

**Supplementary tables 1 - 50**

**Supplementary Table 1 – Search strategy for Ovid MEDLINE(R)**

1.	Prolactinoma/
2.	Prolactinoma*.mp.
3.	Micro?prolactinoma*.mp.
4.	Macro?prolactinoma*.mp.
5.	(prolactin* adj3 (adenoma* or carcinoma* or tumor*)).tw.
6.	Lactotroph.mp. or Lactotrophs/
7.	PRL.ti.
8.	(PRL secreting adj3 (adenoma* or carcinoma* or tumor*)).tw.
9.	prolactin*.ti.
10.	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11.	Dopamine Agonists/
12.	dopamin* agonist*.ti.
13.	cabergolin*.mp. or Cabergoline/
14.	11 or 12 or 13
15.	10 AND 14

**Supplementary Table 2 – Rates for exams, visits, interventions, follow-ups**

<b>Examination / visit / intervention</b>	<b>Unit cost</b>
Specialist visit	€ 20.66 [1]
Blood count	€ 3.17 [1]
Electrocardiogram	€ 11.62 [1]
Glycemia	€ 1.17 [1]
Alkaline Phosphatase (ALP)	€ 1.04 [1]
Creatinine	€ 1.13 [1]
Prothrombin time (PT)	€ 2.85 [1]
Partial thromboplastin time (PTT)	€ 2.85 [1]
Thyrotropin (TSH)	€ 5.46 [1]
Free thyroxine (FT4)	€ 6.36 [1]
Total serum calcium	€ 1.13 [1]
Ordinary hospital stay/day	€ 674.00 [2]
Prolactin	€ 7.13 [1]
Estradiol	€ 9.11 [1]
Testosterone	€ 9.78 [1]
Bone mineral density	€ 31.50 [1]
Cortisol	€ 7.79 [1]
Pituitary MRI with contrast medium	€ 247.50 [1]
Visual field test	€ 16.78 [1]
Serum sodium	€ 1.02 [1]
Potassium	€ 1.02 [1]
Cholesterol	€ 1.04 [1]
Vitamin D	€ 15.86 [1]
Macroprolactin	€ 19.71 [1]
Phosphorus	€ 1.46 [1]
PTH	€ 18.92 [1]
Heart ultrasound	€ 51.65 [1]
Serum Electrophoresis	€ 4.23 [1]
ACTH test 1 mcg	€ 18.50 [1]
Follicle-Stimulating Hormone (FSH)	€ 6.21 [1]
Luteinizing Hormone (LH)	€ 7.20 [1]
IGF-I	€ 10.48 [1]
Computed tomography of the head	€ 120.42 [1]
Aspartate aminotransferase (AST)	€ 1.04 [1]
Alanine aminotransferase (ALT)	€ 1.00 [1]
Gamma-glutamyl transferase (GGT)	€ 1.13 [1]
Bilirubin	€ 1.13 [1]
Urinalysis	€ 2.17 [1]
Optical computed tomography (OCT)	€ 74.88 [1]
Urinary Sodium	€ 2.17 [1]
Prostate specific antigen (PSA)	€ 7.41 [1]
Cholinesterase	€ 1.36 [1]
Nasal endoscopy	€ 14.10 [1]
Blood Urea nitrogen	€ 1.13 [1]
MRI of the brain	€ 166.58 [1]
Lumbar puncture	€ 457.00 [3]
Total calcium	€ 1.13 [1]
Chest X-ray	€ 15.49 [1]
Operating room (hourly rate)	€ 1,225.66 [4]

1. Ministry of Health - Rates for outpatient assistance services; available at: [http://www.salute.gov.it/portale/temi/p2\\_6.jsp?id=1767&area=programmazioneSanitariaLea&menu=lea](http://www.salute.gov.it/portale/temi/p2_6.jsp?id=1767&area=programmazioneSanitariaLea&menu=lea);
2. "Green Paper on Public Expenditure" (2015) - State General Accounting Office - Technical Commission for Public Finance; available at: [http://www.astrid-online.it/static/upload/protected/Libr/Libro\\_Verde\\_Spesa\\_Pubblica.pdf](http://www.astrid-online.it/static/upload/protected/Libr/Libro_Verde_Spesa_Pubblica.pdf);
3. Supplementary Mutual Health - Together Health; available at: [https://www.insiemesalute.org/mutua-sanitaria/insiemesalute.nsf/pdf/tariffario\\_completo\\_insieme\\_salute.pdf](https://www.insiemesalute.org/mutua-sanitaria/insiemesalute.nsf/pdf/tariffario_completo_insieme_salute.pdf);
4. Rossitto, C., Gueli Alletti, S., Romano, F., Fiore, A., Coretti, S., Oradei, M., ... & Scambia, G. (2016). Use of robot-specific resources and operating room times: the case of Telelap Alf-X robotic hysterectomy. *The International Journal of Medical Robotics and Computer Assisted Surgery*, 12(4), 613-619

**Supplementary Table 3 - Acquisition cost of pharmacological alternatives [1]**

Active principle	Cost/mg
Bromocriptine	€ 0.0816
Cabergoline	€ 8.5607
Temozolomide	€ 0.7234
Cefazolin	€ 0.0016
Vancomycin	€ 0.0182
Amoxicillin-clavulanate	€ 0.0007
Hydrocortisone	€ 0.0080
Remifentanil	€ 5.6867
Fentanyl	€ 5.6867
Sufentanil	€ 18.2365
Propofol	€ 0.0144
Sevoflurane <sup>§</sup>	€ 0.3727
Estradiol/drospirenone (estrogenic)	€ 0.2073
Thyroxine	€ 0.6232
Cortisone acetate	€ 0.0184
Desmopressin	€ 418.7891*
Testosterone	€ 0.0080
Acetazolamide	€ 0.0010
Meropenem	€ 0.0136
Fibrin glue (units)	€ 179.5800
Sodium chloride <sup>§</sup>	€ 0.0016

1. Italian Medicines Agency (AIFA); available at: <https://www.aifa.gov.it/liste-farmaci-a-h>

**Supplementary Table 4 – Cost/minute of healthcare professionals and use of the operating room**

	Cost/minute [1]
<b>Physician</b>	€ 0.58
<b>Nurse</b>	€ 0.27
<b>Social health worker</b>	€ 0.23

1. Agency for the Negotiating Representation of Public Administrations (ARAN); available at: <https://www.aranagenzia.it/statistiche-e-pubblicazioni/dati-statistici.html>

**Supplementary Table 5 – Acquisition cost of resources necessary for the delivery of radiation therapy**

Resource	Cost/unit
Needle cannula	€ 0.22 [1]
Thermoplastic mask	€ 100.00 [2]
Linear accelerator - LINAC	€ 42.89 [3]
Gamma knife - Leksell	€ 10.00 [4]

The depreciation cost of the equipment was calculated on the basis of the cost of a linear accelerator of €2,213,000 and a gamma-knife unit of €400,000, assuming that both units are capable of delivering 4000 treatments over the course of their average life, respectively 12 years and 10 years.

1. Lombardy Region - ASST Bergamo West; available at: [https://www.Ospedalegiglio.it/sito/it/fondazione/bandi-e-appalti/download/1173\\_8c668741a110333e37e3eaff7f3b3e4c.html](https://www.Ospedalegiglio.it/sito/it/fondazione/bandi-e-appalti/download/1173_8c668741a110333e37e3eaff7f3b3e4c.html);
2. ASL Rome 1; available at: [https://www.aslroma1.it/uploads/files/53\\_42\\_1907\\_del\\_23.06.2017.pdf](https://www.aslroma1.it/uploads/files/53_42_1907_del_23.06.2017.pdf);
3. Digital administration; available at: <https://www.Ospedale.perugia.it/bandi/procedura-aperta-per-la-fornitura-di-un-accelerator-lineare-linac-corredato-di-strumentazione-fisico-dosimetrica-di-sistemi-for-checking-the-patient-set-up-and-immobilization-systems>;
4. Official Gazette; available at: [https://www.gazzettaufficiale.it/atto/contratti/caricaDettaglioAtto/originario;jsessionid=m4bXaRrkq3FyXQGwhXNwwQ\\_.ntc-as5-guri2b?atto.dataPubblicazioneGazzetta=2016-09-21&atto.codiceRedazionale=TV16BHA11897](https://www.gazzettaufficiale.it/atto/contratti/caricaDettaglioAtto/originario;jsessionid=m4bXaRrkq3FyXQGwhXNwwQ_.ntc-as5-guri2b?atto.dataPubblicazioneGazzetta=2016-09-21&atto.codiceRedazionale=TV16BHA11897)

**Supplementary Table 6 – Hourly earnings by working class and caregiver distribution among working classes [1]**

WORKING CLASS	ANNUAL EARNINGS	HOURLY EARNINGS*	% of caregivers in each working class
Senior executives	€ 101,096.00	€ 48.60	1.30%
Manager (intermediate level)	€ 54,136.00	€ 26.03	4.40%
Employee	€ 30,770.00	€ 14.79	36.00%
Worker/Apprentice	€ 24,780.00	€ 11.91	58.30%
<b>Loss of hourly productivity</b>		<b>€ 14.05</b>	

(\* ) An average of 40 working hours per week was considered

1. Job Pricing: All About Rewards – Salary Outlook 2019: Analysis of the Italian salary market – data updated to the second half of 2018 – Available at: <https://www.jobpricing.it/blog/project/salary-outlook-2019-prima-edition>

**Supplementary Table 7 - Average dosage of drug therapy with cabergoline**

Microprolactinoma	mg/week [C.I.]	Distribution	Annual cost
1 <sup>st</sup> year of treatment	0.94 [0.82-1.05]	Normal	€ 417.33
Subsequent years of treatment	0.67 [0.58-0.75]	Normal	€ 296.77
Macroprolactinoma	mg/week		Annual cost
1 <sup>st</sup> year of treatment	0.67 [0.58-0.75]	Normal	€ 296.77
Subsequent years of treatment	1.38 [1.20-1.55]	Normal	€ 612.09

**Supplementary Table 8 - Diagnostic tests and specialist visits that are provided for the initial classification of the patient - Therapy with cabergoline in microprolactinoma**

	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	2.00 [1.75-2.25]	Normal	€ 41.32
Prolactin	€ 7.13	1.63 [1.42-1.83]	Normal	€ 11.59
Thyrotropin (TSH)	€ 5.46	1.25 [1.10-1.41]	Normal	€ 6.83
Free thyroxine (FT4)	€ 6.36	1.25 [1.10-1.41]	Normal	€ 7.95
Follicle-Stimulating Hormone (FSH)	€ 6.21	1.00 [0.88-1.12]	Normal	€ 6.21
Luteinizing Hormone (LH)	€ 7.20	1.00 [0.88-1.12]	Normal	€ 7.20
Estradiol (E2) in women	€ 3.98	0.88 [0.88-1.13]	Normal	€ 3.98
Testosterone in men	€ 9.78	1.25 [1.10-1.41]	Normal	€ 6.11
Bone mineral density	€ 31.50	0.88 [0.88-1.13]	Normal	€ 13.78
Cortisol	€ 7.79	1.13 [0.99-1.26]	Normal	€ 8.76
IGF-I	€ 10.48	1.25 [1.10-1.41]	Normal	€ 13.11
Pituitary MRI with contrast medium	€ 247.50	1.00 [0.88-1.12]	Normal	€ 247.50
Visual field test	€ 16.78	0.75 [0.66-0.84]	Normal	€ 12.59
Blood count	€ 3.17	0.88 [0.88-1.13]	Normal	€ 2.77
Glycemia	€ 1.17	0.75 [0.66-0.84]	Normal	€ 0.88
Sodium	€ 1.02	0.75 [0.66-0.84]	Normal	€0.77
Potassium	€ 1.02	0.75 [0.66-0.84]	Normal	€0.77
Cholesterol	€ 1.04	0.75 [0.66-0.84]	Normal	€ 0.78
Vitamin D	€ 15.86	0.88 [0.88-1.13]	Normal	€ 13.88
Creatinine	€ 1.13	0.88 [0.88-1.13]	Normal	€ 0.99
Macroprolactin	€ 19.71	1.00 [0.88-1.12]	Normal	€ 19.71
Calcemia	€ 1.13	1.00 [0.88-1.12]	Normal	€ 1.13
Phosphoremia	€ 1.46	1.00 [0.88-1.12]	Normal	€ 1.46
PTH	€ 18.92	1.00 [0.88-1.12]	Normal	€ 18.92
Heart ultrasound	€ 51.65	1.00 [0.88-1.12]	Normal	€ 51.65
ACTH test 1 mcg	€ 18.50	1.00 [0.88-1.12]	Normal	€ 18.50
Serum Electrophoresis	€ 4.23	1.00 [0.88-1.12]	Normal	€ 4.23
<b>TOTAL</b>				<b>€ 523.34</b>

**Supplementary Table 9** - *Diagnostic tests and specialist visits that are provided for the initial classification of the patient - Therapy with cabergoline in macroprolactinoma*

	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Specialist	€ 20.66	2.13 [1.86-2.39]	Normal	€ 43.90
Prolactin	€ 7.13	1.50 [1.31-1.69]	Normal	€ 10.70
Thyrotropin (TSH)	€ 5.46	1.25 [1.10-1.40]	Normal	€ 6.83
Free thyroxine (FT4)	€ 6.36	1.25 [1.10-1.40]	Normal	€ 7.95
Follicle-Stimulating Hormone (FSH)	€ 6.21	1.00 [0.88-1.12]	Normal	€ 6.21
Luteinizing Hormone (LH)	€ 7.20	1.00 [0.88-1.12]	Normal	€ 7.20
Estradiol (E2) in women	€ 9.11	0.88 [0.77-0.98]	Normal	€ 3.98
Testosterone in men	€ 9.78	1.25 [1.10-1.40]	Normal	€ 6.11
Bone mineral density	€ 31.50	0.88 [0.77-0.98]	Normal	€ 27.56
Cortisol	€ 7.79	1.13 [0.99-1.26]	Normal	€ 8.76
IGF-I	€ 10.48	1.25 [1.10-1.40]	Normal	€ 13.11
Pituitary MRI with contrast medium	€ 247.50	1.25 [1.10-1.40]	Normal	€ 309.38
Visual field test	€ 16.78	1.00 [0.88-1.12]	Normal	€ 16.78
Blood count	€ 3.17	0.88 [0.77-0.98]	Normal	€ 2.77
Glycemia	€ 1.17	0.88 [0.77-0.98]	Normal	€ 1.03
Sodium	€ 1.02	0.88 [0.77-0.98]	Normal	€ 0.89
Potassium	€ 1.02	0.88 [0.77-0.98]	Normal	€ 0.89
Cholesterol	€ 1.04	0.88 [0.77-0.98]	Normal	€ 0.91
Vitamin D	€ 15.86	0.88 [0.77-0.98]	Normal	€ 13.88
Creatinine	€ 1.13	0.88 [0.77-0.98]	Normal	€ 0.99
Computed optical tomography (OCT)	€ 74.88	0.67 [0.58- 0.75]	Normal	€ 80.28
ACTH test 1 mcg	€ 18.50	3.00 [2.63-3.37]	Normal	€ 55.49
Calcemia	€ 1.13	1.00 [0.88-1.12]	Normal	€ 1.13
Phosphoremia	€ 1.46	1.00 [0.88-1.12]	Normal	€ 1.46
PTH	€ 18.92	1.00 [0.88-1.12]	Normal	€ 18.92
Heart ultrasound	€ 51.65	1.00 [0.88-1.12]	Normal	€ 51.65
Serum electrophoresis	€ 4.23	1.00 [0.88-1.12]	Normal	€ 4.23
Macroprolactin	€ 19.71	1.00 [0.88-1.12]	Normal	€ 19.71
<b>TOTAL</b>				<b>€ 722.68</b>

**Supplementary Table 10** - Number and type of diagnostic tests and specialist visits that are provided, on an annual basis, for the follow-up of the patient undergoing pharmacological therapy with cabergoline in microprolactinoma

Term	Brief			
	1 <sup>st</sup> year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	2.5 [2.19-2.81]	Normal	51.65
Prolactin	€ 7.13	2.75 [2.41-3.09]	Normal	19.61
Bone mineral density	€ 31.50	0.63 [0.55-0.70]	Normal	19.69
Pituitary MRI	€ 31.50	1 [0.88-1.12]	Normal	247.5
Vitamin D	€ 15.86	1.5 [1.31-1.69]	Normal	23.79
Thyrotropin (TSH)	€ 5.46	1 [0.77-1.12]	Normal	5.46
Free thyroxine (FT4)	€ 6.36	1 [0.77-1.12]	Normal	6.36
Cortisol	€ 1.04	1 [0.77-1.12]	Normal	7.79
Total testosterone (males)	€ 9.78	1 [0.77-1.12]	Normal	4.89
Sodium/potassium	€ 1.02	1 [0.77-1.12]	Normal	2.04
<b>Cost 1st year</b>				<b>388.78</b>
	Medium			
	2nd-5th year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	1.38 [1.20-1.55]	Normal	28.41
Prolactin	€ 7.13	1.38 [1.20-1.55]	Normal	9.8
Bone mineral density	€ 31.50	0.7 [0.61-0.79]	Normal	22.05
Pituitary MRI	€ 31.50	0.62 [0.54-0.69]	Normal	152.63
Vitamin D	€ 15.86	1.12 [0.98-1.26]	Normal	17.71
Thyrotropin (TSH)	€ 5.46	1 [0.77-1.12]	Normal	5.46
Free thyroxine (FT4)	€ 6.36	0.5 [0.44-0.56]	Normal	3.18
Cortisol	€ 1.04	1 [0.77-1.12]	Normal	7.79
Total testosterone (males)	€ 9.78	1 [0.77-1.12]	Normal	4.89
Sodium/potassium	€ 1.02	1 [0.77-1.12]	Normal	2.04
<b>Cost 2nd-5th year</b>				<b>253.96</b>
	Long			
	>5th year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	1.25 [1.10-1.40]	Normal	25.83
Prolactin	€ 7.13	1.19 [1.04-1.33]	Normal	8.47
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	15.75
Pituitary MRI	€ 31.50	0.5 [0.44-0.56]	Normal	123.75
Vitamin D	€ 15.86	0.95 [0.83-1.07]	Normal	15.07
Thyrotropin (TSH)	€ 5.46	1 [0.88-1.12]	Normal	5.46
Free thyroxine (FT4)	€ 6.36	0.5 [0.44-0.56]	Normal	3.18
Cortisol	€ 1.04	1 [0.77-1.12]	Normal	7.79
Total testosterone (males)	€ 9.78	1 [0.77-1.12]	Normal	4.89
Sodium/potassium	€ 1.02	1 [0.77-1.12]	Normal	2.04
<b>Cost &gt;5th year</b>				<b>212.22</b>
<b>TOTAL COST</b>				<b>854.96</b>

**Supplementary Table 11** - Number and type of diagnostic tests and specialist visits that are provided, on an annual basis, for the follow-up of the patient undergoing pharmacological therapy with cabergoline in macroprolactinoma

<b>1<sup>st</sup> year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Specialist	€ 20.66	3.25 [2.85-3.65]	Normal	€ 67.15
Prolactin	€ 7.13	3.25 [2.85-3.65]	Normal	€ 23.17
Free thyroxine (FT4)	€ 6.36	1.63 [1.42-1.83]	Normal	€10 .34
Bone mineral density	€ 31.50	0.63 [0.55-0.70]	Normal	€ 19.69
Cortisol	€ 7.79	1.5 [1.31-1.69]	Normal	€ 11.69
Pituitary MRI	€ 247.50	1.63 [1.42-1.83]	Normal	€ 402.19
Visual field test	€ 16.78	1.38 [1.20-1.55]	Normal	€ 23.07
Vitamin D	€ 15.86	1.25 [1.10-1.40]	Normal	€ 19.83
Blood count	€ 3.17	1 [0.88-1.12]	Normal	€ 3.17
Prostate specific antigen	€ 7.41	1 [0.88-1.12]	Normal	€ 3.71
Testosterone (in men)	€ 9.78	2 [1.75-2.25]	Normal	€ 9.78
Computed optical tomography	€ 120.42	0.67 [0.58-0.75]	Normal	€ 80.28
Echocardiogram	€ 11.62	0	Normal	€ 0.00
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
<b>Cost 1st year</b>				<b>€ 676.09</b>
<b>2nd-5th year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Specialist	€ 20.66	1.88 [1.64-2.11]	Normal	€ 38.74
Prolactin	€ 7.13	2 [1.75-2.25]	Normal	€ 14.26
Free thyroxine (FT4)	€ 6.36	1.25 [1.10-1.40]	Normal	€ 7.95
Bone mineral density	€ 31.50	0.67 [0.88-1.12]	Normal	€ 21.00
Cortisol	€ 7.79	1 [0.88-1.12]	Normal	€ 7.79
Pituitary MRI	€ 247.50	0.98 [0.85-1.10]	Normal	€ 241.31
Visual field test	€ 16.78	0.83 [0.73-0.94]	Normal	€ 13.98
Vitamin D	€ 15.86	1.08 [0.95-1.22]	Normal	€ 17.18
Blood count	€ 3.17	0.88 [0.77-0.98]	Normal	€ 2.77
Prostate specific antigen	€ 7.41	0.94 [0.82-1.05]	Normal	€ 3.47
Testosterone (in men)	€ 9.78	1.25 [1.10-1.40]	Normal	€ 6.11
Computed optical tomography	€ 120.42	0.58 [0.51-0.66]	Normal	€ 70.25
Echocardiogram	€ 11.62	0.33 [0.29-0.37]	Normal	€ 3.83
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
<b>Cost 2nd-5th year</b>				<b>€ 450.70</b>
<b>&gt;5th year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Specialist	€ 20.66	1.33 [1.17-1.50]	Normal	€ 27.55
Prolactin	€ 7.13	1.25 [1.10-1.40]	Normal	€ 8.91
Free thyroxine (FT4)	€ 6.36	1.17 [1.02-1.31]	Normal	€ 7.42
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
Cortisol	€ 7.79	1 [0.88-1.12]	Normal	€ 7.79
Pituitary MRI	€ 247.50	0.64 [0.56-0.72]	Normal	€ 157.99
Visual field test	€ 16.78	0.75 [0.66-0.84]	Normal	€ 12.59
Vitamin D	€ 15.86	1 [0.88-1.12]	Normal	€ 15.86
Blood count	€ 3.17	0.81 [0.71-0.91]	Normal	€ 2.57
Prostate specific antigen	€ 7.41	0.9 [0.79-1.01]	Normal	€ 3.34
Testosterone (in men)	€ 9.78	1.19 [1.04-1.33]	Normal	€ 5.81
Computed optical tomography	€ 120.42	0.58 [0.51-0.66]	Normal	€ 70.25
Echocardiogram	€ 11.62	0.2 [0.18-0.22]	Normal	€ 2.32
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
<b>Cost &gt;5th year</b>				<b>€ 340.18</b>
<b>TOTAL COST</b>				<b>€ 1,466.97</b>
<b>1<sup>st</sup> year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
<b>Specialist</b>	€ 20.66	3.25 [2.85-3.65]	Normal	€ 67.15
<b>Prolactin</b>	€ 7.13	3.25 [2.85-3.65]	Normal	€ 23.17

Free thyroxine (FT4)	€ 6.36	1.63 [1.42-1.83]	Normal	€10 .34
Bone mineral density	€ 31.50	0.63 [0.55-0.70]	Normal	€ 19.69
Cortisol	€ 7.79	1.5 [1.31-1.69]	Normal	€ 11.69
Pituitary MRI	€ 247.50	1.63 [1.42-1.83]	Normal	€ 402.19
Visual field test	€ 16.78	1.38 [1.20-1.55]	Normal	€ 23.07
Vitamin D	€ 15.86	1.25 [1.10-1.40]	Normal	€ 19.83
Blood count	€ 3.17	1 [0.88-1.12]	Normal	€ 3.17
Prostate specific antigen	€ 7.41	1 [0.88-1.12]	Normal	€ 3.71
Testosterone (in men)	€ 9.78	2 [1.75-2.25]	Normal	€ 9.78
Computed optical tomography	€ 120.42	0.67 [0.58-0.75]	Normal	€ 80.28
Echocardiogram	€ 11.62	0	Normal	€ 0.00
Sodium potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
<b>Cost 1st year</b>				<b>€ 676.09</b>
<b>2nd-5th year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Specialist	€ 20.66	1.88 [1.64-2.11]	Normal	€ 38.74
Prolactin	€ 7.13	2 [1.75-2.25]	Normal	€ 14.26
Free thyroxine (FT4)	€ 6.36	1.25 [1.10-1.40]	Normal	€ 7.95
Bone mineral density	€ 31.50	0.67 [0.88-1.12]	Normal	€ 21.00
Cortisol	€ 7.79	1 [0.88-1.12]	Normal	€ 7.79
Pituitary MRI	€ 247.50	0.98 [0.85-1.10]	Normal	€ 241.31
Visual field test	€ 16.78	0.83 [0.73-0.94]	Normal	€ 13.98
Vitamin D	€ 15.86	1.08 [0.95-1.22]	Normal	€ 17.18
Blood count	€ 3.17	0.88 [0.77-0.98]	Normal	€ 2.77
Prostate specific antigen	€ 7.41	0.94 [0.82-1.05]	Normal	€ 3.47
Testosterone (in men)	€ 9.78	1.25 [1.10-1.40]	Normal	€ 6.11
Computed optical tomography	€ 120.42	0.58 [0.51-0.66]	Normal	€ 70.25
Echocardiogram	€ 11.62	0.33 [0.29-0.37]	Normal	€ 3.83
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
<b>Cost 2nd-5th year</b>				<b>€ 450.70</b>
<b>&gt;5th year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Specialist	€ 20.66	1.33 [1.17-1.50]	Normal	€ 27.55
Prolactin	€ 7.13	1.25 [1.10-1.40]	Normal	€ 8.91
Free thyroxine (FT4)	€ 6.36	1.17 [1.02-1.31]	Normal	€ 7.42
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
Cortisol	€ 7.79	1 [0.88-1.12]	Normal	€ 7.79
Pituitary MRI	€ 247.50	0.64 [0.56-0.72]	Normal	€ 157.99
Visual field test	€ 16.78	0.75 [0.66-0.84]	Normal	€ 12.59
Vitamin D	€ 15.86	1 [0.88-1.12]	Normal	€ 15.86
Blood count	€ 3.17	0.81 [0.71-0.91]	Normal	€ 2.57
Prostate specific antigen	€ 7.41	0.9 [0.79-1.01]	Normal	€ 3.34
Testosterone (in men)	€ 9.78	1.19 [1.04-1.33]	Normal	€ 5.81
Computed optical tomography	€ 120.42	0.58 [0.51-0.66]	Normal	€ 70.25
Echocardiogram	€ 11.62	0.2 [0.18-0.22]	Normal	€ 2.32
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
<b>Cost &gt;5th year</b>				<b>€ 340.18</b>
<b>TOTAL COST</b>				<b>€ 1,466.97</b>

**Supplementary Table 12 - Loss of patient productivity stratified by care area - Cabergoline**

	Unit cost	Freq. (n°) [C.I.]	Distribution	% [alpha;beta]	Distribution	Cost/drivers
N° days of absence from work - patient (urban area)	€ 14.05	3.57 [3.23-4.01]	Normal	42.86% [13.86;18.48]	Beta	€ 107.51
N° days of absence from work - patient (rural area)	€ 14.05	3.71 [3.25-4.17]	Normal	57.14% [21.59;142.89]	Beta	€ 149.08
<b>Total</b>				<b>100.00%</b>		<b>€ 256.59</b>



**Supplementary Table 13 – Total treatment cost – Cabergoline**

<b>MICROPROLACTINOMA</b>	<b>1<sup>st</sup> year</b>	<b>Subsequent years (2-5)</b>	<b>Subsequent years (&gt;5)</b>
Pharmacological therapy	€ 417.33	€ 296.77	€ 296.77
First visit	€ 523.34	N/A	N/A
Follow-up	€ 388.78	€ 253.96	€ 212.22
Indirect costs	€ 256.59	€ 256.59	€ 256.59
<b>Total</b>	<b>€ 1,586.04</b>	<b>€ 807.32</b>	<b>€ 765.59</b>
<b>MACROPROLACTINOMA</b>	<b>1<sup>st</sup> year</b>	<b>Subsequent years (2-5)</b>	<b>Subsequent years (&gt;5)</b>
Pharmacological therapy	€ 612.09	€ 370.96	€ 370.96
First visit	€ 722.68	N/A	N/A
Follow-up	€ 676.09	€ 450.70	€ 340.18
Indirect costs	€ 256.59	€ 256.59	€ 256.59
<b>Total</b>	<b>€ 2,267.46</b>	<b>€ 1,078.26</b>	<b>€ 967.74</b>

**Supplementary Table 14 - Mean posology of drug therapy with bromocriptine**

<b>Microprolactinoma</b>	<b>Unit cost</b>	<b>mg/week [C.I.]</b>	<b>Distribution</b>	<b>Annual cost</b>
1 <sup>st</sup> year of treatment	€ 0.0816	23.94 [20.97-26.90]	Normal	€ 101.54
Subsequent years of treatment	€ 0.0816	17.19 [15.06-19.32]	Normal	€ 72.91
<b>Macroprolactinoma</b>	<b>mg/week [C.I.]</b>			<b>Annual cost</b>
1 <sup>st</sup> year of treatment	€ 0.0816	40.03 [35.07-44.99]	Normal	€ 169.81
Subsequent years of treatment	€ 0.0816	33.28 [29.16-37.41]	Normal	€ 141.18

**Supplementary Table 15 - Diagnostic tests and specialist visits that are provided for the initial classification of the patient - Therapy with bromocriptine in microprolactinoma**

	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Specialist	€ 20.66	2.40 [2.10-2.70]	Normal	€ 49.58
Prolactin	€ 7.13	1.40 [1.23-2.70]	Normal	€ 9.98
Thyrotropin (TSH)	€ 5.46	1.00 [0.88-1.12]	Normal	€ 5.46
Free thyroxine (FT4)	€ 6.36	0.60 [0.53-0.67]	Normal	€ 3.82
Follicle-Stimulating Hormone (FSH)	€ 6.21	1.00 [0.88-1.12]	Normal	€ 6.21
Luteinizing Hormone (LH)	€ 7.20	1.00 [0.88-1.12]	Normal	€ 7.20
Estradiol (E2) in women	€ 3.98	0.80 [0.70-0.90]	Normal	€ 3.64
Testosterone in men	€ 9.78	1.00 [0.88-1.12]	Normal	€ 4.89
Bone mineral density	€ 31.50	1.00 [0.88-1.12]	Normal	€ 15.75
Cortisol	€ 7.79	0.60 [0.53-0.67]	Normal	€ 4.67
IGF-I	€ 10.48	1.00 [0.88-1.12]	Normal	€ 10.48
Pituitary MRI with contrast medium	€ 247.50	1.00 [0.88-1.12]	Normal	€ 247.50
Visual field test	€ 16.78	0.60 [0.53-0.67]	Normal	€ 10.07
Blood count	€ 3.17	0.60 [0.53-0.67]	Normal	€ 1.90
Glycemia	€ 1.17	0.60 [0.53-0.67]	Normal	€ 0.70
Sodium	€ 1.02	0.60 [0.53-0.67]	Normal	€ 0.61
Potassium	€ 1.02	0.60 [0.53-0.67]	Normal	€ 0.61
Cholesterol	€ 1.04	0.60 [0.53-0.67]	Normal	€ 0.62
Vitamin D	€ 15.86	0.80 [0.70-0.90]	Normal	€ 12.69
Creatinine	€ 1.13	0.80 [0.70-0.90]	Normal	€ 0.90
Calcemia	€ 1.13	1.00 [0.88-1.12]	Normal	€ 1.13
Phosphoremia	€ 1.46	1.00 [0.88-1.12]	Normal	€ 1.46
PTH	€ 18.92	1.00 [0.88-1.12]	Normal	€ 18.92
Heart ultrasound	€ 51.65	1.00 [0.88-1.12]	Normal	€ 51.65
<b>TOTAL</b>				<b>€ 470.45</b>

**Supplementary Table 16** - *Diagnostic tests and specialist visits that are provided for the initial classification of the patient - Therapy with bromocriptine in macroprolactinoma*

	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	2.80 [2.45-3.15]	Normal	€ 57.85
Prolactin	€ 7.13	1.20 [1.05-1.35]	Normal	€ 8.56
Thyrotropin (TSH)	€ 5.46	1.00 [0.88-1.12]	Normal	€ 5.46
Free thyroxine (FT4)	€ 6.36	1.00 [0.88-1.12]	Normal	€ 6.36
Follicle-Stimulating Hormone (FSH)	€ 6.21	0.80 [0.70-0.90]	Normal	€ 4.96
Luteinizing Hormone (LH)	€ 7.20	0.80 [0.70-0.90]	Normal	€ 5.76
Estradiol (E2) in women	€ 3.98	0.60 [0.53-0.67]	Normal	€ 2.73
Testosterone in men	€ 9.78	1.00 [0.88-1.12]	Normal	€ 4.89
Bone mineral density	€ 31.50	1.00 [0.88-1.12]	Normal	€ 31.50
Cortisol	€ 7.79	0.80 [0.80-0.90]	Normal	€ 6.23
IGF-I	€ 10.48	1.00 [0.88-1.12]	Normal	€ 10.48
Pituitary MRI with contrast medium	€ 247.50	1.00 [0.88-1.12]	Normal	€ 247.50
Visual field test	€ 16.78	1.00 [0.88-1.12]	Normal	€ 16.78
Blood count	€ 3.17	0.80 [0.80-0.90]	Normal	€ 2.53
Glycemia	€ 1.17	0.80 [0.80-0.90]	Normal	€ 0.94
Sodium	€ 1.02	0.80 [0.80-0.90]	Normal	€ 0.82
Potassium	€ 1.02	0.80 [0.80-0.90]	Normal	€ 0.82
Cholesterol	€ 1.04	0.80 [0.80-0.90]	Normal	€ 0.83
Vitamin D	€ 15.86	0.80 [0.80-0.90]	Normal	€ 12.69
Creatinine	€ 1.13	0.80 [0.80-0.90]	Normal	€ 0.90
Computed optical tomography (OCT)	€ 74.88	0.33 [0.29-0.37]	Normal	€ 40.14
Calcemia	€ 1.13	1.00 [0.88-1.12]	Normal	€ 1.13
Phosphoremia	€ 1.46	1.00 [0.88-1.12]	Normal	€ 1.46
PTH	€ 18.92	1.00 [0.88-1.12]	Normal	€ 18.92
Heart ultrasound	€ 51.65	1.00 [0.88-1.12]	Normal	€ 51.65
<b>TOTAL</b>				<b>€ 541.89</b>

**Supplementary Table 17** - *Number and type of diagnostic tests and specialist visits that are provided, on an annual basis, for the follow-up of the patient undergoing pharmacological therapy with bromocriptine in microprolactinoma*

Term	Brief			
	1 <sup>st</sup> year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	2.8 [2.45-3.15]	Normal	€ 57.85
Prolactin	€ 7.13	3.6 [2.15-4.05]	Normal	€ 25.67
Bone mineral density	€ 31.50	0.2 [0.18-0.22]	Normal	€ 6.30
Pituitary MRI with contrast medium	€ 247.50	0.8 [0.70-0.90]	Normal	€ 198.00
Vitamin D	€ 15.86	0.8 [0.70-0.90]	Normal	€ 12.69
<b>Cost 1st year</b>				<b>€ 300.50</b>
	Medium			
	2nd-5th year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	1.4 [1.23-1.57]	Normal	€ 28.92
Prolactin	€ 7.13	1.4 [1.23-1.57]	Normal	€ 9.98
Bone mineral density	€ 31.50	0.33 [0.29-0.37]	Normal	€ 10.50
Pituitary MRI with contrast medium	€ 247.50	0.33 [0.29-0.37]	Normal	€ 82.50
Vitamin D	€ 15.86	0.33 [0.29-0.37]	Normal	€ 5.29
<b>Cost 2nd-5th year</b>				<b>€ 137.19</b>
	Long			
	>5th year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	0.5 [0.44-0.56]	Normal	€ 10.33
Prolactin	€ 7.13	0.7 [0.61-0.79]	Normal	€ 4.99
Bone mineral density	€ 31.50	0.2 [0.18-0.22]	Normal	€ 6.30
Pituitary MRI with contrast medium	€ 247.50	0.33 [0.29-0.37]	Normal	€ 82.50
Vitamin D	€ 15.86	0.33 [0.29-0.37]	Normal	€ 5.29
<b>Cost &gt;5th year</b>				<b>€ 109.41</b>
<b>TOTAL COST</b>				<b>€ 547.10</b>

**Supplementary Table 18 - Number and type of diagnostic tests and specialist visits that are provided, on an annual basis, for the follow-up of the patient undergoing pharmacological therapy with bromocriptine in macroprolactinoma**

1 <sup>st</sup> year				
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	3.8 [3.33-4.27]	Normal	€ 78.51
Prolactin	€ 7.13	3.8 [3.33-4.27]	Normal	€ 27.09
Free thyroxine (FT4)	€ 6.36	1.4 [1.23-1.57]	Normal	€ 8.91
Bone mineral density	€ 31.50	0.2 [0.18-0.22]	Normal	€ 6.30
Cortisol	€ 7.79	1.2 [1.05-1.35]	Normal	€ 9.35
Pituitary MRI	€ 247.50	1.8 [1.58-2.02]	Normal	€ 445.50
Visual field test	€ 16.78	1.6 [1.40-1.80]	Normal	€ 26.85
Vitamin D	€ 15.86	0.8 [0.70-0.90]	Normal	€ 12.69
Blood count	€ 3.17	0.8 [0.70-0.90]	Normal	€ 2.53
Prostate specific antigen	€ 7.41	0.6 [0.53-0.67]	Normal	€ 2.22
Testosterone (in men)	€ 9.78	1.6 [1.40-1.80]	Normal	€ 7.82
Computed optical tomography	€ 120.42	0.33 [0.29-0.37]	Normal	€ 40.14
<b>Cost 1st year</b>				<b>€ 667.92</b>
2nd-5th year				
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	2 [1.75-2.25]	Normal	€ 41.32
Prolactin	€ 7.13	1.6 [1.40-1.80]	Normal	€ 11.41
Free thyroxine (FT4)	€ 6.36	0.8 [0.70-0.90]	Normal	€ 5.09
Bone mineral density	€ 31.50	0.5 [0.29-0.37]	Normal	€ 15.75
Cortisol	€ 7.79	0.8 [0.70-0.90]	Normal	€ 6.23
Pituitary MRI	€ 247.50	0.76 [0.67-0.85]	Normal	€ 188.10
Visual field test	€ 16.78	0.6 [0.53-0.67]	Normal	€ 10.07
Vitamin D	€ 15.86	0.7 [0.61-0.79]	Normal	€ 11.10
Blood count	€ 3.17	0.8 [0.70-0.90]	Normal	€ 2.53
Prostate specific antigen	€ 7.41	0.7 [0.61-0.79]	Normal	€ 2.59
Testosterone (in men)	€ 9.78	1 [0.88-1.12]	Normal	€ 4.89
Computed optical tomography	€ 120.42	0.33 [0.29-0.37]	Normal	€ 40.14
<b>Cost 2nd-5th year</b>				<b>€ 339.23</b>
>5th year				
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	0.8 [0.70-0.90]	Normal	€ 16.53
Prolactin	€ 7.13	0.8 [0.70-0.90]	Normal	€ 5.70
Free thyroxine (FT4)	€ 6.36	0.33 [0.29-0.37]	Normal	€ 2.12
Bone mineral density	€ 31.50	0.26 [0.23-0.29]	Normal	€ 8.19
Cortisol	€ 7.79	0.6 [0.53-0.67]	Normal	€ 4.67
Pituitary MRI	€ 247.50	0.43 [0.38-0.49]	Normal	€ 107.25
Visual field test	€ 16.78	0.33 [0.29-0.37]	Normal	€ 5.59
Vitamin D	€ 15.86	0.66 [0.58-0.74]	Normal	€ 10.47
Blood count	€ 3.17	0.8 [0.70-0.90]	Normal	€ 2.53
Prostate specific antigen	€ 7.41	0.64 [0.56-0.72]	Normal	€ 2.37
Testosterone (in men)	€ 9.78	0.8 [0.70-0.90]	Normal	€ 3.91
Computed optical tomography	€ 120.42	0.33 [0.29-0.37]	Normal	€ 40.14
<b>Cost &gt;5th year</b>				<b>€ 209.49</b>
<b>TOTAL COST</b>				<b>€ 1,216.64</b>

**Supplementary Table 19 - Loss of patient productivity stratified by area of care - Bromocriptine**

	Unit cost	Freq. (n°) [C.I.]	Distribution	% [alpha;beta]	Distribution	Cost/drivers
N° days of absence from work - patient (urban area)	€ 14.05	3.57 [3.13-4.01]	Normal	42.86% [13.86;18.48]	Beta	€ 107.51
N° days of absence from work - patient (rural area)	€ 14.05	3.71 [3.25-4.17]	Normal	57.14% [10.15;7.61]	Beta	€ 149.08
<b>Total</b>				<b>100.00%</b>		<b>€ 256.59</b>

**Supplementary Table 20 - Average dosage of drug therapy with temozolomide**

	Unit cost	mg/week [C.I.]	Distribution	Daily cost
Temozolomide dosage	€ 0.7234	241.67 [211.71-271.62]	Normal	€ 174.83
		Therapy days/month		<b>Cost/cycle</b>
Duration of therapy	-	5.17 [4.53-5.81]	Normal	€ 903.43
		Therapy cycles/year (average)		<b>Total cost</b>
No. of therapy cycles	-	6.14 [5.38-6.90]	Normal	<b>€ 5,549.61</b>

**Supplementary Table 21** - *Diagnostic tests and specialist visits that are provided for the initial classification of the patient - Therapy with temozolomide in macroprolactinoma*

	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	5.71 [5.01-6.42]	Normal	€ 118.06
Prolactin	€ 7.13	5.57 [4.88-6.26]	Normal	€ 39.72
Thyrotropin (TSH)	€ 5.46	2.57 [2.23-2.89]	Normal	€ 14.04
Free thyroxine (FT4)	€ 6.36	2.71 [2.38-3.05]	Normal	€ 17.27
Follicle-Stimulating Hormone (FSH)	€ 6.21	2.00 [1.75-2.25]	Normal	€ 12.41
Luteinizing Hormone (LH)	€ 7.20	2.00 [1.75-2.25]	Normal	€ 14.39
Estradiol (E2) in women	€ 3.98	1.57 [1.38-1.77]	Normal	€ 7.16
Testosterone in men	€ 9.78	2.29 [2.00-2.57]	Normal	€ 11.18
Bone mineral density	€ 31.50	0.71 [0.63-0.80]	Normal	€ 22.50
Cortisol	€ 7.79	2.71 [2.38-3.05]	Normal	€ 21.14
IGF-I	€ 10.48	1.57 [1.38-1.77]	Normal	€ 16.48
Pituitary MRI with contrast medium	€ 247.50	2.71 [2.38-3.05]	Normal	€ 671.79
Visual field test	€ 16.78	3.00 [2.63-3.37]	Normal	€ 50.34
Blood count	€ 3.17	8.14 [7.13-9.15]	Normal	€ 25.80
Glycemia	€ 1.17	4.71 [4.13-5.30]	Normal	€ 5.53
Sodium	€ 1.02	4.71 [4.13-5.30]	Normal	€ 4.81
Potassium	€ 1.02	4.71 [4.13-5.30]	Normal	€ 4.81
Cholesterol	€ 1.04	2.20 [1.93-2.47]	Normal	€ 2.28
Vitamin D	€ 15.86	1.86 [1.63-2.09]	Normal	€ 29.45
Creatinine	€ 1.13	3.57 [3.13-4.01]	Normal	€ 4.03
Aspartate aminotransferase (AST)	€ 1.04	7.00 [6.13-7.87]	Normal	€ 7.26
Alanine aminotransferase (ALT)	€ 1.00	7.00 [6.13-7.87]	Normal	€ 6.98
Gamma-glutamyl transferase (GGT)	€ 1.00	7.00 [6.13-7.87]	Normal	€ 7.90
Alkaline Phosphatase (ALP)	€ 1.04	7.00 [6.13-7.87]	Normal	€ 7.28
Bilirubin	€ 1.13	7.00 [6.13-7.87]	Normal	€ 7.90
<b>TOTAL</b>				<b>€ 1,130.51</b>

**Supplementary Table 22** - *Number and type of diagnostic tests and specialist visits that are provided, on an annual basis, for the follow-up of the patient undergoing pharmacological therapy with temozolomide in macroprolactinoma*

Term	Brief			
	1 <sup>st</sup> year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	4.86 [4.26-5.46]	Normal	€ 100.35
Prolactin	€ 7.13	4.86 [4.26-5.46]	Normal	€ 34.63
Free thyroxine (FT4)	€ 6.36	3.29 [2.88-3.69]	Normal	€ 20.91
Bone mineral density	€ 31.50	1 [0.88-1.12]	Normal	€ 31.50
Cortisol	€ 7.79	3.29 [2.88-3.69]	Normal	€ 25.60
Pituitary MRI with contrast medium	€ 247.50	2.5 [2.19-2.81]	Normal	€ 618.75
Visual field test	€ 16.78	2.29 [2.00-2.57]	Normal	€ 38.35
Vitamin D	€ 15.86	1.71 [1.50-1.93]	Normal	€ 27.19
Blood count	€ 3.17	4.14 [3.63-4.66]	Normal	€ 13.12
PSA (in men)	€ 7.41	0.86 [0.75-0.96]	Normal	€ 3.18
Testosterone (in men)	€ 9.78	1.86 [1.63-2.09]	Normal	€ 9.08
Computed optical tomography (OCT)	€ 120.42	0.6 [0.53-0.67]	Normal	€ 72.25
<b>Cost 1st year</b>				<b>€ 994.91</b>
	Medium			
	2nd-5th year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	3 [2.63-3.37]	Normal	€ 61.98
Prolactin	€ 7.13	3 [2.63-3.37]	Normal	€ 21.39
Free thyroxine (FT4)	€ 6.36	2.4 [2.10-2.70]	Normal	€ 15.27
Bone mineral density	€ 31.50	0.86 [0.75-0.97]	Normal	€ 27.09
Cortisol	€ 7.79	2.2 [1.93-2.47]	Normal	€ 17.14
Pituitary MRI with contrast medium	€ 247.50	2 [1.75-2.25]	Normal	€ 495.00
Visual field test	€ 16.78	2 [1.75-2.25]	Normal	€ 33.56
Vitamin D	€ 15.86	2 [1.75-2.25]	Normal	€ 31.72
Blood count	€ 3.17	2.4 [2.10-2.70]	Normal	€ 7.60
PSA (in men)	€ 7.41	0.8 [0.70-1.58]	Normal	€ 2.97
Testosterone (in men)	€ 9.78	2 [1.75-2.25]	Normal	€ 9.78
Computed optical tomography (OCT)	€ 120.42	0.6 [0.53-0.67]	Normal	€ 72.25

<b>Cost 2nd-5th year</b>				<b>€ 795.75</b>
<b>Long</b>				
<b>&gt;5th year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Specialist	€ 20.66	2.2 [1.93-2.47]	Normal	€ 45.45
Prolactin	€ 7.13	2.2 [1.93-2.47]	Normal	€ 15.69
Free thyroxine (FT4)	€ 6.36	2 [1.75-2.25]	Normal	€ 12.73
Bone mineral density	€ 31.50	0.86 [0.75-0.97]	Normal	€ 27.09
Cortisol	€ 7.79	1.8 [1.58-2.02]	Normal	€ 14.02
Pituitary MRI with contrast medium	€ 247.50	2 [1.75-2.25]	Normal	€ 495.00
Visual field test	€ 16.78	1.8 [1.58-2.02]	Normal	€ 30.20
Vitamin D	€ 15.86	1.8 [1.58-2.02]	Normal	€ 28.55
Blood count	€ 3.17	1.8 [1.58-2.02]	Normal	€ 5.70
PSA (in men)	€ 7.41	0.8 [0.70-1.58]	Normal	€ 2.97
Testosterone (in men)	€ 9.78	1.6 [1.40-1.80]	Normal	€ 7.82
Computed optical tomography (OCT)	€ 120.42	0.6 [0.53-0.67]	Normal	€ 72.25
<b>Cost &gt;5th year</b>				<b>€ 757.47</b>
<b>TOTAL COST</b>				<b>€ 2,548.13</b>

**Supplementary Table 23 - Number and type of diagnostic tests and specialist visits that are provided, on an annual basis, for the additional safety follow-up of the patient undergoing pharmacological therapy with temozolomide in macroprolactinoma**

	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Blood count	€ 3.17	3.40 [2.98-3.82]	Normal	€ 10.77
Glycemia	€ 1.17	3.40 [2.98-3.82]	Normal	€ 3.99
Serum electrophoresis	€ 4.23	3.20 [2.80-3.60]	Normal	€ 13.54
Transaminases (GOT/GPT)	€ 2.03	3.20 [2.80-3.60]	Normal	€ 6.51
Sodium	€ 1.02	3.40 [2.98-3.82]	Normal	€ 3.47
Potassium	€ 1.02	3.40 [2.98-3.82]	Normal	€ 3.47
Creatinine	€ 1.13	3.40 [2.98-3.82]	Normal	€ 3.84
Urinalysis	€ 1.13	3.40 [2.98-3.82]	Normal	€ 6.96
<b>TOTAL</b>				<b>€52.54</b>

**Supplementary Table 24 - Loss of patient productivity stratified by care area - Temozolomide**

	Unit cost	No. of days/year [C.I.]	Distribution	% [alpha;beta]	Distribution	Cost/drivers
N° days of absence from work - patient (urban area)	€ 14.05	3.57 [3.13-4.01]	Normal	42.86% [13.86;18.48]	Beta	€ 107.51
N° days of absence from work - patient (rural area)	€ 14.05	3.71 [3.25-4.17]	Normal	57.14% [10.14-7.61]	Beta	€ 149.08
<b>Total</b>				<b>100.00%</b>		<b>€256.59</b>

**Supplementary Table 25 – Cost of pre-hospitalization procedures – Endoscopic surgery**

	Unit Cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Anesthesia visit	€ 20.66	1.00 [0.88-1.12]	Normal	€ 20.66
Electrocardiogram	€ 11.62	1.00 [0.88-1.12]	Normal	€ 11.62
Chest X-ray	€ 15.49	1.00 [0.88-1.12]	Normal	€ 15.49
Pituitary MRI with contrast medium	€ 247.50	0.71 [0.63-0.80]	Normal	€ 176.79
Computed tomography of the head	€ 120.42	1.00 [0.88-1.12]	Normal	€ 120.42
ENT visit	€ 20.66	1.14 [1.00-1.28]	Normal	€ 23.61
Blood count	€ 3.17	1.29 [1.13-1.45]	Normal	€ 4.07
Creatinine	€ 1.13	1.29 [1.13-1.45]	Normal	€ 1.45
Coagulation tests (AP + PTT)	€ 5.70	1.00 [0.88-1.12]	Normal	€ 5.70
Cholinesterase	€ 1.36	0.80 [0.70-0.90]	Normal	€ 1.09
Urinalysis	€ 2.17	1.00 [0.88-1.12]	Normal	€ 2.17
Eye examination with visual field test	€ 16.78	1.00 [0.88-1.12]	Normal	€ 37.44
OCT	€ 74.88	1.00 [0.88-1.12]	Normal	€ 120.42
Sodium	€ 1.02	1.00 [0.88-1.12]	Normal	€ 1.02
Potassium	€ 1.02	1.00 [0.88-1.12]	Normal	€ 1.02
Glycemia	€ 1.17	1.00 [0.88-1.12]	Normal	€ 1.17
<b>TOTAL</b>				<b>€ 498.60</b>

**Supplementary Table 26 – Cost of pharmacological therapy used during surgery – Endoscopic surgery**

<b>Antibiotics</b>	<b>Unit cost</b>	<b>% usage [alpha;beta]</b>	<b>Distribution</b>	<b>mg/intervention (medium)</b>	<b>Distribution</b>	<b>Cost/ active ingredient</b>
Cefazolin	€ 0.0016	93.33% [0.73;0.05]	Beta	1,334.00 [1168.64-1499.36]	Normal	€ 2.02
Vancomycin	€ 0.0182	6.67% [23.27;325.73]	Beta	1,000.00 [876.04-1123.96]	Normal	€ 1.21
<b>Corticosteroids</b>	<b>Unit cost</b>	<b>% usage [alpha;beta]</b>	<b>Distribution</b>	<b>mg/intervention (medium)</b>	<b>Distribution</b>	<b>Cost/ active ingredient</b>
Hydrocortisone	€ 0.0080	22.50% [19.15;65.96]	Beta	150.00 [131.41-168.59]	Normal	€ 0.27
<b>Opioids</b>	<b>Unit cost</b>	<b>% usage [alpha;beta]</b>	<b>Distribution</b>	<b>mg/intervention (medium)</b>	<b>Distribution</b>	<b>Cost/ active ingredient</b>
Fentanyl	€ 5.6867	100.00%	-	0.21 [0.18-0.23]	Normal	€ 1.17
<b>Anesthetics</b>	<b>Unit cost</b>	<b>% usage [alpha;beta]</b>	<b>Distribution</b>	<b>mg/intervention (medium)</b>	<b>Distribution</b>	<b>Cost/ active ingredient</b>
Remifentanyl	€ 5.6867	100.00%	-	3.94 [3.45-4.43]	Normal	€ 22.39
Propofol	€ 0.0144	100.00%	-	175.00 [153.31-196.69]	Normal	€ 2.52
<b>TOTAL</b>						<b>€ 29.58</b>

**Supplementary Table 27 – Cost of healthcare professionals who intervene during the intervention and structure – Endoscopic surgery**

<b>Healthcare professional</b>	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Physician	€ 0.58	2.29 [2.00-2.57]	Normal	€ 139.97
Nurse	€ 0.27	1.57 [1.38-1.77]	Normal	€ 44.53
Anesthetist	€ 0.58	1.29 [1.13-1.45]	Normal	€ 7 8.73
Assistant	€ 0.23	1.00 [0.88-1.12]	Normal	€ 24.79
Ferrist	€ 0.23	1.00 [0.88-1.12]	Normal	€ 24.79
<b>SUB-TOTAL</b>				<b>€ 312.82</b>
	<b>Unit cost</b>	<b>Minutes [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Operating room cost	€ 20.43	105.71 [92.61-118.82]	Normal	€ 2,159.50
<b>TOTAL</b>				<b>€ 2,472.32</b>

**Supplementary Table 28 – Number and type of examinations and specialist visits that are provided in the post-operative phase - Endoscopic surgery**

	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Pituitary MRI with contrast medium	€ 247.50	0.57 [0.50-0.64]	Normal	€ 141.43
Computed tomography of the head	€ 120.42	0.31 [0.28-0.35]	Normal	€ 37.85
Serum sodium	€ 1.02	3.43 [3.00-3.85]	Normal	€ 3.50
Urinary sodium	€ 2.17	0.71 [0.63-0.80]	Normal	€ 1.55
Serum potassium	€ 1.02	3.43 [3.00-3.85]	Normal	€ 3.50
Potassuria	€ 1.02	0.80 [0.70-0.90]	Normal	€ 0.82
Osmolality (glucose, blood urea nitrogen, sodium)	€ 3.32	1.43 [1.25-1.61]	Normal	€ 4.75
Cortisol	€ 7.79	1.14 [1.00-1.28]	Normal	€ 8.90
Free thyroxine (FT4)	€ 6.36	0.57 [0.50-0.64]	Normal	€ 3.64
Prolactin	€ 7.13	1.14 [1.00-1.28]	Normal	€ 8.15
Nasal endoscopy	€ 14.10	0.43 [0.38-0.48]	Normal	€ 6.04
<b>TOTAL</b>				<b>€ 220.11</b>

**Supplementary Table 29** – *Number and type of examinations and specialist visits that are provided for monitoring patients with surgical complications*

	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Eye examination	€ 20.66	1.20 [1.05-1.35]	Normal	€ 24.79
Visual field examination	€ 16.78	1.14 [1.00-1.28]	Normal	€ 19.18
<b>TOTAL</b>				<b>€ 43.97</b>



**Supplementary Table 30 – Type and average dosage of drug therapies for the management of complications related to endoscopic surgery**

						40% [14.6;21.9]		<b>Beta distribution</b>	
<b>Permanent</b>									
<b>Transient</b>						60.00%		-	
<b>Drug therapies</b>	<b>Unit cost</b>	<b>mg/day</b>	<b>Average duration (months) [C.I]</b>	<b>Distr.</b>	<b>% [alpha;beta]</b>	<b>Distr.</b>	<b>Transient</b>	<b>Permanent</b>	<b>TOTAL</b>
Desmopressin	€ 418.79	0.005	7 [6.13-7.87]	Norm.	9.86% [22.44;205.19]	Beta	€ 26.01	€ 29.72	€ 55.73
Cortisone	€ 0.0184	25	4 [3.50-4.50]	Norm.	8.75% [22.73;236.99]	Beta	€ 2.90	€ 5.81	€ 8.71
Testosterone in men	€ 0.0080	80			21% [19.54;73.51]	Beta	N/A	€ 48.83	€ 48.83
Estroprogestins in women	€ 0.2073	3			11% [22.14;179.13]	Beta	N/A	€ 24.62	€ 24.62
Thyroxine	€ 0.6233	0.2			12.6% [21.72;150.69]	Beta	N/A	€ 5.65	€ 5.65
<b>TOTAL</b>							<b>€ 28.91</b>	<b>€ 114.63</b>	<b>€ 143.54</b>

**Supplementary Table 31 – Occurrence rate and cost of management of CSF fistulas and meningitis related to endoscopic surgery**

<b>CSF fistula (%)</b>									<b>5.71%</b>
	<b>Unit cost</b>	<b>Frequency [alpha;beta]</b>	<b>Distribution</b>	<b>Days</b>	<b>Distribution</b>	<b>Dose/day</b>	<b>Distribution</b>	<b>Cost/drivers</b>	<b>Cost/ driver weighted</b>
Acetazolamide	€ 0.0010	N/A	-	3.00 [2.63-3.37]	Normal	350.00 [306.61-393.39]	Normal	€ 1.06	€ 0.06
Lumbar CSF drainage	€ 154.92	22.50% [19.15-65.96]	Beta	N/A	-	N/A	-	€ 34.86	€ 1.99
Fibrin glue injection	€ 179.58	N/A	-	3.00 [2.63;3.37]	Normal	N/A	-	€ 538.74	€ 30.79
Reintervention	€ 6,204.03	19.00% [20.06-85.52]	Beta	N/A	-	N/A	-	€ 1,139.19	€ 65.10
<b>Total cost CSF fistula</b>								<b>€ 1,713.84</b>	<b>€ 97.93</b>
<b>Meningitis (%)</b>									<b>0.44%</b>
		<b>Frequency [alpha;beta]</b>	<b>Distribution</b>	<b>Days</b>	<b>Distribution</b>	<b>Dose/day</b>	<b>Distribution</b>	<b>Cost/drivers</b>	<b>Cost/ driver weighted</b>
Lumbar puncture	€ 457.00	2.00 [24.48;1199.52]	Beta	N/A	-	N/A	-	€ 420.00	€ 1.86
Antibiotic th. - Meropenem	€ 0.0136	N/A	-	15.00 [13.14-166.86]	Normal	1000.00 [876.04-1123.96]	Normal	€ 203.86	€ 0.90
Reintervention	€ 6,204.03	80.00% [4.2;1.05]	Beta	N/A	-	N/A	-	€ 4,796.58	€ 21.24
<b>Total cost Meningitis</b>								<b>€ 5,420.44</b>	<b>€ 24.00</b>
<b>TOTAL</b>								<b>€ 7,134.28</b>	<b>€ 121.94</b>

**Supplementary Table 32** – Number and type of diagnostic tests and specialist visits provided in the first month following endoscopic surgery

	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Cortisol	€ 7.79	1.14 [1.0-1.28]	Normal	€ 8.90
Free thyroxine (FT4)	€ 6.36	1.14 [1.0-1.28]	Normal	€ 7.27
Prolactin	€ 7.13	1.14 [1.0-1.28]	Normal	€ 8.15
Endocrinological visit	€ 20.66	1.00 [0.88-1.12]	Normal	€ 20.66
ENT visit	€ 20.66	0.57 [0.50-0.64]	Normal	€ 11.81
Neurosurgical visit	€ 20.66	1.14 [1.0-1.28]	Normal	€ 23.61
Testosterone in men	€ 9.78	0.86 [0.75-0.96]	Normal	€ 8.38
Estradiol in women	€ 3.98	0.60 [0.5-0.67]	Normal	€ 5.46
Sodium	€ 1.02	1.43 [1.25-1.61]	Normal	€ 1.46
ACTH test	€ 18.50	0.40 [0.35-0.45]	Normal	€ 7.40
Visual field test	€ 16.78	1.00 [0.88-1.12]	Normal	€ 16.78
<b>TOTAL</b>				<b>€ 119.88</b>

**Supplementary Table 33** – Number and type of diagnostic tests and specialist visits that are provided, on an annual basis, for the follow-up of the patient undergoing endoscopic surgery for microprolactinoma

1 <sup>st</sup> year				
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Cortisol	€ 7.79	2 [1.75-2.25]	Normal	€ 15.58
Free thyroxine (FT4)	€ 6.36	2 [1.75-2.25]	Normal	€ 12.73
Prolactin	€ 7.13	2 [1.75-2.25]	Normal	€ 14.26
Neurosurgical visit	€ 20.66	1.29 [1.13-1.45]	Normal	€ 26.56
Eye examination	€ 20.66	1 [0.88-1.12]	Normal	€ 20.66
Testosterone in men	€ 9.78	2.29 [2.0-2.57]	Normal	€ 11.18
Estradiol in women	€ 3.98	2 [1.75-2.25]	Normal	€ 9.11
Pituitary MRI with contrast medium	€ 247.50	1.43 [1.25-1.61]	Normal	€ 353.57
Bone mineral density	€ 31.50	1 [0.88-1.12]	Normal	€ 31.50
<b>Cost 1st year</b>		1.00		<b>€ 495.14</b>
2nd-5th year				
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Cortisol	€ 7.79	1.4 [1.23-1.57]	Normal	€ 10.91
Free thyroxine (FT4)	€ 6.36	1.6 [1.4-1.8]	Normal	€ 10.18
Prolactin	€ 7.13	1.43 [1.25-1.61]	Normal	€ 10.19
Neurosurgical visit	€ 20.66	0.29 [0.25-0.32]	Normal	€ 5.90
Eye examination	€ 20.66	0.86 [0.75-0.96]	Normal	€ 17.71
Testosterone in men	€ 9.78	1.43 [1.25-1.61]	Normal	€ 6.99
Estradiol in women	€ 3.98	0.86 [0.75-0.96]	Normal	€ 3.90
Pituitary MRI with contrast medium	€ 247.50	0.5 [0.44-0.56]	Normal	€ 123.75
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
<b>Cost 2nd-5th year</b>				<b>€ 205.27</b>
>5th year				
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Cortisol	€ 7.79	1.2 [1.05-1.35]	Normal	€ 9.35
Free thyroxine (FT4)	€ 6.36	1.4 [1.23-1.57]	Normal	€ 8.91
Prolactin	€ 7.13	1.29 [1.13-1.45]	Normal	€ 9.17
Neurosurgical visit	€ 20.66	0.14 [1.13-0.16]	Normal	€ 2.95
Eye examination	€ 20.66	0.86 [0.75-0.96]	Normal	€ 17.71
Testosterone in men	€ 9.78	1.4 [1.23-1.57]	Normal	€ 6.85
Estradiol in women	€ 3.98	0.71 [0.63-0.80]	Normal	€ 3.25
Pituitary MRI with contrast medium	€ 247.50	0.43 [0.38-0.48]	Normal	€ 106.07
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
<b>Cost &gt;5th year</b>				<b>€ 180.00</b>
<b>TOTAL COST</b>				<b>€ 880.42</b>

**Supplementary Table 34** – Number and type of diagnostic tests and specialist visits that are provided, on an annual basis, for the follow-up of patients undergoing endoscopic surgery for macroprolactinoma

<b>1<sup>st</sup> year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Cortisol	€ 7.79	2.29 [2.0-2.57]	Normal	€ 17.81
Free thyroxine (FT4)	€ 6.36	2.29 [2.0-2.57]	Normal	€ 14.54
Prolactin	€ 7.13	2.57	Normal	€ 18.33
Neurosurgical visit	€ 20.66	1.29 [1.4-1.8]	Normal	€ 26.56
Eye examination	€ 20.66	2 [1.75-2.25]	Normal	€ 41.32
Testosterone in men	€ 9.78	2.29 [2.0-2.57]	Normal	€ 11.18
Estradiol in women	€ 3.98	1.6 [1.4-1.8]	Normal	€ 7.29
Pituitary MRI with contrast medium	€ 247.50	1.14 [1.0-1.28]	Normal	€ 282.86
Computed optical tomography	€ 120.42	1 [0.88-1.12]	Normal	€ 120.42
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
Bone mineral density	€ 31.50	1 [0.88-1.12]	Normal	€ 31.50
<b>Cost 1st year</b>				<b>€ 573.85</b>
<b>2nd-5th year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Cortisol	€ 7.79	1.43 [1.25-1.61]	Normal	€ 11.13
Free thyroxine (FT4)	€ 6.36	1.43 [1.25-1.61]	Normal	€ 9.09
Prolactin	€ 7.13	1.71 [1.5-1.93]	Normal	€ 12.22
Neurosurgical visit	€ 20.66	0.9 [0.79-1.01]	Normal	€ 18.59
Eye examination	€ 20.66	1.5 [1.31-1.69]	Normal	€ 30.99
Testosterone in men	€ 9.78	1.43 [1.25-1.61]	Normal	€ 6.99
Estradiol in women	€ 3.98	0.8 [0.7-0.9]	Normal	€ 3.64
Pituitary MRI with contrast medium	€ 247.50	1 [0.88-1.12]	Normal	€ 247.50
Computed optical tomography	€ 120.42	0.37 [0.3-0.42]	Normal	€ 45.16
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
<b>Cost 2nd-5th year</b>				<b>€ 403.10</b>
<b>Long</b>				
<b>&gt;5th year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Cortisol	€ 7.79	1.29 [1.13-1.45]	Normal	€ 10.02
Free thyroxine (FT4)	€ 6.36	1.29 [1.13-1.45]	Normal	€ 8.18
Prolactin	€ 7.13	1.29 [1.13-1.45]	Normal	€ 9.17
Neurosurgical visit	€ 20.66	0.43 [0.38-0.48]	Normal	€ 8.85
Eye examination	€ 20.66	1.3 [1.13-1.45]	Normal	€ 26.86
Testosterone in men	€ 9.78	1.29 [1.13-1.45]	Normal	€ 6.29
Estradiol in women	€ 3.98	0.6 [0.53-0.67]	Normal	€ 2.73
Pituitary MRI with contrast medium	€ 247.50	0.7 [0.61-0.79]	Normal	€ 173.25
Computed optical tomography	€ 120.42	0.38 [0.33-0.42]	Normal	€ 45.16
Sodium/potassium	€ 1.02	<b>1 [0.88-1.12]</b>	Normal	€ 2.04
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
<b>Cost &gt;5th year</b>				<b>€ 308.29</b>
<b>TOTAL COST</b>				<b>€ 1,285.24</b>
<b>1<sup>st</sup> year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Cortisol	€ 7.79	2.29 [2.0-2.57]	Normal	€ 17.81
Free thyroxine (FT4)	€ 6.36	2.29 [2.0-2.57]	Normal	€ 14.54
Prolactin	€ 7.13	2.57	Normal	€ 18.33
Neurosurgical visit	€ 20.66	1.29 [1.4-1.8]	Normal	€ 26.56
Eye examination	€ 20.66	2 [1.75-2.25]	Normal	€ 41.32
Testosterone in men	€ 9.78	2.29 [2.0-2.57]	Normal	€ 11.18
Estradiol in women	€ 3.98	1.6 [1.4-1.8]	Normal	€ 7.29
Pituitary MRI with contrast medium	€ 247.50	1.14 [1.0-1.28]	Normal	€ 282.86
Computed optical tomography	€ 120.42	1 [0.88-1.12]	Normal	€ 120.42
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
Bone mineral density	€ 31.50	1 [0.88-1.12]	Normal	€ 31.50
<b>Cost 1st year</b>				<b>€ 573.85</b>

<b>2nd-5th year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Cortisol	€ 7.79	1.43 [1.25-1.61]	Normal	€ 11.13
Free thyroxine (FT4)	€ 6.36	1.43 [1.25-1.61]	Normal	€ 9.09
Prolactin	€ 7.13	1.71 [1.5-1.93]	Normal	€ 12.22
Neurosurgical visit	€ 20.66	0.9 [0.79-1.01]	Normal	€ 18.59
Eye examination	€ 20.66	1.5 [1.31-1.69]	Normal	€ 30.99
Testosterone in men	€ 9.78	1.43 [1.25-1.61]	Normal	€ 6.99
Estradiol in women	€ 3.98	0.8 [0.7-0.9]	Normal	€ 3.64
Pituitary MRI with contrast medium	€ 247.50	1 [0.88-1.12]	Normal	€ 247.50
Computed optical tomography	€ 120.42	0.37 [0.3-0.42]	Normal	€ 45.16
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
<b>Cost 2nd-5th year</b>				<b>€ 403.10</b>
<b>&gt;5th year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Cortisol2.	€ 7.79	1.29 [1.13-1.45]	Normal	€ 10.02
Free thyroxine (FT4)	€ 6.36	1.29 [1.13-1.45]	Normal	€ 8.18
Prolactin	€ 7.13	1.29 [1.13-1.45]	Normal	€ 9.17
Neurosurgical visit	€ 20.66	0.43 [0.38-0.48]	Normal	€ 8.85
Eye examination	€ 20.66	1.3 [1.13-1.45]	Normal	€ 26.86
Testosterone in men	€ 9.78	1.29 [1.13-1.45]	Normal	€ 6.29
Estradiol in women	€ 3.98	0.6 [0.53-0.67]	Normal	€ 2.73
Pituitary MRI with contrast medium	€ 247.50	0.7 [0.61-0.79]	Normal	€ 173.25
Computed optical tomography	€ 120.42	0.38 [0.33-0.42]	Normal	€ 45.16
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
<b>Cost &gt;5th year</b>				<b>€ 308.29</b>
<b>TOTAL COST</b>				<b>€ 1,285.24</b>

**Supplementary Table 35 – Loss of patient/caregiver productivity – Endoscopic surgery**

	<b>Unit cost</b>	<b>% [alpha;beta]</b>	<b>Distribution</b>	
% patients with caregiver	€ 14.05	6.50% [23.32-335.31]	Beta	<b>€ 85.44</b>
<b>N° days [C.I.]</b>				
Days of convalescence hypothesized	€ 14.05	13.86 [12.14-15.57]	Normal	<b>€ 1,314.51</b>

**Supplementary Table 36 – Cost of pre-hospitalization procedures – Microscopic surgery**

	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Anesthesia visit	€ 20.66	1.00 [0.88-1.12]	Normal	€ 20.66
Electrocardiogram	€ 11.62	1.00 [0.88-1.12]	Normal	€ 11.62
Chest X-ray	€ 15.49	1.00 [0.88-1.12]	Normal	€ 15.49
Pituitary MRI with contrast medium	€ 247.50	0.50 [0.44-0.56]	Normal	€ 123.75
Head CT	€ 120.42	1.00 [0.88-1.12]	Normal	€ 120.42
ENT visit	€ 20.66	1.25 [1.1-1.40]	Normal	€ 25.83
Blood count	€ 3.17	1.50 [1.31-1.69]	Normal	€ 4.75
Creatinine	€ 1.13	1.50 [1.31-1.69]	Normal	€ 1.69
Coagulation tests (AP + PTT)	€ 5.70	1.00 [0.88-1.12]	Normal	€ 5.70
Cholinesterase	€ 1.36	1.00 [0.88-1.12]	Normal	€ 1.36
Urinalysis	€ 1.13	1.00 [0.88-1.12]	Normal	€ 2.17
Eye examination with visual field test	€ 20.66	1.00 [0.88-1.12]	Normal	€ 37.44
OCT	€ 74.88	1.00 [0.88-1.12]	Normal	€ 74.88
<b>TOTAL</b>				<b>€ 445.76</b>

**Supplementary Table 37 – Cost of pharmacological therapy used during surgery – Microscopic surgery**

Antibiotics	Unit cost	% usage [alpha;beta]	Distribution	mg/intervention (medium) [C.I.]	Distribution	Cost/active ingredient
Cefazolin	€ 0.0016	93.33% [0.73;0.05]	Beta	1,334.00 [1168.64-1499.36]	Normal	€ 2.02
Vancomycin	€ 0.0182	6.67% [23.27;325.73]	Beta	1,000.00 [876.04-1123.96]	Normal	€ 1.21
<b>Corticosteroids</b>						
Hydrocortisone	€ 0.0080	22.50% [19.15;65.96]	Beta	150.00 [131.41-168.59]	Normal	€ 0.27
<b>Opioids</b>						
Fentanyl	€ 5.6867	100.00%	-	0.21 [0.18-0.23]	Normal	€ 1.17
<b>Anesthetics</b>						
Remifentanyl	€ 5.6867	100.00%	-	3.94 [3.45-4.43]	Normal	€ 22.39
Propofol	€ 0.0144	100.00%	-	175.00 [153.31-196.69]	Normal	€ 2.52
<b>TOTAL</b>						<b>€ 29.58</b>

**Supplementary Table 38 – Cost of healthcare professionals who intervene during the intervention and structure – Microscopy surgery**

Healthcare professional	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Physician	€ 0.58	1.75 [1.53-1.97]	Normal	€ 108.98
Nurse	€ 0.27	2.00 [1.75-2.25]	Normal	€ 57.63
Anesthetist	€ 0.58	1.50 [1.31-1.69]	Normal	€ 93.41
Assistant	€ 0.23	1.00 [0.88-1.12]	Normal	€ 25.21
Ferrist	€ 0.23	1.00 [0.88-1.12]	Normal	€ 25.21
<b>SUB-TOTAL</b>				<b>€ 310.44</b>
	Unit cost	Minutes [C.I.]	Distribution	Cost/drivers
Operating room cost	€ 20.43	107.50 [94.17-120.83]	Normal	€ 2,159.97
<b>TOTAL</b>				<b>€ 2,506.41</b>

**Supplementary Table 39** - *Number and type of examinations and specialist visits that are provided in the post-operative phase - Microscopic surgery*

	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Pituitary MRI with contrast medium	€ 247.50	1.00 [0.88-1.12]	Normal	€ 247.50
Computed tomography of the head	€ 120.42	0.25 [0.22-0.28]	Normal	€ 30.11
Serum sodium	€ 1.02	1.75 [1.53-1.97]	Normal	€ 1.79
Sodiuria	€ 2.17	0.75 [0.66-0.84]	Normal	€ 1.63
Serum potassium	€ 1.02	2.00 [1.75-2.225]	Normal	€ 2.04
Potassiuria	€ 1.02	0.75 [0.66-0.84]	Normal	€ 0.77
Osmolality (glucose, blood urea nitrogen, sodium)	€ 3.32	2.00 [1.75-2.25]	Normal	€ 6.64
Cortisol	€ 7.79	1.50 [1.31-1.69]	Normal	€ 11.69
Free thyroxine (FT4)	€ 6.36	0.50 [0.44-0.56]	Normal	€ 3.18
Prolactin	€ 7.13	1.50 [1.31-1.69]	Normal	€ 10.70
Nasal endoscopy	€ 14.10	0.25 [0.22-0.28]	Normal	€ 3.53
Urinalysis	€ 1.13	1.00 [0.88-1.12]	Normal	€ 2.17
<b>TOTAL</b>				<b>€ 321.73</b>

**Supplementary Table 40** – *Number and type of examinations and specialist visits that are provided for monitoring patients with surgical complications*

	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Eye examination	€ 20.66	1.25 [1.10-1.40]	Normal	€ 25.83
Visual field examination	€ 16.78	1.25 [1.10-1.40]	Normal	€ 20.98
<b>TOTAL</b>				<b>€ 46.80</b>

**Supplementary Table 41 – Type and average dosage of pharmacological therapies for the management of complications related to microscopic surgery**

								<b>40.00% [4;0.0]</b>	<b>Beta</b>
<b>Permanent</b>								60.00%	-
<b>Transient</b>									
	Unit cost	Average duration (months) [C.I.]	Distribution	usage [alpha;beta]	Distribution	Transient	Permanent	TOTAL	
Desmopressin	€ 418.79	6.00 [5.26-6.74]	Normal	4.75% [21.77;476.55]	Beta	€ 10.74	€ 14.32	€ 25.06	
Cortisone	€ 0.0184	4.00 [3.5-4.5]	Normal	7.50% [23.05;284.28]	Beta	€ 2.49	€ 4.98	€ 7.47	
Testosterone in men	€ 0.0080			7.50% [23.05;284.28]	Beta	N/A	€ 17.44	€ 17.44	
Estroprogestins in women	€ 0.2073			7.50% [23.05;284.28]	Beta	N/A	€ 16.79	€ 16.79	
Thyroxine	€ 0.6232			1.50% [24.61;1616.06]	Beta	N/A	€ 0.67	€ 0.67	
<b>TOTAL</b>						<b>€ 13.23</b>	<b>€ 54.20</b>	<b>€ 67.43</b>	

**Supplementary Table 42 – Occurrence rate and cost of management of CSF fistulas and meningitis related to microscopic surgery**

<b>CSF fistula (%)</b>									<b>5.71%</b>
	Unit cost	Frequency [alpha;beta]	Distribution	Days [C.I.]	Distribution	Dose/day [C.I.]	Distribution	Cost/drivers	Cost/driver weighted
Acetazolamide	€ 0.0010	N/A	-	3.00 [2.63-3.37]	Normal	350.00 [306.61-393.39]	Normal	€ 1.06	€ 0.06
Lumbar CSF drainage	€ 154.92	22.50% [19.15-65.96]	Beta	N/A	-	N/A	-	€ 34.86	€ 1.99
Fibrin glue injection	€ 179.58	N/A	-	3.00 [2.63;3.37]	Normal	N/A	-	€ 538.74	€ 30.79
Reintervention	€ 6,204.03	19.00% [20.06-85.52]	Beta	N/A	-	N/A	-	€ 1,183.27	€ 65.10
<b>Total cost CSF fistula</b>								<b>€ 1,757.92</b>	<b>€ 97.93</b>
<b>Meningitis (%)</b>									<b>0.44%</b>
	Unit cost	Frequency [alpha;beta]	Distribution	Days [C.I.]	Distribution	Dose/day [C.I.]	Distribution	Cost/drivers	Cost/driver weighted
Lumbar puncture	€ 457.00	2.00% [24.48;1199.52]	Beta	N/A	-	N/A	-	€ 420.00	€ 1.86
Antibiotic therapy - Meropenem	€ 0.0136	N/A	-	15.00 [13.14-166.86]	Normal	1000.00 [876.04-1123.96]	Normal	€ 203.86	€ 0.90
Reintervention	€ 6,204.03	80.00% [4.2;1.05]	Beta	N/A	-	N/A	-	€ 4,982.17	€ 21.24
<b>Total Cost Meningitis</b>								<b>€ 5,606.04</b>	<b>€ 24.00</b>
<b>TOTAL</b>								<b>€ 7,363.96</b>	<b>€ 121.94</b>

**Supplementary Table 43 – Number and type of diagnostic tests and specialist visits provided in the first month following microscopic surgery**

	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Cortisol	€ 7.79	1.00 [0.88-1.12]	Normal	€ 7.79
Free thyroxine (FT4)	€ 6.36	1.00 [0.88-1.12]	Normal	€ 6.36
Prolactin	€ 7.13	1.00 [0.88-1.12]	Normal	€ 7.13
Endocrinological visit	€ 20.66	1.00 [0.88-1.12]	Normal	€ 20.66
ENT visit	€ 20.66	0.25	Normal	€ 5.17
Neurosurgical visit	€ 20.66	1.50 [1.31-1.69]	Normal	€ 30.99
Testosterone in men	€ 9.78	0.5 [0.44-0.56]	Normal	€ 2.45
Estradiol in women	€ 3.98	0.5 [0.44-0.56]	Normal	€ 2.28
Sodium	€ 1.02	1.50 [1.31-1.69]	Normal	€ 1.53
ACTH test	€ 18.50	0.25 [0.22-0.28]	Normal	€ 4.62
<b>TOTAL</b>				<b>€ 88.97</b>

**Supplementary Table 44 – Number and type of diagnostic tests and specialist visits that are provided, on an annual basis, for the follow-up of the patient undergoing microscopic surgery in microprolactinoma**

1 <sup>st</sup> year				
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Cortisol	€ 7.79	2.75 [2.41-3.09]	Normal	€ 21.42
Free thyroxine (FT4)	€ 6.36	2.75 [2.41-3.09]	Normal	€ 17.50
Prolactin	€ 7.13	2.25 [1.97-2.53]	Normal	€ 16.04
Neurosurgical visit	€ 20.66	1.25 [1.10-1.41]	Normal	€ 25.83
Eye examination	€ 20.66	0.75 [0.66-0.84]	Normal	€ 15.50
Testosterone in men	€ 9.78	2.75 [2.41-3.09]	Normal	€ 13.45
Estradiol in women	€ 3.98	2.00 [1.75-2.25]	Normal	€ 9.11
Pituitary MRI with contrast medium	€ 247.50	1.75 [1.53-1.97]	Normal	€ 433.13
Bone mineral density	€ 31.50	1 [0.88-1.12]	Normal	€ 31.50
<b>Cost 1st year</b>		1.00		<b>€ 583.46</b>
2nd-5th year				
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Cortisol	€ 7.79	1.50 [1.31-1.69]	Normal	€ 11.69
Free thyroxine (FT4)	€ 6.36	1.75 [1.53-1.97]	Normal	€ 11.14
Prolactin	€ 7.13	1.75 [1.53-1.97]	Normal	€ 12.48
Neurosurgical visit	€ 20.66	0.25 [0.22-0.28]	Normal	€ 5.17
Eye examination	€ 20.66	0.75 [0.66-0.84]	Normal	€ 15.50
Testosterone in men	€ 9.78	1.75 [1.53-1.97]	Normal	€ 8.56
Estradiol in women	€ 3.98	1.00 [0.88-1.12]	Normal	€ 4.55
Pituitary MRI with contrast medium	€ 247.50	0.75 [0.66-0.84]	Normal	€ 185.63
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
<b>Cost 2nd-5th year</b>				<b>€ 270.44</b>
>5th year				
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Cortisol	€ 7.79	1.25 [1.10-1.41]	Normal	€ 9.74
Free thyroxine (FT4)	€ 6.36	1.50 [1.31-1.69]	Normal	€ 9.54
Prolactin	€ 7.13	1.50 [1.31-1.69]	Normal	€ 10.70
Neurosurgical visit	€ 20.66	0.25 [0.22-0.28]	Normal	€ 5.17
Eye examination	€ 20.66	0.75 [0.66-0.84]	Normal	€ 15.50
Testosterone in men	€ 9.78	1.50 [1.31-1.69]	Normal	€ 7.34
Estradiol in women	€ 3.98	0.75 [0.66-0.84]	Normal	€ 3.42
Pituitary MRI with contrast medium	€ 247.50	0.75 [0.66-0.84]	Normal	€ 185.63
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
<b>Cost &gt;5th year</b>				<b>€ 262.76</b>
<b>TOTAL COST</b>				<b>€ 1,116.66</b>
1 <sup>st</sup> year				
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
<b>Cortisol</b>	€ 7.79	2.75 [2.41-3.09]	Normal	€ 21.42
Free thyroxine (FT4)	€ 6.36	2.75 [2.41-3.09]	Normal	€ 17.50



Prolactin	€ 7.13	2.25 [1.97-2.53]	Normal	€ 16.04
Neurosurgical visit	€ 20.66	1.25 [1.10-1.41]	Normal	€ 25.83
Eye examination	€ 20.66	0.75 [0.66-0.84]	Normal	€ 15.50
Testosterone in men	€ 9.78	2.75 [2.41-3.09]	Normal	€ 13.45
Estradiol in women	€ 3.98	2.00 [1.75-2.25]	Normal	€ 9.11
Pituitary MRI with contrast medium	€ 247.50	1.75 [1.53-1.97]	Normal	€ 433.13
Bone mineral density	€ 31.50	1 [0.88-1.12]	Normal	€ 31.50
<b>Cost 1st year</b>		1.00		<b>€ 583.46</b>
<b>2nd-5th year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Cortisol	€ 7.79	1.50 [1.31-1.69]	Normal	€ 11.69
Free thyroxine (FT4)	€ 6.36	1.75 [1.53-1.97]	Normal	€ 11.14
Prolactin	€ 7.13	1.75 [1.53-1.97]	Normal	€ 12.48
Neurosurgical visit	€ 20.66	0.25 [0.22-0.28]	Normal	€ 5.17
Eye examination	€ 20.66	0.75 [0.66-0.84]	Normal	€ 15.50
Testosterone in men	€ 9.78	1.75 [1.53-1.97]	Normal	€ 8.56
Estradiol in women	€ 3.98	1.00 [0.88-1.12]	Normal	€ 4.55
Pituitary MRI with contrast medium	€ 247.50	0.75 [0.66-0.84]	Normal	€ 185.63
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
<b>Cost 2nd-5th year</b>				<b>€ 270.44</b>
<b>&gt;5th year</b>				
	<b>Unit cost</b>	<b>Freq. (n°) [C.I.]</b>	<b>Distribution</b>	<b>Cost/drivers</b>
Cortisol	€ 7.79	1.25 [1.10-1.41]	Normal	€ 9.74
Free thyroxine (FT4)	€ 6.36	1.50 [1.31-1.69]	Normal	€ 9.54
Prolactin	€ 7.13	1.50 [1.31-1.69]	Normal	€ 10.70
Neurosurgical visit	€ 20.66	0.25 [0.22-0.28]	Normal	€ 5.17
Eye examination	€ 20.66	0.75 [0.66-0.84]	Normal	€ 15.50
Testosterone in men	€ 9.78	1.50 [1.31-1.69]	Normal	€ 7.34
Estradiol in women	€ 3.98	0.75 [0.66-0.84]	Normal	€ 3.42
Pituitary MRI with contrast medium	€ 247.50	0.75 [0.66-0.84]	Normal	€ 185.63
Bone mineral density	€ 31.50	0.50 [0.44-0.56]	Normal	€ 15.75
<b>Cost &gt;5th year</b>				<b>€ 262.76</b>
<b>TOTAL COST</b>				<b>€ 1,116.66</b>

**Supplementary Table 45 – Number and type of diagnostic tests and specialist visits that are provided, on an annual basis, for the follow-up of the patient undergoing microscopic surgery in macroprolactinoma**

Term	Brief			
	1 <sup>st</sup> year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Cortisol	€ 7.79	2.5 [2.19-2.81]	Normal	€ 19.48
Free thyroxine (FT4)	€ 6.36	2.75 [2.41-3.09]	Normal	€ 17.50
Prolactin	€ 7.13	2.75 [2.41-3.09]	Normal	€ 19.61
Neurosurgical visit	€ 20.66	1.50 [1.31-1.69]	Normal	€ 30.99
Eye examination	€ 20.66	2.25 [1.97-2.53]	Normal	€ 46.49
Testosterone in men	€ 9.78	2.75 [2.41-3.09]	Normal	€ 13.45
Estradiol in women	€ 3.98	2.25 [1.97-2.53]	Normal	€ 10.25
Pituitary MRI with contrast medium	€ 247.50	1.25 [1.10-1.41]	Normal	€ 309.38
Computed optical tomography	€ 120.42	0.75 [0.66-0.84]	Normal	€ 90.32
Bone mineral density	€ 31.50	1 [0.88-1.12]	Normal	€ 31.50
<b>Cost 1st year</b>		1.00		<b>€ 588.94</b>
	Medium			
	2nd-5th year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Cortisol	€ 7.79	1.50 [1.31-1.69]	Normal	€ 11.69
Free thyroxine (FT4)	€ 6.36	1.75 [1.53-1.97]	Normal	€ 11.14
Prolactin	€ 7.13	1.50 [1.31-1.69]	Normal	€ 10.70
Neurosurgical visit	€ 20.66	1 [0.88-1.12]	Normal	€ 20.66
Eye examination	€ 20.66	1.50 [1.31-1.69]	Normal	€ 30.99
Testosterone in men	€ 9.78	1.75 [1.53-1.97]	Normal	€ 8.56
Estradiol in women	€ 3.98	1.25 [1.10-1.41]	Normal	€ 5.69
Pituitary MRI with contrast medium	€ 247.50	1 [0.88-1.12]	Normal	€ 247.50
Computed optical tomography	€ 120.42	0.25 [0.22-0.28]	Normal	€ 30.11
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
<b>Cost 2nd-5th year</b>				<b>€ 392.77</b>
	Long			
	>5th year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Cortisol	€ 7.79	1.50 [1.31-1.69]	Normal	€ 11.69
Free thyroxine (FT4)	€ 6.36	1.75 [1.53-1.97]	Normal	€ 11.14
Prolactin	€ 7.13	1.75 [1.53-1.97]	Normal	€ 12.48
Neurosurgical visit	€ 20.66	1 [0.88-1.12]	Normal	€ 20.66
Eye examination	€ 20.66	1.50 [1.31-1.69]	Normal	€ 30.99
Testosterone in men	€ 9.78	1.50 [1.31-1.69]	Normal	€ 7.34
Estradiol in women	€ 3.98	1 [0.88-1.12]	Normal	€ 4.55
Pituitary MRI with contrast medium	€ 247.50	0.75 [0.66-0.84]	Normal	€ 185.63
Computed optical tomography	€ 120.42	0.25 [0.22-0.28]	Normal	€ 30.11
Bone mineral density	€ 31.50	0.5 [0.44-0.56]	Normal	€ 15.75
<b>Cost &gt;5th year</b>				<b>€ 330.32</b>
<b>TOTAL COST</b>				<b>€ 1,312.03</b>

**Supplementary Table 46 – Loss of patient/caregiver productivity – Microscopical surgery**

	Unit cost	% [alpha;beta]	Distribution	
% patients with caregivers	€ 14.05	1.25% [24.68-1949.32]	Beta	<b>€ 11.41</b>
		N° days [C.I.]		
Days of convalescence hypothesized	€ 14.05	8.00 [7.01-8.99]	Normal	<b>€ 913.13</b>

**Supplementary Table 47** – Average duration/session and number of sessions of fractionated radiotherapy and radiosurgery operations

	Average duration (min) [C.I]	Distribution	N. of sessions [C.I]	Distribution
Fractional radiotherapy session	47.50 [41.61-53.39]	Normal	22.71 [19.90-25.53]	Normal
Radiosurgery session	30.00 [26.28-33.72]	Normal	1.00 [0.88-1.12]	Normal

**Supplementary Table 48** – Cost of healthcare professionals who intervene during radiation treatment and structure intervention

	Unit cost	No	Distribution	Cost/professional role
<b>Healthcare professionals</b>				
Physician	€ 0.58	1.00 [0.88-1.12]	Normal	€ 274.92
Nurse	€ 0.27	1.00 [0.88-1.12]	Normal	€ 127.22
Anesthetist	€ 0.58	0.33	Normal	€ 91.64
Radiotherapy technician	€ 0.23	1.50 [1.31-1.69]	Normal	€ 166.95
Medical physicist	€ 0.58	1.00 [0.88-1.12]	Normal	€ 274.92
Neurosurgeon	€ 0.58	1.00 [0.88-1.12]	Normal	€ 274.92
<b>Sub-Total</b>				<b>€ 1,210.58</b>
<b>Instrumentation</b>				
Linear accelerator - LINAC	€ 42.89	N/A	-	€ 412.91
Gamma knife - Leksell	€ 10.00	N/A	-	€ 5.76
<b>Sub-Total</b>				<b>€ 418.68</b>
<b>Materials</b>				
Fractional: 1 thermoplastic mask for all sessions	€100.00	1.00 [0.88-1.12]	Normal	€ 100.00
Needle cannula for venous access	€ 0.22	1.00 [0.88-1.12]	Normal	€ 0.22
Physiological solution 0.9% 500 cc	€ 0.0016	1.00 [0.88-1.12]	Normal	€ 0.82
<b>Sub-Total</b>				<b>€ 101.05</b>
	<b>TOTAL</b>			<b>€ 1,730.30</b>

**Supplementary Table 49 – Number and type of diagnostic tests and specialist visits that are provided, on an annual basis, for the follow-up of the patient undergoing radiation therapy**

Term	Brief			
	1 <sup>st</sup> year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	2.38 [2.08-2.67]	Normal	€ 49.07
Prolactin	€ 7.13	2.13 [1.86-2.38]	Normal	€ 15.15
Cortisol	€ 7.79	1.25 [1.10-1.40]	Normal	€ 9.74
Free thyroxine (FT4)	€ 6.36	1.25 [1.10-1.40]	Normal	€ 7.95
Bone mineral density	€ 31.50	1 [0.88-1.12]	Normal	€ 31.50
ACTH test	€ 18.50	1.13 [0.99-1.26]	Normal	€ 20.81
Pituitary MRI with contrast medium	€ 247.50	1.63 [1.42-1.83]	Normal	€ 402.19
Visual field test	€ 16.78	1.25 [1.10-1.40]	Normal	€ 20.98
Vitamin D	€ 15.86	1 [0.88-1.12]	Normal	€ 15.86
Blood count	€ 3.17	1 [0.88-1.12]	Normal	€ 3.17
PSA (in men)	€ 7.41	0.88 [0.76-0.98]	Normal	€ 6.49
Testosterone (in men)	€ 9.78	1 [0.88-1.12]	Normal	€ 9.78
Computed optical tomography (OCT)	€ 120.42	0.83 [0.73-0.94]	Normal	€ 100.35
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
Brain MRI	€ 166.58	0	Normal	€ 0.00
<b>Cost 1st year</b>				<b>€ 695.06</b>
	Medium			
	2nd-5th year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	1.25 [1.10-1.40]	Normal	€ 30.99
Prolactin	€ 7.13	1.25 [1.10-1.40]	Normal	€ 10.70
Cortisol	€ 7.79	1.13 [0.99-1.26]	Normal	€ 8.76
Free thyroxine (FT4)	€ 6.36	1.13 [0.99-1.26]	Normal	€ 7.16
Bone mineral density	€ 31.50	0.79 [0.69-0.88]	Normal	€ 24.75
ACTH test	€ 18.50	1 [0.88-1.12]	Normal	€ 18.50
Pituitary MRI with contrast medium	€ 247.50	1.13 [0.99-1.26]	Normal	€ 278.44
Visual field test	€ 16.78	1 [0.88-1.12]	Normal	€ 16.78
Vitamin D	€ 15.86	0.92 [0.80-1.03]	Normal	€ 14.54
Blood count	€ 3.17	1 [0.88-1.12]	Normal	€ 3.17
PSA (in men)	€ 7.41	0.88 [0.76-0.98]	Normal	€ 6.49
Testosterone (in men)	€ 9.78	1 [0.88-1.12]	Normal	€ 9.78
Computed optical tomography (OCT)	€ 120.42	0.83 [0.73-0.94]	Normal	€ 100.35
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
Brain MRI	€ 166.58	0.5 [0.44-0.56]	Normal	€ 83.29
<b>Cost 2nd-5th year</b>				<b>€ 615.72</b>
	Long			
	>5th year			
	Unit cost	Freq. (n°) [C.I.]	Distribution	Cost/drivers
Specialist	€ 20.66	1.17 [1.02-1.31]	Normal	€ 24.10
Prolactin	€ 7.13	1 [0.88-1.12]	Normal	€ 7.13
Cortisol	€ 7.79	1 [0.88-1.12]	Normal	€ 7.79
Free thyroxine (FT4)	€ 6.36	1 [0.88-1.12]	Normal	€ 6.36
Bone mineral density	€ 31.50	0.79 [0.69-0.88]	Normal	€ 24.75
ACTH test	€ 18.50	1 [0.88-1.12]	Normal	€ 18.50
Pituitary MRI with contrast medium	€ 247.50	0.92 [0.80-1.03]	Normal	€ 226.88
Visual field test	€ 16.78	0.81 [0.71-0.91]	Normal	€ 13.63
Vitamin D	€ 15.86	0.92 [0.80-1.03]	Normal	€ 14.54
Blood count	€ 3.17	1 [0.88-1.12]	Normal	€ 3.17
PSA (in men)	€ 7.41	0.88 [0.76-0.98]	Normal	€ 6.49
Testosterone (in men)	€ 9.78	1 [0.88-1.12]	Normal	€ 9.78
Computed optical tomography (OCT)	€ 120.42	0.75 [0.66-0.84]	Normal	€ 90.32
Sodium/potassium	€ 1.02	1 [0.88-1.12]	Normal	€ 2.04
Brain MRI	€ 166.58	0.5 [0.44-0.56]	Normal	€ 83.29
<b>Cost &gt;5th year</b>				<b>€ 538.76</b>
<b>TOTAL COST</b>				<b>€ 1,849.54</b>

**Supplementary Table 50 – Loss of patient/caregiver productivity – Radiation therapy**

	Unit cost	Days absent from work [C.I.]	Distribution	% [alpha;beta]	Distribution	Cost/figure
Patient						<b>€ 757.19</b>
Caregivers	€14.05	4.67 [4.09-5.25]	Normal	3.64% [24.05; 636.22]	Beta	<b>€ 31.51</b>