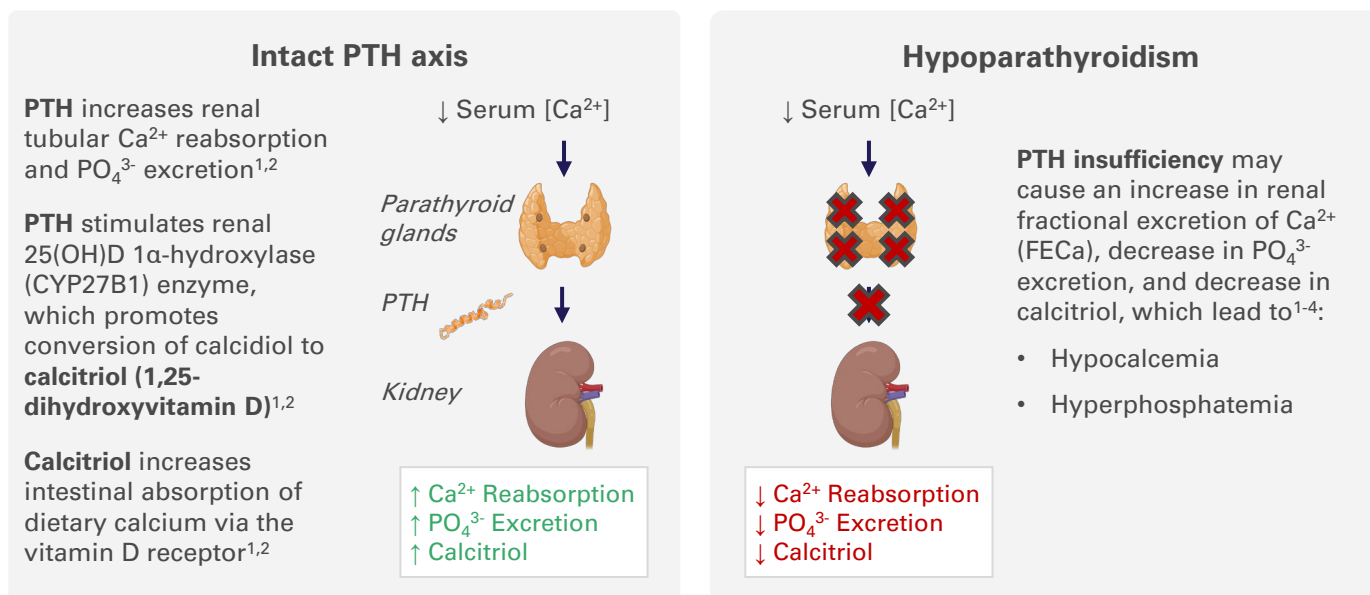


Hypoparathyroidism and Renal Function

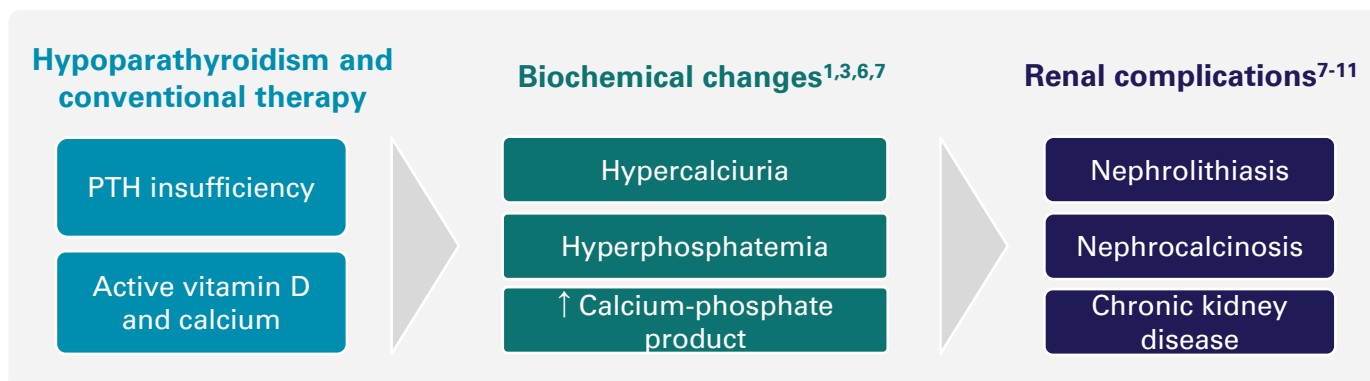
Renal pathophysiology in chronic hypoparathyroidism



Conventional therapy (active vitamin D and calcium) for chronic hypoparathyroidism

- Conventional therapy aims to alleviate hypocalcemia but does not address insufficient PTH levels⁵
- Conventional therapy may lead to increased renal filtered load of Ca^{2+} , hypercalciuria, and nephrotoxic effects^{1,4}

Factors associated with renal complications in individuals with chronic hypoparathyroidism who are managed with conventional therapy^a



The pathophysiological mechanisms of renal complications in chronic hypoparathyroidism are not well established and likely reflect a variety of factors, including PTH insufficiency and adverse renal responses to conventional therapy^{a,12,13}

^aactive vitamin D and calcium

Abbreviations: Ca^{2+} , calcium; PO_4^{3-} , phosphate; PTH, parathyroid hormone

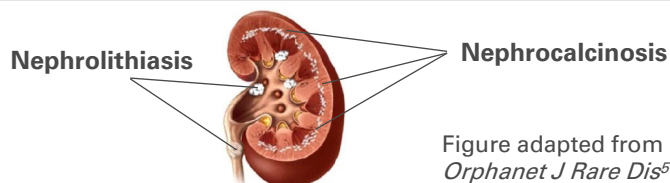
References: 1. Mannstadt M, et al. *Nat Rev Dis Primers*. 2017;3:17055. 2. Shoback D. *N Engl J Med*. 2008;359(4):391-403. 3. Brandi ML, et al. *J Clin Endocrinol Metab*. 2016;101(6):2273-83. 4. Khan AA, et al. *J Bone Miner Res*. 2022;37(12):2568-2585. 5. Khan AA, et al. *Eur J Endocrinol*. 2019;180(3):P1-p22. 6. Rubin MR. *F1000Res*. 2020;9. 7. Shoback DM, et al. *J Clin Endocrinol Metab*. 2016;101(6):2300-2312. 8. Gosmanova EO. *Rev Endocr Metab Disord*. 2021;22(2):297-316. 9. Smith A, et al. Presented ESPE & ESE. May 2025. 10. Reddy NL et al. *Endocr Metab Sci*. 2025.11. Noori W, et al. *Adv Ther*. 2025. 12. Mitchell, D.M., et al. *J Clin Endocrinol Metab*, 2012. 97(12): p. 4507–14. 13. Hamdy, N.A.T., et al. *J Endocrinol Invest*, 2021. 44(7): p. 1437–1446. MED-US-TC-PTH-2600039| May 2026

Hypoparathyroidism and Renal Function

Individuals with chronic hypoparathyroidism who are managed with conventional therapy have an increased risk of renal complications vs. the general population¹⁻⁴

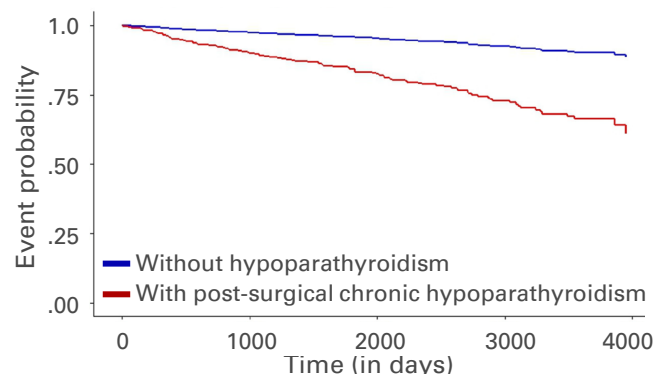
Nephrolithiasis and nephrocalcinosis^{a,1}

For those with chronic hypoparathyroidism, nephrolithiasis has been reported in up to 36% of individuals and nephrocalcinosis has been reported in up to 38% of individuals



Composite renal complications^{b,c,2}

Individuals with post-surgical chronic hypoparathyroidism have a higher probability of composite renal complications

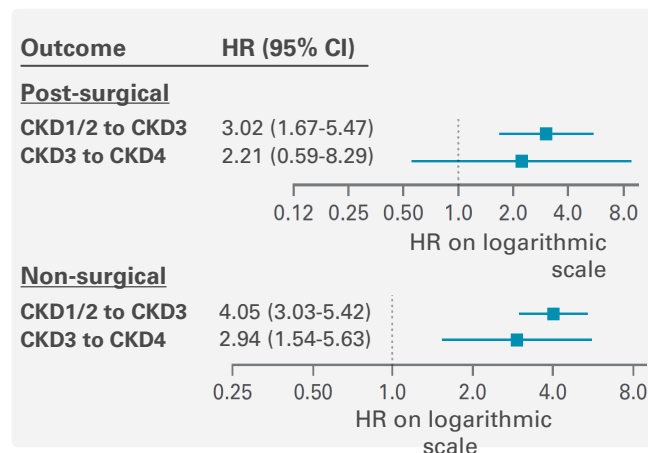


Individuals with post-surgical chronic hypoparathyroidism vs. patients without hypoparathyroidism

Composite renal complications	Hazard ratio (95% CI)	P value
	4.10 (2.25-7.46)	<.001

Chronic kidney disease (CKD) progression^{d,3}

Individuals with chronic hypoparathyroidism who are managed with conventional therapy^e have an increased risk of CKD progression



CKD has been reported in up to 41% of individuals with chronic hypoparathyroidism^{a,1}

Risk of hospitalization for CKD

Individuals with chronic hypoparathyroidism compared with matched controls^{f,6}

Chronic hypoparathyroidism	Hazard ratio (95% CI)	P value
Chronic hypoparathyroidism	3.49 (2.84-4.30)	<.001
Postsurgical	3.34 (2.64-4.23)	<.001
Nonsurgical	3.96 (2.76-5.68)	<.001

Individuals with hypoparathyroidism have an increased risk of hospitalization due to renal complications, such as CKD and renal failure, compared with age- and sex-matched controls^{5,6}

^aIn systematic review of 13 manuscripts, nephrolithiasis and nephrocalcinosis were assessed by diagnostic codes, CT scans, or self-reporting; CKD defined as eGFR <60 mL/min/1.73 m², ≥ stage 3 classification, ICD codes, or self-reporting. ^bRetrospective matched cohort study in England (2007–2020); post-surgical hypoparathyroidism (n=215) matched to patients without hypoparathyroidism (n=2,149) in adjusted cox proportional hazards regression model. ^ccomposite = renal insufficiency, nephrocalcinosis and nephrolithiasis; ^dRetrospective matched cohort study in England (2008–2019); post-surgical (n=215) or non-surgical (n=730) hypoparathyroidism matched to controls (1:10) in cox proportional hazards regression model adjusted for age, sex, and cardiovascular disease. ^eIn post-surgical patients, 71% were managed with calcitriol (≥0.50 µg/day); 73% were managed with calcium (≥600 mg/day). In non-surgical patients, 40% were managed with calcitriol (≥0.50 µg/day); 67% were managed with calcium (≥600 mg/day). ^fSwedish cohort study (1997–2018); Chronic hypoparathyroidism without preexisting CKD (n=1562) matched to controls (n=15620) in cox proportional hazards regression, adjusted for myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, diabetes, and hypertension.

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PTH, parathyroid hormone

References: 1. Gosmanova EO. *Rev Endocr Metab Disord*. 2021;22(2):297-316. 2. Reddy NL et al. *Endocr Metab Sci*. 2025. 3. Smith A, et al. Presented ESPE & ESE. 2025. 4. Díez JJ, et al. *Endocrine*. 2025;88(3):826–835; 5. Cipriani C, et al. *J Endocrinol Invest*. 2024 Aug;47(8):2021-2027; 6. Swartling O, et al. *J Clin Endocrinol Metab*. 2022 Sep 28;107(10):e4098-e4105.