

Cost-effectiveness, Quality of Life, and Patient-reported Outcomes Following Surgery for Primary Hyperparathyroidism

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No Conflicts of Interest To Disclose

Overview

- Anatomy and Function of the Parathyroid Glands
- Pathophysiology/Clinical Presentation of Primary Hyperparathyroidism
- Consensus Conference Treatment Guidelines for “Asymptomatic” Primary Hyperparathyroidism
- Quality-of-Life, Cost-effectiveness and Patient-Reported Outcomes in Primary Hyperparathyroidism

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Indian Rhinoceros



III. *On the Anatomy of the Indian Rhinoceros (Rh. unicornis, L.).*
By Professor OWEN, F.R.S., F.Z.S. &c.

Read Feb. 12, 1850.

PART I.

Introduction. External characters. Position of Viscera.



ity of investigating the internal structure of the Rhinoceros,
: male specimen of the Indian species, *Rhinoceros unicornis, L.*,
Zoological Society, has afforded, enables me to submit to the
ils of its anatomy.
uisite point of comparison with the dimensions and weight of
the animal, which was full-grown and had lived in the men-
ed thirteen feet and a half from the end of the muzzle to the
teen feet in its greatest circumference: its total weight was

Sir Richard Owen
Professor of Comparative Anatomy
Royal College of Surgeons
London



“A small compact yellow glandular body was attached to the thyroid at the point where the veins emerge”

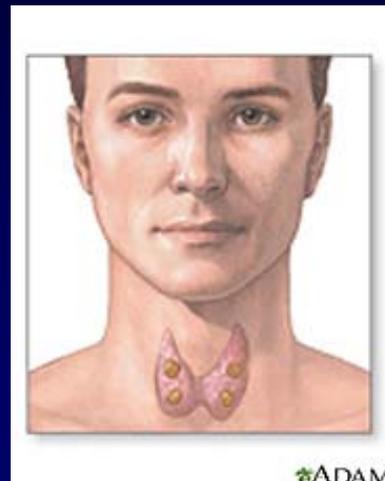
Owen R 1862; Trans Zool Soc Lond 4:31-58

Anatomy

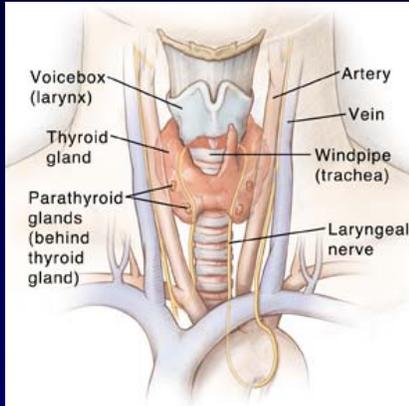
- Ivar Sandström, Swedish medical student

- 1880, published:
“On a new gland in man and several mammals”

- First observed in dog
- Confirmed in rabbit, cat, and horse
- Human cadaver (last major organ to be recognized in humans)

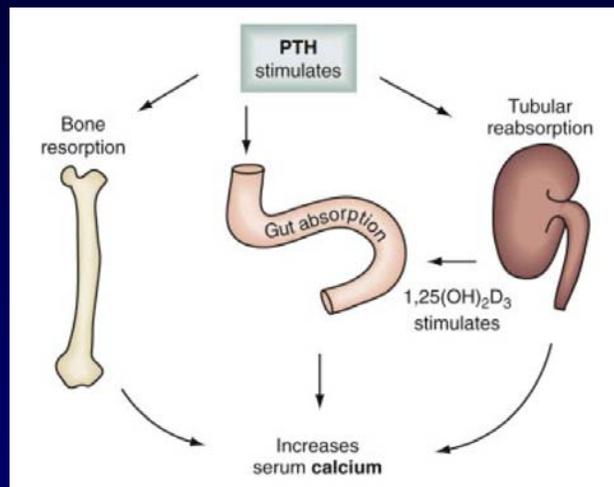


Anatomy



- 4 pea-sized glands behind the thyroid
- Each gland weighs ~35mg
- Ectopic, supernumerary glands possible

Function of the Parathyroids: Calcium Regulation

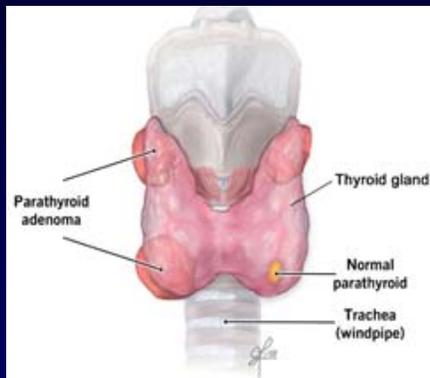


Sabiston Textbook of Surgery

Overview

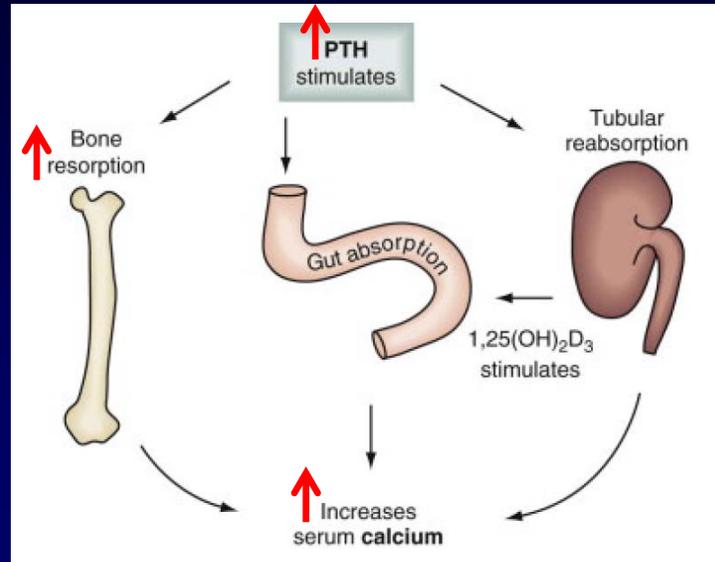
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Pathophysiology of Primary Hyperparathyroidism



- Parathyroid hormone oversecretion
- Usually caused by single parathyroid adenoma (benign tumor)
- Multigland disease is possible
- Can be caused by familial genetic disorders (Multiple Endocrine Neoplasia)

Pathophysiology of Primary Hyperparathyroidism



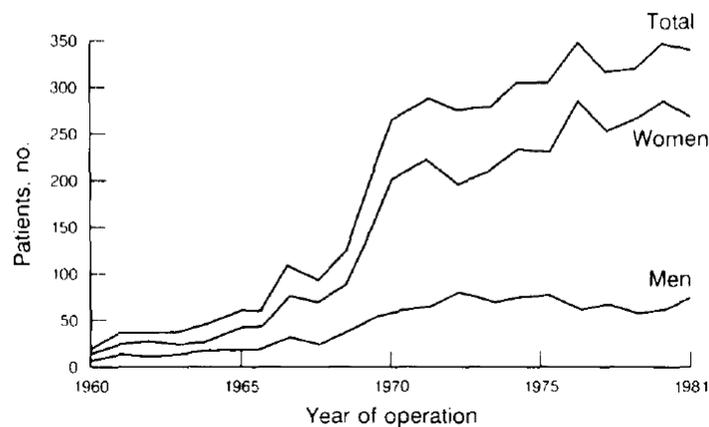
Classic Signs and Symptoms

- Med School Mnemonic
 - “Stones”: kidney stones
 - “Bones”: osteoporosis, fragility fractures
 - “Abdominal Groans”: constipation, peptic ulcers
 - “Psychiatric Moans”: lethargy, fatigue, depression

Diagnosis and Treatment

- Diagnosis is Biochemical
 - Lab tests
 - Serum Calcium: Elevated
 - Serum Parathyroid Hormone (PTH): Elevated
 - Imaging and nuclear medicine localization studies
- Treatment: Surgical removal of the adenoma or hyperplastic glands

EPIDEMIOLOGY OF HYPERPARATHYROIDISM



Number of parathyroid tumors reported to the Swedish cancer registry during 1960-1981.

Am J Epidemiol, 1988; 127:1031-1040.

Table 1. Average Annual Incidence of Primary Hyperparathyroidism in Rochester, Minnesota, from January 1, 1965, through December 31, 1976.

INTERVAL	No. OF YR	No. OF CASES	AVERAGE ANNUAL INCIDENCE*
1/1/65 to 6/30/74	9.5	39	7.8±1.2
7/1/74 to 6/30/75†	1	28	51.1±9.6
7/1/75 to 12/31/76	1.5	23	27.7±5.8

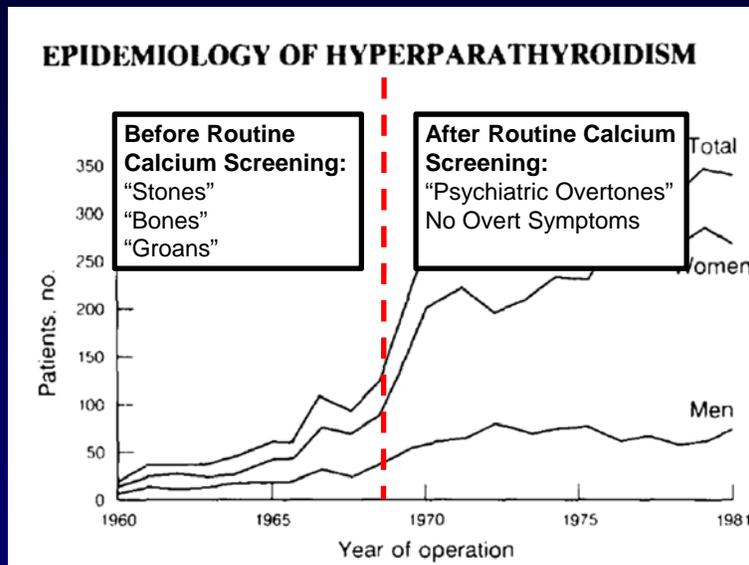
*New diagnoses (mean ±SD) per 100,000 population.

†On 7/1/74, serum calcium measurement was added to 12-unit serum chemistry panel at Mayo clinical laboratories.

The autoanalyzer is to blame

N Engl J Med, 1980; 302:189-93.

Disease Presentation Has Changed



Asymptomatic PHPT

“The clinical profile of patients with documented primary HPT without symptoms or signs commonly attributable to the disease”
-1990 NIH Consensus Development Conference Statement

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U.S. Department of Health & Human Services • National Institutes of Health

NIH Consensus Development Program



- Established 1977
- Jointly sponsored by NIH Office of Disease Prevention and another NIH Institute or Center
- Produce consensus statements on important and controversial topics in medicine
- Goal: Evaluate the available scientific information and develop a statement useful to health professionals and the public at large

Diagnosis and Management of Asymptomatic Primary Hyperparathyroidism

National Institutes of Health
Consensus Development Conference Statement
October 29-31, 1990



- Defined asymptomatic disease
- Established clinical criteria for surgery
- Established observation regimen for asymptomatic patients who do not have surgery

Symptomatic vs. Asymptomatic

- “Some patients may have **one or several vague symptoms that cannot be definitively attributed to primary HPT** but may instead be nonspecific or arise from a coexisting condition. ... for purposes of this conference, such patients **were considered “asymptomatic”**”
- “In contrast, patients who present **significant bone, renal, gastrointestinal or neuromuscular symptoms** are defined as **“symptomatic”** and require surgery.”

J Bone Miner Res. (6):S2, 1990

“Psychiatric Moans” = Asymptomatic?

- “Dr. Purnell pointed out the difficulty of sorting out issues of fatigue and lethargy within the practical limits and time constraints of a typical patient interview.”
- “Many disorders, such as the ‘chronic fatigue syndrome,’ may present in a similar manner.”
- “These symptoms are so difficult to define, even if they could be revealed, that it would be very difficult to use them as an argument for surgery.”

J Bone Miner Res. (6):S2, 1990

Four Consensus Conferences

1990

Diagnosis and Management of Asymptomatic Primary Hyperparathyroidism

National Institutes of Health
Consensus Development Conference Statement
October 29-31, 1990

2002

Summary Statement from a Workshop on Asymptomatic Primary Hyperparathyroidism: A Perspective for the 21st Century

2008

Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism: Summary Statement from the Third International Workshop

2014

Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism: Summary Statement from the Fourth International Workshop

2014 Consensus Guidelines for Surgical Referral

- Serum calcium concentration >1.0 mg/dl above the upper limit of normal
- Bone density T-score of <2.5 at lumbar spine, hip, femoral neck or distal radius
- History of fragility fracture or vertebral fracture
- Creatinine clearance less than 60ml/min
- 24-h urine for calcium >400 mg/day
- Age <50

2014 Consensus Guidelines for Observation-Eligibility of Asymptomatic PHPT Patients

- Annual serum calcium
- Annual serum creatinine
- Bone density scan every 1-2 years, vertebral X-ray or VFA study if clinically indicated (eg height loss or back pain)

J Clin Endocrinol Metab 99:3561-3569, 2014

Early Parathyroidectomy in Asymptomatic Patients

- Improved medical outcomes (bone mineralization)
- Eliminate surveillance costs
- Improved quality-of-life after parathyroidectomy

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Quality-of-Life Studies in Primary Hyperparathyroidism

- Disease specific symptom inventory
- Hospital Anxiety and Depression Scale
- SF-36 Health Survey

Parathyroidectomy Assessment of Symptoms (PAS)

- Visual Analog Scale Questionnaire

- 13 symptoms most likely to respond to parathyroidectomy

Table 2. Items in prospective questionnaire.

Pain in the bones
Feeling tired easily
Mood swings
Feeling “blue” or depressed
Pain in the abdomen
Feeling weak
Feeling irritable
Pain in the joints
Being forgetful
Difficulty getting out of a chair or car
Headaches
Itchy skin
Being thirsty

World J. Surg. 22, 513-519, 1998

Parathyroidectomy Assessment of Symptoms (PAS)

- 203 parathyroidectomies for primary hyperparathyroidism
- Significant improvement in symptom score postoperatively compared to thyroid surgery control patients
- Improvement was durable at 10 years
- No analysis of asymptomatic vs symptomatic patients

World J. Surg. 22, 513-519, 1998
World J. Surg. 26, 942-9, 2002
Surgery. 146(6):1006-13, 2009

Neuropsychological Symptoms

- 24 asymptomatic primary hyperparathyroidism patients and 23 hemithyroidectomy controls in UK administered Hospital Anxiety, Depression and Mood Rating Scale
 - Improvement in all 3 scales in PHPT pts.
 - No improvement in control group
- 25 asymptomatic patients in Japan
 - No improvement on an 8-item questionnaire about neuropsychological symptoms before and after surgery
 - Underpowered

Clin Endocrinol (Oxf). 76(2):196-200, 2012.
Eur Arch Otorhinolaryngol, 265:565-569, 2008

SF-36

- 3 randomized prospective trials of surgery vs. observation in asymptomatic PHPT
- 5% to 25% improvement in SF-36 scores compared to observation
 - Bodily Pain, General Health, Social and Emotional Role Function, Vitality, and Mental Health
- Inconsistent observed differences among 3 studies

J Clin Endocrinol Metab. 89(11):5415-5422. 2004
J Clin Endocrinol Metab. May 2007;92(5):1687-1692.
J Clin Endocrinol Metab. Aug 2007;92(8):3114-3121.

SF-36 and CEA Research

Table III. Quality adjustment factors used in the decision model

<i>Outcome</i>	<i>Life expectancy quality adjustment factor</i>
Stable asymptomatic PHPT	0.987
Cured with RLN damage requiring vocal cord medialization	0.979
Long-term hypoparathyroidism	0.950
Stable asymptomatic disease with RLN damage	0.957
Symptomatic PHPT	0.897
Symptomatic PHPT with RLN damage	0.877

PHPT, Primary hyperparathyroidism; RLN, recurrent laryngeal nerve.

Surgery, 2006; 140:874-82

Cost-Effectiveness Research

Cost-effectiveness analysis of parathyroidectomy for asymptomatic primary hyperparathyroidism

Kyle Zanocco, BS, Peter Angelos, MD, PhD, and Cord Sturgeon, MD, Chicago, Ill

How should age at diagnosis impact treatment strategy in asymptomatic primary hyperparathyroidism?
A cost-effectiveness analysis

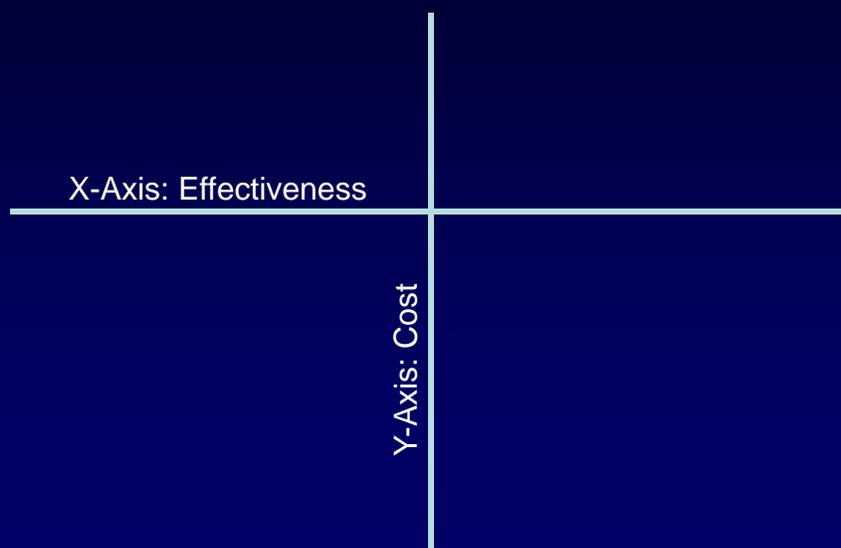
Kyle Zanocco, BS, and Cord Sturgeon, MD, Chicago, Ill

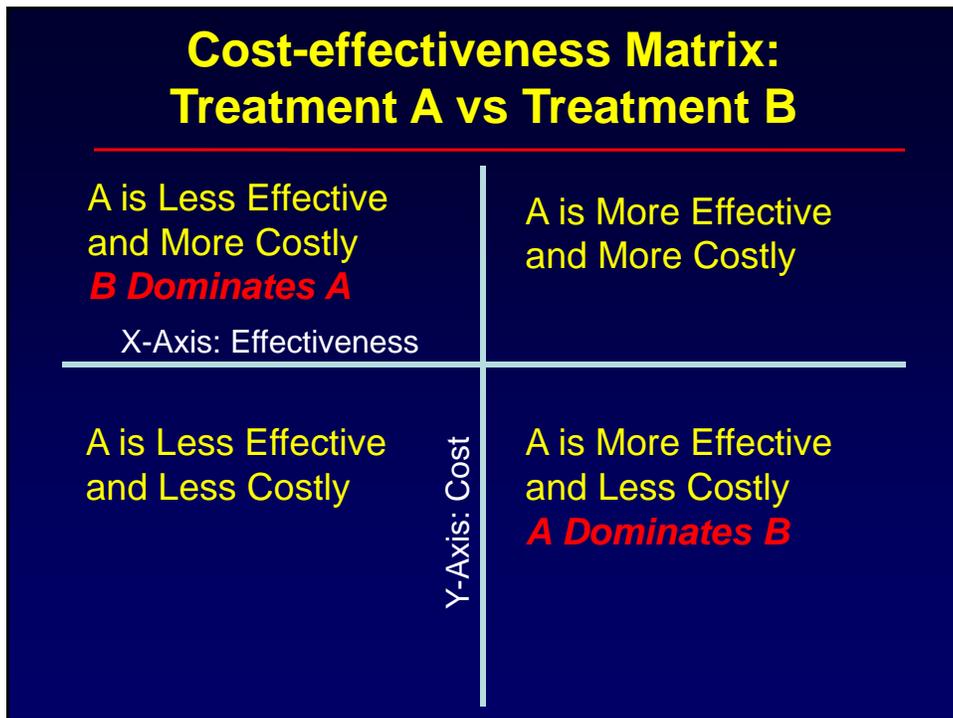
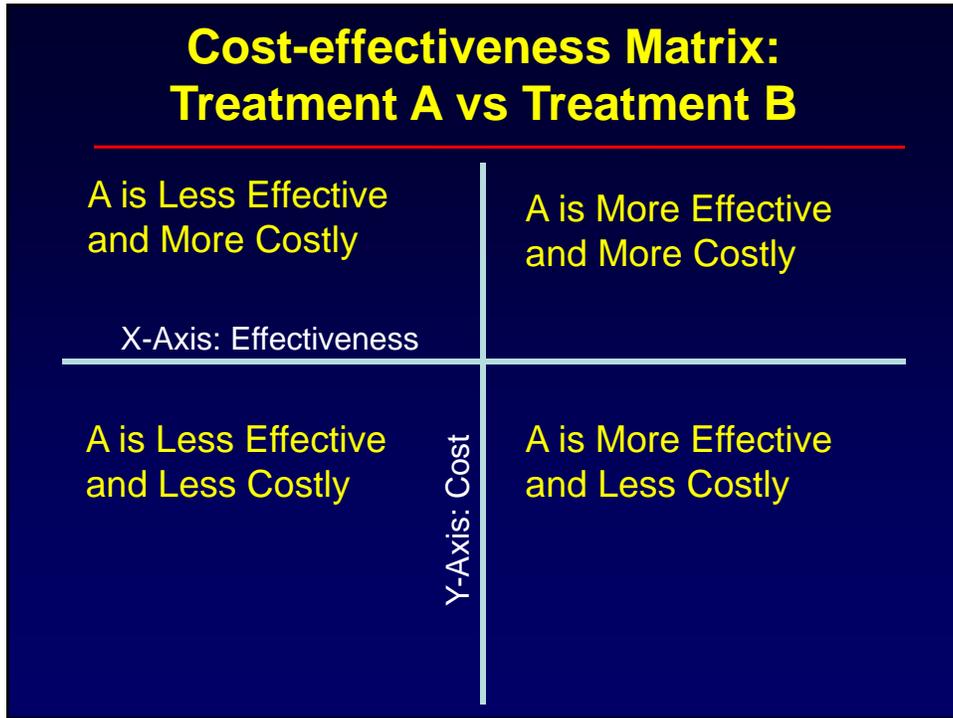
Surgery, 2006; 140:874-82
Surgery, 2008; 144: 290-8.

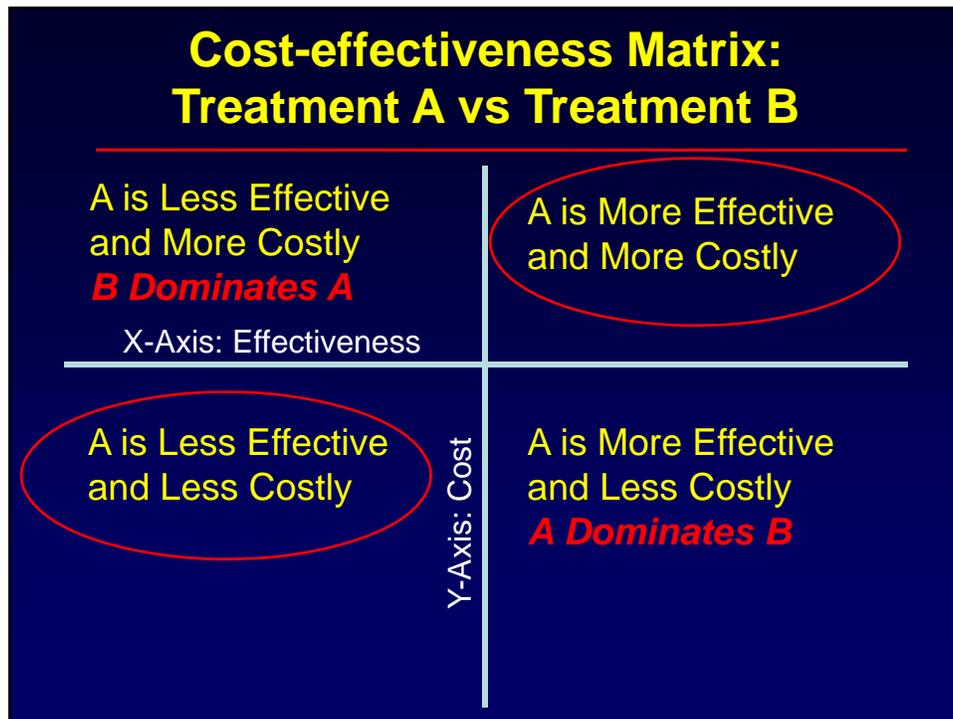
Cost-Effectiveness Analysis (CEA)

- Decision analysis for healthcare. Calculates expected values for costs and effects.
 - Which treatment is more costly?
 - Which treatment is more effective?
 - How much does it cost for treatment to add one year of healthy life? “Buck for your bang” (Incremental cost effectiveness ratio)
 - One year of healthy life =
Quality-adjusted life year (QALY)

Cost-effectiveness Matrix: Treatment A vs Treatment B







Incremental Cost-Effectiveness Ratio (ICER)

Incremental cost-effectiveness ratio =

Additional cost of treatment

QALYs gained

- Comparisons between 2 or more interventions can be made and are expressed as incremental cost effectiveness ratios (ICERs)

Cost-Effectiveness of Selected Interventions¹

Intervention ¹	Incremental Cost-Effectiveness (Cost/QALY)
Beta-blockers after myocardial infarction	<\$10,000
Mammographic screening	\$10,000–\$25,000
Colon-cancer screening	\$10,000–\$25,000
Osteoporosis screening	\$10,000–\$25,000
Hypertension medication	\$10,000–\$60,000
Cholesterol management, as secondary prevention	\$10,000–\$50,000
Implantable cardioverter–defibrillator	\$30,000–\$85,000
Dialysis in end-stage renal disease	\$50,000–\$100,000
Left ventricular assist devices	\$500,000–\$1.4 mil

1. Neumann PJ et al. Medicare and cost-effectiveness analysis. N Engl J Med 2005; 353(14):1516-22.

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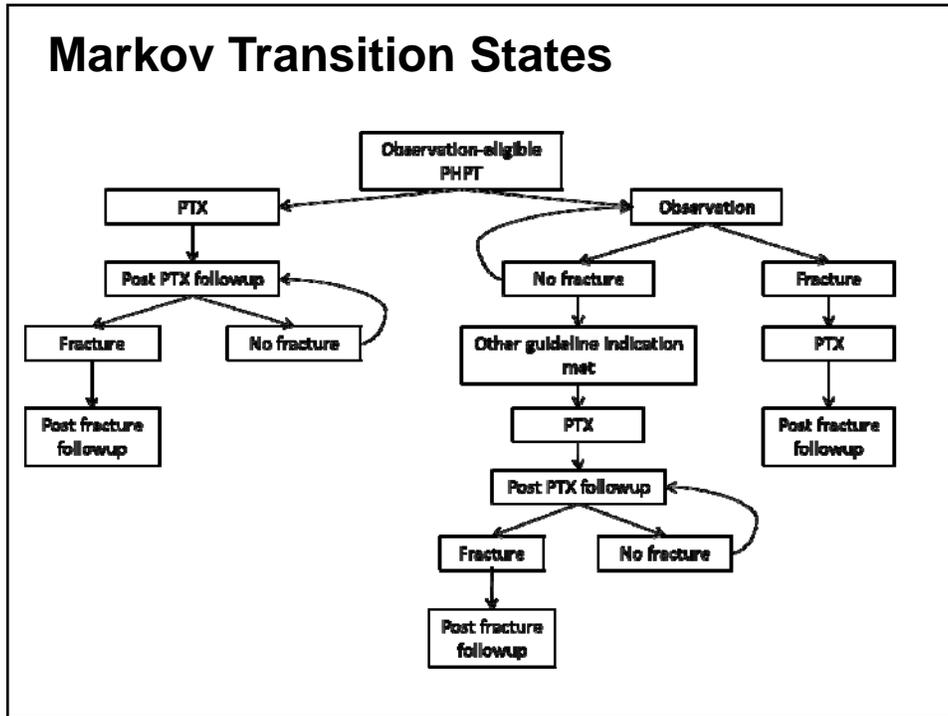
1. Neumann PJ et al. Medicare and cost-effectiveness analysis. N Engl J Med 2005; 353(14):1516-22.

Hypothesis

Parathyroidectomy is cost-effective for patients with asymptomatic primary hyperparathyroidism who are older than 50.

Reference Case Scenario

- Asymptomatic primary hyperparathyroidism patient
- Does not meet NIH criteria for surgery
- Healthy candidate for surgery
- No previous neck surgery
- No MEN syndromes or parathyroid carcinoma



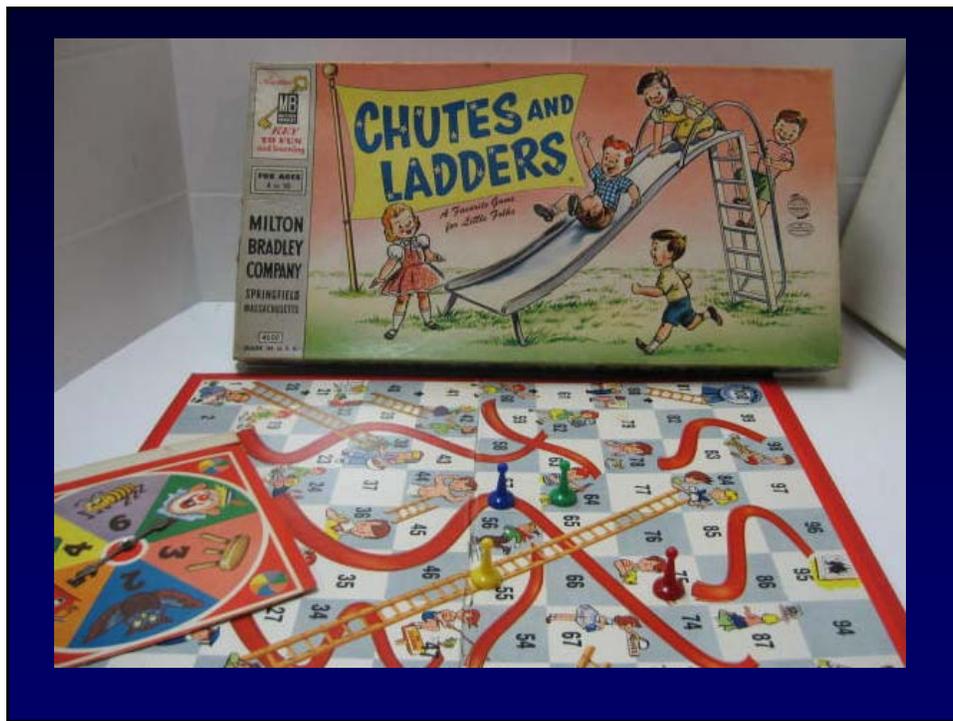
Markov Modeling

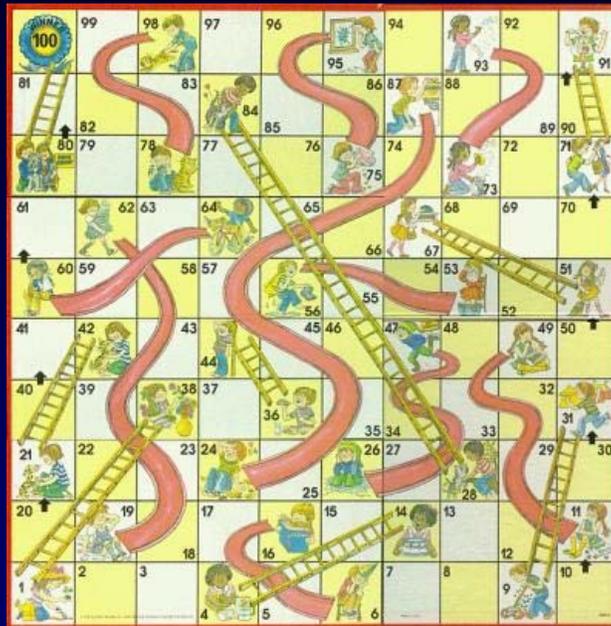
- Markov Chain: A mathematical system that undergoes transitions from one state to another, and the number of states is finite



Andrey Markov 1856-1922

- Health states/QOL that changes over time described with Markov chain
- Allows calculation of future QALYs





No decisions are made during this game, there is a set probability of advancing based only on position you are in. This is a Markov chain.

Outcome Probabilities

Assumption	Probability used	References
Annual probability of progression from asymptomatic disease to symptomatic disease	1.6%	Silverberg
Annual probability of recurrence of hyperparathyroidism following successful PTX	0.68%	Carneiro Hedback
Probability of persistent hyperparathyroidism following initial PTX	5%	Carneiro Hedback
Probability of persistent hyperparathyroidism following redo PTX	10%	al-Fehaily

Surgical Complication Probabilities

Assumption	Probability used	References
Probability of permanent hypoparathyroidism following initial PTX	0.5%	Fahy, Udelsman
Probability of hypoparathyroidism following redo PTX	1%	Fahy, Udelsman
Probability of RLN damage following initial PTX	0.5%	Fahy, Udelsman
Probability of RLN damage following redo PTX	4%	Fahy, Udelsman

Costs: Observation and Pharmacologic Therapy

Monitoring and observation	CPT	Cost
Serum Ca	82310	\$19.46
Serum Creatinine	82565	\$7.16
Bone Density, lumbar spine	76075	\$142.33
Bone Density, forearm and wrist	76076	\$43.27
Follow-up Appointments	99213	\$117.96
<i>Total per year</i>		\$330.18

Pharmacologic Therapy	Dosage	Wholesale Price (quantity)	Estimated Daily Cost	Total Cost Per Year
Cinacalcet	30 mg bid	\$336.96 (30 mg 30.0's)	\$22.46	\$8197.90

Costs: Parathyroidectomy

<i>Hospital Costs</i>	CPT Code	Inpatient PTX	Outpatient PTX	Repeat PTX
PTX, (DRG 289)	60500	\$3,800.78	\$2,534.74	\$3,800.78
Ultrasound	76536	\$64.45	\$64.45	\$64.45
ECG	93005	\$15.93	\$15.93	\$15.93
Parathyroid Imaging	78070	\$149.76	\$149.76	\$149.76
Sestamibi Dose	A9500	\$110.47	\$110.47	\$110.47
<i>Physician Costs</i>				
Anesthesiology	00320	\$225.21	\$225.21	\$296.33
Surgery Office Consult	99242	\$88.66	\$88.66	\$88.66
Surgery PTX	60500	\$916.54	\$916.54	\$1,155.37
Radiology	76536-26	\$26.06	\$26.06	\$26.06
Cardiology	93010	\$8.29	\$8.29	\$8.29
Nuclear Medicine	78070-26	\$39.63	\$39.63	\$39.63
Pathology	88305-26	\$37.69	\$37.69	\$37.69
Total		\$5,483.47	\$4,217.43	\$5,793.42

Methods: QALYs

Outcome	Quality adjustment factor	References
Remission	1.000	
Stable asymptomatic PHPT	0.987	Burney, Sheldon
Stable asymptomatic disease with RLN damage	0.957	Burney, Sheldon, Spector, Vidal-Trecan
Symptomatic PHPT	0.897	Burney, Sheldon
Long term Hypoparathyroidism	0.894	Vidal-Trecan
Remission with RLN damage requiring vocal cord medialization	0.891	Sejean, Spector, Vidal-Trecan
Symptomatic PHPT with RLN damage requiring vocal cord medialization	0.877	Burney, Sheldon, Spector
Permanent hypoparathyroidism and permanent RLN injury requiring vocal cord medialization	0.785	Burney, Sejean, Sheldon, Spector, Vidal-Trecan

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Quality-Adjusted Life Expectancy

- QALY: invented in the 1950s
- Health is a function of length of life and quality of life
- Good for comparing effectiveness of different treatment options for a given disease
- Use to prioritize medical care?
 - Politically sensitive (watch out for death panels, rationing, etc.)

QALE Calculation

- QALE (Quality-adjusted life expectancy = Life Expectancy x Quality Adjustment Factor
- Range of quality-adjustment factors:
 - 0 (death) to 1 (perfect health)
- Negative quality-adjustment factors for states worse than death? A matter of debate

Example: QALE Calculation

- Life expectancy = 10 years
- Quality adjustment factor = 0.8
- What is the QALE?

Estimation of Adjustment Factors

- Techniques
 - Visual analog scale
 - Time trade-off
 - Standard gamble
 - Euro-QOL questionnaire
- Common to all methods: Ask people who don't have the condition in question
 - People with condition overestimate QOL
 - Want to maintain a utilitarian, societal perspective (death panels)

Example: Quality Adjustment Calculation

- What is the quality adjustment factor for permanent iatrogenic hypoparathyroidism?
 - Complication of thyroid and parathyroid surgery
 - Symptoms: weakness, paresthesias
 - Lifelong treatment with calcium and vit-D
 - If severe: trips to ER, frequent serum calcium measurement, calcium infusions, risk of vit-D toxicity, kidney stones

Hypoparathyroidism UK

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The 'Living with Hypoparathyroidism' project

Mandy's story:

'My life has changed dramatically'

Mandy has post surgical hypoparathyroidism following a thyroidectomy for Graves Disease.

She continues: My life has changed dramatically since I became ill. I used to have two jobs, my own flat in a central location, lots of friends and a busy social life. Now I am unable to work, I live quietly in the country with my dog and have become quite isolated. I've lost touch with a lot of my friends since I've moved away, and I don't have the energy to go out much now at all. I'm continually tired and feel old before my time. I look back on my life before my operation, and it feels like I'm looking at a completely different person.'

Visual Analogue Scale

Dead Perfect

0 0.5 1

Prompt: "select a point on this line that represents life with hypoparathyroidism"

Visual Analogue Scale

Dead



Perfect



0

0.5

1



Prompt: "select a point on this line that represents life with hypoparathyroidism"

- Pros: Easy to administer and understand
- Cons: imprecise, no forced tradeoffs

Time Tradeoff

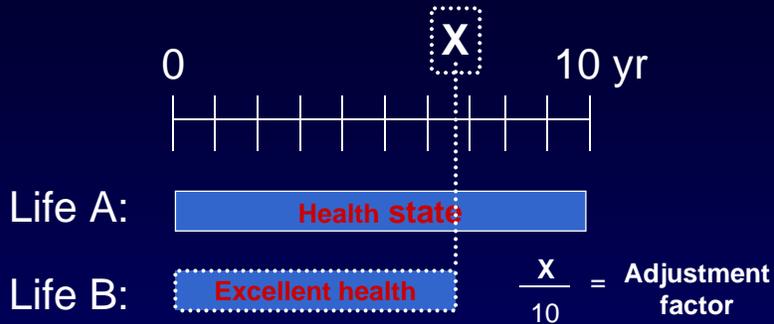


Life A: Health state

Life B: Excellent health $\frac{X}{10} = \text{Adjustment factor}$

Prompt: "Imagine living 10 years with hypopara... how many years out of those 10 would you be willing to give up to be in excellent health for a shorter amount of time?"

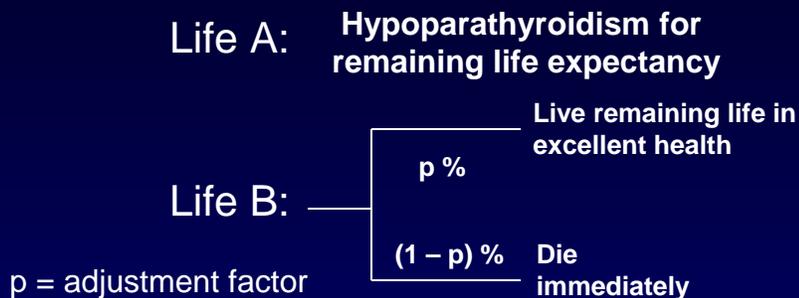
Time Tradeoff



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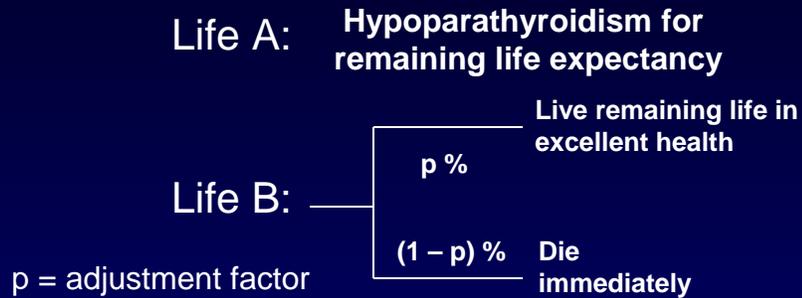
- Pros: Preference-based, precise
- Cons: difficult to administer/understand

Standard Gamble



Prompt: “Imagine there is a new treatment that will cure hypoparathyroidism, restoring you to perfect health. However, this treatment may kill you immediately. Would you undergo this treatment if the chance of survival was 25%, 50%, 90%, 95% ...”

Standard Gamble



- Pros: Preference-based, incorporates attitudes about risk
- Cons: difficult to administer/understand, does not represent a real clinical decision

Euro-QOL and other Surveys

- Survey questions
- Answers converted to adjustment factor based on regression data

Euro-QOL and other Surveys

Prompt: "Imagine you have permanent hypoparathyroidism, circle the most appropriate response:"

Ambulation

- 1: Able to walk around the neighborhood without difficulty
- 2: Able to walk around neighborhood with difficulty, but no walking mobility aid needed
- 3: Able to walk around neighborhood with walking mobility aid
- 4: Able to walk short distances with walking mobility aid, needs wheelchair, other people's assistance for around neighborhood
- 5: Able to walk short distances only with maximal assistance
- 6: Cannot walk at all

Euro-QOL and other Surveys

- Pros
 - Easy to administer
 - Concrete reasoning
- Cons
 - Systematically returns lower quality adjustment factors than the other methods

Differences Among Methods of Quality Adjustment Calculation

• Intermittent Claudication

<u>Method</u>	<u>Adjustment factor</u>
Standard Gamble	0.85
Time Tradeoff	0.74
Visual Analog Scale	0.70
Health Utility Index (Survey)	0.61

JL Bosch, *Qual Life Res* 2000;9(6):591-601.

Quality Adjustment Factors in Thyroid and Parathyroid Surgery

Outcome	Adj. Factor	Method of Calculation	Refs.
Hypothyroid on medication	0.99	Health Utility Index Survey	Muenning ¹
Permanent hypoparathyroidism	0.894 to 0.95	SF-36 Survey, Time-tradeoff	Zanocco ² , Sejean ³
Hypothyroid and Hypoparathyroidism	0.893	Visual Analog Scale	Epstein ⁴
Permanent RLN damage following vocal cord medialization	0.891 to 0.979	SF-36 Survey, Time-tradeoff	Zanocco, Sejean
Hypothyroid and RLN damage	0.881	Health Utility Index Survey, Time-tradeoff	Muenning, Sejean

1. Muennig P, Khan K. Designing and conducting cost-effectiveness analyses in medicine and health care. 1st ed. San Francisco: Jossey-Bass, 2002.
2. Zanocco K et al. Cost-effectiveness analysis of parathyroidectomy for asymptomatic primary hyperparathyroidism. *Surgery* 2005; 140(6):874-81.
3. Sejean K et al. Surgery versus medical follow-up in patients with asymptomatic primary hyperparathyroidism: a decision analysis. *Eur J Endocrinol* 2005; 153(6):915-27.
4. Epstein KA et al. The "abnormal" screening serum thyroxine (T4): analysis of physician response, outcome, cost and health effectiveness. *J Chronic Dis* 1981; 34(5):175-90.

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Permanent hypoparathyroidism	0.894 to 0.95	SF-36 Survey, Time-tradeoff	Zanicco ² , Sejean ³
Hypothyroid and Hypoparathyroidism	0.893	Visual Analog Scale	Epstein ⁴
Permanent RLN damage following vocal cord medialization	0.891 to 0.979	SF-36 Survey, Time-tradeoff	Zanicco, Sejean
Hypothyroid and RLN damage	0.881	Health Utility Index Survey, Time-tradeoff	Muenning, Sejean

1. Muennig P, Khan K. Designing and conducting cost-effectiveness analyses in medicine and health care. 1st ed. San Francisco: Jossey-Bass, 2002.
2. Zanicco K et al. Cost-effectiveness analysis of parathyroidectomy for asymptomatic primary hyperparathyroidism. Surgery 2005; 140(6):874-81.
3. Sejean K et al. Surgery versus medical follow-up in patients with asymptomatic primary hyperparathyroidism: a decision analysis. Eur J Endocrinol 2005; 153(6):915-27.
4. Epstein KA et al. The "abnormal" screening serum thyroxine (T4): analysis of physician response, outcome, cost and health effectiveness. J Chronic Dis 1981; 34(5):175-90.

Methods: Optimal Strategy

Optimal strategy definition:

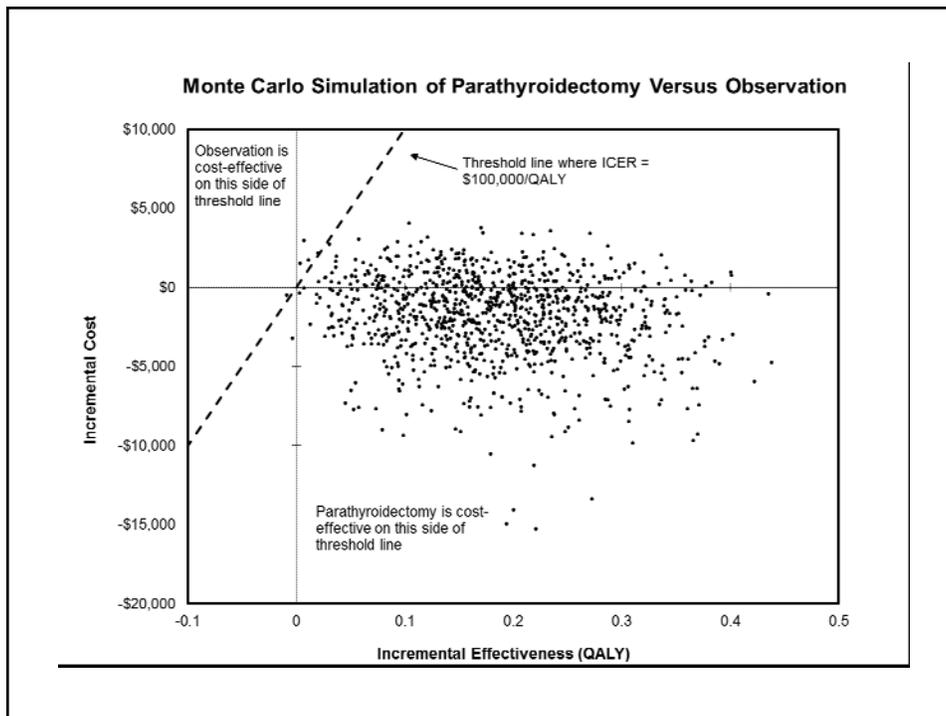
The most effective treatment option (in QALYs) that did not exceed an incremental cost-effectiveness ratio of \$100,000/QALY.

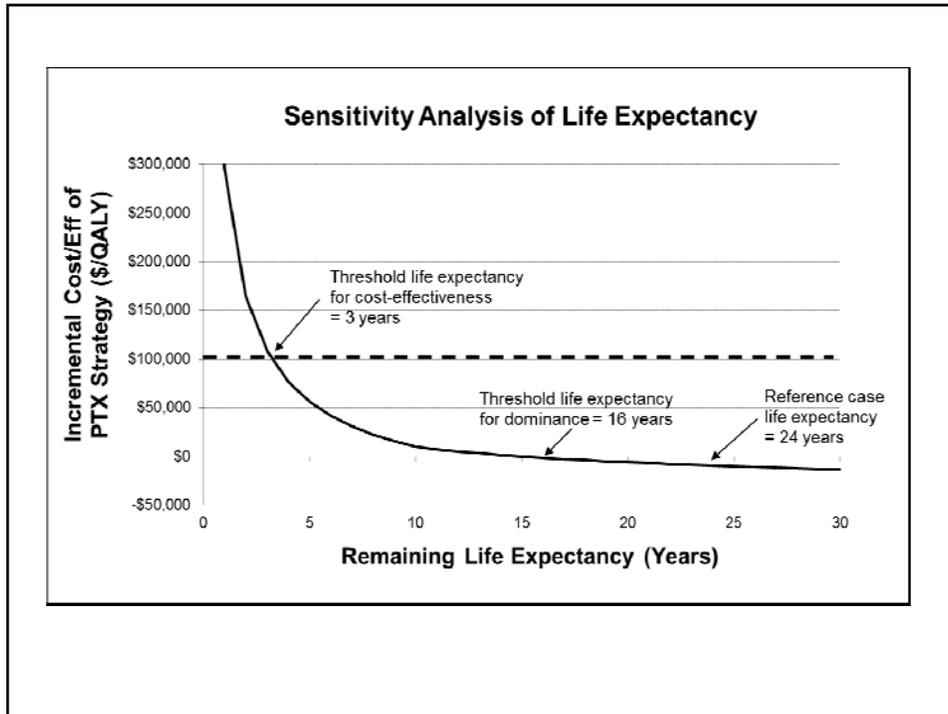
Results: Reference Case

Strategy	Cost	Incremental Cost	Effectiveness (QALYs)	Incremental Effectiveness	Incr. C/E (ICER [†])
Parathyroidectomy	\$6,487	-	17.54*	-	-
Observation	\$8,208	\$1,721	17.35*	-0.19*	Dominated

*quality-adjusted life years, †incremental cost-effectiveness ratio

Observation was **not cost-effective**: more costly and less effective than total thyroidectomy alone





CEA Research

WORKSHOP ON HYPERPARATHYROIDISM

Proceedings

Surgery for Asymptomatic Primary Hyperparathyroidism: Proceedings of the Third International Workshop

Question 6. Is parathyroid surgery cost effective?

Yes, if life expectancy is greater than 3 years

J Clin Endocrinol Metab 94: 366–372, 2009

CEA Research

WORKSHOP ON HYPERPARATHYROIDISM

Proceedings

**Surgery for Asymptomatic Primary
Hyperparathyroidism: Proceedings of the Third
International Workshop**

**Question 6. Is parathyroid surgery cost
effective?**

**Yes, if life expectancy
is greater than 3
years**

And dominant if age<70!

J Clin Endocrinol Metab 94: 366–372, 2009

Quality-of-Life Studies in Primary Hyperparathyroidism

- Disease-specific symptom inventory
- Hospital Anxiety and Depression Scale
- SF-36 Health Survey
- NIH PROMIS®

PROMIS[®]

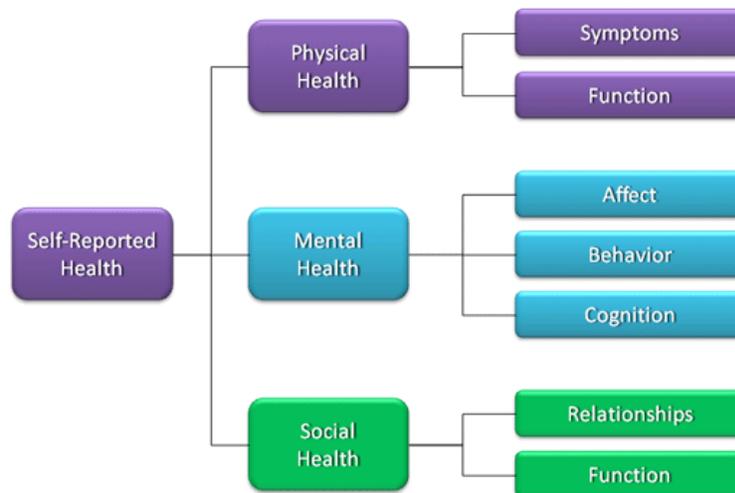
Patient reported outcome measurement system

PROMIS[®] is an efficient, standardized set of tools to measure health-related quality of life

Measures a collection of patient-reported outcomes that are divided into domains

Not disease-specific (allows for comparability across different diseases)

PROMIS Domain Framework



PROMIS Domain Measurement

T-Score is method of measurement for all domains

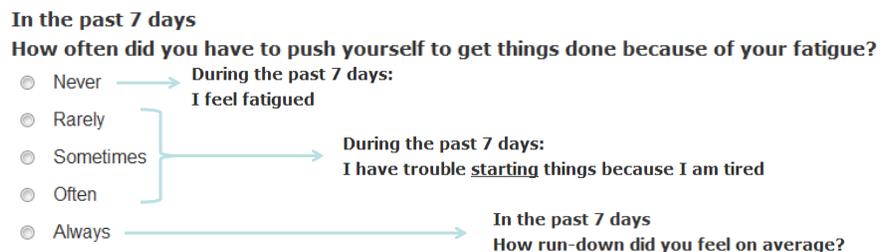
50 = population average

Standard Deviation = 10

Available Computer Adaptive Testing

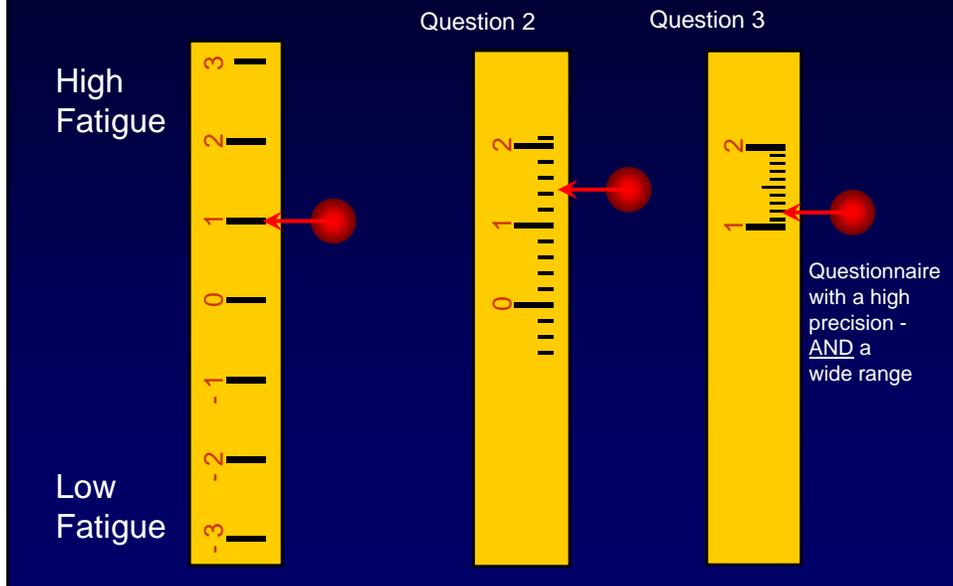
Fatigue: CAT Algorithm

Subsequent items are selected by computer based on previous responses.



CAT will continue until an acceptable standard error is achieved

Fatigue: CAT Algorithm



Measurement of Patient Reported Outcomes in Primary Hyperparathyroidism

- Objective: Measure “softer” symptoms of primary hyperparathyroidism that are not currently part of consensus guidelines recommending surgery.
- Efficiently accomplish measurement during standard clinical encounter.

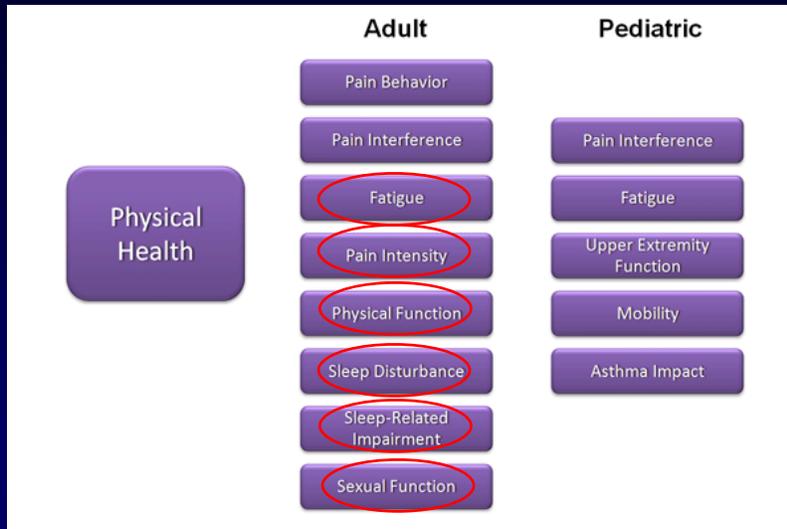
Hypothesis

1. PHPT patients report improved mental and physical health after undergoing successful parathyroidectomy when compared to control patients undergoing surgery for benign thyroid nodules.
2. Improvement after surgery occurs in both “symptomatic” and “asymptomatic” groups as defined by current consensus conference guidelines.

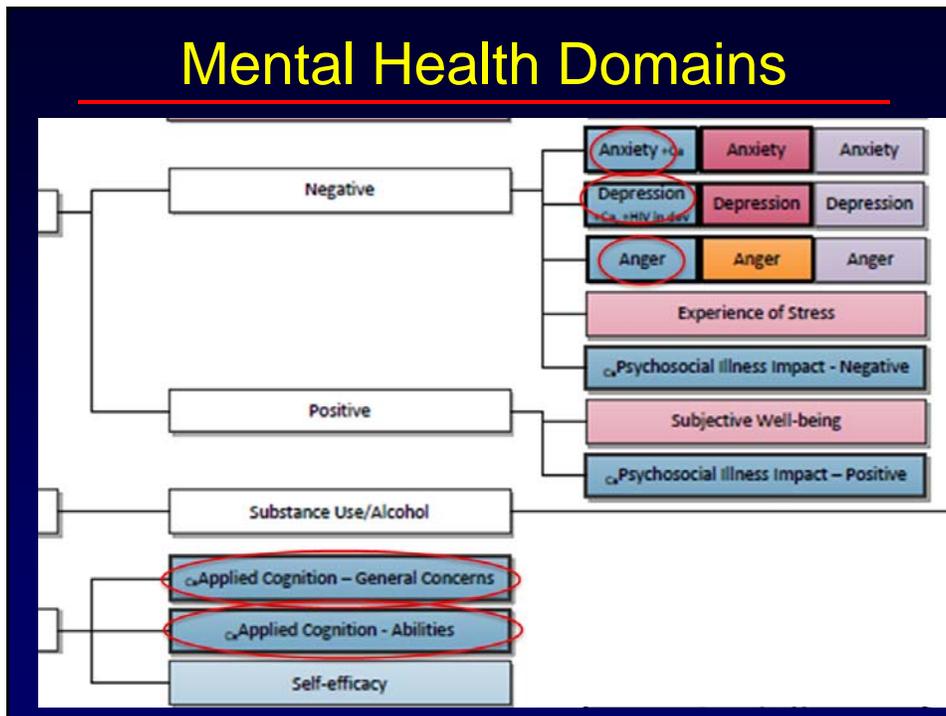
Methods

- Selected relevant health domains (12), literature review and expert opinion
- 6 month prospective enrollment of primary hyperparathyroidism patients and thyroid surgery control patients (September 2012 through February 2013)
- Administered PROMIS item banks during preoperative and 3-week postoperative clinical encounters.

Physical Health Domains

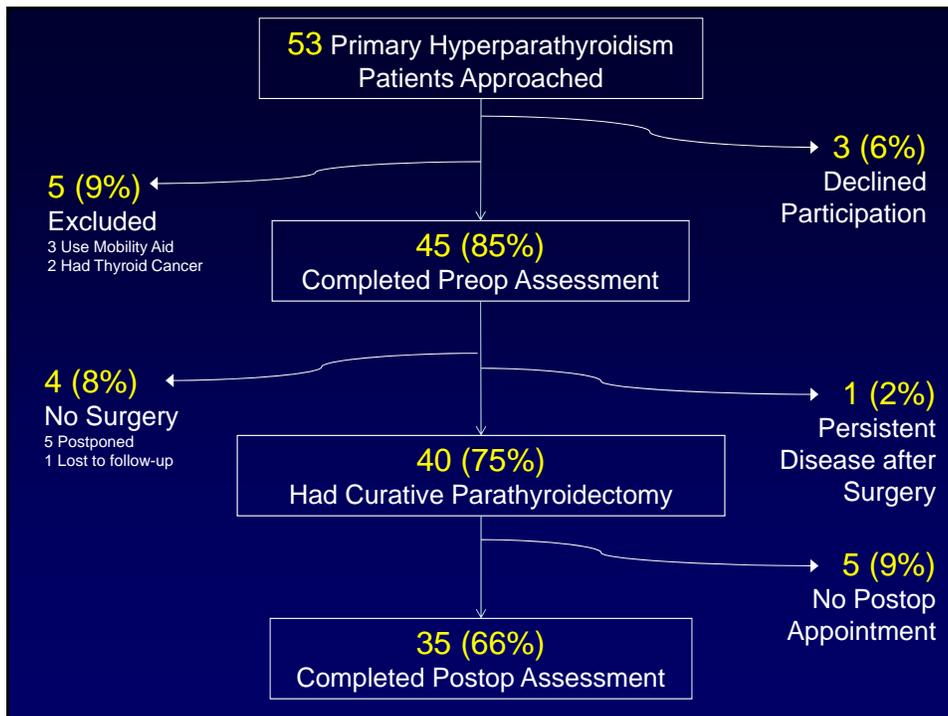


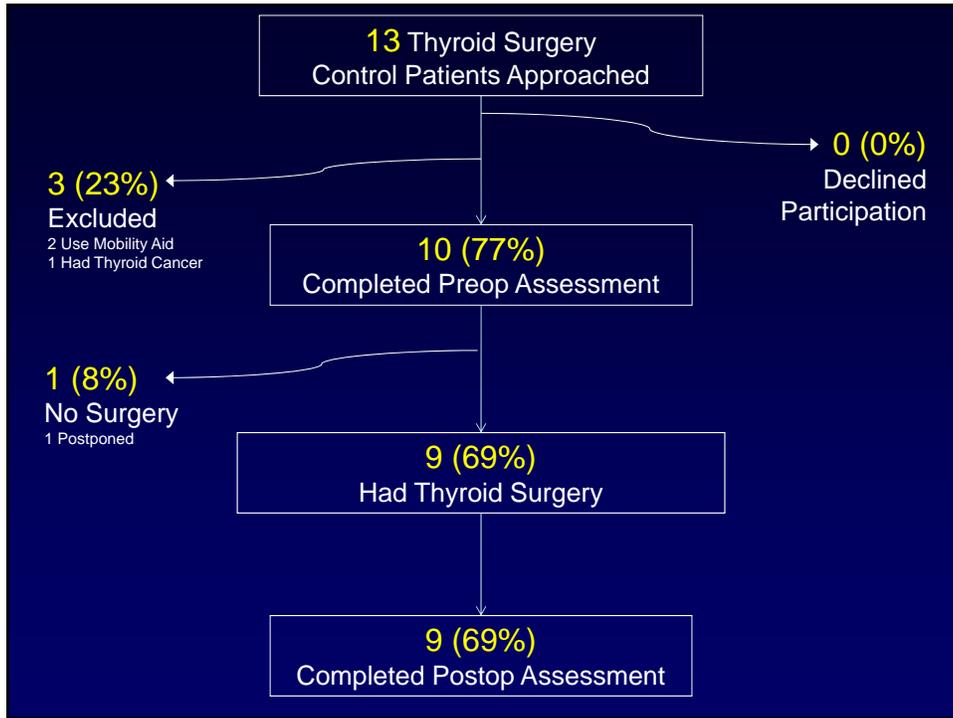
Mental Health Domains



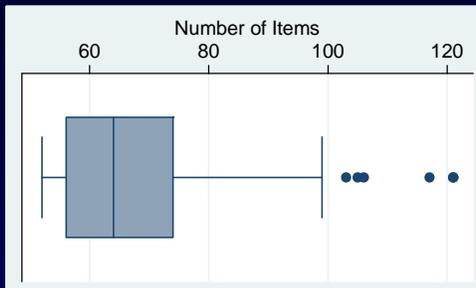
Demographics

	Hyperparathyroidism (n=45)	Benign Thyroid Control (n=10)	P-value
Age (SD)	55 (12.0)	51 (10.1)	0.28
Sex			0.49
Female	36 (80%)	7 (70%)	
Male	9 (20%)	3 (30%)	
Race			0.25
Asian	1 (2%)	0 (0%)	
Black/African Amer.	4 (9%)	3 (30%)	
White	38 (84%)	6 (60%)	
Unknown	2 (4%)	1 (10%)	
Ethnicity			0.65
Hispanic/Latino	3 (7%)	0 (0%)	
Not Hispanic/Latino	31 (69%)	8 (80%)	
Unknown	11 (24%)	2 (20%)	

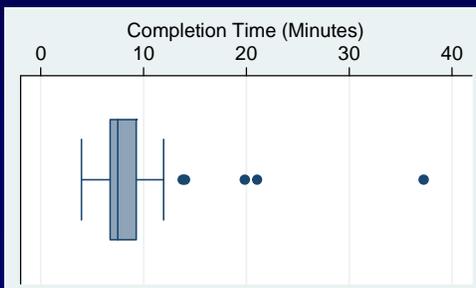




Computer Adaptive Testing Data

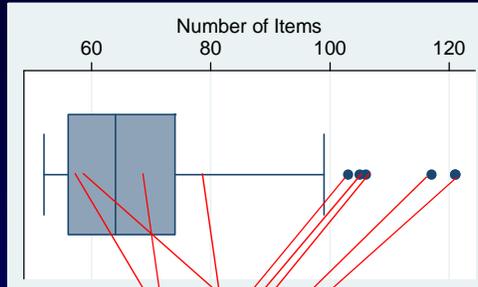


Number of Items
Median: 64 items
Range: 52 to 121

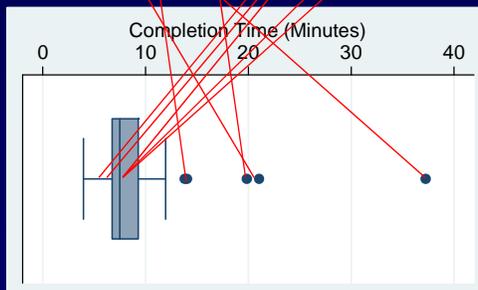


Completion Time
Median: 7.5 Minutes
Range: 4 to 37

Computer Adaptive Testing Data



Number of Items
 Median: 64 items
 Range: 52 to 121



Completion Time
 Median: 7.5 Minutes
 Range: 4 to 37

Preop vs Postop PROMIS T-Scores in Patients with Primary Hyperparathyroidism (n=35)

Domain	Preoperative Score (95% CI)	Postoperative Score (95% CI)	Improvement	P-value
Physical Health				
Fatigue	53.7 (49.1 , 58.3)	44.9 (41.9 , 47.9)	8.8 (5.0 , 12.5)	<0.0001
Interest in Sexual Activity	50.8 (47.1 , 54.5)	52.6 (49.4 , 55.9)	1.8 (-0.5 , 4.1)	0.12
Pain Intensity	38.4 (35.1 , 41.6)	38.1 (35.7 , 40.6)	0.3 (-2.8 , 3.3)	0.87
Physical Function	49.1 (46.3 , 52.0)	51.7 (49.4 , 54.0)	2.6 (0.5 , 4.6)	0.02
Satisfaction with Sex Life	52.6 (47.8 , 57.4)	55.0 (51.0 , 59.0)	2.4 (-0.1 , 4.8)	0.06
Sleep Disturbance	53.1 (49.5 , 56.6)	48.0 (44.7 , 51.2)	5.1 (1.9 , 8.4)	0.003
Sleep-Related Impairment	51.1 (46.6 , 55.5)	44.4 (40.8 , 48.0)	6.7 (3.3 , 10.1)	0.0003
Mental Health				
Anger	52.4 (48.7 , 56.1)	44.5 (42.0 , 46.9)	7.9 (4.5 , 11.3)	<0.0001
Anxiety	53.4 (50.2 , 56.6)	48.4 (45.7 , 51.2)	5.0 (2.6 , 7.3)	0.0002
Cognition – Abilities	45.9 (43.1 , 48.8)	52.9 (50.6 , 55.3)	7.0 (4.4 , 9.6)	<0.0001
Cognition – Gen Concerns	38.1 (33.2 , 43.1)	29.8 (26.4 , 33.1)	8.3 (4.7 , 11.9)	<0.0001
Depression	50.9 (47.9 , 53.9)	44.6 (41.8 , 47.4)	6.2 (3.4 , 9.1)	<0.0001

Preop vs Postop PROMIS T-Scores in Patients with Primary Hyperparathyroidism (n=35)

Domain	Preoperative Score (95% CI)	Postoperative Score (95% CI)	Improvement	P-value
Physical Health				
Fatigue	53.7 (49.1 , 58.3)	44.9 (41.9 , 47.9)	8.8 (5.0 , 12.5)	<0.0001
Interest in Sexual Activity	50.8 (47.1 , 54.5)	52.6 (49.4 , 55.9)	1.8 (-0.5 , 4.1)	0.12
Pain Intensity	38.4 (35.1 , 41.6)	38.1 (35.7 , 40.6)	0.3 (-2.8 , 3.3)	0.87
Physical Function	49.1 (46.3 , 52.0)	51.7 (49.4 , 54.0)	2.6 (0.5 , 4.6)	0.02
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Mental Health				
Anger	52.4 (48.7 , 56.1)	44.5 (42.0 , 46.9)	7.9 (4.5 , 11.3)	<0.0001
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Depression	50.9 (47.9 , 53.9)	44.6 (41.8 , 47.4)	6.2 (3.4 , 9.1)	<0.0001

Preop vs Postop PROMIS T-Scores in Patients with Primary Hyperparathyroidism (n=35)

Domain	Preoperative Score (95% CI)	Postoperative Score (95% CI)	Improvement	P-value
Physical Health				
Fatigue	53.7 (49.1 , 58.3)	44.9 (41.9 , 47.9)	8.8 (5.0 , 12.5)	<0.0001
Interest in Sexual Activity	50.8 (47.1 , 54.5)	52.6 (49.4 , 55.9)	1.8 (-0.5 , 4.1)	0.12
Pain Intensity	38.4 (35.1 , 41.6)	38.1 (35.7 , 40.6)	0.3 (-2.8 , 3.3)	0.87
Physical Function	49.1 (46.3 , 52.0)	51.7 (49.4 , 54.0)	2.6 (0.5 , 4.6)	0.02
Satisfaction with Sex Life	52.6 (47.8 , 57.4)	55.0 (51.0 , 59.0)	2.4 (-0.1 , 4.8)	0.06
Sleep Disturbance	53.1 (49.5 , 56.6)	48.0 (44.7 , 51.2)	5.1 (1.9 , 8.4)	0.003
Sleep-Related Impairment	51.1 (46.6 , 55.5)	44.4 (40.8 , 48.0)	6.7 (3.3 , 10.1)	0.0003
Mental Health				
Anger	52.4 (48.7 , 56.1)	44.5 (42.0 , 46.9)	7.9 (4.5 , 11.3)	<0.0001
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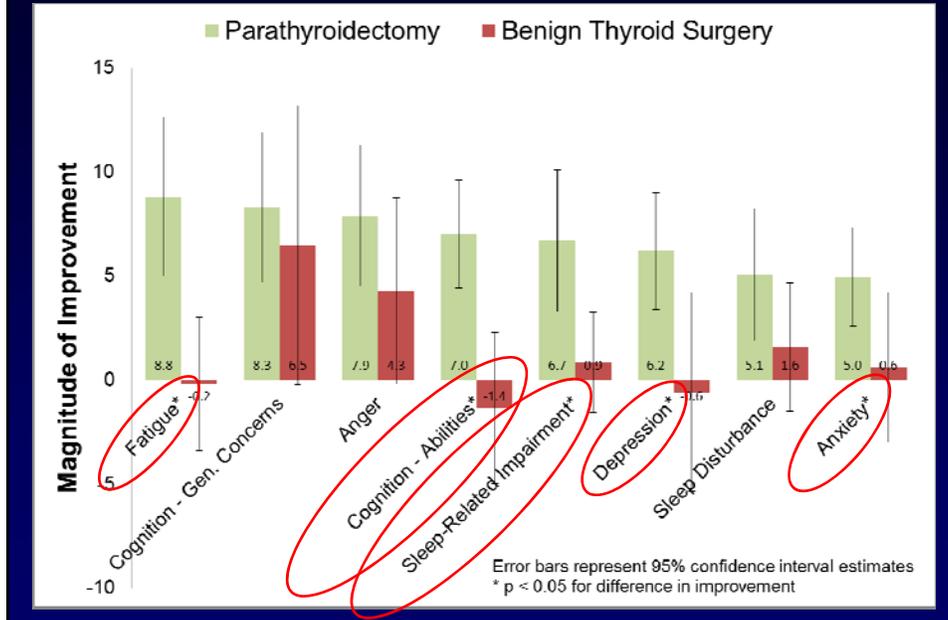
Preop vs Postop PROMIS T-Scores in Control Patients with Thyroid Nodules (n=9)

Domain	Preoperative Score (95% CI)	Postoperative Score (95% CI)	Improvement	P-value
Physical Health				
Fatigue	49.5 (46.8 , 52.2)	49.7 (45.5 , 53.9)	-0.19 (-3.4 , 3.0)	0.90
Interest in Sexual Activity	52.5 (47.1 , 57.9)	52.4 (46.5 , 58.4)	-0.1 (-1.5 , 1.1)	0.90
Pain Intensity	32.0 (29.0 , 35.1)	39.0 (33.5 , 44.4)	-6.9 (-12.7 , -1.2)	0.02
Physical Function	56.4 (52.3 , 60.5)	51.4 (48.8 , 54.0)	-5.1 (-9.2 , -0.9)	0.02
Satisfaction with Sex Life	52.1 (44.2 , 59.9)	52.3 (46.0 , 58.5)	0.2 (-4.2 , 4.6)	0.91
Sleep Disturbance	49.7 (44.7 , 54.8)	48.2 (42.7 , 53.6)	1.6 (-1.5 , 4.7)	0.27
Sleep-Related Impairment	49.5 (46.2 , 52.7)	48.6 (45.0 , 52.2)	0.9 (-1.6 , 3.3)	0.43
Mental Health				
Anger	51.1 (47.6 , 55.4)	47.2 (42.0 , 52.4)	4.3 (-0.2 , 8.8)	0.06
Anxiety	52.1 (48.1 , 56.0)	51.4 (48.1 , 54.8)	0.6 (-3.0 , 4.2)	0.70
Cognition – Abilities	49.5 (45.5 , 53.6)	48.2 (44.1 , 52.3)	-1.4 (-5.0 , 2.3)	0.42
Cognition – Gen Concerns	36.8 (31.8 , 41.8)	30.3 (21.0 , 39.7)	6.5 (-0.2 , 13.2)	0.06
Depression	46.4 (40.9 , 51.8)	46.9 (41.7 , 52.2)	-0.6 (-5.4 , 4.2)	0.79

Preop vs Postop PROMIS T-Scores in Control Patients with Thyroid Nodules (n=9)

Domain	Preoperative Score (95% CI)	Postoperative Score (95% CI)	Improvement	P-value
Physical Health				
Fatigue	49.5 (46.8 , 52.2)	49.7 (45.5 , 53.9)	-0.19 (-3.4 , 3.0)	0.90
Interest in Sexual Activity	52.5 (47.1 , 57.9)	52.4 (46.5 , 58.4)	-0.1 (-1.5 , 1.1)	0.90
Pain Intensity	32.0 (29.0 , 35.1)	39.0 (33.5 , 44.4)	-6.9 (-12.7 , -1.2)	0.02
Physical Function	56.4 (52.3 , 60.5)	51.4 (48.8 , 54.0)	-5.1 (-9.2 , -0.9)	0.02
Satisfaction with Sex Life	52.1 (44.2 , 59.9)	52.3 (46.0 , 58.5)	0.2 (-4.2 , 4.6)	0.91
Sleep Disturbance	49.7 (44.7 , 54.8)	48.2 (42.7 , 53.6)	1.6 (-1.5 , 4.7)	0.27
Sleep-Related Impairment	49.5 (46.2 , 52.7)	48.6 (45.0 , 52.2)	0.9 (-1.6 , 3.3)	0.43
Mental Health				
Anger	51.1 (47.6 , 55.4)	47.2 (42.0 , 52.4)	4.3 (-0.2 , 8.8)	0.06
Anxiety	52.1 (48.1 , 56.0)	51.4 (48.1 , 54.8)	0.6 (-3.0 , 4.2)	0.70
Cognition – Abilities	49.5 (45.5 , 53.6)	48.2 (44.1 , 52.3)	-1.4 (-5.0 , 2.3)	0.42
Cognition – Gen Concerns	36.8 (31.8 , 41.8)	30.3 (21.0 , 39.7)	6.5 (-0.2 , 13.2)	0.06
Depression	46.4 (40.9 , 51.8)	46.9 (41.7 , 52.2)	-0.6 (-5.4 , 4.2)	0.79

Comparison to Controls



Postoperative Improvement Stratified by Presence of Consensus Criteria for Parathyroidectomy

Domain	Met Criteria (95% CI) (n=25)	Did Not Meet Criteria (95% CI) (n=10)	P-value
Physical Health			
Fatigue	9.1 (4.4 , 13.8)	8.0 (0.8 , 15.2)	0.79
Interest in Sexual Activity	-0.2 (-2.2 , 1.8)	6.4 (0.6 , 12)	0.03
Pain Intensity	-0.4 (-4.0 , 3.2)	1.9 (-4.7 , 8.5)	0.51
Physical Function	2.8 (0.0 , 5.6)	2.1 (-0.3 , 4.5)	0.71
Satisfaction with Sex Life	0.9 (-1.2 , 2.9)	5.7 (-1.6 , 13.0)	0.17
Sleep Disturbance	4.1 (0.6 , 7.7)	7.6 (-0.7 , 15.8)	0.41
Sleep-Related Impairment	5.8 (2.0 , 9.5)	9.0 (0.6 , 17.4)	0.44
Mental Health			
Anger	8.2 (3.7 , 12.6)	7.3 (2.0 , 12.5)	0.78
Anxiety	4.7 (1.9 , 7.5)	5.7 (0.4 , 11.0)	0.71
Cognition – Abilities	5.3 (2.9 , 7.7)	11.2 (4.2 , 18.3)	0.10
Cognition – Gen Concerns	7.2 (2.8 , 11.7)	3.1 (3.9 , 18.1)	0.34
Depression	5.2 (2.0 , 8.3)	8.9 (1.8 , 16.1)	0.30

Postoperative Improvement Stratified by Presence of Consensus Criteria for Parathyroidectomy

Domain	Met Criteria (95% CI) (n=25)	Did Not Meet Criteria (95% CI) (n=10)	P-value
Physical Health			
Fatigue	9.1 (4.4 , 13.8)	8.0 (0.8 , 15.2)	0.79
Interest in Sexual Activity	-0.2 (-2.2 , 1.8)	6.4 (0.6 , 12)	0.03
Pain Intensity	-0.4 (-4.0 , 3.2)	1.9 (-4.7 , 8.5)	0.51
Physical Function	2.8 (0.0 , 5.6)	2.1 (-0.3 , 4.5)	0.71
Satisfaction with Sex Life	0.9 (-1.2 , 2.9)	5.7 (-1.6 , 13.0)	0.17
Sleep Disturbance	4.1 (0.6 , 7.7)	7.6 (-0.7 , 15.8)	0.41
Sleep-Related Impairment	5.8 (2.0 , 9.5)	9.0 (0.6 , 17.4)	0.44
Mental Health			
Anger	8.2 (3.7 , 12.6)	7.3 (2.0 , 12.5)	0.78
Anxiety	4.7 (1.9 , 7.5)	5.7 (0.4 , 11.0)	0.71
Cognition – Abilities	5.3 (2.9 , 7.7)	11.2 (4.2 , 18.3)	0.10
Cognition – Gen Concerns	7.2 (2.8 , 11.7)	3.1 (3.9 , 18.1)	0.34
Depression	5.2 (2.0 , 8.3)	8.9 (1.8 , 16.1)	0.30

Conclusions

- PROMIS is an efficient clinical assessment platform for patient-reported outcomes in primary hyperparathyroidism
- Short-term improvement in several domains of physical and mental health after parathyroidectomy
- Additional data needed to assess long term durability of improvement

Future directions

- Sample size is major limitation
- Multicenter, automated, e-mail and Web-based
- Modeling: do calcium and parathyroid hormone levels predict lower quality of life?

Acknowledgements

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 - Michael Yeh, MD
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- Northwestern Section of Endocrine Surgery
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- Northwestern Department of Medical Social Sciences
 - David Cella, PhD, Zeeshan Butt, PhD

Thank You For Your Attention

David Geffen School of Medicine
UCLA Department of Surgery
Section of Endocrine Surgery



David Geffen
School of Medicine

UCLA Health