

Payer and Societal Benefit of Peginterferon Beta-1a versus Subcutaneous Interferon Beta-1a in Patients with Relapsing-Remitting Multiple Sclerosis in Italy

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Conclusions

- The results suggest PEG-IFN1a versus SC-IFN1a for the treatment of RRMS in Italy is a potential cost-saving strategy that could moderate healthcare resource use and improve patient outcomes.
- The clinical and economic benefits of treating the SC-IFN1a population (n = 6,665) with PEG-IFN1a results in €175 million from a National Health Service (NHS) perspective and rises to €417 million in savings from a societal perspective.
- The majority (61%) of savings from the NHS perspective are the result of offsets in disability, while the greatest savings (45%) from a societal perspective are due to offsets in permanent sick leave.

Introduction

- Multiple sclerosis (MS) is a chronic neurodegenerative disease that affects the central nervous system and causes pathological inflammatory, demyelinating and neurodegenerative changes (1).
- The estimated prevalence in 2015 was more than 109,000 MS patients in Italy (2).
 - The Italian MS patient society (AISM) estimates that there are 122,000 patients in Italy with an incidence of 3,400 cases per year (3). An estimated 12 new cases per year occur in Sardinia (3).
- MS has a large economic impact on Italian society and a significant impact on quality of life.
 - Mean utility and total annual costs were 0.735 and €22,900 at Expanded Disability Status Scale (EDSS) of 0–3, 0.534 and €40,100 at EDSS of 4–6.5, and 0.135 and €53,300 at EDSS of 7–9 (4).
- The DMTs considered as suitable for treating mild and moderate forms of MS are the different formulations of interferon beta, glatiramer acetate (GA), triflunomide and dimethyl fumarate.
 - More, specifically subcutaneous pegylated interferon (peginterferon) beta-1a (PEG-IFN1a) and subcutaneous interferon beta-1a (SC-IFN1a) are among the most commonly used interferons indicated for the treatment of patients with relapsing-remitting multiple sclerosis (RRMS) in Italy.
- Studies have compared relative costs and health outcomes of PEG-IFN1a and SC-IFN1a.
 - Previous cost-effectiveness analyses suggest that PEG-IFN1a is a dominant treatment strategy compared to SC-IFN1a, but analyses have focused only on Scotland and the United States (5,6).
 - A recent cost-effectiveness analysis published in 2018 for Italy found PEG-IFN1a to be a dominant treatment strategy compared to SC-IFN1a from both the National Health Service (NHS) and Societal perspective, but no published studies have yet conducted this analysis considering the total population of RRMS patients using SC-IFN1a while providing detailed clinical and economic results (7).

Objectives

- To evaluate the clinical and economic benefits of treatment with peginterferon beta-1a (PEG-IFN1a) vs. subcutaneous interferon beta-1a 44 mcg (SC-IFN1a) for RRMS patients in Italy.

Methods

Design

- A cost-consequence evaluation comparing PEG-IFN1a to SC-IFN1a was performed using a Markov cohort model and country-specific data (year 2018) relating to clinical events and costs from a NHS and societal perspective in Italy.
 - The model counterfactually estimates the clinical and economic consequences of treating all SC-IFN1a patients in Italy with PEG-IFN1a based on current SC-IFN1a market share.
 - Disability levels (as measured by EDSS scores) are characterized by a Markov process with a 10-year time horizon and three-month cycle lengths.

Inputs

- The model framework (Figure 1) included country-specific and -independent patient distribution across disability health states (4), transition probabilities for confirmed disability worsening (CDW) (8), and costs of relapse (9), and disability status (10).
 - The number of RRMS patients treated with SC-IFN1a in Italy was 6,665 (11).
 - Costs, resource utilization, and baseline EDSS distribution were specific to Italy (4,12).
- Data sources included peer reviewed literature and real-world market research (Table 1).
 - The CDW hazard ratio and the annualized relapse rate (ARR) risk ratio for clinical outcomes of PEG-IFN1a and SC-IFN1a were estimated from an indirect treatment comparison (13).
 - The RRMS populations treated with SC-IFN1a are from March 2018 real world utilization (11).
 - Cost of relapses and disability were drawn from a cross-sectional cost of illness study (8,12).
 - Costs were inflation adjusted to €2018 (14).

Analysis

- Analyses were performed per patient and for the entire SC-IFN1a population.
- The clinical and economic outcomes evaluated included:
 - Clinical: relapses, quality-adjusted life years (QALYs), time spent with EDSS ≤ 3 and ≥ 6.
 - Economic: drug cost, direct and indirect disability and relapse management cost differences.

Results

- PEG-IFN1a was shown to slow disability worsening, with fewer patients progressing (Table 2).
 - PEG-IFN1a was shown to slow disability worsening versus SC-IFN1a, with 12.4% fewer (57.8% versus 70.1%) patients progressing to EDSS ≥ 6.0. More patients remained at EDSS ≤ 3 (20.6% versus 9.4%; difference = 11.2%).
- The use of PEG-IFN1a in place of SC-IFN1a lead to a comparable number of relapses (Table 2).
 - An average of 8.75 versus 8.76 relapses per patient and 61,403 versus 61,448 relapses per SC-IFN1a population (n = 6,665) for PEG-IFN1a and SC-IFN1a, respectively.
- For the entire SC-IFN1a population (n = 6,665), PEG-IFN1a was shown to lower health resource utilization (HRU) across multiple types of services, including inpatient and outpatient services (Table 3).
 - The largest declines in resource utilization were seen for PEG-IFN1a versus SC-IFN1a for total days as an inpatient at a rehabilitation center (saved/spared 16,977 days or 14.4% reduction), number of days at a nursing home (saved 13,012 days or 10.4% reduction), and number of day visits at a rehabilitation center (saved 49,562 day visits or 11.5% reduction).
- PEG-IFN1a was shown to lower cumulative/overall costs, per patient (Figure 2) as well as at a population-level (Table 4).
 - Total direct cost savings per patient for PEG-IFN1a versus SC-IFN1a when including treatment, relapse, and disability would approach €174 million (€24,923 per patient).
 - Relapse costs declined slightly with an average cost of €20,126 versus €20,165 per patient or €141,172,768 versus €141,444,025 per SC-IFN1a population (n = 6,665) for PEG-IFN1a and SC-IFN1a, respectively.
 - Disability costs declined by €15,151 per patient (€106.3 million per SC-IFN1a population) for PEG-IFN1a versus SC-IFN1a, largely driven by reduced informal care (€6,452 savings per patient or €45.3 million savings per SC-IFN1a population) and inpatient care costs (€ 3,549 savings per patient or €24.9 million savings per SC-IFN1a population) (Figure 3).
- Total indirect cost savings per patient for PEG-IFN1a versus SC-IFN1a when including work leave, sick leave and early retirement would approach €241.9 million (€34,487 per patient).
 - Short-term absence costs increased for PEG-IFN1a versus SC-IFN1a by €11.1 million (€1,583 per patient).
 - Permanent sick leave, early retirement, and long-term non-permanent sick leave costs declined for PEG-IFN1a versus SC-IFN1a by €186.4 million (€26,569 per patient), €64.2 million (€9,148 per patient), and €2.5 million (€352 per patient), respectively.

Figure 1. Model Framework

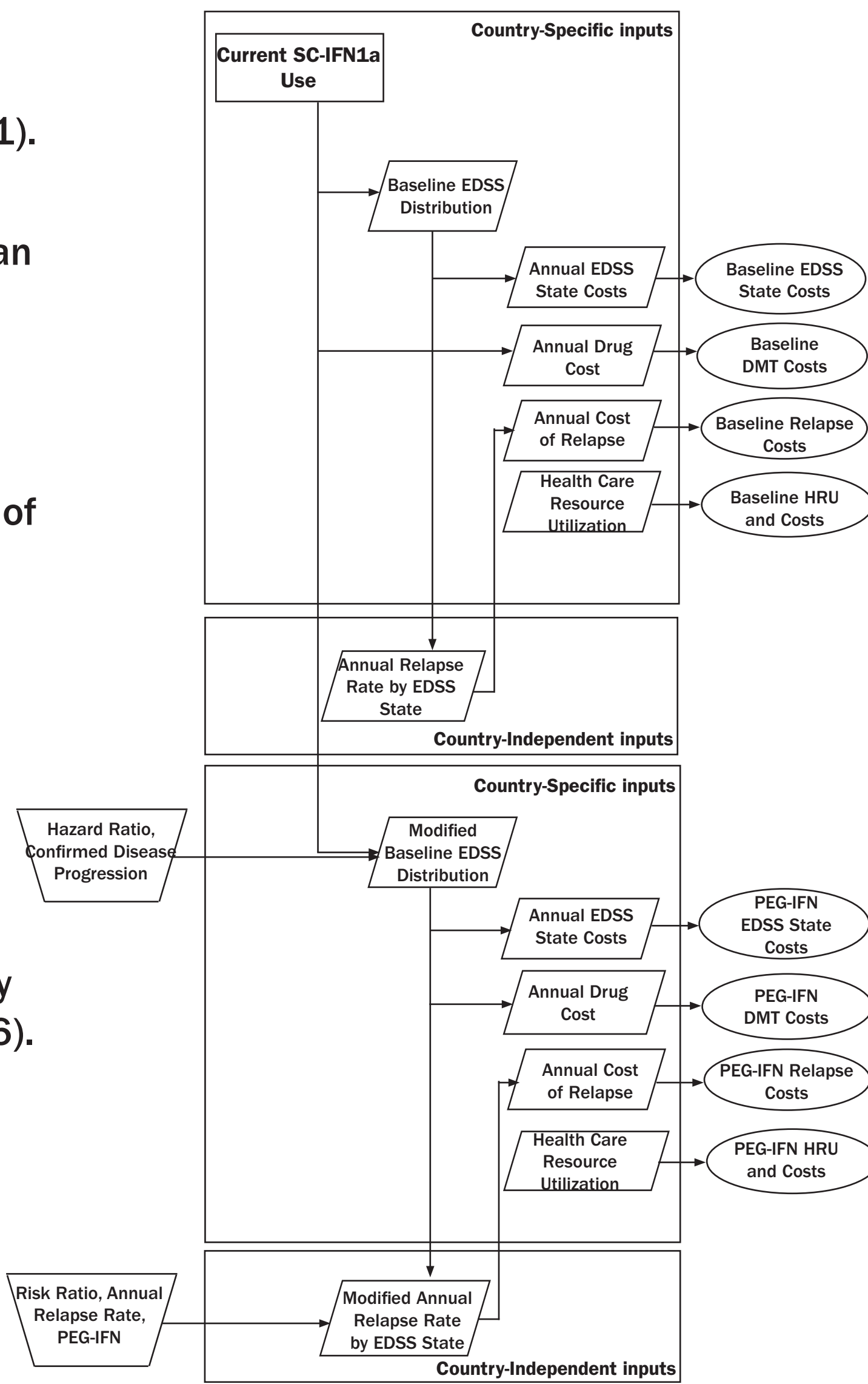


Table 1. Model Inputs

Description	Model Parameter
IFN1a 44 mcg Clinical Inputs	
Number of Patients on SC-IFN1a 44 mcg (March 2018) ¹	6,665
Annual Relapse Rate, Risk Ratio (SC-IFN1a 44 mcg vs Placebo) ²	0.660
Annual Relapse Rate, Risk Ratio (PEG-IFN1a vs SC-IFN1a 44 mcg) ³	0.984
6-Month Confirmed Disability Worsening, Hazard Ratio (IFN1a 44 mcg vs Placebo) ⁴	0.780
6-Month Confirmed Disability Worsening, Hazard Ratio (PEG-IFN1a vs IFN1a 44 mcg) ⁵	0.553
EDSS Distribution, ARR Rates & Costs	
EDSS Distribution	
EDSS 0	8%
EDSS 1	26%
EDSS 2	27%
EDSS 3	23%
EDSS 4	11%
EDSS 5	2%
EDSS 6	3%
EDSS 7	0%
EDSS 8	0%
EDSS 9	0%
Annual Rate of Relapse*	
EDSS 0	1.26
EDSS 1	1.32
EDSS 2	1.32
EDSS 3	1.35
EDSS 4	1.36
EDSS 5	1.43
EDSS 6	1.18
EDSS 7	1.23
EDSS 8	1.23
EDSS 9	1.23
Annual Cost	
EDSS 0	€ 1,639
EDSS 1	€ 2,475
EDSS 2	€ 4,720
EDSS 3	€ 8,348
EDSS 4	€ 8,214
EDSS 5	€ 16,909
EDSS 6	€ 16,581
EDSS 7	€ 29,290
EDSS 8	€ 28,695
EDSS 9	€ 46,692
Cost of Relapse	
PEG-IFN1a over 30 Days	€ 956
SC-IFN1a 44 mcg over 30 Days	€ 1,101

*The annual rate of relapse is not specific to Italy.
EDSS: expanded disability status scale; PEG-IFN1a: pegylated interferon (peginterferon) beta-1a; SC-IFN1a: subcutaneous interferon beta-1a.

Table 2. Relapses, Disability Status and Quality-Adjusted Life Years Over 10 Years

Treatment	Relapses	EDSS ≤ 3 (% of Patients)	EDSS ≥ 6 (% of Patients)	Quality-Adjusted Life Years (QALYs)
Per Patient				
PEG-IFN1a	8.75	20.6%	57.8%	5.04
SC-IFN1a	8.76	9.4%	70.1%	4.80
Differences	- 0.01	+ 11.2%	- 12.4%	+ 0.24
SC-IFN1a Population (n = 6,665)				
PEG-IFN1a	61,403	1,410	3,943	33,263
SC-IFN1a	61,448	643	4,779	31,052
Differences	45	+ 767	- 836	+ 2,211

PEG-IFN1a: pegylated interferon (peginterferon) beta-1a; SC-IFN1a: subcutaneous interferon beta-1a.

Table 3. Health Resource Utilization and Differences over 10 Years (n = 6,665)

Type of Resource Use	PEG-IFN1a	SC-IFN1a	Difference	% Reduction
Number of inpatient admissions	51,920	52,995	- 1,075	-2.0%
Number of day case admissions	143,984	143,849	135	+ 0.1%
Number of days as inpatient at rehabilitation center	101,180	118,157	- 16,977	- 14.4%
Number of day visits at rehabilitation center	382,099	431,661	- 49,562	- 11.5%
Number of days at a nursing home, sheltered living	111,770	124,781	- 13,012	- 10.4%
Number of consultations*	2,214,111	2,446,316	- 232,204	- 9.5%
Number of investigations and tests (any investigation)	367,346	363,719	+ 3,627	+ 1.0%
Number of blood tests	279,871	277,763	+ 2,107	+ 0.8%

*with doctors, specialists and other healthcare professionals (any consultation).

PEG-IFN1a: pegylated interferon (peginterferon) beta-1a; SC-IFN1a: subcutaneous interferon beta-1a.

Figure 2. Average Annual Costs per Patient for PEG-IFN1a and SC-IFN1a

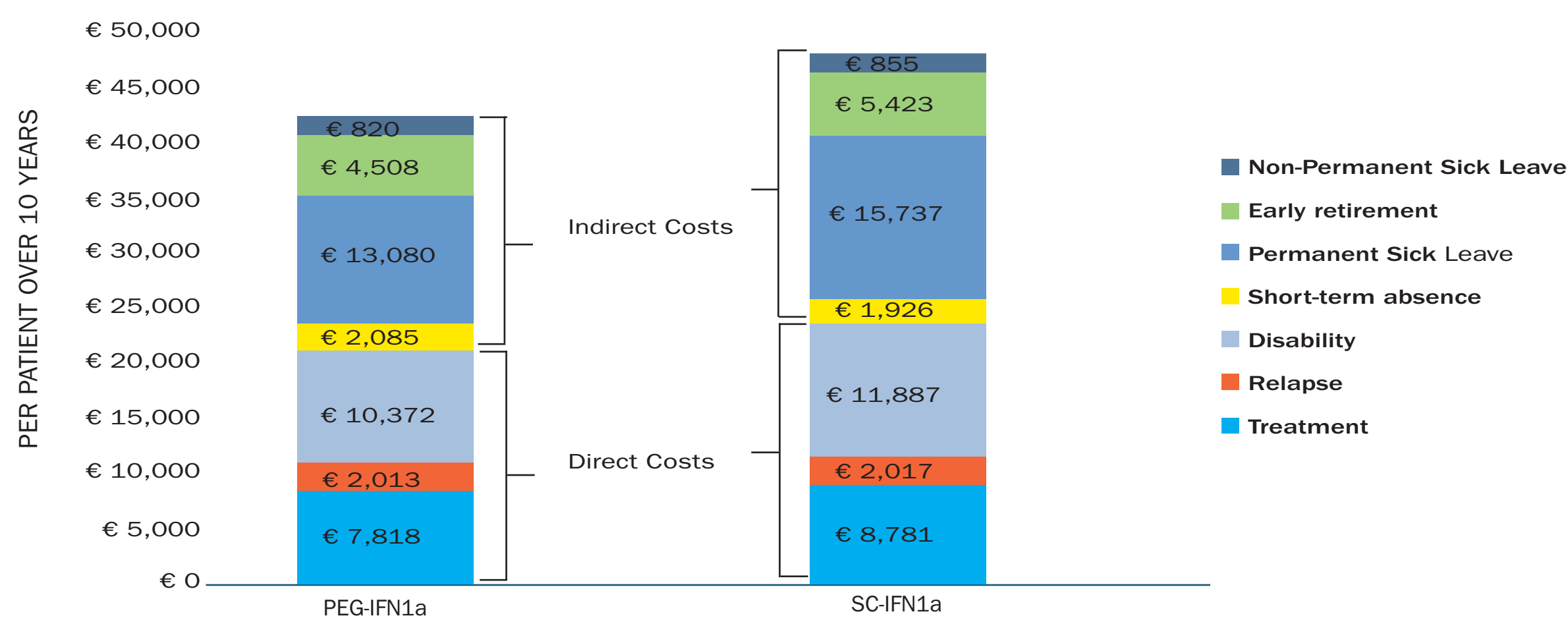
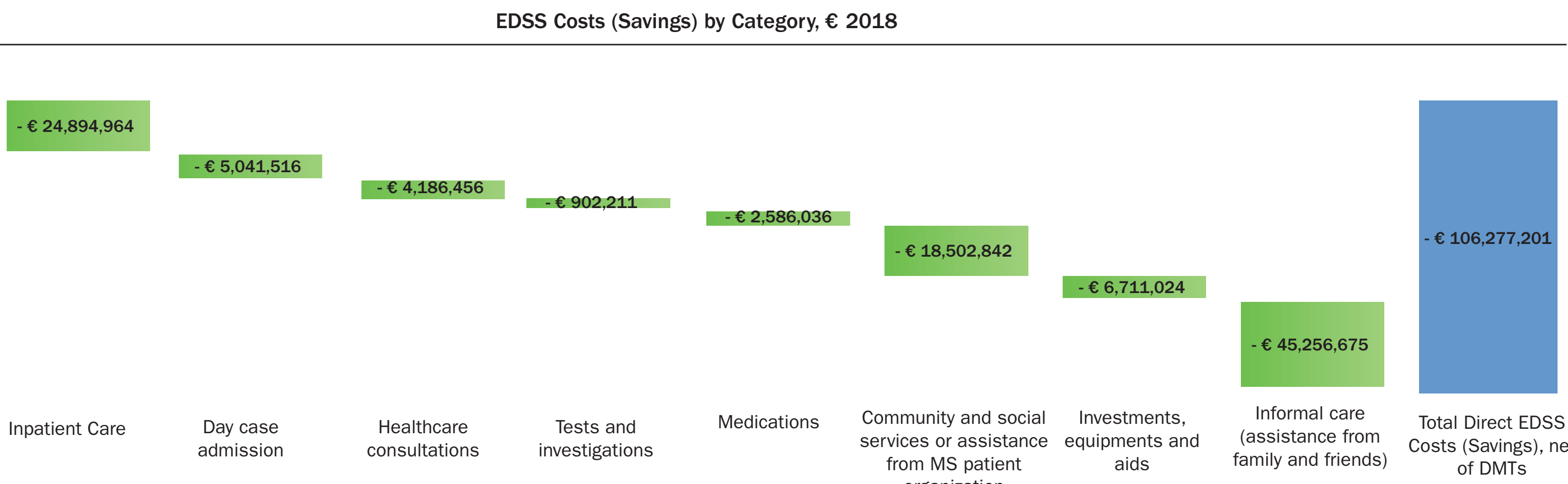


Table 4. Average Annual Costs per Patient for PEG-IFN1a and SC-IFN1a

Type of Resource Use	PEG-IFN1a	SC-IFN1a	Difference	% Reduction
National Health Service (Direct)				
Total Direct	€ 36,569	€ 41,080	(€ 4,511)	- 11.0%
Treatment	€ 14,151	€ 15,913	(€ 1,762)	- 11.1%
Relapse	€ 3,643	€ 3,650	(€ 7)	- 0.2%
Disability	€ 18,775	€ 21,517	(€ 2,743)	- 12.7%
Societal (Indirect)				
Total Indirect	€ 37,094	€ 43,337	(€ 6,243)	- 14.4%
Short-term Absence	€ 3,774	€ 3,487	€ 287	+ 8.2%
Permanent Sick Leave	€ 23,677	€ 28,486	(€ 4,809)	- 16.9%
Early retirement	€ 8,160	€ 9,816	(€ 1,656)	- 16.9%
Non-Permanent Sick Leave	€ 1,484	€ 1,547	€ 64	- 4.1%
Total (Direct and Indirect)	€ 73,663	€ 84,417	(€ 10,754)	- 12.7%

PEG-IFN1a: pegylated interferon (peginterferon) beta-1a; SC-IFN1a: subcutaneous interferon beta-1a.

Figure 3. Total Direct Population (n = 6,665) Savings for Disability by Service Over 10 Years for PEG-IFN1a over SC-IFN1a



EDSS: expanded disability status scale; PEG-IFN1a: pegylated interferon (peginterferon) beta-1a; SC-IFN1a: subcutaneous interferon beta-1a.