

Revised European Society of Endocrinology Clinical Practice Guideline: Treatment of Chronic Hypoparathyroidism in Adults

Jens Bollerslev,^{1,*}  Ottilia Buch,² Luís Miguel Cardoso,³ Neil Gittoes,⁴ Pascal Houillier,^{5,6,7} Leonie van Hulsteijn,^{8,9}  Ozer Makay,^{10,11}  Claudio Marcocci,¹² J. Carl Pallais,¹³ Stefan Pilz,¹⁴  Lars Rejnmark,¹⁵ Maria Yavropoulou,¹⁶ and Olaf M. Dekkers^{9,17,18} 

¹Faculty of Medicine, University of Oslo, 0372 Oslo, Norway

²Endocrinology Centre, York and Scarborough Teaching Hospitals NHSFT, YO31 8HE York, UK

³Local Health Unity of Coimbra, and Institute for Research and Innovation in Health of the University of Porto, 4099-002 Porto, Portugal

⁴Centre for Endocrinology, Diabetes and Metabolism, University of Birmingham & Queen Elizabeth Hospital, Birmingham B15 2GW, UK

⁵Service de Physiologie, Hôpital Européen Georges-Pompidou, Assistance Publique - Hôpitaux de Paris, 75015 Paris, France

⁶Centre de Référence des Maladies Rares du Calcium et du Phosphate, Endo-ERN, 75015 Paris, France

⁷Centre de Recherche des Cordeliers, INSERM, Sorbonne Université, Université Paris Cité, 75006 Paris, France

⁸European Society of Endocrinology, Bristol BS32 4QW, UK

⁹Department of Clinical Epidemiology, Leiden University Medical Center, 2333 ZA Leiden, The Netherlands

¹⁰Özel Sağlık Hospital, Centre for Endocrine Surgery, 35000 Izmir, Türkiye

¹¹Aristotle University, School of Medicine, Thessaloniki 54124, Greece

¹²Department of Clinical and Experimental Medicine, University of Pisa, 56126 Pisa, Italy

¹³Division of Endocrinology, Diabetes, and Hypertension, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 02115, USA

¹⁴Department of Internal Medicine, Division of Endocrinology and Diabetology, Medical University of Graz, 8010 Graz, Austria

¹⁵Department of Endocrinology and Metabolism, Aarhus University Hospital, 8200 Aarhus, Denmark

¹⁶First Department of Propaedeutic and Internal Medicine, National and Kapodistrian University of Athens, LAIKO General Hospital of Athens, Centre of Excellence for Rare Endocrine Diseases (CERED), Athens 115 27, Greece

¹⁷Department of Endocrinology and Metabolism, Leiden University Medical Center, 2333 ZA Leiden, The Netherlands

¹⁸Department of Clinical Epidemiology, Aarhus University, 8200 Aarhus, Denmark

*Corresponding author: Jens Bollerslev. Email: jens.bollerslev@medisin.uio.no

Abstract

In the present European Society of Endocrinology (ESE) clinical guideline, we present recommendations for the diagnosis, management, and monitoring of chronic hypoparathyroidism (HypoPT) in adults. Management of HypoPT has changed since the first ESE clinical guideline was published in 2015, as has the knowledge on patient burden of the disease, and the understanding of associated morbidities. In line with the ESE policy, the 2015 guidelines were updated based on up-to-date scientific evidence.

As HypoPT is an orphan disease, strong evidence for most outcomes is scarce and recommendations were based on careful synthesis of the literature and expert opinion. Postsurgical HypoPT should be defined as persisting more than 12 months following surgery; recovery could be expected even thereafter (clinical question I [Q I]). For Q II (optimal treatment of chronic HypoPT), relevant data regarding conventional treatment are lacking for clinically relevant endpoints and long-term effects. PTH replacement therapy reduces the pill burden of conventional therapy, improves various biochemical parameters, and potentially improves QoL. We cannot recommend a substantial role for parathyroid allotransplantation in the treatment of chronic HypoPT (Q III).

In conclusion, we present recommendations for the diagnosis, management, and monitoring of chronic HypoPT in adults, to give health care providers practical clinical guidance on the management of this condition. The guideline can serve as a source for preparation of educational materials to empower patients and clinicians.

Keywords: Hypoparathyroidism, hypocalcaemia, PTH replacement therapy, vitamin D

Received: October 25, 2025. Accepted: October 27, 2025

© The Author(s) 2025. Published by Oxford University Press on behalf of European Society of Endocrinology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

1. Summary of Recommendations

1. Diagnosis

R.1.1 We recommend considering a diagnosis of chronic hypoparathyroidism (HypoPT) in a patient with persistent hypocalcaemia and inappropriately low or inappropriately normal parathyroid hormone (PTH) levels.

R.1.2 We recommend genetic testing and/or family screening in a patient with nonsurgical HypoPT without other obvious aetiology.

2. General goals of management in chronic hypoparathyroidism

R.2.1 We recommend treatment for HypoPT to be personalised and centred on the patient's overall well-being with therapeutic goals that optimise quality of life (QoL), minimise symptoms of hypocalcaemia, improve long-term prognosis, and maintain calcium levels within the lower part or slightly below the reference range. (Good clinical practice)

R.2.2 We recommend providing information/education that enables patients to recognise the possible symptoms of hypo- or hypercalcaemia and/or complications of their disease. (Good clinical practice)

R.2.3 We suggest aiming for normal 24-hour urinary calcium excretion. (⊕○○○)

R.2.4 We suggest aiming for phosphate levels within the reference range. (⊕○○○)

R.2.5 We suggest aiming for magnesium levels within the reference range. (⊕○○○)

R.2.6 We suggest aiming at an adequate vitamin D status (25(OH)D level ≥ 75 nmol/L [> 30 ng/mL]). (⊕○○○)

3. Treatment

R.3.1 We recommend treatment of all patients with chronic HypoPT who have symptoms of hypocalcaemia and/or an albumin-adjusted calcium level < 2.0 mmol/L (< 8.0 mg/dL) \approx ionised calcium (iCa^{2+}) < 1.00 mmol/L.

R.3.2 We suggest offering treatment to patients with chronic HypoPT, even if apparently asymptomatic, if albumin-adjusted calcium levels are between 2.0 mmol/l (8.0 mg/dL or iCa^{2+} 1.00 mmol/L) and the lower limit of the reference range to assess whether this may improve their well-being. (Good clinical practice)

R.3.3 We recommend treatment with vitamin D.

R.3.3.1 We recommend treatment with an activated vitamin D analogue if available (e.g., alfacalcidol or calcitriol). (⊕○○○)

R.3.3.2 If activated vitamin D analogues are not available, we suggest treatment with supraphysiological doses of calciferol (preferentially cholecalciferol, i.e., vitamin D₃). (⊕○○○)

R.3.3.3 We recommend titration of vitamin D analogue doses aiming at calcium levels within the target range with patients being free of symptomatic hypocalcaemia and biomarkers within the target range. (⊕○○○)

R.3.4 We recommend assuring an adequate calcium intake.

R.3.4.1 We suggest a dietary elemental calcium intake of about 800-1000 mg/day in adults (non-pregnant) (European Food Safety Authority¹).

R.3.4.2 We suggest using calcium supplements if blood calcium levels in the target range cannot be achieved by treatment with activated vitamin D analogues in combination with an adequate dietary calcium intake. (⊕○○○)

R.3.4.3 We recommend that elemental calcium supplementation greater than 500 mg daily should be taken in smaller doses and spread throughout the day.

R.3.5 We recommend PTH replacement therapy patients with chronic HypoPT who continue to have signs or symptoms of HypoPT despite optimised treatment with (activated) vitamin D and adequate calcium intake. (⊕⊕○○)

R.3.5.1 We suggest to titrate the dose of PTH replacement therapy to achieve sustained calcium levels in the target range without the need for concurrent activated vitamin D treatment or calcium supplements.

R.3.5.2 We suggest to consider treatment with PTH replacement therapy in patients with one of the following despite optimised conventional treatment:

- Frequent fluctuations in calcium levels, or symptomatic hypocalcaemia
- Impaired quality of life attributable to chronic HypoPT
- Reduced kidney function (eGFR < 60 mL/min per 1.73m²)
- Hypercalciuria (calcium excretion > 7.5 mmol/24-hour [300 mg/24-hour] in men, and > 6.25 mmol/24-hour in women [250 mg/24-hour]; or > 0.1 mmol/kg/24-hour [4 mg/kg/24-hour] in both sexes)
- Hyperphosphataemia

R.3.5.3 If PTH replacement therapy is initiated, we suggest evaluating the treatment effects after 6-12 months, depending on treatment goals. (Good clinical practice)

R.3.6 In the presence of hypercalciuria, we suggest measures to lower urinary calcium excretion, which may include decreased doses of calcium supplements and/or activated vitamin D analogues, a low sodium chloride intake (< 6 g NaCl or < 2.4 g sodium/day), and/or addition of treatment with a thiazide diuretic. If these measures are not effective in normalising hypercalciuria, while maintaining calcium levels within the target range, we suggest PTH replacement therapy. (⊕○○○)

R.3.7 In the presence of hyperphosphataemia, we suggest dietary interventions and/or adjustment of treatment with calcium supplements and vitamin D analogues. If these measures are not effective in normalising hyperphosphataemia while maintaining calcium levels within the target range, we suggest PTH replacement therapy. (⊕○○○)

R.3.8 In a patient with hypomagnesaemia, we suggest measures to increase magnesium levels. (⊕○○○)

R.3.9 Ensure replete levels of vitamin D by using a daily vitamin D supplement (cholecalciferol or ergocalciferol; vitamin D₃ or D₂) of 800-2000IU (20-50 μ g).

4. Monitoring

R.4.1 We suggest measuring PTH levels once a year, as appropriate, to assess endogenous function for potential recovery.

- R.4.2 We recommend routine biochemical monitoring of circulating levels of ionised, or albumin-adjusted total calcium, phosphate, magnesium, and creatinine (estimated glomerular filtration rate [eGFR]), as well as assessment of symptoms of hypocalcaemia and hypercalcaemia at regular time intervals (e.g., every 3-6 months).
- R.4.3 Following changes in therapy, we recommend biochemical monitoring every 1-2 weeks.
- R.4.4 When receiving conventional treatment, we suggest monitoring of 24-hour urinary calcium at regular time intervals (e.g., every 1-2 years).
- R.4.5 We recommend against routine renal imaging, but perform renal imaging (ultrasound or computed tomography) if there are clinical or laboratory features suggestive of nephrolithiasis, nephrocalcinosis, or unexplained decline in renal function.
- R.4.6 We suggest monitoring for the development of signs or symptoms of co-morbidities at regular time intervals (e.g., yearly).
- R.4.7 We suggest assessing fracture risk as recommended for the general population.
5. Special circumstances
- Autosomal dominant hypocalcaemia*
- R.5.1 We recommend close monitoring of patients with autosomal dominant hypocalcaemia (ADH), who are being treated with calcium and/or activated vitamin D, as such patients may be at greater risk of hypercalcaemia and renal complications.
- Pregnancy and breastfeeding*
- R.5.2 We suggest treatment with activated vitamin D analogues and calcium supplements as in non-pregnant women.
- R.5.3 We recommend monitoring ionised calcium and/or albumin-adjusted calcium levels regularly (e.g., every 3 - 4 weeks) throughout pregnancy and lactation and even more frequently (e.g., weekly) during the 4 weeks before and after delivery, aiming to keep calcium levels at the lower end of the normal range.
- R.5.4 We recommend that a paediatrician and/or neonatologist be informed of maternal HypoPT and be involved in the immediate care and monitoring of the infant for potential consequences related to both maternal treatment and the underlying maternal disorder.

2. Clinical considerations in chronic hypoparathyroidism

2.1 Aetiology and Epidemiology

Hypoparathyroidism (HypoPT) is an endocrine disease characterised by low calcium and undetectable or inappropriately low (insufficient) circulating parathyroid hormone (PTH) levels²⁻⁵. It is a rare condition, designated an orphan disease by the European Commission in January, 2014, (EU/3/13/1210), http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/orphans/2014/01/human_orphan_001301.jsp&mid=WC0b01ac058001d12b.

HypoPT is the only major endocrine disorder in which the missing hormone, PTH, is not routinely replaced⁶⁻⁸. Functionally, HypoPT represents a dual hormonal deficiency, as levels of activated vitamin D (1,25-dihydroxyvitamin D [1,25(OH)₂D], calcitriol) are reduced due to absent PTH stimulation of renal 1 α -hydroxylase⁹.

The prevalence of HypoPT ranges from 6.4 to 38/100.000, and the vast majority (75% or more) is due to neck surgery^{6,8,10-12}, i.e., secondary to thyroid or parathyroid surgery, termed postsurgical HypoPT^{6-8,13}. The annual incidence of HypoPT varies by region, ranging from 0.8 to around 7 per 100.000 inhabitants, most likely reflecting differences in the completeness and representativeness of background registries¹⁴. HypoPT may have an autoimmune pathogenesis^{13,15}, and in many such patients, the cause is a bi-allelic mutation in the *AIRE* (autoimmune regulator of endocrine function) gene^{13,16-18}. The main targets of autoantigens in *AIRE*-related autoimmunity are the calcium-sensing receptor (CaSR) and NACHT leucine-rich protein 5 (NALP5)¹⁹. In general, autoimmune polyendocrine syndromes occur in the setting of autoimmune polyendocrine syndromes, but isolated autoimmune forms of HypoPT may also occur²⁰, such as that caused by activating antibodies to CaSR²¹. In addition, other rare genetic conditions can cause HypoPT, either as part of a syndrome (e.g., DiGeorge Syndrome²², which tends to be sporadic but can be familial), or as an isolated endocrinopathy (e.g., autosomal dominant hypocalcaemia type 1 [ADH1]), caused by pathogenic gain-of-function variants in *CASR*¹³ (see [Table 1](#)). An emerging mechanism of nonsurgical HypoPT relates to the increasing use of immune therapies, including immune checkpoint inhibitors for malignancies and related diseases^{23,24}. Other rare causes of HypoPT include, for example, parathyroid gland radiation injury, haemochromatosis, granulomatous diseases, or metastatic cancers²⁵.

2.2 Postsurgical Hypoparathyroidism

Postsurgical HypoPT persisting for more than 6–12 months in adults is usually secondary to thyroid surgery but may occur following parathyroidectomy or other operations on the neck²⁶. Overall, between 2-10% of patients undergoing total thyroidectomy, particularly when combined with central/lateral lymph node dissection for thyroid cancer, will develop permanent HypoPT^{27,28}.

Postsurgical HypoPT is associated with young age, female sex, underlying Graves' disease, unilateral or bilateral lymphadenectomy, gross extrathyroidal extension of thyroid cancer, early postoperative hypocalcaemia (within 24 hours of thyroidectomy), accidental parathyroidectomy, intraoperative parathyroid biopsies during surgery for hyperparathyroidism, the presence of parathyroid tissue in the operative specimen, and parathyroid auto-transplantation²⁹. Most importantly, the number of functioning parathyroid glands remaining *in situ* postoperatively is a key determinant of the risk of developing postoperative hypocalcaemia (16% for cases with 1-2 preserved glands, 6% for 3 glands, and 2.5% for four glands)²⁸⁻³⁰. All these factors correlate with reduced PTH secretion immediately following surgery. If the PTH concentration is > 10 pg/mL (1.05 pmol/L) 12 to 24 hours after surgery, progression to permanent HypoPT is very unlikely. However, many patients with lower PTH levels may still recover from postoperative HypoPT¹³.

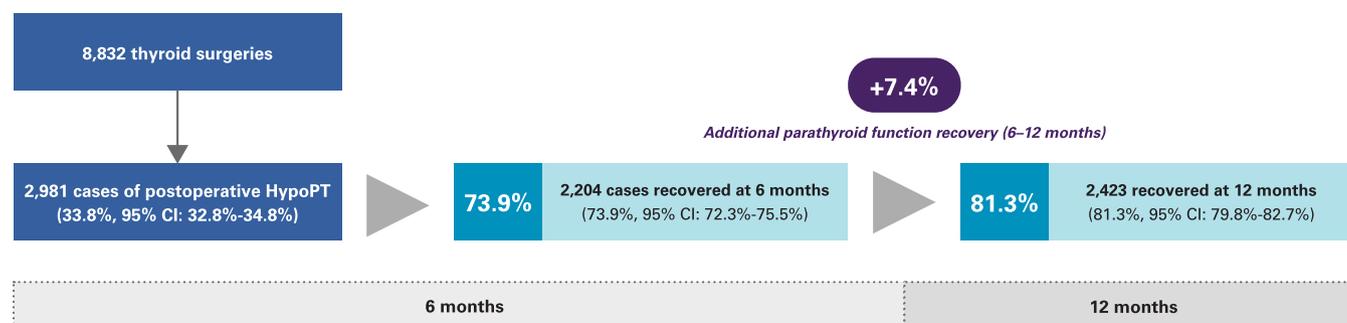
Notably, in patients with preoperative hypercalcaemia, such as in primary hyperparathyroidism, calcium levels may take several days to normalise after surgery, during which PTH levels may be very low²⁸⁻³¹. Additional risk factors for postsurgical HypoPT include obesity³² and severe vitamin D deficiency³³.

Table 1. Genetic Aetiologies of Hypoparathyroidism.

Condition	OMIM Phenotype #	Gene/Chromosome	Syndromic features
Isolated hypoparathyroidism due to pathogenic variants or deletions/insertions in:			
ADH1	601198	CASR	Hypomagnesemia, hypercalciuria, possible Bartter syndrome
ADH2	615361	GNA11	Hypomagnesemia, hypercalciuria
FIH1	146200	PTH	
FIH2	618883	GCM2	
HYPX	307700	Chromosome Xq27.1 (SOX3)	
Syndromes of hypoparathyroidism with damage to the parathyroid glands due to pathogenic variants in:			
APS1	240300	AIRE	Primary adrenal insufficiency, mucocutaneous candidiasis, other autoimmune conditions, ectodermal dystrophy
Syndromes of hypoparathyroidism with impaired parathyroid gland formation due to pathogenic variants or deletions in:			
DiGeorge syndrome 1	188400	Chromosome 22q11 (TBX1)	Thymic hypoplasia with immune deficiencies, heart malformations, cleft palate, dysmorphic facies, cognitive impairment, developmental delay, psychiatric disorders
DiGeorge syndrome 2	601362	Chromosome 10p14 (NEBL)	
Barakat syndrome	146255	GATA3	Sensorineural deafness, renal dysplasia
CHARGE syndrome (Hall-Hittner syndrome)	214800	CHD7	Coloboma, Heart defects, Atresia choanae, Retardation of growth and development, Genital abnormalities, Ear abnormalities
Kabuki syndrome	147920	KMT2D*	Dysmorphic facies, developmental delay, growth retardation, cardiac, and skeletal abnormalities
Sanjad-Sakati syndrome (Kenny-Caffey syndrome type 1)	241410/ 244460	TBCE**	Growth retardation, short stature, dysmorphic facies, developmental delay, seizures, intellectual disability
Kenny-Caffey syndrome, dominant (type 2)	127000	FAM111A**	Growth retardation, short stature, craniofacial abnormalities, seizures, and cortical thickening and medullary stenosis of long bones
Osteocraniostenosis	602361		Gracile bone dysplasia with thin and fragile bones, craniofacial abnormalities, microphthalmia
Kearns-Sayre syndrome	530000	Mitochondrial DNA	Mitochondrial encephalomyopathy, progressive ophthalmoplegia, pigmentary retinopathy, cardiac abnormalities
Pearson marrow-pancreas syndrome	557000		Anaemia, cytopenias, pancreatic insufficiency, lactic acidosis
MELAS	540000		Mitochondrial encephalomyopathy, lactic Acidosis, stroke-like episodes, seizures
Mitochondrial trifunctional protein deficiency syndrome	609015/ 620300	HADHA/HADHB	Cardiomyopathy, hypoglycaemia, lethargy, hypotonia, rhabdomyolysis, neuropathy, liver disease
Long-chain hydroxyacyl-CoA dehydrogenase deficiency	609016	HADHA	Hypoglycaemia, myopathy, rhabdomyolysis, cardiomyopathy, hepatomegaly, neuropathy, pigmentary retinopathy, liver disease
Medium-chain acyl-CoA dehydrogenase deficiency	201450	ACADM	Hypoglycaemia, lethargy, vomiting, seizures, fatty liver
Smith-Lemli-Opitz syndrome	270400	DHCR7	Microcephaly, intellectual dysfunction, hypotonia, facial dysmorphism, syndactyly, genital abnormalities

Data in Table 1 were derived from Mannstadt et al.¹³, *Cerqueira et al.²⁷³, and **Schight et al.²⁷⁴.

ADH1, autosomal dominant hypocalcaemia 1; ADH2, autosomal dominant hypocalcaemia 2; FIH1, Familial isolated hypoparathyroidism 1; FIH2, Familial isolated hypoparathyroidism 2; HYPX, hypoparathyroidism X-linked recessive; APS1, autoimmune polyendocrine syndrome type 1; MELAS, mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes.

**Figure 1.** Recovery of postsurgical HypoPT 6 and 12 months after thyroid surgery.

About 60-70% of cases of postoperative hypocalcaemia resolves within four to six weeks after surgery (transient HypoPT); the rest remains with HypoPT characterised by low PTH levels and the need for continued treatment, at least

for a period, but still with a chance for recovery; other clinical variables lose predictive value at this stage^{28,30}.

Importantly, a substantial proportion of patients with postoperative HypoPT will recover in the period between 6 to 12

months following surgery³⁴⁻³⁷, see **Figure 1**. Therefore, we here define postoperative chronic HypoPT in adults as HypoPT of more than 12 months duration following neck surgery. However, it is important to stress that some patients may still regain sufficient parathyroid function even several years after surgery³⁵.

Overdiagnosis of thyroid cancer can lead to unnecessary surgery and is a potential contributor to preventable HypoPT cases and should be carefully minimised^{38,39}. Efforts to preserve parathyroid gland function and reduce the risk of postsurgical HypoPT have led to the introduction of near-infrared autofluorescence (NIRAF), as an intraoperative adjunct to improve parathyroid gland visibility during surgery⁴⁰. By using near-infrared light and NIRAF characteristics of the parathyroid tissue, surgeons can obtain high-contrast imaging in real-time, with the potential to preserve the glands. The use of indocyanine green (ICG) to enhance fluorescence imaging enables the real-time assessment and direct imaging of tissue perfusion and vascularisation⁴¹. Standardisation of the technique, as well as long-term randomised controlled studies, are required to truly assess any sustained beneficial effect of NIRAF on parathyroid function⁴².

2.3 Complications and Renal Implications of Chronic Hypoparathyroidism in Adults

Compared to the general population, patients with chronic HypoPT experience a lower quality of life (QoL), characterised by musculoskeletal and neuropathic pain, fatigue, weakness, increased anxiety, and a potentially higher risk of depression^{6,8,10,43-48}. Similarly, cohort studies have shown an increased risk of hospitalisation for depression and affective disorders, as well as for renal impairment and infections^{8,44,48-50}. The risk of ischaemic heart disease and cataracts is increased in nonsurgical HypoPT, whereas data from patients with postsurgical HypoPT are inconsistent^{8,10,44,50,51}. The discrepancy between the two conditions may be disease- and exposure-time-specific⁴.

HypoPT is associated with an increased circulating calcium-phosphate product. Loss of renal PTH action decreases renal tubular reabsorption of calcium and the excretion of phosphate, causing hypercalciuria and hyperphosphataemia, respectively⁵². Patients with chronic HypoPT have an increased risk of renal complications, such as renal stones, renal insufficiency, and a higher risk of needing renal replacement therapy^{8,48,49,51,53,54}; see **Table 2**. Impaired renal function has been associated with duration of disease and time with hypercalcaemia^{48,53}. However, despite keen interest in improving the management of HypoPT, large cohort studies describing typical treatment patterns, optimised target laboratory parameters, and rates of complications are scarce. Data on mortality have been conflicting so far. A recent study found increased mortality in patients with nonsurgical HypoPT⁵¹, while others did not find this association¹⁰. A recent synthesis of these studies showed an increased all-cause mortality of 80% (Hazard Ratio 1.8, 95% CI 1.49–2.17) in patients with HypoPT in general⁵⁰.

2.4 Pregnancy and breastfeeding

Pregnancy and lactation pose substantial short-term challenges to maternal calcium homeostasis. These challenges are met by production of parathyroid hormone-related protein (PTHrP) by the placenta followed by a vigorous

Table 2. Co-morbidities which may occur with an increased prevalence in patients with hypoparathyroidism^{8,10,44,48,50,51,111,125,216,229,275-279}.

Organ system	Co-morbidity
Renal	Renal stone disease [§] Impaired renal function [§] Renal calcifications [§]
Immunological Neuropsychiatric	Infections [§] Neuropsychiatric diseases Seizures [§] Depression [§] Anxiety Sleep disorders Fatigue Impaired quality of life [§]
Musculoskeletal	Muscle stiffness/pain Joint/bone pain Proximal humerus fractures*
Cardiovascular	Ischemic heart disease ^{§*} Heart failure Cardiac arrhythmias ^{§*} Stroke*
Central nervous system Eyes	Intracerebral calcifications* Cataract [§]

[§]Co-morbidities with a statistically significant association with hypoparathyroidism. *An increased risk has only been documented in nonsurgical hypoparathyroidism.

production of activated vitamin D, stimulating intestinal calcium and phosphate absorption. These changes result in a low to suppressed endogenous PTH secretion and higher levels of urinary calcium⁵⁵⁻⁵⁷. As pregnancy progresses, PTHrP production increases. PTHrP synthesis rises even further during nursing because it is abundantly produced in lactating mammary tissue⁵⁶.

Pregnant and nursing women with HypoPT are at considerable risk for both hypercalcaemia and hypocalcaemia⁵⁵⁻⁵⁷. Poor control of maternal HypoPT and resulting hypocalcaemia during pregnancy can cause miscarriage, stillbirth, premature labour, and even neonatal death⁵⁶⁻⁵⁹. Maternal hypocalcaemia can impair neonatal skeletal development and trigger compensatory hyperparathyroidism in the newborn. This may lead to skeletal deformities, fractures, parathyroid hyperplasia, and other complications (e.g., respiratory distress, poor feeding, hypotonia)^{56,57}. Conversely, maternal overtreatment, resulting in hypercalcaemia, can suppress foetal parathyroid development, causing neonatal hypocalcaemia^{57,59}.

2.5 Conventional treatment

Treatment of chronic HypoPT aims to relieve symptoms of hypocalcaemia, improve patients' well-being (QoL), and long-term prognosis. Conventional treatment includes sufficient calcium intake by diet, with or without calcium supplements, plus activated vitamin D treatment (e.g., calcitriol, alfalcidol or calcifediol (referred to as activated vitamin D analogues for ease of reading throughout the manuscript), while maintaining adequate vitamin D and magnesium status (see **Figure 2** and **Table 3**). Hyperphosphataemia^{60,61} and hypercalciuria^{62,63} should be addressed, if needed.

Seemingly asymptomatic patients with mild hypocalcaemia and without hypocalcaemic symptoms should be considered to receive oral therapy, as nonspecific symptoms (e.g., fatigue, brain fog, anxiety) may improve with treatment. Dietary calcium intake should be optimised, according to guidelines for the general population^{64,65}. Magnesium deficiency should be

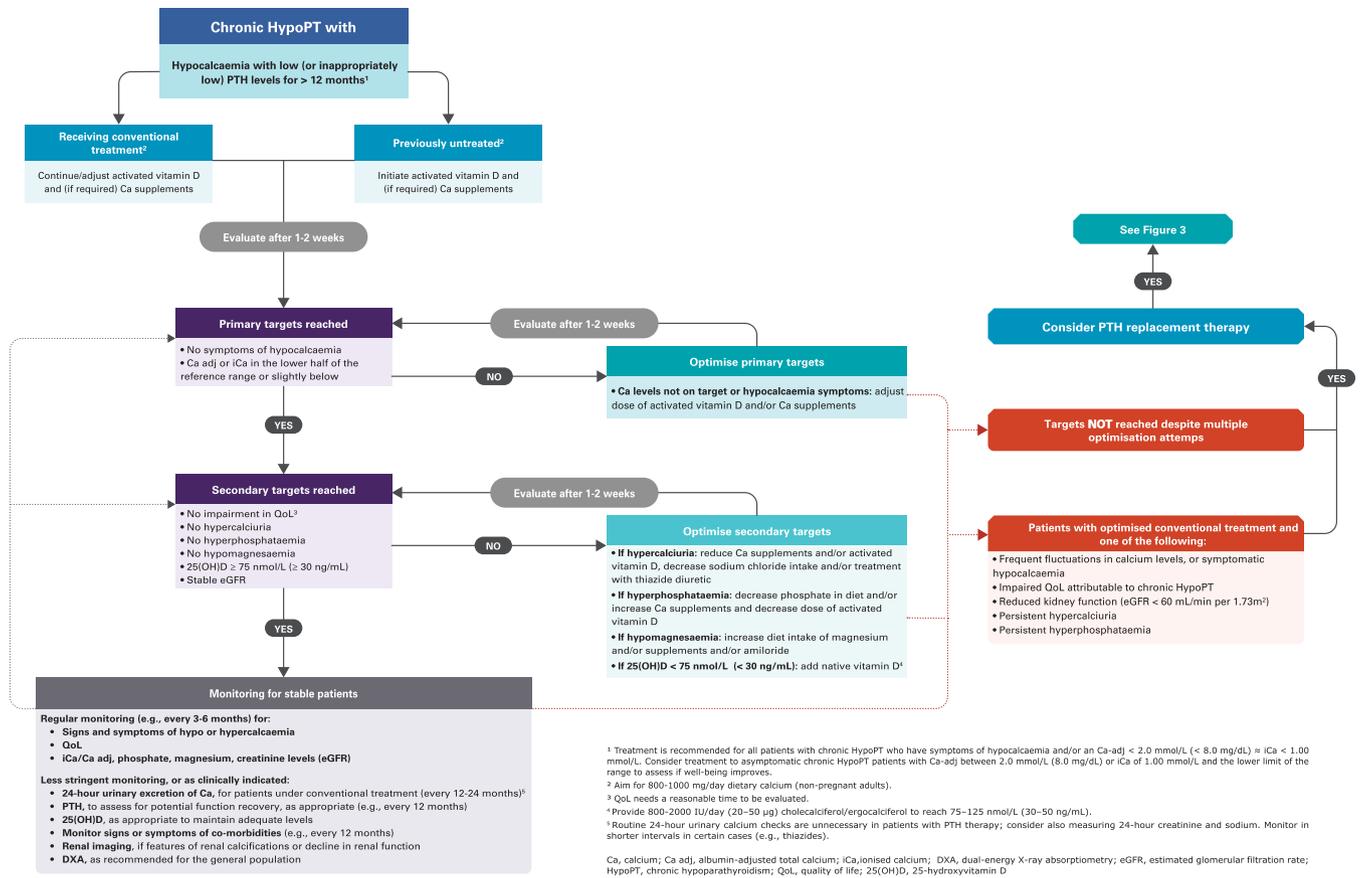


Figure 2. Chronic hypoparathyroidism treatment algorithm.

Table 3. Vitamin D metabolites in the management of chronic hypoparathyroidism¹.

Medication	Typical dose	Time to onset of action	Time to offset of action
Calcitriol	0.25-2.0 µg	1-2 days	2-3 days
1,25(OH) ₂ D	once or twice daily		
Alfacalcidol ²	0.5-4 µg once daily	1-2 days	5-7 days
1α(OH)D ₃			
Dihydroxycholesterol ²	0.3-1.0 mg	4-7 days	7-21 days
	once daily		
Vitamin D ₂ (ergocalciferol) or vitamin D ₃ (cholecalciferol) ³	25,000–200,000 IU daily	10-14 days	14-75 days

¹Derived from Shoback¹²¹.

²Alfacalcidol and dihydroxycholesterol are rapidly activated in the liver to 1,25(OH)₂D and 25(OH)D dihydroxycholesterol, respectively.

³These compounds could be used in a setting where activated vitamin D metabolites are not available and/or too expensive.

corrected, as profound hypomagnesaemia *per se* inhibits PTH secretion and action (functional hypoparathyroidism)⁶⁶. In cases of symptomatic severe hypocalcaemia, the use of intravenous calcium should be considered for a limited period (see 5.3 Treatment).

2.6 PTH replacement therapy

PTH replacement therapy with synthetic or recombinant human (rh) PTH analogues is an attractive option for patients with persistent signs and symptoms of chronic HypoPT. The N-terminal part of the PTH molecule [PTH(1-34)] binds with high affinity to the PTH receptors (PTH1R and PTH2R), which are widely distributed in the human body⁶⁷.

Since the first ESE Guideline on the management of chronic HypoPT in 2015³, numerous initiatives have emerged for new treatment strategies. rhPTH(1-84) (Natpara®, US and Natpar®, Europe) was approved by the FDA (U.S. Food and Drug Administration) in 2015, later by the EMA (European Medicines Agency) based on multiple clinical trials. However, the drug was withdrawn from the market at the end of 2024 (Takeda Discontinuation of NATPARA® [parathyroid hormone]).

In general, substitution therapy with intact PTH(1-84) or PTH(1-34), has been promising in maintaining normocalcaemia, lowering phosphate levels, reducing urinary calcium excretion, and potentially improving patient well-being (QoL) (see Clinical Question II)⁶⁸⁻⁷². In most studies, PTH has

been administered in a non-physiological manner (i.e., once-daily injection), compared to its continuous episodic endogenous pattern of secretion. Due to the short plasma half-life after subcutaneous injection, i.e., about 1 hour for PTH(1-34)⁷³ and 3 hours for PTH(1-84)^{74,75}, once-daily injections are not expected to cause sustained PTH activity. Studies on injections twice a day so far have been scarce. However, a recent study comparing once daily versus twice-daily equipotent injections of PTH(1-84) in patients with chronic HypoPT, without supplemental calcium intake, found no clinically significant differences between the two regimes, although the statistical power was low⁷⁶. For PTH(1-34), twice-daily injections for HypoPT showed less fluctuations in calcium levels compared with once daily injections^{77,78}. The same authors compared twice-daily injections with infusion pumps of PTH(1-34) in patients with postsurgical HypoPT, and found the latter application superior for various biochemical endpoints, and the most physiological approach⁷⁹. However, in the clinic, PTH(1-34) has until recently only been available for the treatment of osteoporosis, administered as a fixed 20 microgram once-a-day injection. Although off-label use of this drug for HypoPT (once or twice injections daily) has been tried, this application has been limited by challenges in achieving precise dose titration^{69,80}.

Several pharmacodynamic, safety, and clinical studies have recently demonstrated promising results with palopegteriparatide, a pegylated form of PTH(1-34) that provides active PTH within the physiological range over a 24-hour dosing interval⁸¹⁻⁸⁴. Following pivotal clinical trials, palopegteriparatide (Yorvipath®) was approved by the EMA and the FDA for the treatment of chronic HypoPT in 2023 and 2024, respectively, and is currently the only approved PTH replacement treatment on the market. Additional therapies are currently under development, including and oral PTH analogue¹¹³, a calcilytic agent (encaloret) and a selective PTHR1 agonist (eneboparatide), with phase 2 results recently published for the latter two^{85,86}.

3. Methods

3.1 Guideline working group

This guideline revision was initiated by the European Society of Endocrinology (ESE). The chair (J.B.) was appointed by the ESE Clinical Committee. O.D. served as the methodology lead, L.v.H. joined the guideline working group for methodology and organisational support. Members of the working group (authors) were appointed by the chairs and approved by the ESE Clinical Committee: endocrinologists (N.G., C.M., J.C.P. (Endocrine Society Representative), S.P., L.R., and M.Y.), a nephrologist (P.H.), and an endocrine surgeon (O.M.). O.B. served as ESE Nurse Representative and L.M.C. (endocrinologist) as EYES Representative. The working group had in-person meetings in May and October 2024 and several virtual meetings. All participants completed conflict of interest forms (see [Supplementary Table 1](#)).

The guideline panel collaborated with the following patient representatives: Liz Glenister (UK), Natalie Grosset (France), Tanja Richter and Frauke Sieger (Germany), and Helen Dahl-Hansen and Perny-Ann Nilsen (Norway). Before publication, a draft of the guideline was reviewed by three experts in the field (see [Acknowledgements](#)). Revision of the guideline was based on feedback from the Endocrine Society's Clinical Committee, and ESE members following a presentation at

the Joint Congress of ESE and ESPE (European Society of Paediatric Endocrinology) 2025, in Copenhagen. All comments and suggestions were discussed and implemented as deemed appropriate by the working group (see [Supplementary Table 10](#)).

3.2 Target group

This document was developed for healthcare providers of patients with chronic HypoPT and serves as a source document for the preparation of educational materials to be published on the ESE website to empower patients with chronic HypoPT and their clinicians.

3.3 Aims

The overall purpose of this guideline is to provide clinicians with practical guidance for the management of patients with chronic HypoPT in adults. In clinical practice, both the recommendations and the clinical judgment of treating physicians should be considered. Recommendations may need adaptation to local circumstances.

3.4 Endorsement by other societies

To achieve wide acceptance of the guideline within the clinical community of the different disciplines involved in the management of chronic HypoPT in adults, the draft of the guideline document was submitted to several other professional/learned societies. The following societies endorsed the present guideline: the European Society of Endocrine Surgeons, the Endocrine Society of Australia.

3.5 Summary of methods used for guideline development

The methods used have been described in more detail previously^{3,87}. In short, the guideline used GRADE (Grading of Recommendations Assessment, Development and Evaluation) as a methodological base. The first step was to define clinical questions (see section 3.6), the second being a systematic literature search (see section 3.7). After including relevant articles, we 1) estimated an average effect for specific outcomes (if possible), and 2) rated the quality of the evidence. The quality of evidence behind the recommendations is classified as very low (⊕○○○), low (⊕⊕○○), moderate (⊕⊕⊕○) or high (⊕⊕⊕⊕).

For the recommendations we considered: 1) the quality of the evidence, 2) the balance of desirable and undesirable outcomes, and 3) values and preferences (patient preferences, goals for health, costs, management inconvenience, feasibility of implementation, etc)^{3,87}. The recommendations are worded as “*recommend*” (strong recommendation) or “*suggest*” (weak recommendation). It is important to emphasise that there is no direct translation from the (quality of) evidence to the strength of a recommendation, and there might be situations when a recommendation is strong even if the quality of evidence is low⁸⁸. Recommendations based on good clinical practice were not graded. Recommendations were derived from a majority consensus of the guideline development panel, but substantive disagreements could be acknowledged in the manuscript. All recommendations provided are accompanied by an explanation (“reasoning”).

3.6 Clinical questions and eligibility criteria

In the 2015 guideline, chronic HypoPT was defined as HypoPT persisting for more than 6 months³. Acknowledging that the statement from the Second International Workshop on the management of HypoPT defined postsurgical chronic HypoPT as persisting for more than 12 months after surgery⁸⁹, we decided to systematically review the literature on the time to recovery of parathyroid function after surgery.

We updated the literature review of optimal treatment for chronic HypoPT in adults, both for conventional treatment and PTH replacement therapy. Since the 2015 guideline³, more data have become available regarding the use of PTH replacement therapy^{84,90,91}. For PTH replacement therapy, results were stratified according to the biological half-life of the drug. In addition, the guideline panel noticed an emerging interest of patients in parathyroid allotransplantation, especially those with uncontrolled HypoPT despite medical treatment⁹², and decided to explore the evidence.

The clinical questions for the systematic reviews are summarised in [Table 4](#). Eligible study designs were observational cohort studies, crossover studies, case-control studies, and RCTs. To answer questions on treatment effects in a meaningful way, studies had to compare two different treatment regimens, either in a direct comparison or in a formal pre-post design. Surveys were excluded. Eligible articles were required to present data on adult patients (≥ 18 years), with a minimum of 10 patients to reduce the risk of selection bias. Studies primarily selecting patients with end-stage renal disease were excluded. Eligible studies were restricted to languages familiar to the authors (English, French, German, and Dutch).

For clinical question I (recovery of HypoPT after 6 and 12 months), the number of persons with recovery of HypoPT at re-testing (numerator) and the total number of persons with HypoPT at baseline (denominator) were used to estimate the incidence of recovery. For intervention studies, the duration of intervention needed to be ≥ 4 weeks. The outcomes of treatment effects of the updated literature review included endpoints of the original guideline³ (i.e., mortality, QoL, calcium levels in serum or plasma and urine - including the incidence of hypercalcaemia, chronic kidney disease (CKD), and renal calcifications - defined as symptoms or episodes of nephrolithiasis or nephrocalcinosis, cramps, tetany and seizures, cardiovascular disease - defined as the incidence of major adverse cardiovascular events, and disability or sick leave), supplemented with the following endpoints after discussion within the guideline panel and consultation with patient representatives (see section 3.1): phosphate levels, neuropsychological endpoints, bone markers, fractures or bone mineral density (BMD), pill burden, increased susceptibility to infection, cataract, gastrointestinal symptoms, and pain (bone, muscle, and nerves).

3.7 Description of search and selection of literature

PubMed, MEDLINE, Embase, Web of Science, and Cochrane Library were searched with the help of a specialised librarian to identify potentially relevant studies. The literature searches for questions I, II, and III were performed in June 2024, September 2024, and November 2024, respectively. Searches can be found in [Appendix 1](#) (see section on [supplementary materials](#) at the end of this guideline). Since clinical question II (optimal treatment) was an update of the literature review of the original guideline³, the search was conducted from the

date of the search of the original guideline, i.e., from 2013 onwards. The outcome “bone” was not assessed in the original guideline but deemed an outcome of major interest by the guideline panel; for reasons of completeness, studies published before 2013 were also included for this outcome.

All studies obtained from the searches were entered into reference manager software (EndNote X21, Clarivate Analytics, Philadelphia, PA) and titles and abstracts were screened. Potentially relevant studies were retrieved for detailed assessment. References of included studies were assessed for additional relevant articles.

4. Summary and interpretation of evidence from the systematic reviews

4.1 Clinical question I: What is the incidence of recovery from postoperative HypoPT 6 and 12 months after thyroid surgery?

Fourteen studies assessing the recovery of postsurgical HypoPT were included^{34-37,93-102}. See [Supplementary Table 2](#) and [Supplementary Table 3](#) for details and the GRADE assessment. Overall, the evidence quality was moderate based on a serious risk of bias concerning outcome measurement (i.e., no standard protocol for assessing recovery of parathyroid function) and loss to follow-up (mostly not reported). It was not possible to stratify results for patients undergoing parathyroid auto-transplantation.

Of the 8,832 patients (data from 14 studies) undergoing thyroid surgery, 2,981 developed postoperative hypoparathyroidism (33.8%, [Figure 1](#)). Six months after surgery, 73.9% of these 2,981 patients had recovered parathyroid function (i.e., 91.2% of the total cohort had normal parathyroid function), while 12 months after surgery, this number had increased to 81.3% (93.7% of the total cohort). In total, 558 of 8832 patients undergoing thyroid surgery had chronic HypoPT 1 year after thyroid surgery, i.e., 6.3% of the total cohort.

From these data, we conclude that between 6 and 12 months after thyroid surgery, an additional 7.4% of patients recovered parathyroid function. The guideline panel deemed this a clinically relevant proportion and decided to define postsurgical HypoPT from 6 months following surgery in the original guideline³ to 12 months after surgery, in accordance with recent recommendations⁸⁹. Several studies reported patients regaining parathyroid function ≥ 1 year after surgery^{34,35,95,98,102}; however, since standard follow-up protocols were lacking, it is uncertain if this resulted from delayed weaning from supplementation therapy rather than actual recovery.

4.2 Clinical question II: What is the optimal treatment for adult patients with chronic HypoPT?

4.2.1 Conventional treatment

Although many studies have published prevalence data on outcomes of interest in chronic HypoPT patients on conventional treatment, these studies did not compare different conventional treatment *strategies*, e.g., different supplement dosages or different target calcium levels. Therefore, these studies did not inform regarding optimal conventional treatment regimens. Another complicating factor was that several outcomes, e.g., CKD, QoL, and fractures are dependent on disease duration (time exposure) and ageing by itself. These

Table 4. Clinical questions.

Clinical question	Search criteria			Papers included (n)
	Population	Intervention	Comparison	
<i>Question I:</i> What is the incidence of recovery from postoperative HypoPT 6 and 12 months after surgery?	Adults with postsurgical HypoPT	-	-	14 34-36,37,93-102
<i>Question II:</i> What is optimal treatment for adult patients with chronic HypoPT?	Adults with chronic (≥ 1 year) HypoPT	PTH/conventional therapy ≥ 4 weeks	PTH/conventional therapy/placebo/no intervention	Conventional treatment: 4 ¹⁰³⁻¹⁰⁶ PTH replacement therapy: 19 ^{46,69,71,72,80,82,83,85,90,107-116}
<i>Question III:</i> What is the effect of parathyroid allotransplantation in HypoPT treatment?	Individuals with HypoPT	Parathyroid allotransplantation	PTH/conventional therapy/placebo/no intervention	3 117-119

HypoPT = hypoparathyroidism, PTH = parathyroid hormone, QoL = quality of life, CKD = chronic kidney disease, CVD = cardiovascular disease, BMD = bone mineral density.

time-dependent outcomes require long-term observational studies to adequately disentangle underlying disease effects (i.e., chronic HypoPT) versus treatment effects.

We defined conventional treatments as treatment regimens based on formulations of activated vitamin D and/or calcium. We could only include two observational studies and two RCTs assessing optimal treatment regimens of conventional treatment; a total of 170 patients with chronic HypoPT, ~75% females, were included¹⁰³⁻¹⁰⁶. See [Supplementary Table 4](#) for study details and description of outcomes; GRADE evidence is presented in [Supplementary File 5](#). Overall, the quality of the evidence was very low, based on concerns regarding the selection of patients, confounding factors and small study cohorts.

A small, double-blind crossover study (n = 24) reported no difference in serum calcium and phosphorus, or urinary calcium between calcium carbonate versus calcium citrate; however, gastrointestinal tolerance of calcium citrate was higher¹⁰⁴. Biochemical control also did not differ between various preparations of activated vitamin D analogues in two studies with a total of 79 patients^{105,106}. Biochemical control did appear to improve in patients with an adequate increase in dietary calcium intake (i.e., elemental 1000 - 1200 mg daily), while maintaining their regular doses of activated vitamin D and calcium supplements¹⁰³. Importantly, the intervention duration was too short, and the sample sizes were too small in these four studies to draw firm conclusions. From the results of this systematic review, it is apparent that relevant data regarding optimal conventional treatment regimens are lacking, particularly for clinically relevant endpoints and long-term effects.

4.2.2 PTH replacement therapy

Nineteen studies assessing the efficacy of PTH replacement therapy in a total of 2069 patients (79% women) with chronic HypoPT were included. Eleven studies assessed PTH(1-84) treatment^{46,71,72,90,107-113} and seven studies PTH(1-34) treatment^{69,80,82,83,114-116}, of which four used teriparatide^{69,80,114,116}, two palopegteriparatide^{82,83}, and one oral PTH¹¹⁵. A single study reported on the PTHR1 agonist, enboparatide⁸⁵. There were six RCTs^{46,72,82,83,111,116}, two cohort studies with historical controls^{107,109}, and eleven open-label intervention studies making pre-post comparisons^{69,71,80,85,90,108,110,112-115}. Details of included studies and descriptive results per outcome can be found in [Supplementary Table 6](#); the description of the GRADE evidence is in [Supplementary File 7](#). Except for the RCTs on pill burden, for which the quality of evidence was moderate (large effect), the quality of the evidence was very low for all other outcomes, with concerns on small sample sizes, selection of patients, and, depending on the outcome, concerns on possible confounder adjustment and assessment of outcome.

Pill burden and biochemical parameters. The results of the systematic review showed that PTH replacement therapy reduced the pill burden of conventional therapy (as assessed by 11 studies) while improving biochemical parameters (as assessed by 13 studies). Reductions in activated vitamin D analogues and calcium supplementation were observed by PTH(1-84) therapy^{72,90,108,112}, with some studies reporting discontinuation of these supplements in over 60% of the study cohort¹⁰⁸. With PTH(1-34) therapy, conventional therapy

dosages could also be markedly reduced^{69,80,83,115} or completely discontinued in a majority of the study cohort^{80,82,83}. PTHR1 agonist therapy enabled the discontinuation of activated vitamin D analogues in 92% and calcium supplements in 88% of patients⁸⁵.

With PTH(1-84) treatment, an increase in calcium levels^{108,110,111} and a decline in, or continuous normalisation of phosphate levels were observed^{72,90,108,110-113}. There were mixed results for 24-hour urine calcium excretion. Two studies reported a decrease in urinary calcium excretion^{90,112} with percentages of hypercalciuria decreasing from 69.2% at baseline to 33.3% after three years of treatment for women, and 66.7% to 34% for men¹¹². Two other studies reported an increase in 24-hour urine calcium excretion, albeit remaining within the normal range^{108,110}.

With PTH(1-34) treatment, calcium levels either increased^{69,80} or remained within normal range^{82,83,115}. Phosphate levels remained within the normal range (palopegteriparatide)^{82,83} or decreased^{69,80}. All studies with PTH(1-34) treatment observed a significant, or a trend towards, a decrease in 24-hour urine calcium excretion^{69,80,82,83,114,115}.

These results apply to the short- as well as the long-acting PTH(1-34) preparations, although too few studies were included to make proper comparisons between the two therapies.

QoL. There are limited data indicating that short-term PTH(1-34) treatment can improve various aspects of QoL compared to baseline (teriparatide, oral PTH)^{69,80,115} or to placebo (palopegteriparatide)^{82,83}. For PTH(1-84) treatment, results were inconsistent; two studies found improvement in several QoL domains compared to baseline^{71,90,113}, while others found no difference^{110,111}.

Renal and cardiovascular outcomes. PTH(1-84) treatment did seem to improve renal and cardiovascular outcomes in observational studies. PTH(1-84) treatment maintained renal function within the normal range¹⁰⁸ and lowered the risk of developing CKD, eGFR decline or a cardiovascular event compared to conventional treatment; adjusted Hazard Ratio 0.47 (95% CI 0.25-0.87), 0.35 (95% CI 0.13-0.89) and 0.25 (95% CI 0.08-0.81), respectively, after five years of follow-up^{107,109}. Renal function also improved with palopegteriparatide: after 26 weeks, mean eGFR rose by 7.9 ± 10.4 ml/min per 1.73 m^2 with treatment and generally remained unchanged by 1.9 ± 8.6 ml/min per 1.73 m^2 in the placebo group (p < 0.001)⁸³. Well-designed, long-term RCTs are, however, needed to confirm these potential positive results, with adequate outcome measures assessing renal function, e.g., cystatin C.

No data were found on cardiovascular outcomes for PTH(1-34) treatment or PTHR1 agonist treatment.

Bone. Biochemical markers of bone turnover were assessed in eight studies and consistently increased after initiation with PTH treatment^{46,80,82,85,90,116}, stabilising to steady-state values above pretreatment levels during long-term treatment^{110,112}. Although this reflects exposure to the physiologic bone-remodelling effects of PTH, effects on BMD were inconsistent^{46,110,112,113,116}, and it is currently not known if this translates to a clinically relevant endpoint such as fracture rates.

Overall, most studies have so far been hypothesis-generating only, with the need for future prospective,

randomised controlled studies (hypothesis testing) on hard endpoints such as patient outcomes and markers of morbidity, to establish the true value of PTH replacement therapy beyond biochemical control.

We were not able to stratify results for HypoPT aetiology.

4.3 Clinical question III: What is the effect of parathyroid allotransplantation in HypoPT treatment?

Three studies assessing the results of 141 parathyroid allotransplantations in 109 patients were included¹¹⁷⁻¹¹⁹. Details of the included studies can be found in [Supplementary Table 8](#), and the description of the GRADE evidence is provided in [Supplementary Table 9](#). Overall, the evidence was very low, based on a serious risk of bias concerning adjustment for confounding factors, heterogeneity of intervention and measurement of outcome, and imprecision due to small patient numbers.

A small cohort study ($n = 10$) reported functioning allografts in 70% of patients after one year, which led to the discontinuation of conventional therapy in these patients¹¹⁷. Another study ($n = 14$) reported a reduction of daily conventional therapy dosages two years after parathyroid allotransplantation, but discontinuation in none¹¹⁸. The largest study, comprising 85 patients, reported 57% functioning allografts directly after transplantation, and a mean cellular allograft survival of 6.3 ± 13.1 months¹¹⁹.

In conclusion, small, short-term studies show functioning allografts one year after transplantation although this comes at the cost of immunosuppression use.

Based on the available evidence, we cannot recommend a role for parathyroid allotransplantation in the treatment of chronic HypoPT.

5. Recommendations and rationale for the recommendations

5.1 Diagnosis

R.1.1 We recommend considering a diagnosis of chronic hypoparathyroidism (HypoPT) in a patient with persistent hypocalcaemia and inappropriately low or inappropriately normal parathyroid hormone (PTH) levels.

Reasoning: Hypocalcaemia is defined as an ionised or albumin-adjusted total calcium level below the lower limit of the reference range. Measurements of ionised or total calcium mostly reflect local traditions. However, ionised calcium measurements might improve diagnostic accuracy¹²⁰, and may be preferred in pregnancy, see section 5.5. A specific cut-off limit for PTH levels in the presence of hypocalcaemia cannot be defined. If parathyroid function is intact, hypocalcaemia is normally associated with (markedly) increased PTH levels (secondary hyperparathyroidism). In accordance, a diagnosis of HypoPT may be considered in a patient with hypocalcaemia if PTH levels are low in the reference range, which is inappropriately normal in the setting of hypocalcaemia^{121,122}.

Remarks: Magnesium. Magnesium depletion impairs the secretion of PTH, causing a state of functional HypoPT and impairs effective PTH actions in target tissues. If magnesium levels are low, this should be corrected before diagnosing a patient with chronic HypoPT¹²³.

Remarks: Postsurgical HypoPT. Recovery of parathyroid function in patients with postsurgical HypoPT increased from 73.9% to 81.3% between six months and one year after surgery (see [Clinical Question I](#)). Therefore, chronic HypoPT should not be diagnosed within the first year following surgery (12-month cut-off). In the case of postoperative HypoPT, we advise close monitoring of calcium and PTH levels.

R.1.2 We recommend genetic testing and/or family screening in a patient with nonsurgical HypoPT without other obvious aetiology.

Reasoning: Nonsurgical HypoPT may be due to various reasons¹³. If no obvious cause can be established, we recommend genetic testing for inherited forms of HypoPT, which include isolated or syndromic aetiologies¹³. Family history may be negative when pathogenic variants occur *de novo* or have variable clinical features. Genetic testing refines the clinical diagnosis, may guide targeted therapies, could help predict other medical conditions, and can help to assess the risk for family members. For example, individuals with autosomal dominant hypocalcaemia type 1 (ADH1) caused by activating variants in *CASR* may benefit from a targeted negative allosteric modulator of the calcium-sensing receptor that can promote PTH secretion and renal calcium reabsorption⁸⁶. Genetic testing may be of particular importance to younger individuals, as a genetic diagnosis may allow for genetic counselling about future pregnancy plans. Genetic information may also prompt monitoring for other possible complications that may accompany HypoPT (see [Table 1](#))¹³. Access to genetic testing may vary in different settings and may be limited by availability and costs.

5.2 General goals of management in chronic hypoparathyroidism

R.2.1 We recommend treatment for HypoPT to be personalised and centred on the patient's overall well-being with therapeutic goals that optimise QoL, minimise symptoms of hypocalcaemia, improve long-term prognosis, and maintain calcium levels within the lower part or slightly below the reference range. (Good clinical practice)

Reasoning: Patients with chronic HypoPT suffer from varying degrees of physical, mental, and emotional health impairments. Although treatment may alleviate symptoms, QoL is not fully normalised in most cases¹²⁴. Fluctuations in calcium levels, a high pill burden, hyperphosphataemia, hypercalciuria, and renal complications are limitations of conventional therapy with calcium and activated vitamin D.

The main therapeutic goals are to enhance the patient's overall well-being and maintain albumin-adjusted calcium levels or ionised calcium levels in the lower part of the reference range or slightly below. Based on normal physiology, maintaining circulating calcium levels in the low-normal range may reduce urinary calcium excretion, lower the risk of hypercalcaemia and hyperphosphataemia, and potentially support residual parathyroid function recovery^{125,126}. Some patients may require higher calcium levels for symptom relief. If raising calcium levels to the upper part of the normal range improves well-being, this may be acceptable, as there is no evidence of specific harm from this approach. However, the elevated

calcium level resulting from conventional treatment comes at the expense of increased urinary calcium excretion.

It is important to emphasise that no firm evidence exists on the long-term benefits (or harms) of achieving these therapeutic goals. Consequently, treatment decisions should avoid compromising QoL or imposing significant burdens on the patient, such as undesirable lifestyle changes (i.e., dietary habits) or adverse effects of therapy.

For patients not adequately managed with conventional therapy, PTH replacement therapy may improve biochemical parameters and enhance QoL (see R.3.5.2 and Clinical Question II). However, these therapies are significantly more expensive, posing accessibility challenges for many individuals and limiting their widespread use. Therefore, where available and affordable, PTH replacement therapy should be considered for patients not adequately controlled on conventional therapy and based on the individual needs of the patient.

R.2.2 We recommend providing information/education that enables patients to recognise the possible symptoms of hypo- or hypercalcaemia and/or complications of their disease. (Good clinical practice)

Reasoning: As stated in section 5.4, we suggest monitoring patients at regular time intervals. Circulating calcium levels may, however, change, and complications may emerge at any time, with or without apparent reasons. Thus, we find it of importance to empower patients with knowledge of symptoms and of co-morbidities and drugs that may affect the course of their disease.

Table 5. Symptoms patients should be informed of to allow for early detection of hypo- or hypercalcaemia.

	Hypocalcaemia ^{50,61,66}	Hypercalcaemia ^{66,280}
CNS	Depression Irritability Confusion or disorientation Seizures	Weakness Headache Drowsiness Confusion or disorientation Poor memory Reduced concentration
Neuromuscular	Numbness and tingling (paraesthesia) in circumoral and acral areas (fingers, toes) Spasms/twitches Cramps	Muscle weakness
Cardiovascular	Fast, slow, or irregular heart rate Symptoms of congestive heart failure	Fast, slow, or irregular heart rate Hypertension
Gastrointestinal	Abdominal cramps	Loss of appetite Nausea/vomiting Abdominal pain Constipation
Renal	-	Polyuria Hypotension due to renal NaCl wasting Dry mouth and/or increased thirst
Respiratory	Shortness of breath Wheezing Throat tightness	

Table 2 shows co-morbidities which may occur with an increased prevalence in HypoPT.

Table 5 shows symptoms of hypo- and hypercalcaemia, of which patients should be informed.

Table 6 lists drugs, conditions, and diseases which may interfere with calcium homeostasis. If a patient is diagnosed with one of the diseases or initiates treatment with one of the drugs, this may necessitate changes in the medical treatment of HypoPT to maintain target calcium levels. For further useful information, we suggest referring patients to the Patient Information Leaflet on the treatment of Chronic Hypoparathyroidism in Adults ([hypoparathyroidismpatientleaflet.pdf](#)). A standardised European Emergency Card for Adult Patients with Hypoparathyroidism has been published, containing relevant medical information to guide emergency management of either hypocalcaemia or hypercalcaemia ([A Standardised European Emergency Card for Adult Patients with Hypoparathyroidism | ESE](#)). The Patient Information Leaflet and the Emergency Card are available in several languages.

R.2.3 We suggest aiming for normal 24-hour urinary calcium excretion. (⊕○○○)

Reasoning: In a patient with intact parathyroid function, hypercalciuria is considered a risk factor for renal stone formation. Because PTH increases the renal tubular reabsorption of calcium, chronically low PTH levels make hypercalciuria a common feature of HypoPT on conventional therapy. The risk of renal stone disease is increased in HypoPT^{8,44}. It is not possible to predict 24-hour urinary calcium excretion based on a circulating calcium value, and there is limited and conflicting evidence as to whether the risk of forming or passing renal stones is associated with the amount of urinary calcium excreted in patients with HypoPT^{49,127-133}. Moreover, it is important to note that other urine parameters besides calcium may increase (e.g., low volume, low urinary citrate or high uric acid, oxalate, or phosphate) or decrease (e.g., high volume or magnesium) the risk of renal stone formation. However, assuming that the pathogenesis of renal stone disease is similar in HypoPT, as in hypercalciuric individuals with normal parathyroid function, it is reasonable to aim for a normal 24-hour urinary calcium excretion¹²⁶, in order to decrease renal stone formation¹³⁴. Algorithms using 24-hour urinary collection and spot samples for estimating stone risk have also been proposed^{127,135,136}, offering potential avenues for future research and clinical application.

Remarks: autosomal dominant hypocalcaemia. Particular attention should be paid to patients with ADH in whom hypercalciuria may occur at low-normal serum calcium levels because of both decreased PTH action and increased renal CaSR signalling. In patients with symptoms of hypocalcaemia, hypercalciuria may be further increased when treated with conventional therapy^{13,137,138}.

General Remarks: We recommend measuring 24-hour urinary calcium excretion when stable serum calcium target values and satisfactory well-being have been obtained, particularly when using conventional therapy, since hypercalciuria is less common using PTH replacement therapy, see 4.2.2 Clinical question II. Urinary calcium excretion is higher in men compared to women. No clinical intervention studies have been conducted to guide target calcium excretion. The risk of

Table 6. Drug therapy and diseases that may interfere with calcium and phosphate homeostasis potentially necessitating changes in monitoring and therapy of patients with chronic hypoparathyroidism.

Drug/disease	Mechanism	Possible adverse effects in HypoPT	Action
Loop diuretics	Increased urinary calcium losses	May aggravate hypercalciuria and lower serum calcium levels ²⁸¹	Avoid if possible
Thiazide diuretics	Decreased urinary calcium losses ²⁸²	May increase serum calcium levels ²⁸³	May be used in a patient with HypoPT (see text, section 5.3)
Systemic glucocorticoids	Decreased intestinal calcium absorption	May precipitate hypocalcaemia ²⁸⁴	Avoid if possible Otherwise, use minimum effective dose and consider steroid sparing medications
Antiresorptive drugs	Decreased bone turnover	May cause hypocalcaemia ^{285,286}	Rarely needed, as HypoPT is a state of (very) low bone turnover
Proton pump inhibitors (PPI)	May cause hypomagnesaemia ²⁸⁷ May impair bioavailability of calcium in the intestine	May lower serum calcium levels ²⁸⁸ and cause symptoms similar to hypocalcaemia	Avoid if possible – otherwise magnesium supplements as needed, and use calcium citrate
Chemotherapy: Cisplatin, 5-Fluorouracil, Leucovorin	Cisplatin causes renal damage leading to a functional defect in magnesium reabsorption, while it also decreases the activity of 1-alpha-hydroxylase. Leucovorin/5-fluorouracil can also independently induce hypocalcaemia ²⁸⁹	May lower serum calcium levels and cause symptoms similar to hypocalcaemia	Magnesium and/or vitamin D supplements, as needed
Cardiac glycosides (e.g., digoxin)	Cardiac glycosides inhibit the Na ⁺ /K ⁺ ATPase, which in turn increases intracellular calcium, through reducing Na ⁺ /Ca ²⁺ exchange Hypercalcaemia may predispose to digoxin toxicity, while hypocalcaemia may reduce the efficacy of digoxin ²⁹⁰	Arrhythmias	Avoid if possible. If needed, close monitoring by a cardiologist
Diarrhoea/gastrointestinal disease	May reduce intestinal absorption of calcium and vitamin D	May cause hypocalcaemia	Close monitoring of serum calcium levels with dose adjustments as needed
Changes in (correction of) acid-base balance* ²⁹¹	The affinity of calcium to bind to proteins in serum is highly pH dependent – only the free fraction is physiological active	Correction of metabolic alkalosis may cause hypercalcaemia Correction of metabolic acidosis may cause hypocalcaemia** May cause hypercalcaemia	
Immobilisation	Increased bone resorption. In healthy individuals, PTH and 1,25-dihydroxyvitamin D levels are suppressed.		
Hungry bone syndrome	Severe and prolonged hypocalcaemia due to rapid calcium shift into the bone ²⁹²	Except for parathyroidectomy may also occur in thyroidectomy due to thyrotoxicosis ²⁹³ and osteoblastic metastasis due to prostate cancer ²⁹⁴	Close monitoring of serum calcium levels with dose adjustments as needed
Intravenous iron infusion (notably ferric carboxymaltose) ²⁹⁵	Increases circulating concentrations of biologically active FGF-23 in patients with iron deficiency anaemia	May cause transient ²⁹⁶ or even severe and protracted ^{297,298} hypophosphataemia	Avoid if possible/close monitoring of Ca/PO4 product for several weeks after intravenous iron infusion, particularly in patients under PTH replacement therapy ²⁹⁹ Consider changing to tenofovir alafenamide or other non-tenofovir-based regimen
Tenofovir disoproxil fumarate (TDF) used in first-line treatment of human immunodeficiency virus infection and in hepatitis B virus infection ^{300,301}	Induces renal proximal tubular dysfunction	May cause hypophosphataemia and osteomalacia	
Immune check point inhibitors (mainly PD-1 and PD-L1 inhibitors) ^{24,302-306}	Immune tolerance disruption- Antiparathyroid and calcium-sensing receptor-activating autoantibodies may be detectable	May rarely cause autoimmune HypoPT (largely irreversible) between 3 weeks and 7 months of treatment	Close monitoring/Long-term treatment with an activated vitamin D and calcium supplements

(continued)

Table 6. Continued

Drug/disease	Mechanism	Possible adverse effects in HypoPT	Action
Pregnane X receptor ligands** ³⁰⁷	Upregulate the expression of the 24-hydroxylases (CYP24A1 and CYP3A4) leading to increased degradation of 1,25-dihydroxy vitamin D	May induce hypocalcaemia	Consider modifying doses of activated vitamin D

HypoPT, hypoparathyroidism; PD-1, programmed cell death-ligand 1; PTH, parathyroid hormone.
 *Changes in the free (ionised) fraction of calcium (Ca^{2+}) cannot be monitored by measuring total calcium levels. Many laboratories report serum Ca^{2+} levels adjusted to a neutral pH value (pH 7.4), which does not reflect the actual serum Ca^{2+} level in a patient with disturbances in acid-base balance. If so, patients may have symptoms despite (apparently) normal calcium levels and Ca^{2+} levels at actual pH should be requested.
 ** As pH decreases, more H^+ ions compete for binding sites on proteins like albumin, causing more calcium to be released and increasing the physiologically active free fraction. Conversely, increasing pH values increase the negative charge on proteins, leading to increased calcium binding and a decrease in free ionized calcium.
 *** Including antibiotics (rifampicin), anti-epileptic drugs (phenytoin, carbamazepine), anti-inflammatory/steroids (dexamethasone), antiretroviral drugs (ritonavir, saquinavir), antineoplastic drugs (cyclophosphamide, taxol (paclitaxel), epirubicin, tamoxifen), other drugs (nifedipine, spironolactone, cyproterone acetate, clotrimazole) or herbal products (hyperforin, Kava kava).

developing calcium stone disease increases continuously, in a nonlinear manner, with urinary calcium excretion. It is therefore difficult to provide a threshold below which the risk becomes negligible. Nevertheless, we suggest aiming at calcium excretion <7.5 mmol/24-hour (300 mg/24-hour) in men, and <6.25 mmol/24-hour in women (250 mg/24-hour); or <0.1 mmol/kg/24-hour (4 mg/kg/24-hour) in both sexes. Creatinine and sodium excretion should be measured in parallel to assess the completeness of the collection and sodium intake, respectively. In patients with hypercalciuria, reduction in calcium intake, a sodium-restricted diet, and thiazide diuretic use can be considered (see R.3.5).

R.2.4 We suggest aiming for phosphate levels within the reference range. (⊕○○○)

Reasoning: HypoPT is characterised by a relatively high circulating phosphate level and a higher-than-normal calcium-phosphate product. This is attributable to the lack of the phosphaturic effect of PTH, as well as an enhanced intestinal absorption of phosphorus, due to activated vitamin D treatment (conventional treatment)^{25,121}. The risk of extra-skeletal calcifications, including nephrocalcinosis and cataracts, is increased in HypoPT. It is generally assumed that this is related to high phosphate levels and an increased calcium-phosphate product; therefore, it seems reasonable to aim for keeping phosphate levels within the normal range¹³⁹.

R.2.5 We suggest aiming for magnesium levels within the reference range. (⊕○○○)

Reasoning: Magnesium is central to several physiological processes, including the secretion and actions of PTH. Low circulating magnesium levels may cause functional HypoPT by blunting the (residual) capacity of the parathyroid glands to secrete PTH¹⁴⁰. Moreover, low magnesium may cause hypocalcaemia-like symptoms by itself¹⁴¹. Accordingly, it seems reasonable to aim at keeping serum magnesium levels within the reference range.

Although more than 99% of the exchangeable total body magnesium is located intracellularly, routine clinical measurements are limited to serum or plasma magnesium levels. Hypomagnesaemia - considered when magnesium concentration is below 0.7 mmol/L - is common, particularly in subjects with comorbid conditions and medications (like diuretics and proton pump inhibitors)¹⁴¹. Despite its limitations as a proxy for intracellular magnesium status, circulating magnesium levels remain the standard measure in clinical practice and should be monitored and optimised in HypoPT.

R.2.6 We suggest aiming at an adequate vitamin D status (25(OH)D level ≥ 75 nmol/L [30 ng/mL]). (⊕○○○)

Reasoning: Vitamin D insufficiency has been associated with adverse effects on skeletal, as well as extra-skeletal health¹⁴². Severe vitamin D deficiency is associated with symptoms of myopathy, and patients with HypoPT frequently report neuromuscular symptoms, which may be exacerbated by concomitant vitamin D deficiency^{25,111,143}. To ensure that symptoms are not caused by vitamin D deficiency, an adequate vitamin D status should be ensured. A concentration of

25-hydroxyvitamin D (25(OH)D) above 75 nmol/L (30 ng/mL) may be considered adequate¹⁴⁴.

Remarks: Treatment with activated vitamin D analogues does not guarantee an adequate vitamin D status, as measured by circulating 25(OH)D levels. As vitamin D (calciferol) and its metabolite 25(OH)D itself may be of importance to several cellular processes and may undergo hydroxylation to 1,25(OH)₂D catalysed by local hydroxylases in different tissues¹⁴⁵, it seems reasonable to ensure sufficient 25(OH)D levels, despite treatment with activated vitamin D analogues.

5.3 Treatment

R.3.1 We recommend treatment of all patients with chronic HypoPT who have symptoms of hypocalcaemia and/or an albumin-adjusted calcium level < 2.0 mmol/L (< 8.0 mg/dL) \approx ionised calcium (iCa²⁺) < 1.00 mmol/L.

R.3.2 We suggest offering treatment to patients with chronic HypoPT, even if apparently asymptomatic, if albumin-adjusted calcium levels are between 2.0 mmol/L (8.0 mg/dL or iCa²⁺ 1.00 mmol/L) and the lower limit of the reference range to assess whether this may improve their well-being. (Good clinical practice)

Reasoning: In chronic HypoPT, symptoms of hypocalcaemia may vary widely, from asymptomatic to life-threatening, such as seizures, cardiac failure, bronchospasm, and laryngospasm^{25,121,125,146}. In a life-threatening hypocalcaemia emergency, 90-180 mg elemental calcium, e.g., preferably 1-2 ampules calcium gluconate (containing 1 g calcium gluconate per ampule) is administered over 10 to 20 minutes, followed by a slower intravenous calcium infusion, e.g., 10 ampules containing about 900 mg elemental calcium into 1 litre of 5% dextrose or saline at a starting rate of 100 mL/h. In addition to close monitoring of calcium levels and ECG, oral therapy with calcium supplements and activated vitamin D (e.g., calcitriol 0.25 or 0.5 μ g twice daily) should be started¹⁴⁷.

While it is obvious to recommend treatment of patients with severe symptoms of hypocalcaemia, it is unclear whether asymptomatic patients with biochemical hypocalcaemia should be treated. No limit of calcium levels has been defined below which treatment is unquestionably needed. Symptoms of hypocalcaemia do not translate directly to circulating calcium levels. Sudden fluctuations in calcium levels may cause symptoms, even if average calcium levels are (almost) normal. On the other hand, no apparent symptoms may be present, despite low calcium levels, if the hypocalcaemia has developed slowly or has been present for a longer period. In a patient with intact parathyroid function, calcium levels are tightly regulated within a narrow range^{145,148}. It seems likely that patients with no complaints of hypocalcaemia, despite (very) low calcium levels, have adapted to a new calcium homeostasis, which may have blunted their symptoms of hypocalcaemia. We consider it reasonable to offer treatment to asymptomatic patients with chronic HypoPT, since treatment might improve their well-being (Figure 2). An exception is for patients with ADH1, where lower calcium levels in asymptomatic patients might be tolerated, see section 5.1. If no improvements

occur following 6-12 months of therapy, the need for treatment may be reconsidered, especially if hypocalcaemia is mild.

R.3.3 We recommend treatment with vitamin D.

R.3.3.1 *If available, we recommend treatment with an activated vitamin D analogue (e.g., alfacalcidol or calcitriol). (⊕○○○).*

R.3.3.2 *If activated vitamin D analogues are not available, we suggest treatment with supraphysiological doses of calciferol (preferentially cholecalciferol, i.e., vitamin D₃). (⊕○○○).*

R.3.3.3 *We recommend titration of vitamin D analogue doses aiming at calcium levels within the target range, with patients being free of symptomatic hypocalcaemia and biomarkers within the target range. (⊕○○○)*

Reasoning: HypoPT is a disease with a deficiency of two hormones (PTH and 1,25(OH)₂D), as PTH normally facilitates the hydroxylation of 25(OH)D to 1,25(OH)₂D, and activated vitamin D stimulates the intestinal calcium absorption. There are no comparative studies guiding the optimal treatment with vitamin D (dose and type). Prior to the development of activated vitamin D analogues, calciferol (ergocalciferol [vitamin D₂] or cholecalciferol [vitamin D₃]) were used, as small amounts of 25(OH)D are converted to 1,25(OH)₂D, even if PTH is low as in HypoPT¹⁴⁹. If supraphysiological doses of calciferol (typical 25.000-200.000 IU/day, 625-5000 μ g/day) are used, this may result in normocalcaemia with very high circulating concentrations of 25(OH)D (typically 500-1000 nmol/L, 200-400 ng/mL). Importantly, this treatment with supraphysiological calciferol doses should only be considered in special circumstances or in healthcare settings with no access to activated vitamin D analogues, as this therapy is only based on historical observations, rarely used today and associated with the risk of vitamin D toxicity. Following the development of activated vitamin D analogues, small case series showed that normocalcaemia could be achieved if HypoPT was treated with activated vitamin D analogues^{150,151}. Today, activated vitamin D analogues are preferred due to shorter plasma half-life, allowing for dose titration at shorter time intervals compared with calciferol (Table 3). Moreover, in the case of intoxication, calcium levels normalise faster if patients are treated with activated vitamin D analogues^{152,153}. Alfacalcidol (1 α -hydroxyvitamin D) or calcitriol (1,25(OH)₂D) are mainly used. Effects on long-term clinical outcomes of the different analogues have not been compared head-to-head in HypoPT. In terms of calcaemic effects, calcitriol is approximately twice as potent as alfacalcidol, as shown in a randomised controlled trial¹⁵⁴. To maintain calcium levels within the target range, the daily dose must be carefully titrated, as the dose needed varies between patients. Daily doses of calcitriol are typically 0.25-2.0 μ g, equal to a daily dose of 0.5-4.0 μ g of alfacalcidol¹⁵⁵ (Table 3). We suggest treatment with calcitriol once or twice daily or with using alfacalcidol, once daily as opposed to divided doses for the following reasons: 1) Changes in circulating or urinary calcium are similar regardless of whether identical calcitriol doses per day are given once daily or twice daily^{156,157}, 2) The onset of effect of active vitamin D analogues on intestinal calcium absorption and calcium levels is

delayed with no significant difference for intravenous versus oral calcitriol treatment¹⁵⁸, 3) Although the plasma half-life of calcitriol is only several hours, the half-life of its biological effects on calcium metabolism is more than 24 hours^{159,160}, and 4) To minimize pill burden. We acknowledge that there is limited evidence and controversy in the literature regarding whether once-daily doses or divided doses of active vitamin D analogues is preferred. We therefore encourage further studies on this issue.

If calcium levels are slightly outside the target range, or if a patient is complaining of symptoms, the daily dose of activated vitamin D can be gradually changed (Figure 2), i.e., the daily dose of alfacalcidol may be changed by 0.5 µg, corresponding to a 0.25 µg change in the dose of calcitriol. Larger changes in dose may be needed in case of severe hypo- or hypercalcaemia and treatment initiation (e.g., daily doses of 1.0 to 2.0 µg of alfacalcidol or 0.5 to 1.0 µg calcitriol, which roughly equals the normal daily calcitriol production rate of a human)¹⁶¹. To allow for the achievement of a new steady-state, dose adjustments should not be performed more frequently than at 2-3 day time intervals¹⁶². If only minor symptoms or biochemical disturbances are to be adjusted, weeks may be allowed to pass between dose adjustments. Of note, the measurement of calcium levels is subject to variations. Because of the long half-life of calciferol, if a patient is receiving treatment with supraphysiological doses of calciferol, 2-3 months are needed between dose adjustments before a new steady state has emerged.

R.3.4 We recommend assuring an adequate calcium intake.

R.3.4.1 We suggest a dietary elemental calcium intake of about 800-1000 mg/day in adults (non-pregnant) (European Food Safety Authority¹).

R.3.4.2 We suggest using calcium supplements if blood calcium levels in the target range cannot be achieved by treatment with activated vitamin D analogues in combination with an adequate dietary calcium intake. (⊕○○○).

R.3.4.3 We recommend that elemental calcium supplementation greater than 500 mg daily should be taken in smaller doses and spread throughout the day.

Reasoning: An adequate daily intake of calcium from diet and/or supplements is advisable for several reasons, including for bone health. In HypoPT, hypocalcaemia is mainly caused by the lack of 1,25(OH)₂D due to PTH deficiency. Thereby, it seems rational to substitute with activated vitamin D and not to aim for obtaining normocalcaemia by supplying very high amounts of calcium supplements. Most patients with HypoPT have normal calcium absorption if conditions allow, i.e., if adequate 1,25(OH)₂D is present. Accordingly, most patients with HypoPT do not need a (very) high calcium intake to achieve normocalcaemia, and selected patients can be well managed without any calcium supplements^{49,163}. A high calcium intake can help to achieve calcium levels in the target range (and lower the dose of activated vitamin D needed), but it is not feasible as the principal component in the treatment of HypoPT, as it causes a high pill burden. Intake of calcium causes only a transient increase in circulating calcium levels. Moreover, the absorptive capacity of the intestine is probably saturated by an intake of 500 mg of elemental calcium in one ingestion¹⁶⁴. Thus, routine high-dose calcium supplements are discouraged,

but higher doses may be selectively useful in defined situations and administered in divided doses throughout the day^{165,166}.

However, it is noteworthy that calcium binds phosphorus in the intestine and may thereby lower circulating phosphate levels¹⁶⁷. Thus, in selected cases, high doses of calcium from supplements may be advantageous. Furthermore, extra intake of calcium alone may be recommended on an *as-required* basis if a patient is only experiencing symptoms of hypocalcaemia occasionally.

Intake of calcium from dietary sources is physiologic and considered equivalent to intake from supplements^{103,168}. Different calcium salts are available as supplements. Of note, 500 mg elemental calcium equals to 1250 mg calcium carbonate (40% elemental calcium) and to 2385 mg calcium citrate (21% elemental calcium). Calcium carbonate is most often used and is less expensive than other calcium preparations. However, calcium carbonate requires an acidic environment for absorption and should, therefore, be taken together with a meal¹⁶⁸. Calcium citrate can be used in patients with achlorhydria or receiving treatment with proton pump inhibitors (PPI), as well as in patients who prefer to take supplements outside mealtimes¹⁶⁶, see Table 6. Calcium citrate, compared with calcium carbonate, was also associated with lower urinary oxalate excretion and may therefore mitigate the risk of nephrolithiasis¹⁰⁴.

Bariatric surgery, especially Roux-en-Y gastric bypass, frequently causes intestinal calcium malabsorption^{169,170}. Therefore, higher doses of oral calcium supplements than in patients with conserved intestinal absorption may be needed. Calcium citrate rather than calcium carbonate may be recommended because achlorhydria is frequently associated. Furthermore, high oral calcium intake is useful to decrease intestinal oxalate absorption and limit hyperoxaluria¹⁷¹.

Coexistence of hypothyroidism is common in patients with postsurgical HypoPT. Due to interference with L-thyroxine absorption, calcium supplements should not be taken together with thyroxine substitution¹⁷².

R.3.5 We recommend PTH replacement therapy in patients with chronic HypoPT who continue to have signs or symptoms of HypoPT despite optimised treatment with (activated) vitamin D and adequate calcium intake. (⊕⊕○○)

R.3.5.1 We suggest to titrate the dose of PTH replacement therapy to achieve sustained calcium levels in the target range without the need for concurrent activated vitamin D treatment or calcium supplements.

R.3.5.2 We suggest to consider treatment with PTH replacement therapy in patients with one of the following despite optimised conventional treatment.

- Frequent fluctuations in calcium levels, or symptomatic hypocalcaemia
- Impaired quality of life attributable to chronic HypoPT
- Reduced kidney function (eGFR < 60 mL/min per 1.73m²)
- Hypercalciuria (calcium excretion >7.5 mmol/24-hour [300 mg/24-hour] in men, and > 6.25 mmol/24-hour in women [250 mg/24-hour]; or > 0.1 mmol/kg/24-hour [4 mg/kg/24-hour] in both sexes)
- Hyperphosphataemia

R.3.5.3 *If PTH replacement therapy is initiated, we suggest evaluating the treatment effects after 6-12 months, depending on treatment goals. (Good clinical practice).*

Reasoning: There is a potential for recovering parathyroid function in postsurgical HypoPT (even after years; see **Clinical Question I**). Accordingly, in patients managed with conventional treatment, calcium levels should be in the lower half or slightly below the reference range (i.e., in the target range) to stimulate any remaining parathyroid cells to secrete PTH, and to avoid suppression of parathyroid gland function.

Target ranges for calcium levels may differ for patients on conventional treatment by activated vitamin D analogues versus replacement formulations with sustained PTH effects. As the PTH effects of increasing renal calcium reabsorption and decreasing renal phosphate reabsorption are minimal (if at all present) in chronic HypoPT patients, the aim to increase calcium levels with activated vitamin D treatment comes at the expense of increased risk of hypercalciuria (risk of urinary stones) and hyperphosphataemia. Therefore, aiming at low normal or slightly below the lower limit of normal calcium levels is reasonable for conventional treatment, to minimise adverse treatment effects when targeting higher calcium levels. Conversely, treatment with formulations with sustained PTH effects simultaneously increases endogenous activated vitamin D (calcitriol) levels (due to increased conversion of 25(OH)D to 1,25(OH)₂D/calcitriol), and restores PTH effects on renal calcium reabsorption and urinary phosphate excretion, thereby mitigating the risk of hypercalciuria and hyperphosphataemia¹⁷³. Therefore, in patients with chronic HypoPT treated with PTH replacement therapy, the optimal trade-off between minimising hypocalcaemic symptoms while minimising the risk of adverse treatment effects by, e.g., hypercalciuria or hyperphosphataemia, may shift towards higher target ranges for calcium levels, as compared to conventional treatment. Thus, we consider it reasonable to aim for a target calcium level within the lower half of the normal range (but not below) in patients on PTH replacement therapy. For these patients, it may also be reasonable to aim for calcium levels within the normal range as recorded before the occurrence of HypoPT, even if in the upper half of the normal range. Targeting calcium levels in the upper half of the reference range may also be reasonable if required for optimising symptoms and QoL and when paying particular attention to avoid overtreatment reflected by, e.g., hypercalcaemia and hypercalciuria.

Palopegteriparatide is currently (i.e., 2025) the only available (EMA and FDA) PTH analogue approved for the treatment of chronic HypoPT and causes a sustained PTH effect⁸¹. Although clinical trials have shown beneficial effects of treatment with palopegteriparatide^{82,83}, the guideline panel acknowledges that long-term safety and outcome data (e.g., on fracture rates, cardiovascular health, or renal endpoints) are not yet available. Moreover, availability and reimbursement criteria may differ between countries, which must be considered when treatment decisions are made.

After a subcutaneous injection of palopegteriparatide, free PTH(1-34) is slowly released into the circulation, providing stable concentrations throughout the day (half-life is about 60 hours)⁸¹ with steady circulating calcium concentrations and no need for treatment with activated vitamin D or calcium supplements in the majority of patients. The starting dose is one daily subcutaneous injection of 18 µg, see **Figure 3**.

Activated vitamin D should be omitted on the same day that PTH treatment is initiated. However, reduced doses of activated vitamin D (usually half the dose) should be maintained if calcium levels are very low (e.g., total calcium < 2.07 mmol/L [< 8.3 mg/dL]). Doses of palopegteriparatide are adjusted according to calcium levels with up or down titration once a week (with a maximum change of ± 3 µg/day each week). Concomitant doses of activated vitamin D and calcium are adjusted, aiming at calcium levels within the target range without the need for activated vitamin D or calcium supplements^{83,174}. We acknowledge that some patients will remain in need of concurrent treatment with activated vitamin D and calcium supplements. Palopegteriparatide can be dosed in the range of 6-60 µg/day (the FDA limit is currently 30 µg/day, as per the label). A dose > 30 µg/day is administered as two subcutaneous injections (simultaneously). The package leaflet of the drug provides further information on how best to titrate the drug (Yorvipath®, INN-palopegteriparatide).

In addition to stabilising calcium concentrations, clinical trials on the treatment of chronic HypoPT with palopegteriparatide have shown improvement in QoL, reductions in renal calcium excretion, increased eGFR, and normalisation of phosphate levels and the calcium-phosphate product^{82,83} (see **Clinical Question II**).

For the purposes of the above, frequent fluctuations in calcium levels are considered if 3 or more adjustments per year are needed in doses of activated vitamin D and/or calcium supplements to maintain a calcium concentration in the target range. Such patients are considered inadequately controlled by conventional therapy and usually suffer from a significant disease burden with likewise frequent and costly demands on healthcare resources^{175,176}. These patients might benefit from PTH replacement therapy.

Impaired QoL attributable to chronic HypoPT is multifaceted¹⁷⁷, including a high pill burden, lack of energy with reduced psychological well-being, and impairment of physical - (frequent symptoms of hypo-/hypercalcaemia including neuromuscular irritability with muscle spasms and pain) and cognitive- (brain fog, reduced memory, difficulties in concentrating/focusing) function. The parameters, measures, and extent to which reduced QoL is attributed to HypoPT that justifies PTH replacement therapy are currently not specifically defined and require individual decision-making. Certain disease-specific questionnaires may aid in the assessment of QoL in HypoPT patients and inform treatment decisions regarding PTH replacement therapy¹²⁴.

HypoPT is associated with an increased risk of renal complications^{8,25,54,125}. Kidney function (creatinine-based eGFR) decreases in patients with HypoPT on conventional treatment^{81,178}, but improves in response to treatment of chronic HypoPT with palopegteriparatide. This effect was more pronounced if eGFR at the start of treatment was below 60 mL/min per 1.73 m²; e.g., 52 weeks of treatment with palopegteriparatide in HypoPT patients with a baseline eGFR below 60 mL/min per 1.73 m² resulted in a mean (standard deviation) increase of 11.5 (11.3) mL/min per 1.73 m²¹⁷⁹. Accordingly, it seems reasonable to offer this treatment to patients with impaired kidney function. However, it must be acknowledged that an effect of palopegteriparatide on tubular creatinine secretion rather than filtration has not been ruled out.

Effects of replacement with palopegteriparatide should be evaluated 6-12 months after starting the treatment.

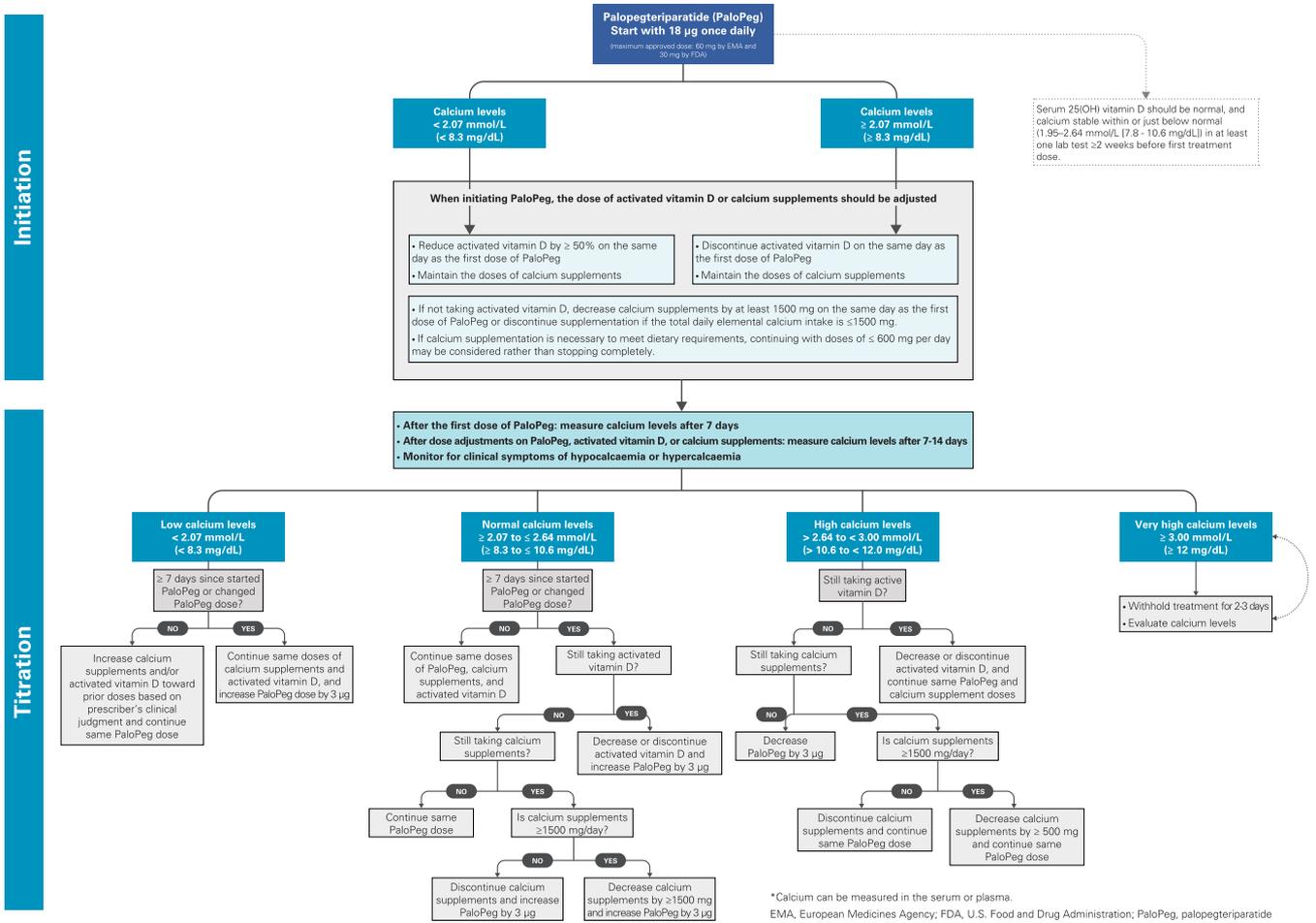


Figure 3. Palopegteriparatide treatment algorithm.

However, if the circumstances that led to the start of treatment (R.3.5.2) did not improve, it should be considered whether the new treatment is of value for the patient.

If palopegteriparatide must be discontinued, frequent monitoring of calcium levels (e.g., every 2 to 3 days) is recommended until disease control is re-established with conventional therapy. Due to its prolonged half-life, calcium levels may remain relatively stable for several days. However, the pharmacologic effect of a single dose diminishes gradually, with no meaningful biological activity expected beyond 10 to 14 days. To minimise the risk of hypocalcaemia following discontinuation, conventional therapy should be reinstated promptly. Patients can be advised to resume calcium and activated vitamin D in the same dose as prior to starting palopegteriparatide. At present, no studies have evaluated the optimal strategy for discontinuing palopegteriparatide. It remains unclear whether abrupt cessation or a gradual tapering approach (e.g., reducing the dose by 3 µg every 2-3 days until cessation) is preferable.

Apart from palopegteriparatide, a sustained PTH effect can be achieved by pump-therapy or through several daily subcutaneous injections with PTH(1-34) or PTH(1-84). As PTH(1-84) therapy has recently been withdrawn from the market, only PTH(1-34) is available, but it has not been marketed for the treatment of HypoPT. However, PTH(1-34) is used off-label in some countries, and clinical studies have shown a beneficial effect compared to conventional treatment^{68,69,79}. In an open-label phase 2 study,

eneboparatide, an agonist of the PTHR1 receptor, has been effective and safe for disease control in chronic HypoPT⁸⁵. Eneboparatide is thus a potential new treatment for patients with chronic HypoPT that still requires further study results and approval by regulatory authorities before use in patient care⁸⁵.

R.3.6 In the presence of hypercalcaemia, we suggest measures to lower urinary calcium excretion, which may include decreased doses of calcium supplements and/or activated vitamin D analogues, a low sodium chloride intake (< 6 g NaCl or < 2.4 g sodium/day) and/or addition of treatment with a thiazide diuretic. If these measures are not effective in normalising hypercalcaemia, while maintaining calcium levels within the target range, we suggest PTH replacement therapy. (⊕○○○)

Reasoning: In the general population, high renal calcium excretion is associated with an increased risk of renal calcifications. In HypoPT, the risk of renal complications is increased^{8,63,125,180}, but only insufficient data are available on whether a high urinary calcium excretion in HypoPT is associated with this increased risk. However, it seems reasonable to aim to normalise the 24-hour urinary calcium (Figure 2), even though formal scientific proof is lacking. Replacement therapy with a sustained PTH effect has demonstrated lowering urinary calcium in HypoPT¹⁷⁴.

No data exist on whether dietary recommendations are useful in reducing urinary calcium in HypoPT. In patients with intact parathyroid function, urinary calcium is positively associated with the intake of calcium and sodium chloride^{181,182}. Accordingly, it may be helpful to reduce the intake of sodium chloride to < 6 g/day^{183,184}. See also the European Association of Urology 2024 Guidelines on Urolithiasis: EAU Guidelines on Urolithiasis - Uroweb, and [Figure 2](#). If patients are receiving treatment with a high daily dose of calcium supplements, the daily dose of activated vitamin D may be increased to allow for reducing the dose of calcium supplements. If dietary recommendations or changes in the daily dose of calcium supplements and/or activated vitamin D analogues do not sufficiently reduce urinary calcium excretion, treatment with a thiazide diuretic may be considered ([Figure 2](#)). Treatment with a thiazide diuretic is associated with a lowering of urinary calcium in patients with HypoPT^{63,185-188} and can be considered in patients with hypercalcaemia. Pharmacological management of urolithiasis includes treatment with a thiazide diuretic in case of hypercalcaemia¹⁸⁹. A calcium-sparing effect of thiazides may also allow for reduced doses of calcium supplements. The addition of amiloride to a thiazide may further lower urinary calcium losses and decrease the risk of hypokalaemia. Moreover, amiloride may lower renal magnesium excretion^{46,190}. However, no data are available on whether thiazides reduce the risk of renal complications in HypoPT. If a thiazide diuretic is prescribed, it should be noted that the hypocalcaemic effect is dose-dependent, and treatment should preferably be combined with sodium restriction (85). A relatively high dose administered twice daily is often needed to lower 24-hour urinary calcium, i.e., hydrochlorothiazide 50 mg twice daily or bendroflumethiazide 5 mg twice daily. Thiazide-like diuretics (e.g., chlorthalidone and indapamide) may, however, be administered only once daily as they have a longer duration of action. Risks of adverse effects increase with dose, and potential adverse effects should be monitored early (1-2 weeks) and closely during treatment, including blood electrolyte disturbances, decrease in eGFR and potentially reduced blood pressure. In case of calcium nephrolithiasis, the other metabolic risk factors (volume, oxalate, citrate, animal protein consumption) must be assessed and corrected, (see EAU Guidelines on Urolithiasis - Uroweb). HypoPT patients with nephrolithiasis and hypercalcaemia despite optimised conventional therapy are candidates for PTH replacement therapy.

R.3.7 In the presence of hyperphosphataemia, we suggest dietary interventions and/or adjustment of treatment with calcium supplements and vitamin D analogues. If these measures are not effective in normalising hyperphosphataemia while maintaining calcium levels within the target range, we suggest PTH replacement therapy. (⊕○○○)

Reasoning: High phosphate levels and/or a high calcium-phosphate product are presumed to increase the risk of extra-skeletal calcifications, interventions aiming at normalising these biochemical indices should be considered¹⁹¹ ([Figure 2](#)), although evidence from trials is lacking. Patients may be advised to reduce their intake of dietary sources rich in phosphate. As calcium binds phosphate in the intestine and calcitriol increases intestinal absorption of phosphorous, it

may be considered to titrate therapy so that the daily intake of calcium supplements (together with a meal) is increased, which may allow for a decrease in daily dose of activated vitamin D analogues. Following such changes, 24-hour urinary calcium should be measured to ensure that patients have not developed severe hypercalcaemia. No data exist on the use of phosphate binders in HypoPT. Of note, studies in patients with chronic kidney disease (mostly not on dialysis) have suggested increased mortality and risk of vascular calcifications in patients on treatment with calcium-containing versus calcium-free phosphate binders¹⁹². It is unknown whether lowering phosphate levels in HypoPT by increasing calcium intake is of benefit or harm to patients.

R.3.8 In a patient with hypomagnesaemia, we suggest measures to increase magnesium levels. (⊕○○○)

Reasoning: Low magnesium levels are often reported in HypoPT, and marked magnesium deficiency may cause symptoms like hypocalcaemia¹⁴¹. In addition to HypoPT, other causes of hypomagnesaemia must be considered, including treatment with certain diuretics and PPIs¹⁹³. To normalise magnesium levels, a diet rich in magnesium (e.g., leafy greens, nuts, and whole grains) and/or treatment with magnesium supplements or amiloride can be considered^{190,194}. Magnesium supplements are not always well tolerated due to gastrointestinal adverse events. Various magnesium salts can be prescribed, based on the tolerance of the individual patient. Amiloride has been shown (in patients with an intact parathyroid function) to act as a magnesium-sparing diuretic^{190,195}.

Of note, magnesium is mainly present in the intracellular compartment, distributed in soft tissue (19%), muscle (27%), and bone (53%). Only 0.8% of magnesium is found in the circulation, with 0.3% in serum and 0.5% in erythrocytes¹⁹⁶. As mentioned above, circulating magnesium levels do not provide an accurate proxy of magnesium status. If magnesium levels are chronically low, a magnesium retention test may be considered. This involves administering 0.5 mmol of magnesium per kg of body weight in 500 mL of saline as an intravenous infusion over 6 hours. The test should be avoided in cases of severe renal impairment, and the dose should be reduced in patients with mild renal dysfunction. This test helps determine whether the patient has intracellular magnesium depletion. If 24-hour urinary magnesium excretion is < 50% of the infused amount, magnesium deficiency is likely present, and the infusion itself will serve as treatment¹⁹⁷⁻¹⁹⁹.

R.3.9 Ensure replete levels of vitamin D by using a daily vitamin D supplement (cholecalciferol or ergocalciferol; vitamin D₃ or D₂) of 800-2000 IU (20-50 µg).

Reasoning: Vitamin D is of importance for many physiological processes, including calcium homeostasis. In otherwise healthy individuals, PTH secretion starts to rise if concentrations of 25(OH)D, the accepted marker of vitamin D status, decrease. Vitamin D deficiency may thus increase the requirement for PTH in mineral metabolism. There is no clear threshold for vitamin D sufficiency, but at a circulating 25(OH)D level ≥ 75 nmol/L (30 ng/mL), PTH secretion to compensate for a poor vitamin D status is considered minimal, if at all present²⁰⁰⁻²⁰². The vast majority of patients will effectively

and safely achieve levels of 25(OH)D \geq 75 nmol/L (30 ng/mL) if vitamin D (cholecalciferol or ergocalciferol; vitamin D₃ or D₂) is supplemented at a dose of 800-2000 IU/day (20-50 μ g/day)²⁰³⁻²⁰⁸. A reasonable target range for vitamin D status in chronic HypoPT patients may be 25(OH)D of 75 to 125 nmol/L (30 to 50 ng/mL)¹²².

5.4. Monitoring

R.4.1 We suggest measuring PTH levels once a year, as appropriate, to assess endogenous function for potential recovery.

Reasoning: Recovery of chronic postsurgical HypoPT following years after the initial diagnosis, although rare, has been reported^{35,94,209-211}. In a case series of four individuals, recovery of parathyroid function was documented up to 8 and 16 years after the initial diagnosis following treatment with PTH(1-84) for 36 to 63 months²⁰⁹. Underlying mechanisms may involve the potential effects of PTH in enhancing vascularisation of the remaining parathyroid tissue or the reduction of calcium and vitamin D supplements that are well-known negative regulators of parathyroid function²¹²⁻²¹⁵. A few patients may regain sufficient parathyroid function even after several years. This possibility should be tested periodically by lowering treatment doses (including PTH analogues if used), measurement of PTH and calcium, and assessment of related symptoms. Of importance, in certain types of non-surgical HypoPT, PTH secretion may also be reestablished (e.g., autoimmune HypoPT).

R.4.2 We recommend routine biochemical monitoring of circulating levels of ionised, or albumin-adjusted total calcium, phosphate, magnesium, and creatinine (estimated glomerular filtration rate [eGFR]), as well as assessment of symptoms of hypocalcaemia and hypercalcaemia at regular time intervals (e.g., every 3-6 months).

Reasoning: In a patient with HypoPT on stable therapy, calcium levels and renal function may change without an obvious cause and without causing noticeable symptoms. On the other hand, hypocalcaemia-related symptomatology may be present, yet unrecognised despite maintaining calcium levels within the normal range, imposing a significant negative impact on the patient's QoL²¹⁶. Although there are currently no data defining optimal monitoring of patients with HypoPT, it seems reasonable to offer biochemical screening and clinical assessment of related symptomatology to patients at regular time intervals (Figure 2).

As no straightforward relationship exists between calcium levels and hypocalcaemic symptoms, the occurrence of hypocalcaemic symptoms should be evaluated at regular time intervals to ensure that the treatment provides relief of symptoms without causing adverse effects.

R.4.3 Following changes in therapy, we recommend biochemical monitoring every 1-2 weeks.

Reasoning: If the daily dose of activated vitamin D or calcium is changed, or if a new treatment is introduced (such as thiazide diuretics), circulating levels of calcium, phosphate, magnesium, and creatinine (together with eGFR) should be

closely monitored for the first weeks (Figure 2). This also applies to the change from conventional to PTH replacement therapy. In case of severe hypo- or hypercalcaemia, more frequent monitoring (e.g., several times a week) may be needed, but not earlier than 2 to 3 days after adjusting conventional therapy.

R.4.4 When receiving conventional treatment, we suggest monitoring of 24-hour urinary calcium at regular time intervals (e.g., every 1-2 years).

Reasoning: Hypercalciuria is a well-known risk factor for renal calcifications^{126,134-136}, and although currently no data exist on patients with HypoPT, assessment of 24-hour urinary calcium, sodium, and creatinine at regular time intervals may allow for early intervention, in case hypercalciuria is present.

Vitamin D status should be normal when measuring 24-hour urinary calcium²¹⁷. In addition, high dietary sodium and increased urinary sodium excretion are known to significantly increase calcium excretion. Therefore, a low-sodium diet should be advised, especially in the presence of hypercalciuria²¹⁸⁻²²¹.

No data, however, are available on whether these measures will help to reduce long-term morbidity. Monitoring of urinary calcium at shorter time intervals may be considered in cases where specific treatment targeting lowering urinary calcium is advised (e.g., thiazide diuretics) and in patients requiring higher than generally recommended calcium levels.

As stated in R.3.5, PTH replacement therapy decreases renal excretion of calcium, wherefore we do not suggest monitoring 24-hour urinary calcium routinely during treatment with PTH analogues.

R.4.5 We recommend against routine renal imaging but perform renal imaging (ultrasound or CT) if there are clinical or laboratory features suggestive of nephrolithiasis, nephrocalcinosis, or unexplained decline in renal function.

Reasoning: Renal imaging upon diagnosis or during monitoring is generally not recommended but may be considered in patients with additional risk factors of nephrolithiasis, such as positive family history, type of hypoparathyroidism (e.g., ADH1), duration of treatment for HypoPT, arterial hypertension, diabetes, obesity, or gout²²²⁻²²⁴. For people with CKD, a change in eGFR of > 20% and/or a doubling of the urinary albumin-over-creatinine ratio on a subsequent test exceeds the expected variability and warrants further evaluation²²⁵. eGFR and albuminuria should be assessed at least annually.

R.4.6 We suggest monitoring for the development of signs or symptoms of co-morbidities at regular time intervals (e.g., yearly).

Reasoning: HypoPT is associated with multiple co-morbidities (Table 2). While the risk for renal complications is well-established, particularly for chronic kidney failure, hypercalciuria, nephrolithiasis, and nephrocalcinosis, the causality with other complications is less well-understood. Increased cardiovascular risk has been reported in patients with HypoPT, and the risk for cardiovascular events appears to

increase with the duration of the disease^{8,48,226}. Increased risk of basal ganglia calcifications is also associated with HypoPT and varies with the severity of the disease, its aetiology, or the duration of treatment^{227,228}. However, patients with basal ganglia calcifications do not appear to have an increased risk of neurological conditions or musculoskeletal symptoms. Patients with HypoPT are also at increased risk of neuropsychiatric disorders (i.e., depression, bipolar affective disorder, anxiety)^{10,44,229}, and infections^{44,48,230}, but the underlying mechanisms and whether both surgical and non-surgical forms are equally affected remain to be elucidated.

Early detection of complications may be of importance, which is why it seems reasonable to assess whether patients are experiencing symptoms, which may indicate emerging complications. However, so far, screening for comorbidities in chronic HypoPT has not shown a beneficial effect in terms of a favourable cost-benefit outcome.

As certain drugs/diseases and conditions may interfere with the treatment of HypoPT, awareness of concomitant medication is relevant (Table 6).

R.4.7 We suggest assessing fracture risk as recommended for the general population.

Reasoning: The relationship between HypoPT and bone health is complex. The absence of parathyroid hormone leads to low bone turnover, thereby increasing bone mineral density (BMD) by up to around 30%, and reducing the loss of BMD during the ageing process, despite having risk factors for osteoporosis²³¹⁻²³³. Data on the risk of fragility fractures, however, is limited, and an increase in the overall risk of fractures has not been consistently reported^{44,51,234}. A recent meta-analysis reported an increased risk of vertebral fractures in patients with nonsurgical HypoPT²³⁵, but an increased risk of vertebral fractures has also been reported in postsurgical HypoPT²³⁶. Furthermore, high BMD readings on DXA may not accurately represent the risk of fractures or the true state of bone health in patients with HypoPT^{237,238}. In addition, the female preponderance in postsurgical hypoparathyroidism and certain presurgical conditions, such as Graves' disease or corticosteroid use, may affect the baseline risk for bone disease and should be taken into consideration when evaluating the individual patient. A recent cross-sectional study based on the Canadian National Hypoparathyroidism Registry reported that 35% of postmenopausal women had osteoporosis by BMD or prior fragility fracture, and three men ≥ 50 had osteoporosis by BMD or fragility fracture (33.3%; $n = 3/9$)²³⁹. A large registry study from Sweden, published after our systematic reviews were conducted, reported no difference in major osteoporotic fractures of patients with HypoPT versus matched controls (HR 0.93; 95% CI 0.69-1.26)²⁴⁰. However, patients with HypoPT had a higher risk of vertebral fractures (HR 1.55; 95% CI 1.12-2.14) and a lower risk of femur fractures (HR 0.70; 95% CI 0.50-0.98) compared to controls. Despite being more often diagnosed with osteoporosis (HR 1.54; 95% CI 1.21-1.95), HypoPT patients were less frequently prescribed osteoporosis medication (HR 0.69; 95% CI 0.54-0.88) compared to controls²⁴⁰.

Therefore, patients with chronic HypoPT should be screened for risk factors for fragility fractures (including measurement of BMD by dual-energy X-ray absorptiometry (DXA), as in the general population, and a closer follow-up

may be required for postmenopausal women and men > 50 years. For patients treated with PTH analogues, an initial decrease in BMD has been reported, and as the long-term effects of this treatment are unknown, more frequent monitoring of fracture risk factors with or without BMD may be considered¹⁷⁴. Patients with osteoporosis or low-energy fractures should be considered for pharmacological therapy as per general population guidelines, bearing in mind the potential risk of (aggravation) of hypocalcaemia when antiresorptive treatment is initiated.

5.5 Special circumstances

Autosomal dominant hypocalcaemia

R.5.1 We recommend close monitoring of patients with autosomal dominant hypocalcaemia (ADH), who are being treated with calcium and/or activated vitamin D, as such patients may be at greater risk of hypercalciuria and renal complications.

Reasoning: ADH is classified into two subtypes based on the gene involved: ADH1, caused by activating variants in the calcium-sensing receptor (CASR) gene^{241,242}, and ADH2, caused by activating variants in the alpha subunit ($G\alpha 11$) of the associated G-protein (GNA11)^{243,244}, see Table 1. A diagnosis of ADH can be established through genetic testing^{241,242,244}. The gain-of-function mutations cause a lowering of the calcium set-point in the parathyroid glands. At equivalent calcium levels, patients with ADH have lower PTH levels than normal individuals. In a strict sense, this is not a state of HypoPT, as the parathyroid glands are well preserved, although less responsive to a hypocalcaemic challenge²⁴⁵. The CaSR and GNA11 are also expressed in the renal tubule, and renal calcium excretion is often markedly increased in patients with ADH who are at increased risk of renal complications^{241,246,247}. Asymptomatic patients should, in general, not be treated unless calcium levels are very low and there is no hypercalciuria¹³⁸. Because of enhanced CaSR sensing, increasing calcium levels may further suppress PTH secretion and exacerbate urinary calcium excretion. Therefore, target serum calcium levels may be lower in ADH than in other forms of hypoparathyroidism where renal calcium handling is less affected²⁴⁸. Besides conventional treatment, thiazide diuretics are prescribed in some patients with ADH to reduce urinary calcium excretion^{63,186,241,249}. Calcilytics, which act as antagonists to the CaSR and increase PTH levels, are promising new therapies for ADH⁸⁶. Encaleret, an oral calcilytic, has shown efficacy and safety in a phase 2b trial in 13 patients with ADH1 and is currently being evaluated in a multinational phase 3 trial⁸⁶.

In general, the frequency of monitoring will be dependent on the clinical situation and whether any change in treatment is introduced, see Figure 2.

Pregnancy and breastfeeding

R.5.2 We suggest treatment with activated vitamin D analogues and calcium supplements as in non-pregnant women.

Reasoning: Case series and registry data indicate an increased risk of pregnancy complications in women with chronic HypoPT, including higher rates of induced labour, preterm

birth, lower birth weight, blood transfusions, and congenital anomalies^{55,58,250}. However, robust data from cohort studies or randomised controlled trial data are lacking, but most women with chronic HypoPT have uncomplicated pregnancies and give birth to healthy babies^{55,58,250}.

Activated vitamin D treatment and calcium supplements are the mainstay of HypoPT treatment during pregnancy and lactation. This conventional treatment should remain unchanged when a sufficiently well-controlled woman with HypoPT becomes pregnant, unless initial evaluation after conception reveals the need for adjustment^{57,59,251}. PTH replacement therapy is currently not recommended for use during pregnancy outside of clinical studies. However, case reports of women treated with either subcutaneous PTH(1-84) injections or continuous subcutaneous PTH(1-34) infusions throughout pregnancy have been described with favourable outcomes and no teratogenic effects²⁵²⁻²⁵⁵. While we currently do not recommend PTH replacement therapy during pregnancy, it might be considered for individual patients who are inadequately controlled by conventional therapy. This position may evolve as additional evidence on safety becomes available. Thiazides should be discontinued before conception or once pregnancy is confirmed due to potential risks but could be used with caution in the second and third trimesters after careful risk-benefit assessment⁵⁷.

Although group comparisons of women with HypoPT indicate no significant changes in calcium levels from pre-pregnancy to pregnancy, there is notable inter-individual variability²⁵⁶⁻²⁵⁸. While many women do not require a change in their conventional treatment during pregnancy, a substantial proportion requires adjustments, with either increased or decreased doses of activated vitamin D and/or calcium supplements²⁵⁶⁻²⁶¹. These treatment changes are, however, not predictable and may vary throughout pregnancy with a tendency towards higher dosage requirements in the third trimester²⁵⁶⁻²⁵⁸. Therefore, pre-pregnancy counselling is essential, with optimisation of calcium and vitamin D status prior to conception, and ongoing shared care between endocrinology and obstetrics to ensure maternal and foetal safety.

Towards the end of pregnancy and during lactation, rising PTHrP levels may cause hypercalcaemia unless calcium and activated vitamin D dosages are significantly reduced in the days after, and sometimes even in the days up to, delivery. In some cases, conventional treatment can be temporarily discontinued during lactation^{256-258,262}. After weaning, maternal hormone changes gradually subside, leading to increased dosage requirements for activated vitamin D and calcium. Generally, women with HypoPT stabilise on a similar, if not the same, medical regimen as pre-pregnancy, but careful adjustment and monitoring are essential to ensure smooth transitions.

R.5.3 We recommend monitoring ionised calcium and/or albumin-adjusted calcium levels regularly (e.g., every 3 - 4 weeks) throughout pregnancy and lactation and even more frequently (e.g., weekly) during the 4 weeks before and after delivery, aiming to keep calcium levels at the lower end of the normal range.

Reasoning: Calcium falls in normal pregnancy due to haemodilution-induced reductions in serum albumin levels,

whereas ionised calcium and albumin-adjusted calcium remain stable^{263,264}. Thus, in pregnant women with HypoPT, ionised calcium and/or albumin-adjusted calcium levels are the preferred parameters for monitoring. Frequent monitoring (e.g., every 3 - 4 weeks) is essential because of the common and unpredictable changes in dosage requirements of activated vitamin D and calcium supplements^{57,251,265}. Levels of calcium are recommended to be kept at the lower end or lower half of the normal range in pregnant women with chronic HypoPT⁵⁷. Maternal hypo- and hypercalcaemia should be avoided during pregnancy.

During lactation, there are high rates of bone resorption due to mammary tissue production of PTHrP²⁶⁶. The onset of the PTHrP-induced rise in calcium levels during lactation usually occurs in the first few days after delivery, but the timing may vary. Hypercalcaemia is commonly encountered in nursing women with HypoPT, if activated vitamin D therapy is not reduced quickly after delivery^{259,266-270}. Hypercalcaemia after delivery has even been reported in women who did not breast-feed²⁷¹. Therefore, activated vitamin D and calcium supplements are generally reduced immediately postpartum with close biochemical monitoring indicated to detect rapid and unpredictable change in calcium levels. Some women, however, may develop hypocalcaemia immediately postpartum before the further physiologic effects of PTHrP become evident, underscoring the need for more frequent monitoring of calcium levels (e.g., weekly) in the four weeks before and after delivery^{57,262,266}. After weaning, activated vitamin D and calcium supplements should be gradually re-escalated with close follow-up as maternal hormones return to pre-pregnancy levels and a new steady state is achieved. In the rare event that PTH replacement therapy is required during lactation, it may be (re-)started a few weeks after delivery, though clinical data are insufficient.

R.5.4 We recommend that a paediatrician and/or neonatologist be informed of maternal HypoPT and be involved in the immediate care and monitoring of the infant for potential consequences related to both maternal treatment and the underlying maternal disorder.

Reasoning: Depending on the ease and degree of control of the maternal calcium and phosphate levels during pregnancy, the neonate may be at greater risk of disordered parathyroid function and calcium levels postnatally. The neonate is at risk for suppressed PTH secretion, manifested as neonatal hypocalcaemia, if the mother has been hypercalcaemic during pregnancy. Alternatively, the infant may demonstrate secondary hyperparathyroidism with bone demineralisation and its consequences, if the mother has been significantly hypocalcaemic during pregnancy. The intensity of monitoring of the newborn may depend on maternal calcium levels during pregnancy and on underlying disease in case of maternal non-surgical HypoPT. A rough guidance for newborn monitoring is to undertake serial ionised calcium monitoring, starting on day two of life and typically repeating every 48 hours during the first week⁵⁷. Routine newborn vitamin D supplementation, according to local or national guidelines, should be ensured^{57,272}.

Acknowledgments

The authors of the guideline would like to thank and acknowledge Sigridur Björnsdóttir, Michael Mannstadt and Salvatore Minisola for their expert review. We are also grateful for all the valuable and critical comments of members of the European Society of Endocrinology. The comments of the reviewers, as well as our responses, are available in [Supplementary Table 10](#).

In addition, the authors would like to thank J.W. Schoones for his help in conducting the literature searches.

Funding

This work is supported by the European Society of Endocrinology.

Conflict of interest: Conflicts of interest are stated in [Supplementary Table 1](#).

References

- EFSA Panel on Dietetic Products, N. and Allergies, Scientific Opinion on Dietary Reference Values for calcium. *EFSA Journal*, 2015. 13(5): p. 4101.
- Shoback, D.M., *et al.*, Presentation of Hypoparathyroidism: Etiologies and Clinical Features. *J Clin Endocrinol Metab*, 2016. 101(6): p. 2300-12.
- Bollerslev, J., *et al.*, European Society of Endocrinology Clinical Guideline: Treatment of chronic hypoparathyroidism in adults. *Eur J Endocrinol*, 2015. 173(2): p. G1-G20.
- Bollerslev, J., *et al.*, MANAGEMENT OF ENDOCRINE DISEASE: Unmet therapeutic, educational and scientific needs in parathyroid disorders. *Eur J Endocrinol*, 2019.
- Brandi, M.L., *et al.*, Management of Hypoparathyroidism: Summary Statement and Guidelines. *J Clin Endocrinol Metab*, 2016. 101(6): p. 2273-83.
- Astor, M.C., *et al.*, Epidemiology and Health-Related Quality of Life in Hypoparathyroidism in Norway. *J Clin Endocrinol Metab*, 2016. 101(8): p. 3045-53.
- Clarke, B.L., Epidemiology and Complications of Hypoparathyroidism. *Endocrinol Metab Clin North Am*, 2018. 47(4): p. 771-782.
- Underbjerg, L., *et al.*, Cardiovascular and renal complications to postsurgical hypoparathyroidism: a Danish nationwide controlled historic follow-up study. *J Bone Miner Res*, 2013. 28(11): p. 2277-85.
- Bikle, D.D., Vitamin D metabolism, mechanism of action, and clinical applications. *Chem Biol*, 2014. 21(3): p. 319-29.
- Underbjerg, L., *et al.*, The Epidemiology of Nonsurgical Hypoparathyroidism in Denmark: A Nationwide Case Finding Study. *J Bone Miner Res*, 2015. 30(9): p. 1738-44.
- Powers, J., *et al.*, Prevalence and incidence of hypoparathyroidism in the United States using a large claims database. *J Bone Miner Res*, 2013. 28(12): p. 2570-6.
- Hasegawa, M., *et al.*, Prevalence and characteristics of post-operative and nonoperative chronic hypoparathyroidism in Japan: a nationwide retrospective analysis. *JBMR Plus*, 2024. 8(9): p. ziae100.
- Mannstadt, M., *et al.*, Hypoparathyroidism: Genetics and Diagnosis. *J Bone Miner Res*, 2022. 37(12): p. 2615-2629.
- Yang, Y.Y., *et al.*, Hypoparathyroidism: Similarities and differences between Western and Eastern countries. *Osteoporos Int*, 2025. 36(3): p. 391-402.
- Betterle, C., *et al.*, Addison's disease: a survey on 633 patients in Padova. *Eur J Endocrinol*, 2013. 169(6): p. 773-84.
- Humbert, L., *et al.*, Lessons from prospective longitudinal follow-up of a French APECED cohort. *J Clin Endocrinol Metab*, 2024.
- Cranston, T., *et al.*, Spectrum of germline AIRE mutations causing APS-1 and familial hypoparathyroidism. *Eur J Endocrinol*, 2022. 187(1): p. 111-122.
- Bruserud, O., *et al.*, A Longitudinal Follow-up of Autoimmune Polyendocrine Syndrome Type 1. *J Clin Endocrinol Metab*, 2016. 101(8): p. 2975-83.
- Alimohammadi, M., *et al.*, Autoimmune polyendocrine syndrome type 1 and NALP5, a parathyroid autoantigen. *N Engl J Med*, 2008. 358(10): p. 1018-28.
- Betterle, C., S. Garelli, and F. Presotto, Diagnosis and classification of autoimmune parathyroid disease. *Autoimmun Rev*, 2014. 13(4-5): p. 417-22.
- Teisseyre, M., O. Moranne, and S. Renaud, Late diagnosis of chronic hypocalcemia due to autoimmune hypoparathyroidism. *BMJ Case Rep*, 2021. 14(6).
- Lima, K., *et al.*, Hypoparathyroidism and autoimmunity in the 22q11.2 deletion syndrome. *Eur J Endocrinol*, 2011. 165(2): p. 345-52.
- Trevisani, V., *et al.*, Endocrine immune-related adverse effects of immune-checkpoint inhibitors. *Expert Rev Endocrinol Metab*, 2023. 18(5): p. 441-451.
- Lupi, I., *et al.*, Activating Antibodies to The Calcium-sensing Receptor in Immunotherapy-induced Hypoparathyroidism. *J Clin Endocrinol Metab*, 2020. 105(5).
- Bilezikian, J.P., *et al.*, Hypoparathyroidism in the adult: epidemiology, diagnosis, pathophysiology, target-organ involvement, treatment, and challenges for future research. *J Bone Miner Res*, 2011. 26(10): p. 2317-37.
- van Dijk, S.P.J., *et al.*, Management of Postthyroidectomy Hypoparathyroidism and Its Effect on Hypocalcemia-Related Complications: A Meta-Analysis. *Otolaryngol Head Neck Surg*, 2024. 170(2): p. 359-372.
- Koimtzis, G.D., *et al.*, What are the real rates of temporary hypoparathyroidism following thyroidectomy? It is a matter of definition: a systematic review. *Endocrine*, 2021. 73(1): p. 1-7.
- Sitges-Serra, A., Etiology and Diagnosis of Permanent Hypoparathyroidism after Total Thyroidectomy. *J Clin Med*, 2021. 10(3).
- Edafe, O., *et al.*, Systematic review and meta-analysis of predictors of post-thyroidectomy hypocalcaemia. *Br J Surg*, 2014. 101(4): p. 307-20.
- Lorente-Poch, L., *et al.*, Importance of in situ preservation of parathyroid glands during total thyroidectomy. *Br J Surg*, 2015. 102(4): p. 359-67.
- Ning, K., *et al.*, Risk factors of transient and permanent hypoparathyroidism after thyroidectomy: a systematic review and meta-analysis. *Int J Surg*, 2024. 110(8): p. 5047-5062.
- Taye, A., *et al.*, Post-thyroidectomy emergency room visits and readmissions: Assessment from the Collaborative Endocrine Surgery Quality Improvement Program (CESQIP). *Am J Surg*, 2020. 220(4): p. 813-820.
- Vaitsi, K.D., *et al.*, Preoperative Vitamin D Deficiency is a Risk Factor for Postthyroidectomy Hypoparathyroidism: A Systematic Review and Meta-Analysis of Observational Studies. *J Clin Endocrinol Metab*, 2021. 106(4): p. 1209-1224.
- Roberts, S.L., *et al.*, Incidence of post-surgical hypoparathyroidism (POSH) after total thyroidectomy. *Br J Oral Maxillofac Surg*, 2023. 61(10): p. 679-685.
- Villarroya-Marquina, I., *et al.*, Time to parathyroid function recovery in patients with protracted hypoparathyroidism after total thyroidectomy. *Eur J Endocrinol*, 2018. 178(1): p. 103-111.
- Wang, W., *et al.*, Prediction of permanent hypoparathyroidism by parathyroid hormone and serum calcium 24 h after thyroidectomy. *Am J Otolaryngol*, 2018. 39(6): p. 746-750.
- Zhang, Q., *et al.*, Clinical application of parathyroid autotransplantation in endoscopic radical resection of thyroid carcinoma. *Front Oncol*, 2022. 12: p. 942488.
- Pizzato, M., *et al.*, The epidemiological landscape of thyroid cancer worldwide: GLOBOCAN estimates for incidence and

- mortality rates in 2020. *Lancet Diabetes Endocrinol*, 2022. 10(4): p. 264-272.
39. Li, M., *et al.*, Evolving epidemiological patterns of thyroid cancer and estimates of overdiagnosis in 2013-17 in 63 countries worldwide: a population-based study. *Lancet Diabetes Endocrinol*, 2024. 12(11): p. 824-836.
 40. Tjahjono, R., *et al.*, Methods of identification of parathyroid glands in thyroid surgery: A literature review. *ANZ J Surg*, 2021. 91(9): p. 1711-1716.
 41. Benmiloud, F., *et al.*, Parathyroid vascular anatomy using intraoperative mapping angiography: the PARATLAS study. *Br J Surg*, 2025. 112(3).
 42. Safia, A., *et al.*, The impact of using near-infrared autofluorescence on parathyroid gland parameters and clinical outcomes during total thyroidectomy: a meta-analytic study of randomized controlled trials. *Int J Surg*, 2024. 110(6): p. 3827-3838.
 43. Siggelkow H, C.B., Germak J *et al*, Impact of Chronic Hypoparathyroidism on Health-Related Quality of Life: Findings from a 13-Country Patient Survey. *Journal of the Endocrine Society* 2019.
 44. Underbjerg, L., *et al.*, Postsurgical hypoparathyroidism—risk of fractures, psychiatric diseases, cancer, cataract, and infections. *J Bone Miner Res*, 2014. 29(11): p. 2504-10.
 45. Sikjaer, T., *et al.*, Hypoparathyroidism: changes in brain structure, cognitive impairment, and reduced quality of life. *J Bone Miner Res*, 2024. 39(7): p. 855-866.
 46. Sikjaer, T., *et al.*, The effect of adding PTH(1-84) to conventional treatment of hypoparathyroidism: a randomized, placebo-controlled study. *J Bone Miner Res*, 2011. 26(10): p. 2358-70.
 47. Underbjerg, L., T. Sikjaer, and L. Rejnmark, Health-related quality of life in patients with nonsurgical hypoparathyroidism and pseudohypoparathyroidism. *Clin Endocrinol (Oxf)*, 2018. 88(6): p. 838-847.
 48. Underbjerg, L., T. Sikjaer, and L. Rejnmark, Long-Term Complications in Patients With Hypoparathyroidism Evaluated by Biochemical Findings: A Case-Control Study. *J Bone Miner Res*, 2018. 33(5): p. 822-831.
 49. Ridder, L.O., *et al.*, Determinants of hypercalciuria and renal calcifications in chronic hypoparathyroidism: A cross-sectional study. *Clin Endocrinol (Oxf)*, 2021. 95(2): p. 286-294.
 50. Yao, L., *et al.*, Complications, Symptoms, Presurgical Predictors in Patients With Chronic Hypoparathyroidism: A Systematic Review. *J Bone Miner Res*, 2022. 37(12): p. 2642-2653.
 51. Vadiveloo, T., *et al.*, Increased mortality and morbidity in patients with chronic hypoparathyroidism: A population-based study. *Clin Endocrinol (Oxf)*, 2019. 90(2): p. 285-292.
 52. Peacock, M., Hypoparathyroidism and the Kidney. *Endocrinol Metab Clin North Am*, 2018. 47(4): p. 839-853.
 53. Luk, Y., *et al.*, Long-term kidney outcomes in patients with permanent hypoparathyroidism after total thyroidectomy for benign disease: A population-based study. *Surgery*, 2024. 176(3): p. 700-707.
 54. Swartling, O., *et al.*, Kidney Complications and Hospitalization in Patients With Chronic Hypoparathyroidism: A Cohort Study in Sweden. *J Clin Endocrinol Metab*, 2022. 107(10): p. e4098-e4105.
 55. Khan, A.A., *et al.*, MANAGEMENT OF ENDOCRINE DISEASE: Hypoparathyroidism in pregnancy: review and evidence-based recommendations for management. *Eur J Endocrinol*, 2019. 180(2): p. R37-R44.
 56. Kovacs, C.S., Maternal Mineral and Bone Metabolism During Pregnancy, Lactation, and Post-Weaning Recovery. *Physiol Rev*, 2016. 96(2): p. 449-547.
 57. Bollerslev, J., *et al.*, European Expert Consensus on Practical Management of Specific Aspects of Parathyroid Disorders in Adults and in Pregnancy: Recommendations of the ESE Educational Program of Parathyroid Disorders. *Eur J Endocrinol*, 2022. 186(2): p. R33-R63.
 58. Bjornsdottir, S., *et al.*, Women With Chronic Hypoparathyroidism Have Low Risk of Adverse Pregnancy Outcomes. *J Clin Endocrinol Metab*, 2021. 106(11): p. 3312-3319.
 59. Callies, F., *et al.*, Management of hypoparathyroidism during pregnancy—report of twelve cases. *Eur J Endocrinol*, 1998. 139(3): p. 284-9.
 60. Cernaro, V., *et al.*, Phosphate binders for the treatment of chronic kidney disease: role of iron oxyhydroxide. *Int J Nephrol Renovasc Dis*, 2016. 9: p. 11-9.
 61. Cooper, M.S. and N.J. Gittoes, Diagnosis and management of hypocalcaemia. *BMJ*, 2008. 336(7656): p. 1298-302.
 62. Kiam, J.S., *et al.*, UK national chronic hypoparathyroidism audit. *Clin Endocrinol (Oxf)*, 2022. 97(5): p. 562-567.
 63. Porter, R.H., *et al.*, Treatment of hypoparathyroid patients with chlorthalidone. *N Engl J Med*, 1978. 298(11): p. 577-81.
 64. Atkinson, S.A., Defining the process of Dietary Reference Intakes: framework for the United States and Canada. *Am J Clin Nutr*, 2011. 94(2): p. 655S-7S.
 65. Ross, A.C., *et al.*, The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *J Clin Endocrinol Metab*, 2011. 96(1): p. 53-8.
 66. Tinawi, M., Disorders of Calcium Metabolism: Hypocalcemia and Hypercalcemia. *Cureus*, 2021. 13(1): p. e12420.
 67. Bollerslev, J., E. Sjøstedt, and L. Rejnmark, Cardiovascular consequences of parathyroid disorders in adults. *Ann Endocrinol (Paris)*, 2021. 82(3-4): p. 151-157.
 68. Santonati, A., *et al.*, PTH(1-34) for Surgical Hypoparathyroidism: A Prospective, Open-Label Investigation of Efficacy and Quality of Life. *J Clin Endocrinol Metab*, 2015. 100(9): p. 3590-7.
 69. Palermo, A., *et al.*, PTH(1-34) for Surgical Hypoparathyroidism: A 2-Year Prospective, Open-Label Investigation of Efficacy and Quality of Life. *J Clin Endocrinol Metab*, 2018. 103(1): p. 271-280.
 70. Vokes, T.J., *et al.*, Recombinant Human Parathyroid Hormone Effect on Health-Related Quality of Life in Adults With Chronic Hypoparathyroidism. *J Clin Endocrinol Metab*, 2018. 103(2): p. 722-731.
 71. Tabacco, G., *et al.*, Quality of Life in Hypoparathyroidism Improves With rhPTH(1-84) Throughout 8 Years of Therapy. *J Clin Endocrinol Metab*, 2019. 104(7): p. 2748-2756.
 72. Clarke, B.L., *et al.*, Effects of parathyroid hormone rhPTH(1-84) on phosphate homeostasis and vitamin D metabolism in hypoparathyroidism: REPLACE phase 3 study. *Endocrine*, 2017. 55(1): p. 273-282.
 73. Satterwhite, J., *et al.*, Pharmacokinetics of teriparatide (rhPTH[1-34]) and calcium pharmacodynamics in postmenopausal women with osteoporosis. *Calcif Tissue Int*, 2010. 87(6): p. 485-92.
 74. Clarke, B.L., *et al.*, Pharmacokinetics and pharmacodynamics of subcutaneous recombinant parathyroid hormone (1-84) in patients with hypoparathyroidism: an open-label, single-dose, phase I study. *Clin Ther*, 2014. 36(5): p. 722-36.
 75. Sikjaer, T., *et al.*, PTH(1-84) replacement therapy in hypoparathyroidism: a randomized controlled trial on pharmacokinetic and dynamic effects after 6 months of treatment. *J Bone Miner Res*, 2013. 28(10): p. 2232-43.
 76. Ing, S.W., *et al.*, A Phase I Randomized Trial of Once-Daily Versus Twice-Daily Recombinant Human Parathyroid Hormone (1-84) for Hypoparathyroidism. *JBMR Plus*, 2023. 7(7): p. e10758.
 77. Winer, K.K., *et al.*, Effects of once versus twice-daily parathyroid hormone 1-34 therapy in children with hypoparathyroidism. *J Clin Endocrinol Metab*, 2008. 93(9): p. 3389-95.
 78. Winer, K.K., *et al.*, A randomized, cross-over trial of once-daily versus twice-daily parathyroid hormone 1-34 in treatment of hypoparathyroidism. *J Clin Endocrinol Metab*, 1998. 83(10): p. 3480-6.
 79. Winer, K.K., *et al.*, Synthetic human parathyroid hormone 1-34 replacement therapy: a randomized crossover trial comparing

- pump versus injections in the treatment of chronic hypoparathyroidism. *J Clin Endocrinol Metab*, 2012. 97(2): p. 391-9.
80. Marcucci, G., *et al.*, Chronic hypoparathyroidism and treatment with teriparatide. *Endocrine*, 2021. 72(1): p. 249-259.
 81. Karpf, D.B., *et al.*, A Randomized Double-Blind Placebo-Controlled First-In-Human Phase 1 Trial of TransCon PTH in Healthy Adults. *J Bone Miner Res*, 2020. 35(8): p. 1430-1440.
 82. Khan, A.A., *et al.*, PaTH Forward: A Randomized, Double-Blind, Placebo-Controlled Phase 2 Trial of TransCon PTH in Adult Hypoparathyroidism. *J Clin Endocrinol Metab*, 2022. 107(1): p. e372-e385.
 83. Khan, A.A., *et al.*, Efficacy and Safety of Parathyroid Hormone Replacement With TransCon PTH in Hypoparathyroidism: 26-Week Results From the Phase 3 PaTHway Trial. *J Bone Miner Res*, 2023. 38(1): p. 14-25.
 84. Rejnmark, L., *et al.*, Palopegteriparatide Treatment Improves Renal Function in Adults with Chronic Hypoparathyroidism: 1-Year Results from the Phase 3 PaTHway Trial. *Adv Ther*, 2024. 41(6): p. 2500-2518.
 85. Takacs, I., *et al.*, An Open-label Phase 2 Study of Eneboparatide, a Novel PTH Receptor 1 Agonist, in Hypoparathyroidism. *J Clin Endocrinol Metab*, 2024. 109(9): p. 2199-2209.
 86. Gafni, R.I., *et al.*, Efficacy and Safety of Encalaret in Autosomal Dominant Hypocalcemia Type 1. *N Engl J Med*, 2023. 389(13): p. 1245-1247.
 87. Dekkers, O.M., P. Burman, and E.S.E.C. Committee, ESE guidelines, why and how. *Eur J Endocrinol*, 2015. 173(2): p. E1-2.
 88. Andrews, J.C., *et al.*, GRADE guidelines: 15. Going from evidence to recommendation—determinants of a recommendation's direction and strength. *J Clin Epidemiol*, 2013. 66(7): p. 726-35.
 89. Khan, A.A., *et al.*, Management of Hypoparathyroidism. *J Bone Miner Res*, 2022. 37(12): p. 2663-2677.
 90. Khan, A.A., *et al.*, Open-label extension of a randomized trial investigating safety and efficacy of rhPTH(1-84) in hypoparathyroidism. *JBMR Plus*, 2024. 8(3): p. ziad010.
 91. Mannstadt, M., *et al.*, Safety and Efficacy of 5 Years of Treatment With Recombinant Human Parathyroid Hormone in Adults With Hypoparathyroidism. *J Clin Endocrinol Metab*, 2019. 104(11): p. 5136-5147.
 92. Stevenson, A. and R. Mihai, Patients' views about parathyroid transplantation for post-thyroidectomy hypoparathyroidism. *Langenbecks Arch Surg*, 2018. 403(5): p. 623-629.
 93. Al-Dhahri, S.F., *et al.*, Factors predicting post-thyroidectomy hypoparathyroidism recovery. *World J Surg*, 2014. 38(9): p. 2304-10.
 94. Arshad, M.F., *et al.*, Parathyroid hormone of ≥ 1.6 pmol/L at 6 months is associated with recovery in 'long-term' post-surgical hypoparathyroidism. *Eur Thyroid J*, 2022. 11(3).
 95. Diez, J.J., *et al.*, Prevalence and risk factors for hypoparathyroidism following total thyroidectomy in Spain: a multicentric and nation-wide retrospective analysis. *Endocrine*, 2019. 66(2): p. 405-415.
 96. Guglielmetti, L., *et al.*, How Long Does It Take to Regain Normocalcaemia in the Event of Postsurgical Hypoparathyroidism? A Detailed Time Course Analysis. *J Clin Med*, 2022. 11(11).
 97. Herranz Gonzalez-Botas, J. and D. Lourido Piedrahita, Hypocalcaemia after total thyroidectomy: incidence, control and treatment. *Acta Otorrinolaringol Esp*, 2013. 64(2): p. 102-7.
 98. Kim, B.W., *et al.*, Parathyroid score can predict the duration of required calcium supplementation after total thyroidectomy. *PLoS One*, 2017. 12(3): p. e0174088.
 99. Proye, C., *et al.*, [The parathyroid risk in thyroid surgery. Argument against the early postoperative prescription of vitamin D. Experience with 729 thyroidectomies in 1988]. *Chirurgie*, 1990. 116(6-7): p. 493-500.
 100. Razack, M.S., *et al.*, Total thyroidectomy for Graves' disease. *Head Neck*, 1997. 19(5): p. 378-83.
 101. Ritter, K., *et al.*, Hypoparathyroidism after total thyroidectomy: incidence and resolution. *J Surg Res*, 2015. 197(2): p. 348-53.
 102. Xing, Z., *et al.*, Surgical strategy when identifying less than four parathyroid glands during total thyroidectomy: a retrospective cohort study. *Gland Surg*, 2021. 10(1): p. 10-22.
 103. Canat, M.M., *et al.*, The effects of adequate dietary calcium intake in patients with hypoparathyroidism non-adherent to treatment: a prospective randomized controlled trial. *Rev Assoc Med Bras* (1992), 2023. 69(11): p. e20230406.
 104. Naciu, A.M., *et al.*, Calcium Citrate Versus Calcium Carbonate in the Management of Chronic Hypoparathyroidism: A Randomized, Double-Blind, Crossover Clinical Trial. *J Bone Miner Res*, 2022. 37(7): p. 1251-1259.
 105. Stamm, B., *et al.*, The Influence of Conventional Treatment on Symptoms and Complaints in Patients With Chronic Postsurgical Hypoparathyroidism. *JBMR Plus*, 2022. 6(2): p. e10586.
 106. Streeeten, E.A., *et al.*, Hypoparathyroidism: Less Severe Hypocalcemia With Treatment With Vitamin D2 Compared With Calcitriol. *J Clin Endocrinol Metab*, 2017. 102(5): p. 1505-1510.
 107. Ayodele, O., *et al.*, Lower Risk of Cardiovascular Events in Adult Patients with Chronic Hypoparathyroidism Treated with rhPTH(1-84): A Retrospective Cohort Study. *Adv Ther*, 2022. 39(8): p. 3845-3856.
 108. Marcucci, G., *et al.*, Multicenter retro-prospective observational study on chronic hypoparathyroidism and rhPTH (1-84) treatment. *J Endocrinol Invest*, 2022. 45(9): p. 1653-1662.
 109. Rejnmark, L., *et al.*, The risk of chronic kidney disease development in adult patients with chronic hypoparathyroidism treated with rhPTH(1-84): A retrospective cohort study. *Clin Endocrinol (Oxf)*, 2023. 98(4): p. 496-504.
 110. Rubin, M.R., *et al.*, Extended Treatment With Recombinant Human Parathyroid Hormone (1-84) in Adult Patients With Chronic Hypoparathyroidism. *Endocr Pract*, 2024. 30(3): p. 200-208.
 111. Sikjaer, T., *et al.*, Effects of PTH(1-84) therapy on muscle function and quality of life in hypoparathyroidism: results from a randomized controlled trial. *Osteoporos Int*, 2014. 25(6): p. 1717-26.
 112. Watts, N.B., *et al.*, Long-Term Safety and Efficacy of Recombinant Human Parathyroid Hormone (1-84) in Adults With Chronic Hypoparathyroidism. *J Endocr Soc*, 2023. 7(5): p. bvad043.
 113. Rubin, M.R., *et al.*, Therapy of hypoparathyroidism with intact parathyroid hormone. *Osteoporos Int*, 2010. 21(11): p. 1927-34.
 114. Gafni, R.I., *et al.*, Hypocitraturia Is an Untoward Side Effect of Synthetic Human Parathyroid Hormone (hPTH) 1-34 Therapy in Hypoparathyroidism That May Increase Renal Morbidity. *J Bone Miner Res*, 2018. 33(10): p. 1741-1747.
 115. Ish-Shalom, S., *et al.*, Safety and Efficacy of Oral Human Parathyroid Hormone (1-34) in Hypoparathyroidism: An Open-Label Study. *J Bone Miner Res*, 2021. 36(6): p. 1060-1068.
 116. Winer, K.K., *et al.*, Long-term treatment of hypoparathyroidism: a randomized controlled study comparing parathyroid hormone-(1-34) versus calcitriol and calcium. *J Clin Endocrinol Metab*, 2003. 88(9): p. 4214-20.
 117. Aysan, E., *et al.*, Parathyroid Allotransplant With a New Technique: A Prospective Clinical Trial. *Exp Clin Transplant*, 2016. 14(4): p. 431-5.
 118. Goncu, B., *et al.*, The Challenge of Preoperative Panel Reactive Antibody Positivity in Parathyroid Transplantation. *Exp Clin Transplant*, 2024. 22(Suppl 1): p. 233-242.
 119. Nawrot, I., *et al.*, Allotransplantation of cultured parathyroid progenitor cells without immunosuppression: clinical results. *Transplantation*, 2007. 83(6): p. 734-40.
 120. Ong, G.S., *et al.*, The importance of measuring ionized calcium in characterizing calcium status and diagnosing primary hyperparathyroidism. *J Clin Endocrinol Metab*, 2012. 97(9): p. 3138-45.
 121. Shoback, D., Clinical practice. Hypoparathyroidism. *N Engl J Med*, 2008. 359(4): p. 391-403.

122. Khan, A.A., *et al.*, Evaluation and Management of Hypoparathyroidism Summary Statement and Guidelines from the Second International Workshop. *J Bone Miner Res*, 2022. 37(12): p. 2568-2585.
123. Kannan, S., *et al.*, Estimation of magnesium in patients with functional hypoparathyroidism. *Indian J Endocrinol Metab*, 2014. 18(6): p. 821-5.
124. Buttner, M., S. Singer, and K. Taylor, Quality of life in patients with hypoparathyroidism receiving standard treatment: an updated systematic review. *Endocrine*, 2024. 85(1): p. 80-90.
125. Mitchell, D.M., *et al.*, Long-term follow-up of patients with hypoparathyroidism. *J Clin Endocrinol Metab*, 2012. 97(12): p. 4507-14.
126. Rathod, A., *et al.*, Association of urinary calcium excretion with serum calcium and vitamin D levels. *Clin J Am Soc Nephrol*, 2015. 10(3): p. 452-62.
127. Gronemeyer, K., *et al.*, Renal complications in chronic hypoparathyroidism - a systematic cross-sectional assessment. *Front Endocrinol (Lausanne)*, 2023. 14: p. 1244647.
128. Kovaleva, E.V., *et al.*, The Russian Registry of Chronic Hypoparathyroidism. *Front Endocrinol (Lausanne)*, 2022. 13: p. 800119.
129. Lopes, M.P., *et al.*, Hypoparathyroidism and pseudohypoparathyroidism: etiology, laboratory features and complications. *Arch Endocrinol Metab*, 2016. 60(6): p. 532-536.
130. Saha, S., *et al.*, Nephrocalcinosis, Renal Dysfunction, and Calculi in Patients With Primary Hypoparathyroidism on Long-Term Conventional Therapy. *J Clin Endocrinol Metab*, 2020. 105(4).
131. Cherchir, F., *et al.*, Long-term complications of permanent hypoparathyroidism in adults: prevalence and associated factors. *Endocrine*, 2024. 84(3): p. 1164-1171.
132. Khan, A.A., *et al.*, Canadian national hypoparathyroidism registry: an overview of hypoparathyroidism in Canada. *Endocrine*, 2021. 72(2): p. 553-561.
133. Mazoni, L., *et al.*, Renal complications and quality of life in post-surgical hypoparathyroidism: a case-control study. *J Endocrinol Invest*, 2022. 45(3): p. 573-582.
134. Coe, F.L., A. Evan, and E. Worcester, Pathophysiology-based treatment of idiopathic calcium kidney stones. *Clin J Am Soc Nephrol*, 2011. 6(8): p. 2083-92.
135. Tiselius, H.G., A proposed method for approximate estimates of the ion-activity products of calcium oxalate and calcium phosphate in spot-urine samples or in urine samples collected during less well defined periods of time. *Urolithiasis*, 2013. 41(2): p. 105-9.
136. Tiselius, H.G., *Metabolic risk-evaluation and prevention of recurrence in stone disease: does it make sense?* *Urolithiasis*, 2016. 44(1): p. 91-100.
137. Yamamoto, M., *et al.*, Comparison of hypocalcemic hypercalciuria between patients with idiopathic hypoparathyroidism and those with gain-of-function mutations in the calcium-sensing receptor: is it possible to differentiate the two disorders? *J Clin Endocrinol Metab*, 2000. 85(12): p. 4583-91.
138. De Coster, T., *et al.*, Management of autosomal dominant hypocalcemia type 1: Literature review and clinical practice recommendations. *J Endocrinol Invest*, 2025. 48(4): p. 831-844.
139. Caudarella, R., *et al.*, Hyperphosphatemia: effects on bone metabolism and cardiovascular risk. *J Endocrinol Invest*, 2007. 30(6 Suppl): p. 29-34.
140. Rodriguez-Ortiz, M.E., *et al.*, Magnesium modulates parathyroid hormone secretion and upregulates parathyroid receptor expression at moderately low calcium concentration. *Nephrol Dial Transplant*, 2014. 29(2): p. 282-9.
141. Salinas, M., *et al.*, Improving diagnosis and treatment of hypomagnesemia. *Clin Chem Lab Med*, 2024. 62(2): p. 234-248.
142. Bouillon, R., *et al.*, Skeletal and Extraskeletal Actions of Vitamin D: Current Evidence and Outstanding Questions. *Endocr Rev*, 2019. 40(4): p. 1109-1151.
143. Rejnmark, L., L. Underbjerg, and T. Sikjaer, Therapy of hypoparathyroidism by replacement with parathyroid hormone. *Scientifica (Cairo)*, 2014. 2014: p. 765629.
144. Giustina, A., *et al.*, Consensus Statement on Vitamin D Status Assessment and Supplementation: Whys, Whens, and Hows. *Endocr Rev*, 2024. 45(5): p. 625-654.
145. Hobaus, J., *et al.*, Role of calcium, vitamin D, and the extrarenal vitamin D hydroxylases in carcinogenesis. *Anticancer Agents Med Chem*, 2013. 13(1): p. 20-35.
146. Khan, M.I., S.G. Waguespack, and M.I. Hu, Medical management of postsurgical hypoparathyroidism. *Endocr Pract*, 2011. 17 Suppl 1: p. 18-25.
147. Turner, J., N. Gittoes, and P. Selby, SOCIETY FOR ENDOCRINOLOGY EMERGENCY ENDOCRINE GUIDANCE: Emergency management of acute hypocalcaemia in adult patients. *Endocr Connect*, 2019. 8(6): p. X1.
148. O'Seaghda, C.M., *et al.*, Common variants in the calcium-sensing receptor gene are associated with total serum calcium levels. *Hum Mol Genet*, 2010. 19(21): p. 4296-303.
149. Mautalen, C.A., Total urinary hydroxyproline excretion after administration of Vitamin D to patients with hypoparathyroidism. *J Clin Endocrinol Metab*, 1970. 31(5): p. 595-9.
150. Davies, M., *et al.*, 1,25-dihydroxycholecalciferol in hypoparathyroidism. *Lancet*, 1977. 1(8002): p. 55-9.
151. Hill, L.F., *et al.*, Treatment of hypoparathyroidism with 1,25-dihydroxycholecalciferol. *Clin Endocrinol (Oxf)*, 1976. 5 Suppl: p. 167S-173S.
152. Kanis, J.A., R.G. Russell, and R. Smith, Physiological and therapeutic differences between vitamin D, its metabolites and analogues. *Clin Endocrinol (Oxf)*, 1977. 7 Suppl: p. 191s-201 s.
153. Kanis, J.A. and R.G. Russell, Rate of reversal of hypercalcaemia and hypercalciuria induced by vitamin D and its 1alpha-hydroxylated derivatives. *Br Med J*, 1977. 1(6053): p. 78-81.
154. Saha, S., V. Sreenivas, and R. Goswami, Alfacalcidol vs Calcitriol in the Management of Patient With Hypoparathyroidism: A Randomized Controlled Trial. *J Clin Endocrinol Metab*, 2021. 106(7): p. 2092-2102.
155. Okano, K., *et al.*, Comparative efficacy of various vitamin D metabolites in the treatment of various types of hypoparathyroidism. *J Clin Endocrinol Metab*, 1982. 55(2): p. 238-43.
156. Bailie, G.R. and C.A. Johnson, Comparative review of the pharmacokinetics of vitamin D analogues. *Semin Dial*, 2002. 15(5): p. 352-7.
157. Levine, B.S., *et al.*, Pharmacokinetics and biologic effects of calcitriol in normal humans. *J Lab Clin Med*, 1985. 105(2): p. 239-46.
158. Bianchi, M.L., *et al.*, No difference in intestinal strontium absorption after an oral or an intravenous 1,25(OH)2D3 bolus in normal subjects. For the European Study Group on Vitamin D in children with renal failure. *J Bone Miner Res*, 1999. 14(10): p. 1789-95.
159. Brickman, A.S., *et al.*, Comparison of effects of 1 alpha-hydroxy-vitamin D3 and 1,25-dihydroxy-vitamin D3 in man. *J Clin Invest*, 1976. 57(6): p. 1540-7.
160. Stuss, M., M. Michalska-Kasiczak, and E. Sewerynek, Clinical efficacy and safety of use of alfacalcidol and calcitriol in daily endocrinological practice. *Endokrynol Pol*, 2023. 74(1): p. 16-24.
161. Bilezikian, J.P., *et al.*, Management of Hypoparathyroidism: Present and Future. *J Clin Endocrinol Metab*, 2016. 101(6): p. 2313-24.
162. Seino, Y., *et al.*, Circulating 1 alpha,25-dihydroxyvitamin D levels after a single dose of 1 alpha,25-dihydroxyvitamin D3 or 1 alpha-hydroxyvitamin D3 in normal men. *Bone Miner*, 1987. 2(6): p. 479-85.
163. Al-Sharefi, A., *et al.*, Is calcium supplementation always needed in patients with hypoparathyroidism? *Clin Endocrinol (Oxf)*, 2019. 90(6): p. 775-780.
164. Heaney, R.P., P.D. Saville, and R.R. Recker, Calcium absorption as a function of calcium intake. *J Lab Clin Med*, 1975. 85(6): p. 881-90.

165. Harvey, J.A., M.M. Zobitz, and C.Y. Pak, Dose dependency of calcium absorption: a comparison of calcium carbonate and calcium citrate. *J Bone Miner Res*, 1988. 3(3): p. 253-8.
166. Straub, D.A., Calcium supplementation in clinical practice: a review of forms, doses, and indications. *Nutr Clin Pract*, 2007. 22(3): p. 286-96.
167. Malberti, F., Hyperphosphataemia: treatment options. *Drugs*, 2013. 73(7): p. 673-88.
168. Recker, R.R. and R.P. Heaney, The effect of milk supplements on calcium metabolism, bone metabolism and calcium balance. *Am J Clin Nutr*, 1985. 41(2): p. 254-63.
169. Mangan, A., *et al.*, Iron and Vitamin D/Calcium Deficiency after Gastric Bypass: Mechanisms Involved and Strategies to Improve Oral Supplement Disposition. *Curr Drug Metab*, 2019. 20(3): p. 244-252.
170. Schafer, A.L., Vitamin D and intestinal calcium transport after bariatric surgery. *J Steroid Biochem Mol Biol*, 2017. 173: p. 202-210.
171. Witting, C., *et al.*, Pathophysiology and Treatment of Enteric Hyperoxaluria. *Clin J Am Soc Nephrol*, 2021. 16(3): p. 487-495.
172. Zamfirescu, I. and H.E. Carlson, Absorption of levothyroxine when coadministered with various calcium formulations. *Thyroid*, 2011. 21(5): p. 483-6.
173. Yao, L., *et al.*, Parathyroid Hormone Therapy for Managing Chronic Hypoparathyroidism: A Systematic Review and Meta-Analysis. *J Bone Miner Res*, 2022. 37(12): p. 2654-2662.
174. Clarke, B.L., *et al.*, Efficacy and Safety of TransCon PTH in Adults with Hypoparathyroidism: 52-Week Results From the Phase 3 PaTHway Trial. *J Clin Endocrinol Metab*, 2024.
175. Deering, K.L., *et al.*, Economic burden of patients with post-surgical chronic and transient hypoparathyroidism in the United States examined using insurance claims data. *Orphanet J Rare Dis*, 2024. 19(1): p. 164.
176. Bjornsdottir, S., *et al.*, Epidemiology and Financial Burden of Adult Chronic Hypoparathyroidism. *J Bone Miner Res*, 2022. 37(12): p. 2602-2614.
177. Siggelkow, H., *et al.*, Burden of illness in not adequately controlled chronic hypoparathyroidism: Findings from a 13-country patient and caregiver survey. *Clin Endocrinol (Oxf)*, 2020. 92(2): p. 159-168.
178. Ayodele, O., *et al.*, Five-Year Estimated Glomerular Filtration Rate in Adults with Chronic Hypoparathyroidism Treated with rhPTH(1-84): A Retrospective Cohort Study. *Adv Ther*, 2022. 39(11): p. 5013-5024.
179. Rejnmark, L., *et al.*, Palopegteriparatide Treatment Improves Renal Function in Adults with Chronic Hypoparathyroidism: 1-Year Results from the Phase 3 PaTHway Trial. *Adv Ther*, 2024. 41(6): p. 2500-2518.
180. Gosmanova, E.O., *et al.*, Risk of Chronic Kidney Disease and Estimated Glomerular Filtration Rate Decline in Patients with Chronic Hypoparathyroidism: A Retrospective Cohort Study. *Adv Ther*, 2021. 38(4): p. 1876-1888.
181. el-Hajj Fuleihan, G., *et al.*, Calcium-regulated renal calcium handling in healthy men: relationship to sodium handling. *J Clin Endocrinol Metab*, 1998. 83(7): p. 2366-72.
182. Karp, H.J., M.E. Ketola, and C.J. Lamberg-Allardt, Acute effects of calcium carbonate, calcium citrate and potassium citrate on markers of calcium and bone metabolism in young women. *Br J Nutr*, 2009. 102(9): p. 1341-7.
183. Akram, M., *et al.*, Urological Guidelines for Kidney Stones: Overview and Comprehensive Update. *J Clin Med*, 2024. 13(4).
184. McCarron, D.A., *et al.*, Urinary calcium excretion at extremes of sodium intake in normal man. *Am J Nephrol*, 1981. 1(2): p. 84-90.
185. Kurznel, R.B. and G.A. Hagen, Use of thiazide diuretics to reduce the hypercalciuria of hypoparathyroidism during pregnancy. *Am J Perinatol*, 1990. 7(4): p. 333-6.
186. Newman, G.H., M. Wade, and D.J. Hosking, Effect of bendrofluzide on calcium reabsorption in hypoparathyroidism. *Eur J Clin Pharmacol*, 1984. 27(1): p. 41-6.
187. Parfitt, A.M., Thiazide-induced hypercalcemia in vitamin D-treated hypoparathyroidism. *Ann Intern Med*, 1972. 77(4): p. 557-63.
188. Santos, F., M.J. Smith, and J.C. Chan, Hypercalciuria associated with long-term administration of calcitriol (1,25-dihydroxy vitamin D3). Action of hydrochlorothiazide. *Am J Dis Child*, 1986. 140(2): p. 139-42.
189. Abou Chakra, M., *et al.*, Established and recent developments in the pharmacological management of urolithiasis: an overview of the current treatment armamentarium. *Expert Opin Pharmacother*, 2020. 21(1): p. 85-96.
190. Maschio, G., *et al.*, Prevention of calcium nephrolithiasis with low-dose thiazide, amiloride and allopurinol. *Am J Med*, 1981. 71(4): p. 623-6.
191. Cannata-Andia, J.B. and M. Rodriguez-Garcia, Hyperphosphataemia as a cardiovascular risk factor – how to manage the problem. *Nephrol Dial Transplant*, 2002. 17 Suppl 11: p. 16-9.
192. Ketteler, M., *et al.*, Revisiting KDIGO clinical practice guideline on chronic kidney disease-mineral and bone disorder: a commentary from a Kidney Disease: Improving Global Outcomes controversies conference. *Kidney Int*, 2015. 87(3): p. 502-28.
193. Epstein, M., S. McGrath, and F. Law, Proton-pump inhibitors and hypomagnesemic hypoparathyroidism. *N Engl J Med*, 2006. 355(17): p. 1834-6.
194. Lubi, M., *et al.*, Magnesium supplementation does not affect blood calcium level in treated hypoparathyroid patients. *J Clin Endocrinol Metab*, 2012. 97(11): p. E2090-2.
195. Murdoch, D.L., *et al.*, A comparison of the potassium and magnesium-sparing properties of amiloride and spironolactone in diuretic-treated normal subjects. *Br J Clin Pharmacol*, 1993. 35(4): p. 373-8.
196. Workinger, J.L., R.P. Doyle, and J. Bortz, Challenges in the Diagnosis of Magnesium Status. *Nutrients*, 2018. 10(9).
197. Fatemi, S., *et al.*, Effect of experimental human magnesium depletion on parathyroid hormone secretion and 1,25-dihydroxyvitamin D metabolism. *J Clin Endocrinol Metab*, 1991. 73(5): p. 1067-72.
198. Gullestad, L., *et al.*, The magnesium loading test: reference values in healthy subjects. *Scand J Clin Lab Invest*, 1994. 54(1): p. 23-31.
199. Ozono, R., *et al.*, Systemic magnesium deficiency disclosed by magnesium loading test in patients with essential hypertension. *Hypertens Res*, 1995. 18(1): p. 39-42.
200. in *Dietary Reference Intakes for Calcium and Vitamin D*, A.C. Ross, *et al.*, Editors. 2011: Washington (DC).
201. Jorde, R. and G. Grimnes, Serum PTH is not a good marker for defining a threshold for vitamin D deficiency. *Endocr Connect*, 2020. 9(5): p. 396-404.
202. Lips, P., Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. *Endocr Rev*, 2001. 22(4): p. 477-501.
203. Luttmann-Gibson, H., *et al.*, Serum 25-hydroxyvitamin D in the VITamin D and Omega-3 Trial (VITAL): Clinical and demographic characteristics associated with baseline and change with randomized vitamin D treatment. *Contemp Clin Trials*, 2019. 87: p. 105854.
204. Pludowski, P., *et al.*, Vitamin D Supplementation: A Review of the Evidence Arguing for a Daily Dose of 2000 International Units (50 microg) of Vitamin D for Adults in the General Population. *Nutrients*, 2024. 16(3).
205. Pilz, S., *et al.*, Effect of Two Different Multimicronutrient Supplements on Vitamin D Status in Women of Childbearing Age: A Randomized Trial. *Nutrients*, 2017. 9(1).
206. Cashman, K.D., *et al.*, Estimation of the dietary requirement for vitamin D in free-living adults ≥ 64 y of age. *Am J Clin Nutr*, 2009. 89(5): p. 1366-74.
207. Mazess, R.B., H.A. Bischoff-Ferrari, and B. Dawson-Hughes, Vitamin D: Bolus Is Bogus-A Narrative Review. *JBMR Plus*, 2021. 5(12): p. e10567.

208. Zittermann, A., *et al.*, Long-term supplementation with 3200 to 4000 IU of vitamin D daily and adverse events: a systematic review and meta-analysis of randomized controlled trials. *Eur J Nutr*, 2023. 62(4): p. 1833-1844.
209. Cusano, N.E., *et al.*, Recovery of parathyroid hormone secretion and function in postoperative hypoparathyroidism: a case series. *J Clin Endocrinol Metab*, 2013. 98(11): p. 4285-90.
210. Lambert, L.A., *et al.*, Surgical treatment of hyperparathyroidism in patients with multiple endocrine neoplasia type 1. *Arch Surg*, 2005. 140(4): p. 374-82.
211. Kim, S.M., *et al.*, Recovery from Permanent Hypoparathyroidism After Total Thyroidectomy. *Thyroid*, 2015. 25(7): p. 830-3.
212. Carter, W.B., *et al.*, Parathyroid-induced angiogenesis is VEGF-dependent. *Surgery*, 2000. 128(3): p. 458-64.
213. Rashid, G., *et al.*, Parathyroid hormone stimulates the endothelial expression of vascular endothelial growth factor. *Eur J Clin Invest*, 2008. 38(11): p. 798-803.
214. Drake, M.T., *et al.*, Effects of intermittent parathyroid hormone treatment on osteoprogenitor cells in postmenopausal women. *Bone*, 2011. 49(3): p. 349-55.
215. Cantley, L.K., *et al.*, 1,25-Dihydroxyvitamin D3 suppresses parathyroid hormone secretion from bovine parathyroid cells in tissue culture. *Endocrinology*, 1985. 117(5): p. 2114-9.
216. Arlt, W., *et al.*, Well-being, mood and calcium homeostasis in patients with hypoparathyroidism receiving standard treatment with calcium and vitamin D. *Eur J Endocrinol*, 2002. 146(2): p. 215-22.
217. Bussey, A.D. and J.M. Bruder, Urinary calcium excretion in primary hyperparathyroidism: relationship to 25-hydroxyvitamin d status. *Endocr Pract*, 2005. 11(1): p. 37-42.
218. Yatabe, M.S., *et al.*, Effects of a high-sodium diet on renal tubule Ca²⁺ transporter and claudin expression in Wistar-Kyoto rats. *BMC Nephrol*, 2012. 13: p. 160.
219. Nordin, B.E., *et al.*, The nature and significance of the relationship between urinary sodium and urinary calcium in women. *J Nutr*, 1993. 123(9): p. 1615-22.
220. WHO, *in Guideline: Sodium Intake for Adults and Children*. 2012, World Health Organization (WHO): Geneva.
221. Aparicio, A., *et al.*, Estimation of salt intake assessed by urinary excretion of sodium over 24 h in Spanish subjects aged 7-11 years. *Eur J Nutr*, 2017. 56(1): p. 171-178.
222. Abate, N., *et al.*, The metabolic syndrome and uric acid nephrolithiasis: novel features of renal manifestation of insulin resistance. *Kidney Int*, 2004. 65(2): p. 386-92.
223. Hill, A.J., *et al.*, Incidence of Kidney Stones in the United States: The Continuous National Health and Nutrition Examination Survey. *J Urol*, 2022. 207(4): p. 851-856.
224. Weinberg, A.E., *et al.*, Diabetic severity and risk of kidney stone disease. *Eur Urol*, 2014. 65(1): p. 242-7.
225. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*, 2024. 105(4 s): p. S117-s314.
226. Underbjerg, L., T. Sikjaer, and L. Rejnmark, Cardiovascular findings in patients with nonsurgical hypoparathyroidism and pseudohypoparathyroidism: A cohort study. *Clin Endocrinol (Oxf)*, 2019. 90(4): p. 592-600.
227. Zavatta, G., *et al.*, Basal Ganglia Calcification Is Associated With Local and Systemic Metabolic Mechanisms in Adult Hypoparathyroidism. *J Clin Endocrinol Metab*, 2021. 106(7): p. 1900-1917.
228. David, K., *et al.*, Long-term complications in patients with chronic hypoparathyroidism: a cross-sectional study. *Eur J Endocrinol*, 2019. 180(1): p. 71-78.
229. Kim, S.H., *et al.*, Prevalence and complications of nonsurgical hypoparathyroidism in Korea: A nationwide cohort study. *PLoS One*, 2020. 15(5): p. e0232842.
230. Puliani, G., *et al.*, Impaired Immune Function in Patients With Chronic Postsurgical Hypoparathyroidism: Results of the EMPATHY Study. *J Clin Endocrinol Metab*, 2021. 106(5): p. e2215-e2227.
231. Abugassa, S., *et al.*, Bone mineral density in patients with chronic hypoparathyroidism. *J Clin Endocrinol Metab*, 1993. 76(6): p. 1617-21.
232. Fujiyama, K., *et al.*, Attenuation of postmenopausal high turnover bone loss in patients with hypoparathyroidism. *J Clin Endocrinol Metab*, 1995. 80(7): p. 2135-8.
233. Touliatos, J.S., *et al.*, Hypoparathyroidism counteracts risk factors for osteoporosis. *Am J Med Sci*, 1995. 310(2): p. 56-60.
234. Chawla, H., *et al.*, Vertebral Fractures and Bone Mineral Density in Patients With Idiopathic Hypoparathyroidism on Long-Term Follow-Up. *J Clin Endocrinol Metab*, 2017. 102(1): p. 251-258.
235. Pal, R., *et al.*, Fracture risk in hypoparathyroidism: a systematic review and meta-analysis. *Osteoporos Int*, 2021. 32(11): p. 2145-2153.
236. Rejnmark, L. and L. Underbjerg, Fracture Risk in Patients with Hypoparathyroidism. *Curr Osteoporos Rep*, 2023. 21(5): p. 632-636.
237. Furstenberg, A., J. Buscombe, and A. Davenport, Overestimation of lumbar spine calcium with dual energy X-ray absorptiometry scanning due to the prescription of lanthanum carbonate in patients with chronic kidney disease. *Am J Nephrol*, 2010. 32(5): p. 425-31.
238. Fidan, N., *et al.*, Bone mineral density and biochemical markers of bone metabolism in predialysis patients with chronic kidney disease. *J Investig Med*, 2016. 64(4): p. 861-6.
239. Khan, A.A., *et al.*, Skeletal health status among patients with chronic hypoparathyroidism: results from the Canadian National Hypoparathyroidism Registry (CNHR). *Osteoporos Int*, 2025.
240. Bjornsdottir, S., *et al.*, Increased risk of vertebral fractures and reduced risk of femur fractures in patients with chronic hypoparathyroidism: a Nationwide cohort study in Sweden. *J Bone Miner Res*, 2025.
241. Roszko, K.L., *et al.*, Autosomal Dominant Hypocalcemia Type 1: A Systematic Review. *J Bone Miner Res*, 2022. 37(10): p. 1926-1935.
242. Charoengam, N., P. Wattanachayakul, and M. Mannstadt, CASRdb: A Publicly Accessible Comprehensive Database for Disease-Associated Calcium-Sensing Receptor Variants. *J Clin Endocrinol Metab*, 2025. 110(2): p. 297-302.
243. Nesbit, M.A., *et al.*, Mutations affecting G-protein subunit alpha11 in hypercalcemia and hypocalcemia. *N Engl J Med*, 2013. 368(26): p. 2476-2486.
244. Howles, S.A., *et al.*, GNA11 Variants Identified in Patients with Hypercalcemia or Hypocalcemia. *J Bone Miner Res*, 2023. 38(6): p. 907-917.
245. Heath, H., 3rd, *et al.*, Clustered inactivating mutations and benign polymorphisms of the calcium receptor gene in familial benign hypocalciuric hypercalcemia suggest receptor functional domains. *J Clin Endocrinol Metab*, 1996. 81(4): p. 1312-7.
246. Lienhardt, A., *et al.*, Activating mutations of the calcium-sensing receptor: management of hypocalcemia. *J Clin Endocrinol Metab*, 2001. 86(11): p. 5313-23.
247. Thakker, R.V., Genetic developments in hypoparathyroidism. *Lancet*, 2001. 357(9261): p. 974-6.
248. Roszko, K.L., R.D. Bi, and M. Mannstadt, Autosomal Dominant Hypocalcemia (Hypoparathyroidism) Types 1 and 2. *Front Physiol*, 2016. 7: p. 458.
249. Sato, K., *et al.*, Hydrochlorothiazide effectively reduces urinary calcium excretion in two Japanese patients with gain-of-function mutations of the calcium-sensing receptor gene. *J Clin Endocrinol Metab*, 2002. 87(7): p. 3068-73.
250. Hochberg, A., *et al.*, Pregnancy, delivery and neonatal outcomes among women with hypoparathyroidism-A population-based study. *Clin Endocrinol (Oxf)*, 2023. 99(6): p. 525-532.

251. Kovacs, C.S. and H. Fuleihan Gel, Calcium and bone disorders during pregnancy and lactation. *Endocrinol Metab Clin North Am*, 2006. 35(1): p. 21-51, v.
252. Shulman, D., Subcutaneous Infusion of rhPTH(1-34) During Pregnancy and Nursing in a Woman With Autosomal Dominant Hypoparathyroidism 1. *J Endocr Soc*, 2022. 6(5): p. bvac031.
253. Ilany, J., I. Vered, and O. Cohen, The effect of continuous subcutaneous recombinant PTH (1-34) infusion during pregnancy on calcium homeostasis - a case report. *Gynecol Endocrinol*, 2013. 29(9): p. 807-10.
254. Appelman-Dijkstra, N.M. and S. Pilz, Approach to the Patient: Management of Parathyroid Diseases Across Pregnancy. *J Clin Endocrinol Metab*, 2023. 108(6): p. 1505-1513.
255. Liao, E.P. and N.E. Cusano, Use of rhPTH(1-84) for hypoparathyroidism during early pregnancy and lactation. *Endocrinol Diabetes Metab Case Rep*, 2023. 2023(2).
256. Hartogsohn, E.A.R., *et al.*, Changes in treatment needs of hypoparathyroidism during pregnancy and lactation: A case series. *Clin Endocrinol (Oxf)*, 2020. 93(3): p. 261-268.
257. Marcucci, G., *et al.*, Hypoparathyroidism and pseudohypoparathyroidism in pregnancy: an Italian retrospective observational study. *Orphanet J Rare Dis*, 2021. 16(1): p. 421.
258. Wang, J.J., *et al.*, Changes in Serum Calcium and Treatment of Hypoparathyroidism During Pregnancy and Lactation: A Single-center Case Series. *J Clin Endocrinol Metab*, 2021. 106(12): p. e5054-e5063.
259. Caplan, R.H. and E.A. Beguin, Hypercalcemia in a calcitriol-treated hypoparathyroid woman during lactation. *Obstet Gynecol*, 1990. 76(3 Pt 2): p. 485-9.
260. Sadeghi-Nejad, A., J.I. Wolfsdorf, and B. Senior, Hypoparathyroidism and pregnancy. *Treatment with calcitriol*. *JAMA*, 1980. 243(3): p. 254-5.
261. Salle, B.L., *et al.*, Hypoparathyroidism during pregnancy: treatment with calcitriol. *J Clin Endocrinol Metab*, 1981. 52(4): p. 810-3.
262. Kovacs, C.S., Calcium and Phosphate Metabolism and Related Disorders During Pregnancy and Lactation, in *Endotext*, K.R. Feingold, *et al.*, Editors. 2000: South Dartmouth (MA).
263. Graham, W.P., 3rd, *et al.*, Effect of Pregnancy and of the Menstrual Cycle on Hypoparathyroidism. *J Clin Endocrinol Metab*, 1964. 24: p. 512-6.
264. Kovacs, C.S., Bone development and mineral homeostasis in the fetus and neonate: roles of the calciotropic and phosphotropic hormones. *Physiol Rev*, 2014. 94(4): p. 1143-218.
265. Cooper, M.S., Disorders of calcium metabolism and parathyroid disease. *Best Pract Res Clin Endocrinol Metab*, 2011. 25(6): p. 975-83.
266. Mather, K.J., C.L. Chik, and B. Corenblum, Maintenance of serum calcium by parathyroid hormone-related peptide during lactation in a hypoparathyroid patient. *J Clin Endocrinol Metab*, 1999. 84(2): p. 424-7.
267. Cundy, T., *et al.*, Remission of hypoparathyroidism during lactation: evidence for a physiological role for prolactin in the regulation of vitamin D metabolism. *Clin Endocrinol (Oxf)*, 1987. 26(6): p. 667-74.
268. Markestad, T., *et al.*, Vitamin D metabolism in normal and hypoparathyroid pregnancy and lactation. *Case report*. *Br J Obstet Gynaecol*, 1983. 90(10): p. 971-6.
269. Rude, R.K., M.R. Haussler, and F.R. Singer, Postpartum resolution of hypocalcemia in a lactating hypoparathyroid patient. *Endocrinol Jpn*, 1984. 31(3): p. 227-33.
270. Shomali, M.E. and D.S. Ross, Hypercalcemia in a woman with hypoparathyroidism associated with increased parathyroid hormone-related protein during lactation. *Endocr Pract*, 1999. 5(4): p. 198-200.
271. Wright, A.D., G.F. Joplin, and H.G. Dixon, Post-partum hypercalcemia in treated hypoparathyroidism. *Br Med J*, 1969. 1(5635): p. 23-5.
272. Munns, C.F., *et al.*, Global Consensus Recommendations on Prevention and Management of Nutritional Rickets. *J Clin Endocrinol Metab*, 2016. 101(2): p. 394-415.
273. Cerqueira, B.P., *et al.*, Kabuki and CHARGE syndromes: overlapping symptoms and diagnostic challenges. *Einstein (Sao Paulo)*, 2025. 23: p. eRC1142.
274. Schigt, H., *et al.*, Expanding the Phenotypic Spectrum of Kenny-Caffey Syndrome. *J Clin Endocrinol Metab*, 2023. 108(9): p. e754-e768.
275. Hadker, N., *et al.*, Understanding the burden of illness associated with hypoparathyroidism reported among patients in the PARADOX study. *Endocr Pract*, 2014. 20(7): p. 671-9.
276. Hamdy, N.A.T., *et al.*, Burden of illness in patients with chronic hypoparathyroidism not adequately controlled with conventional therapy: a Belgium and the Netherlands survey. *J Endocrinol Invest*, 2021. 44(7): p. 1437-1446.
277. Ketteler, M., *et al.*, Risk of Nephrolithiasis and Nephrocalcinosis in Patients with Chronic Hypoparathyroidism: A Retrospective Cohort Study. *Adv Ther*, 2021. 38(4): p. 1946-1957.
278. Cusano, N.E., *et al.*, The effect of PTH(1-84) on quality of life in hypoparathyroidism. *J Clin Endocrinol Metab*, 2013. 98(6): p. 2356-61.
279. Cusano, N.E., *et al.*, Therapy of hypoparathyroidism with PTH(1-84): a prospective four-year investigation of efficacy and safety. *J Clin Endocrinol Metab*, 2013. 98(1): p. 137-44.
280. Bilezikian, J.P., *et al.*, Primary hyperparathyroidism. *Nat Rev Dis Primers*, 2016. 2: p. 16033.
281. Grieff, M. and D.A. Bushinsky, Diuretics and disorders of calcium homeostasis. *Semin Nephrol*, 2011. 31(6): p. 535-41.
282. Nijenhuis, T., *et al.*, Enhanced passive Ca²⁺ reabsorption and reduced Mg²⁺ channel abundance explains thiazide-induced hypocalcemia and hypomagnesemia. *J Clin Invest*, 2005. 115(6): p. 1651-8.
283. Griebeler, M.L., *et al.*, Thiazide-Associated Hypercalcemia: Incidence and Association With Primary Hyperparathyroidism Over Two Decades. *J Clin Endocrinol Metab*, 2016. 101(3): p. 1166-73.
284. Ruppe, M.D., Medications that affect calcium. *Endocr Pract*, 2011. 17 Suppl 1: p. 26-30.
285. Gao, S., *et al.*, Hypocalcemia Event Associated with Denosumab: A Real-World Study from FDA Adverse Event Reporting System (FAERS) Database. *Ther Innov Regul Sci*, 2025. 59(1): p. 135-141.
286. Liamis, G., H.J. Milionis, and M. Elisaf, A review of drug-induced hypocalcemia. *J Bone Miner Metab*, 2009. 27(6): p. 635-42.
287. Tamura, T., *et al.*, Omeprazole- and esomeprazole-associated hypomagnesaemia: data mining of the public version of the FDA Adverse Event Reporting System. *Int J Med Sci*, 2012. 9(5): p. 322-6.
288. Recker, R.R., Calcium absorption and achlorhydria. *N Engl J Med*, 1985. 313(2): p. 70-3.
289. Verzicco, I., *et al.*, Electrolyte Disorders Induced by Antineoplastic Drugs. *Front Oncol*, 2020. 10: p. 779.
290. Khandelwal, R., *et al.*, A Comprehensive Review on Unveiling the Journey of Digoxin: Past, Present, and Future Perspectives. *Cureus*, 2024. 16(3): p. e56755.
291. Wang, S., *et al.*, pH effects on measurements of ionized calcium and ionized magnesium in blood. *Arch Pathol Lab Med*, 2002. 126(8): p. 947-50.
292. Jain, N. and R.F. Reilly, Hungry bone syndrome. *Curr Opin Nephrol Hypertens*, 2017. 26(4): p. 250-255.
293. Michie, W., *et al.*, Mechanism of hypocalcaemia after thyroidectomy for thyrotoxicosis. *Lancet*, 1971. 1(7698): p. 508-14.
294. Riveros, H.A., *et al.*, Hungry bone syndrome: persistent hypocalcemia related to osteoblastic bone metastases of prostate cancer. *J Palliat Med*, 2013. 16(12): p. 1496-7.
295. Strubbe, M., *et al.*, No longer to be ignored: Hypophosphatemia following intravenous iron administration. *Rev Endocr Metab Disord*, 2025. 26(1): p. 125-135.

296. Schouten, B.J., *et al.*, FGF23 elevation and hypophosphatemia after intravenous iron polymaltose: a prospective study. *J Clin Endocrinol Metab*, 2009. 94(7): p. 2332-7.
297. Blazevic, A., J. Hunze, and J.M. Boots, Severe hypophosphatemia after intravenous iron administration. *Neth J Med*, 2014. 72(1): p. 49-53.
298. Mani, L.Y., *et al.*, Severe hypophosphatemia after intravenous administration of iron carboxymaltose in a stable renal transplant recipient. *Transplantation*, 2010. 90(7): p. 804-5.
299. Ovejero, D., *et al.*, PTH and FGF23 Exert Interdependent Effects on Renal Phosphate Handling: Evidence From Patients With Hypoparathyroidism and Hyperphosphatemic Familial Tumoral Calcinosis Treated With Synthetic Human PTH 1-34. *J Bone Miner Res*, 2022. 37(2): p. 179-184.
300. Mateo, L., *et al.*, Hypophosphatemic osteomalacia induced by tenofovir in HIV-infected patients. *Clin Rheumatol*, 2016. 35(5): p. 1271-9.
301. Herlitz, L.C., *et al.*, Tenofovir nephrotoxicity: acute tubular necrosis with distinctive clinical, pathological, and mitochondrial abnormalities. *Kidney Int*, 2010. 78(11): p. 1171-7.
302. Kreze, A., *et al.*, Hypoparathyroidism: an uncommon adverse effect of treatment with durvalumab. *Endocr Oncol*, 2022. 2(1): p. K21-K24.
303. Piranavan, P., *et al.*, Immune Checkpoint Inhibitor-Induced Hypoparathyroidism Associated With Calcium-Sensing Receptor-Activating Autoantibodies. *J Clin Endocrinol Metab*, 2019. 104(2): p. 550-556.
304. Trinh, B., *et al.*, Inflammation-induced hypoparathyroidism triggered by combination immune checkpoint blockade for melanoma. *J Immunother Cancer*, 2019. 7(1): p. 52.
305. Umeguchi, H., *et al.*, Autoimmune-Related Primary Hypoparathyroidism Possibly Induced by the Administration of Pembrolizumab: A Case Report. *J Oncol Pract*, 2018. 14(7): p. 449-451.
306. Win, M.A., *et al.*, Acute symptomatic hypocalcemia from immune checkpoint therapy-induced hypoparathyroidism. *Am J Emerg Med*, 2017. 35(7): p. 1039 e5-1039 e7.
307. Pascucci, J.M., *et al.*, Possible involvement of pregnane X receptor-enhanced CYP24 expression in drug-induced osteomalacia. *J Clin Invest*, 2005. 115(1): p. 177-86.