

con il patrocinio di



**UniSR**  
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**I.R.C.C.S. Ospedale  
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**CORSO DI AGGIORNAMENTO**

**NUOVE TRAIETTORIE  
NELLA CURA**

**DELL'IPOPARATIROIDISMO**



OSPEDALE  
SAN RAFFAELE



**UniSR**  
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**II SESSIONE - Diagnosi e clinica  
dell'ipoparatiroidismo**

**Complicanze ossee**

Dr. Luigi di Filippo

Institute of Endocrine and Metabolic Sciences

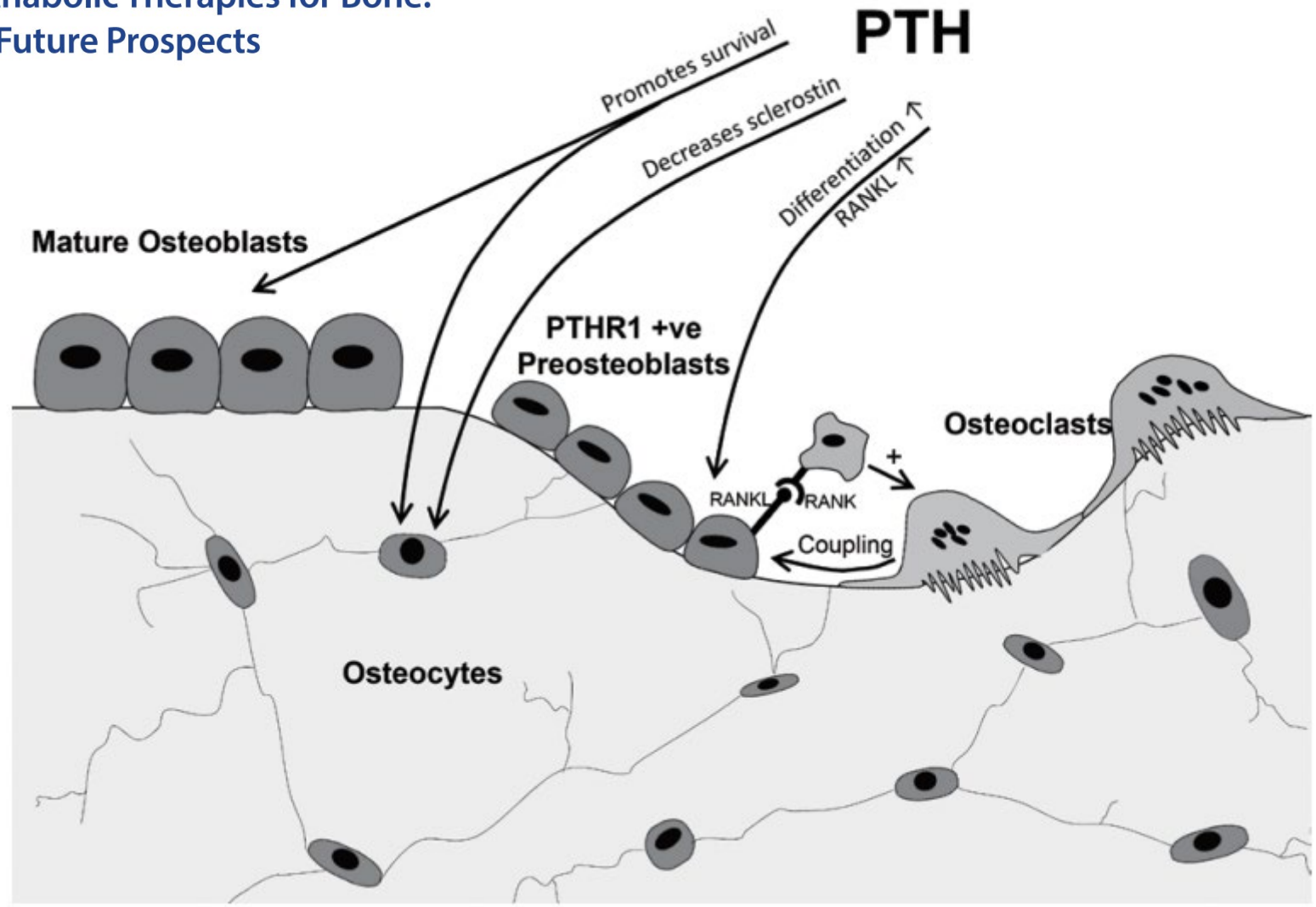
Università Vita-Salute San Raffaele

IRCCS Ospedale San Raffaele, Milano

# PTH e osso

## Bone Biology and Anabolic Therapies for Bone: Current Status and Future Prospects

T. John Martin



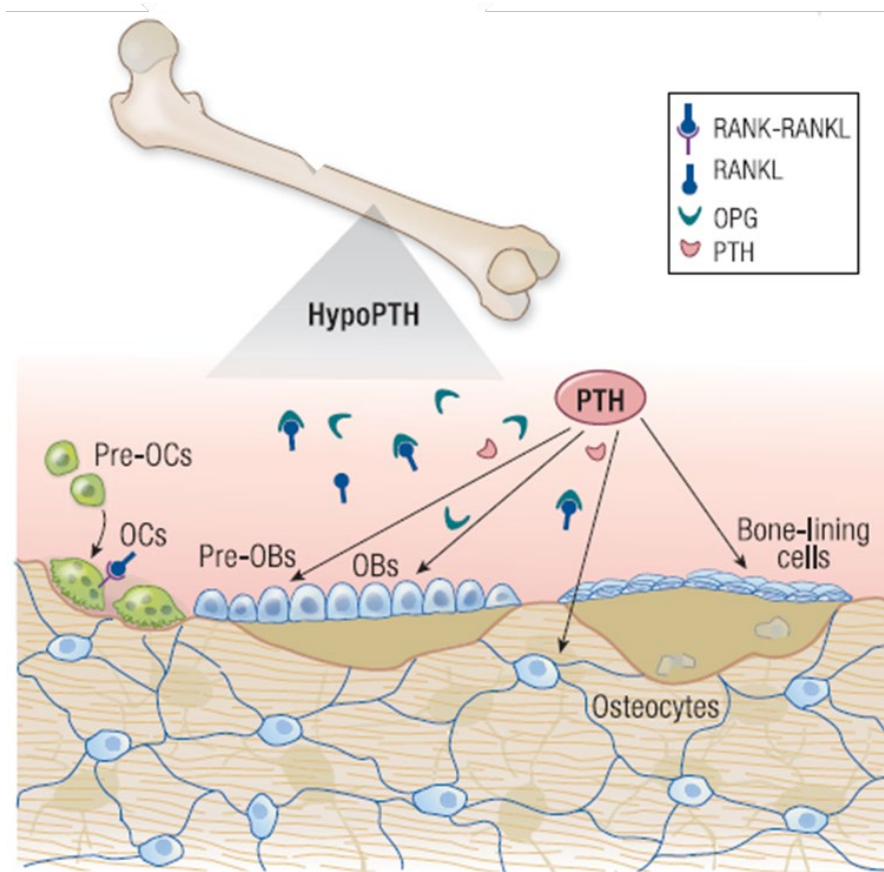
# Patologie paratiroidiee e osso

Endocrine Reviews, 2025, 00, 1–45  
https://doi.org/10.1210/endrev/bnaf010  
Advance access publication 3 April 2025  
Review



## Bone in Parathyroid Diseases Revisited: Evidence From Epidemiological, Surgical and New Drug Outcomes

Afroditi Roumpou,<sup>1,\*</sup> Andrea Palermo,<sup>2,3,\*</sup> Symeon Tournis,<sup>4</sup> Valeria Hasenmajer,<sup>5,6</sup> Janice L. Pasieka,<sup>7</sup> Gregory Kaltsas,<sup>8,9</sup> Andrea Isidori,<sup>5,6,1</sup> and Eva Kassi<sup>8,9,10,†</sup>



Bone aspects	Serum calcium	aBMD +vBMD	Histo Histomorphometry	Bone turnover/ markers	TBS Trabecular bone score	Fracture risk
Postsurgical hypoparathyroidism (PH)	↓	↑	↓	↓	—	ND
Non-surgical hypoparathyroidism (Ns-hypoPTH)	↓	↑	↓	↓	—	↑ Spine
PTH (1-84)	↔	↑ Trabecular/spine ↓ Cortical/radius, tibia	↑	↑	↑	ND
PTH (1-34)	↔	↑ Total hip — Spine/femoral neck ↓ Total radius	↑	↑	ND	—
TransCon PTH	↔	ND	ND	↑	ND	ND

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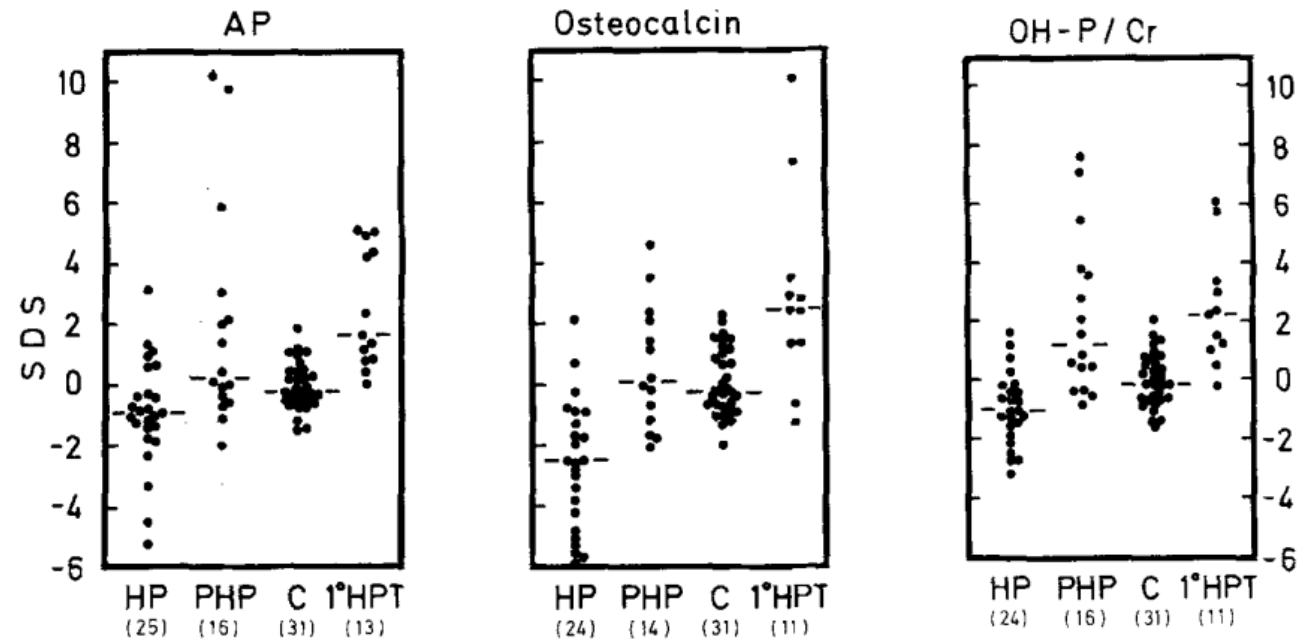
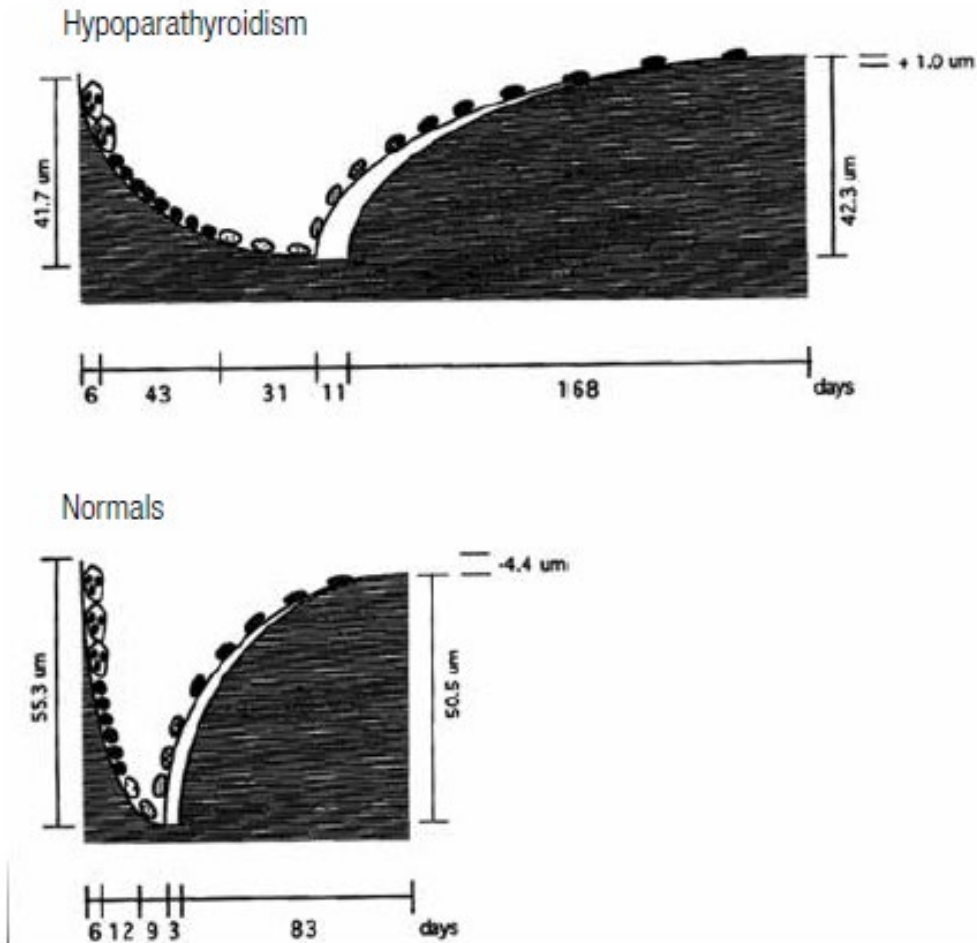
# Ipoparatiroidismo e turnover osseo

## Bone Histomorphometry in Hypoparathyroid Patients Treated With Vitamin D

B. L. LANGDAHL, L. MORTENSEN, A. VESTERBY, E. F. ERIKSEN, and P. CHARLES

## Biochemical markers of bone turnover, intact serum parathyroid hormone and renal calcium excretion in patients with pseudohypoparathyroidism and hypoparathyroidism before and during vitamin D treatment

K. Kruse, U. Kracht, K. Wohlfart, and U. Kruse

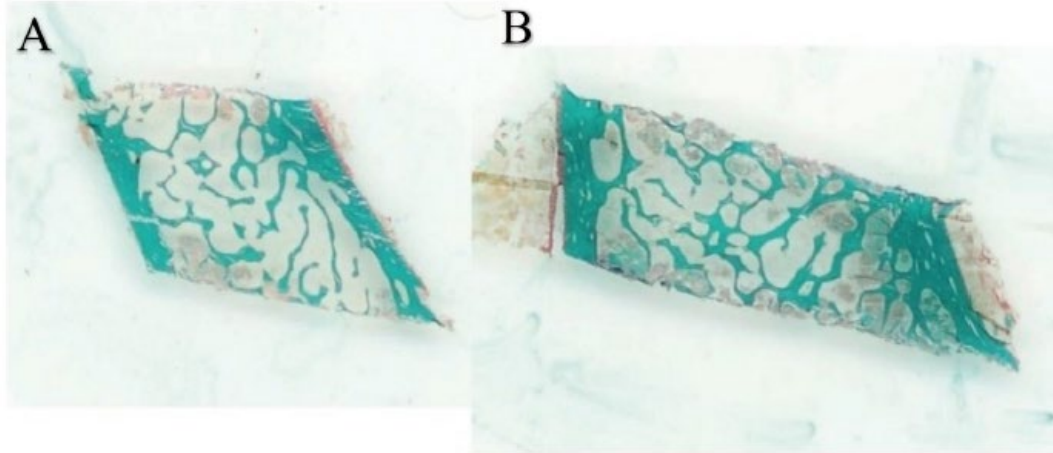


# Ipoparatiroidismo e dati istomorfometrici

## Dynamic and Structural Properties of the Skeleton in Hypoparathyroidism

Mishaela R Rubin, David W Dempster, Hua Zhou, Elizabeth Shane, Thomas Nickolas, James Sliney Jr, Shonni J Silverberg, and John P Bilezikian

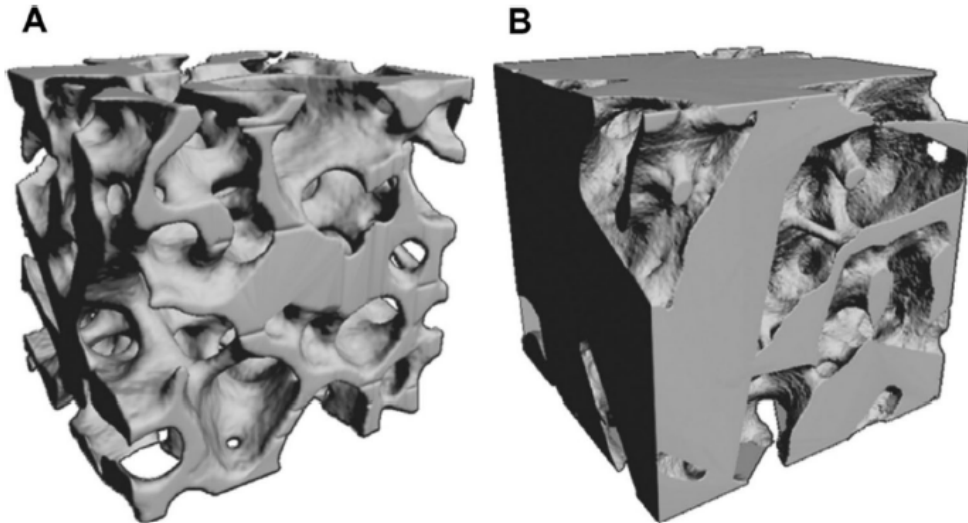
“Iliac crest biopsies from a control (A) and hypoparathyroidism (B): increase in cancellous bone volume and cortical thickness”



## Three Dimensional Cancellous Bone Structure in Hypoparathyroidism

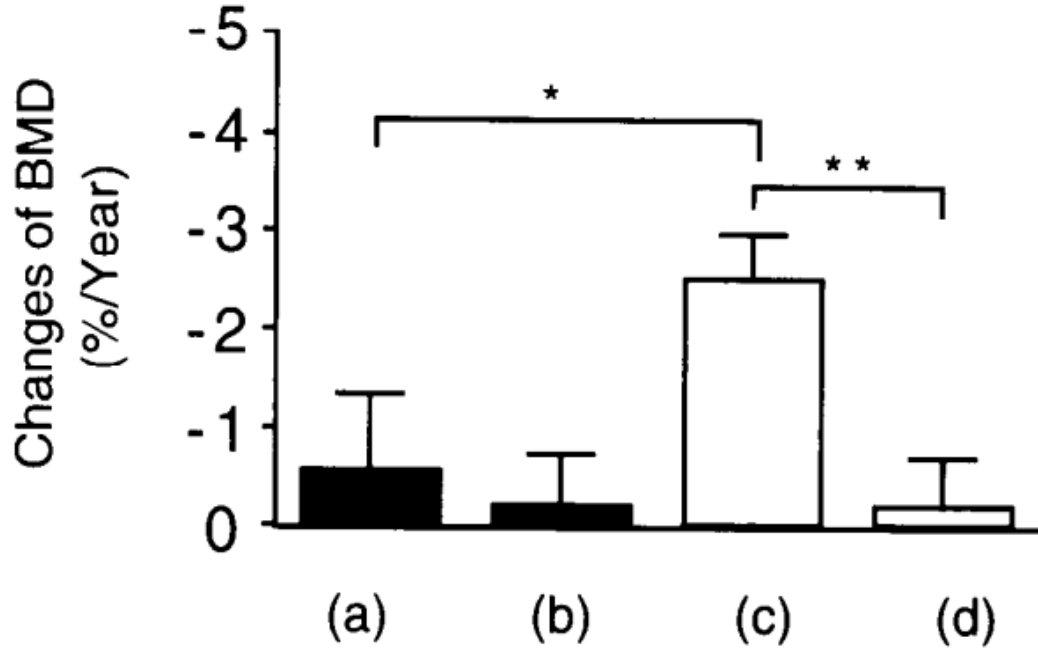
Mishaela R. Rubin<sup>1</sup>, David W. Dempster<sup>2</sup>, Thomas Kohler<sup>3</sup>, Martin Stauber<sup>3</sup>, Hua Zhou<sup>2</sup>, Elizabeth Shane<sup>1</sup>, Thomas Nickolas<sup>1</sup>, Emily Stein<sup>1</sup>, James Sliney Jr.<sup>1</sup>, Shonni J. Silverberg<sup>1</sup>, John P. Bilezikian<sup>1</sup>, and Ralph Müller<sup>3</sup>

“uCT images of cancellous bone from a control (A) and hypoparathyroidism (B): dense trabecular structure in hypoparathyroidism”



## Attenuation of Postmenopausal High Turnover Bone Loss in Patients with Hypoparathyroidism\*

KAORU FUJIYAMA, TAKESHI KIRIYAMA, MASAKO ITO, KEISUKE NAKATA, SHUNICHI YAMASHITA, NAOKATA YOKOYAMA, AND SHIGENOBU NAGATAKI



## Increased Bone Mineral Density in Patients with Chronic Hypoparathyroidism

FREDRIECH K. W. CHAN, SAU-CHEUNG TIU, KIN-LAM CHOI, CHEUNG-HEI CHOI, ALICE P. S. KONG, AND CHI-CHUNG SHEK

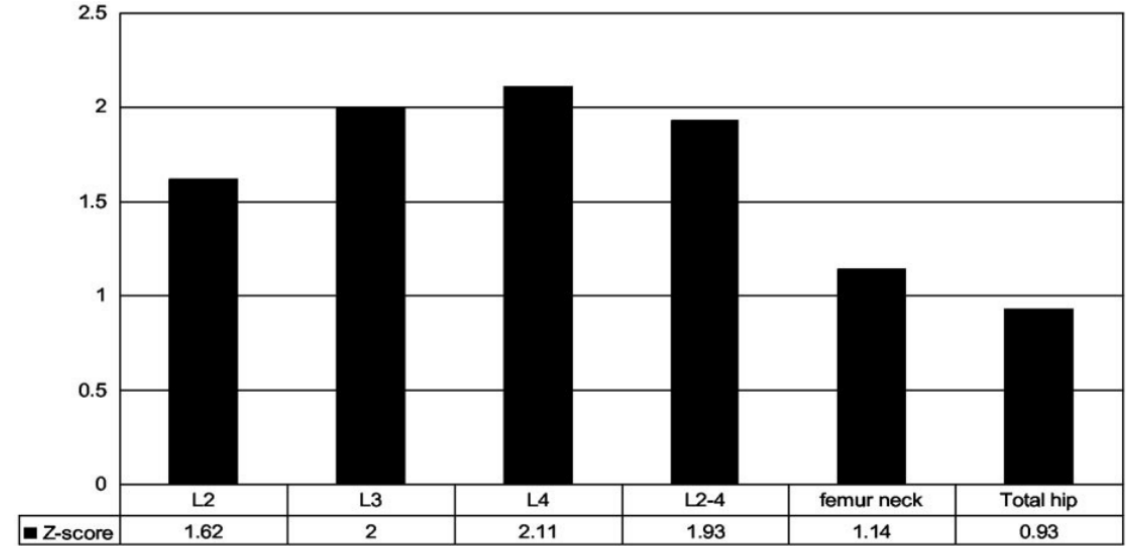


FIG. 1. Mean Z-scores for the BMD of lumbar vertebra, femur neck, and total hip in patients with hypoparathyroidism ( $P < 0.001$ ).

# Ipoparatiroidismo e BMD

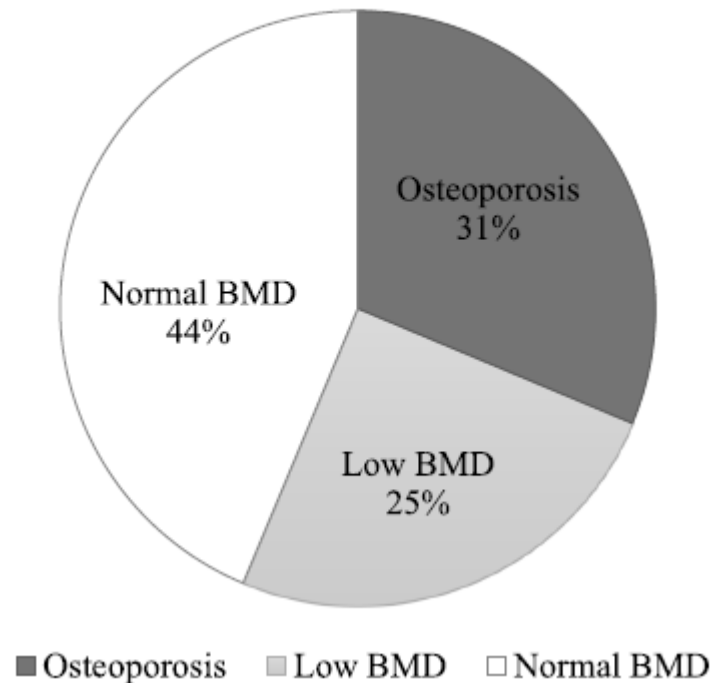
ORIGINAL ARTICLE



## Skeletal health status among patients with chronic hypoparathyroidism: results from the Canadian National Hypoparathyroidism Registry (CNHR)

Aliya A. Khan<sup>1,3,12</sup> · Hajar AbuAlrob<sup>2</sup> · Dalal S. Ali<sup>1</sup> · Zayd Al Kassem<sup>3</sup> · Abdulrahman Almoulia<sup>3</sup> · Habiba Afifi<sup>3</sup> · Manoela Braga<sup>1</sup> · Alice Cheng<sup>4</sup> · Jouma Malhem<sup>3</sup> · Adam Millar<sup>5</sup> · Emmett Morgante<sup>3</sup> · Parwana Muhammad<sup>3</sup> · Terri L. Paul<sup>6</sup> · Ally Prebtani<sup>1</sup> · Zubin Punthakee<sup>1</sup> · Tayyab Khan<sup>6</sup> · Sarah Khan<sup>3</sup> · Muhammad Shrayyef<sup>7</sup> · Stan Van Uum<sup>6</sup> · James Edward Massey Young<sup>8</sup> · Maria Luisa Brandi<sup>9,10</sup> · Michel Ovize<sup>11</sup> · Blandine Weiss<sup>11</sup>

### BMD Distribution in Postmenopausal Women with Hypoparathyroidism



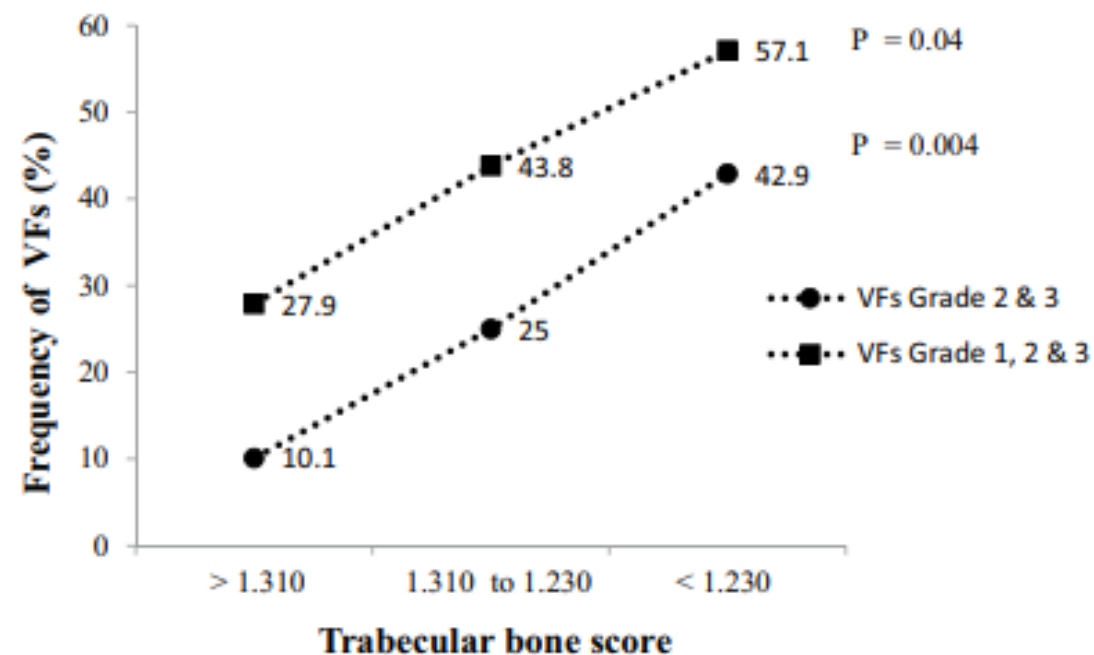
**Table 4** Correlation analysis between duration of disease and BMD

Variable	<i>N</i>	Correlation coefficient ( <i>r</i> )	<i>p</i> -value
L1-L4 BMD (gm/cm <sup>2</sup> )	84	0.317	0.0034
Femoral neck BMD (gm/cm <sup>2</sup> )	87	0.272	0.0107
Total hip BMD (gm/cm <sup>2</sup> )	86	0.280	0.0090
1/3 radial BMD (gm/cm <sup>2</sup> )	79	0.091	0.4230

## Vertebral fractures, trabecular bone score and their determinants in chronic hypoparathyroidism

S. Saha<sup>1</sup> · V. Mannar<sup>1</sup> · D. Kandasamy<sup>2</sup> · V. Sreenivas<sup>3</sup> · R. Goswami<sup>1</sup>

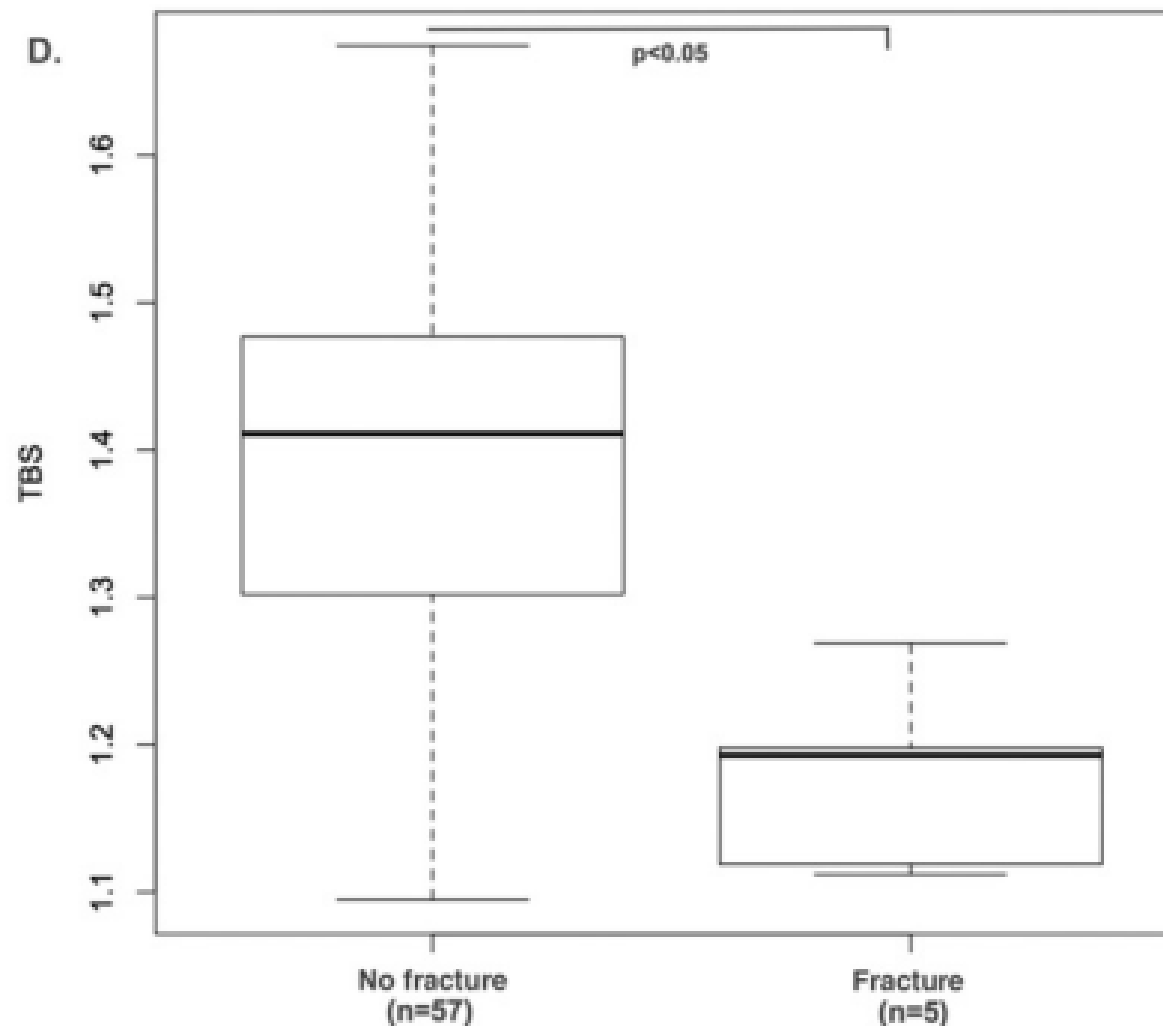
Characteristic	cHypoPT (n = 152)	Controls (n = 152)	P
<b>BMD (g/cm<sup>2</sup>)</b>			
L1-4 AP spine	1.232 ± 0.229	0.982 ± 0.116	<0.001
Femoral neck	0.922 ± 0.178	0.783 ± 0.110	<0.001
Trochanter	0.756 ± 0.134	0.665 ± 0.072	<0.001
Total hip	1.040 ± 0.161	0.917 ± 0.103	<0.001
Ultradistal-forearm	0.457 ± 0.078	0.450 ± 0.061	0.41
Mid-forearm	0.610 ± 0.075	0.611 ± 0.060	0.85
Proximal-forearm	0.716 ± 0.082	0.703 ± 0.069	0.14
Total forearm	0.588 ± 0.072	0.584 ± 0.058	0.62
<b>Trabecular bone score</b>			
Mean ± SD	1.411 ± 0.091	1.334 ± 0.093	<0.001
< 1.230 (n, %)	7 (4.6)	23 (15.1)	
1.230—1.310 (n, %)	16 (10.5)	35 (23.0)	
> 1.310 (n, %)	129 (84.9)	94 (61.8)	<0.001



# Ipoparatiroidismo e bone quality

## Predictors of Poor Bone Microarchitecture Assessed by Trabecular Bone Score in Postsurgical Hypoparathyroidism

Eliane Naomi Sakane,<sup>1</sup> Maria Carolina Camargo Vieira,<sup>1</sup> Marise Lazaretti-Castro,<sup>1</sup>  
and Sergio Setsuo Maeda<sup>1</sup>



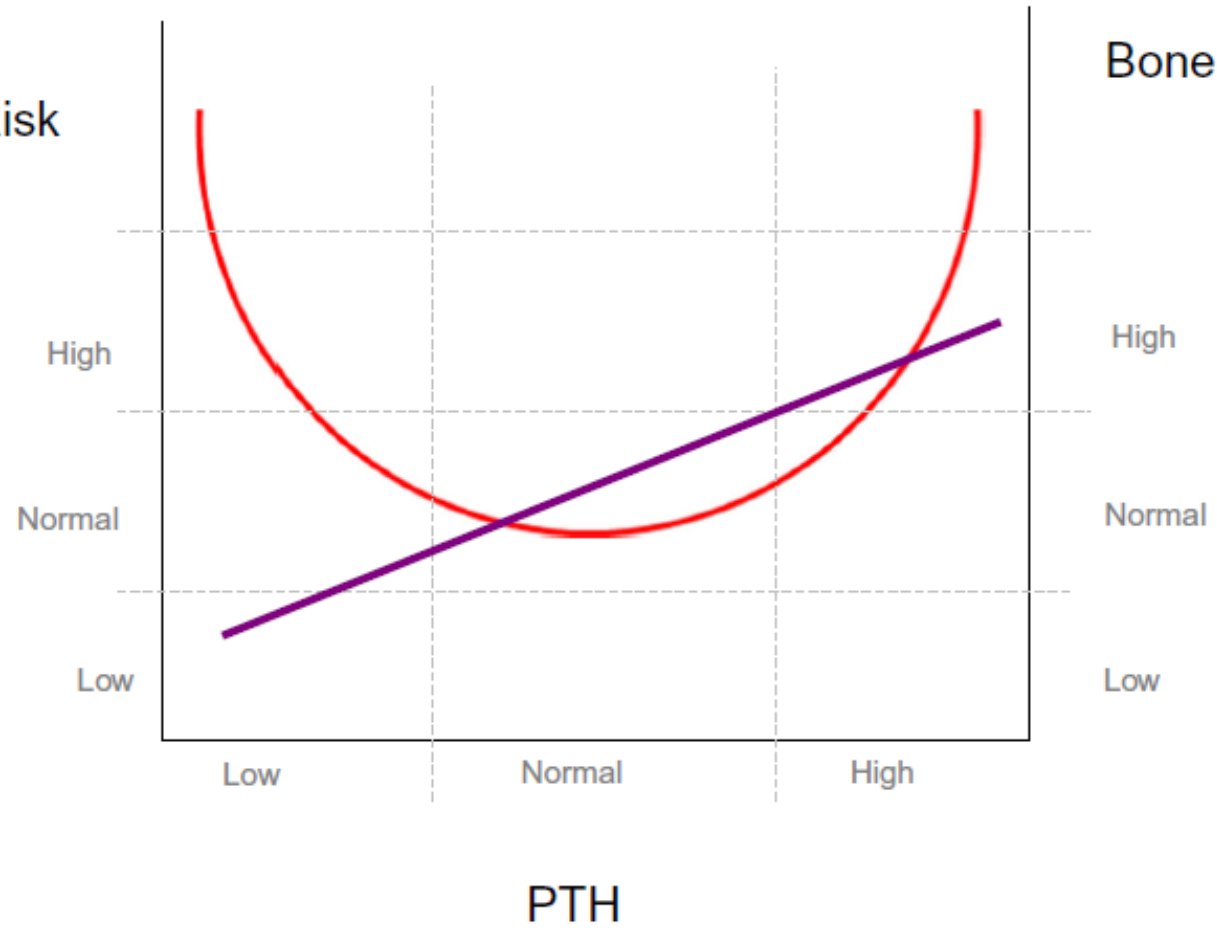
# Ipoparatiroidismo e fratture

Reviews in Endocrine and Metabolic Disorders (2019) 20:295–302  
<https://doi.org/10.1007/s11154-019-09507-x>

## Risk of vertebral fractures in hypoparathyroidism

Anna Maria Formenti<sup>1</sup> • Francesco Tecilazich<sup>1</sup> • Raffaele Giubbini<sup>2</sup> • Andrea Giustina<sup>1</sup>

Vertebral  
Fracture Risk



Bone Metabolism

Proposed U-shape model of increased morphometric vertebral fracture risk in case of defect or excess of parathyroid hormone

# Ipoparatiroidismo e fratture

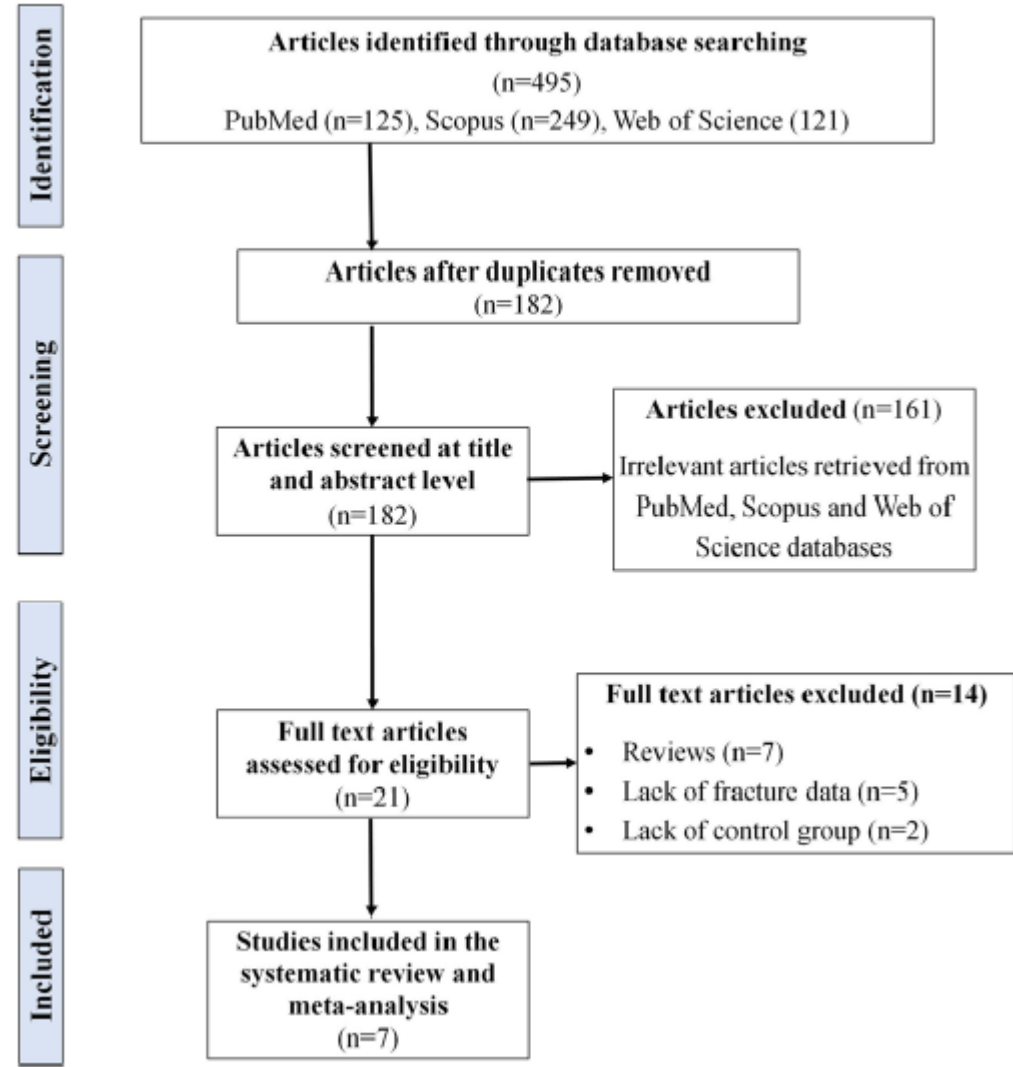


Osteoporosis International (2021) 32:2145–2153  
<https://doi.org/10.1007/s00198-021-05966-8>

REVIEW

## Fracture risk in hypoparathyroidism: a systematic review and meta-analysis

R. Pal<sup>1</sup> · S.K. Bhadada<sup>1</sup> · S. Mukherjee<sup>1</sup> · M. Banerjee<sup>2</sup> · A. Kumar<sup>3</sup>



# Ipoparatiroidismo e fratture

## Fracture risk in hypoparathyroidism: a systematic review and meta-analysis

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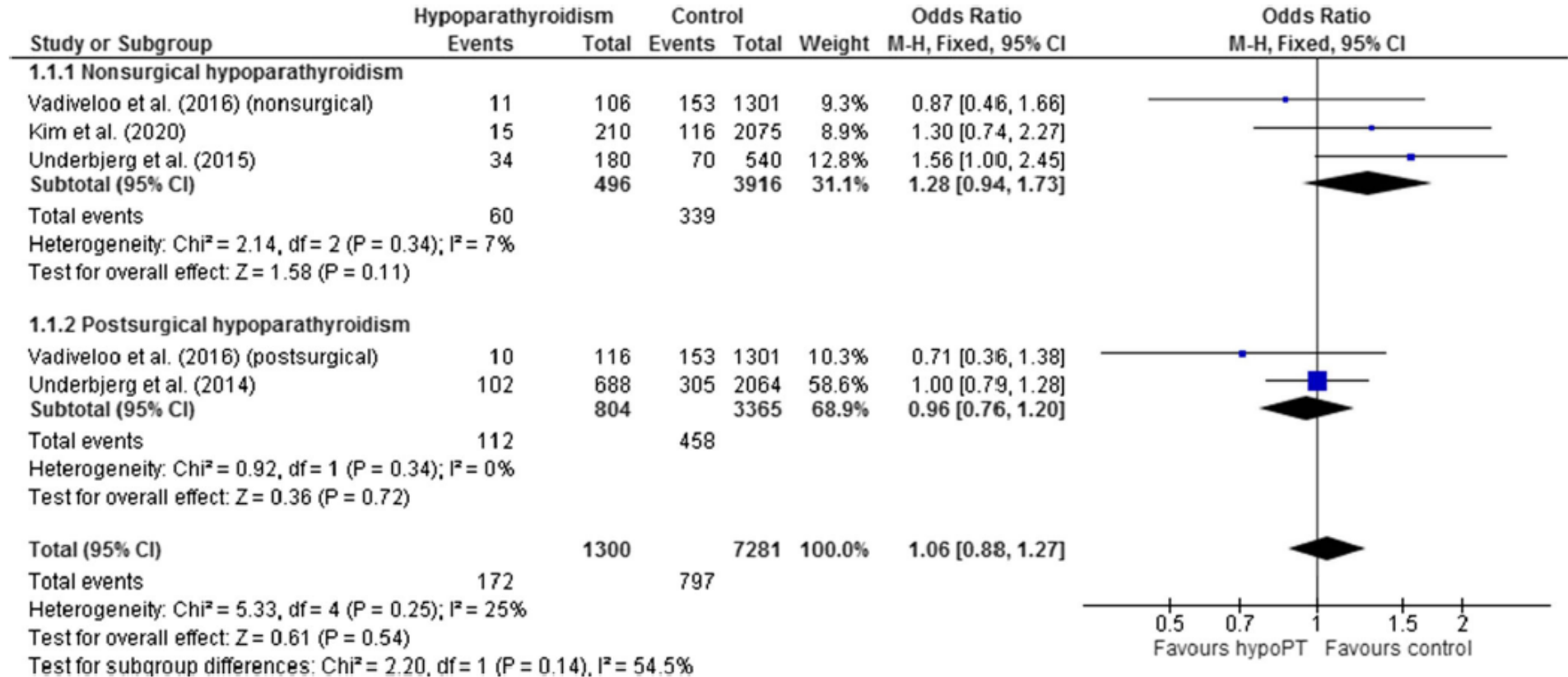


Fig. 2 Forest plot with subgroup analysis showing the risk of *any* fractures in patients with hypoparathyroidism (hypoPT) as compared to non-hypoPT controls

# Ipoparatiroidismo e fratture

## Fracture risk in hypoparathyroidism: a systematic review and meta-analysis

R. Pal<sup>1</sup> · S.K. Bhadada<sup>1</sup> · S. Mukherjee<sup>1</sup> · M. Banerjee<sup>2</sup> · A. Kumar<sup>3</sup>

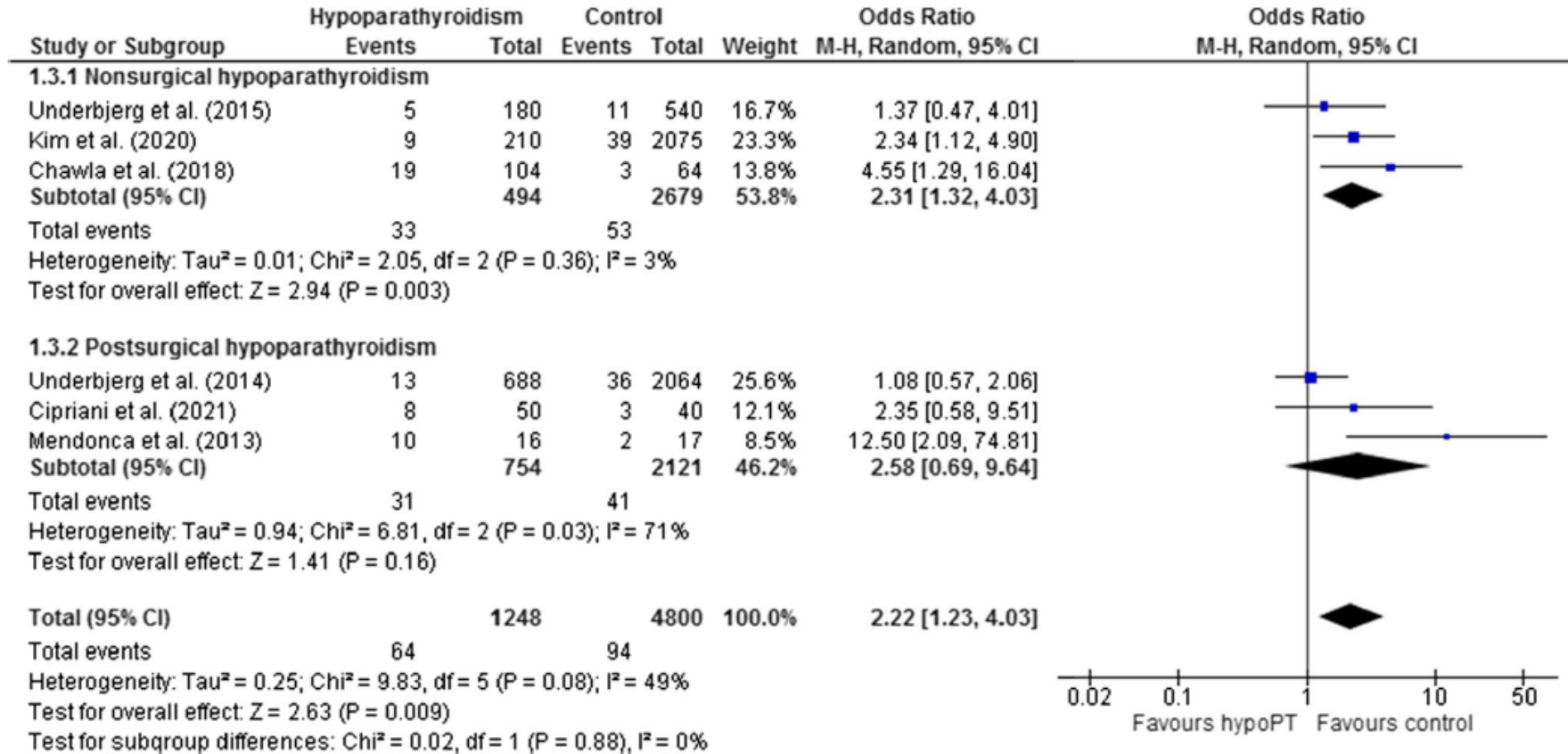


Fig. 3 Forest plot with subgroup analysis showing the risk of *vertebral* fractures in patients with hypoparathyroidism (hypoPT) as compared to non-hypoPT controls

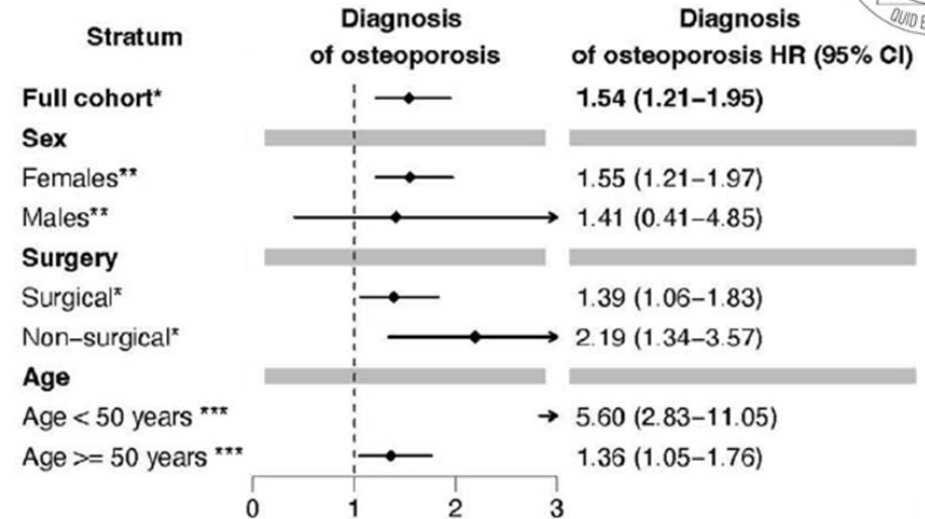
# Ipoparatiroidismo e fratture

Journal of Bone and Mineral Research, 2025, 00, 1–8  
<https://doi.org/10.1093/jbmr/zjaf061>  
 Advance access publication: May 5, 2025  
 Research Article



## Increased risk of vertebral fractures and reduced risk of femur fractures in patients with chronic hypoparathyroidism: a nationwide cohort study in Sweden

Sigrídur Björnsdóttir<sup>1,\*</sup>, Wafa Kamal<sup>1,2</sup>, Michael Mannstadt<sup>3</sup>, Outi Mäkitie<sup>4,5</sup>, Tim Spelman<sup>6</sup>, Olle Kämpe<sup>2,7</sup>, Bente L. Langdahl<sup>8</sup>



**Table 2.** The risk of fractures (HR (95% CI)) in patients with chronic hypoparathyroidism compared to controls.

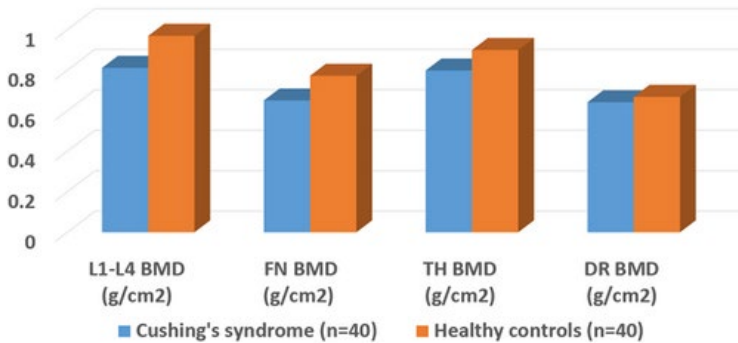
Fractures <sup>a</sup> , n (%)	Cases (n = 1915)	Controls (n = 15 838)	HR (95% CI)	p-value
Vertebral fractures	49 (2.6)	267 (1.7)	1.55 (1.12, 2.14)	.008
Pelvic fractures	11 (0.6)	94 (0.6)	0.92 (0.48, 1.78)	.809
Femur	39 (2.0)	460 (2.9)	0.70 (0.50, 0.98)	.038
Proximal humerus	25 (1.3)	309 (2.0)	0.69 (0.46, 1.06)	.09
Forearm	57 (3.0)	577 (3.6)	0.94 (0.71, 1.25)	.676

<sup>a</sup> Adjusted for comorbidities, age, and sex. Bold values indicate statistical significance ( $p < 0.05$ ).

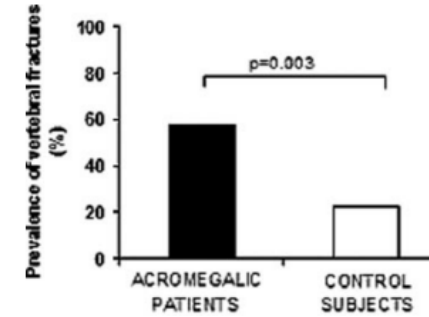
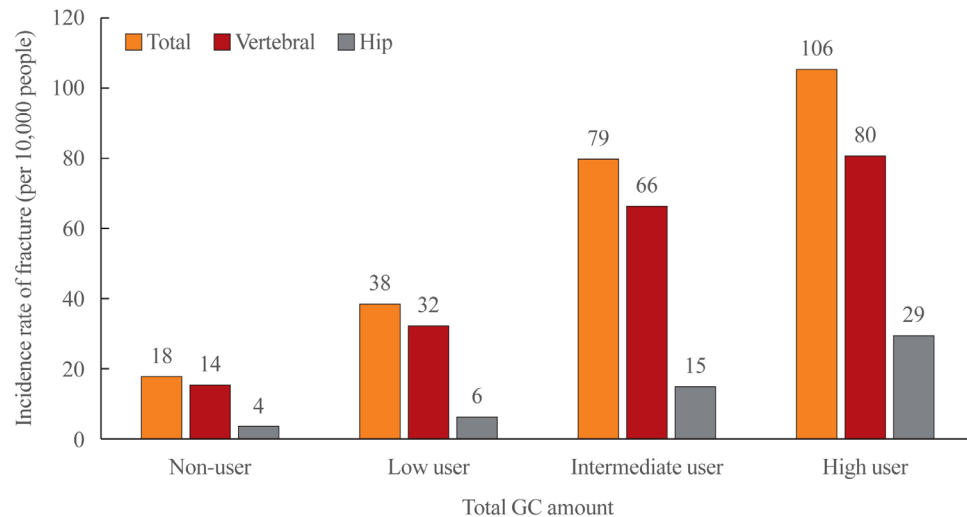
# Fratture e osteoporosi secondarie

## Trabecular bone score and bone mineral density as indices of skeletal fragility in endogenous Cushing's syndrome

Bone Mineral Density (BMD) in endogenous Cushing's syndrome (n=40) vs healthy controls (n=40)

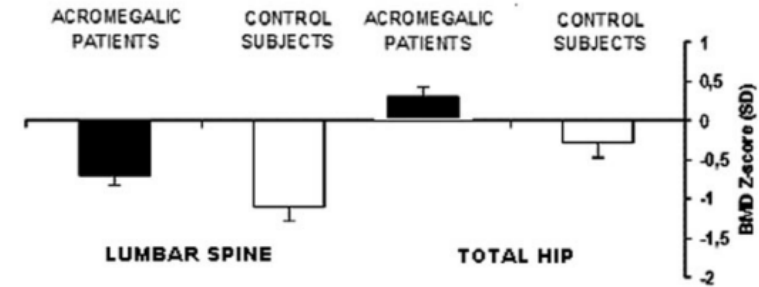


## Effects of Systemic Glucocorticoid Use on Fracture Risk: A Population-Based Study



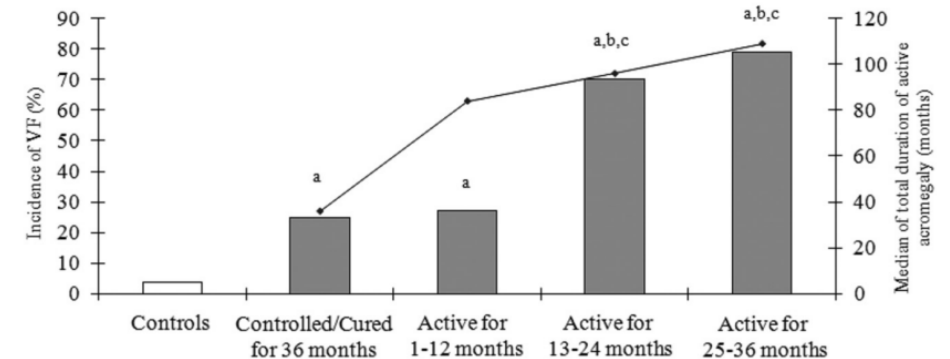
## Prevalence of Vertebral Fractures in Men with Acromegaly

Gherardo Mazziotti, Antonio Bianchi, Stefania Bonadonna, Vincenzo Cimino, Ilaria Patelli, Alessandra Fusco, Alfredo Pontecorvi, Laura De Marinis, and Andrea Giustina



## Vertebral Fractures in Patients With Acromegaly: A 3-Year Prospective Study

G. Mazziotti, A. Bianchi, T. Porcelli, M. Mormando, F. Maffezzoni, A. Cristiano, A. Giampietro, L. De Marinis, and A. Giustina



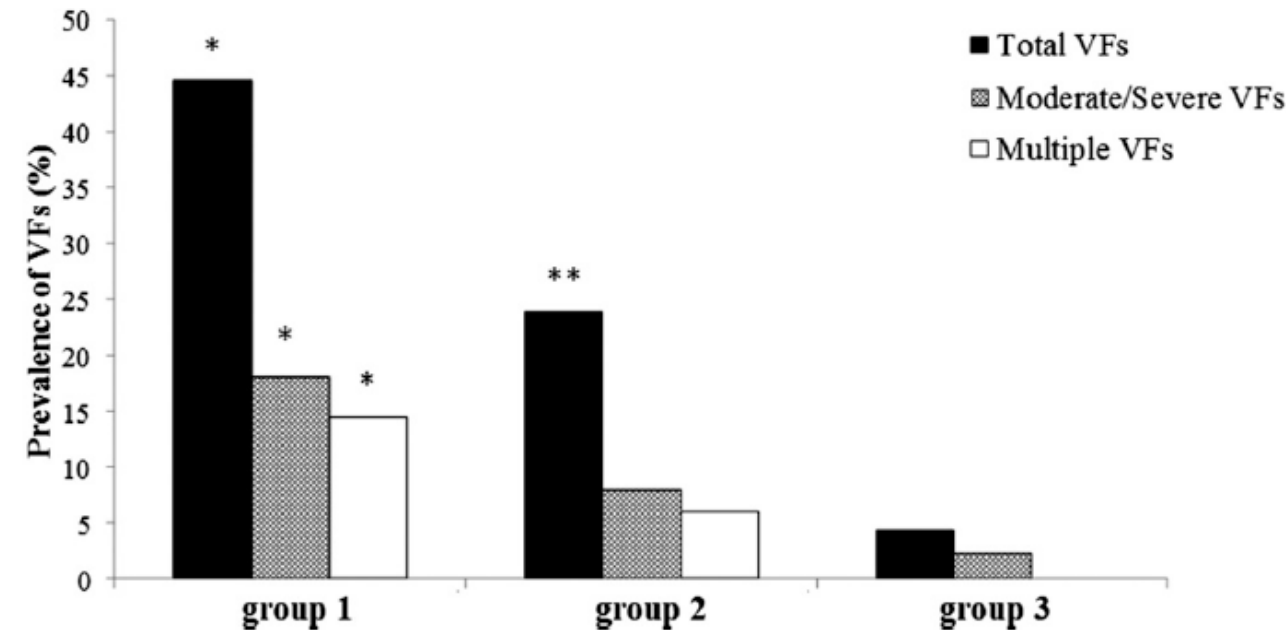
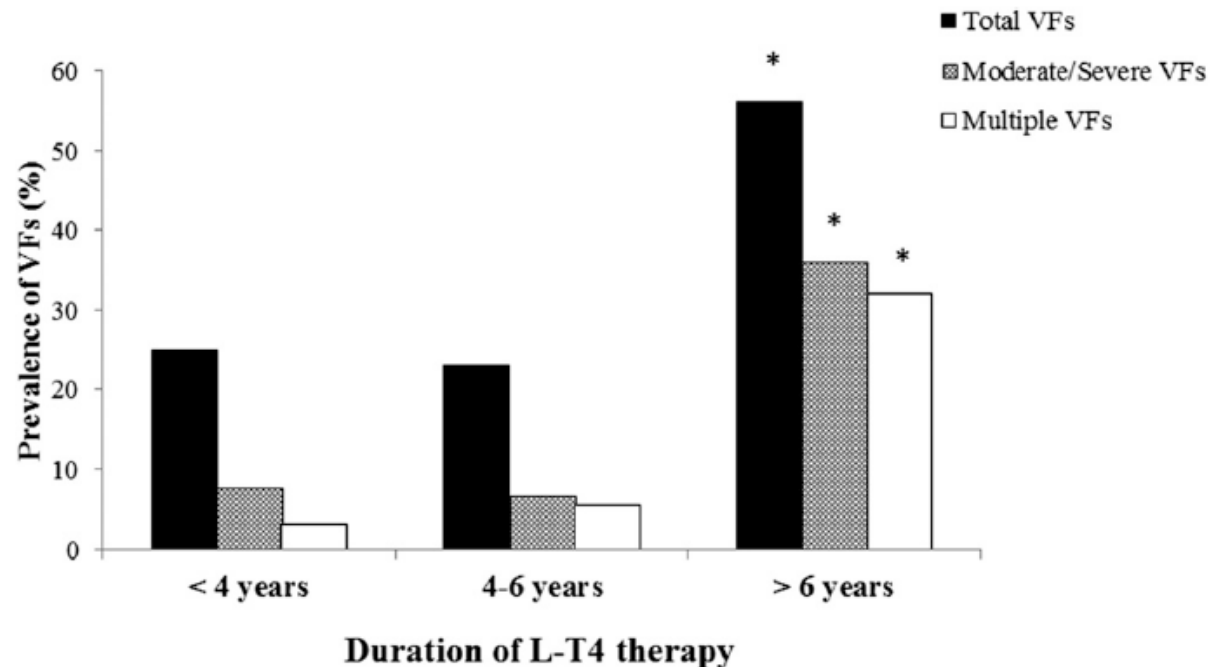
# Fratture e terapia soppressiva

## High Prevalence of Radiological Vertebral Fractures in Women on Thyroid-Stimulating Hormone–Suppressive Therapy for Thyroid Carcinoma

Gherardo Mazziotti,<sup>1</sup> Anna Maria Formenti,<sup>2</sup> Stefano Frara,<sup>3</sup> Roberto Olivetti,<sup>1</sup> Giuseppe Banfi,<sup>4,5</sup> Maurizio Memo,<sup>2</sup> Roberto Maroldi,<sup>6</sup> Raffaele Giubbini,<sup>7</sup> and Andrea Giustina<sup>3</sup>

**Table 2. Results of Multivariate Logistic Regression Analysis, Using Total VFs as the Dependent Variable**

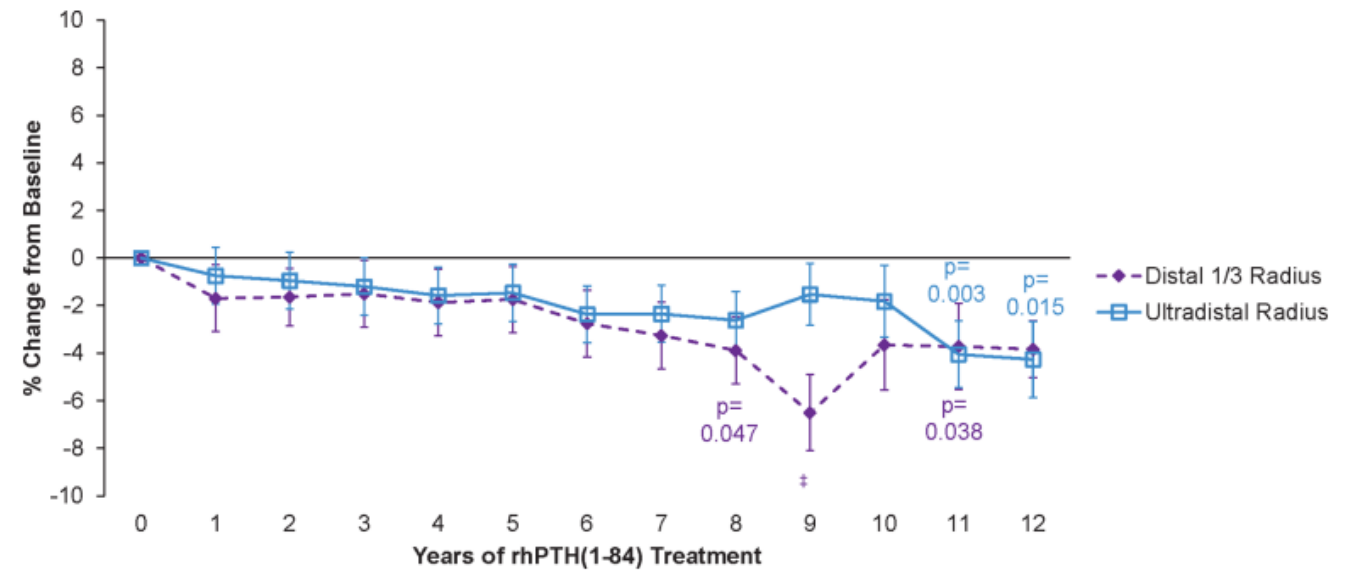
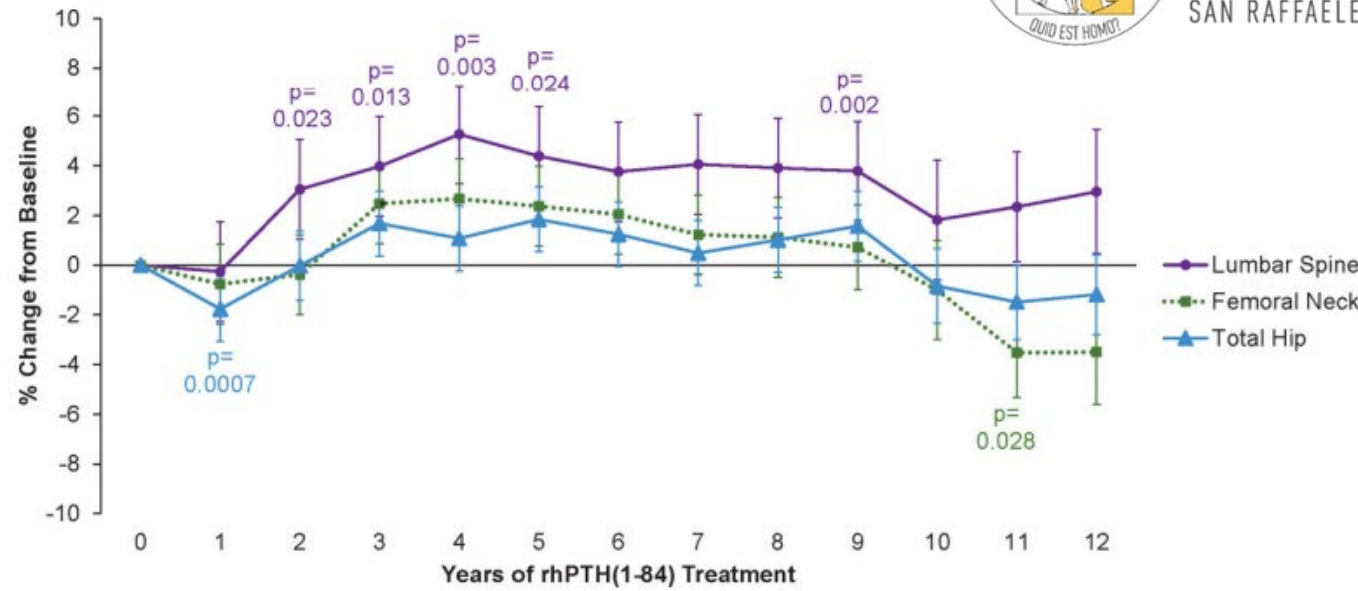
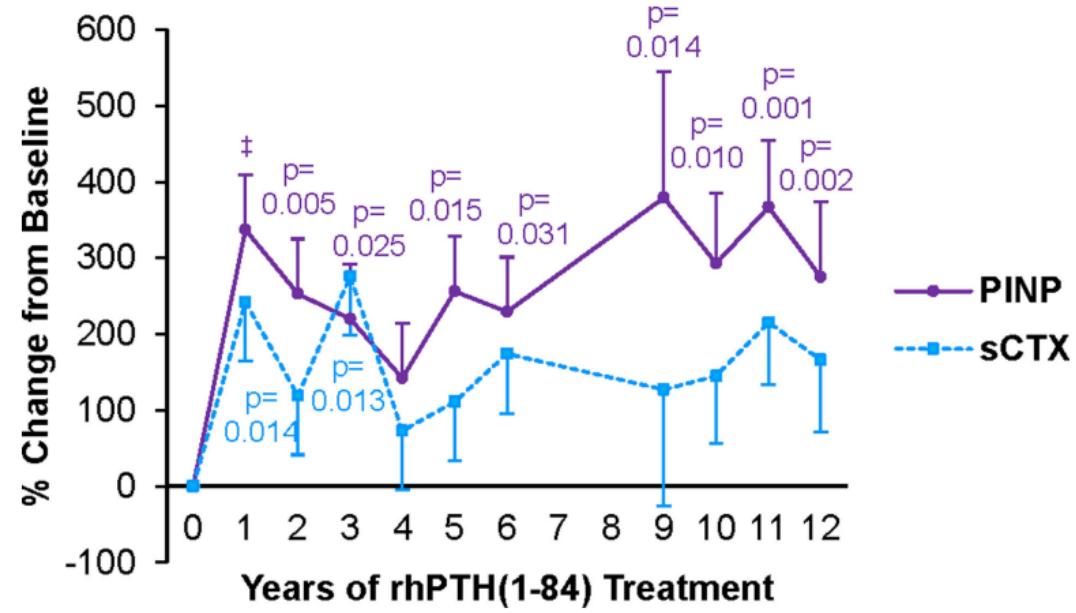
	Odds Ratio	95% CI	P Value
Age	1.08	1.02–1.14	0.01
Osteoporosis	3.64	1.01–13.25	0.05
L-T4 dose	0.97	0.96–1.01	0.06
Duration of L-T4 therapy	1.12	1.02–1.23	0.02
TSH <0.5 mU/L	25.04	2.62–238.88	0.005
TSH 0.5–1.0 mU/L	10.38	1.67–64.45	0.01
Serum FT4 value	0.99	0.77–1.26	0.92
RAI therapy	3.35	0.59–18.97	0.17
Treatment with vitamin D3 plus calcium	0.65	0.42–1.02	0.06



# PTH (1-84) ed effetti ossei

## The Clinical and Skeletal Effects of Long-Term Therapy of Hypoparathyroidism with rhPTH(1-84)

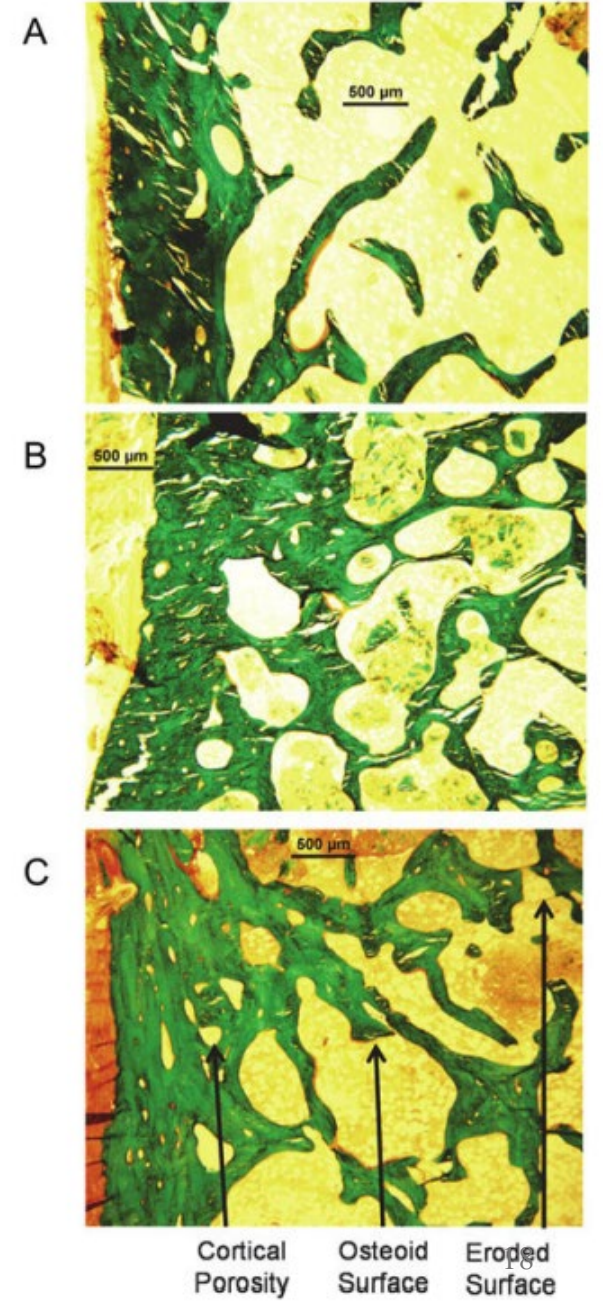
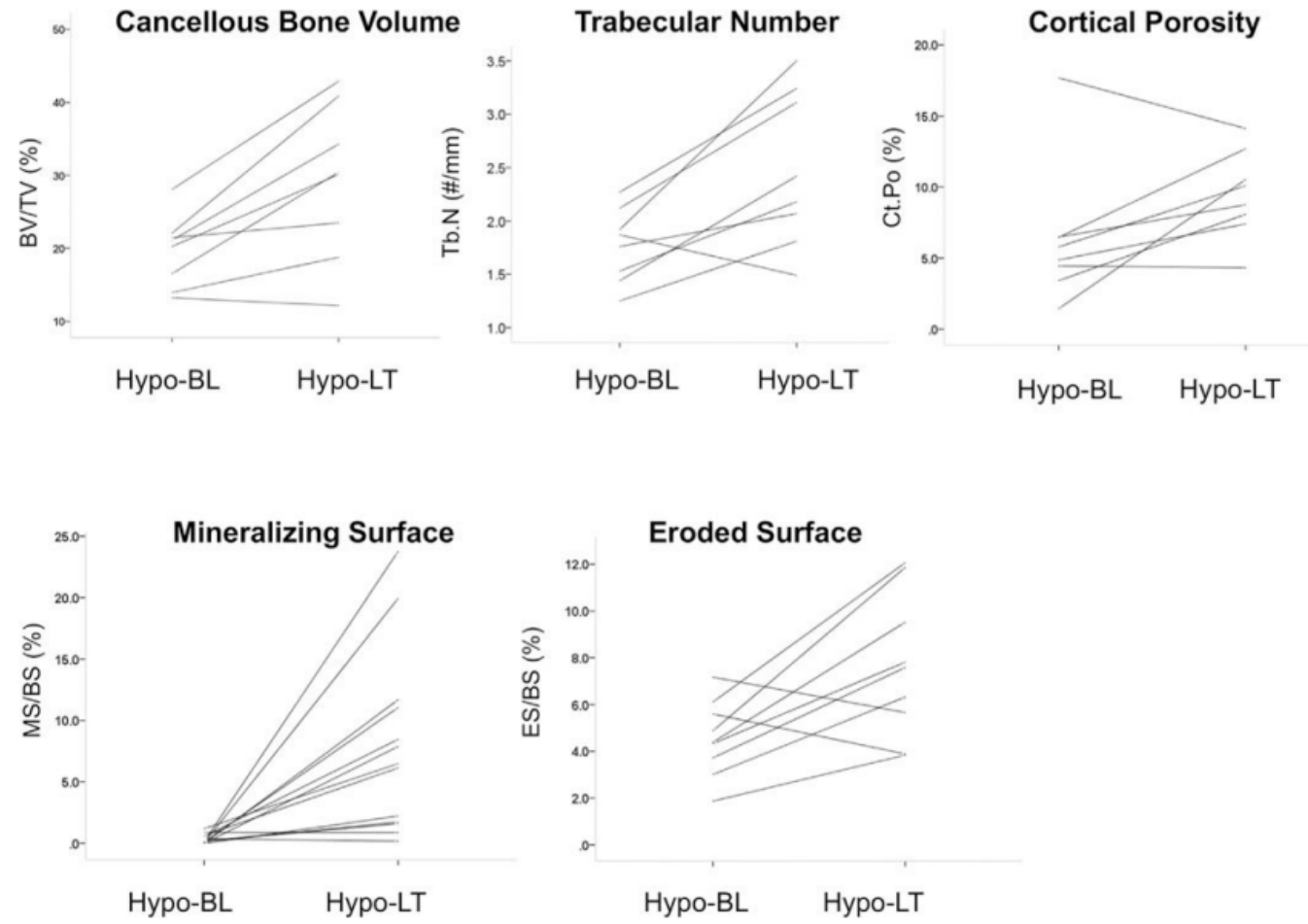
Sanchita Agarwal<sup>1</sup>, Donald J. McMahon<sup>1</sup>, Juliet Chen<sup>2</sup>, Aiden Crossfield<sup>1</sup>, Jason Fernando<sup>1</sup>, John P. Bilezikian, MD<sup>1</sup>, Natalie E. Cusano, MD<sup>3</sup>, Mishaela R. Rubin, MD<sup>1</sup>



# PTH (1-84) ed effetti ossei

## The Effects of Long-term Administration of rhPTH(1-84) in Hypoparathyroidism by Bone Histomorphometry

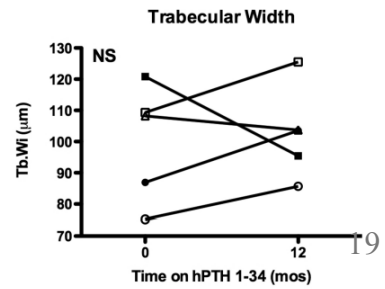
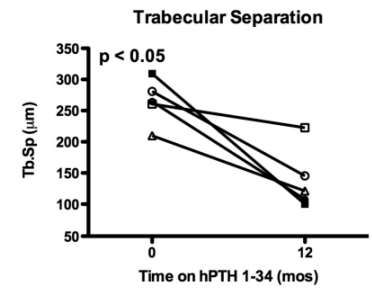
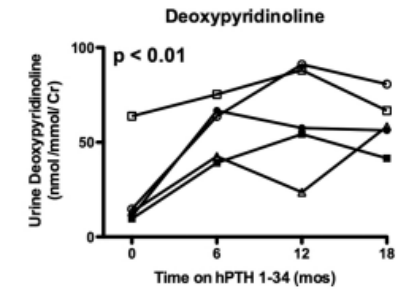
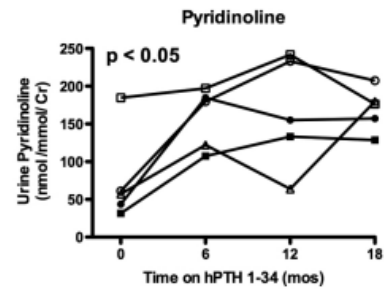
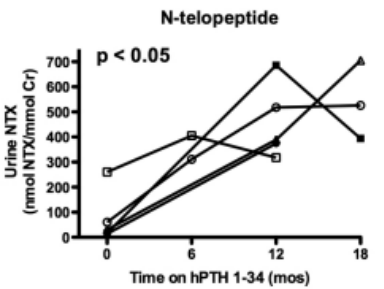
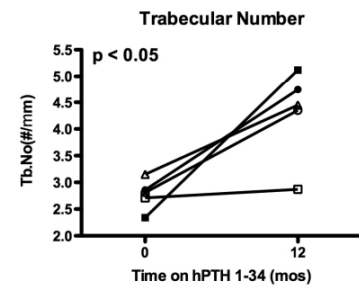
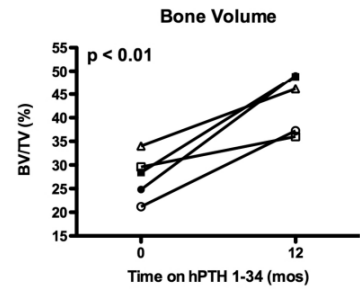
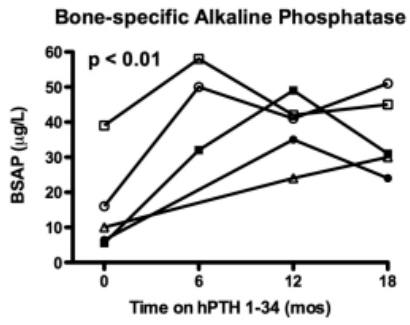
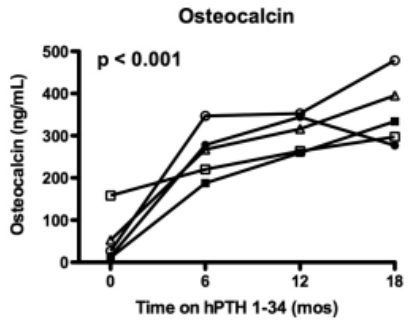
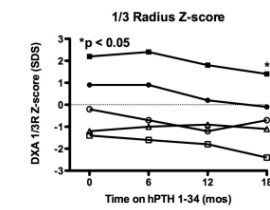
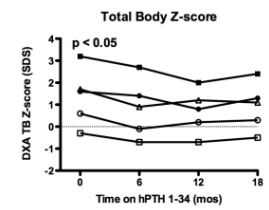
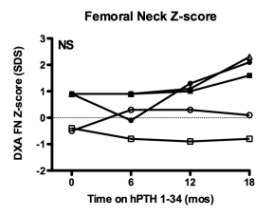
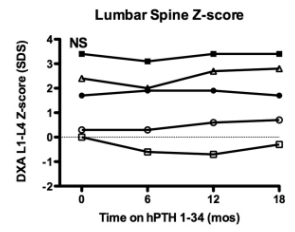
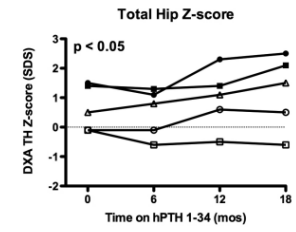
Mishaela R Rubin<sup>1</sup>, Hua Zhou<sup>2</sup>, Natalie E Cusano<sup>1</sup>, Rukshana Majeed<sup>1</sup>, Beatriz Omeragic<sup>1</sup>, Maximo Gomez<sup>1</sup>, Thomas L Nickolas<sup>1</sup>, David W Dempster<sup>2,3</sup>, and John P Bilezikian<sup>1</sup>



# Teriparatide PTH (1-34) ed effetti ossei

## Daily Parathyroid Hormone 1-34 Replacement Therapy for Hypoparathyroidism Induces Marked Changes in Bone Turnover and Structure

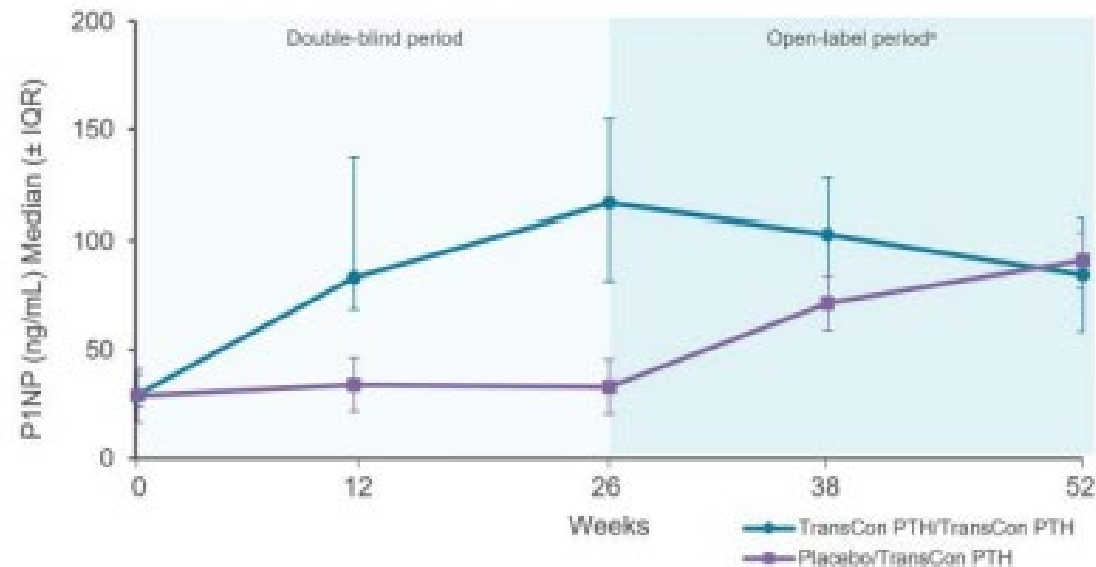
Rachel I. Gafni, MD<sup>1</sup>, Jaime S. Brahim, DDS, MS<sup>2</sup>, Panagiota Andreopoulou, MD<sup>3</sup>, Nisan Bhattacharyya, PhD<sup>1</sup>, Marilyn H. Kelly, RN, MSN<sup>1</sup>, Beth A. Brillante, RN, MBA<sup>1</sup>, James C. Reynolds, MD<sup>4</sup>, Hua Zhou, MD<sup>5</sup>, David W. Dempster, PhD<sup>5</sup>, and Michael T. Collins, MD<sup>1</sup>



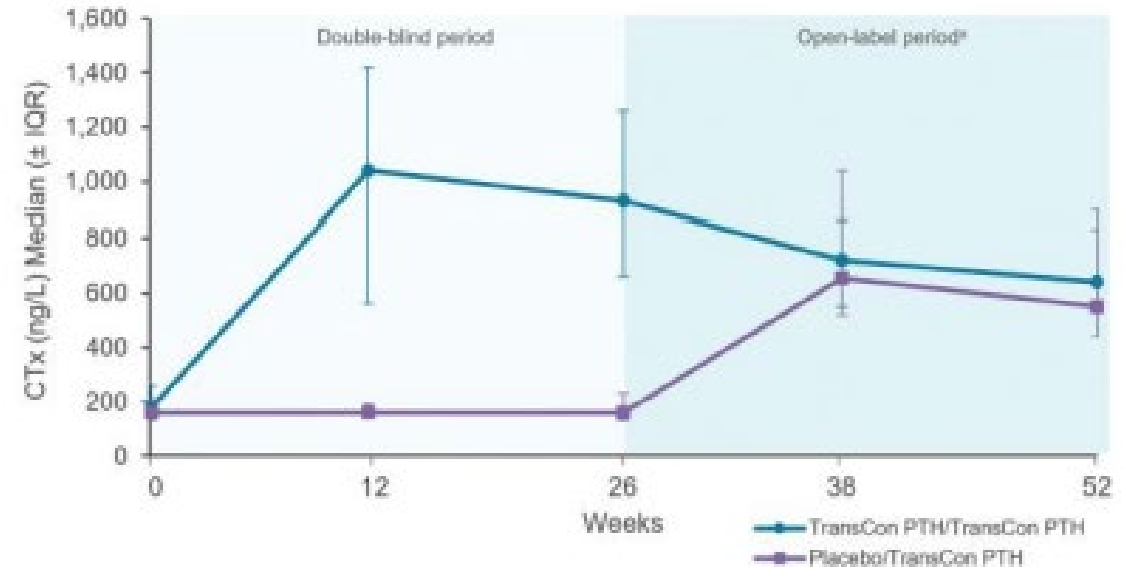
## Efficacy and Safety of TransCon PTH in Adults With Hypoparathyroidism: 52-Week Results From the Phase 3 PaTHway Trial

Bart L. Clarke,<sup>1</sup> Aliya A. Khan,<sup>2</sup> Mishaela R. Rubin,<sup>3</sup> Peter Schwarz,<sup>4</sup> Tamara Vokes,<sup>5</sup> Dolores M. Shoback,<sup>6</sup> Claudia Gagnon,<sup>7,8</sup> Andrea Palermo,<sup>9,10</sup> Lisa G. Abbott,<sup>11,12</sup> Lorenz C. Hofbauer,<sup>13</sup> Lynn Kohlmeier,<sup>14</sup> Filomena Cetani,<sup>15</sup> Susanne Pihl,<sup>16</sup> Xuebei An,<sup>17</sup> Alden R. Smith,<sup>18</sup> Bryant Lai,<sup>19</sup> Jenny Ukena,<sup>19</sup> Christopher T. Sibley,<sup>19</sup> Aimee D. Shu,<sup>19</sup> and Lars Rejnmark<sup>20</sup>

### A Procollagen Type 1 N-Terminal Propeptide (P1NP)



### B C-Terminal Telopeptide of Type 1 Collagen (CTx)



## Long-term efficacy and safety of palopegteriparatide treatment in adults with chronic hypoparathyroidism: 4-year results from the phase 2 path forward trial

[Andrea Palermo](#)<sup>1</sup>, [Aliya Khan](#)<sup>2</sup>, [Mishaela Rubin](#)<sup>3</sup>, [Peter Schwarz](#)<sup>4</sup>, [Bart L. Clarke](#)<sup>5</sup>, [Uberto Pagotto](#)<sup>6</sup>, [Elena Tsourdi](#)<sup>7</sup>, [Filomena Cetani](#)<sup>8</sup>, [Rajesh Jain](#)<sup>9</sup>, [Carol Zhao](#)<sup>10</sup>, [Michael Ominsky](#)<sup>10</sup>, [Bryant Lai](#)<sup>10</sup>, [Jenny Ukena](#)<sup>10</sup>, [Christopher Sibley](#)<sup>10</sup>, [Aimee Shu](#)<sup>10</sup> & [Lars Rejnmark](#)<sup>11</sup>

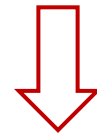
Mean CTx and P1NP increased from the low end of normal at baseline, peaked by week 26, and declined thereafter and remained stable above baseline levels through week 214.

The elevated baseline mean BMD Z-scores trended towards age- and sex-matched norms at the lumbar spine, femoral neck, and total hip and largely stabilized after 26 weeks of treatment, remaining above zero through week 214.

Changes in Z-scores were larger in participants with longer duration of hypoparathyroidism but were similar across the population when considering sex and age/menopausal status.

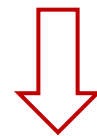
# Conclusioni

- Dati istomorfometrici rilevano un impatto soprattutto a carico dell'osso trabecolare
- Osso dinamico: ridotto turnover e rimodellamento



Come valutare l'impatto osseo nell'ipoPTH?

- BTMs di neoformazione e riassorbimento → ridotti
- Quali tools diagnostici:
  - BMD sottostima il danno?
  - Pochi dati sulla qualità dell'osso
  - Morfometria vertebrale → ruolo centrale



Qual è l'impatto delle nuove terapie sostitutive sull'osso?

- Riattivazione costante e sostenuta dei marker di rimodellamento osseo
- Non ancora noto impatto su rischio fratturativo

# Ringraziamenti



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