

Yorvipath (Palopegteriparatide) Reduces Pill Burden and Stabilizes Serum Calcium in Postsurgical Hypoparathyroid Patients with Persistent Symptomatic Hypocalcemia: A Real-World Case Series

Blair Hume^{1*}, Brittany Henderson MD, ECNU^{1*}
Charleston Thyroid Center

¹ Charleston Thyroid Center, Mount Pleasant SC

Introduction

Chronic hypoparathyroidism (HypoPT) is an endocrine disorder characterized by deficient or absent parathyroid hormone production, resulting in symptomatic hypocalcemia. Conventional therapy with calcium and activated vitamin D often results in fluctuating serum calcium levels, recurrent symptoms, and a high daily pill burden that can negatively affect quality of life. Long-term supplementation may also contribute to complications such as nephrocalcinosis, nephrolithiasis, and soft tissue calcification.

Palopegteriparatide (Yorvipath), a sustained-release parathyroid hormone replacement therapy approved in 2024, offers a physiologic treatment approach with the potential to improve biochemical stability and symptom control [Figure 1]. This study aimed to evaluate the effects of Yorvipath on serum calcium levels, supplemental calcium and vitamin D requirements, and symptom burden in patients with chronic HypoPT treated in a real-world clinical setting.

Methods

- A retrospective chart review was conducted at a single thyroid specialty clinic identifying patients with persistently symptomatic postsurgical HypoPT on conventional treatment who initiated palopegteriparatide between January 2025 and the present.
- Longitudinal serum albumin-corrected calcium levels were collected before and after treatment initiation.
- Additional data including calcium supplementation, calcitriol and vitamin D3 dosages, hydrochlorothiazide use, total daily pill burden, Yorvipath dosage, and patient-reported symptoms and clinical outcomes were collected.
- Four patients met inclusion criteria for analysis [Table 1].

Mechanism of Action

- Yorvipath is a prodrug of PTH(1-34) given as a once-daily subcutaneous injection for hypoparathyroidism in adults — designed as true hormone *replacement*, not intermittent dosing of a peptide, making it different than the pulsed administration of Forteo™, Tymlos™, and Natpara (rhPTH1-84) (*now removed from the market*).
- Sustained release from the TransCon depot maintains free PTH(1-34) within the physiologic range across the entire 24-hour dosing interval — an infusion-like, flat exposure profile (effective half-life ~60 hours vs ~1-2 hours for free PTH 1-34).
- The sustained release delivery restores the full spectrum of PTH physiology around the clock including renal distal tubular calcium reabsorption, phosphate excretion, activation of 1α-hydroxylase (endogenous calcitriol production), and normalized bone turnover.

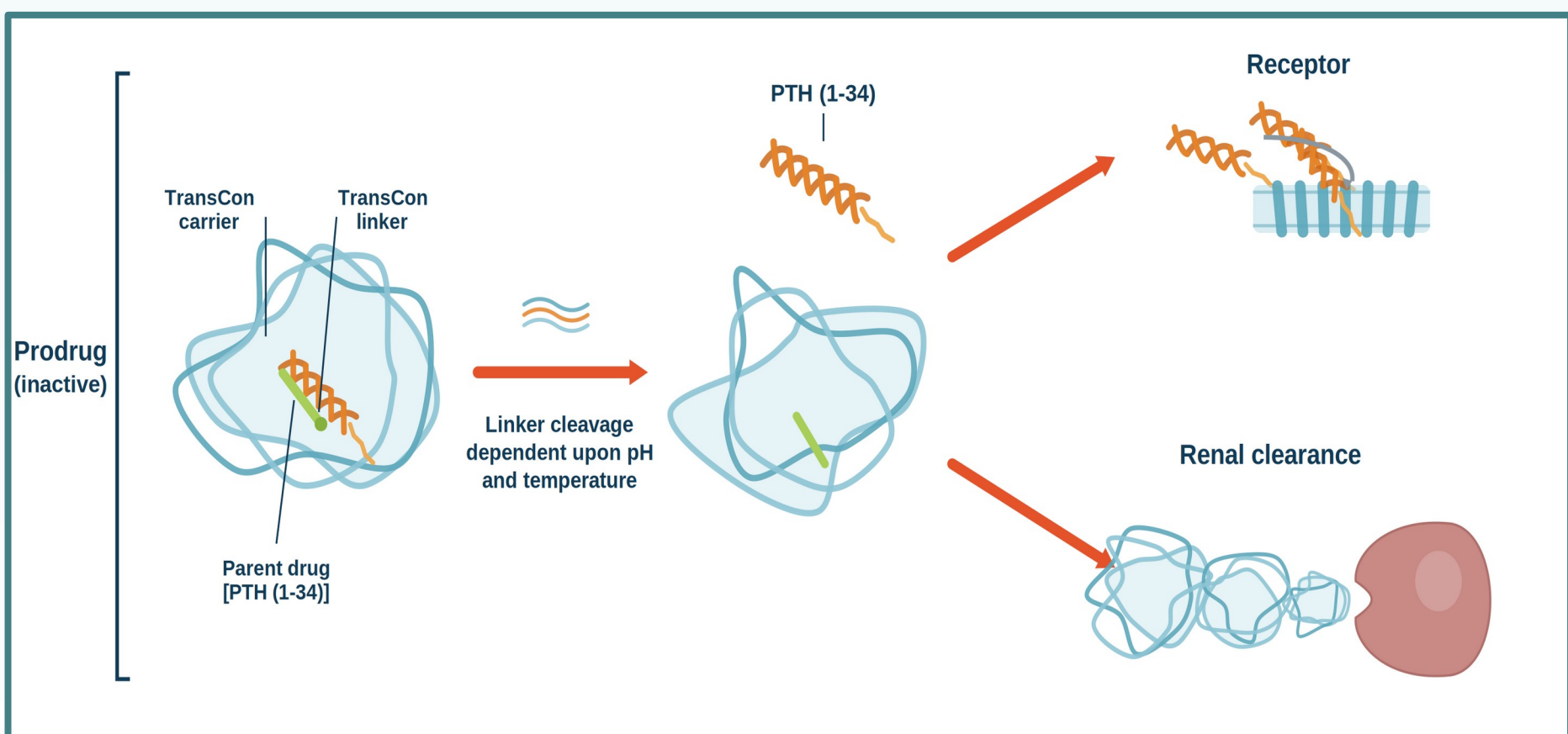


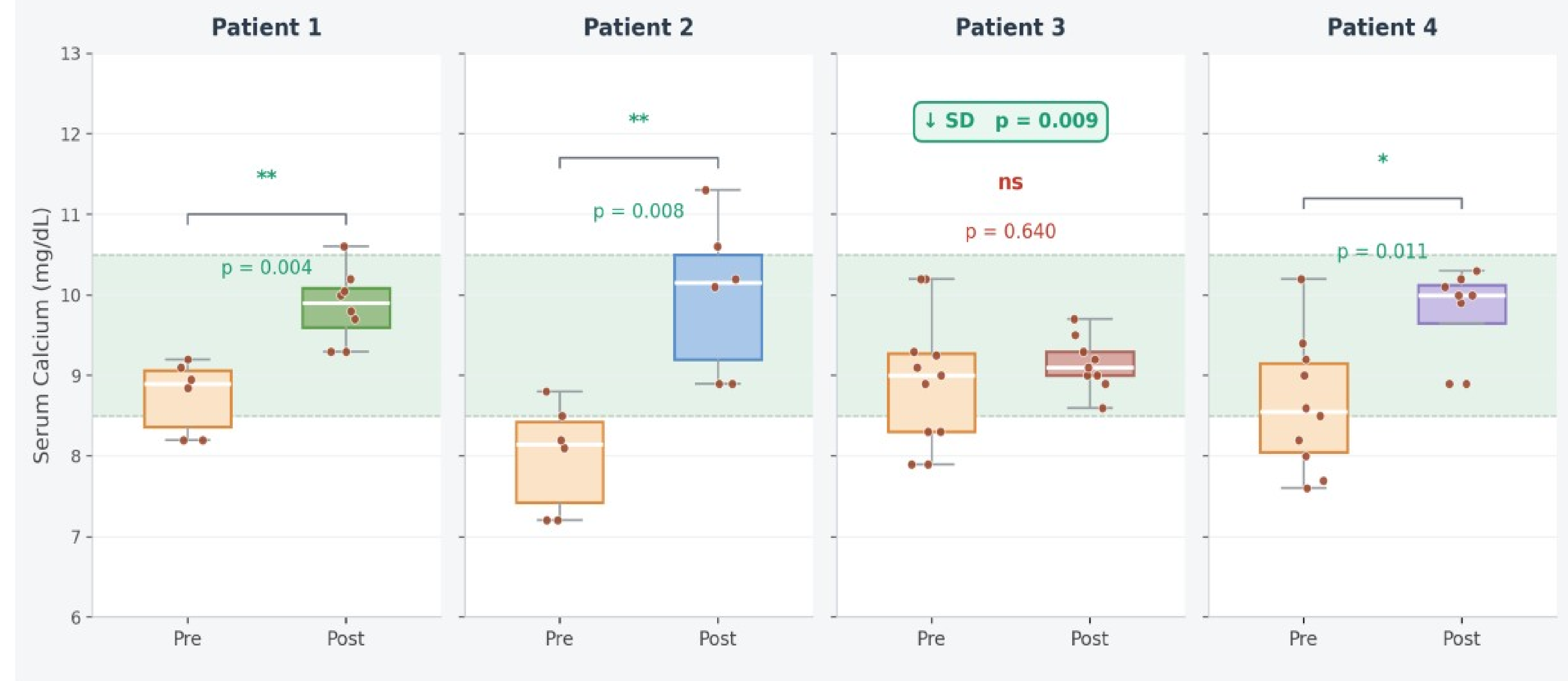
Figure 1. Yorvipath (palopegteriparatide) Mechanism of Action. Yorvipath is an inactive prodrug in which PTH(1-34) is transiently linked to an inert TransCon carrier. pH- and temperature-dependent linker cleavage (approximately pH 7.4 and temperature 37°C) steadily releases active PTH(1-34), which binds the PTH1 receptor, similar to endogenous hormone; the carrier is cleared renally.

Results

Table 1. Patient Characteristics — Hypoparathyroidism Treated with Yorvipath				
Characteristic	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	48	35	37	37
Sex	Female	Female	Female	Female
Ethnicity	White	White	White	White
Indication for thyroidectomy	PTC (thyroid cancer)	Hashitoxicosis (Hashimoto's)	FTC + PTC (thyroid cancer)	PTC (thyroid cancer)
Cause of hypoparathyroidism	Post-op thyroidectomy	Post-op TT (2 PTGs removed)	Post-op TT (PTG autotransplant)	Post-op TT (multiple surgeries)
Yorvipath start	Jun 2025	Sep 2025	May 2025	Aug 2025
Pre-Yorvipath Calcium (elemental mg/day)	800 mg/day (Ca Citrate)	2,400 mg/day (Ca Citrate)	800 mg/day (CaCO ₃ /flums)	1,000 mg/day (Ca supplement)
Pre-Yorvipath Calcitriol (mcg/day)	1.0 mcg/day (0.5 mcg BID)	1.0 mcg/day (0.5 mcg BID)	0.5 mcg/day (0.5 mcg QD)	0.5 mcg/day (0.5 mcg QD)
Pre-Yorvipath Vitamin D3	None (not taking)	5,000 IU/day	Weekly dose (dose NOS)	5,000 IU 2x/week
Pre-Yorvipath HCTZ	No	No	Yes (12.5 mg/day)	Yes (12.5 mg/day)
Pre-Yorvipath Magnesium	Magnesium (dose NOS)	Magnesium (dose NOS)	Not documented	Not documented
Post-Yorvipath Medications	Yorvipath 12 mcg/day (no supplements)	Yorvipath 15 mcg/day (no supplements)	Yorvipath 12 mcg/day + Vitamin D3 weekly (dose NOS)	Yorvipath 18 mcg/day + Vitamin D3 5,000 IU QOD

Table 1. Patient Characteristics (n=4 patients). The average patient age was 39 years old; a majority were Caucasian females. 75% of patients underwent thyroidectomy for thyroid cancer, with the last undergoing surgical intervention for Hashitoxicosis. The average daily dose of calcium pre-Yorvipath was 1,250 mg daily with an average dose of calcitriol at 0.75 mcg/day. 50% of patients were on HCTZ and/or Magnesium to help maintain serum calcium. Post-Yorvipath, most patients were either on no supplements or elective vitamin D3. The mean dose of Yorvipath was 14.25 mcg per day.

Distribution of Serum Calcium: Pre vs Post Yorvipath



Patient 3: reduction in serum calcium standard deviation, one-sided F-test p = 0.009 (variability test, distinct from the mean-comparison p-values shown). Illustrative — estimated from figure data; verify against source data.

Figure 2. Improvement in Serum Calcium and Reduction in Calcium Distribution Pre and Post Yorvipath (n=4 patients). Serum calcium significantly increased in patients 1, 2, and 4 post-Yorvipath. Patient 3 maintained normocalcemia but had a significant reduction in calcium variability, measured by standard deviation, post-Yorvipath (p=0.009) and no instances of hypoglycemia.

Results

- Three out of four patients experienced significant improvements in calcium levels after transitioning to Yorvipath compared to conventional treatment (p<0.01); the fourth patient remained normocalcemic after the transition with significant improvement in standard deviation (p=0.009) [Figure 2].
- While on conventional treatment, all four patients intermittently experienced hypocalcemia and widely fluctuating calcium levels; there were no episodes of hypocalcemia after transition to Yorvipath and only two episodes of hypercalcemia (10.9 and 11.3 mg/dL, respectively) that occurred immediately after transition and resolved with titration off supplements.
- All patients experienced a decrease in average pill burden associated with HypoPT from 8.75 pills/day to 0.5 pills/day (a 94% reduction from conventional therapy) [Figure 3].
- All four patients experienced an improvement of symptoms, including increased mental clarity, decreased depression, and complete resolution of numbness/tingling. Mild adverse events (AEs) of hypotension and headache were reported in one patient and completely resolved with down titration of Yorvipath and dosing at bedtime.

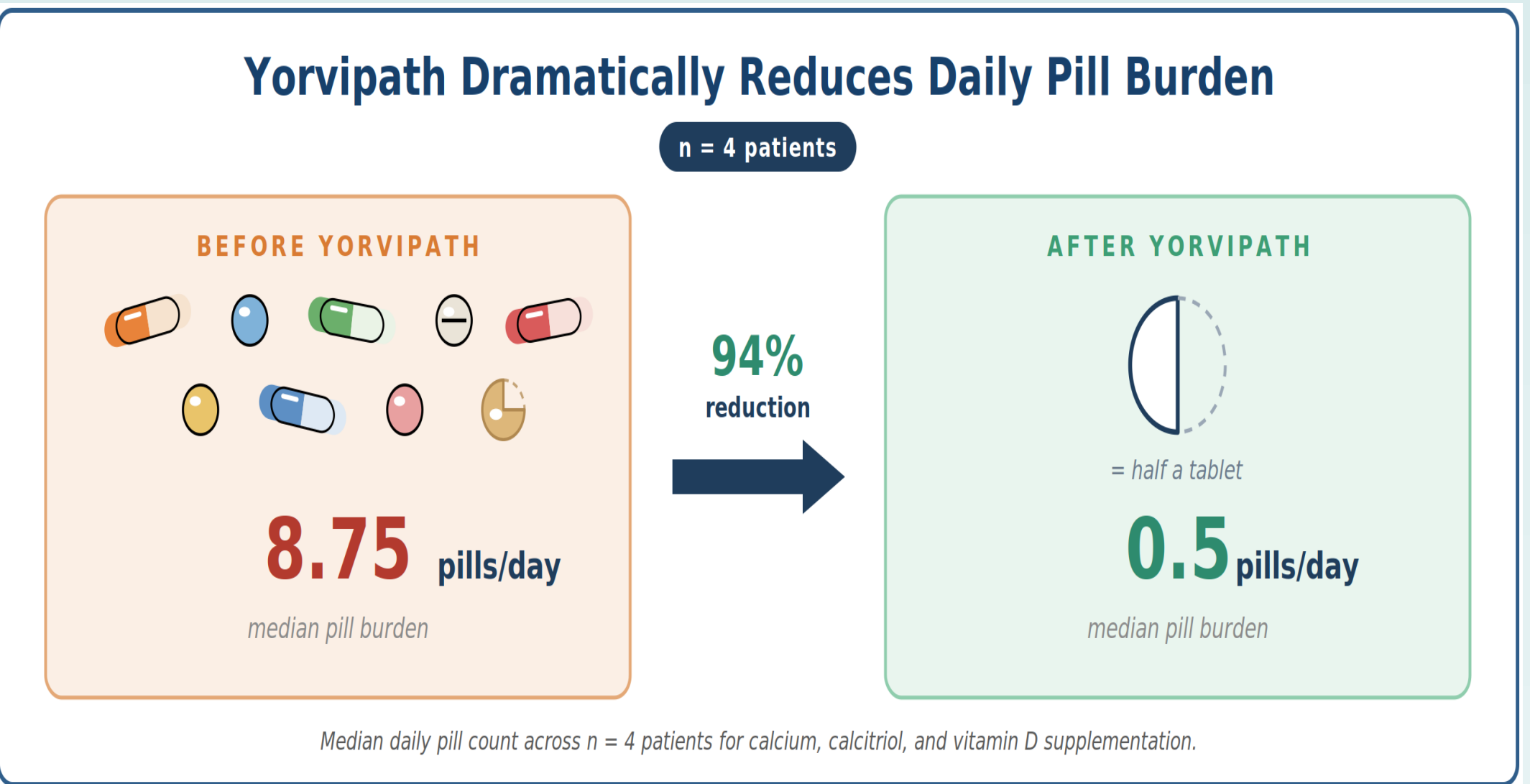


Figure 3. Meaningful Reduction In Daily Pill Burden on Yorvipath. Pill burdens can negatively impact patient quality of life (QOL) and, over time, can contribute to tissue calcification in basal ganglia, kidney, heart and other organs. Among postoperative hypothyroid patients requiring daily oral thyroid medication, finding time to space thyroid medicines at least 2-4 hours from calcium can disrupt QOL and significantly impact thyroid medication absorption by altering gastric pH. In our study, daily pill burden fell by 94% on Yorvipath from an average of 8.75 pills/day on conventional therapy to 0.5 pills per day.

Conclusions

- These real-world findings suggest that palopegteriparatide effectively stabilizes serum calcium, reduces treatment burden, and improves quality of life in patients with postsurgical hypoparathyroidism beyond conventional therapy.
- Larger, long-term clinical studies are needed to further characterize the biochemical and symptomatic effects of Yorvipath and evaluate its long-term efficacy and safety in the management of hypoparathyroidism.

References

- Khan AA, Bilezikian JP, Brandt ML, Clarke BL, Gittoes NJ, Pasieka JL, Rejnmark L, Shoback DM, Potts JT, Guyatt GH, Mannstadt M. Evaluation and Management of Hypoparathyroidism: Summary Statement and Guidelines from the Second International Workshop. *J Bone Miner Res.* 2022;37(12):2568–2585. doi:10.1002/jbmr.4691
- Bjornsson S, Ing S, Mitchell DM, Sikjaer T, Underbjerg L, Hassan-Smith Z, et al. Epidemiology and Financial Burden of Adult Chronic Hypoparathyroidism. *J Bone Miner Res.* 2022. doi:10.1002/jbmr.4675
- Khan AA, et al. Best practice recommendations for the diagnosis and management of hypoparathyroidism. *Metabolism* (Elsevier). 2025. (PII S0026-0495(25)00204-5).
- Khan AA, Rubin MR, Schwarz P, Vokes T, Shoback DM, et al. Efficacy and Safety of Parathyroid Hormone Replacement With TransCon PTH in Hypoparathyroidism: 26-Week Results From the Phase 3 PaHway Trial. *J Bone Miner Res.* 2023;38(1):14–25.
- Clarke BL, Khan AA, Rubin MR, Schwarz P, Vokes T, Shoback DM, et al. Efficacy and Safety of TransCon PTH in Adults With Hypoparathyroidism: 52-Week Results From the Phase 3 PaHway Trial. *J Clin Endocrinol Metab.* 2025;110(4):951–960. doi:10.1210/clinem/dgae693
- YORVIPATH (palopegteriparatide) Prescribing Information. Ascendis Pharma, Inc.; 2024. (FDA approval announced August 12, 2024.)
- Singh N, Singh PN, Hershman JM. Effect of Calcium Carbonate on the Absorption of Levothyroxine. *JAMA.* 2000;283(21):2822–2825. doi:10.1001/jama.283.21.2822
- Singh N, Weisler SL, Hershman JM. The Acute Effect of Calcium Carbonate on the Intestinal Absorption of Levothyroxine. *Thyroid.* 2001;11(10):967–971. doi:10.1089/105072501753211046
- Shahid, S. R., Shahid, K., Ehsan, S., Khalid, M., & Waafra, A. (2026). Advancing hypoparathyroidism treatment: FDA approval of Palopegteriparatide as a promising orphan drug. *Annals of medicine and surgery* (2012), 88(2), 1209–1212. <https://doi.org/10.1097/MS9.00000000000004734>