

Innovazione organizzativa
nei percorsi di diagnosi,
cura, follow-up

Focus on
IPOPARIROIIDISMO

REGIONE EMILIA-ROMAGNA

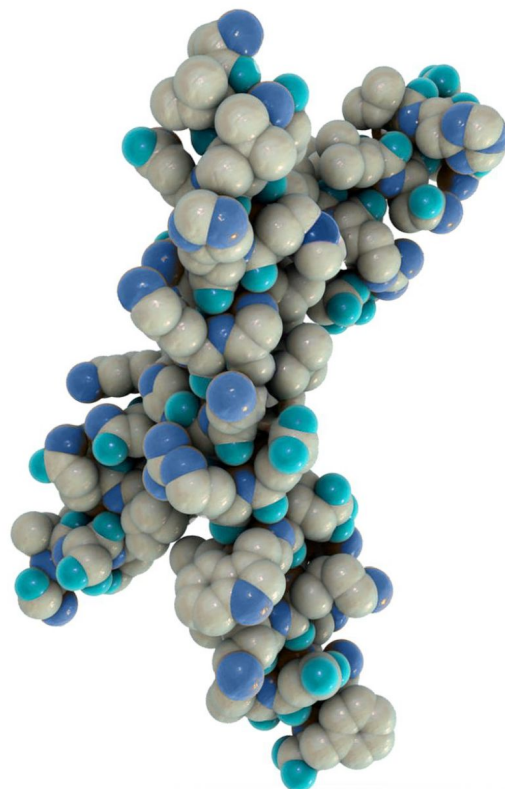


BOLOGNA

STARHOTELS EXCELSIOR
V.le Pietro Pietramellara, 51



19 GIUGNO 2025
dalle 10.00 alle 13.30



Ipoparatiroidismo oggi

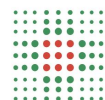
**Epidemiologia regionale, burden
socio-sanitario, cutting edge della ricerca e
prospettive di cura**

Dott. Guido Zavatta

**UOC Endocrinologia e Prevenzione e Cura del Diabete
– Prof. Pagotto
IRCCS AOU Bologna**



ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA



SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA

Azienda Ospedaliero - Universitaria di Bologna

IRCCS Istituto di Ricovero e Cura a Carattere Scientifico

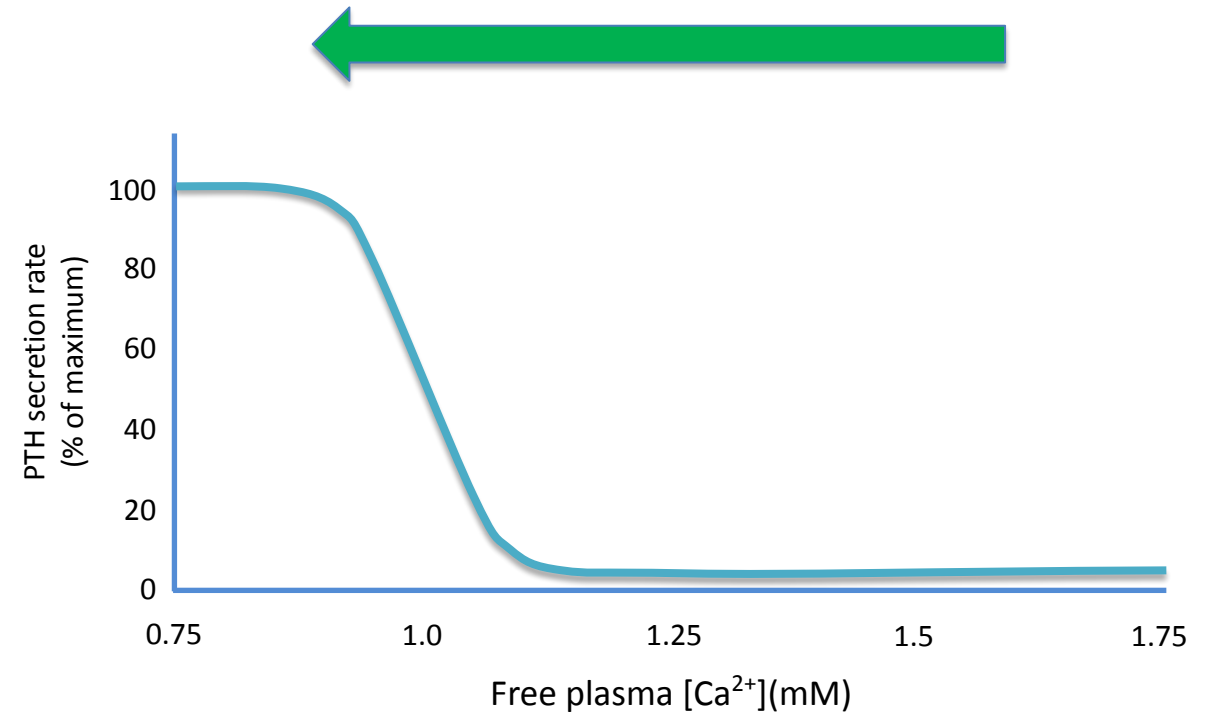
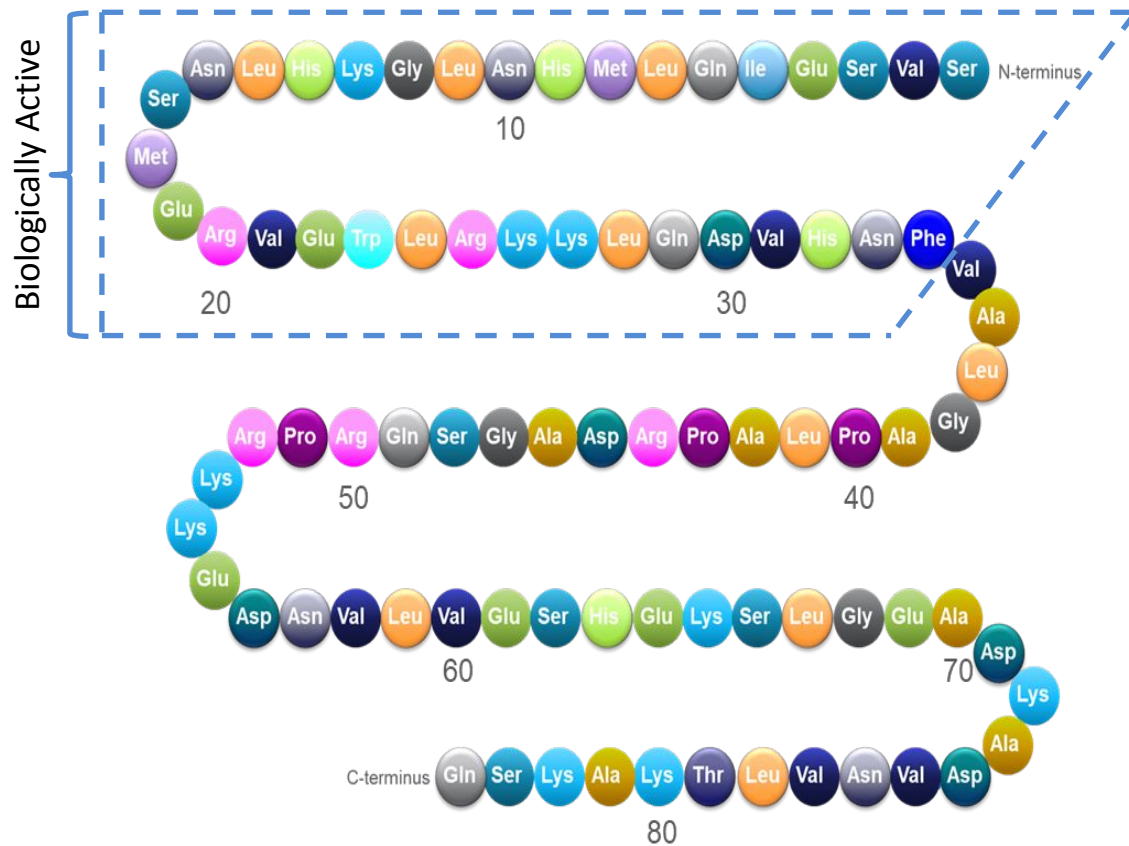
POLICLINICO DI **SANT'ORSOLA**

Una malattia in un certo senso invisibile

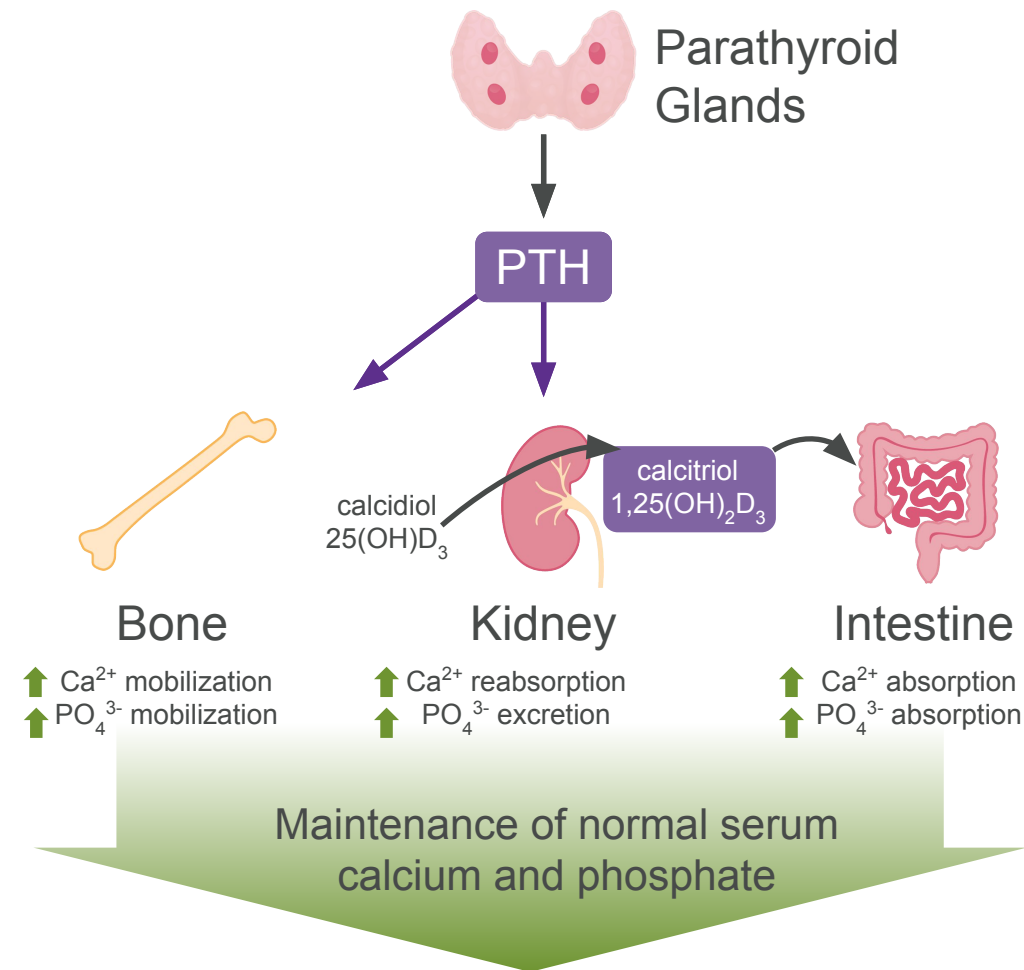
- *Anna, 32 anni. “Ogni giorno prendo 12 pillole tra calcio e supplementi vari. Ho crampi, ansia, e non riesco a guidare. Se dormo con una mano sotto il cuscino sento sempre le formiche. Quasi nessuno conosce la mia malattia.”*
- L'ipoparatiroidismo è una malattia rara e cronica
- Malattia rara: poco conosciuta
- Sintomi spesso sottovalutati o attribuiti ad altro
- La malattia 'passa in secondo piano' rispetto ad altre malattie più conosciute

Cosa è il PTH o paratormone

PTH (secreted) 84 residues



Cosa fa il paratormone

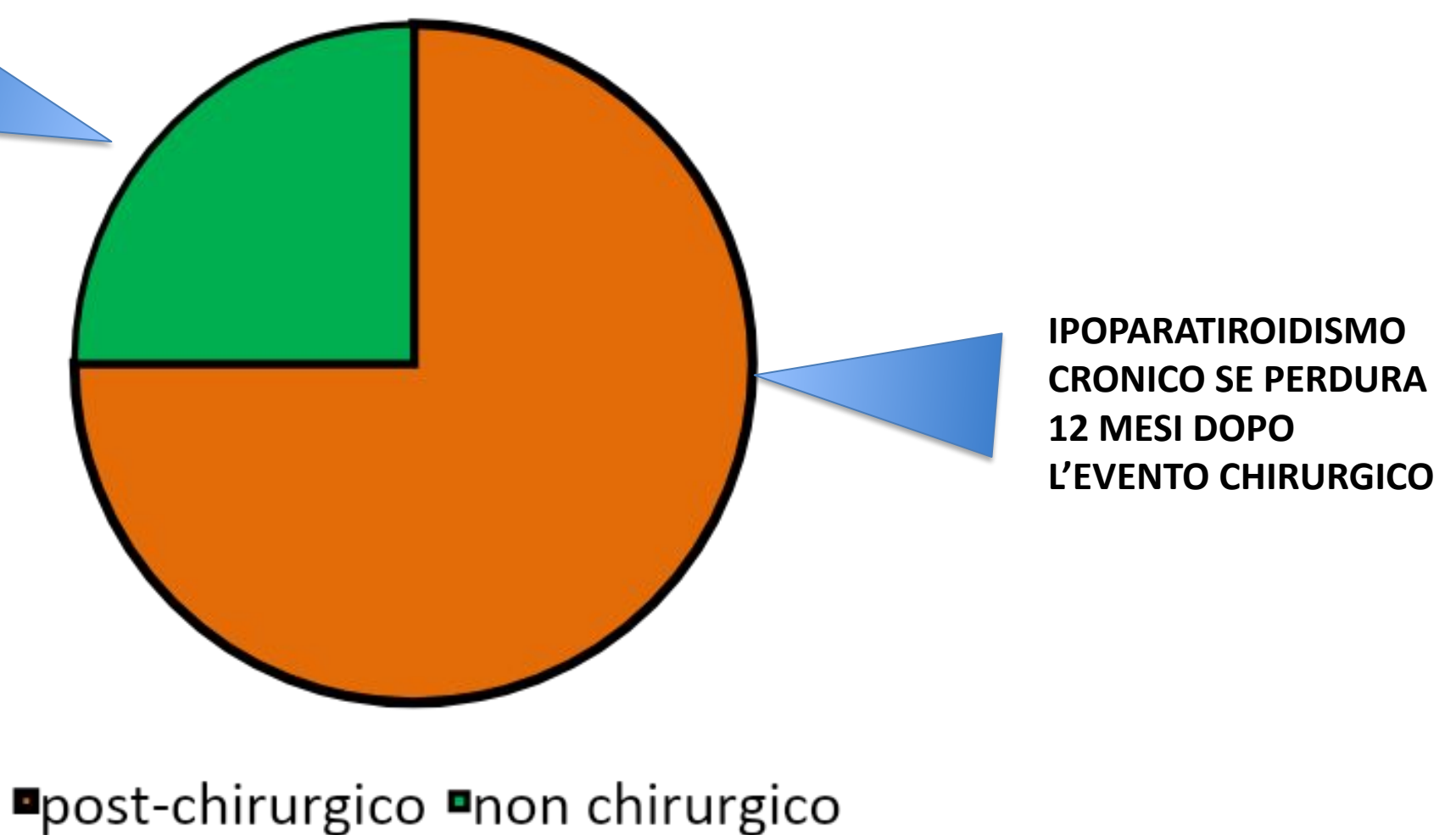


Cos'è l'ipoparatiroidismo

- Deficit di PTH (ormone paratormone)
- Sconvolge l'equilibrio calcio-fosforo

Perché ci si ammala di ipoparatiroidismo?

Di una quota non si
conosce ancora la causa



IPOPARI TIROIDISMO

Epidemiologia regionale



Ipoparatiroidismo: prevalenza europea

Hypoparathyroidism

rare endocrine disease caused by insufficient levels of parathyroid hormone (PTH)

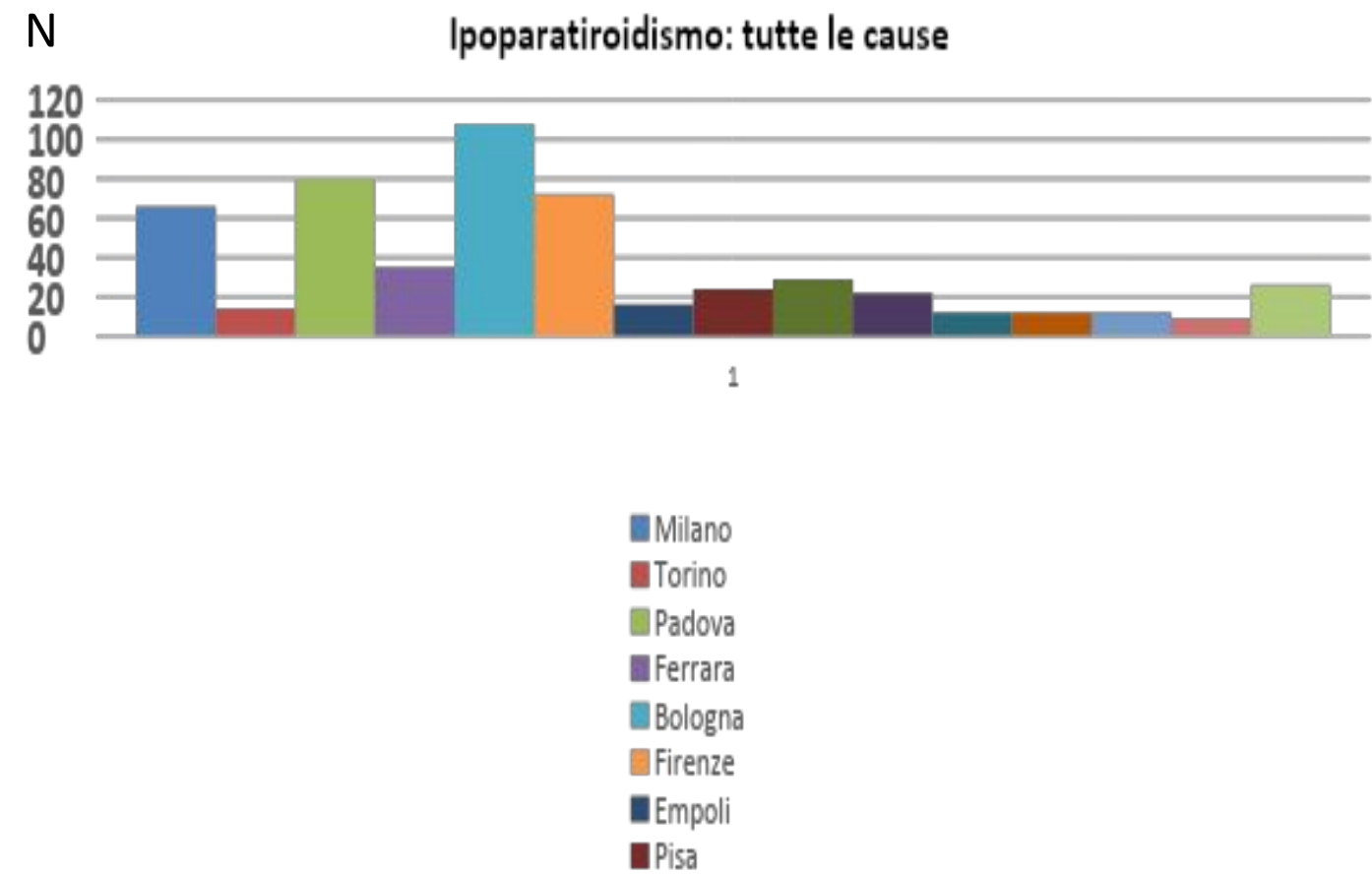


Estimated Prevalence in the EU

3.1 in 10,000 individuals

Prevalence estimated from targeted literature review of EU published studies utilizing case ascertainment methodology and combining separate metanalysis for both non-surgical and post-surgical hypoparathyroidism.

Epidemiologia: Italia



N=509



16 centri italiani

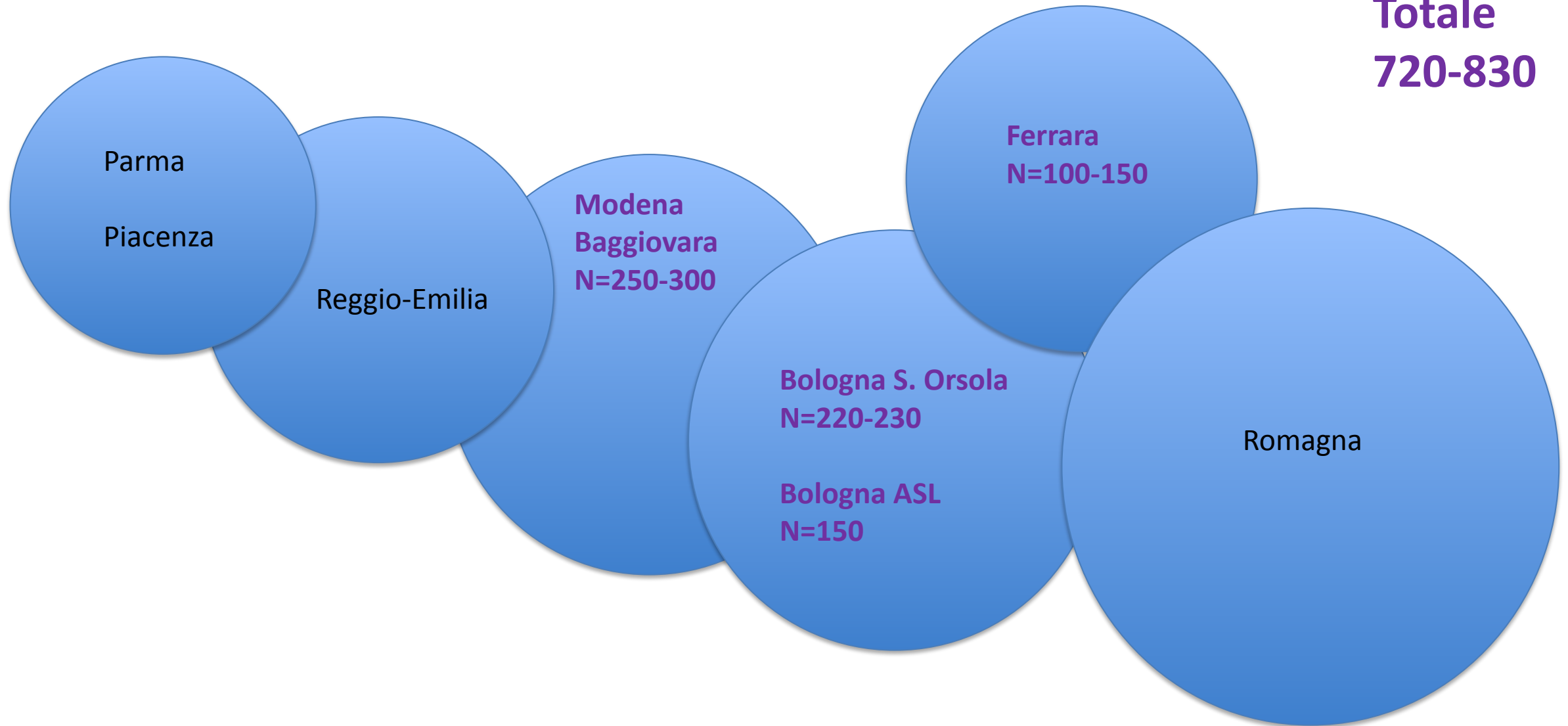


27.1%

Focus Emilia-Romagna

- **Emilia-Romagna: ~4,5 milioni abitanti**
- **Stima proporzionale: 750–1.200 pazienti**
- **EXPERTISE:** aziende ospedaliere, aziende ospedaliero-universitarie

Focus Emilia-Romagna: quanti pazienti?



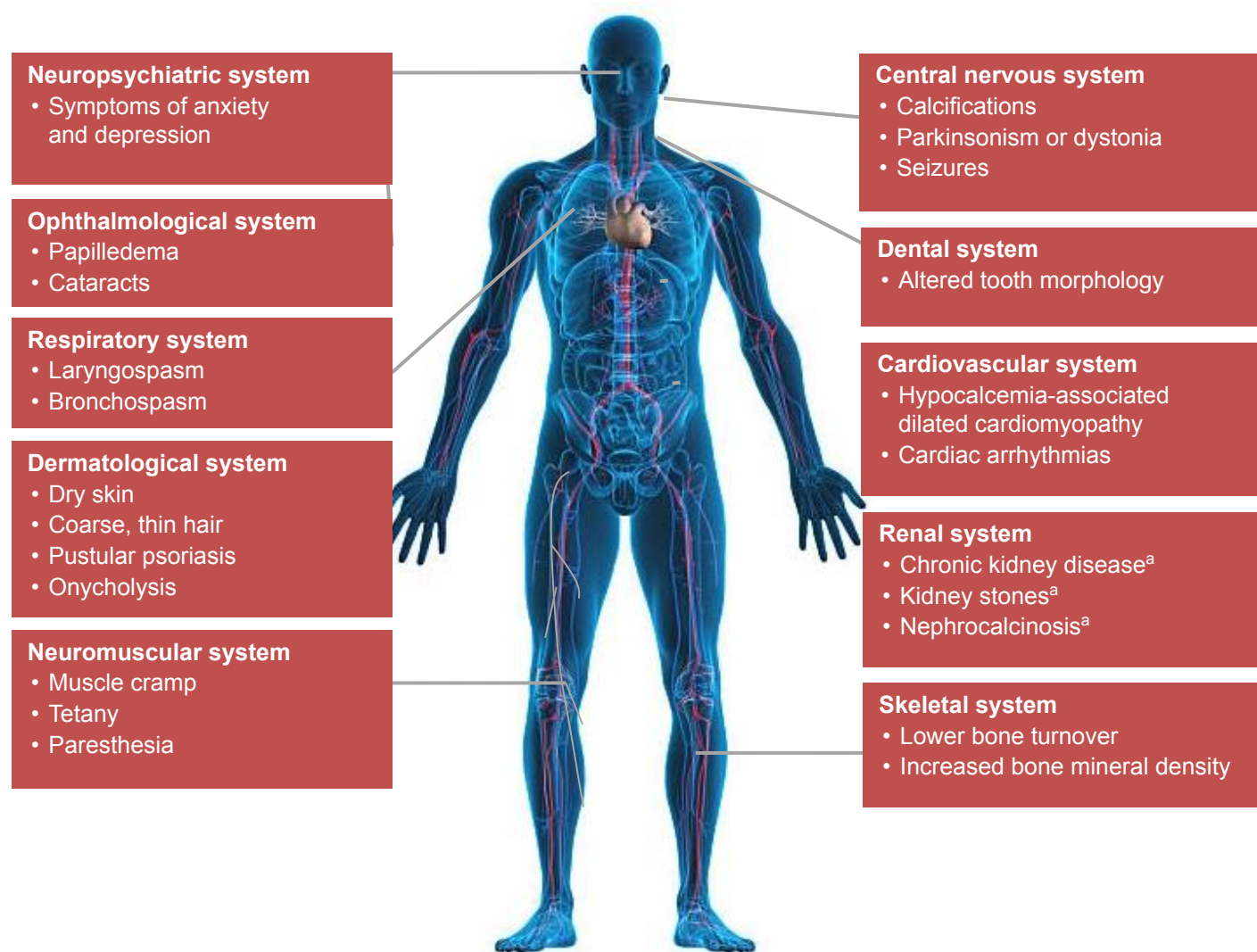
IPOPARIROIDISMO

Burden socio-sanitario

Differenze (?)

	Ipoparatiroidismo non-chirurgico	Ipoparatiroidismo post-chirurgico
Età di insorgenza	MINORE	MAGGIORE
Esposizione all'ipocalcemia	MAGGIORE	MINORE
Durata di malattia	MAGGIORE	MINORE
Durata della terapia convenzionale	MAGGIORE	MINORE
Complicanze	Probabilmente maggiori	Probabilmente minori

Manifestazioni cliniche: carenza di PTH + terapia convenzionale



1. Mannstadt M, et al. Nat Rev Dis Primers. 2017;3:17055.
2. Bilezikian JP, et al. J Bone Miner Res. 2011;26(10):2317-2337

Complicanze dell'ipoparatiroidismo

	Postsurgical	Non-surgical	
Mortality	0.98 (0.76–1.26)	1.25 (0.90–1.73)	No difference to controls
Renal insufficiency	3.10 (1.73–5.55)*	6.01 (2.45 - 14.75)*	Increased risk to controls
Nephrolithiasis	4.02 (1.64–9.90)*	0.80 (0.17–3.85)	Reduced risk to controls
Ischemic heart disease	1.09 (0.83–1.45)	2.01 (1.31–3.09)*	Increased risk to controls
Stroke	1.09 (0.73–1.64)	1.84 (0.95–3.54)	No difference to controls
Arrhythmia	1.11 (0.79–1.57)	1.78 (0.96–3.30)	No difference to controls
Seizures	3.8 (2.2–6.8)*	10.05 (5.39–18.72)*	Increased risk to controls
Cataract	1.17 (0.66–2.09)	4.21 (2.13–8.34)*	Increased risk to controls
Neuropsychiatric	2.01 (1.16–3.50)*	2.45 (1.78–3.35)*	Increased risk to controls
Infections	1.42 (1.20–1.67)*	1.94 (1.55–2.44)*	Increased risk to controls
Fractures	1.03 (0.83–1.29)	1.40 (0.93–2.11)	No difference to controls
Any cancer	0.83 (0.61–1.13)	0.44 (0.24–0.82)*	Reduced risk to controls
GI cancer	0.62 (0.42–0.92)*	0.29 (0.07–1.25)	Reduced risk to controls

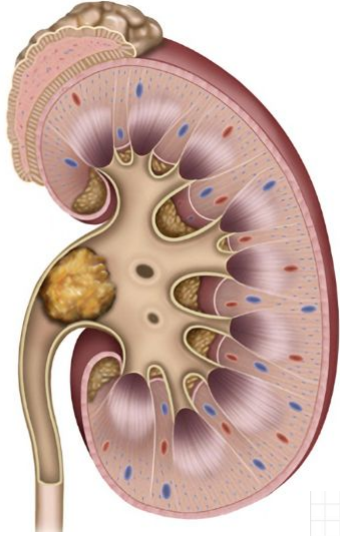
* P < 0.05

GI, gastrointestinal

1. Underbjerg L, et al. *J Bone Miner Res.* 2013;28:2277-2285;
2. Underbjerg L et al. *J Bone Miner Res.* 2014; 29 (11): 2504–2510;
3. Underbjerg L et al. *J Bone Miner Res.* 2015; 30(9):1738-44.

Hazard ratio (95% confidence interval)

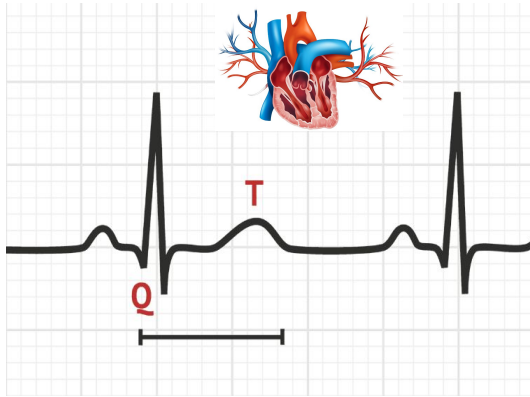
Rischio di complicanze (HR) rispetto alla popolazione generale: organi bersaglio



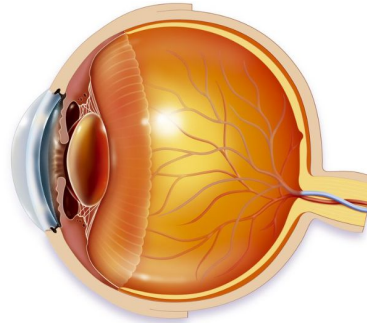
IRC: 3,67

Nefrolitiasi/
Nefrocalcinosi: 1,88

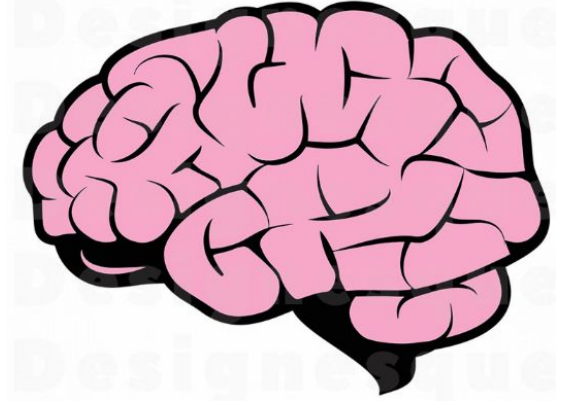
Ipoparatiroidismo cronico



Aritmie: 1,37
Cardiopatia
ischemica: 1,26



Cataratta: 2,13



Crisi convulsiva: 3,22
Depressione: 1,89

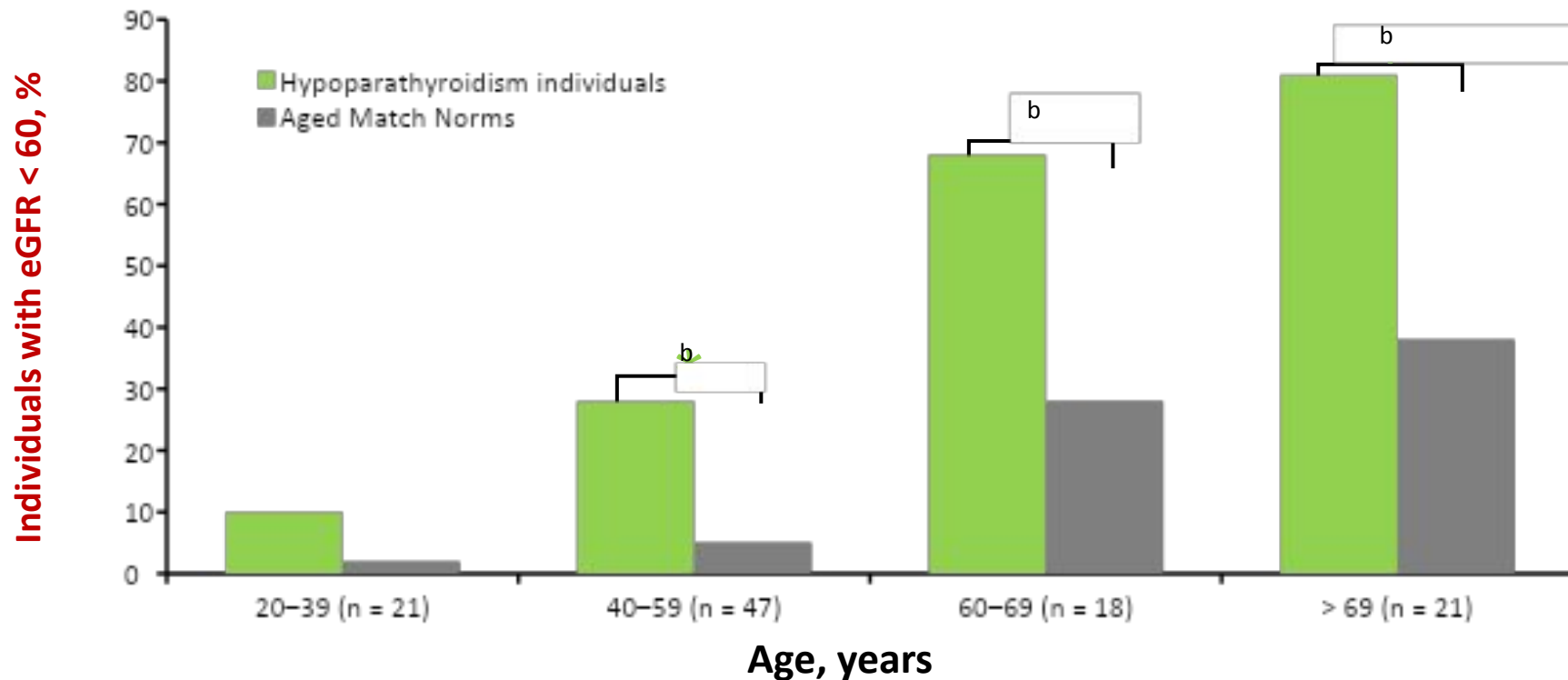


Infezioni: 2,30

(++urinarie e
respiratorie)

Ipoparatiroidismo e rischio di malattia renale

A chart review of 120 patients was conducted to evaluate serum and urine laboratory results and renal and brain imaging via a clinical patient data registry in individuals with permanent hypoparathyroidism. **41% of the individuals had an eGFR of 60 ml/min ·1.73m² or below consistent with chronic kidney disease stage 3 or higher¹**



Individuals with chronic hypoparathyroidism receiving long-term treatment with conventional therapy may have an increased risk of renal complications²

eGFR, estimated glomerular filtration rate

^aExcludes individuals < 18 years of age and those with previous renal transplant (n=13) leaving a final group of 107 individuals.

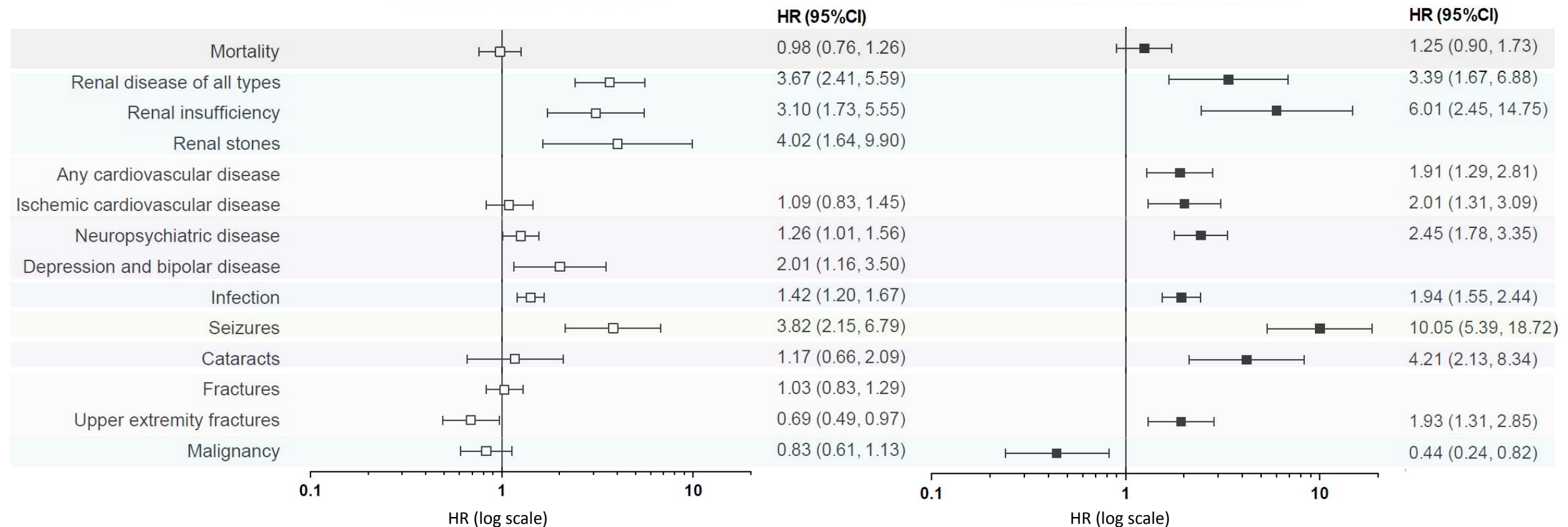
^bP<0.001 for comparison by one-sample t test

1. Mitchell DM, et al. *J Clin Endocrin Metab.* 2012;97:4507-4514. 2. Gosmanova EO, et al. *Endocr Metab Disord.* 2021;22(2):297-316..

Rischio di ospedalizzazione per complicanza

Postsurgical hypoparathyroidism

Nonsurgical hypoparathyroidism



Underbjerg L, et al. *J Bone Miner Res.* 2013;28(11):2277-2285.

Underbjerg L, et al. *J Bone Miner Res.* 2014;29(11):2504-2510. 3. Underbjerg L, et al. *J Bone Miner Res.* 2015;30(9):1738-1744.

Complicanze dell'ipoparatiroidismo - Italia

	Complications	HypoPT (14,579 hospitalizations)
➡	Cardiovascular disease	OR 2 (95% CI 1.6–2.5)
➡	Cancer	OR 40 (95% CI 31.8–52.6)
➡	Infection	In women only: OR 1.3 (95% CI 1.1–1.6)
➡	Renal failure	OR 48 (95% CI 24.5–94.7)
	Psychiatric disease	OR 0.13 (95% CI 0.1–0.2)
	Upper airway tract infections and pneumonia	OR 0.2 (95% CI 0.1–0.3)
➡	Seizures	OR 1.6 (95% CI 1.4–1.9)
➡	Nephrolithiasis	OR 1.6 (95% CI 1.1–2.4)
➡	Cognitive impairment	In women only: OR 2.3 (95% CI 1.19)
	Skin	OR 0.3 (95% CI 0.2–0.4)

Ma tra tutte le complicanze?.....

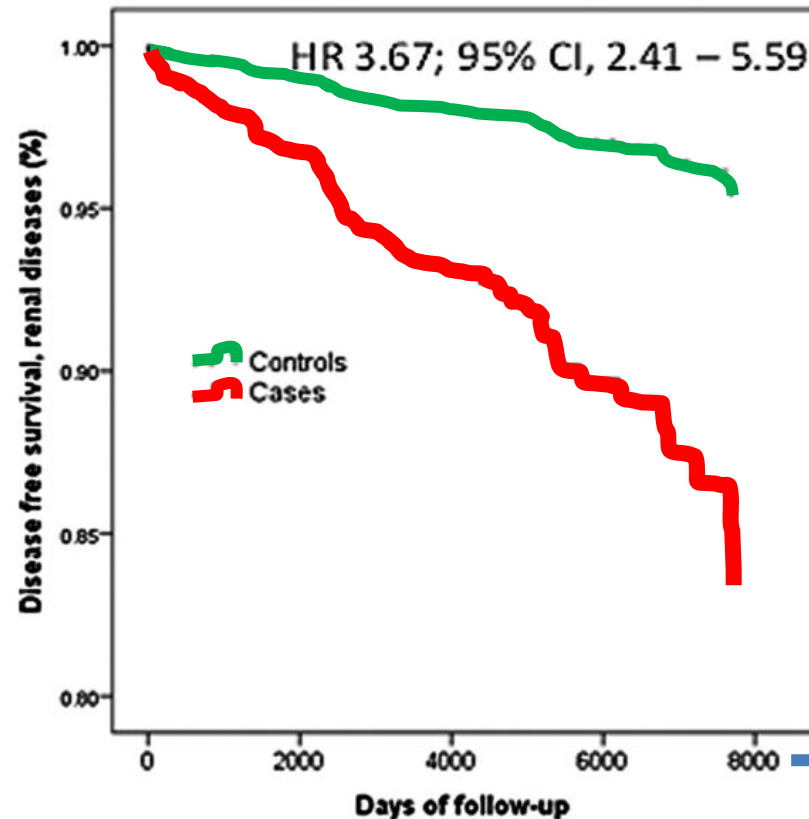


Renal insufficiency	5 ^(12-14,18,20)	9264/45,253	6.22 (5.74–6.74)	3.67 (2.44–5.52)
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Yao et al. JBMR 2022

Rischio inaccettabile!

Ipoparatiroidismo
post-chirurgico da
cause non
maligne



Rischio di
ospedalizzazione per
IR o nefrolitiasi

(R aggiustato per DM
o precedente
nefropatia)

8000/365 =
21 anni

ORIGINAL ARTICLE

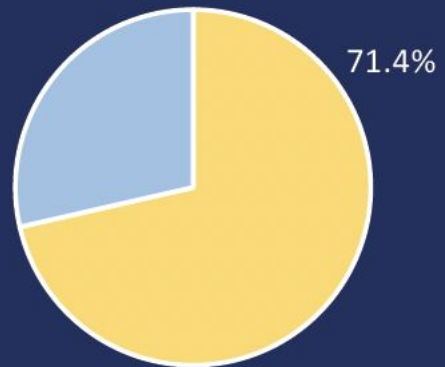
JBMR®

2013

Cardiovascular and Renal Complications to
Postsurgical Hypoparathyroidism: A Danish
Nationwide Controlled Historic Follow-Up Study

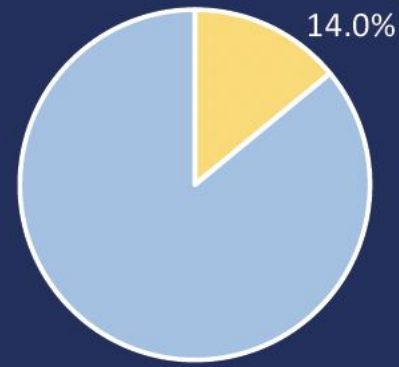
Line Underbjerg, Tanja Sikjaer, Leif Mosekilde, and Lars Rejnmark
Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Tage Hansens Gade (THG), Aarhus, Denmark

Non-Surgical
Hypoparathyroidism



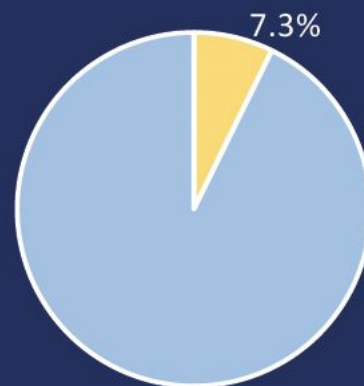
n = 20/28

Post-Surgical
Hypoparathyroidism



n = 16/114

Age- and Sex-
Matched Controls

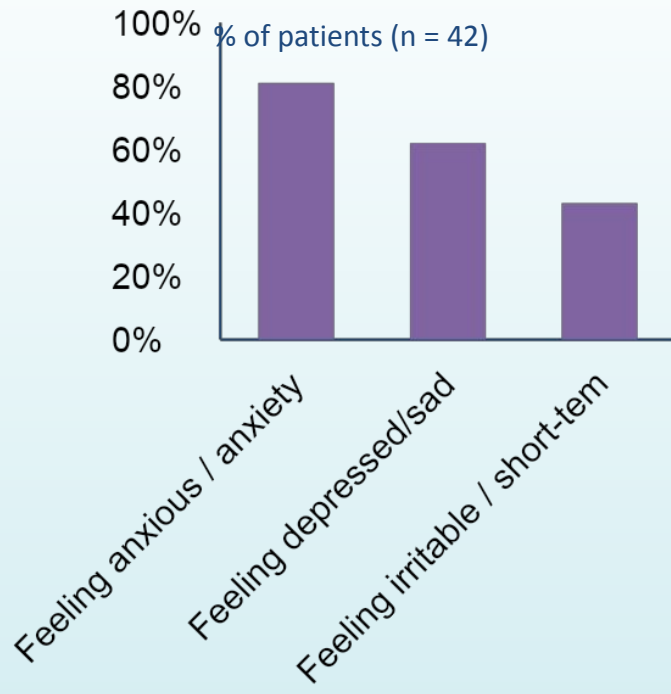


n = 31/426

La qualità di vita è ridotta

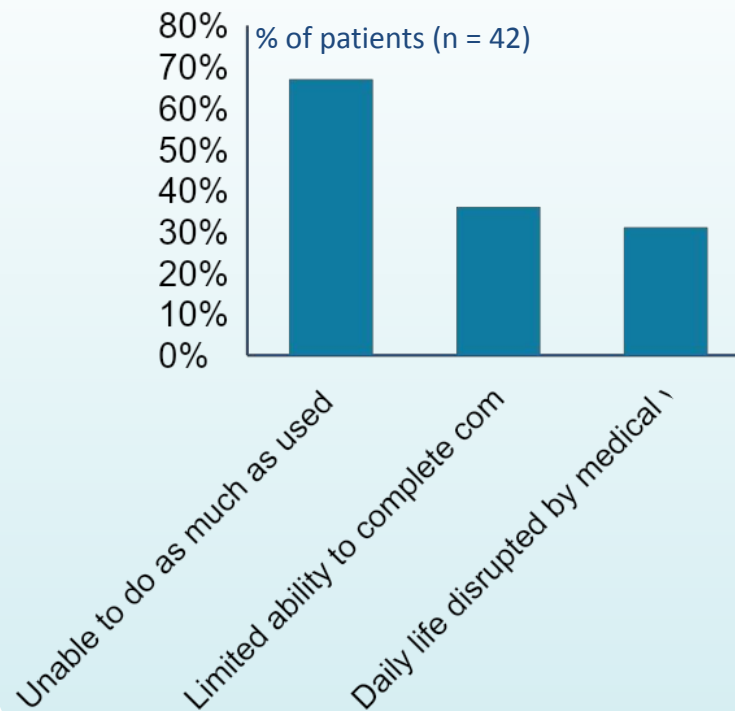
100% of Patients Reported Psychological Impacts

Psychological Impacts



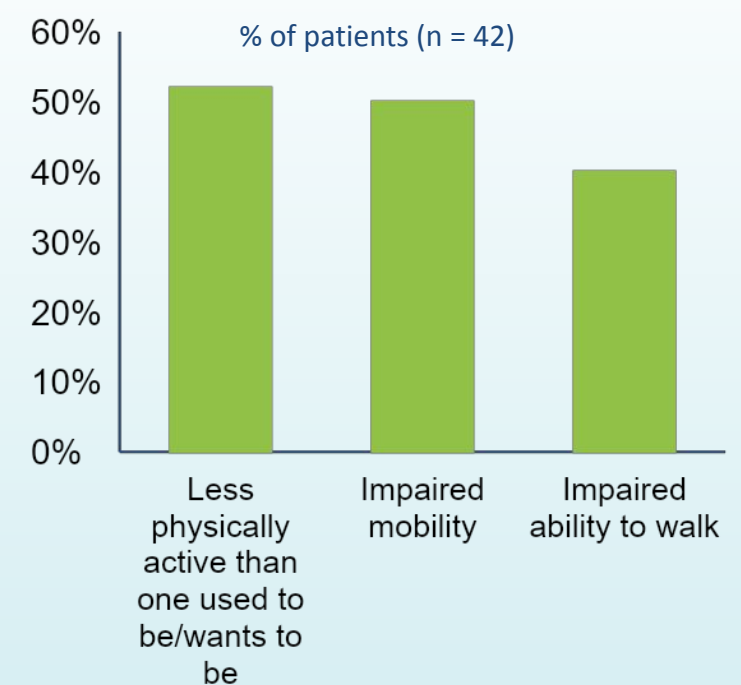
95% of Patients Reported Interference with Daily Life

Impacts on Daily Life



95% of Patients Reported Impacts on Physical Functioning

Impacts on Physical Functioning



Impatto sulla vita quotidiana

- Oltre l'85% dei pazienti riferisce riduzione significativa della qualità di vita
- Terapie multiple giornaliere, frequenti accessi a visite/esami
- Sintomi fluttuanti e invalidanti
- Difficoltà a lavorare, vivere in autonomia
- Crisi ipocalcemiche acute → accessi in PS/ospedalizzazioni

Il costo della 'non-cura'

- Visite ripetute, esami frequenti, ospedalizzazioni
- Terapia a base di supplementi non risolve la patologia
- Costi diretti stimati (dati USA adattati): 10.000–15.000 €/anno/paziente
- Costi indiretti: perdita produttività, caregiver, burn-out

Research | [Open access](#) | Published: 18 April 2024

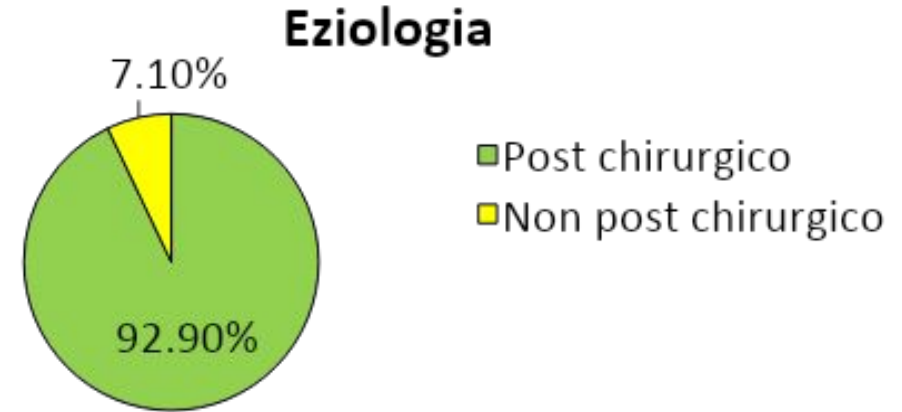
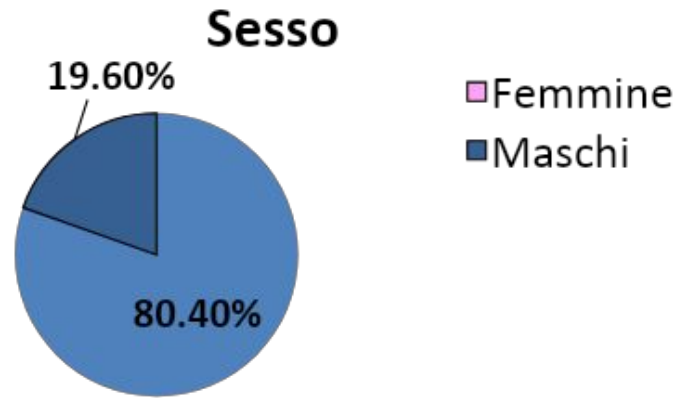
Economic burden of patients with post-surgical chronic and transient hypoparathyroidism in the United States examined using insurance claims data

[Kathleen L Deering](#) , [Niccole J Larsen](#), [Patrick Loustau](#), [Blandine Weiss](#), [Soraya Allas](#), [Michael D Culler](#), [Qing Harshaw](#) & [Deborah M. Mitchell](#)

[Orphanet Journal of Rare Diseases](#) **19**, Article number: 164 (2024) | [Cite this article](#)

1543 Accesses | **2** Citations | **1** Altmetric | [Metrics](#)

I nostri dati (Endo s. Orsola)



Dosi medie terapia:

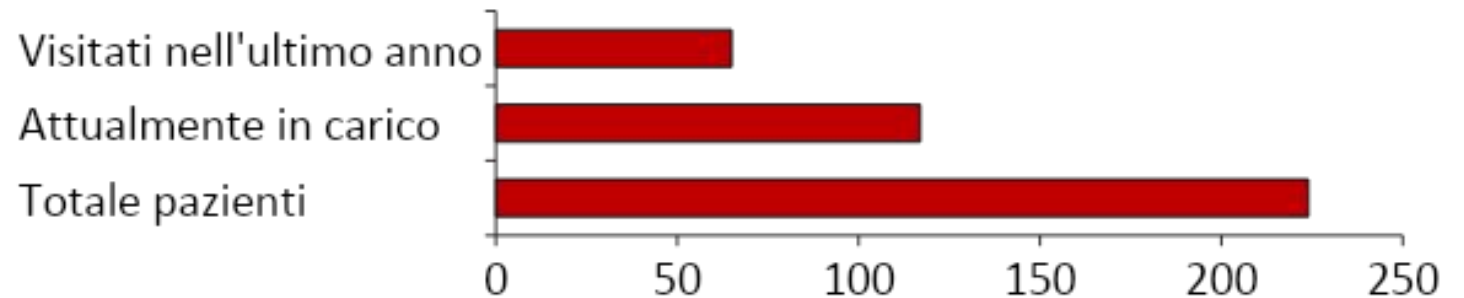
Calcio carbonato: 1334 mg al giorno

Calcitriolo: 54 mcg al giorno



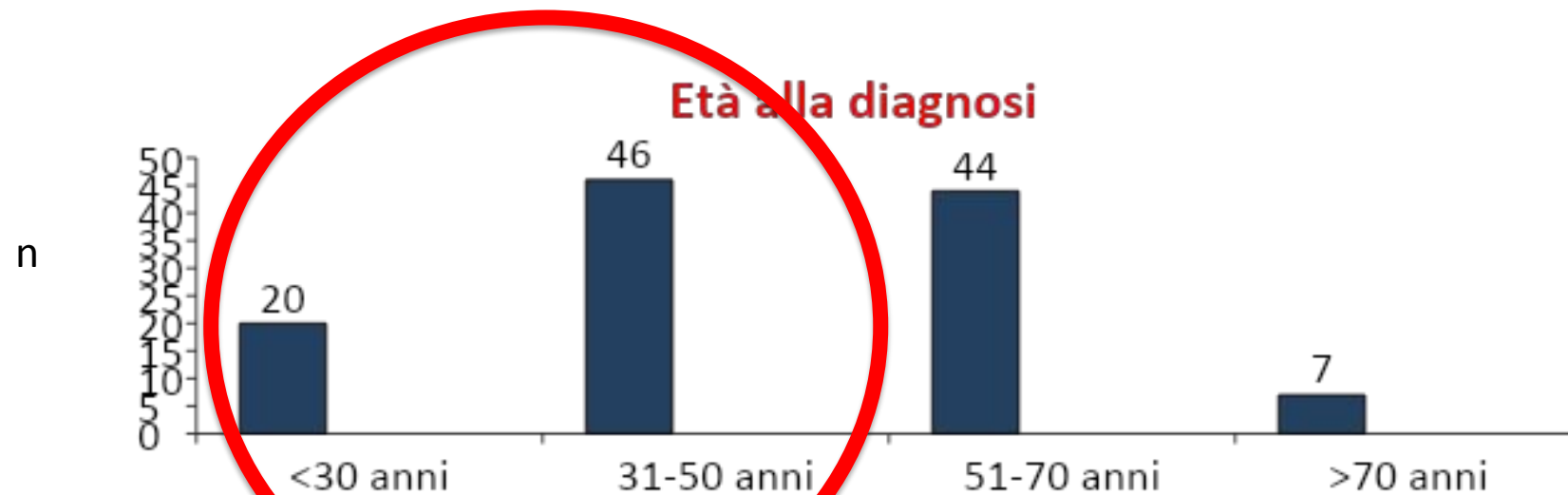
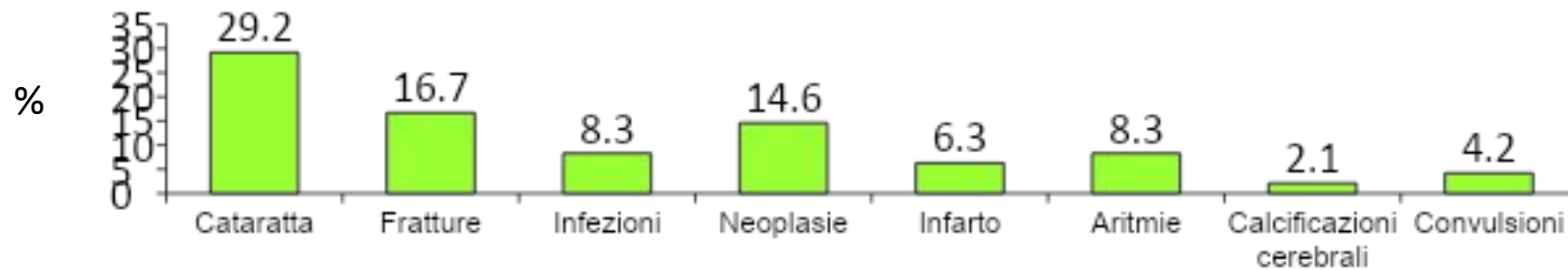
Pazienti in teriparatide

N= 10



Come stanno nostri pazienti (Endocrinologia, Policlinico di S. Orsola)

Prevalenza percentuale complicanze



IPOPARIROIDISMO

**Cutting edge della
ricerca e prospettive di
cura**

Terapie oggi

- Calcio + vitamina D attiva = terapia sintomatica
- Non fisiologica → rischi renali e calcificazioni
- 1 paziente su 2 ha sintomi non controllati
- Terapia sostitutiva con palopegteriparatide disponibile in Europa ma non rimborsata in Italia

Trattamento 'convenzionale' dell'ipoparatiroidismo

Conventional Therapy

- Oral calcium¹
- Active vitamin D or analogs¹

Additional Therapies

- Magnesium supplements^{1,2}
- Thiazide diuretics when necessary to help manage hypercalciuria and low salt diet¹
- Phosphate binders and low phosphate diet, if necessary, to control hyperphosphatemia¹

Parathyroid Hormone

- Guidelines state that when conventional therapy is deemed unsatisfactory, consider the use of parathyroid hormone^{2a}

^aUse of conventional therapy as first-line therapy rather than administration of parathyroid hormone in individuals with chronic hypoparathyroidism was classified as a weak recommendation

1. Brandi ML, et al. *J Clin Endocrinol Metab.* 2016;101(6):2273-2283.
2. Khan AA, et al. *J Bone and Miner Res.* 2022;37(12): 2568-2585.

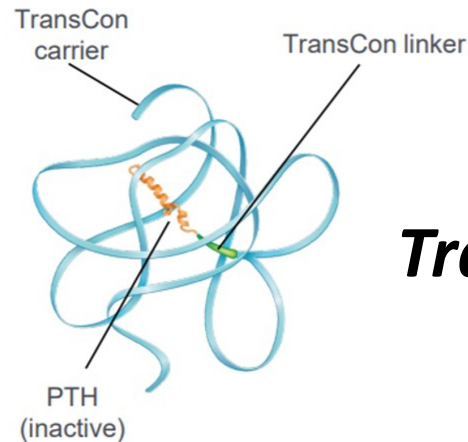
Ma c'è un prima e un dopo...

EMA: 17/11/2023

FDA: 09/08/2024

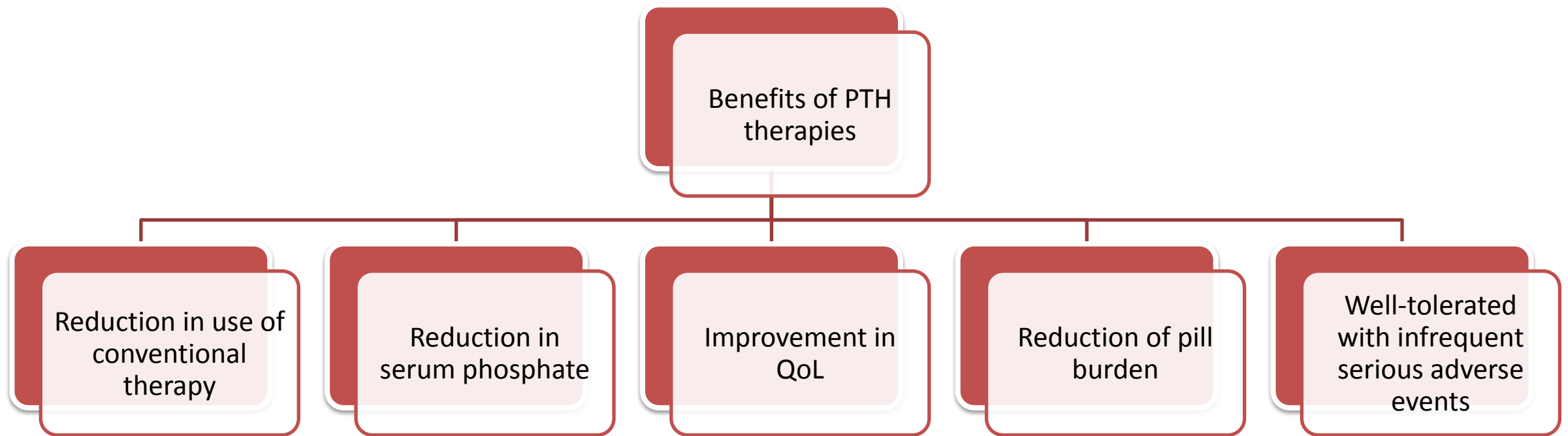
Past

Future



Benefici delle terapie a base di PTH rispetto alla terapia convenzionale

A systematic review and meta-analysis of 7 randomized trials was conducted to evaluate the benefits of PTH therapy in comparison to conventional therapy in individuals with chronic hypoparathyroidism



PTH, parathyroid hormone; QoL, quality of life

Khan AA, et al. *J Bone and Miner Res.* 2022;37(12): 2568-2585.

Quando la terapia convenzionale è ritenuta insoddisfacente?

Inadequate control with conventional therapy^a

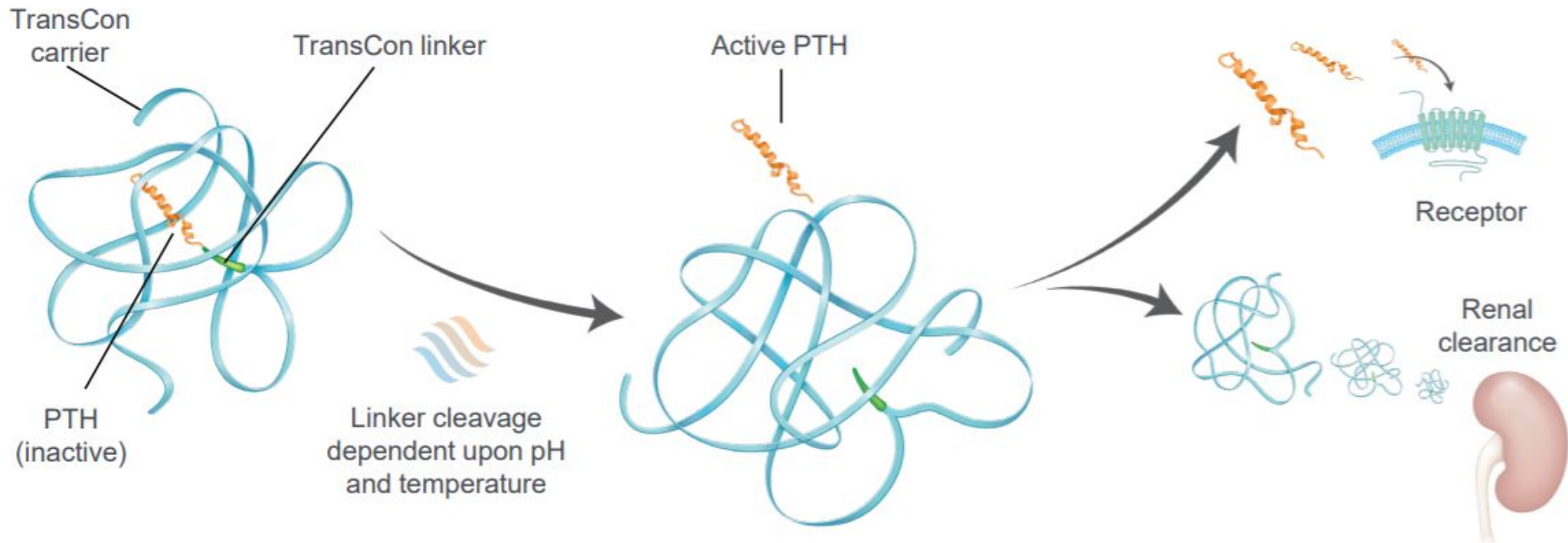
- Symptomatic hypocalcemia
- Hyperphosphatemia
- Renal insufficiency
- Hypercalciuria
- Poor quality of life

Other individuals who may benefit from PTH therapy

- Poor compliance or malabsorption
- Intolerant of large doses of calcium and active vitamin D
- Requiring high doses of conventional therapy (calcium >2 g/day or active vitamin D >2 µg/day)

^aInadequate control is considered to be any of the following

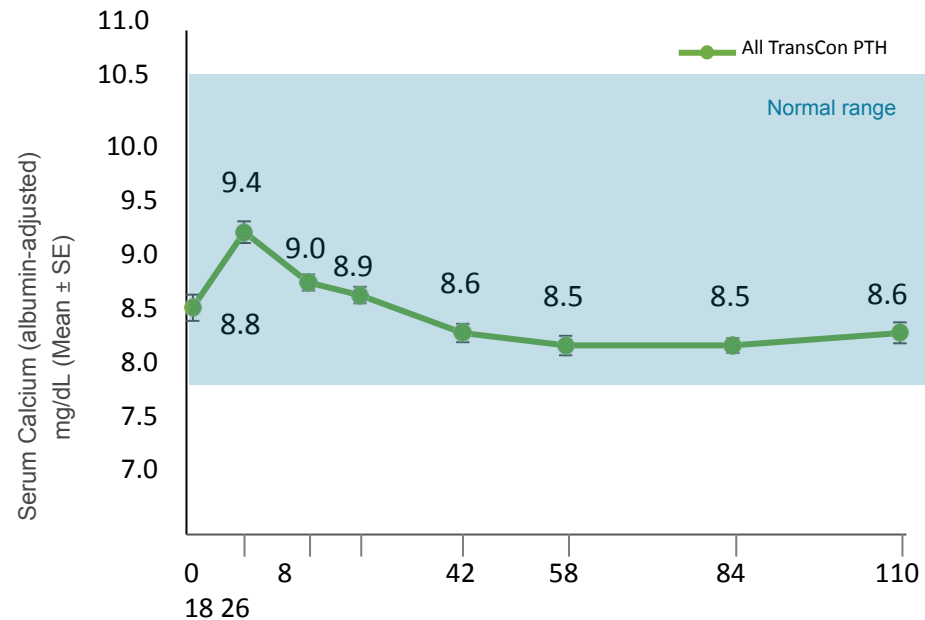
Meccanismo d'Azione del Palopegteriparatide



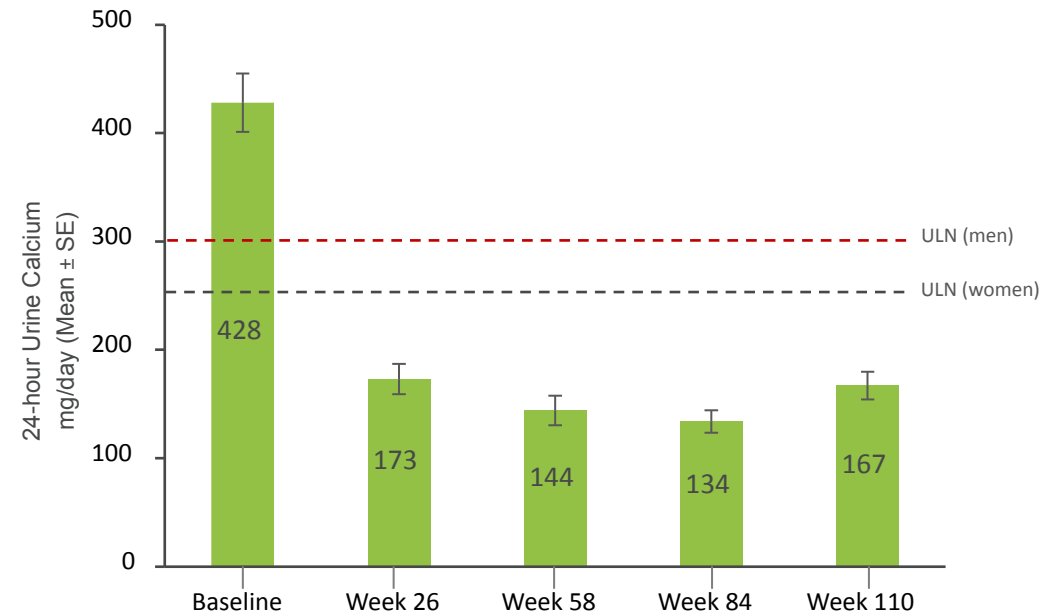
Pro-farmaco di teriparatide PTH(1-34) legato a un trasportatore mPEG tramite un linker proprietario. Permette un rilascio prolungato di teriparatide per 24 ore, simulando l'ormone nativo o un'infusione continua di PTH.

Risposta calcemica e calciurica a palopegteriparatide

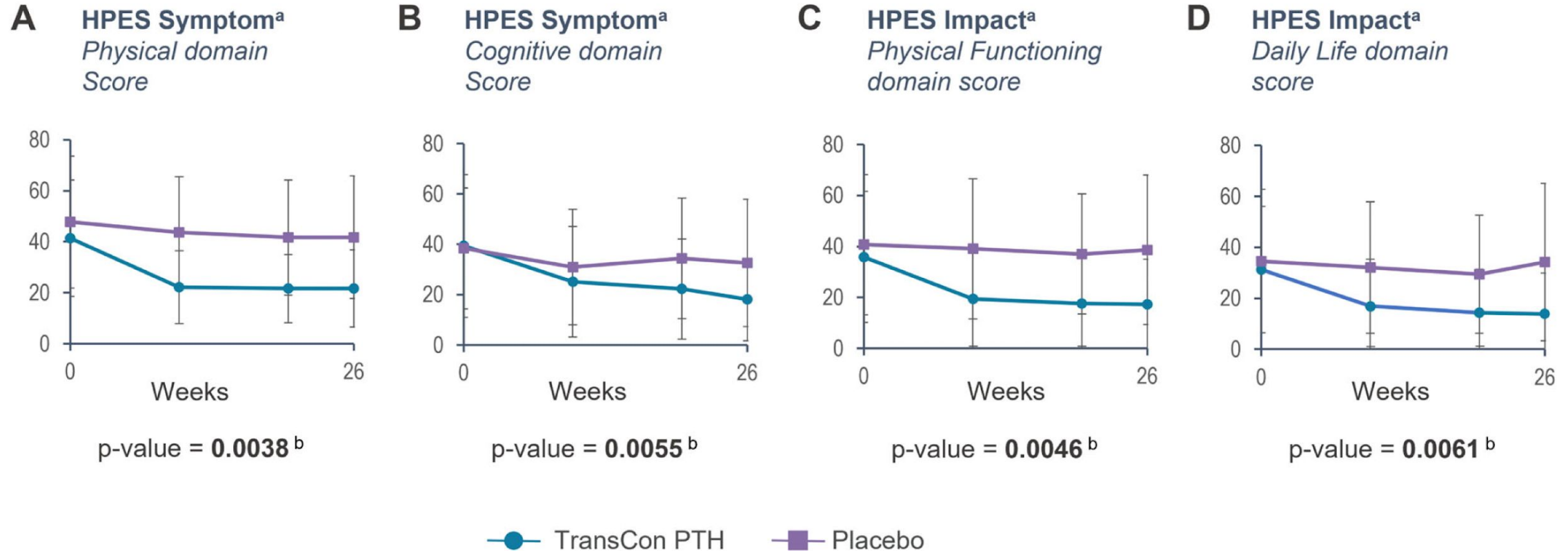
Calcio sierico



Calcio urinario delle 24 ore



Palopegteriparatide: qualità di vita



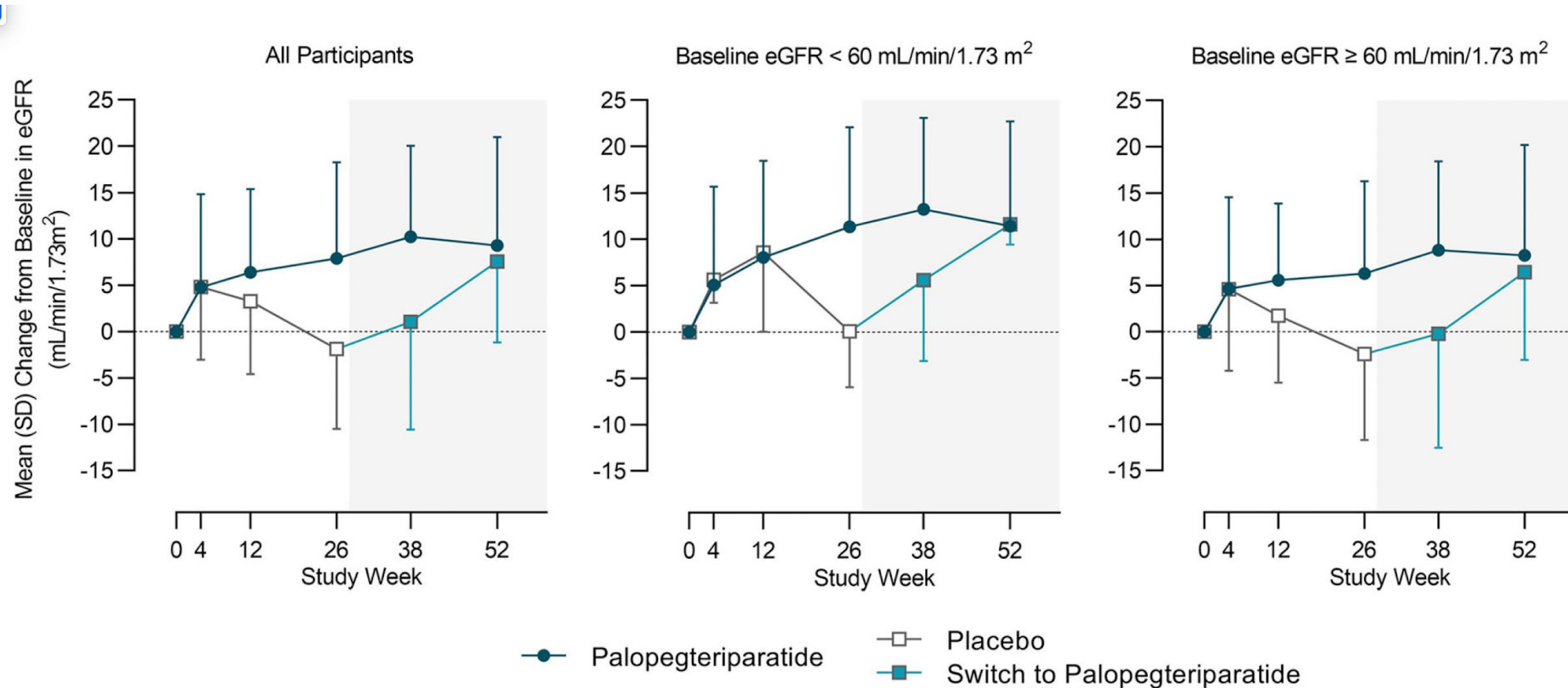
Khan AA, et al. Efficacy and Safety of Parathyroid Hormone Replacement With TransCon PTH in Hypoparathyroidism: 26-Week Results From the Phase 3 PaTHway Trial. J Bone Miner Res. 2023

Palopegteriparatide: dati a 12 mesi (RCT + open label)

Table 1. PaTHway trial open-label extension multi-component efficacy endpoint at week 52

	Total TransCon PTH (N = 82)
Participants with data on all criteria at week 52, n	78
Participants meeting the multi-component endpoint at week 52 (responders), n	63
Proportion, % (95% CI) ^a	81 (70, 89)
Number of participants meeting each component, n (%)	
Albumin-adjusted serum calcium within the normal range ^b	67 (86)
Independence from active vitamin D ^c	78 (100) 
Independence from therapeutic doses of calcium ^d	74 (95) 

La funzione renale dopo 12 mesi di palopegteriparatide:



**Nel 43% dei pazienti
GFR aumenta di
almeno 10 ml/min**

Rejnmark L, et al. Palopegteriparatide Treatment Improves Renal Function in Adults with Chronic Hypoparathyroidism: 1-Year Results from the Phase 3 PaTHway Trial.

IPOPARIROIIDISMO

OGGI

- **Malattia deve ricevere maggiore attenzione da parte di tutta la comunità medica alla luce di elevati tassi di morbidità**
- **I pazienti devono essere indirizzati ai Centri Esperti nella gestione della patologia per ridurre il rischio di complicanze a lungo termine**
- **Per la prima volta nella storia della patologia è stata approvata una terapia che sostituisce il paratormone**

OGGI

Ipotiroidismo



Ormone Tiroideo

Diabete mellito tipo 1



Insuline

GRAZIE

Morbo di Addison



Idrocortisone + idrocortisone a lento rilascio

IPOPARIROIDISMO



Calcio e calcitriolo

TERAPIA SOSTITUTIVA