PCR272

Humanistic and Economic Burden Associated with Idiopathic Pulmonary Fibrosis (IPF): Summary of Evidence from Systematic Literature Reviews (SLRs)

Diana Weidlich[1], Rashi Tomer[2], Geetika Kainthla[2], Sheetal Sharma[2], Malgorzata L. Kaczynska[1]

1. Boehringer Ingelheim, Germany. 2. ZS Associates, New Delhi, India

Background & Objectives

- Idiopathic pulmonary fibrosis (IPF) is the most common interstitial lung disease (ILD), characterised by chronic progressive fibrosis, worsening of lung function and dyspnoea and a median survival from diagnosis of 3–5 years [1,2]
- Patients with IPF experience cough, fatigue, loss of emotional well-being, and social isolation. As the disease progresses, the symptom burden increases and further impairs health-related quality of life (HRQoL) [3-5]
- Two systematic literature reviews (SLRs) were conducted to assess the general humanistic and economic burden associated with IPF

Methods

- Two SLRs followed Cochrane/PRISMA [6] guidelines to identify literature published between January 2014 and September 2023. Searches in Embase, MEDLINE, EconLit and Cochrane Library were supplemented with additional grey literature and conference searching
- Key outcomes assessed for humanistic burden included generic scales and disease specific scales
- Key outcomes assessed for economic burden included direct cost, indirect cost, and HCRU. All prices were inflated and converted to 2024, EUR; original values are reported alongside in brackets. Total direct cost included, but was not limited to, medication cost and non-medication cost, medical costs, facility costs, and pharmacy costs and outpatient, inpatient service and pharmacy costs.

Results

- Search and selection details are presented in Figure 1 and Figure 2

Figure 1: PRISMA diagram for humanistic burden

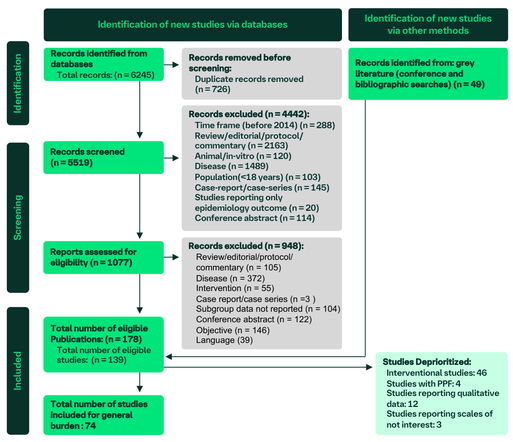
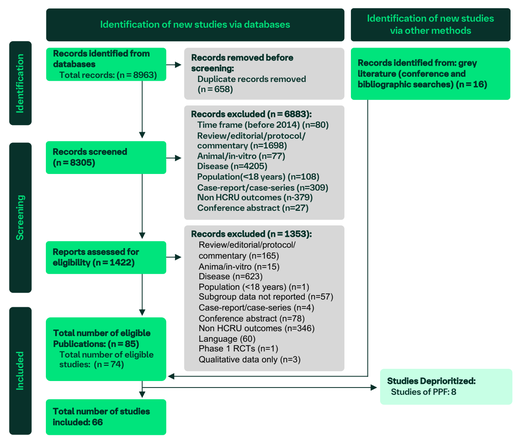


Figure 2: PRISMA diagram for economic burden

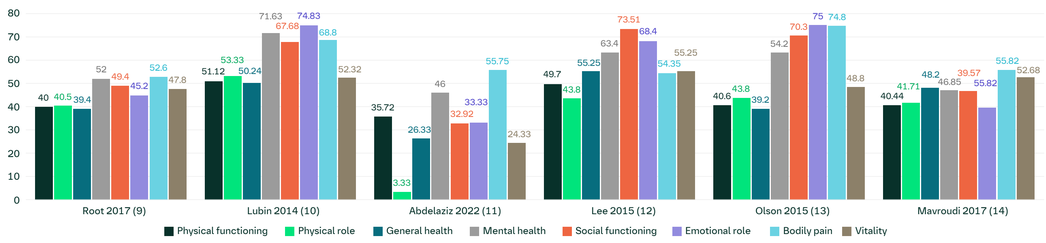


Abbreviations
PPF, progressive pulmonary fibrosis; HCRU, healthcare resource utilisation; RCT, randomised controlled trial.

Key findings of the Humanistic burden SLR

- A total of 74 general humanistic burden studies were included. The majority of the evidence identified was from European countries, the US, and Japan. Most studies utilised measurement tools such as the 36-Item Short Form Survey (SF-36) (0 [worst health] to100 [best health]), EuroQoL Five-Dimensional instrument (EQ-5D) (utility index 0 [dead] to 1 [best possible health]; visual analogue scale (VAS) 0 [worst imaginable health state] to 100 [best imaginable health state]), St. George's Respiratory Questionnaire (SGRQ) (0 [no health impairment] to 100 [maximum health impairment]), Modified Medical Research Council (mMRC) Dyspnea Scale (0 [lower disability] to 4 [greater disability]), and King's Brief Interstitial Lung Disease (K-BILD) (0 [worst health status] to 100 [best health status]) to assess HRQoL in patients with IPF
- **SF-36**: Sixteen studies reported HRQoL in patients with IPF as assessed by the SF-36 tool. The SF-36 summary score for physical and mental components was given in six studies. In all six studies, the score for the physical component (with mean (SD) ranging from 37 (10) [7] to 54.9 (7.8) [8]) was lower compared with that of the mental component (with mean (SD) ranging from 43 (14) [7] to 62.4 (5.9) [8]), showing that IPF has a larger impact on physical function than on the mental well-being of patients. Figure 3 shows mean baseline scores of SF-36 domains in the six studies [9-14]. Patients with severe IPF scored lower on the SF-36, compared with those with mild to moderate IPF (Mean(SD) 32 (11.4) vs 59.1 (17.8)) and scores for all subscales of the SF-36, with the exception of bodily pain, decreased as the MRC Dyspnea grade increased [15, 16]

Figure 3: Mean baseline scores of SF-36 domains

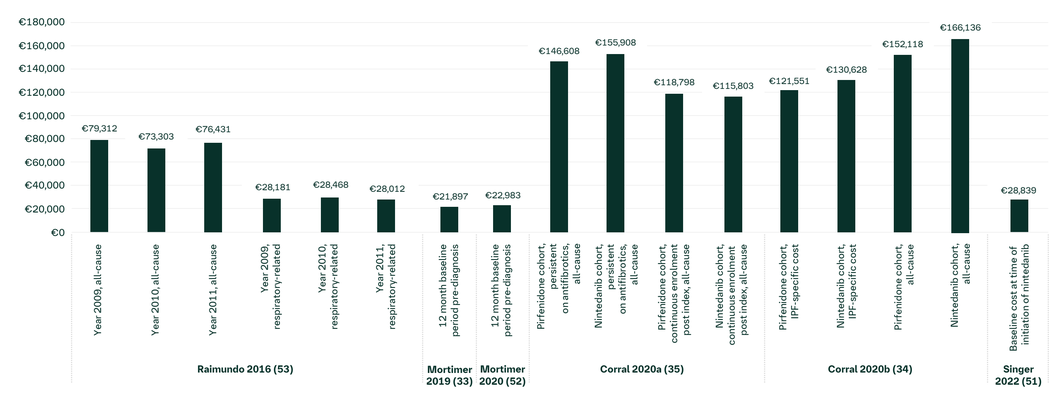


- **EQ-5D**: Sixteen studies reported the HRQoL in patients with IPF using EQ-5D. The baseline mean (SD) EQ-5D-5L score ranged from 0.589 (0.29) [17] to 0.79 (0.15) [18] and the mean (SD) EQ-5D VAS score ranged from 61.1 (19.2) [19] to 69 (18) [20]
- **SGRQ**: Thirty-nine studies assessed HRQoL in patients with IPF using SGRQ. Almost half of the studies found total mean SGRQ scores of >40 (16 studies), indicating poor HRQoL in patients with IPF. The mean SGRQ score (SD) for symptom domain across 14 studies ranged from 34.4 (22.4) [21] to 74.37 (12.04) [11], for activity domain ranged from 38.4 (25.9) [22] to 73.1 (25.9) [23] , and for impact domain ranged from 15.38 (17.3) [24] to 65.35 (12.02) [11]. Patients with moderate-to-severe disease compared with those with mild disease (53.22 (16.72) vs 40.91 (14.63)) as well as elderly patients compared with non-elderly patients (49.4 (20.1) vs 47.2 (20.8)) had numerically higher mean SGRQ total scores [25, 26]
- **mMRC**: Twenty-six studies assessed HRQoL in patients using the mMRC Dyspnea scale. Of the 11 studies that reported the distribution of mMRC grades at baseline, the majority found that patients had an mMRC score ≥2, illustrating that a higher proportion of IPF patients suffer from breathlessness. People with FVC % predicted ≤75% had higher mean mMRC compared to FVC% predicted >75% (mean (SD): 2.93 (0.87) vs 2.38 (1.03), p<0.001) [27]
- **K-BILD**: Eighteen studies assessed the HRQoL of patients with IPF using the K-BILD scale. The baseline total mean K-BILD score ranged from 48.2 [28] to 73.1 [29]. Six studies reported domain scores, and the score results showed that the impact of IPF was greater in the breathlessness and activity domains compared with the psychological domain. Patients with moderate disease had numerically lower total K-BILD, chest symptom, and psychological domain scores compared with those with mild disease, although values were not statistically different (mean (SD) total score for mild disease 67 (10.3) vs moderate disease 60 (6.6), p=0.058) [30]
- Symptoms such as depression and anxiety (baseline mean Hospital Anxiety and Depression Scale [HADS] anxiety score range 3.46 [24] to 6.2 [31], and HADS depression score range 3.86 [21] to 6 [31]), breathlessness (baseline mMRC score range 0.81 [32] to 2.71 [27]), and cough (baseline mean CQLQ score 47.26) impacted patients' HRQoL and emotional well-being [27, 32]

Key findings of the Economic burden SLR

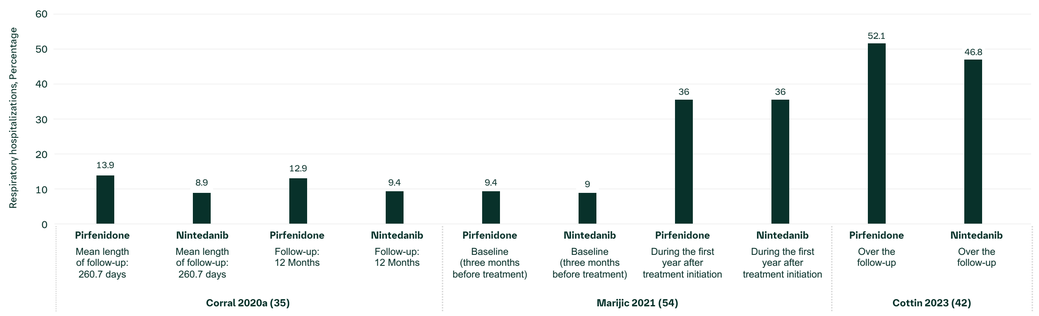
- A total of 66 studies examined the economic burden associated with IPF before and after the introduction of antifibrotics. The majority of the evidence identified was from European countries and the US
  - **Direct cost:** Worldwide, the economic burden of IPF is substantial, with hospitalisation and medication expenses reported as the main cost drivers
    - US: Total estimated direct cost (varied types of cost) per patient per year (PPPY) ranged from €21,897 [33] to €166,136 [34] ($21,184 [2019 USD] to $144,072 [2015 USD])(Figure 4) pre- and post- introduction of antifibrotics, respectively. Medication cost is one of the main drivers of IPF-related cost [35]. Pharmacy costs accounted for the largest share of total costs per month followed by costs for inpatient services [34], which is underpinned by a similar finding in a study by Dempsey 2021 [36]

Figure 4: Total direct cost in the US, PPPY



  - Canada: Total estimated annual direct cost (varied types of cost) PPPY ranged from €6,627 to €51,773 ($8,267 [2016 CAD] to $65,697 [2017 CAD]) pre- and post- introduction of antifibrotics, respectively [37, 38]
  - Europe (UK, France, Germany, Spain and Finland): Total estimated annual direct cost (varied types of cost) PPPY ranged from €3,122 to €36,537 (€2,973 [2022 EUR] to €34,351 [2021 EUR]) post-approval of antifibrotics [39,40]
  - Australia: Two studies reported direct cost data for Australia. Total estimated annual direct cost PPPY was reported in one study as €22,614 ($31,655 [2021 AUD, 95% CI: 27,723 to 35,757]) [41]. The primary cost drivers were anti-fibrotic medications (61% of total direct costs), hospital admissions (13%), and medications for comorbidities (7%)
- **Indirect cost:** Patients with IPF experience greater indirect cost through loss of work productivity, early retirement, sick leave compensations, and job losses
  - France: The mean indirect HCRU cost, covering sick leave compensations and transportation expenses, was higher for patients treated with nintedanib compared with those treated with pirfenidone although this difference was not statistically significant (€1,121 vs €892; p=0.09) [42]
  - Spain: Indirect costs which encompassed missed workdays due to the disease and informal caregiver expenses did not significantly differ across predicted FVC groups. Patients with lower FVC% predicted at baseline received more help from caregivers (FVC<50% vs FVC 50–80% vs FVC>80%: 40. 9% vs 17.8 % vs 16.7%) [43]
  - The estimated annual indirect cost (productivity loss) was €14,513 PPPY in the UK (£11,378 [2011/2012 GBP]) and €9,249 PPPY in Canada ($11,737 [2017 CAD]) [44,45]
- **HCRU:** HCRU and costs for patients with IPF are high, with major contributors being facility charges, inpatient services, and costs associated with comorbidities and respiratory-related hospitalisation [33, 34, 41, 46, 47] . Respiratory-related hospitalisation for overall population ranged from 8.9% [35] to 54.2 % [48] at varying time points. Respiratory hospitalisation in patients receiving antifibrotics was reported in three studies and is depicted in Figure 5 . Oxygen supplementation for the overall population including home oxygen therapy, oxygen supplementation at hospital, and other oxygen therapies ranged from 2.9 % [43] to 93.3% [49] at varying time points with or without intervention

Figure 5: Respiratory-related hospitalisations in patients with antifibrotics



Conclusions

The results of the current SLR suggest that IPF poses a high burden on the HRQoL of the patients that further deteriorates over time. IPF has more impact on the physical function than the mental well-being of patients. Patient's HRQoL is especially impacted by the respiratory symptoms, such as breathlessness, and cough, depression and anxiety. The identified measurement tools were in alignment with those identified in a systematic review and meta-analysis conducted by Cox et al 2020 that reported SGRQ, SF36, and EQ-5D to be the most frequently used instruments to measure HRQoL in IPF [50]

Healthcare costs associated with IPF are substantial. Comorbidities associated with IPF complicate pathways for treatment, leading to increased costs, including treatment/pharmacy costs, HCRU (respiratory and non-respiratory-related hospitalisation costs), loss of productivity, and other non-medical costs

References
1. Copeland CR, Lancaster LH. Front Med-Lausanne. 2021;8.
2. Tzouvelekis A, et al.Pulm Pharmacol Ther. 2017;42:21-4.
3. Belkin A, Swigris JJ. Curr Opin Pulm Med. 2013;19(5):474-9.
4. King CS, Nathan SD. Lancet Resp Med. 2017;5(1):72-84.
5. Kreuter M et al. Respir Res. 2019.
6. Page MJ et al.BMJ. 2021:372.
7. Machado FVC et al. Bmj Open Respir Res. 2021;8(1).
8. Sikora M et al. Resp Physiol Neurobi. 2023;313.
9. Root ED et al. BMC Pulm Med. 2017;17(1):154.
10. Lubin M et al. Chest. 2014;145(6):1333-8.
11. Abdelaziz AA et al. Egypt J Chest Dis Tu. 2022;71(1):108-13.
12. Lee RNC et al. Qjm-Int J Med. 2015;108(4):315-23.
13. Olson AL et al. Expert Rev Resp Med. 2015;9(3):361-7.
14. Mavroudi M et al. Sleep Breath.2017;22(2):393-400.
15. Kozu R, Jenkins S, Senjyu H. Arch Phys Med Rehab. 2014;95(5):950-5.
16. Bors M et al. Chron Resp Dis. 2015;12(4):365-72.
17. Giltay L et al. Am J Resp Crit Care. 2021;203(9).
18. Scallan C et al. Eur Respir J. 2022;59(1).
19. Wuyts WA et al. Pulm Ther. 2022;8(2):181-94.
20. Cox IA et al. Qual Life Res. 2023;32(2):473-93.
21. Badenes-Bonet D et al. Bmc Pulmonary Medicine. 2022;22(1).
22. Matsuda T et al. Internal Med. 2017;56(13):1637-44.
23. Morsi TS, Ghobashy S, Younis G. Egypt J Chest Dis Tu. 2014;63(3):731-43.
24. Lee YJ, C et al. Plos One. 2017;12(9).
25. Hoyer N et al. Bmj Open Respir Res. 2022;9(1).
26. Leuschner G et al. Front Med-Lausanne. 2020;7.
27. Kim JW et al. Chron Resp Dis. 2021;18.
28. Veit T et al. J Clin Med. 2023;12(11).
29. Atkins CP et al. Sarcoidosis Vasc Dif . 2016;33(2):130-8.
30. Davis R, et al. Bmc Pulmonary Medicine. 2021;21(1).
31. Nishiyama O et al. Respir Investig. 2018;56(1):57-63.
32. Park H et al.Korean J Intern Med. 2022;37(2):387-+.
33. Mortimer K et al. BMC Pulmonary Medicine. 2019;19:1-13.
34. Corral M et al. Journal of Comparative Effectiveness Research. 2020;9(13):933-43.
35. Corral M, DeYoung K, Kong AM. BMC Pulmonary Medicine. 2020;20:1-12.
36. Dempsey TM et al. Annals of the American Thoracic Society. 2021;18(7):1121-8.
37. Tarride J-E et al. ClinicoEconomics and Outcomes Research. 2018:127-37.
38. Kalluri M et al. Annals of the American Thoracic Society. 2020;17(6):706-13.
39. Kreuter M et al. Respiratory Research. 2022;23(1):62.
40. Marijic P et al. Respiratory research. 2021;22:1-11.
41. Cox IA et al. The European Journal of Health Economics. 2023;24(7):1121-39.
42. Cottin V et al.Respiratory Medicine and Research. 2023;83:100951.
43. Rodríguez-Nieto MJ et al. PharmacoEconomics. 2023;41(8):999-1010.
44. Wilson EC et al. Pharmacoeconomics. 2014;32:87-99.
45. Algamdi M et al. Chest. 2019;156(5):887-95.
46. Kalluri M et al. Journal of Pain and Symptom Management. 2018;55(2):420-6.
47. Alqalyoobi S, Fernández Pérez ER, Oldham JM. BMC Pulmonary Medicine. 2020;20:1-11.
48. Teramachi R et al. Respiratory medicine. 2018;143:147-52.
49. Faverio P et al. 2021;11(9):1623.
50. Cox IA et al. Eur Respir Rev. 2020;29(158).
51. Singer D et al .Journal of Medical Economics. 2022;25(1):532-40.
52. Mortimer KM et al. Respiration. 2020;99(2):108-18.
53. Raimundo K et al . BMC pulmonary medicine. 2016;16:1-8
54. Marijic P et al. Respiratory research. 2021;22:1-11.

Disclosures
Diana Weidlich and Malgorzata L. Kaczynska are employees of Boehringer Ingelheim International GmbH. Rashi Tomer, Geetika Kainthla, Sheetal Sharma (ZS Associates, New Delhi, India) have supported the literature review, which was funded by Boehringer Ingelheim International GmbH.

Acknowledgements
This study was supported and funded by Boehringer Ingelheim International GmbH. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors did not receive payment related to the development of the poster. Boehringer Ingelheim was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations.

Boehringer Ingelheim