Nutritional D versus Active Vitamin D: Which One to Choose?

Activate Vitamin D

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Use of activate Vitamin D in CKD patients

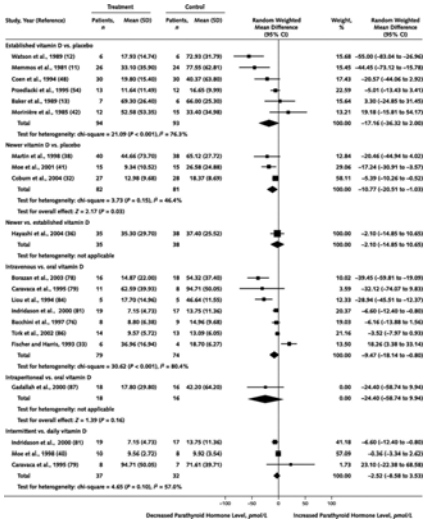
- Secondary hyperparathyroidism
- Proteinuria
- Hypertension
- Left Ventricular Hypertrophy
- Mortality

Meta-analysis: Vitamin D Compounds in Chronic Kidney Disease

- 76 trials, 3,667 participants
- Mortality only reported in 8 trials (627 patients)
- “Beneficial effects on patient-level outcomes are unproven”

Palmer et al. Ann of Intern Med. 2007

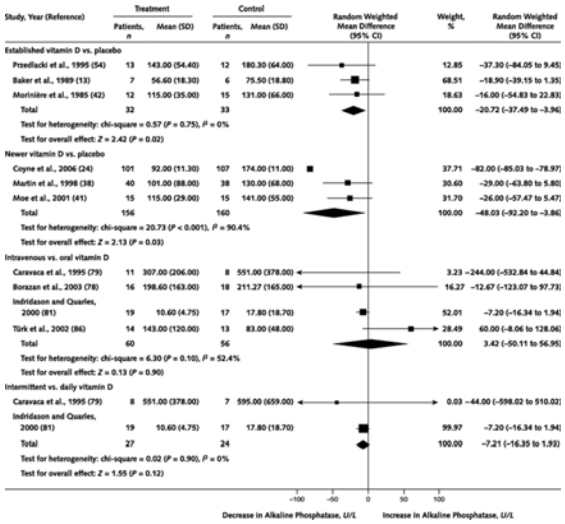
Effect of vitamin D versus placebo or other comparator interventions on the end-of-treatment PTH concentration in people with chronic kidney disease



Palmer, S. C. et. al. Ann Intern Med 2007;147:840-853

Annals of Internal Medicine

Effect of vitamin D vs. placebo or other comparator interventions on end-of-treatment serum alkaline phosphatase levels in CKD



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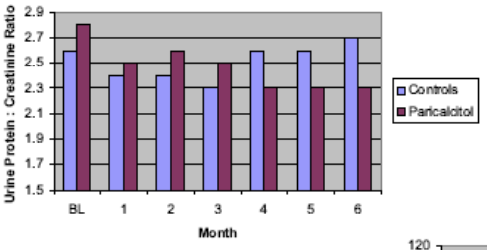
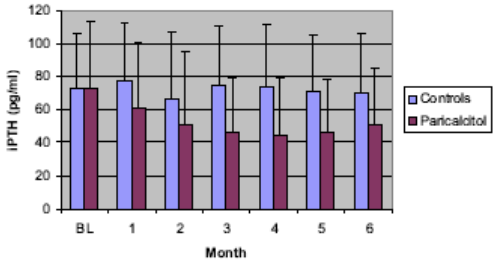
Oral Paricalcitol in the Treatment of Patients With CKD and Proteinuria: A Randomized Trial

Steven Fishbane, MD, Harini Chittineni, MD, Michal Packman, MD, Paula Dutka, RN, Nicole Ali, MD, and Nicole Durie, MD

Am J Kidney Dis 54:647-652.



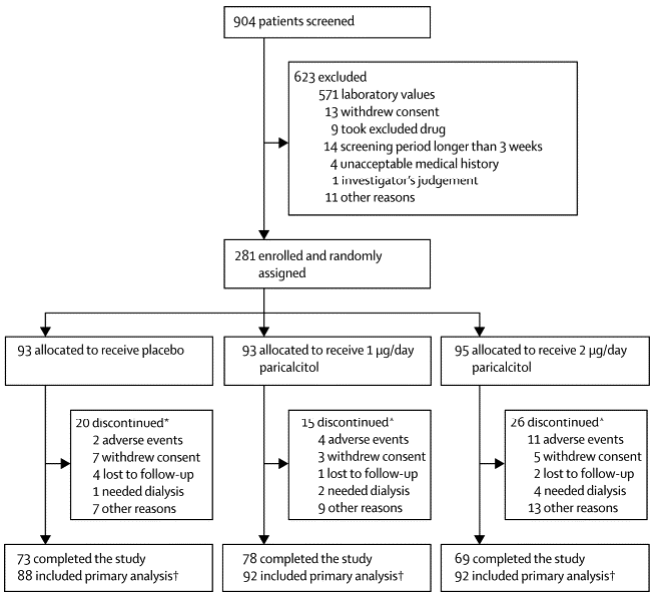
Double-blind placebo controlled trial of paricalcitol in 61 patients with eGFR 15-90 (mean 35ml/min/1.73m^2)



Selective vitamin D receptor activation with paricalcitol for reduction of albuminuria in patients with type 2 diabetes (VITAL study): a randomised controlled trial

de Zeeuw *et al.* The Lancet 2010

- 281 enrolled patients from 9 different countries
- Type 2 diabetics
- eGFR 15-90 ml/min/1.73m^2
- albuminuria (100-3,000 mg/g)
- ACE inhibitor or ARBs
- Serum calcium <9.8 mg/dL
- PTH 35-500 pg/mL



de Zeeuw *et al.* The Lancet 2010

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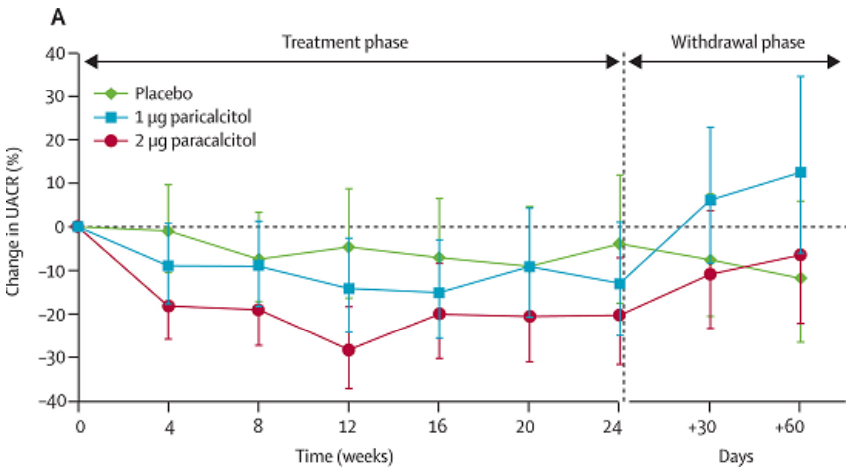

de Zeeuw *et al.* The Lancet 2010

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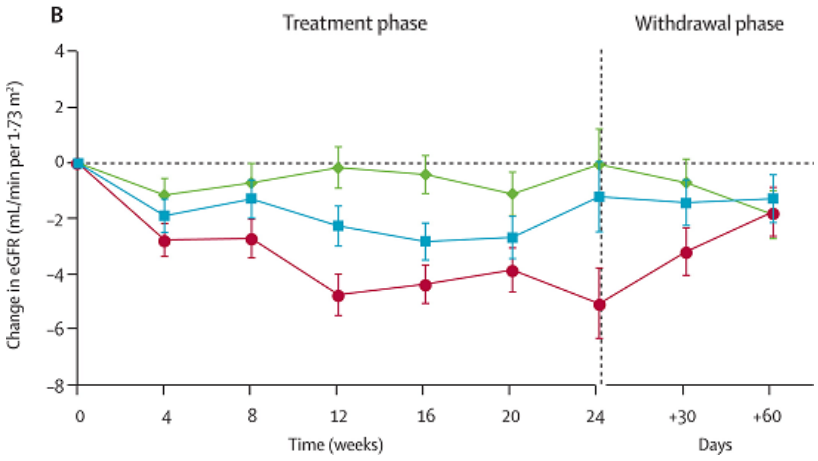

de Zeeuw *et al.* The Lancet 2010

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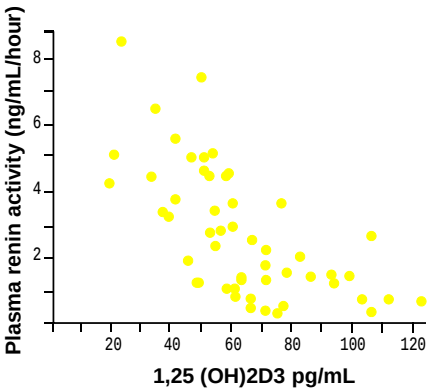
Low Serum 1-25D Levels Are Associated With High Levels of Plasma Renin Activity

Variable	Normo-tensive (n=0)	Low renin (n=20)	Normal renin (n=18)	High renin (n=13)
Plasma renin activity (ng/mL/h)	2.4±0.51	0.65±0.08	1.98±0.32	4.59±0.52
PTH (pg/mL)	244±21	433±38	318±22	242±37
$1,25(OH)_2D_3$ (pg/mL)	53.9±5.3	75.4±5.5	57.2±4.3	43.1±4.6



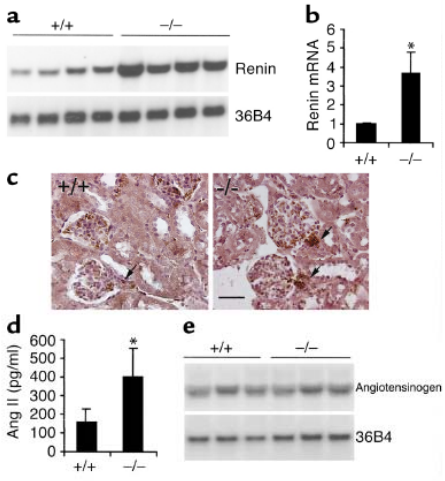
Resnick LM. *Ann Intern Med*. 1986;105:649-654.

1,25-Dihydroxyvitamin D_3 is a negative endocrine regulator of the renin-angiotensin system

See related Commentary on pages 155–156.

Yan Chun Li,[1] Juan Kong,[1] Minjie Wei,[1] Zhou-Feng Chen,[2] Shu Q. Liu,[3] and Li-Ping Cao[1]

[1]Department of Medicine, University of Chicago, Chicago, Illinois, USA
[2]Department of Anesthesiology, Washington University School of Medicine, St. Louis, Missouri, USA
[3]Department of Biomedical Engineering, Northwestern University, Evanston, Illinois, USA



J. Clin. Invest. **110**:229–238 (2002).

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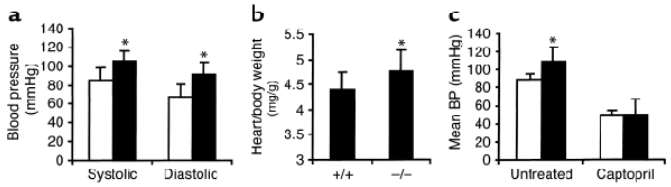

Figure 2
Effect of VDR inactivation on blood pressure and heart weight/body weight ratio. (a) Systolic and diastolic blood pressures of wild-type (white bars) and VDR$^{-/-}$ (black bars) mice. *P < 0.01 vs. corresponding wild-type mice; n = 9 for wild-type mice; n = 8 for VDR$^{-/-}$ mice. (b) Ratio of heart weight to body weight of wild-type and VDR$^{-/-}$ mice. *P < 0.05 vs. wild-type mice; n = 9 in each genotype. (c) Mean blood pressure (BP) of wild-type (white bars) and VDR$^{-/-}$ (black bars) mice untreated or treated with captopril for 5 days. *P < 0.05 vs. corresponding untreated wild-type mice; n = 4 in each genotype in each group.

J. Clin. Invest. **110**:229–238 (2002).

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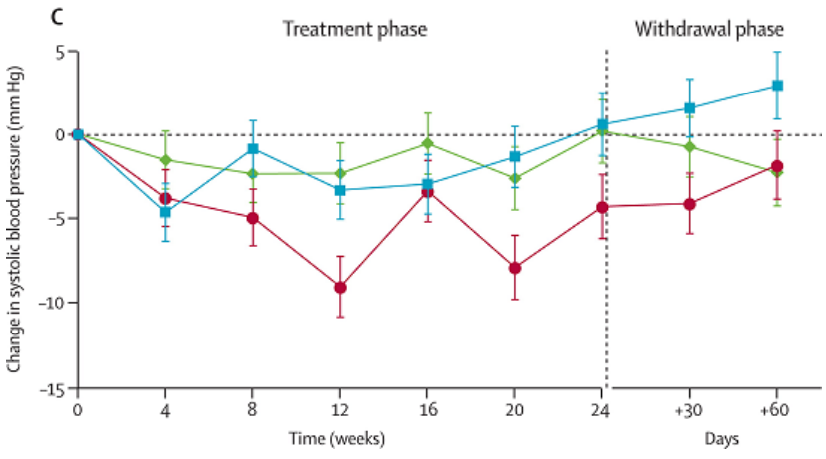

de Zeeuw *et al.* The Lancet 2010

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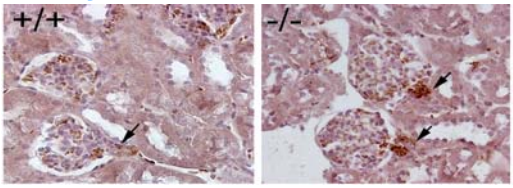
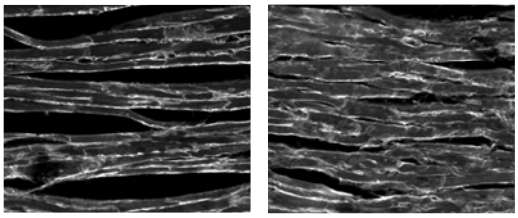
Renal and Cardiac Effects: VDR Knockout Mice

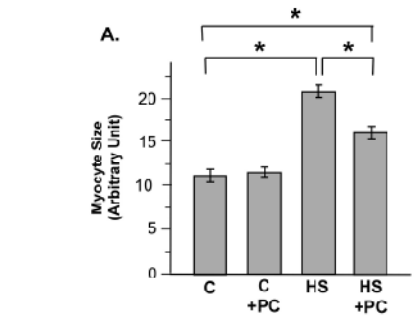
Kidney Cortex With Anti-renin Anti-serum

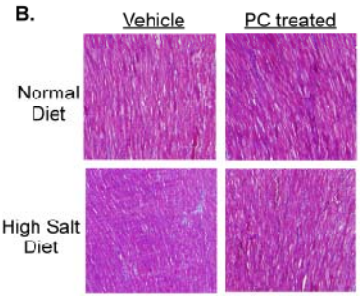


Left Ventricular Cardiac Myocytes



1. Li YC, et al. *J Clin Invest*. 2002;110:229-238.
2. Xiang G, et al. *Am J Physiol*. 2005;288:e125-132.





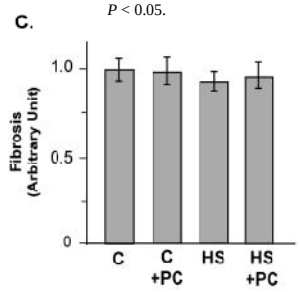


Fig. 5. Myocyte hypertrophy and fibrosis measures. (*A*) HS diet leads to cardiomyocyte hypertrophy, whereas PC attenuates this response. Cardiomyocyte area was measured by using the GNU Image Manipulation Program (GIMP; Open Source). Mean value for each group (C, $n = 4$; C+PC, $n = 5$; HS, $n = 5$; HS+PC = 4, 25 cells per animal); *, $P < 0.05$. (*B*) Representative Masson's trichrome staining of the heart sections. (*C*) There were no significant differences in cardiac fibrosis in all experimental groups. Mean value for each group (C, $n = 4$; C+PC, $n = 5$; HS, $n = 5$; HS+PC = 4; 3-4 fields at ´20 objective per animal were measured), *, $P < 0.05$.

Bodyak et al. (2007) Proc. Natl. Acad. Sci. USA 104, 16810-16815

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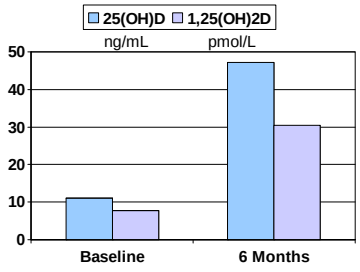
Observational Associations Between Activated Vitamin D Use and Survival in Dialysis Patients

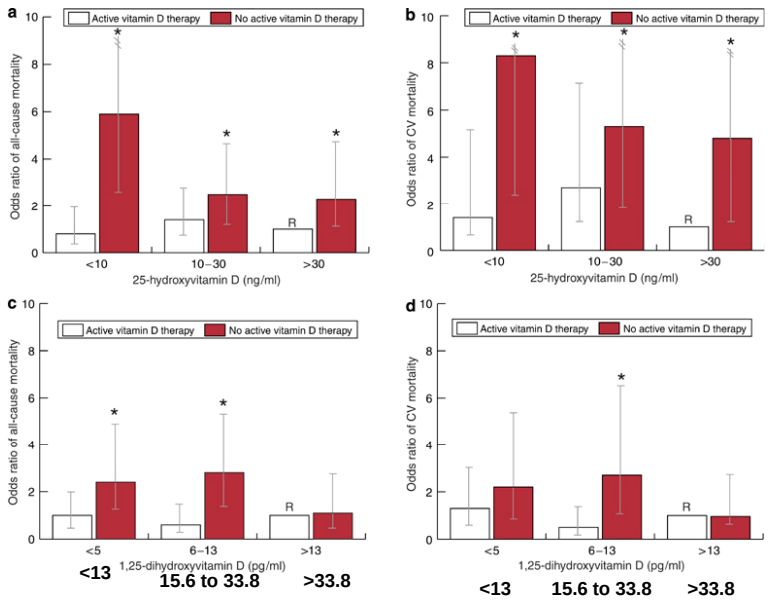
Teng *et al*, J Am Soc Nephrol, 2005	Any VDRA	N=51,037
Melamed *et al*, Kidney Int., 2006	Calcitriol	N=1007
Tentori *et al.* Kidney Int., 2006	Any VDRA	N=7731
Kalantar-Zadeh *et al.* Kidney Int., 2006	Paricalcitol	N=58,058
Shoji *et al.* Nephrol Dial Transplant, 2004	Alfacalcidol	N=242
Wolf *et al.* J Am Soc Nephrol, 2008	Any VDRA	N=9303
Shinaberger *et al.* Clin J Am Soc Nephrol, 2008	Paricalcitol	N=34,307
Kovesdy *et al.* Archives of Internal Med. 2008	Calcitriol	N=520
Shoben *et al.* J Am Soc Nephrol, 2008	Calcitriol	N=1418
Tentori *et al.* Nephrol Dial Transplant, 2009	Any VDRA	N=38,066

Evidence for Persistent Vitamin D 1-Alpha-Hydroxylation in Hemodialysis Patients: Evolution of Serum 1,25-Dihydroxycholecalciferol after 6 Months of 25-Hydroxycholecalciferol Treatment

C. Jean et al. Nephron Clin Pract 2008

- 43 Hemodialysis patients given 400 – 1200 IU of Vitamin D3 daily for 6 months
- Mean 1,25(OH)2D levels post therapy 30.5 +/- 15 pmol/L





Wolf et al. *Kidney Int* 2007

Conclusions

- Patients with CKD have deficiencies of 25(OH)D and 1,25 (OH)2D
- Randomized clinical trials have shown a benefit for active Vitamin D in:
  - Albuminuria
  - Hypertension
- Associations between active Vitamin D use and:
  - Mortality