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Lazzaro C, Lopiano L, Cocito D.

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# Subcutaneous vs intravenous administration of immunoglobulin in chronic inflammatory demyelinating polyneuropathy: an Italian cost-minimization analysis

Carlo Lazzaro<sup>1</sup>, Leonardo Lopiano<sup>2</sup> and Dario Cocito<sup>2</sup>

<sup>1.</sup> Studio di Economia Sanitaria, Via Stefanardo da Vimercate, 19, 20128 Milan, Italy

<sup>2.</sup> UOA Neurologia 2, Dipartimento di Neuroscienze, University of Turin, Turin, Italy

Carlo Lazzaro

Email: carlo.lazzaro@tiscalinet.it

## Abstract

Prior researches have suggested that home-based subcutaneous immunoglobulin (SCIG) is equally effective and can be less expensive than hospital-based intravenous immunoglobulin (IVIG) in treating chronic inflammatory demyelinating polyneuropathy (CIDP) patients. This economic evaluation aims at comparing costs of SCIG vs IVIG for CIDP patients in Italy. A 1-year model-based cost-minimization analysis basically populated via neurologists' opinion was undertaken from a societal perspective. Health care resources included immunoglobulin; drugs for premedication and complications (rash, headache, and hypertension) management; time of various health care professionals; pump for SCIG self-administration; infusion disposables. Non-health care resources encompassed transport and parking; losses of working and leisure time for patients and caregivers. Unit or yearly costs for resources valuation were mainly obtained from published sources. Costs were expressed in Euro (€) 2013. An extensive one-way sensitivity analysis (OWSA) and a scenario SA tested the robustness of the base case findings. Overall costs per patient amount to €49,534.75 (SCIG) and €50,895.73 (IVIG); saving in favour of SCIG reaches €1360.98. For both SCIG and IVIG, the cost driver was immunoglobulin (94.06 vs 86.06 % of the overall costs, respectively). Sensitivity analyses confirmed the consistency of the baseline results. SCIG may be a cost-saving therapy for Italian CIDP patients.

**Keywords:** Chronic inflammatory demyelinating polyneuropathy CIDP Immunoglobulin SCIG IVIG Cost-minimization analysis

## Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired immune-mediated inflammatory disorder [1]. The course of CIDP may be chronic progressive, stepwise, or monophasic [2].

Although CIDP is not age or gender-dependent, it is more frequent in older individuals and males [1]. Older age groups are more likely to have a chronic progressive course of CIDP, whereas a relapsing-remitting pattern is frequently observed in younger patients [3].

The crude prevalence rate of CIDP in different countries has been reported to range between 0.8 and 7.7 per 100,000 population [4–6], and falls in between these extremes (3.58 per 100,000 population) for two North-Western Italian Regions (Piedmont and Valle d'Aosta) [7].

Prior researches have suggested that home-based subcutaneous immunoglobulin (SCIG) is equally effective and can be less expensive than hospital-based intravenous immunoglobulin (IVIG) in treating CIDP patients, due to savings on nursing and medical resources [8, 9].

Expanding on the unique Italian economic evaluation on this topic [9], this article reports on methods and result of a 1-year model-based cost-minimization analysis [10] aimed at comparing cost of SCIG vs IVIG for CIDP patients in Italy from the societal perspective [10].

## Methods

As the economic evaluation was not an empirical study, no ethics board approval was requested.

### Cost-minimization analysis

Cost-minimization analysis compares solely in terms of cost two or more health care technologies proved to be equivalent in terms of clinical effectiveness [10, 11].

### Resource identification and quantification

Consistently with the societal standpoint, health care and non-health care resources were identified and quantified based on neurologists' opinion and research hypotheses (Table 1).

Table 1: Resource identification and quantification

Item	SCIG	IVIG	Source
Health care resources			
Training for SCIG self-administration			
Nurse time	2 sessions, 2.5 h each	–	Experts' opinion
Therapy			
Premedication	–	Antihistaminic (10 mg per os) corticosteroid (4 mg iv)	Experts' opinion and research hypotheses
Immunoglobulin	960 g per year <sup>a</sup>	960 g per year <sup>a</sup>	Experts' opinion
GP consultation for recipes	2 per year	12 per year	Experts' opinion
LHA admittances for receiving immunoglobulin, disposable and self-infusion pump	4 per year	–	Experts' opinion

Item	SCIG	IVIG	Source
LHA pharmacist time for delivering immunoglobulin, disposable and self-infusion pump	1.32 h per year	–	Research hypotheses
Administration			
Number of administrations	96 per year <sup>b</sup>	24 per year <sup>c</sup>	Experts' opinion
Neurologist time	–	0.50 h per administration	Experts' opinion
Nurse time	–	1 h per administration	Experts' opinion
Self-infusion pump	1 self-infusion pump 50 ml	–	Experts' opinion
Disposables	1 50 ml syringe	1 needle	Experts' opinion
	1 multi subcutaneous drug delivery device	1 tubing	
Follow-up			
Neurologist time	2 visits per year, 0.50 h each	2 visits per year, 0.50 h each	Experts' opinion
Electromyography (12 single nerves)	1 per year	1 per year	Experts' opinion
Complications <sup>d</sup>			
Neurologist time for rash; headache; hypertension	–	0.50 h for rash; headache; hypertension	Experts' opinion
Other specialist time for rash; headache; hypertension	–	0.025 h for rash; headache; hypertension	Experts' opinion
Nurse time	–	0.33 h for rash;	Experts'

Item	SCIG	IVIG	Source
		headache; hypertension; 0.25 h for difficult iv	opinion
Drug for rash	–	Antihistaminic (10 mg per os for 1 day)e corticosteroid (4 mg iv for 1 day)	Experts' opinion
Drug for headache	–	paracetamol (2 g suppositories per diem for 2.5 days)	Experts' opinion
Drug for hypertension	–	Amlodipine besylate (5 mgper os for 1 day) furosemide (20 mg iv for 1 day)	Experts' opinion
Non-health care resources			
Training for SCIG self-administration			
Transport	12 km per session	–	Experts' opinion
Parking	3 h per session	–	Experts' opinion and research hypotheses
Therapy			
Transport	3 km per LHA admittance	–	Research hypotheses
Parking	0.75 h per LHA admittance	–	Research hypotheses
Administration			
Transport	–	12 km per administration	Experts' opinion
Parking	–	3.5 h per administration	Experts' opinion and research

Item	SCIG	IVIG	Source
			hypotheses
Follow-up			
Transport	12 km per follow-up visit	12 km per follow-up visit	Research hypotheses
Parking	1.5 h per follow-up visit	1.5 h per follow-up visit	Research hypotheses
Complications			
Parking	–	1.30 h rash; headache; hypertension; 0.75 h for difficult iv	Experts' opinion and research hypotheses
Productivity losses <sup>f</sup>			
Training for SCIG self-administration			
Patient	4.5 h each per session	–	Experts' opinion
Caregiver <sup>g</sup>	4.5 h each per session	–	Experts' opinion
Therapy			
Patients time (admittance to GP surgery)	1 h per admittance	1 h per admittance	Research hypotheses
Patients time (admittance to LHA)	1.25 h per admittance	–	Research hypotheses
Administration			
Patient	–	5 h per administration	Experts' opinion
Caregiver <sup>h</sup>	–	5 h per administration	Experts' opinion
Follow-up			

Item	SCIG	IVIG	Source
Patient	3 h per follow-up visit	3 h per follow-up visit	Experts' opinion
Caregiver <sup>g,h</sup>	3 h per follow-up visit	3 h per follow-up visit	Experts' opinion
Complications			
Patient	–	0.80 h rash; headache; hypertension; 0.25 h for difficult iv	Experts' opinion and research hypotheses
Caregiver <sup>h</sup>	–	0.80 h rash; headache; hypertension; 0.25 h for difficult iv	Experts' opinion and research hypotheses
Leisure time losses			
Administration	1.25 h per administration	–	Experts' opinion

GP general practitioner, LHA Local Health Authority, IVIG intravenous immunoglobulin, SCIG subcutaneous immunoglobulin

<sup>a</sup>Assuming a 80 kg patient, 1 g per kilo per month for 12 months

<sup>b</sup>That is, 8 administrations per month per 12 months

<sup>c</sup>That is, 2 administrations per month per 12 months

<sup>d</sup>Proportion of complications per IVIG administration: rash: 0.25; headache: 0.50; hypertension: 0.50; difficult iv: 0.40. Patients may report more than one complication

<sup>e</sup>Proportion of IVIG patients needing 10 mg per os for further 7 days: 0.10

<sup>f</sup>Proportion of employed patients and housewives for SCIG and IVIG patients: 0.46 and 0.14, respectively. The same proportions were assumed for caregivers, too

<sup>f</sup>Proportion of SCIG patients needing caregivers' support (training for self-administration and follow-up visits): 0.04

<sup>h</sup>Proportion of IVIG patients needing caregivers' support (administration sessions; follow-up visits and complications): 0.40

Health care resources included immunoglobulin, drugs for premedication and management of the complications (rash, headache, and hypertension) following infusion (IVIG only) [8, 9], time of neurologist, nurse, general practitioner (GP), other specialist (IVIG only), Local Health Authority (LHA) pharmacist (SCIG only), pump for self-administration (SCIG only), and infusion disposables.



Assuming a patient weight of 80 kg, a monthly infusion scheme of 1 g of immunoglobulin per kg was considered. SCIG patients were assumed to self-administer 10 g of immunoglobulin twice per week (i.e. 96 administrations per year), and IVIG patients to receive 40 g of immunoglobulin twice per month in two subsequent days (i.e. 24 administrations per year) in hospital setting.

Non-health care resources encompassed transport and parking, as well as losses of working and leisure time for patients and caregivers.

Distance back and forth between patients' home and hospital (LHA) was estimated at 12 (6) km and travelled by car, whereas a walking distance of 2 km between patients' home and GP surgery was considered.

Parking duration was assumed to be 0.5 h longer than patients and caregivers' time loss, considering that they prefer to pay an extra amount for parking to avoid possible fines should any delay on scheduled parking time occur.

For both SCIG and IVIG, the proportion of employed patients and housewives was estimated at 0.46 and 0.14, respectively (the same proportions were assumed for caregivers), whereas the proportion of patients needing caregivers' support (i.e. informal car) [10, 11] was estimated at 0.04 (SCIG) and 0.4 (IVIG).

Patients and their caregivers were supposed to lose working time for attending two hospital-based training sessions for learning immunoglobulin self-administration only once before starting treatment (SCIG only); accessing GP surgery for recipes concerning neurologist visits, immunoglobulin infusions, and follow-up; accessing LHA for receiving immunoglobulin, disposables, and self-infusion pump (SCIG only); undergoing immunoglobulin administration in hospital setting (IVIG only), follow-up, and complications management (IVIG only).

Time spent by patients and caregivers included the distance travelled back and forth between home and hospital, LHA and GP surgery.

As no disruption in daily activities was assumed for SCIG patients, they were supposed to lose leisure time instead of working time for immunoglobulin self-administration.

Due to the limited time horizon, mortality was not taken into account.

### **Resource valuation**

Unit or yearly costs for resource valuation were grouped into three categories that focus on who actually funds a given health care or non-health care resource [10] (Table 2)

*Table 2: Unit or yearly costs for resource valuation (costs in €2013)*

Item	SCIG	<u>IVIG</u>	Source
Health care sector costs			
Nurse (per h)	21.24	21.24	[9, 28]
Neurologist (per h)	55.90	55.90	[9, 28]

<b>Item</b>	<b>SCIG</b>	<b><u>IVIG</u></b>	<b>Source</b>
Other specialist (per h)	–	55.90	[9, 28]
GP (per consultation)	21.71	21.71	[9, 28]
LHA pharmacist (per h)	39.27	–	[12, 28]
Immunoglobulin (per g)	48.54	45.63	Weighted average tender price negotiated between pharmaceuticals and five Italian Regions, 1st quarter 2013; [18]
Antihistaminic (10 mg per os)	–	0.22	[15]
Corticosteroid (4 mg vial iv)	–	0.55	[15]
Paracetamol (1 g suppository)	–	0.46	[15]
Amlodipine besylate (5 mg per os)	–	0.13	[15]
Furosemide (20 mg vial iv)		0.41	[15]
Disposables (per administration)	–	19.88	[9, 28]
Electromyography(12 nerves)	123.96 <sup>a</sup>	123.96 <sup>a</sup>	[16]
Patients and their family costs			
Out-of-pocket expenses			
Transport (per km)	0.26 <sup>b</sup>	0.26 <sup>b</sup>	[14]
Parking (per h)	1.50	1.50	Average hourly cost in three Northern Italy towns
Productivity losses			
Average gross cost (per h)—employed	30.20	30.20	[25–28]

Item	SCIG	IVIG	Source
Average gross cost (per h)—housewife	14.34	14.34	[22, 23, 26–28]
Leisure time losses			
Average net cost (per h)—employed c	13.86	–	[25, 28]
Other sectors costs			
Self-infusion pump (per year)	202	–	Average market price for Italy
Disposables (per administration)	10.16	–	Average market price for Italy

*GP general practitioner, IVIG intravenous immunoglobulin, LHA Local Health Authority; SCIG subcutaneous immunoglobulin*

<sup>a</sup>*That is, €10.33 per nerve*

<sup>b</sup>*Domestic brand (displacement: 1,400 cubic centimetres; horse power: 70; unleaded fuel engine)*

<sup>c</sup>*For valuing SCIG patient's time devoted to self-administration only*

The first category includes costs for drugs, inpatient and outpatient health care services provided by health care facilities and professionals within the health care sector (hospital, LHA, and GP).

The second category gathers patients' and their families' out-of-pocket expenses for health and non-health care resources, as well as productivity and leisure time losses incurred by patients and caregivers.

The third category includes costs borne by other sectors, such as those related to self-infusion pump and disposables (SCIG only), as in Italy these items are usually provided and funded by pharmaceuticals producing immunoglobulin, with no charge for hospital, LHA or patient.

Monetary values for resources different from patients, caregivers, and housewives' time were obtained from published sources [9, 12–15], estimated using tariffs for funding health care providers in Italy [16] assuming that they were a good proxy of the actual costs [17], or retrieved via ad hoc researches (immunoglobulin; parking; self-infusion pump and disposables for SCIG).

Immunoglobulin was valued using the average tender price per gram negotiated between pharmaceuticals and five Italian Regions (North East: 1; North West: 1; Centre: 1; South: 2) during the 1st quarter 2013, weighted for the relative population [18] to take into account potential differences in the exposition to immunoglobulin at local level.

Consistently with the useful life for a SCIG self-infusion pump, a 5-year straight-line depreciation approach [10] was adopted for calculating the yearly cost of this device. Therefore, the yearly cost of a SCIG self-infusion pump equals one-fifth of its purchase cost. No maintenance or replacement cost for SCIG self-infusion pump was considered.

Health care sector costs do not include a share of overheads to be attributed to LHA and hospital. No co-payment for drugs or health care services was included among out-of-pocket expenses, as in Italy CIDP patients can apply for a disease-based exemption [19].

Time off paid work (leisure time) was valued using the average gross (net) annual wage rate for different professional categories, whereas housewives' time was costed using the average gross hourly cost of a patient companion [20–27].

All costs were expressed in Euro (€) 2013 and updated to this year according to proper inflation rates whenever necessary [28].

Yearly costs for patient on SCIG or IVIG and their difference were calculated.

Since the economic evaluation stretches over 1-year time horizon, no discounting procedure was performed [10, 11].

### **Statistical analysis**

For most of the parameters included in the model, the 95 % confidence interval (95 % CI) was calculated via the percentile method [29, 30].

An appropriate statistical distribution was given to each parameter and a reasonable coefficient of variation was applied to their base case estimate to obtain the standard error (SE) [30–32]. The SE for proportions was calculated assuming a sample of 100 patients (Table 3).

*Table 3: Parameters distribution (costs in €2013)*

<b>Item</b>	<b>Point estimate</b>	<b>CV (%)</b>	<b>SE</b>	<b>Parameter distribution for 95 % CI calculation</b>	<b>95 % CI</b>
Patient weight	80	10	8.00	Gamma	65.09;96.42
Number of administrations (per year)					
SCIG	96	10	9.60	Gamma	78.11;115.71
IVIG	24	10	2.4	Gamma	19.53; 28.93
Number of LHA admittances (per year) <sup>a</sup>	4	24	0.96	Gamma	2.35; 6.09
Hours per administration					
SCIG	1.25	10	0.13	Gamma	1.02;1.51
IVIG	5	10	0.50	Gamma	4.07;6.03
Transport					

<b>Item</b>	<b>Point estimate</b>	<b>CV (%)</b>	<b>SE</b>	<b>Parameter distribution for 95 % CI calculation</b>	<b>95 % CI</b>
Km <sup>b</sup>	12	40	4.80	Gamma	4.52;23.08
Cost (per km)	0.26	10	0.03	Normal	0.21;0.32
Parking cost (per h)	1.50	10	0.15	Normal	1.21;1.79
Average gross cost (per h)					
Employed	29.24	10	2.92	Normal	23.51;34.97
Housewife	15.12	10	1.51	Normal	12.16;18.09
Average net cost (per h)					
Employed	13.45	10	1.34	Normal	10.81;16.08
Nurse cost (per h)	21.24	10	2.12	Normal	17.08;25.40
Neurologist cost (per h)	55.90	10	5.59	Normal	44.94;66.85
Other specialist cost (per h)	55.90	10	5.59	Normal	44.94;66.85
LHA pharmacist cost (per h)	39.27	10	3.93	Normal	31.57;46.97
Cost of GP (per consultation)	21.71	10	2.17	Normal	17.46;25.97
Cost of immunoglobulin (per g)					
SCIG	48.54	0.03	1.46	Normal	45.68;51.39
IVIG	45.63	0.03	1.37	Normal	42.94;48.31
Cost of self-infusion pump (per year) <sup>a</sup>	202	10	20.20	Normal	162.41;241.59
Cost of disposables (per administration)					

Item	Point estimate	CV (%)	SE	Parameter distribution for 95 % CI calculation	95 % CI
SCIG	10.16	10	1.02	Normal	8.17;12.15
IVIG	19.88	10	1.99	Normal	15.98;23.78
Cost of electromyography (12 nerves)	123.96	10	12.40	Normal	99.66;148.26
Proportion of employed (patients and caregivers)	0.46	–	0.05 <sup>c</sup>	Beta	0.36;0.56
Proportion of housewives (patients and caregivers)	0.14	–	0.03 <sup>c</sup>	Beta	0.08;0.21
Proportion of patients needing caregivers' support					
SCIG	0.04	–	0.02 <sup>c</sup>	Beta	0.01;0.09
IVIG	0.40	–	0.05 <sup>c</sup>	Beta	0.31;0.50
Proportion of rash <sup>d</sup>	0.25	–	0.04 <sup>c</sup>	Beta	0.17;0.34
Proportion of headache <sup>d</sup>	0.50	–	0.05 <sup>c</sup>	Beta	0.40;0.60
Proportion of hypertension <sup>d</sup>	0.50	–	0.05 <sup>c</sup>	Beta	0.40;0.60
Proportion of difficult iv <sup>d</sup>	0.40	–	0.05 <sup>c</sup>	Beta	0.31;0.50

CV coefficient of variation (CV = SE/Point estimate), GP general practitioner, IVIG intravenous immunoglobulin, LHA Local Health Authority, OWSA one-way sensitivity analysis, SCIG subcutaneous immunoglobulin, SE standard error, 95 % CI 95 % confidence interval

<sup>a</sup>SCIG only

<sup>b</sup>Distance between patients' home and hospital

<sup>c</sup>SE was calculated assuming a sample of 100 patients. Therefore, no CV was assumed

<sup>d</sup>IVIG only

No hypothesis testing was undertaken.

## **Sensitivity analysis**

Sensitivity analysis (SA) allows for uncertainty in economic evaluation of health care programmes [10, 11]. A one-way SA (OWSA)—in which model parameters were changed one at a time by replacing the base case estimate with the lower and the upper limits of 95 % CI while keeping the other parameters at their baseline levels [10, 11]—was carried out on: hourly cost of health care professionals, patients, caregivers, and parking; cost of immunoglobulin, disposables, self-infusion pump for SCIG, and electromyography; patient weight; number of administrations per year and their duration; number of LHA admittances per year (SCIG only); distance between patient’s home and hospital; proportion of employed patients, housewives and caregivers; and frequency of complications for (IVIG only).

The results of OWSA were plotted on a Tornado chart. The y and x axes of Tornado chart crossed at the base case result.

A scenario SA [10, 11] was performed to investigate the impact on base case results due to shifting the cost for self-infusion pump and disposables for SCIG from pharmaceuticals to hospital or patient and their family budget.

## **Results**

### **Base case analysis**

Overall costs per patient amount to €49,534.75 and €50,895.73 for SCIG and IVIG, respectively; saving in favour of SCIG reaches €1,360.98 (Table 4).

*Table 4: Base case analysis—cost-minimization analysis (costs in €2013)*

<b>Item</b>	<b>SCIG (%) (A)</b>	<b>IVIG (%) (B)</b>	<b>Saving for SCIG (%) (B–A)</b>
Health care sector costs			
Training for SCIG self-administration			
Nurse time	106.19 (0.21)	–(0.00)	–106.19 (–7.80)
Therapy			
Premedication	–(0.00)	18.44 (0.04)	18.44 (1.35)
Immunoglobulin	46,593.81 (94.06)	43,800.90 (86.06)	–2,792.91 (–205.21)
GP consultation for recipes	43.43 (0.09)	260.57 (0.51)	217.14 (15.95)
LHA pharmacist time for delivering immunoglobulin and disposable	52.36 (0.11)	–(0.00)	–52.36 (–3.85)

<b>Item</b>	<b>SCIG (%) (A)</b>	<b>IVIG (%) (B)</b>	<b>Saving for SCIG (%) (B-A)</b>
Administration			
Neurologist time	-(0.00)	670.75 (1.32)	670.75 (49.28)
Nurse time	-(0.00)	509.72 (1.00)	509.72 (37.45)
Disposables	-(0.00)	477.12 (0.94)	477.12 (35.06)
Follow-up			
Neurologist time	55.90 (0.11)	55.90 (0.11)	-(0.00)
Electromyography	123.96 (0.25)	123.96 (0.24)	-(0.00)
Complications			
Neurologist time	-(0.00)	838.43 (1.65)	838.43 (61.61)
Other specialist time	-(0.00)	41.92 (0.08)	41.92 (3.08)
Nurse time	-(0.00)	258.05 (0.51)	258.05 (18.96)
Drug for rash	-(0.00)	5.51 (0.01)	5.51 (0.41)
Drug for headache	-(0.00)	27.60 (0.05)	27.60 (2.03)
Drug for hypertension	-(0.00)	6.52 (0.01)	6.52 (0.48)
Total health care sector costs	46,975.64 (94.83)	47,095.38 (92.53)	119.74 (8.80)
Patients and their family costs			
Out-of-pocket expenses			
Training for SCIG self-administration			
Transport	6.35 (0.01)	-(0.00)	-6.35 (-0.47)
Parking	9.00 (0.02)	-(0.00)	-9.00 (-0.66)
Therapy			



<b>Item</b>	<b>SCIG (%) (A)</b>	<b>IVIG (%) (B)</b>	<b>Saving for SCIG (%) (B-A)</b>
Transport	3.17 (0.01)	-(0.00)	-3.17 (-0.23)
Parking	4.50 (0.01)	-(0.00)	-4.50 (-0.33)
Administration			
Transport	-(0.00)	76.19 (0.15)	76.19 (5.60)
Parking	-(0.00)	126.00 (0.25)	126.00 (9.26)
Follow-up			
Transport	6.35 (0.01)	6.35 (0.01)	-(0.00)
Parking	4.50 (0.01)	4.50 (0.01)	-(0.00)
Complications			
Parking	-(0.00)	71.55 (0.14)	71.55 (5.26 %)
Productivity losses			
Training for SCIG self-administration			
Patient	139.75 (0.28)	-(0.00)	-139.75 (-10.27)
Caregiver	5.59 (0.01)	-(0.00)	-5.59 (-0.41)
Therapy			
Patients/caregiver time (access to GP surgery)	31.06 (0.06)	186.34 (0.37)	155.28 (11.41)
Patients/caregiver time (access to LHA)	77.64 (0.16)	-(0.00)	-77.64 (-5.70)
Administration			
Patient	-(0.00)	1,863.39 (3.66)	1,863.39 (136.92)
Caregiver	-(0.00)	745.36 (1.46)	745.36 (54.77)

Item	SCIG (%) (A)	IVIG (%) (B)	Saving for SCIG (%) (B-A)
Follow-up			
Patient	93.17 (0.19)	93.17 (0.18)	-(0.00)
Caregiver	3.73 (0.01)	37.27 (0.07)	33.54 (2.46)
Complications			
Patient	-(0.00)	421.59 (0.83)	421.59 (30.98)
Caregiver	-(0.00)	168.64 (0.33)	168.64 (12.39)
Leisure time losses			
Administration	996.94 (2.01 %)	-(0.00)	-996.94 (-73.25)
Total patients and their family costs	1,381.75 (2.79)	3,800.35 (7.47)	2,418.60 (177.71)
Other sectors costs			
Administration			
Infusion pump	202 (0.41)	-(0.00)	-202.00 (-14.84)
Disposables	975.36 (1.97)	-(0.00)	-975.36 (-71.67)
Total other sectors costs	1,177.36 (2.38)	-(0.00)	-1,177.36 (-86.51)
Overall costs	49,534.75 (100.00)	50,895.73 (100.00)	1,360.98 (100.00)

*GP general practitioner, IVIG intravenous immunoglobulin, LHA Local Health Authority, SCIG subcutaneous immunoglobulin*

For both SCIG and IVIG, health care sector costs (94.83 vs 92.53 % of the overall costs, respectively) are driven by immunoglobulin (94.06 vs 86.06 % of the overall costs, respectively).

Conversely, the impact of out-of-pocket expenses, working and leisure time losses is limited, especially for SCIG (2.79 vs 7.47 % of the overall costs, respectively). Saving in favour of SCIG is mainly explained by a

lower need for informal care (€9.32 vs €951.26) and reduced time losses due to immunoglobulin administration (€996.94 vs €1,863.39).

Eventually, other sector costs show a quite negligible effect on overall costs for SCIG (2.38 %).

### Sensitivity analysis

For the sake of brevity, only the results of OWSA concerning the ten parameters causing the widest variation in base case findings are reported on the Tornado chart (Fig. 1).

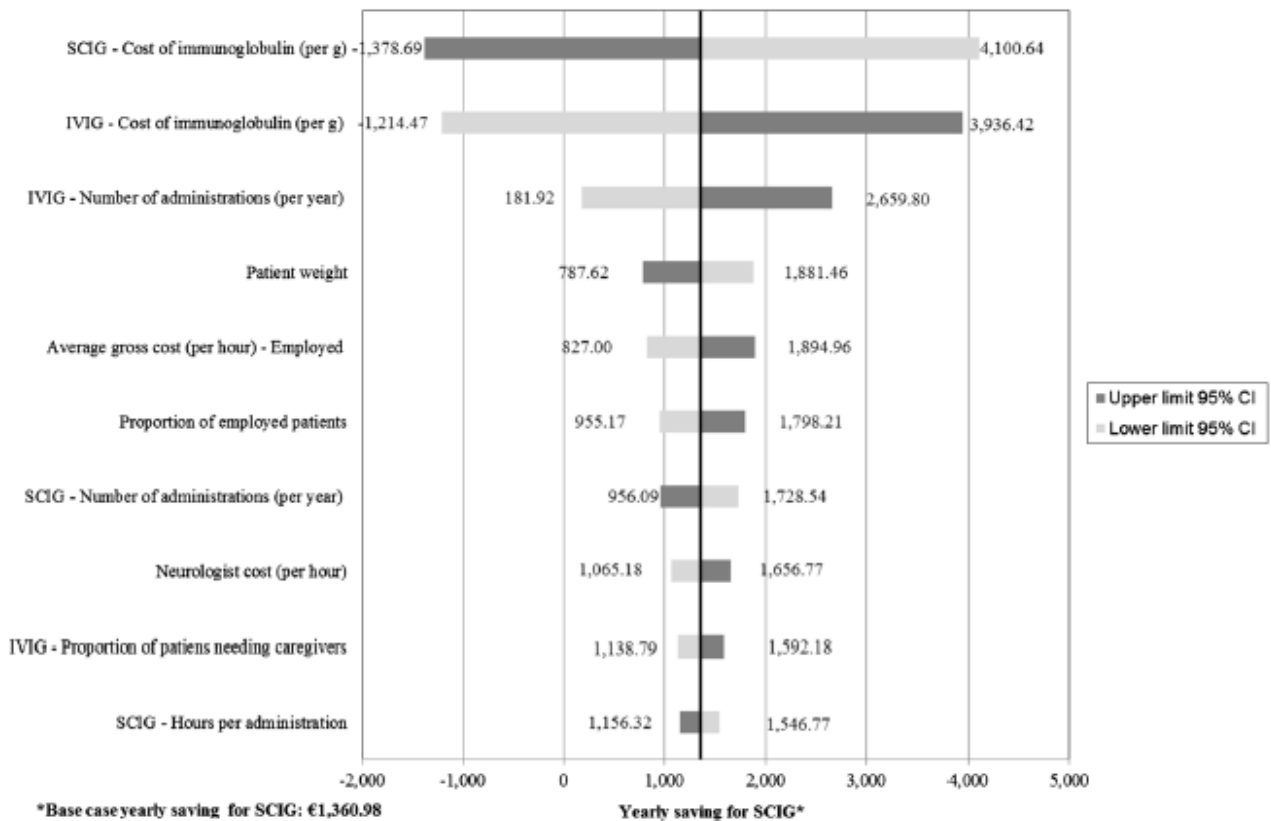


Fig. 1

OWSA—cost-minimization analysis (savings in €2013). IVIG intravenous immunoglobulin; OWSA one-way sensitivity analysis; SCIG subcutaneous immunoglobulin; 95 % CI 95 % confidence interval

Consistently with the base case results, changing the cost per gram of immunoglobulin has the highest impact on the baseline findings. Replacing the base case cost per gram for SCIG with the 95 % CI limits remarkably influences savings for SCIG (€4,100.64 or +201.30 % vs baseline results; -€1,378.69 or -201.30 % vs baseline results). Differences against base case saving for SCIG are slightly lower when the cost per gram for IVIG is changed in the same fashion (€3,936.42 or +189.23 % vs baseline results; -€1,214.47 or -189.23 % vs baseline results).

As IVIG administration is more time consuming than SCIG self-administration for health professionals, patients and caregivers, setting the number of IVIG administrations per year at the 95 % CI limits obviously affects saving for SCIG (€2,659.80 or +95.43 % vs baseline results; €181.92 or -86.63 % vs baseline results).

Conversely, changing in the same way the number of SCIG self-administrations per year has only a mild effect on base case findings (€1,728.54 or +27.01 % vs baseline results; €956.09 or –29.75 % vs baseline results).

Interestingly, even if pharmaceuticals producing SCIG ceased to provide self-infusion pump and disposables free of charge and costs related to those essential components for SCIG therapy (€1,177.36) were shifted to hospital or patient and their family budget, the overall saving in favour of SCIG would remain unvaried (€1,360.98) (Table 5).

*Table 5: Scenario SA—Cost-minimization analysis (costs in €2013)*

<b>Item</b>	<b>SCIG (%) (A)</b>	<b>IVIg (%) (B)</b>	<b>Saving for SCIG (%) (B–A)</b>
Base case analysis			
Total health care sector costs	46,975.64 (94.83)	47,095.38 (92.53)	119.74 (8.80)
Total patients and their family costs	1,381.75 (2.79)	3,800.35 (7.47)	2,418.60 (177.71)
Total other sectors costs	1,177.36 (2.38)	–(0.00)	–1,177.36 (–86.51)
Overall costs	49,534.75 (100.00)	50,895.73 (100.00)	1,360.98 (100.00)
Scenario sensitivity analysis—cost for self- infusion pump and disposables for SCIG shifted from pharmaceuticals to hospital budget			
Total health care sector costs	48,153.00 (97.21)	47,095.38 (92.53)	–1,057.62 (–77.71)
Total patients and their family costs	1,381.75 (2.79)	3,800.35 (7.47)	2,418.60 (177.71)
Total other sectors costs	–(0.00)	–(0.00)	–(0.00)
Overall costs	49,534.75 (100.00)	50,895.73 (100.00)	1,360.98 (100.00)
Scenario sensitivity analysis—cost for self- infusion pump and disposables for SCIG shifted from pharmaceuticals to patient and their family budget			
Total health care sector costs	46,975.64 (94.83)	47,095.38 (92.53)	119.74 (8.80)
Total patients and their	2,559.11 (5.17)	3,800.35 (7.47)	1,241.24 (91.20)

Item	SCIG (%) (A)	IVIG (%) (B)	Saving for SCIG (%) (B-A)
family costs			
Total other sectors costs	-(0.00)	-(0.00)	-(0.00)
Overall costs	49,534.75 (100.00)	50,895.73 (100.00)	1,360.98 (100.00)

*IVIG intravenous immunoglobulin, SA sensitivity analysis, SCIG subcutaneous immunoglobulin*

## Discussion

By adopting a 1-year time horizon and the Italian societal perspective, this model-based cost-minimization analysis confirms that, given the same effectiveness [8, 9], SCIG seems cost saving when compared with IVIG. If only half of the prevalent 2,126 CIDP patients estimated for Italy [7, 18] were prescribed SCIG instead of IVIG, saving for society and health care sector would reach €1.45 and €0.13 million, respectively.

It is worth noting that, even without adjusting for inflation, the base case saving in favour of SCIG could have been fourfold if the standard cost per gram of IVIG reported by the Italian National Blood Centre (€49.95, 2011 values) [33] instead of the weighted average tender price had been used.

This is the first Italian economic evaluation that compares SCIG vs IVIG in CIDP patients following a viewpoint wider than the third-party payer perspective. Therefore, saving in favour of SCIG is higher than the one previously reported in the unique cost-minimization analysis on the same topic performed in Italy [9] because, consistently with the adopted standpoint, that research did not include cost categories other than health care sector costs funded by Piedmont Health Service.

The results of our research support the evidence that preferring SCIG vs IVIG generates saving also for hospital. Interestingly, saving at hospital level is due to a sort of “informal partnership” between health care sector and pharmaceuticals producing SCIG. However, scenario SA proved that, under the societal viewpoint, the overall saving in favour of SCIG would not change event if costs for self-infusion pump and disposables were borne by hospital or patient and their family instead of pharmaceuticals producing SCIG.

As SCIG self-administration affects patients’ leisure time only, the potential productivity loss for society due to CIDP is higher for IVIG. How the absence of disruption in working and daily activities, as well as the time saved from moving back and forth between home and hospital for immunoglobulin administration, improves SCIG patients’ health-related quality of life (HRQoL) is still debated [9, 34] and shall benefit from further investigations on samples of patients of adequate size.

This economic evaluation has two main limitations. Firstly, due to a remarkable lack of patient level comparative research on the health economics of SCIG vs IVIG in CIDP, our cost-minimization analysis is based on a model that relied heavily on experts’ opinions about resource consumption and loss induced by CIDP management. However, modelling was previously utilized for the economic evaluation of CIDP treatment in Canada and Italy [1, 9]. Moreover, supporting Italian decision-makers in choosing between SCIG and IVIG on the grounds of the results of a model-based cost-minimization analysis is, in all likelihood, better than providing them with no guidance at all [35, 36].

The second limitation rests on the fact that the health care professionals whose qualified opinions were substantive for model population work in the same neurological department, which is at the forefront in CIDP treatment in Italy [37]. Therefore, model assumptions may have been different had a random sample of Italian neurological wards dealing with CIDP treatment been drawn for this research.

Being aware of the above-mentioned limitations, we tested the robustness of the base case findings via an extensive OWSA and a scenario SA.

In conclusion, the results of our research would endorse SCIG for CIDP treatment also from an economic point of view. However, as our results are far from being conclusive, there is an apparent necessity to carry out long-term empirical studies that can contribute to address the health economic and HRQoL issues related to the comparison of SCIG vs IVIG in treating CIDP patients in Italy.

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## Conflict of interest

Authors declare no conflict of interest.

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