# Economic Burden Of Idiopathic Pulmonary Fibrosis In Spain: The OASIS Study

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## INTRODUCTION

- Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive and fatal disease of unknown cause, occurring primarily in older adults, limited to the lungs, and associated with the histopathologic and/or radiologic pattern of usual interstitial pneumonia. [1]
- As the disease progresses, patients' lung function declines with the consequent worsening of dyspnea and quality of life impairment. [2]
- It is estimated that IPF affects about 7,500 people in Spain. [3]
- The overall burden associated with IPF patients in Spain is still unknown. According to a Delphi panel study, management of patients with IPF in Spain has a high economic impact on the national health system, especially for those patients with rapid disease progression and occurrence of IPF exacerbations. [4]
- It was of great interest to develop studies analyzing the Cost-of-illness to define the magnitude of the disease in monetary terms and the main determinants of IPF costs.

## AIM

- This study aims to estimate and compare the economic impact of IPF according to forced vital capacity (FVC) % predicted level in adult patients through estimation of direct and indirect costs associated with the disease during 1 year.
- Secondary objectives aimed to explore the determinants of IPF costs and the cost variation associated to FVC decline along the study.

## METHODS

### Study design

- The OASIS Study is a prospective, observational, multicentric study based on newly collected data of patients with a confirmed diagnosis of IPF in secondary care settings (Pulmonology Services) followed during 12 months.
- As per clinical practice, three visits per patient were performed (baseline, the closest visit to 6 months –T6- and 12 months after baseline –T12-).
  - The inclusion period was from December 2017 to July 2018. The mean (standard deviation (SD)) follow-up were 12.40 (1.07) months.
- A total of 204 patients ≥ 40 years of age diagnosed with IPF according to last ATS/ERS/JRS/ALAT IPF guideline [1], who met the selection criteria were included from 28 sites in Spain. Patients were classified in 3 groups according to their FVC at baseline: FVC < 50 %, FVC 50-80% and FVC >80%.
- Total annual direct and indirect IPF-related costs per patient were estimated in the cost evaluable population (N=180):
  - The use of resources was collected at T6 and/or T12 in addition to those related to exacerbations.
  - The direct costs over the 12-months follow-up period were quantified by multiplying the reported units of resource use by the unitarian cost obtained from Spanish databases. Indirect costs were estimated using the cost-opportunity for informal caregiver and considering the salary cost according to the Spanish Statistics National Institute.
  - Costs were converted to 2018 euros using the published consumer price index.
  - Total annual costs were calculated at patient level as the sum of direct health costs, direct non-health costs and indirect costs. A list of included sources of costs is provided in Table 1.

***Table 1.*** *Annual IPF-associated sources of costs included in the OASIS study.*

| |
|---|
| **Direct costs** |
| Direct health costs<br>• Visits (primary care visits, secondary care visits, emergency room visits)<br>• Hospitalizations<br>• ICU hospitalizations<br>• Outpatient tests<br>• Non-pharmacological treatment<br>• Pharmacological treatment (Pharmacological doses and costs) |
| Direct non-health costs<br>• Transport<br>• Paid caregivers<br>• Orthoprosthetic material<br>• Financial aid and social services<br>• Structural changes |
| **Indirect costs** |
| • Patients' days off work along 12 months<br>• Informal caregiver (time dedicated to patient care with IPF) |

- Bivariate exploratory methods and multivariate linear models were used to explore factors related to costs.
- To estimate cost variation associated to FVC decline, patients were classified according their relative FVC decline along the study in 3 subgroups: >10%, 10% to 5%, <5%.

## RESULTS

### Population characteristics

- 77% of patients were male, average age (SD) 70.8 (7.6) years diagnosed with IPF 1.92 years ago, in average (Table 2).
- At baseline, FVC was <50%, 50–80% and >80% in 10.8%, 74.5% and 14.7% of patients, respectively (Table 2).

***Table 2.*** *Characteristics of patients at baseline.*

| Characteristic | FVC <50% N=22 | FVC 50-80% N=152 | FVC >80% N= 30 |
|---|---|---|---|
| % male, n (%) | 18 (81.8%) | 120 (78.9%) | 19 (63.3%) |
| Age (years), mean (SD) | 70.32 (8.52) | 71.36 (7.21) | 68.33 (8.54) |
| Time since IPF diagnosis to baseline visit (years), mean (SD) | 2.00 (1.69) | 1.95 (1.91) | 1.73 (1.67) |
| Smoking habit, n (%) | | | |
| Non smokers | 8 (36.4%) | 48 (31.6%) | 8 (26.7%) |
| Former smokers[2] | 14 (63.6%) | 101 (66.4%) | 20 (66.7%) |
| Smokers | 0 (0.0%) | 3 (2.0%) | 2 (6.7%) |
| IPF associated comorbidities, n (%) | | | |
| Yes | 18 (81.8%) | 110 (72.4%) | 19 (63.3%) |
| No | 4 (18.2%) | 42 (27.6%) | 11 (36.7%) |
| Occupational or environmental exposure factors, n (%) | | | |
| Yes | 10 (45.5%) | 75 (49.3%) | 12 (40.0%) |
| No | 12 (54.5%) | 73 (48.0%) | 18 (60.0%) |
| Unknown | 0 (0.0%) | 4 (2.6%) | 0 (0.0%) |
| Lung function, mean (SD) | | | |
| FVC post BD (L) | 1.68 (0.41) | 2.53 (0.63) | 3.34 (0.94) |
| FVC post BD (%) | 50.00 (10.02) | 75.95 (13.33) | 98.23 (16.65) |
| Six-minute walk test, mean (SD) | | | |
| Distance (m) | 376.45 (122.65) | 449.78 (92.71) | 472.55 (103.70) |
| Patients receiving antifibrotic treatment, n (%) | | | |
| Yes | 16 (72.7%) | 129 (84.9%) | 21 (70.0%) |
| No | 6 (27.3%) | 23 (15.1%) | 9 (30.0%) |

FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; L: litre; n: number of patients; SD: standard deviation.

### Annual IPF-related costs

- 180 patients were evaluable for costs analysis.
- The mean total annual IPF-related costs per patient was 23,661.21 €, with statistically significant differences (p=0.0002) between groups: 38,923.57 € for the FVC<50% group, 22,613.68 € for the FVC 50-80% group and 20,369.94 € for the FVC>80% group (Table 3).
  - Statistically significant differences were observed among FVC% predicted groups in the annual direct and annual non-direct costs (p=0.0007 and p<0.0001, respectively).

***Table 3.*** *Annual IPF-related costs in the total sample and according to FVC % predicted value at baseline (euros).*

| | Total sample N=180 | FVC <50% N=15 | FVC 50-80% N=140 | FVC >80% N=25 | P-value |
|---|---|---|---|---|---|
| **Total annual IPF-related costs*** | | | | | |
| Mean (SD) | 23661.21 (15385.65) | 38923.57 (29263.42) | 22613.68 (12873.07) | 20369.94 (11955.91) | 0.0002 |
| **Annual direct health IPF-related costs** | | | | | |
| Mean (SD) | 23345.67 (15109.35) | 37183.17 (28465.86) | 22425.64 (12788.42) | 20195.31 (12159.89) | 0.0007 |
| **Annual direct non-health IPF-related costs** | | | | | |
| Mean (SD) | 278.48 (1173.93) | 1657.63 (3148.58) | 149.25 (701.58) | 174.63 (589.43) | <0.0001 |
| **Annual indirect IPF-related costs** | | | | | |
| Mean (SD) | 37.07 (293.59) | 82.77 (320.58) | 38.79 (316.50) | 0.00 (0.00) | 0.6839 |

*Total costs were included for patients with a follow-up of at least 6 months.
FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; SD: standard deviation.

- Annual **direct health IPF-related costs** had the greatest weight in total annual IPF-related costs per patient. Pharmacological treatments and cost of hospitalization-days contributed the most to direct health costs (mean of 19,565.11 € and 1,453.5 €, respectively) (Table 4).
  - Patients with lower FVC% predicted at baseline reported significantly higher direct health costs associated with primary and secondary care visits, hospitalization-days, hospitalizations-ICU and non-pharmacological treatments costs than those with a more preserved FVC % predicted at baseline.

***Table 4.*** *Annual direct health IPF-related costs in the total sample and according to FVC % predicted value at baseline (euros).*

| | Total sample N= 180 | FVC <50% N=15 | FVC 50-80% N=140 | FVC >80% N=25 | P-value |
|---|---|---|---|---|---|
| **Primary care visits** | | | | | |
| Mean (SD) | 30.25 (66.49) | 71.74 (90.74) | 28.65 (66.90) | 14.35 (29.89) | 0.0244 |
| **Secondary care visits (specialized care visits)** | | | | | |
| Mean (SD) | 404.17 (338.78) | 607.95 (534.94) | 382.18 (313.46) | 405.07 (302.07) | 0.0485 |
| **Emergency visits (primary care visits)** | | | | | |
| Mean (SD) | 9.15 (42.35) | 24.95 (78.33) | 9.09 (40.62) | 0.00 (0.00) | 0.1971 |
| **Emergency visits (hospital)** | | | | | |
| Mean (SD) | 62.06 (181.44) | 114.57 (191.22) | 63.83 (192.65) | 20.62 (75.56) | 0.2776 |
| **Hospitalizations- admission in emergency room** | | | | | |
| Mean (SD) | 129.19 (783.89) | 134.69 (329.91) | 129.01 (847.50) | 126.88 (599.61) | 0.9995 |
| **Hospitalizations- days of hospitalization** | | | | | |
| Mean (SD) | 1453.57 (6452.10) | 8145.45 (19166.86) | 868.91 (3203.53) | 712.56 (2489.51) | 0.0001 |
| **Hospitalizations- in ICU** | | | | | |
| Mean (SD) | 392.87 (2735.68) | 2946.52 (7775.85) | 189.42 (1665.71) | 0.00 (0.00) | 0.0006 |
| **Outpatients tests (laboratory test, pulmonary function test, other examinations)** | | | | | |
| Mean (SD) | 740.18 (646.44) | 1010.86 (1057.31) | 737.39 (625.29) | 593.39 (363.03) | 0.1408 |
| **Pharmacological treatment (except treatments administered in hospitalization)** | | | | | |
| Mean (SD) | 19565.11 (12070.96) | 21637.08 (12806.64) | 19617.80 (11896.47) | 18026.87 (12893.07) | 0.6560 |
| **Non-Pharmacological treatment (except treatments administered in hospitalization)** | | | | | |
| Mean (SD) | 382.17 (1303.33) | 2337.70 (3669.64) | 236.86 (610.68) | 22.57 (78.46) | <0.0001 |
| **End of life (palliative care)** | | | | | |
| Mean (SD) | 176.94 (610.99) | 151.67 (587.40) | 162.50 (588.01) | 273.00 (754.53) | 0.6994 |

*Total costs were included for patients with a follow-up of at least 6 months.
FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; n: number of patients; SD: standard deviation.

- The mean **direct non-health IPF-related costs** was 278.48 €, with statistically significant differences between FVC% predicted groups (Table 5).
  - Higher costs were observed among patients with lower FVC% predicted, who reported a higher use of transport in taxi, ambulance, need for formal caregiver and orthopedic material.
  - Transport in ambulance cost was the cost with greatest weight to the direct non-health IPF-related costs.

***Table 5.*** *Annual direct non-health IPF-related costs in the total sample and according to FVC % predicted value at baseline (euros).*

| | Total sample N=180 | FVC <50% N=15 | FVC 50-80% N=140 | FVC >80% N=25 | P-value[1] |
|---|---|---|---|---|---|
| **Transport in taxi** | | | | | |
| Mean (SD) | 5.28 (57.28) | 62.81 (195.12) | 0.05 (0.62) | 0.00 (0.00) | 0.0002 |
| **Transport in ambulance (€/service)** | | | | | |
| Mean (SD) | 109.69 (516.15) | 506.26 (1023.17) | 82.14 (464.45) | 26.04 (130.18) | 0.0065 |
| **Formal caregiver** | | | | | |
| Mean (SD) | 78.96 (917.38) | 878.24 (3152.29) | 7.42 (87.81) | 0.00 (0.00) | 0.0017 |
| **Orthopaedic material** | | | | | |
| Mean (SD) | 25.77 (152.96) | 126.32 (333.59) | 13.07 (108.95) | 36.59 (182.96) | 0.0218 |
| **Economic aid** | | | | | |
| Mean (SD) | 21.00 (209.53) | 84.00 (325.33) | 18.00 (212.98) | 0.00 (0.00) | 0.4437 |
| **Structural adaptations** | | | | | |
| Mean (SD) | 37.78 (362.97) | 0.00 (0.00) | 28.57 (338.06) | 112.00 (560.00) | 0.5252 |

*Total costs were included for patients with a follow-up of at least 6 months.
FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; n: number of patients; SD: standard deviation.

- Regarding **indirect IPF-related costs**, the annual mean (SD) cost for informal caregiver was 37.07 (293.59) €, with no differences between FVC% predicted groups (p=0.6339). None of the patients reported days-off from paid work along 12 months.

### Determinants of costs

- Determinants to increase the total annual IPF- related costs in patients with FVC 50-80% were:
  - To have pulmonary emphysema associated with IPF (p=0.0223): total annual IPF-related costs decreased 9,207.12 € in patients who had not pulmonary emphysema.
  - To receive antifibrotic treatment (p<0.0001): total annual IPF related costs decreased 20,557.00 € in patients who were not treated with antifibrotics.

### Costs associated with FVC decline

- No differences in total annual IPF-related costs were observed among FVC decline subgroups (Table 6).
  - Higher total annual IPF-related costs were observed in patients among the FVC decline <5%. Most of the patients in this group were patients with an already significantly impaired pulmonary function (Table 6).

***Table 6.*** *Total annual IPF-related costs associated with relative FVC decline along 12 months (euros).*

| | FVC decline (Relative change) >10% N=42 | From 10% to 5% N= 23 | <5% N= 75 | P-value |
|---|---|---|---|---|
| **Total annual IPF-related costs** | | | | |
| Mean (SD) | 22537.96 (13102.84) | 19816.40 (10688.54) | 26760.56 (17577.99) | 0.2682 |

*Total costs were included for patients with a follow-up of at least 6 months.
FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; n: number of patients; SD: standard deviation.

## CONCLUSIONS

- **In Spain, IPF is associated with a high economic burden which is significantly higher among patients with a more impaired FVC at baseline.**
- **Total annual IPF-related costs were estimated in 23661 € per patient, the direct cost having the greatest weight to the total costs.**
- **Either having pulmonary emphysema associated with IPF or being treated with antifibrotics are related with increasing the annual IPF-related costs.**
- **Maintaining patients at early disease stages by slowing IPF progression seems relevant to reduce the economic impact of IPF.**

## References

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