

# Parathyroid Hormone Hyper- and Hypoparathyroidism Effect of Treatment and Long-term Follow-up Studies

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## ABSTRACT

**Background:** High or low parathyroid hormone (PTH) can be challenging in diagnosis and treatment. The prevalence and natural history of normocalcemic hyperparathyroidism (nHPT) are still not known. The knowledge gap regarding fracture risk, other comorbidities, and mortality in nHPT in the population is deep. Hypoparathyroidism (HypoPT) is the only endocrine disease for which there is no substitution of the missing hormone, PTH. A fraction of the natural PTH, teriparatide (PTH 1-34), is used in the treatment of severe osteoporosis.

**Aims and methods:** The aim was to study the prevalence of fractures, morbidity, and mortality in individuals with nHPT and HypoPT. The self-reported Health-Related Quality of Life (HRQoL) for patients with HypoPT compared with age-matched controls from the population was studied with validated generic questionnaires, the EuroQol-5 dimensions visual analogue scale and the Short Form-36. The effects on bone, fractures and HRQoL of daily administration of teriparatide (PTH 1-34) were investigated in patients with severe osteoporosis in comparison with the population and a placebo-treated control group with osteoporosis during 10 years of follow-up. The hypothesis was that nHPT in men and women from the population would lead to higher morbidity and mortality and that HRQoL was low in patients with HypoPT and osteoporosis but improved in osteoporotic patients treated with teriparatide.

**Results:** nHPT was common in the population, up to 11%, and did not progress to primary hyperparathyroidism (pHPT) up to 21 years later. No increase in comorbidity or mortality was observed in nHPT. Subjects with HypoPT had lower HRQoL, fewer fractures and no increased morbidity or mortality in comparison with the population. One out of five patients with HypoPT would benefit from other treatment than the calcium and active vitamin D therapy traditionally used. Teriparatide increased bone mineral density and decreased fracture frequency up to 10 years after treatment start. HRQoL was low in osteoporotic women and did not improve with treatment.

**Conclusion:** The newly described clinical phenotype, nHPT, was common in the population but did not lead to pHPT, more fractures or higher morbidity or mortality during up to 21 years of follow-up. HRQoL was low in subjects with HypoPT and in women with severe osteoporosis. Teriparatide had an anabolic effect on osteoporotic bone and favorable effect on fractures after 10 years but HRQoL was unaffected.

**Keywords:** Calcium, Hyperparathyroidism, Hypoparathyroidism, Vitamin D, Population, Fractures, Cardiovascular disease, Quality of Life, Comorbidity, Teriparatide, Osteoporosis

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### Avhandlingen baseras på följande delarbeten

- I. Kontogeorgos G, Trimpou P, Laine CM, Oleröd G, Lindahl A, Landin-Wilhelmsen K. Normocalcaemic, vitamin D-sufficient hyperparathyroidism - high prevalence and low morbidity in the general population: A long-term follow-up study, the WHO MONICA project, Gothenburg, Sweden. *Clin Endocrinol (Oxf)*. 2015 Aug; 83(2):277-84. doi:10.1111/cen.12819. Epub 2015 Jun 15.
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- IV. Kontogeorgos G, Krantz E, Trimpou P, Laine CM, Landin-Wilhelmsen K. Teriparatide treatment in severe osteoporosis - a controlled 10-year follow-up study. *BMC Musculoskelet Disord*. 2022 Nov 24;23(1):1011. doi: 10.1186/s12891-022-05987-2.

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