

Supplementary Materials

1. Inputs Data

Table S1 – Tariff for Exams¹, Consultations, Interventions, Follow-ups

Exam/Consultation/Intervention	Unit Cost	Exam/Consultation/Intervention	Unit Cost
Specialist consultation	€ 20.66	Thyroid-stimulating hormone (TSH)	€ 5.46
S-protein electrophoresis	€ 4.23	Calcitonin	€ 14.41
Parathyroid hormone (PTH)	€ 18.92	Total calcium	€ 1.13
Complete blood count (CBC)	€ 3.17	Prolactin	€ 7.13
Electrocardiogram (ECG)	€ 11.62	Cortisol	€ 7.79
Magnetic resonance imaging - neck	€ 153.60	Sodium	€ 1.02
Computed tomography - neck	€ 97.65	Potassium	€ 1.02
X-ray - neck	€ 15.24	Vitamin D	€ 15.86
Cytology examination	€ 14.10	Aspartate aminotransferase (AST)	€ 1.04
Ultrasound - neck	€ 28.41	Alanine aminotransferase (ALT)	€ 1.00
Thyroid scintigraphy	€ 33.36	Gamma-glutamyl transferase (gamma GT)	€ 1.13
Albumin	€ 1.42	Cholinesterase	€ 1.36
Gastrin	€ 14.08	X-ray - chest	€ 15.49
Lipase	€ 2.58	Inpatient stay per day	€ 674.00 ²
Amylase	€ 1.84	24-hour urinary calcium	€ 1.70
X-ray - hand	€ 14.20	Ionized calcium	€ 5.25
X-ray - skull	€ 22.21	Phosphaturia	€ 1.15
Intravenous urography	€ 89.35	PET-CT 18-Fluoro-Choline	€ 1,071.65
X-ray - abdomen	€ 19.37	Phosphatemia	€ 1.35
Fibrinogen	€ 12.18	C-terminal telopeptide	€ 14.75
Renal ultrasound	€ 34.09	Urinary citrate	€ 3.70
Bone densitometry	€ 36.58	Urinary oxalate	€ 9.15
X-ray - spine	€ 100.89	Histological examination	€ 27.17
Magnesium	€ 1.55	Urinary metanephries	€ 16.50
Bone alkaline phosphatase	€ 12.33	Plasma metanephries	€ 56.00
Alkaline phosphatase (ALP)	€ 1.04	X-ray of other specified sites	€ 14.98
Creatinine	€ 1.13	Vertebral morphometry	€ 17.30
Corticotropin (ACTH)	€ 18.50	Trabecular Bone Score (TBS) assessment	€ 43.38
Growth hormone (GH)	€ 10.48	Speech therapy rehabilitation	€ 45.00
Prothrombin time (PT)	€ 2.85	Free thyroxine (FT4)	€ 6.36
Partial thromboplastin time (PTT)	€ 2.85	Operating room / minute	€ 4.59 ³

Table S2 – Acquisition cost of pharmacological alternatives⁴

Active Ingredient	Cost/mg	Active Ingredient	Cost/mg
Cholecalciferol	€ 0.000060	Droperidol	€ 3.24
Calcifediol	€ 2.216383	Propofol	€ 0.025061
Cinacalcet	€ 0.074458	Rocuronium	€ 0.118016
Alendronic acid	€ 0.029515	Remifentanyl	€ 5.650000
Sodium risedronate	€ 0.050788	Saline solution	€ 0.003923
Sodium ibandronate	€ 0.066182	Antibiotic (cefazolin)	€ 0.002724
Zoledronate	€ 25.546531	NSAID (ketoprofen)	€ 0.007284
Clodronic acid	€ 0.013852	Cortisone	€ 0.016529
Denosumab	€ 2.837513	Paracetamol	€ 0.000242
Indapamide	€ 0.050189	Teriparatide\$	€ 10.614641
Hydrochlorothiazide	€ 0.001860	Calcitriol*	€ 0.376113
Chlorthalidone	€ 0.002052	Calcium carbonate	€ 0.000107
Lidocaine	€ 0.003145	Calcium gluconate	€ 0.000165 ⁵
Midazolam	€ 0.432726	Alendronate	€ 0.029515
Fentanyl	€ 5.650000		

(*) dosage in units; (\$) dosage in micrograms

Table S3 – Cost per minute for healthcare professionals

Professional Role	Cost/Minute ⁶
Specialist Doctor	€ 0.58
Nurse	€ 0.27
Healthcare Assistant	€ 0.23

Table S4 – Acquisition cost of resources required for performing parathyroidectomy

Resource	Cost/Unit	Resource	Cost/Unit
BiClamp forceps	€ 25.03 ⁷	Scalpel	€ 15.38 ⁸
Electrosurgical unit	€ 14.34 ⁹	Surgical swabs	€ 0.18 ^{10(p1)}
Gauze	€ 0.10 ¹¹	Dressing 8x15	€ 0.54 ^{12(p3)}
Surgical sponge	€ 2.20 ¹³	Emodren (low suction drainage)	€ 6.50 ¹⁴
Jackson-Pratt drain	€ 3.07 ¹⁵	Vicryl round suture	€ 6.00 ¹⁶
Sterile material package	€ 24.52 ¹⁷	Monocryl suture	€ 7.25 ¹⁸
Neuromonitoring	€ 33.88 ^{19(p6)}	Prolene for intradermal sutures	€ 6.93 ²⁰
Suture thread	€ 6.00 ¹⁶	Hemostatic cellulose patch (Emoxicel)	€ 75.60 ²¹
Surgical drape	€ 2.16 ²²	Metal clip	€ 0.46 ²³

Table S5 – Hourly Earnings by Job Class and Caregiver Distribution Across Job Classes

Class	Annual Earnings ²⁴	Hourly Earnings*	% of Caregivers in Each Job Class ²⁴
Executives	€ 101,096.00	€ 48.60	1.30%
Managers (Intermediate Level)	€ 54,136.00	€ 26.03	4.40%
Employees	€ 30,770.00	€ 14.79	36.00%
Workers/Apprentices	€ 24,780.00	€ 11.91	58.30%
Hourly Productivity Loss	-	€ 14.05	-

(*) Calculations are based on an average of 40 working hours per week.

2. Outputs Data

2.1. Framework at start

2.1.1. Procedures for the diagnosis of PHPT

Table S6 – Number and Types of Tests Performed for the Diagnosis of Hyperparathyroidism

Test/Consultation	NO.	Cost/Driver
Endocrinology consultation	2.14	€ 44.14
Total calcium	2.31	€ 2.61
Ionized calcium	1.74	€ 9.12
Urinary calcium	1.63	€ 2.76
Phosphatemia	2.08	€ 2.81
Urinary phosphorus	1.11	€ 1.28
Serum albumin	1.71	€ 2.43
Serum protein electrophoresis	0.92	€ 1.03
Serum creatinine	1.83	€ 2.07
Urinary creatinine	1.55	€ 1.74
25OH-Vitamin D	1.67	€ 26.43
Parathyroid hormone (PTH)	2.21	€ 41.78
Alkaline phosphatase	1.33	€ 1.39
Magnesium	0.90	€ 1.39
Anti-transglutaminase antibodies (reflex)	0.39	€ 2.13
Complete blood count (CBC)	1.13	€ 3.56
Serum sodium	0.58	€ 0.60
Serum potassium	0.58	€ 0.60
Electrocardiogram (ECG)	0.49	€ 5.66
X-ray - neck	0.10	€ 1.45
Ultrasound - neck	1.10	€ 31.25
Parathyroid scintigraphy	0.84	€ 27.94
CT scan - neck	0.39	€ 59.14

MRI - neck	0.09	€ 8.88
PET-CT 18-Fluoro-Choline	0.26	€ 277.65
Cytological examination	0.09	€ 1.31
Total		€ 561.15

2.1.2. Procedures for the evaluation of comorbidities and complications

Table S7 – Number and Types of Tests Performed for the Evaluation of Comorbidities and Complications

Test/Consultation	NO.	Cost/Driver
TSH reflex	0.82	€ 4.47
Calcitonin	0.52	€ 7.47
Urinary metanephrines	0.14	€ 2.33
Plasma metanephrines	0.26	€ 14.31
Prolactin (PRL)	0.45	€ 3.18
Corticotropin (ACTH)	0.44	€ 8.05
Serum cortisol	0.43	€ 3.31
Urinary cortisol	0.15	€ 1.13
Growth hormone (GH)	0.42	€ 4.35
IGF-1	0.46	€ 4.83
Gastrin	0.47	€ 6.65
Urinary citrate	0.30	€ 1.11
Urinary oxalate	0.24	€ 2.24
Amylase	0.29	€ 0.53
Lipase	0.29	€ 0.74
Bone alkaline phosphatase	1.06	€ 13.12
C-terminal telopeptide (CTX)	0.99	€ 14.62
Renal ultrasound	1.00	€ 34.09
Bone densitometry	1.00	€ 36.58
X-ray - spine	0.87	€ 87.77
X-ray - hands	0.15	€ 2.09
Neuropsychological evaluation	0.13	€ 2.64
X-ray - skull	0.13	€ 2.84
X-ray of other specified sites	0.06	€ 0.92
Urography	0.04	€ 3.97
Abdominal X-ray	0.14	€ 2.80
Trabecular Bone Score (TBS) during densitometry	1.00	€ 43.38
Vertebral morphometry	1.00	€ 17.30
Total		€ 326.81

2.2. Surgical strategies: Parathyroidectomy

2.2.1. Preoperative Therapies

Table S8 – Active Ingredients and Average Dosage of Preoperative Pharmacological Therapies

Ingredient	Average Dosage	Min	Max	Therapy Duration (months)	T Min	T Max	Average Cost	Min	Max	% of Use	Weighted Cost	Min	Max
Cholecalciferol (UI/month)	46,944.44	16,222.22	83,888.89	7.40	2.00	22.00	€ 20.88	€ 1.95	€ 110.95	77.30 %	€ 16.14	€ 1.51	€ 85.77
Cinacalcet (mg/day)	38.33	23.33	73.33	5.83	1.22	13.33	€ 499.49	€ 63.70	€ 2,184.09	26.00 %	€ 129.87	€ 16.56	€ 567.86
Alendronate (mg/week)	88.13	73.13	114.38	11.25	3.14	29.14	€ 117.05	€ 27.13	€ 393.52	21.25 %	€ 24.87	€ 5.77	€ 83.62
Risedronate (mg/month)	63.75	35.00	35.00	6.75	0.33	13.33	€ 21.85	€ 0.59	€ 23.70	4.17 %	€ 0.91	€ 0.02	€ 0.99
Ibandronate (mg/month)	100.00	100.00	100.00	12.00	0.00	0.00	€ 79.42	€ 0.00	€ 0.00	1.25 %	€ 0.99	€ 0.00	€ 0.00
Zoledronate (mg/year)	4.67	2.60	4.60	18.00	0.00	36.00	€ 178.83	€ 0.00	€ 352.54	25.83 %	€ 47.54	€ 1.35	€ 92.42
Denosumab (mg/6 months)	60.00	40.00	60.00	16.50	5.00	36.00	€ 468.19	€ 94.58	€ 1,021.50	8.13 %	€ 38.04	€ 7.68	€ 83.00
Hydrochlorothiazide (mg/day)	25.00	12.50	50.00	6.00	0.00	0.00	€ 8.37	€ 0.00	€ 0.00	1.67 %	€ 0.14	€ 0.00	€ 0.00
Weighted Total Cost											€ 258.51	€ 32.89	€ 913.66

2.2.2. Pre-Hospitalization Procedures

Table S9 – Number and Types of Tests/Consultations Performed During the Pre-Hospitalization phase

Test/Consultation	NO.	Cost/Driver
Complete blood count (CBC)	1.00	€ 3.17
Prothrombin activity (PT)	0.80	€ 2.28
Partial thromboplastin time (PTT)	0.80	€ 2.28
Fibrinogen	0.60	€ 7.31
Cholinesterase	0.67	€ 0.90
Serum creatinine	1.00	€ 1.13
Serum sodium	1.00	€ 1.02
Serum potassium	1.00	€ 1.02
Aspartate aminotransferase (AST)	1.00	€ 1.04
Alanine aminotransferase (ALT)	1.00	€ 1.00
Gamma-glutamyl transferase (gamma GT)	0.89	€ 1.00
ECG and cardiology consultation	0.90	€ 29.05
ENT consultation and laryngoscopy	0.93	€ 19.21
Chest X-ray	1.00	€ 15.49
Anesthesiology consultation	1.00	€ 20.66
Serum calcium	1.50	€ 1.69
Parathyroid hormone (PTH)	1.00	€ 18.92
Vitamin D 25-OH	1.00	€ 15.86
Parathyroid hormone	1.00	€ 18.92
Total		€ 161.95

2.2.3. Pharmacological Therapy Used During Surgery

Table S10 – Active Ingredients and Average Dosage Used During Parathyroidectomy Surgery

Active Ingredient	Dosage (mg/surgery - average)	Cost/Active Ingredient
Lidocaine	30.00	€ 0.09
Midazolam	7.83	€ 3.39
Fentanyl	0.30	€ 1.70
Droperidol	1.25	€ 4.05
Propofol	384.40	€ 9.63
Rocuronium	60.00	€ 7.08
Remifentanyl	0.90	€ 5.09
Saline solution	625.00	€ 2.45
Antibiotic (cefazolin)	2000.00	€ 5.45
NSAID (ketoprofen)	30.00	€ 0.22
Cortisone	337.33	€ 5.58
Paracetamol	1000.00	€ 0.24
Total		€ 44.96

2.2.4. Materials/Devices Used

Table S11 – Types of Materials Used and Average Frequency During Parathyroidectomy Surgery

Resource	NO./Day	Cost/Driver
Big Clamp	0.17	€ 4.17
Electrosurgical unit	0.71	€ 10.24
Scalpel	1.00	€ 15.38
Surgical swabs	1.00	€ 0.18
Suture thread	1.17	€ 7.00
Neuromonitoring	0.51	€ 17.22
Jackson-Pratt drain	0.53	€ 1.61
Gauze	10.00	€ 0.99
Surgical drape	2.29	€ 4.93
Sponge	6.71	€ 14.77
Sterile material package	0.83	€ 20.43
Low suction drainage (Emodren)	0.60	€ 3.90
Vicryl round suture	2.00	€ 12.00

Monocryl	0.86	€ 6.21
Dressing 8 x 15	0.86	€ 0.46
Manually loaded metal clips	10.00	€ 4.58
Hemostatic cellulose patch (Emoxicel)	1.00	€ 75.60
Prolene for intradermal sutures	1.00	€ 6.93
Surgical glue	1.00	€ 0.00
Total		€ 206.63

2.2.5. Intraoperative Procedures

Table S12 – Types of Intraoperative Procedures (Parathyroidectomy Surge

Procedure	Number of Determinations per Surgery	Total Cost
Intraoperative PTH measurement	2.41	€ 45.59

2.2.6. Hospital length of Stay

Table S13 – Length of Hospital Stay for Patients Undergoing Parathyroidectomy

Parameter	Days	Total Cost
Hospital stay duration	1.97	€ 1,329.62

2.2.7. Healthcare Professionals & Facility

Table S14 – Resource Allocation During Hospital Stay for Parathyroidectomy Patients

Parameter	Value	Cost
Average Surgery Duration (min)	42.22	
Professional Role	NO.	Cost/Professional
Doctor	1.86	€ 45.42
Nurse	1.75	€ 19.81
Anesthesiologist	1.13	€ 27.52
Assistant	1.13	€ 11.14
Scrub Nurse	1.00	€ 11.32
Sub-Total Personnel		€ 115.21
Operating Room		€ 193.82
Total		€ 309.02

2.2.8. Follow-up

2.2.8.1. Standard Postoperative Course

Table S15 – Costs Incurred During the First Year for Patients Undergoing Parathyroidectomy with a Standard Postoperative Course

Parameter	%	Cost/Driver
% of patients with a standard course	95.02%	
Visit/Test/Treatment	NO.	Cost/Driver
Endocrinology consultation	1.54	€ 31.85
Surgical consultation	1.08	€ 22.38
Total calcium	2.29	€ 2.59
Serum albumin	1.59	€ 2.26
Ionized calcium	1.38	€ 7.25
Phosphatemia	1.45	€ 1.96
Parathyroid hormone (PTH)	2.04	€ 38.62
Serum creatinine	1.41	€ 1.59
25(OH) Vitamin D plasma	1.83	€ 29.08
Bone alkaline phosphatase	1.04	€ 12.85
C-terminal telopeptide (CTX)	0.91	€ 13.41
Urinary calcium	1.23	€ 2.09
Histological examination	1.00	€ 27.17
TSH reflex	0.75	€ 4.07
Neck ultrasound	0.56	€ 8.59
Renal ultrasound	0.68	€ 23.24
Bone densitometry	0.78	€ 28.35
Calcium therapy	N/A	€ 0.43
Bisphosphonate therapy (20.00%)	N/A	€ 21.49

Calcitriol/alfacalcidol therapy	N/A	€ 1.13
Cholecalciferol/calcifediol therapy	N/A	€ 115.18
Total		€ 395.57
Weighted Total		€ 375.89

2.2.8.2. Postoperative Course with Acute Complications

Table S16 – Costs Incurred During the First Year for Patients with Acute Postoperative Complications

Parameter	NO.	Cost/Driver
% of patients with acute complications	2.54%	
Visit/Test/Treatment	NO.	Cost/Driver
Endocrinology consultation	1.95	€ 40.38
Surgical consultation	0.95	€ 19.72
ENT consultation	1.55	€ 32.12
Reoperation	0.47	€ 1,333.45
Anesthesiology consultation	0.51	€ 10.45
Electrocardiogram (ECG)	0.60	€ 6.98
Complete blood count (CBC)	1.10	€ 3.48
Total calcium	2.27	€ 2.56
Serum albumin	1.91	€ 2.71
Ionized calcium	1.64	€ 8.59
Phosphatemia	1.73	€ 2.33
Parathyroid hormone (PTH)	1.86	€ 35.26
Serum creatinine	1.77	€ 2.00
25(OH) Vitamin D plasma	1.82	€ 28.84
Calcium infusion	0.60	€ 0.01
Calcitriol therapy	0.63	€ 5.30
Neck ultrasound	0.80	€ 12.21
Total		€ 1,546.40
Weighted Total		€ 39.32

2.2.8.3. Postoperative Course with Chronic Complications

Table S17 – Costs Incurred During the First Year for Patients with Chronic Postoperative Complications

Parameter	NO.	Cost/Driver
% of patients with chronic complications	2.43%	
Visit/Test/Treatment	NO.	Cost/Driver
Endocrinology consultation	2.09	€ 43.20
Surgical consultation	1.00	€ 20.66
Speech therapy rehabilitation	1.61	€ 181.02
Electrocardiogram (ECG)	0.37	€ 4.33
TSH reflex	0.92	€ 5.02
Total calcium	2.73	€ 3.08
Serum albumin	1.82	€ 2.58
Ionized calcium	2.00	€ 10.50
Phosphatemia	2.27	€ 3.07
Parathyroid hormone (PTH)	2.45	€ 46.44
Serum creatinine	1.91	€ 2.15
25(OH) Vitamin D plasma	1.91	€ 30.28
Urinary calcium	1.20	€ 19.03
Urinary phosphorus	0.70	€ 11.10
Magnesium	0.44	€ 0.46
Thyroxine therapy	N/A	€ 6.36
Calcium therapy	N/A	€ 4.83
Calcitriol/alfacalcidol therapy	N/A	€ 8.46
Cholecalciferol/calcifediol therapy	N/A	€ 9.60
Teriparatide	0.001	€ 2.12
Total		€ 414.29
Weighted Total		€ 10.07

2.2.9. Indirect Costs

Table S18 – Productivity Loss Associated with Parathyroidectomy for Patients and Caregivers

Category	Days	Cost
Hospital stay	1.97	€ 221.71
Postoperative recovery (convalescence)	5.66	€ 636.51
Sub-Total – Patient		€ 858.21
% of patients with caregiver	7.78%	€ 66.80
Total Productivity Loss		€ 925.01

2.3. Non-Surgical Treatments

2.3.1. Pharmacological Therapy

Table S19 – Active Ingredients and Average Dosage of Pharmacological Therapies

Ingredient	Average Dosage	Min	Max	Therapy Duration (months)	Min	Max	Total Cost	Min	Max	% of Use	Weighted Cost (percentage)	Min	Max
Cholecalciferol (IU/month)	49,666.67	26,714.29	90,285.71	23.14	8.40	50.00	€ 69.10	€ 13.49	€ 271.39	81.70%	€ 56.46	€ 11.02	€ 221.73
Calcifediol (mg/month)	0.26	0.15	0.30	10.00	6.00	6.00	€ 5.66	€ 1.99	€ 3.99	1.71%	€ 0.10	€ 0.03	€ 0.07
Cinacalcet (mg/day)	35.50	26.67	70.00	16.86	5.29	27.86	€ 1,336.73	€ 314.85	€ 4,355.77	29.32%	€ 391.93	€ 92.31	€ 1,277.11
Alendronate (mg/week)	93.89	100.71	100.71	29.33	11.14	58.29	€ 325.15	€ 132.49	€ 693.04	20.00%	€ 65.03	€ 26.50	€ 138.61
Risedronate (mg/month)	62.50	70.00	73.33	22.50	18.00	24.00	€ 71.42	€ 63.99	€ 89.39	3.38%	€ 2.41	€ 2.16	€ 3.02
Ibandronate (mg/month)	125.00	125.00	125.00	15.00	18.00	24.00	€ 124.09	€ 148.91	€ 198.55	0.86%	€ 1.06	€ 1.28	€ 1.70
Zoledronate (mg/year)	5.00	5.00	5.00	26.57	12.00	42.00	€ 317.81	€ 127.73	€ 447.06	37.86%	€ 120.31	€ 48.36	€ 169.25
Denosumab (mg/6 months)	60.00	60.00	60.00	27.43	10.80	40.43	€ 778.29	€ 306.45	€ 1,147.30	15.10%	€ 117.52	€ 46.27	€ 173.24
Indapamide (mg/day)	6.25	6.25	6.25	6.00	6.00	6.00	€ 56.46	€ 56.46	€ 56.46	1.25%	€ 0.71	€ 0.71	€ 0.71
Hydrochlorothiazide (mg/day)	15.63	12.50	29.17	12.00	12.00	12.00	€ 10.46	€ 8.37	€ 19.53	3.75%	€ 0.39	€ 0.31	€ 0.73
Chlorthalidone (mg/day)	6.25	6.25	12.50	0.00	0.00	0.00	€ 0.00	€ 0.00	€ 0.00	1.25%	€ 0.00	€ 0.00	€ 0.00
Weighted Total Cost											€ 755.92	€ 228.95	€ 1,986.16

2.3.2. Follow-up

Table S20 – Types and Annual Frequency of Specialist Visits and Diagnostic Tests for Monitoring Patients Undergoing Pharmacological Therapy

Visit/Test	NO. / Year	Cost/Driver
Endocrinology consultation	1.56	€ 32.14
Serum creatinine	1.40	€ 1.58
Total calcium	1.50	€ 1.69
Serum albumin	1.40	€ 1.99
Ionized calcium	1.14	€ 5.99
Urinary calcium	1.03	€ 1.76
Phosphatemia	1.40	€ 1.89
Urinary phosphorus	0.62	€ 0.71
Alkaline phosphatase	1.10	€ 1.14
Parathyroid hormone (PTH)	1.50	€ 28.38
Neck ultrasound	0.50	€ 7.62
Parathyroid scintigraphy	0.17	€ 5.67
Renal ultrasound	0.73	€ 24.89
Bone densitometry	0.57	€ 20.85
Spine X-ray	0.39	€ 38.84
Bone alkaline phosphatase	0.85	€ 10.48
C-terminal telopeptide (CTX)	0.80	€ 11.80
Total		€ 197.42

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