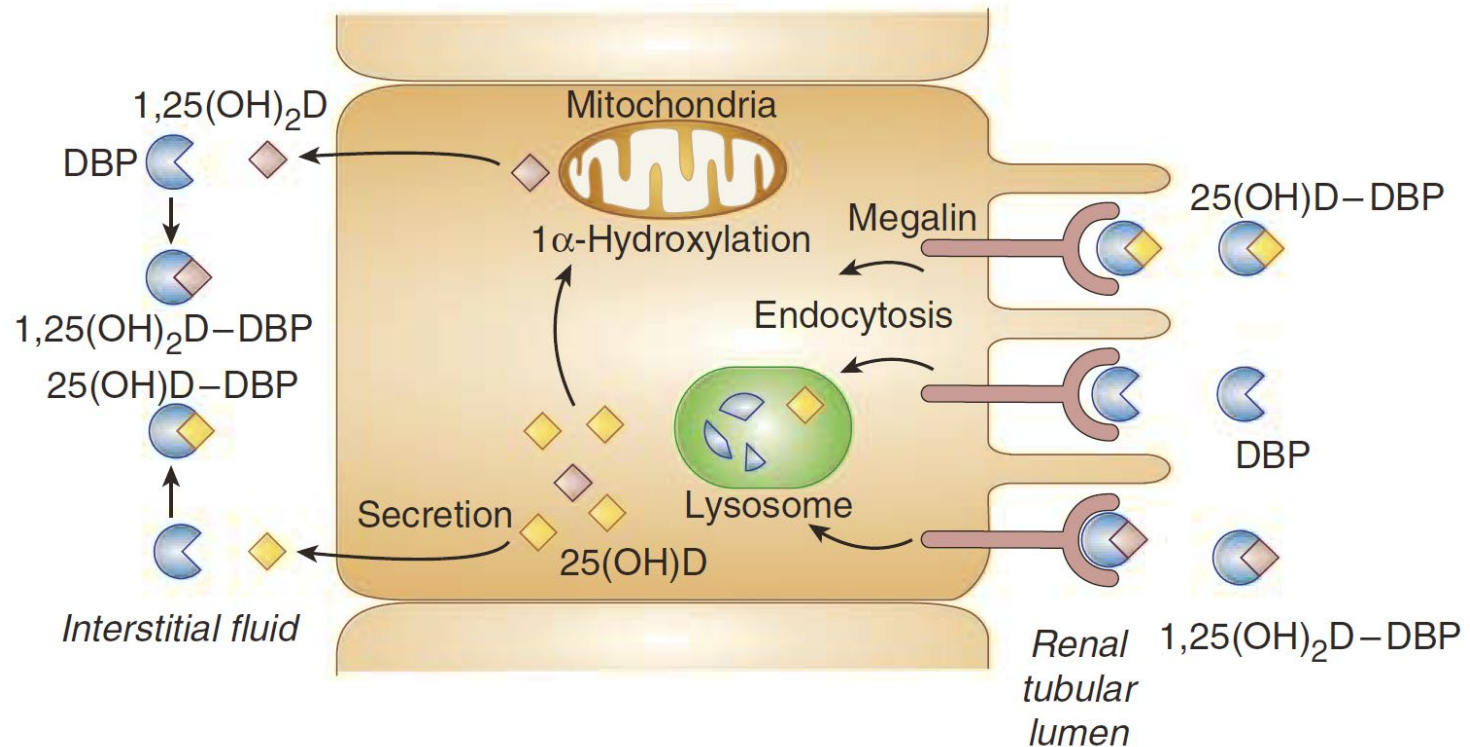
# T3 / T4



## ... und Vitamin D?

# Nur freies Vitamin D kann die Zellmembran passieren





Megalin-vermittelte 25 (OH) Vitamin D- oder 1,25 (OH)<sub>2</sub> Vitamin D-Aufnahme findet man hauptsächlich **in den prox. Tubuli der Niere, der Plazenta und der Nebenschilddrüse.** Anderen Gewebe nehmen nur freies 25 (OH) Vitamin D über die Zellmembran auf.

Variable, units	Free 25(OH)D, pg/mL	Total 25(OH)D, ng/mL
BSAP, µg/mL	-0.203, p<0.001	-0.108, p=0.038
LDL, mg/dL	-0.191, p<0.001	0.033, p=0.539
Free T3, pg/mL	-0.172, p=0.001	-0.114, p=0.029
LDL/HDL ratio	-0.164, p=0.002	-0.076, p=0.154
PTH, pg/mL	-0.138, p=0.008	-0.227, p<0.001
WBC count, 10 <sup>3</sup> /µL	-0.138, p=0.029	0.018, p=0.774
Gestational age, weeks	-0.134, p=0.021	0.081, p=0.165
RDW, %	-0.126, p=0.047	-0.110, p=0.084
DBP, mg/L	-0.121, p=0.022	0.161, p=0.002
Platelet count, 10 <sup>3</sup> /µL	-0.120, p=0.059	-0.093, p=0.145
HDL, mg/dL	-0.032, p=0.546	0.178, p=0.001
Phosphate, U/L	0.012, p=0.820	0.080, p=0.124
MCV, fL	0.036, p=0.567	0.099, p=0.120
Sodium, mmol/L	0.043, p=0.417	0.054, p=0.313
MCHC, g/dL	0.061, p=0.334	0.029, p=0.652
MCH, pg	0.062, p=0.334	0.093, p=0.144
RBC count, 10 <sup>6</sup> /µL	0.065, p=0.302	0.013, p=0.835
TSH, uU/mL	0.084, p=0.108	0.050, p=0.336
Hemoglobin, g/dL	0.105, p=0.079	0.050, p=0.403
Free T4, ng/dL	0.106, p=0.041	-0.071, p=0.176
Hematocrit, %	0.107, p=0.091	0.068, p=0.288
Urea, mg/dL	0.114, p=0.032	0.008, p=0.887
Albumin, g/dL	0.127, p=0.015	-0.088, p=0.092
Calcium, mmol/L	0.141, p=0.007	0.060, p=0.251
Adiponectin, µg/mL	0.142, p=0.008	0.054, p=0.307
Zinc, µmol/L	0.217, p=0.090	0.029, p=0.822
Vitamin B12, pg/mL	0.246, p<0.001	0.099, p=0.062
Vitamin B6, ng/mL	0.246, p<0.001	0.122, p=0.024
Maternal age, years	0.251, p<0.001	0.194, p<0.001

Spearman's rho color gradient
-0.2>rho>-0.3
-0.1>rho>-0.2
0.0>rho>-0.1
0.0<rho<0.1
0.1<rho<0.2
0.2<rho<0.3

## Comparison of Free and Total 25-hydroxyvitamin D in Normal Human Pregnancy

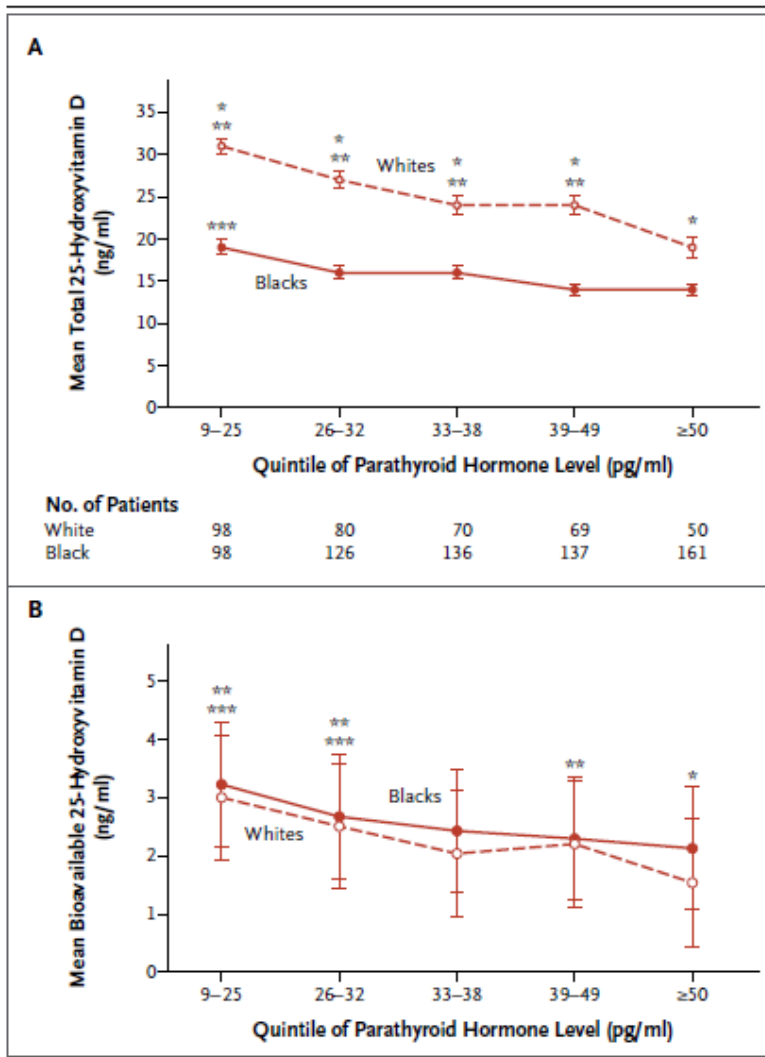
Tsuyprykov O, Buse C, Skoblo R, Haq A, Hoher B.  
J Steroid Biochem Mol Biol. 2019, n pressi

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Vitamin D–Binding Protein and Vitamin D Status of Black Americans and White Americans

Camille E. Powe, M.D., Michele K. Evans, M.D., Julia Wenger, M.P.H.,  
Alan B. Zonderman, Ph.D., Anders H. Berg, M.D., Ph.D., Michael Nalls, Ph.D.,  
Hector Tamez, M.D., M.P.H., Dongsheng Zhang, Ph.D.,  
Ishir Bhan, M.D., M.P.H., S. Ananth Karumanchi, M.D.,  
Neil R. Powe, M.D., M.P.H., M.B.A., and Ravi Thadhani, M.D., M.P.H.



Total and Bioavailable 25-Hydroxyvitamin D Levels among Homozygous Blacks and Whites with Similar Parathyroid Hormone Levels. Within quintiles of parathyroid hormone values, blacks generally had lower levels of total 25-hydroxyvitamin D levels than whites (Panel A) but similar levels of bioavailable 25-hydroxyvitamin D (Panel B). I bars indicate standard.

One asterisk denotes  $P < 0.01$  for the comparisons between blacks and whites within the quintile, two asterisks  $P < 0.01$  for the comparison with the highest quintile among whites, and three asterisks  $P < 0.01$  for the comparison with the highest quintile among blacks.

Powe C. et al. N Engl J Med 2013; 369:1991-2000

## Urinary vitamin D3 metabolites in normal humans and patients with the nephrotic syndrome.

Group	<i>n</i>	25OHD <sub>3</sub> ng/24 hr.	24,25(OH) <sub>2</sub> D <sub>3</sub> ng/24 hr.	1,25(OH) <sub>2</sub> D <sub>3</sub> pg/24 hr.
Normal subjects (mean ± S.D.)	7	10 ± 6	N.D.	N.D.
Nephrotic patients (mean + S.D.)	7	529 ± 149 <sup>a</sup>	23 ± 10	246 ± 104

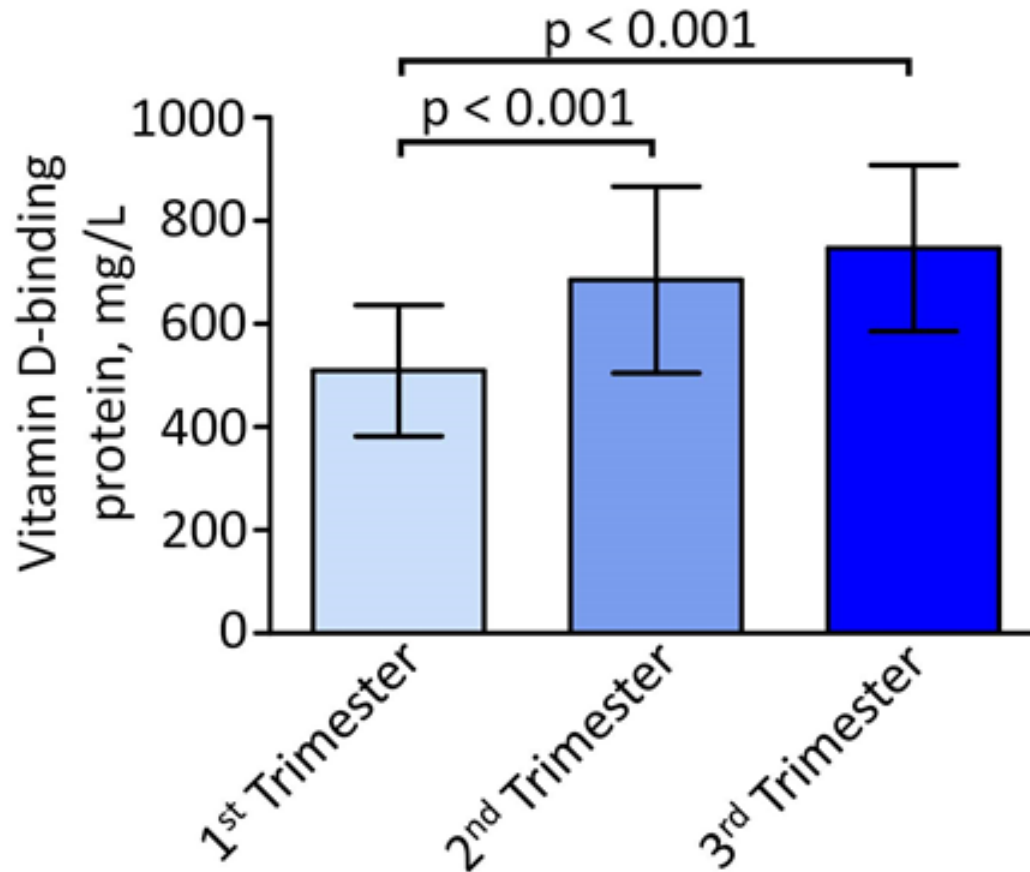
Metab Bone Dis Relat Res. 1982;4(1):7-15. doi:  
10.1016/0221-8747(82)90003-0.



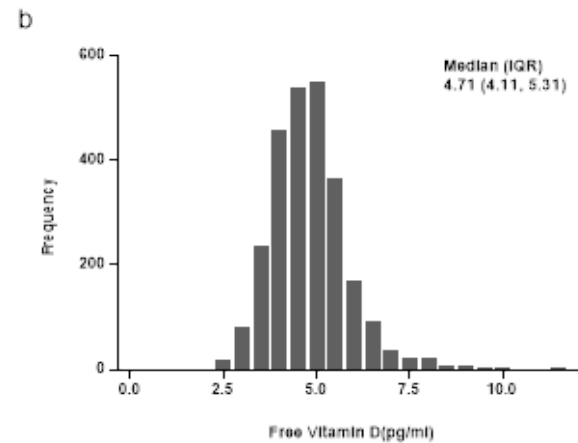
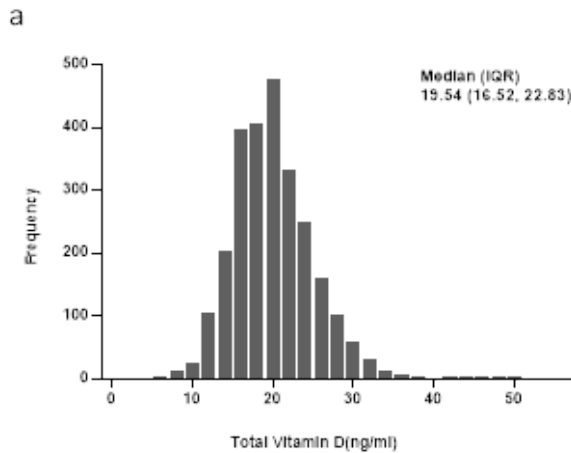
Reference intervals for measured and calculated free 25-hydroxyvitamin D in normal pregnancy.

Tsuprykov O, Buse C, Skoblo R, Haq A, Hocher B.

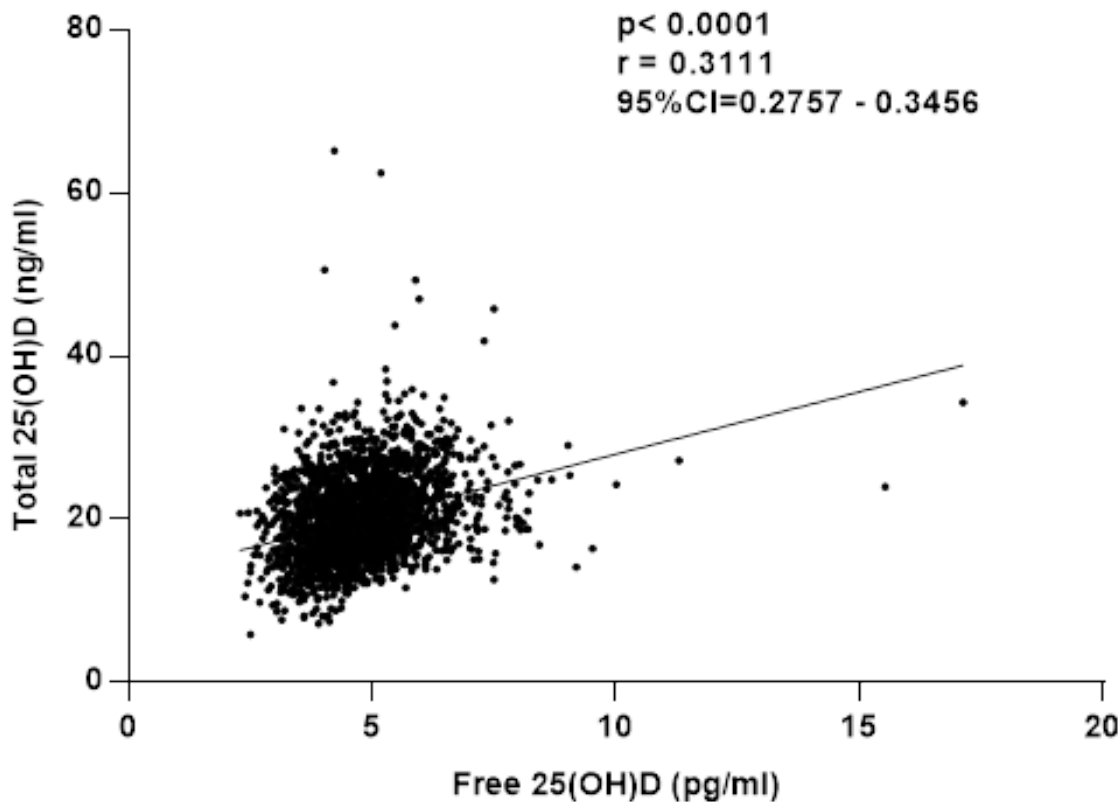
J Steroid Biochem Mol Biol. 2018 Jul;181:80-87. doi: 10.1016/j.jsbmb.2018.03.005 ■



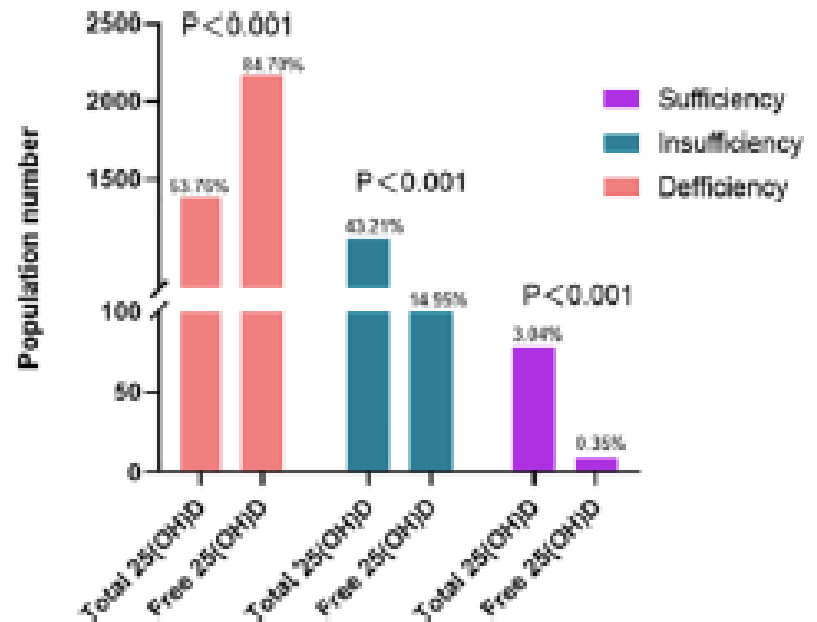
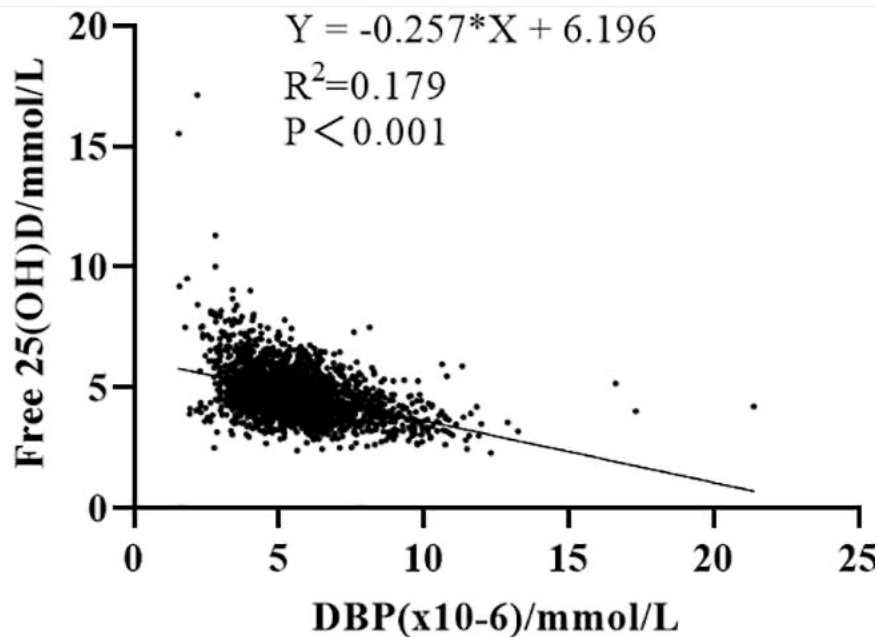
**.Changes in serum levels of vitamin D-binding protein throughout pregnancy**



C



Cai S, .....Hoche B.  
Impact of vitamin D on human  
embryo implantation-a  
prospective cohort study in  
women undergoing fresh embryo  
transfer. Fertil Steril. 2020 Oct  
7:S0015-0282(20)32206-8. doi:  
10.1016/j.fertnstert.2020.09.005.



**Die Konzentration des Vitamin-D-Bindungsproteins korreliert sehr gut mit dem Grad des E2-Anstiegs nach ovarieller Stimulation.**

**DBP ist invers mit dem freien 25(OH)D korreliert, was darauf hindeutet, dass der Anteil des freien, bioverfügbaren 25(OH)D während der ovariellen Stimulation durch die E2-stimulierte DBP-Synthese abnimmt.**

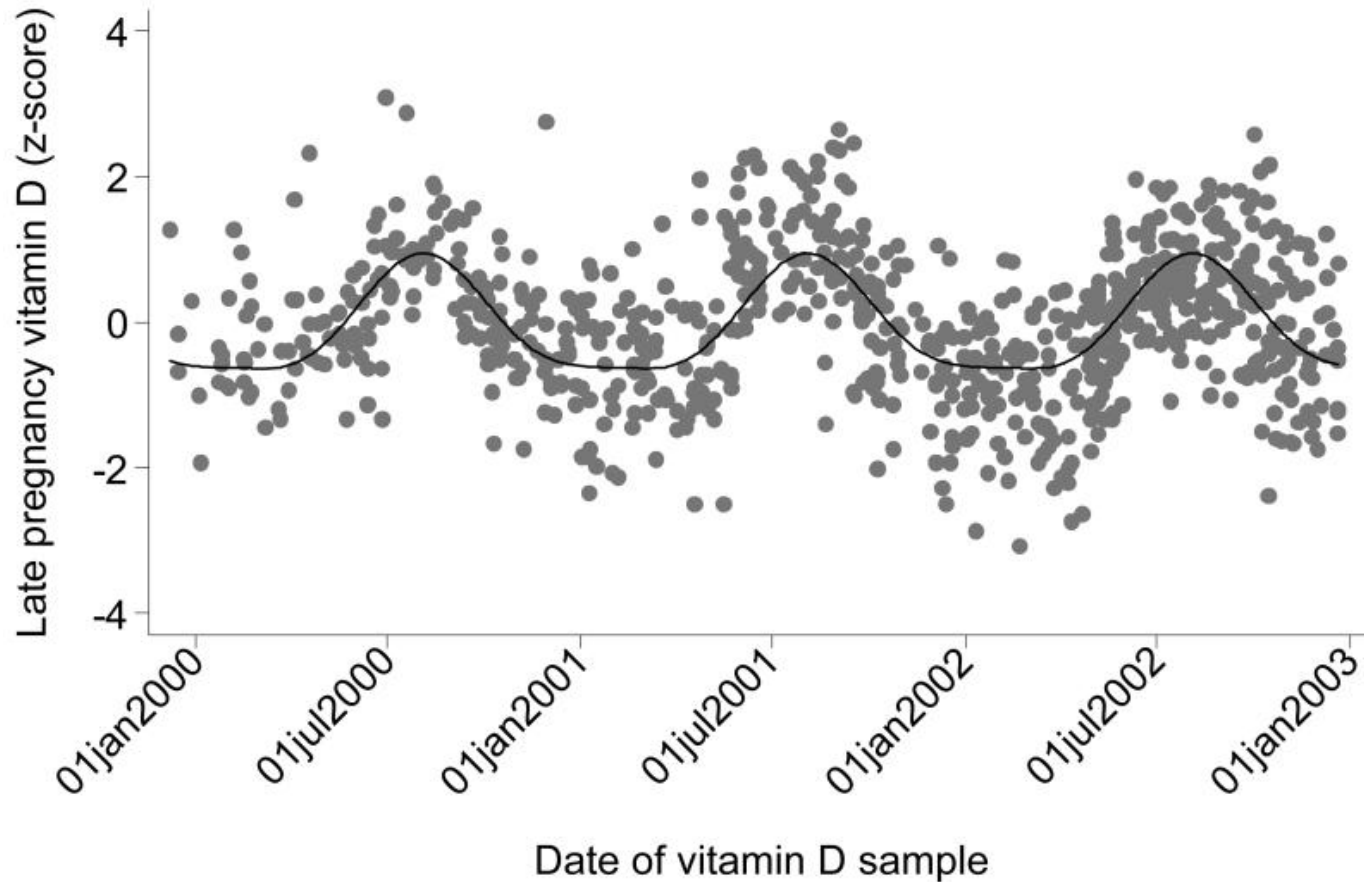
Chen, ... Hocher .Front Endocrinol (Lausanne). 2024 May 23;15:1401975. doi: 10.3389/fendo.2024.1401975.

# Vitamin D Binding Protein und damit total 25 (OH) Vitamin D wird beeinflusst durch

- Sex steroids
- Liver function
- Kidney diseases
- Genetic background

**Messungen vom bioaktiven freies 25 (OH) Vitamin D sind unabhängig von diesen Störgrößen**

# Fourier analysis of maternal vitamin D status in late pregnancy



# Vitamin D in der Schwangerschaft

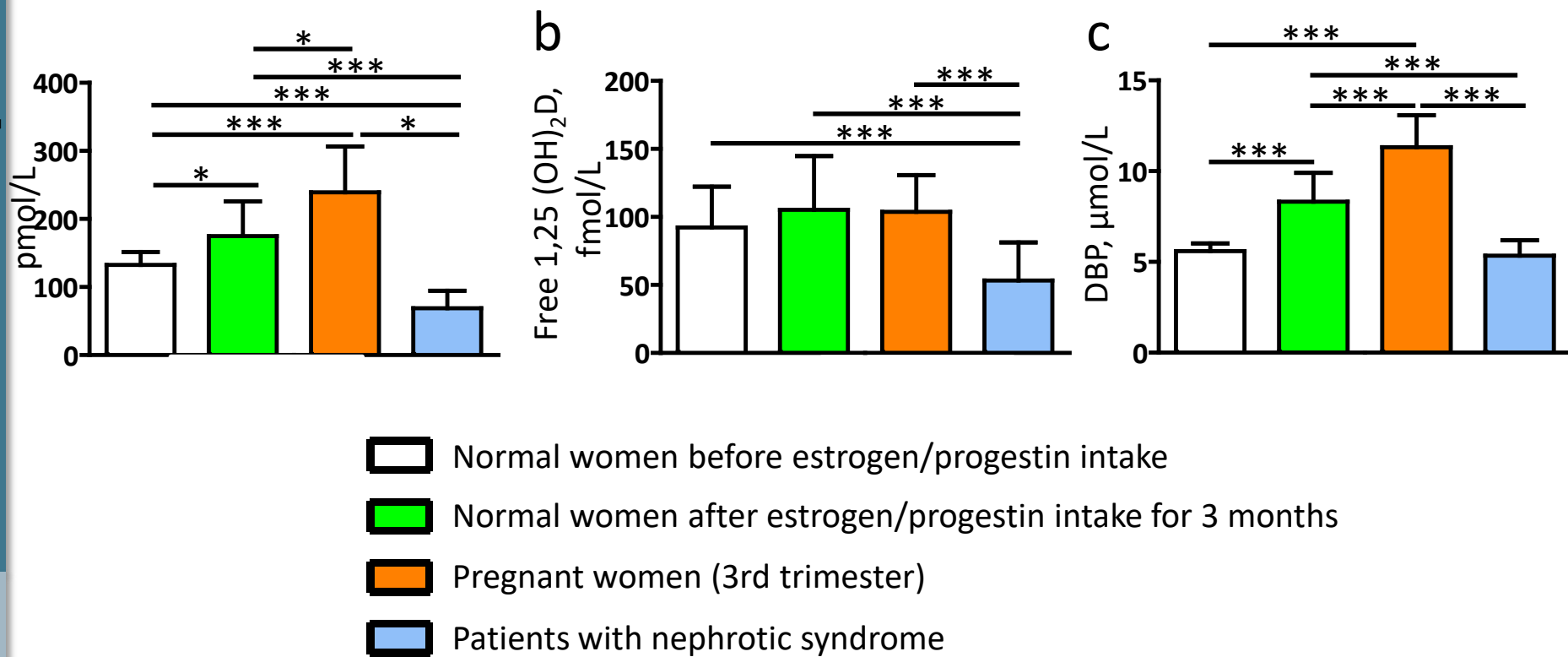
Maternal characteristics	Term maternal plasma 25(OH)D (n=547)			Significant group differences
	<1 nmol/L (n =37)	≥1 to <25 nmol/L (n = 361)	≥25 nmol/L (n = 149)	
Maternal age, y	29.8 ± 7.0	30.9 ± 6.3	31.1 ± 5.4	n.s
Ethnicity (Caucasian, other), %	83.8/16.2	84.8/15.2	96.0/4.0	p=0.002
Education (low,medium, high), %	27.0/45.9/27.0	16.9/47.1/36.0	6.0/48.3/45.6	p=0.002
Income (low, medium, high),%	54.1/32.4/13.5	39.3/37.3/23.4	29.3/40.8/29.9	p=0.039
Maternal height, cm	163.9 ± 7.2	166.3 ± 6.9	168.9 ± 5.7	p<0.0001
Maternal weight before pregnancy, kg	58.1 ± 9.2	63.9 ± 15.1	62.7 ± 11.3	p=0.053
Body mass index before pregnancy, kg/m <sup>2</sup>	21.7 ± 3.3	23.1 ± 5.1	22.0 ± 3.8	p=0.023
Mean weight 3rd trimester, kg	69.4 ± 9.6	77.1 ± 14.8	76.4 ± 12.3	p=0.007
Hypertension before/during pregnancy, %	0/2.7	3.6/10.8	4.7/8.1	n.s.
Diabetes mellitus before/during pregnancy, %	2.7/10.8	1.7/10.9	0.7/5.4	n.s.
Mean systolic blood pressure 3rd trimester, mmHg	112.9 ± 13.0	114.5 ± 11.4	115.3 ± 8.7	n.s.
Mean diastolic blood pressure 3rd trimester, mmHg	66.9 ± 7.2	69.5 ± 7.5	70.3 ± 6.8	p=0.043
Smoking before/during pregnancy, %	37.8/18.9	41.6/16.1	41.2/12.8	n.s.
Plasma 25OHD, [nmol/L]	below level of detection	9.8 ± 6.4	42.5 ± 19.5	p<0.0001
Primigravida/primipara, %	35.1/45.9	41.6/55.4	43.6/63.1	n.s./p=0.02
Season of birth (summer; other; %)	16.2/83.8	29.1/70.9	55.7/44.3	p<0.0001
Mode of delivery (spontaneous, vag. OP; c-section;)	43.2/8.1/48.6	60.7/9.1/30.2	59.7/5.4/34.9	n.s
Gestational age at delivery, d	260.1 ± 21.8	272.0 ± 15.4	271,6 ± 16.3	p<0.0001
Birthweight, g	2791.4 ± 776.1	3286.2 ± 640.7	3255.3 ± 588.3	p<0.0001
Birthlength, cm	47.7 ± 4.8	50.4 ± 3.5	49.9 ± 3.7	p<0.0001
Child head circumference, cm	33.5 ± 2.7	34.5 ± 1.8	34.5 ± 1.9	n.s.
Child sex, male/female, %	51.4/48.6	51.5/48.5	53.7/46.3	n.s.
Apgar score at 5 min	8.3 ± 1.9	9.2 ± 1.2	9.0 ± 1.5	p=0.001
Apgar score at 10 min	8.9 ± 1.8	9.4 ± 1.3	9.3 ± 1.4	n.s.

# Opposite correlation of 25-hydroxy-vitamin D- and 1,25-dihydroxy-vitamin D-metabolites with gestational age, bone- and lipid-biomarkers in pregnant women.

Sci Rep. 2021 Jan 21;11(1):1923. doi: 10.1038/s41598-021-81452-9.

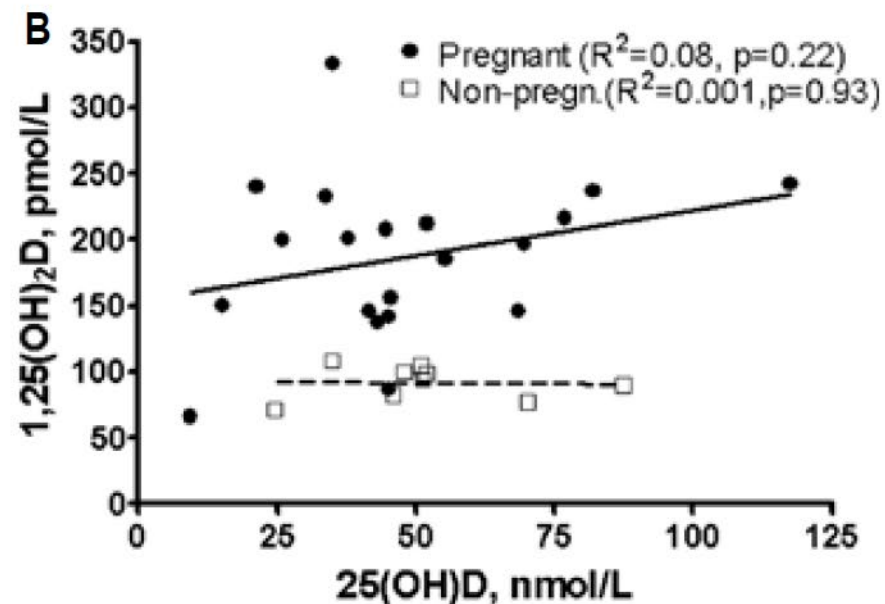
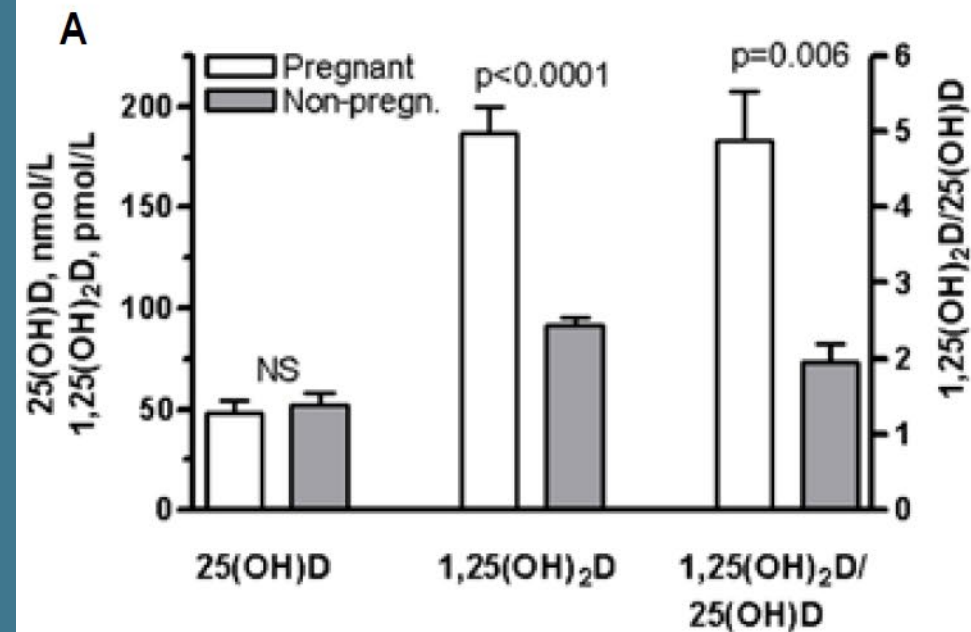
	Total 25(OH)D, ng/mL	Free 25(OH)D, pg/mL	Bioavailable 25(OH)D, ng/mL	Total 1,25(OH) <sub>2</sub> D, pg/mL	Free 1,25(OH) <sub>2</sub> D, pg/mL	Bioavailable 1,25(OH) <sub>2</sub> D, pg/mL	Spearman's rho color gradient
<b>Age and gestational age</b>							-0.5>rho>-0.6
Age, years	<b>0.218, p&lt;0.001</b>	<b>0.235, p&lt;0.001</b>	<b>0.227, p&lt;0.001</b>	0.027, p=0.572	0.078, p=0.109	0.091, p=0.062	-0.4>rho>-0.5
Gestational age, days <sup>5</sup>	0.095, p=0.081	<b>-0.198, p&lt;0.001</b>	<b>-0.350, p&lt;0.001</b>	<b>0.597, p&lt;0.001</b>	<b>0.244, p&lt;0.001</b>	-0.045, p=0.413	-0.3>rho>-0.4
<b>Bone turnover biomarkers</b>							-0.2>rho>-0.3
PTH, pg/mL	<b>-0.292, p&lt;0.001</b>	<b>-0.266, p&lt;0.001</b>	<b>-0.256, p&lt;0.001</b>	<b>-0.163, p=0.001</b>	<b>-0.184, p&lt;0.001</b>	<b>-0.210, p&lt;0.001</b>	-0.1>rho>-0.2
BSAP, µg/mL	<b>-0.155, p=0.001</b>	<b>-0.253, p&lt;0.001</b>	<b>-0.287, p&lt;0.001</b>	<b>0.145, p=0.003</b>	0.021, p=0.673	-0.067, p=0.172	0.0>rho>-0.1
Calcium, mmol/L	0.080, p=0.098	<b>0.234, p&lt;0.001</b>	<b>0.369, p&lt;0.001</b>	<b>-0.278, p&lt;0.001</b>	-0.074, p=0.131	<b>0.182, p&lt;0.001</b>	0.0<rho<0.1
Phosphate, U/L	<b>0.097, p=0.046</b>	0.041, p=0.403	0.050, p=0.305	0.003, p=0.946	-0.096, p=0.050	-0.090, p=0.066	0.1<rho<0.2
DBP, mg/L	<b>0.152, p=0.002</b>	<b>-0.290, p&lt;0.001</b>	<b>-0.399, p&lt;0.001</b>	<b>0.570, p&lt;0.001</b>	-0.019, p=0.702	<b>-0.229, p&lt;0.001</b>	0.2<rho<0.3
<b>Lipid metabolism biomarkers</b>							0.3<rho<0.4
LDL, mg/dL	0.049, p=0.315	<b>-0.174, p&lt;0.001</b>	<b>-0.300, p&lt;0.001</b>	<b>0.464, p&lt;0.001</b>	<b>0.193, p&lt;0.001</b>	-0.004, p=0.420	0.4<rho<0.5
HDL, mg/dL	<b>0.228, p&lt;0.001</b>	0.094, p=0.057	0.031, p=0.527	<b>0.333, p&lt;0.001</b>	<b>0.178, p&lt;0.001</b>	0.093, p=0.059	0.5<rho<0.6
LDL/HDL ratio	<b>-0.099, p=0.044</b>	<b>-0.228, p&lt;0.001</b>	<b>-0.308, p&lt;0.001</b>	<b>0.232, p&lt;0.001</b>	0.071, p=0.153	<b>-0.104, p=0.036</b>	
Adiponectin, µg/mL	0.063, p=0.202	<b>0.140, p=0.005</b>	<b>0.168, p=0.001</b>	<b>-0.123, p=0.012</b>	-0.045, p=0.362	0.018, p=0.718	
<b>Thyroid gland-associated biomarkers</b>							
Free T3, pg/mL	<b>-0.114, p=0.018</b>	<b>-0.144, p=0.003</b>	<b>-0.120, p=0.013</b>	-0.040, p=0.415	-0.088, p=0.073	-0.070, p=0.153	
Free T4, ng/dL	<b>-0.095, p=0.049</b>	0.087, p=0.074	<b>0.216, p&lt;0.001</b>	<b>-0.413, p&lt;0.001</b>	<b>-0.203, p&lt;0.001</b>	0.028, p=0.571	
TSH, uU/mL	0.021, p=0.670	0.000, p=0.996	-0.005, p=0.916	-0.020, p=0.674	-0.087, p=0.075	-0.095, p=0.052	
<b>Hematological biomarkers</b>							
Hemoglobin, g/dL	0.063, p=0.252	<b>0.203, p&lt;0.001</b>	<b>0.298, p&lt;0.001</b>	<b>-0.226, p&lt;0.001</b>	-0.008, p=0.881	<b>0.177, p=0.001</b>	
RBC count, 10 <sup>6</sup> /µL	0.016, p=0.784	<b>0.119, p=0.042</b>	<b>0.208, p&lt;0.001</b>	<b>-0.215, p&lt;0.001</b>	-0.056, p=0.338	0.104, p=0.074	
WBC count, 10 <sup>7</sup> /µL	0.051, p=0.379	-0.062, p=0.287	-0.098, p=0.092	<b>0.231, p&lt;0.001</b>	0.088, p=0.130	0.031, p=0.600	
Platelet count, 10 <sup>3</sup> /µL	-0.084, p=0.148	-0.062, p=0.295	-0.026, p=0.654	-0.109, p=0.060	<b>-0.117, p=0.045</b>	-0.060, p=0.310	
MCV, fL	<b>0.116, p=0.046</b>	<b>0.145, p=0.013</b>	<b>0.146, p=0.013</b>	0.031, p=0.598	0.084, p=0.153	0.110, p=0.060	
MCH, pg	0.101, p=0.083	<b>0.123, p=0.035</b>	0.110, p=0.061	0.065, p=0.263	<b>0.122, p=0.037</b>	<b>0.135, p=0.021</b>	
MCHC, g/dL	0.004, p=0.940	0.004, p=0.945	-0.027, p=0.649	0.091, p=0.118	<b>0.134, p=0.022</b>	<b>0.115, p=0.049</b>	
RDW, %	-0.095, p=0.101	-0.102, p=0.081	-0.094, p=0.110	-0.073, p=0.207	-0.109, p=0.062	<b>-0.129, p=0.028</b>	
Hematocrit, %	0.090, p=0.120	<b>0.228, p&lt;0.001</b>	<b>0.333, p&lt;0.001</b>	<b>-0.239, p&lt;0.001</b>	-0.034, p=0.562	<b>0.158, p=0.007</b>	
<b>Other biomarkers</b>							
Urea, mg/dL	0.026, p=0.597	<b>0.161, p=0.001</b>	<b>0.240, p&lt;0.001</b>	<b>-0.360, p&lt;0.001</b>	<b>-0.224, p&lt;0.001</b>	-0.082, p=0.098	
Albumin, g/dL	-0.056, p=0.247	<b>0.185, p&lt;0.001</b>	<b>0.377, p&lt;0.001</b>	<b>-0.533, p&lt;0.001</b>	<b>-0.272, p&lt;0.001</b>	0.075, p=0.126	
Vitamin B6, ng/mL	<b>0.178, p&lt;0.001</b>	<b>0.367, p&lt;0.001</b>	<b>0.458, p&lt;0.001</b>	<b>-0.277, p&lt;0.001</b>	-0.025, p=0.623	<b>0.164, p=0.001</b>	
Vitamin B12, pg/mL	<b>0.130, p=0.008</b>	<b>0.280, p&lt;0.001</b>	<b>0.363, p&lt;0.001</b>	<b>-0.246, p&lt;0.001</b>	-0.069, p=0.164	<b>0.102, p=0.038</b>	
Sodium, mmol/L	0.086, p=0.081	0.081, p=0.104	0.082, p=0.098	0.043, p=0.380	0.024, p=0.629	0.032, p=0.526	
Zinc, µmol/L	-0.020, p=0.867	0.163, p=0.171	<b>0.275, p=0.020</b>	<b>-0.396, p=0.001</b>	<b>-0.297, p=0.011</b>	-0.001, p=0.992	

**25(OH)D-Metaboliten und 1,25(OH)<sub>2</sub>D-Metaboliten korrelierten mit Knochen- und Lipid-Biomarkern in entgegengesetzter Richtung -> unterschiedliche Wirkung von 25(OH)D und 1,25(OH)<sub>2</sub>D am nukleären VD-Rezeptor ?**



Total 1,25(OH)<sub>2</sub>D, free 1,25(OH)<sub>2</sub>D and DBP concentrations in **normal women before (N, V) and after 3 months of estrogen/ progestagen intake (E, W)**, in pregnant women (P, K) and in patients with **nephrotic syndrome (K, L)**. The dotted lines indicate reference ranges (\*P , 0.05, \*\*\*P , 0.001). van Hoof et al. European Journal of Endocrinology (2001) 144 391-396





- **1-alpha Hydroxylase ist hochreguliert in der Schwangerschaft**
- **1-alpha Hydroxylase wandelt 25OH in 1,25OH um**

Parameter, units		Total 25(OH)D, ng/ml	Free 25(OH)D, pg/ml	Spearman's rank
FAI	Rho Value	-0.199	-0.166	-0.15 >rho> p<0.05
	p value	<0.0001	<0.0001	-0.10 >rho> p<0.05
LH,	Rho Value	-0.153	-0.101	-0.05 >rho> p<0.05
	p value	0.001	0.027	0.00 >rho> p<0.05
Testosteronel	Rho Value	-0.131	-0.143	0.00 <rho< p>0.05
	p value	0.003	0.001	0.05 <rho< p<0.05
AMH	Rho Value	-0.127	-0.088	0.10 <rho< p<0.05
	p value	0.004	0.049	0.20 <rho< p<0.05
LH/FSH	Rho Value	-0.119	-0.100	0.30 <rho< p<0.05
	p value	0.009	0.029	
Androstendion	Rho Value	-0.104	-0.083	
	p value	0.02	0.063	
TSH	Rho Value	-0.1	-0.121	
	p value	0.025	0.007	
DHEAS	Rho Value	-0.1	-0.078	
	p value	0.024	0.08	
PR	Rho Value	-0.074	-0.093	
	p value	0.097	0.036	
17-Hydroxy- progesterone	Rho Value	-0.073	-0.072	
	p value	0.108	0.11	
T4	Rho Value	-0.068	-0.037	
	p value	0.13	0.413	
FSH, mIE/ml	Rho Value	-0.063	0.012	
	p value	0.173	0.802	
Adiol,	Rho Value	-0.048	-0.042	
	p value	0.288	0.343	
DHT	Rho Value	-0.034	-0.028	
	p value	0.442	0.534	
Progesterone	Rho Value	-0.028	-0.015	
	p value	0.527	0.734	
Free T3	Rho Value	-0.027	-0.068	
	p value	0.543	0.13	
Estrone	Rho Value	-0.008	0.076	
	p value	0.969	0.706	
	Rho Value	0.035	0.051	

## Vitamin D und PCOS

- Dies ist die erste Studie, in der **totales 25(OH)D** und **direkt gemessenes freies 25(OH)D** in einer relativ großen Kohorte von gesunden jungen Frauen im **reproduktionsfähigem Alter (n=508)** verglichen wurde.
- **Insbesondere Androgene, aber auch LH und AMH sind sowohl mit freiem als auch mit Gesamt-25(OH)D invers korreliert -> Hormonkonstellation beim PCOS (Androgene erhöht, AMH erhöht)**

Chu C, Tsuprykov O, Chen X, Elitok S, Krämer BK, Hochar B. Relationship Between Vitamin D and Hormones Important for Human Fertility in Reproductive-Aged Women. Front Endocrinol (Lausanne). 2021 Apr 14;12:666687. doi: 10.3389/fendo.2021.666687.

# Maternal Vitamin D Deficiency and Risk for Preeclampsia

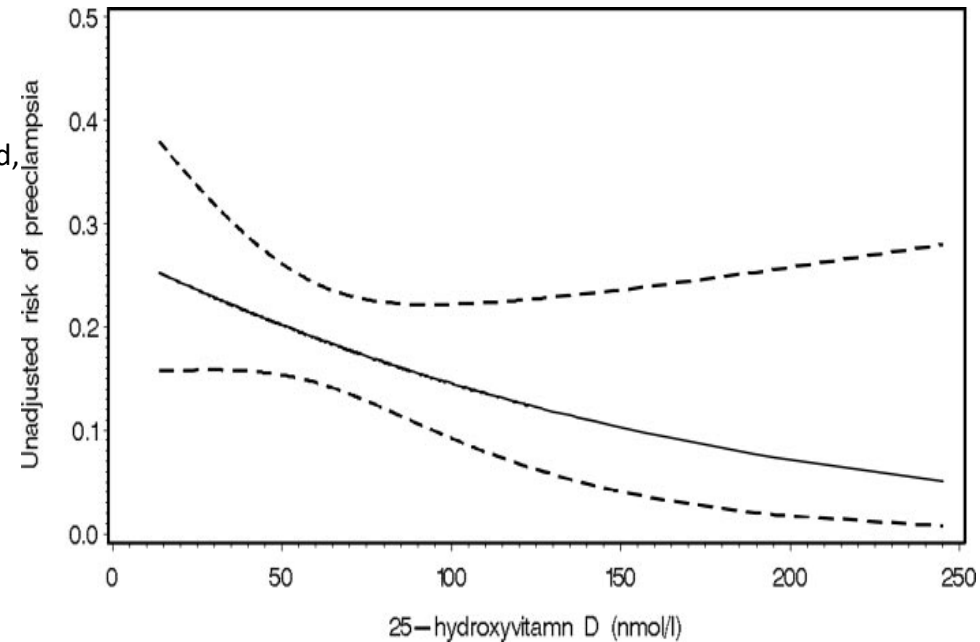
J Clin Endocrinol Metab. 2007 Sep; 92(9): 3517–3522.

## ■ Methods

- Case study of Vitamin D levels in preeclamptic women >16 wks compared to non-preeclamptic women

## ■ Results

- As maternal serum vitamin D concentrations increased, risk of preeclampsia decreased.
- Neonates born to preeclamptic mothers more likely to have poor Vitamin D status than neonates of controls

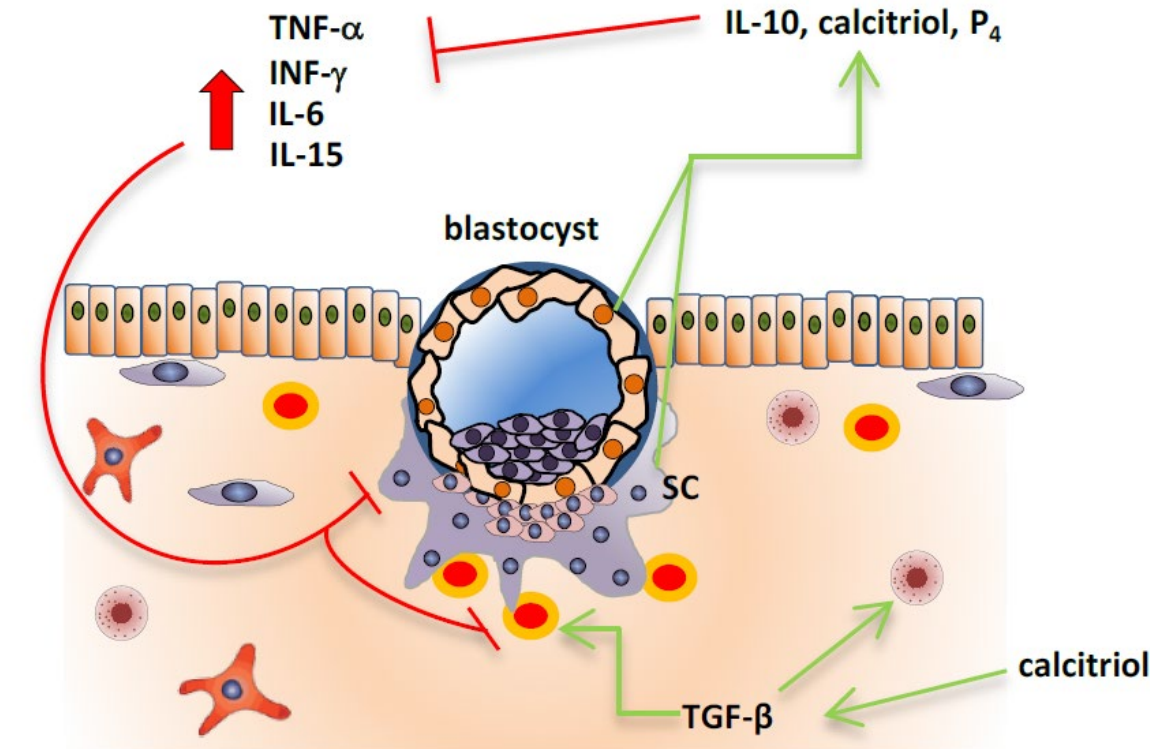


**Studien belegen, dass ein niedriger mütterlicher Vitamin-D-Status mit einem erhöhten Risiko nachteiliger Schwangerschaftsausgänge verbunden ist. Interventionelle Studien zeigen, dass eine Vitamin-D-Supplementierung während der Schwangerschaft den mütterlichen und neonatalen Vitamin-D-Status optimiert.**

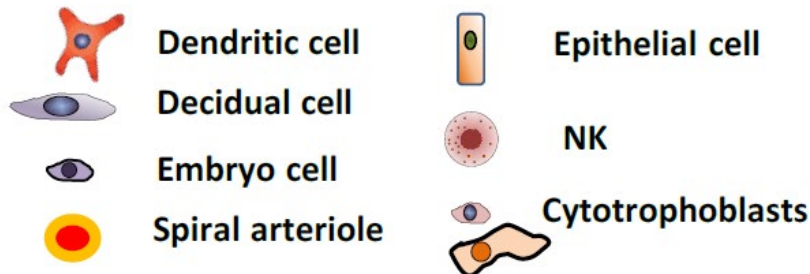
Curr Opin Obstet Gynecol. 2014 Dec;26(6):438-47. doi: 10.1097/GCO.0000000000000117

TNF-controls trophoblast growth and invasion of maternal spiral arteries, limiting excessive trophoblastic penetration.

TGF- $\beta$  interacts with its receptor endoglin in blood vessels and controls trophoblast invasion/penetration. TGF- $\beta$  produced by macrophages interacts with NK cells, making them accept trophoblasts while avoiding them to kill fetal cells.



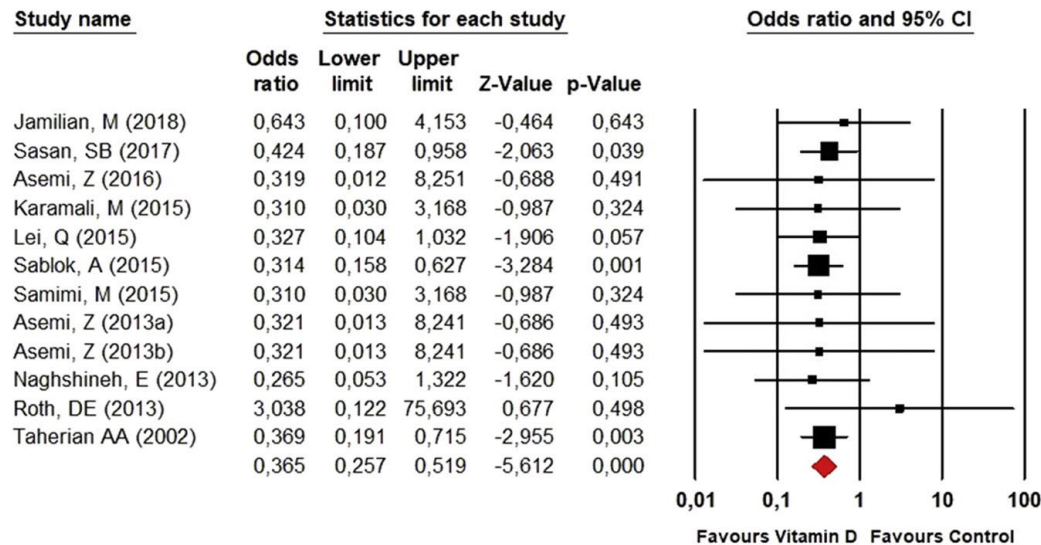
**Um eine übermäßige Entzündung zu verhindern, die zur Abstoßung des fetalen Allotransplantats führen könnte, wirken Calcitriol, IL-10 und Progesteron (P4), die von dezidualen Zellen produziert werden, Trophoblasten und Syncytiotrophoblasten als entzündungshemmende Faktoren, die das immunologische Milieu modulieren.**



Meta-analyses

## Vitamin D supplementation and incident preeclampsia: A systematic review and meta-analysis of randomized clinical trials

### *Risk of incident preeclampsia*



# Vitamin D and the outcome of IVF/ICSI

Research | [Open Access](#) | Published: 09 February 2018

## Whether vitamin D was associated with clinical outcome after IVF/ICSI: a systematic review and meta-analysis

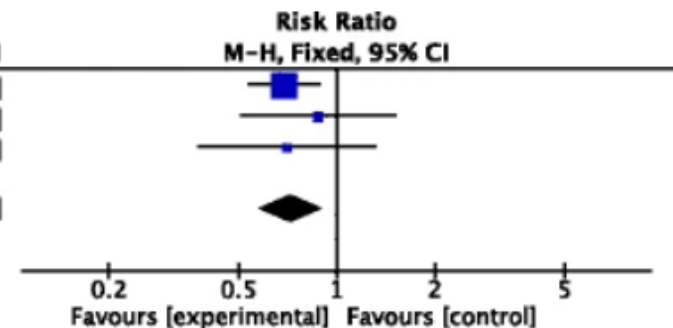
[Jing Zhao](#), [Xi Huang](#), [Bin Xu](#), [Yi Yan](#), [Qiong Zhang](#) & [Yanping Li](#) 

*Reproductive Biology and Endocrinology*. 16, Article number: 13 (2018) | [Cite this article](#)

1911 Accesses | 8 Citations | 41 Altmetric | [Metrics](#) 

**Patientinnen mit Vitamin-D-Mangel haben eine niedrigere Lebendgeburtenrate nach IVF (RR: 0.72 (95% CI, 0.58, 0.90; P = 0.004))**

Study or Subgroup	deficient group		sufficient group		Weight	Risk Ratio
	Events	Total	Events	Total		M-H, Fixed, 95% CI
Polyzos 2014	78	239	61	129	68.3%	0.69 [0.53, 0.89]
Rudick 2012	11	39	48	149	17.2%	0.88 [0.50, 1.52]
Rudick 2014	8	26	32	73	14.5%	0.70 [0.37, 1.32]
<b>Total (95% CI)</b>		<b>304</b>		<b>351</b>	<b>100.0%</b>	<b>0.72 [0.58, 0.90]</b>
Total events	97		141			
Heterogeneity: $\text{Chi}^2 = 0.60$ , $\text{df} = 2$ ( $P = 0.74$ ); $I^2 = 0\%$						
Test for overall effect: $Z = 2.88$ ( $P = 0.004$ )						



29.05.2024 17:18

Forschungsergebnisse, Wissenschaftliche Publikationen

## Der Blutdruck bestimmt den Erfolg einer künstlichen Befruchtung



Kontrolle des Blutdrucks auch während der Schwangerschaft | **Copyright:** Pixabay, kostenlose Nutzung | **Download**

Studie mit **73462 Patientinnen** von Wissenschaftlern der Central South University, Changsha, China, der Universität Heidelberg und des IMD Berlin demonstriert die Bedeutung des Blutdrucks für die Lebendgeburtsrate nach IVF Behandlung auch bei Frauen mit **scheinbar normalen Blutdruck**

Ma S, ..... , Hocher B. Inverse association of pre-pregnancy Systolic Blood Pressure and Live Birth Rate in normotensive women undergoing IVF/ICSI. Fertil Steril. 2024 May 21:S0015-0282(24)00460-6. doi: 10.1016/j.fertnstert.2024.05.150.

- Fetal programming



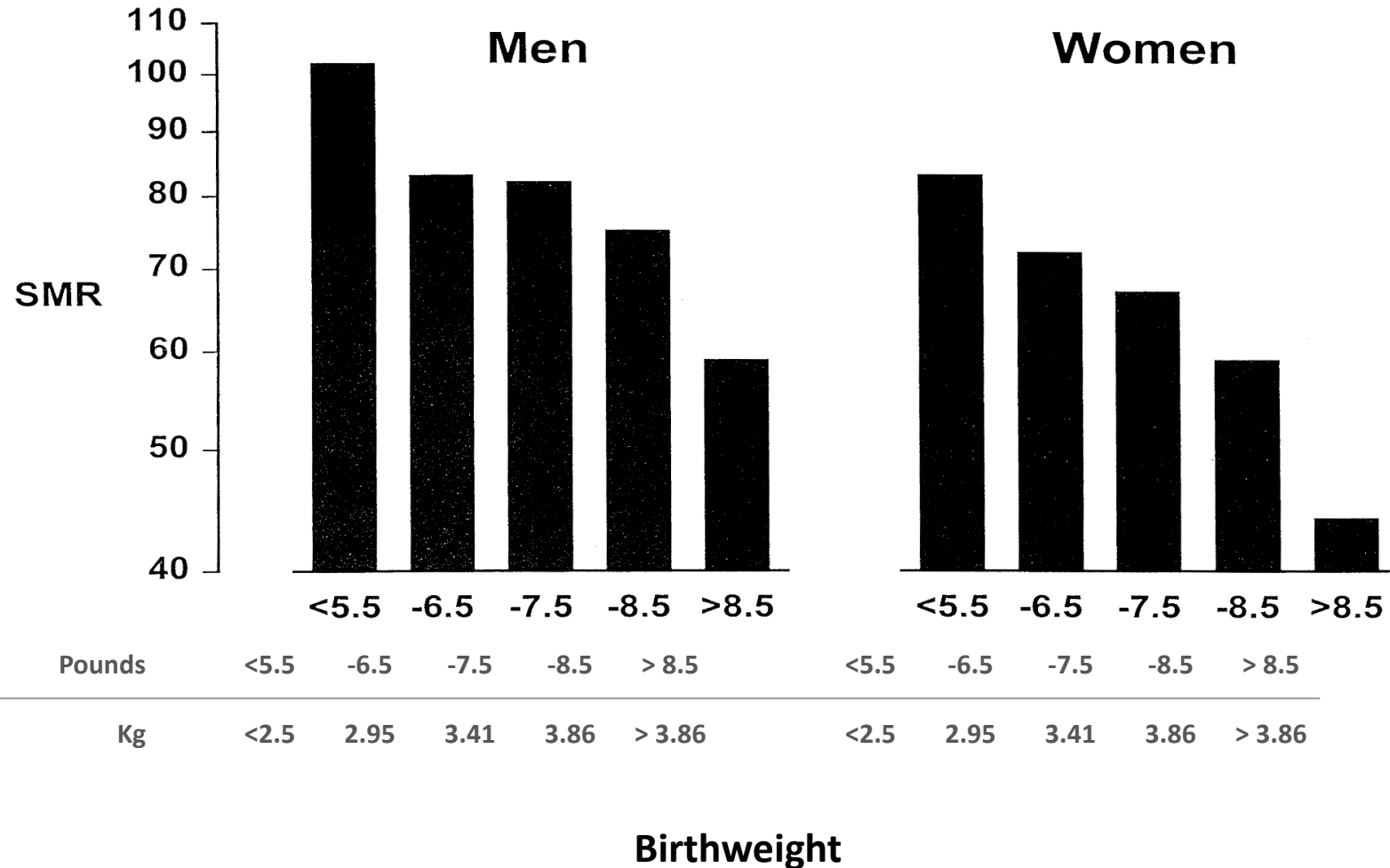
**David Barker**



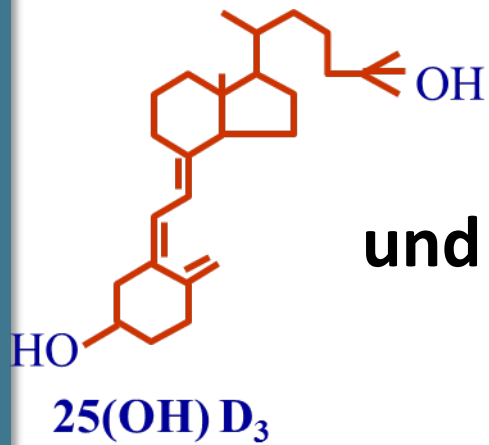
Ein Ereignis in einer "kritischen", frühen Phase des Lebens, das die Struktur und Funktion von Herz-Kreislauforganen dauerhaft verändert und zu damit zu Herz-Kreislauf-Erkrankungen im Erwachsenenalter führt.



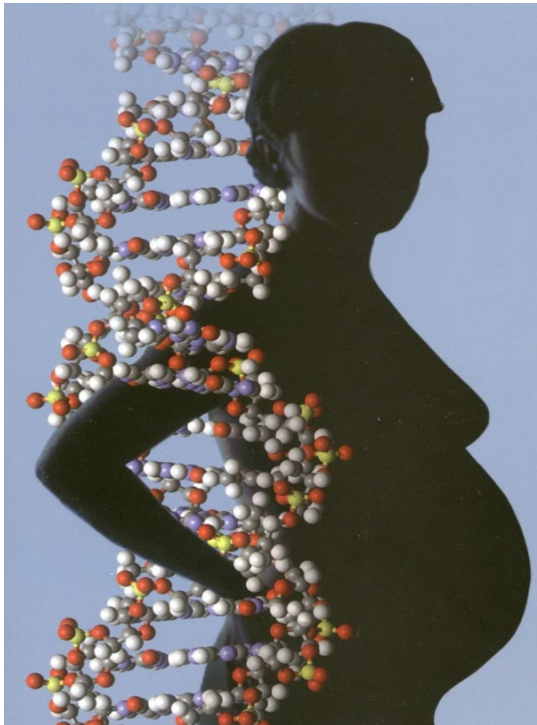
# Standardisierte Sterblichkeitsraten für koronare Herzkrankheit bei 15726 Erwachsenen aus Hertfordshire unter 65 Jahren



Barker DJ, Osmond C. Lancet. 1986 May 10;1(8489):1077-81. doi: 10.1016/s0140-6736(86)91340-1.



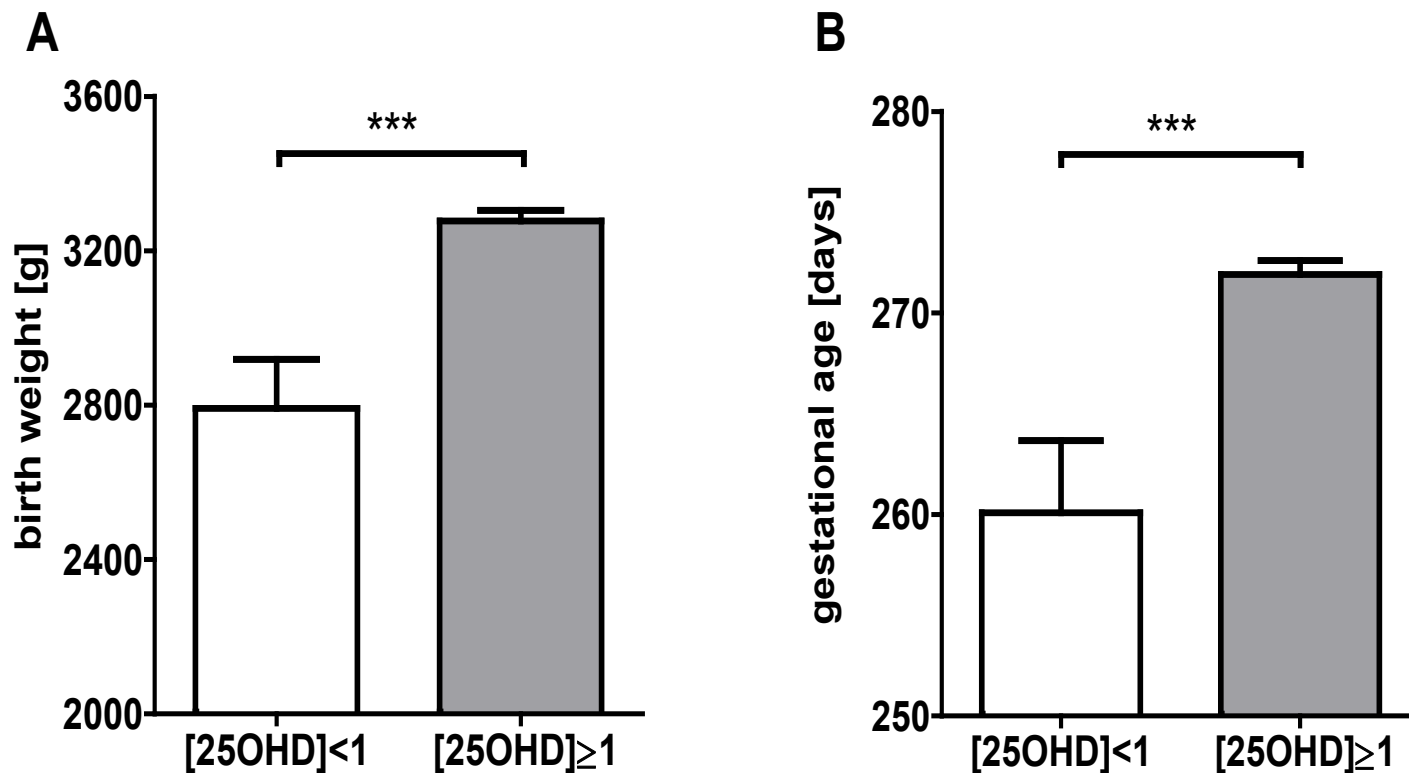
## und Fetal Programming



Maternal Vitamin D Status during  
Pregnancy act on the Offspring via:

1. DNA methylation
2. histone modifications
3. non-coding microRNAs

# Maternal Vitamin D Deficiency and Fetal Programming – Lessons learned from Humans and Mice

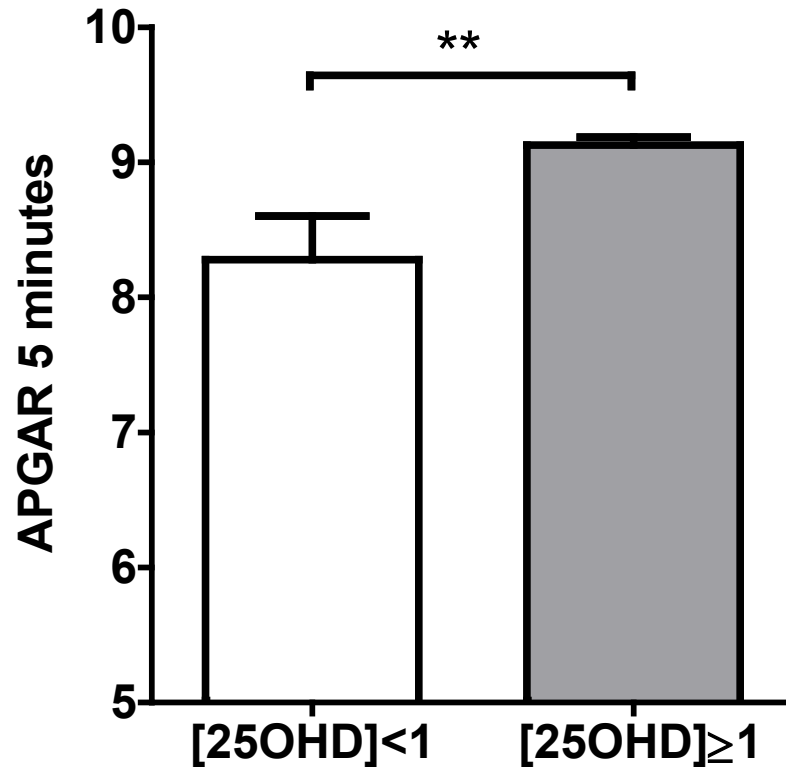


Birth weight in kilograms (A; 2791.4±776.1g vs. 3277.2±625.4g; p<0.0001) and gestational age in days (B; 260.1±3.6 days vs. 271.9±0.7 days; p<0.0001) of mothers with 25OHD levels below and above the threshold of detection,

**Diese Studie zeigt einen Zusammenhang zwischen mütterlichem 25OHD und dem Geburtsgewicht der Nachkommen. Die Wirkung von 25OHD auf das Geburtsgewicht scheint durch den Vitamin D Effekt auf das Gestationsalter bedingt zu sein.**

Reichetzer et al.; Kidney Blood Press Res.; 2014

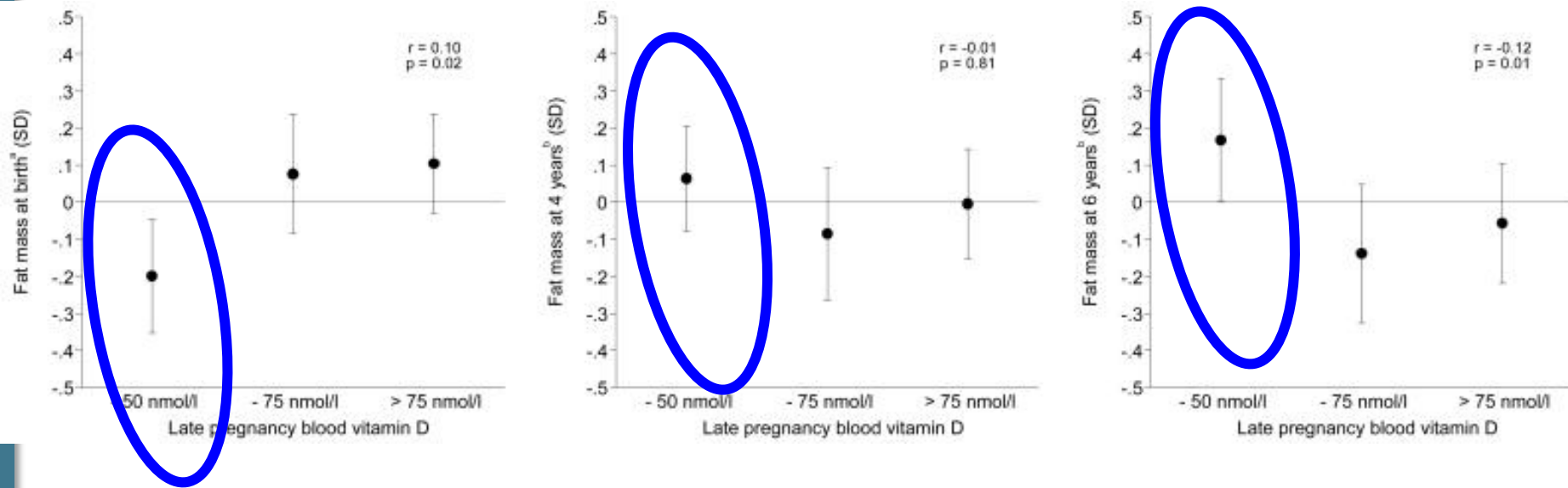
## Maternal Vitamin D Deficiency and Fetal Programming – Lessons learned from Humans and Mice



**This study demonstrates an independent association between maternal 25OHD and offspring's APGAR score**

Reichetzedder, ... , Hocher; Kidney Blood Press Res.; 2014

# Mean (95% CI) fat mass at birth, 4 years and 6 years according to maternal vitamin D status in late pregnancy

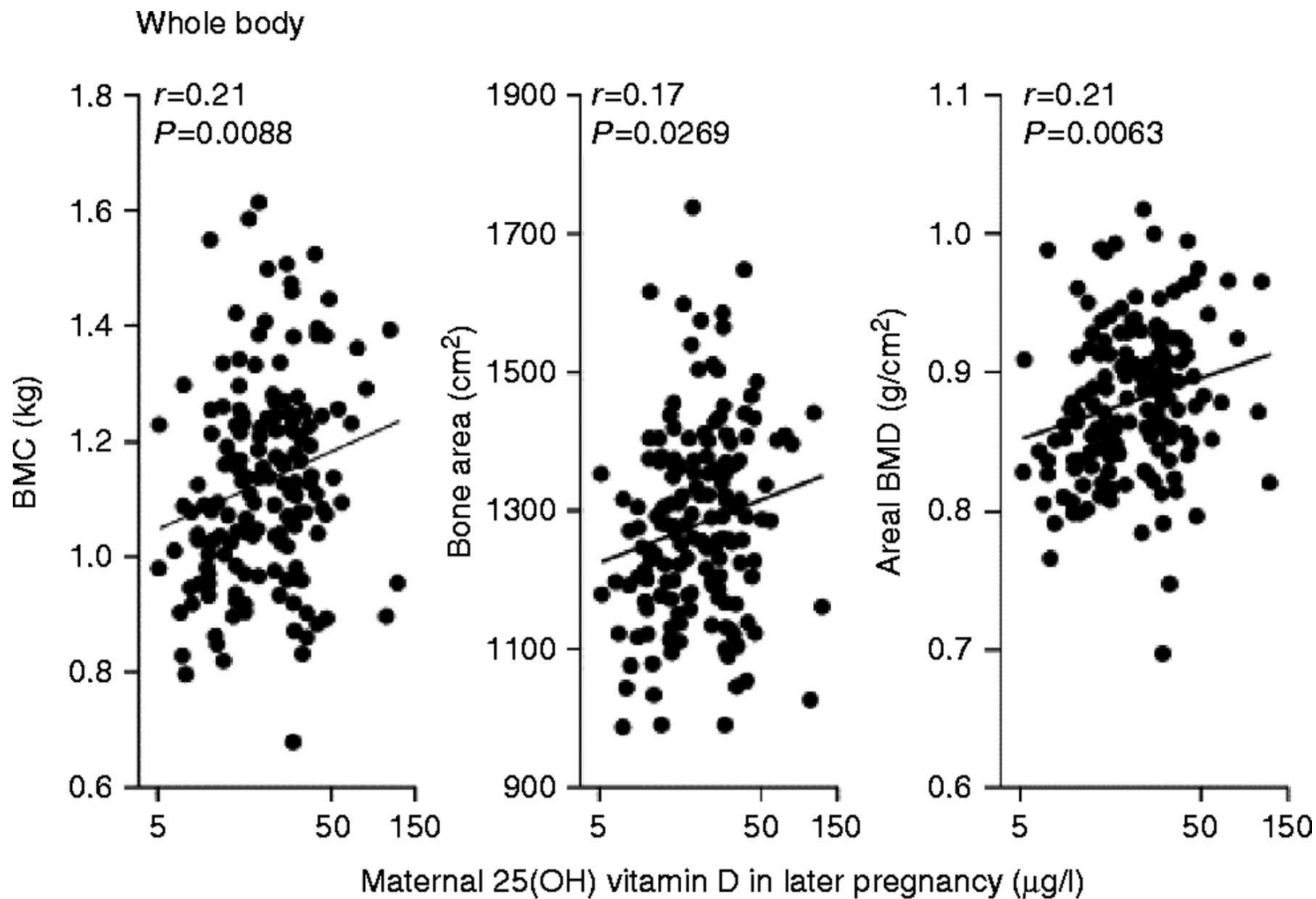


## Mean (95% CI) fat mass at birth, 4 years and 6 years according to maternal vitamin D status in late pregnancy

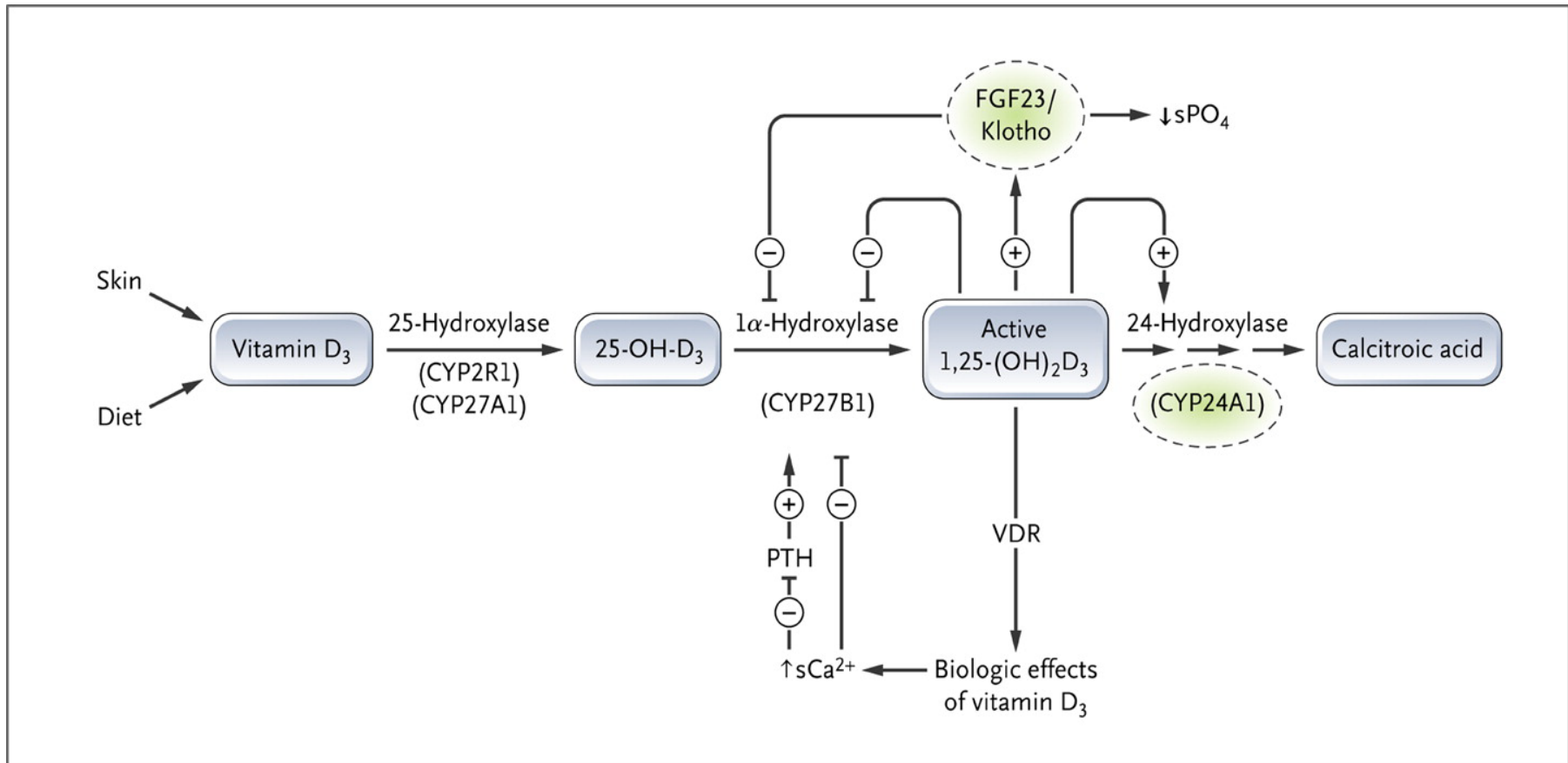
<sup>a</sup>Adjusted for sex, gestation, age at measurement, age squared, length, maternal educational attainment, smoking in pregnancy, pre-pregnancy BMI, height, parity, social class and IOM weight gain categories

<sup>b</sup>Adjusted for sex, age, height, maternal educational attainment, smoking in pregnancy, pre-pregnancy BMI, height, parity, social class, IOM weight gain categories, breastfeeding duration, vitamin D intake at 3 years, and physical activity at 3 years

# Maternal 25(OH)D concentration in late pregnancy and childhood bone mass at age 9 years.



# Vitamin D Metabolism with Selected Candidate Genes



# Is vitamin D supplementation always a good idea ?????

The NEW ENGLAND JOURNAL of MEDICINE

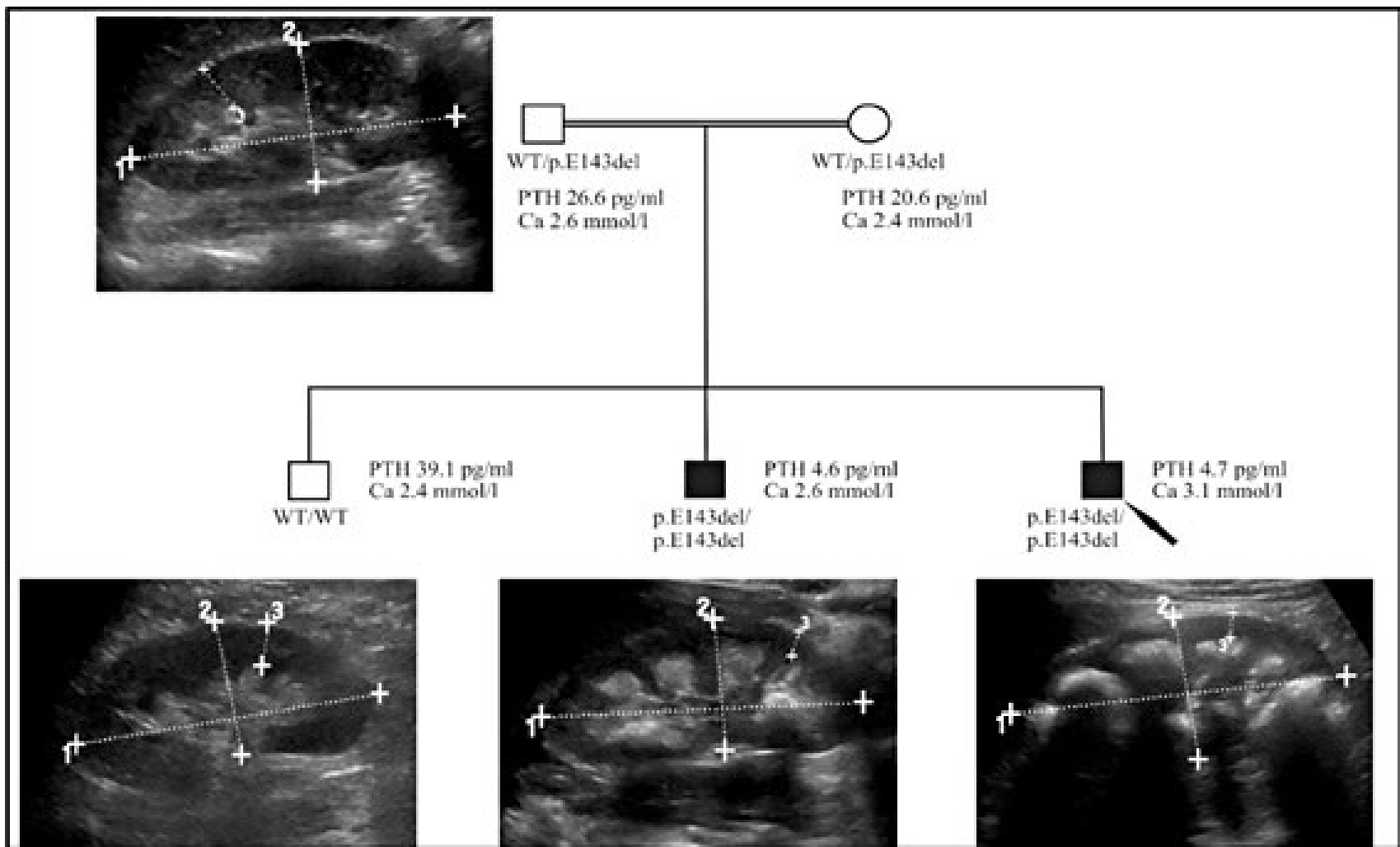
ORIGINAL ARTICLE

## Mutations in *CYP24A1* and Idiopathic Infantile Hypercalcemia

Karl P. Schlingmann, M.D., Martin Kaufmann, Ph.D., Stefanie Weber, M.D., Andrew Irwin, B.Sc., Caroline Goos, Ulrike John, M.D., Joachim Misselwitz, M.D., Günter Klaus, M.D., Eberhard Kuwertz-Bröking, M.D., Henry Fehrenbach, M.D., Anne M. Wingen, M.D., Tülay Güran, M.D., Joost G. Hoenderop, Ph.D., René J. Bindels, Ph.D., David E. Prosser, Ph.D., Glenville Jones, Ph.D., and Martin Konrad, M.D.

ABSTRACT





Pedigree and clinical key findings. The index patient (arrow) is homozygous for the *CYP24A1* mutation, as is his 28 year old brother (p.E143del/p.E143del). The parents are heterozygous (WT/p.E143del) for the *CYP24A1* mutation and the third brother is not affected, displaying the wild-type allele homozygously (WT/WT). Both affected brothers show suppressed PTH levels (normal value 15-65 pg/ml), but hypercalcemia is an inconsistent finding. The mildly affected brother shows moderate medullary enhancement on ultrasound, whereas the index patient has profound medullary calcifications.

# Superelemente und Vitamine in der Schwangerschaft – Bedeutung für Mutter und Kind

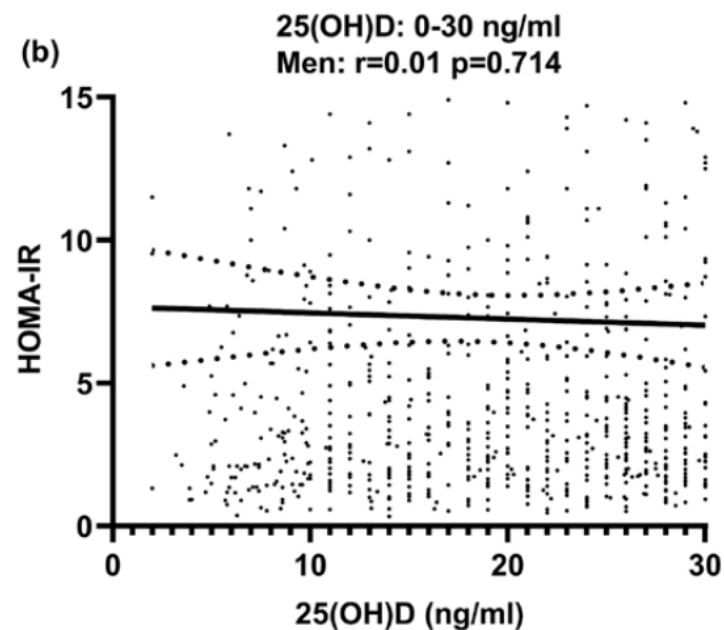
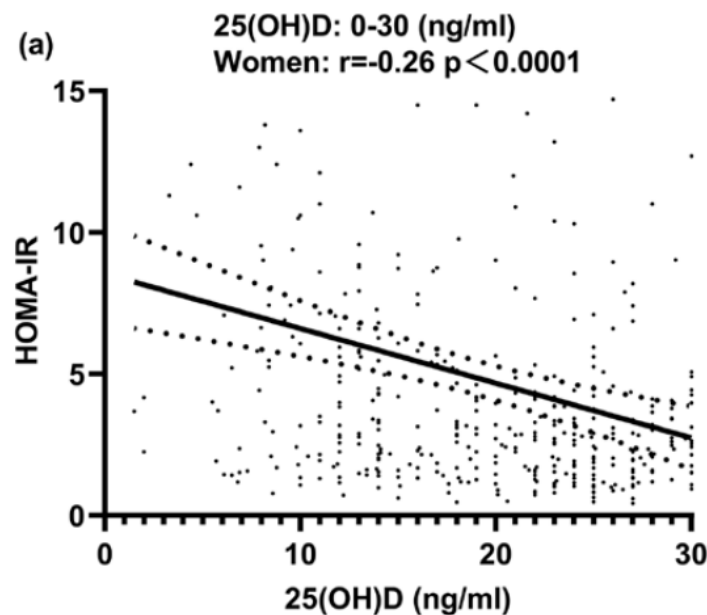
- Warum sollte man freies Vitamin D messen
- Vitamin D und Schwangerschaft/Reproduktionsmedizin
- Vitamin D und Schwangerschafts-Diabetes
- Zusammenfassung



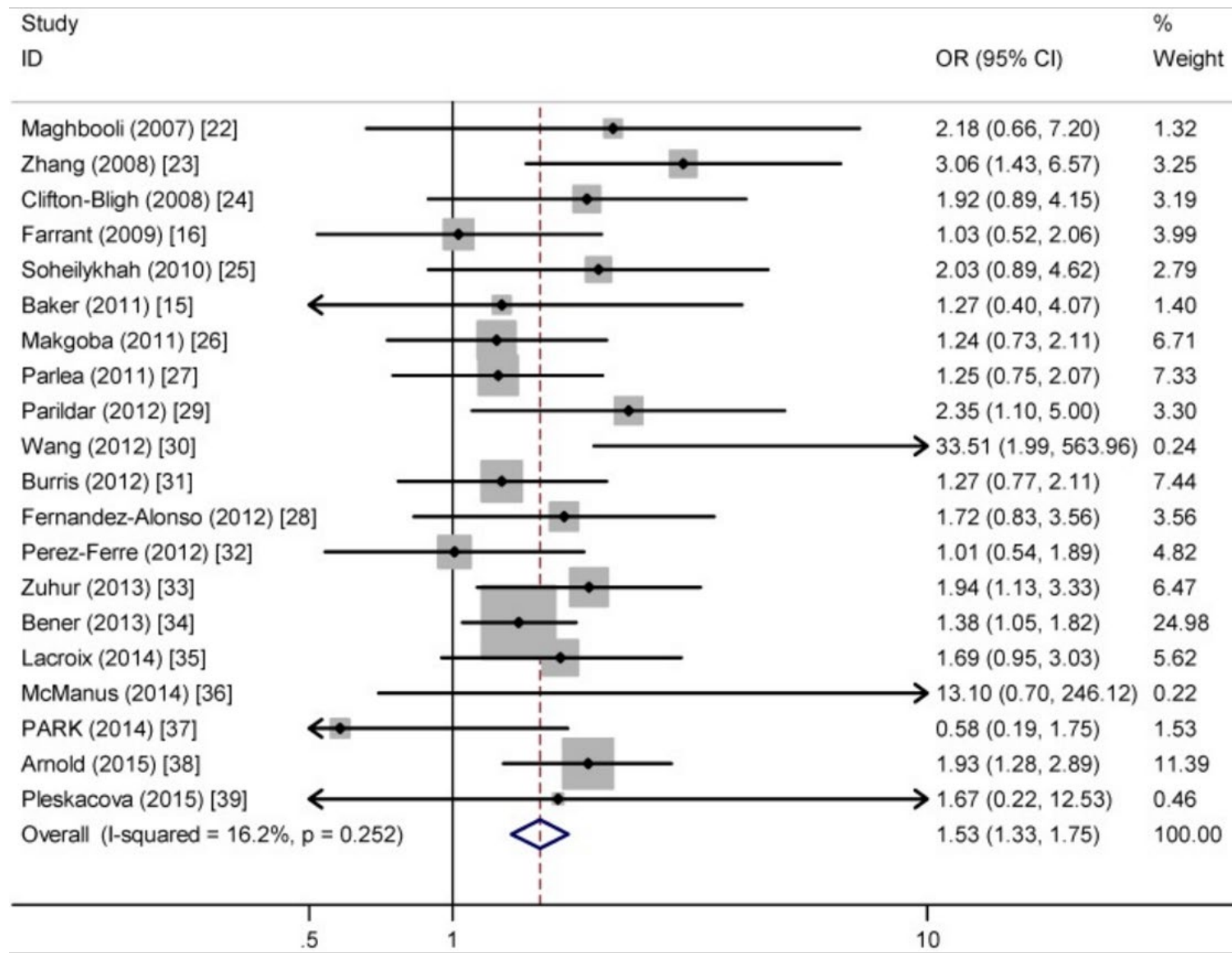
Clinical Research Article

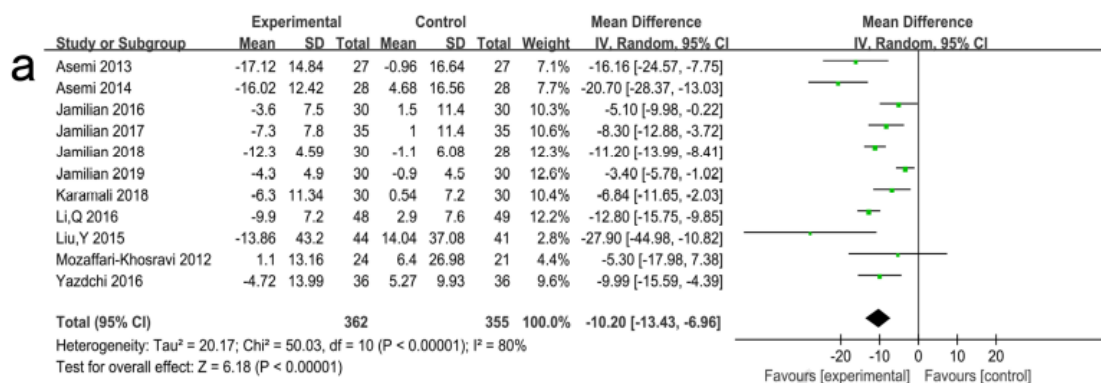
# Sex-Dependent Association of Vitamin D With Insulin Resistance in Humans

Xin Chen,<sup>1,2,\*</sup> Chang Chu,<sup>1,2,\*</sup> Cornelia Doebis,<sup>3</sup> Volker von Baehr,<sup>3</sup> and Berthold Hocher<sup>1,3,4,5</sup>



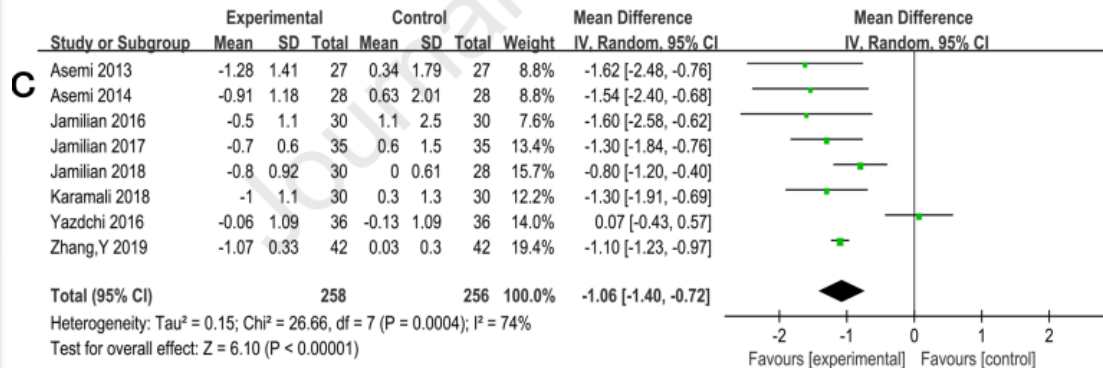
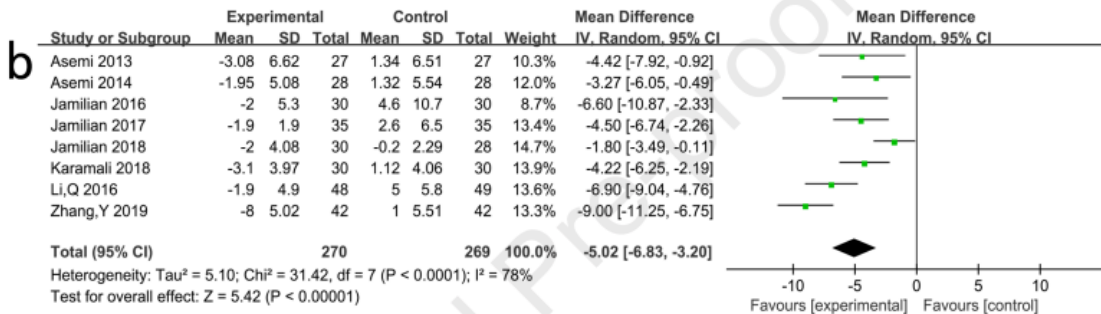
# Meta-analysis of the association between **vitamin D deficiency** and risk of gestational diabetes mellitus (GDM)





The effects of **vitamin D supplementation** on glycemic control and maternal-neonatal outcomes in women with established gestational diabetes mellitus: A systematic review and meta-analysis.

Clin Nutr. 2021 May;40(5):3148-3157.



Forest plot:

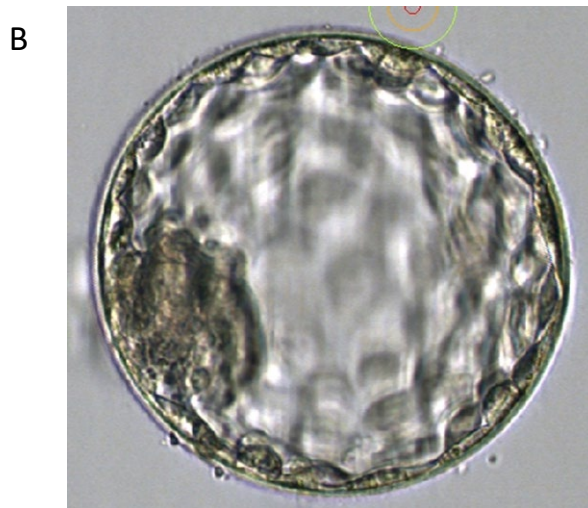
(a) Nüchtern-Zucker

(b) Insulin

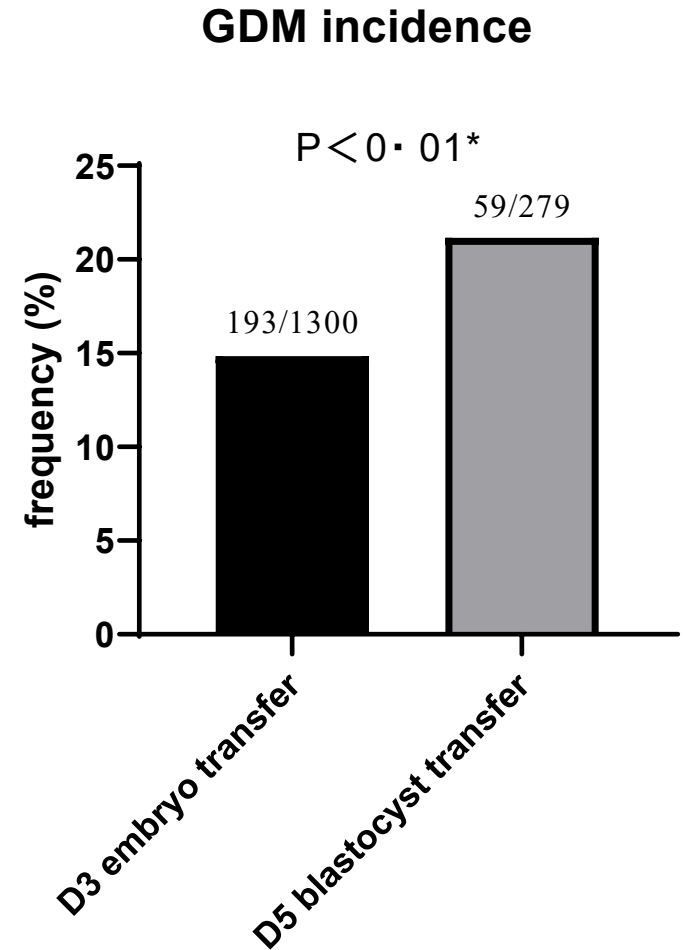
(c) HOMA-IR.

# Blastocyst Transfer: A Risk Factor for Gestational Diabetes Mellitus in Women Undergoing In Vitro Fertilization.

Chen H, .... Hocher B . *J Clin Endocrinol Metab.* 2022;107(1):e143-e152. doi:10.1210/clinem/dgab594



C



**Vitamin D – Mangel im Kulturmedium ???**

# Was hat Hocher gesagt \_

- **Der totale 25(OH) Vitamin D Spiegel hängt wesentlich von Faktoren ab, die unabhängig sind von der endokrinologischen Funktion von Vitamin D (E2-Status Leberfunktion, Nierenfunktion, genetischer Hintergrund)**
- **Freies Vitamin D korreliert besser mit klinischen Endpunkten im Vergleich zu totalem Vit D**
- **Vitamin-D-Mangel ist mit männlicher und weiblicher Unfruchtbarkeit assoziiert**
- **Vitamin-D-Mangel ist mit GDM und Eklampsie assoziiert**
- **Vitamin-D-Mangel während der Schwangerschaft ist mit Frühgeburt, niedrigem Geburtsgewicht, Fettleibigkeit bei Kindern, Knochengesundheit der Nachkommen und kardiometabolischen Erkrankungen der Nachkommen im späteren Leben verbunden**
- **Der freie Vitamin-D-Spiegel hängt von genetischen Variationen innerhalb des Vitamin-D-Stoffwechsels, dem Vitamin-D-bindenden Protein und auch von epigenetischen Veränderungen ab.**
- **Die Konzentration von freiem 25 (OH) Vitamin D ist während einer normalen Schwangerschaft weitgehend konstant, während die Konzentration von 1,25 (OH)<sup>2</sup> Vit D während der Schwangerschaft deutlich ansteigt.**
- **Freies, bioverfügbares 25(OH)D nimmt während der ovariellen Stimulation bei künstlicher Befruchtung durch die E2-stimulierte DBP-Synthese ab**
- **Seltene genetische Varianten im Vitamin D Metabolismus verursachen fatale Hypercalzämien**

# Was sollte wann bestimmt werden

- Freies 25 (OH) Vitamin D und 1,25 (OH)<sub>2</sub> vor Schwangerschaft Mann und Frau
- PTH und FGF23 sind sehr empfindliche endokrine Marker für zu hohe und zu niedrige Spiegel
- Freies 25 (OH) Vitamin D und 1,25 (OH)<sub>2</sub> Vitamin D im ersten und zweiten Trimester





Ruprecht-Karls-Universität Heidelberg



**Vielen Dank  
für Ihre Aufmerksamkeit!**