



EMPIRE
(IPF)

European **M**ulti**P**artner **I**PF **R**Egistry 3rd international SC meeting

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EMPIRE (European MultiPartner IPF REgistry)

- International, multicentre, observational, non-interventional registry of IPF patients in Central and Eastern Europe
- Currently involved 5 countries (CZ, SK, PL, HU, RS)
 - Turkey is ready to join (waiting for contract)
 - In process of negotiation – Russia, Israel?
 - Do not have information on Croatia
- Currently entered more than 800 patients



Sponsors

- Contract with Boehringer Ingelheim RCV is signed till the end of the year 2016
- New contract for another period will be prepared
- Currently working on contract with Boehringer Ingelheim Turkey – contract with RCV is not covering Turkey and needs to be separate contract with BI Turkey
- Probably another companies will be interested to join the registry – Roche





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Involved countries

Current status of EMPIRE – involved countries

- Czech Republic (10 sites)
- Hungary (5 sites)
- Poland (6 sites)
- Slovakia (6 sites)
- Serbia (1 site)
- Turkey - **in progress**



Representation of countries in EMPIRE registry

N = 724

	N (%)
Czech Republic	512 (70.7 %)
Poland	107 (14.8 %)
Slovakia	54 (7.5 %)
Hungary	37 (5.1 %)
Serbia	14 (1.9 %)



Number of patient according to countries

Country	Number of newly entered patients in 2016	Total number of patients
Czech Republic	22	539
Slovakia	10	64
Poland	26	135
Hungary	16	54
Serbia	1	15
Total	75	807

Status on the date: 8.3.2016





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Meeting minutes – 2nd SC

Minutes from 2nd SC meeting

- **What do we store from patients?**
 - Blood
 - Lung tissue
 - BALF
- **Czech Republic response:**
 - Blood – not generally, only for the genetic projects within the studies (Schwartz, epidemiology of IPF from the Czech registry), and previously for biomarkers
 - Lung tissue – the samples are only those embedded in paraffin at the department of pathology
 - BALF – in most cases we store supernatant for biomarkers for our grant supported research of biomarkers.



Minutes from 2nd SC meeting

- **Hungary response:**
 - We can access histology blocks if surgical biopsy was performed.
 - In our center most BAL are stored, and cytopsin form BALs on slides. Additionally we have from all new IPF patient serum and plasma.





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Technical issue

Feedback from analyst

- Based on entered data and processed analysis some inconsistency in data occurred:

Inconsistency in forms therapy and FUP

- when treatment starts, no data about spirometry are usually available
- This can be solved if PI will enter FUP and treatment at the same or at least close date



Feedback from analyst

Long-term follow up of patient

- Extremely high values of VC (in some patients grow and it should fall in patients with IPF)
- Long-term survival





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Publication in progress

Processed analytical outputs and abstracts

- Does early diagnosis of idiopathic pulmonary fibrosis matter? Real- life results from the EMPIRE registry (Vašáková et al.)
- Influence of HRCT on prognosis of patients with IPF (Vašáková et al.)
- Effect of pirfenidone on decline of lung functions in comparison with other treatment modalities in Czech patients with IPF (Žurková et al.)
- Influence of parameters on survival of patients with IPF (Doubková et at.)



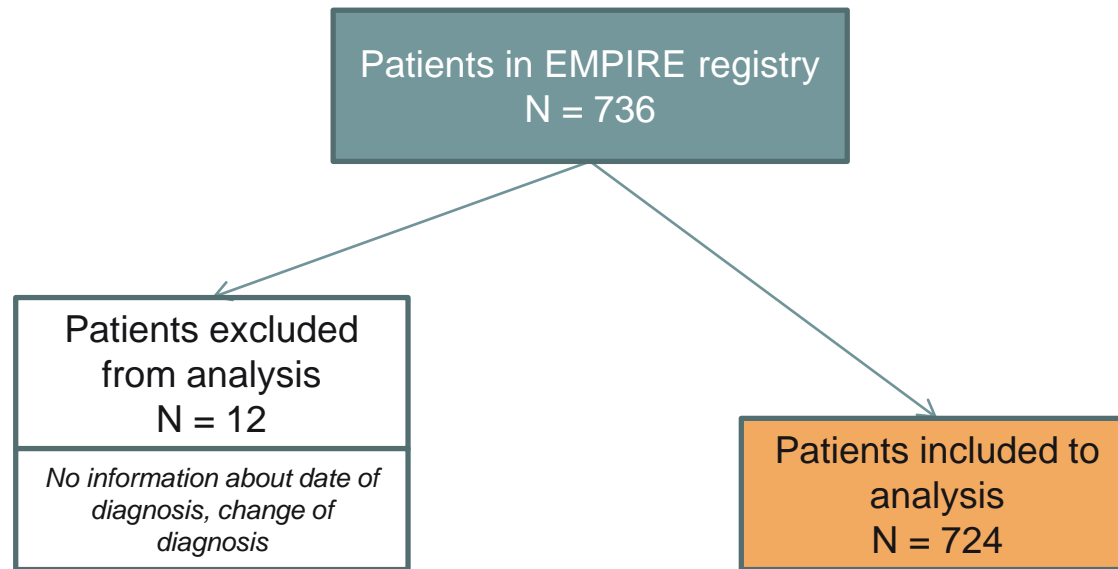


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Data analysis

Data export 31DEC2015

Selection of data set for analysis



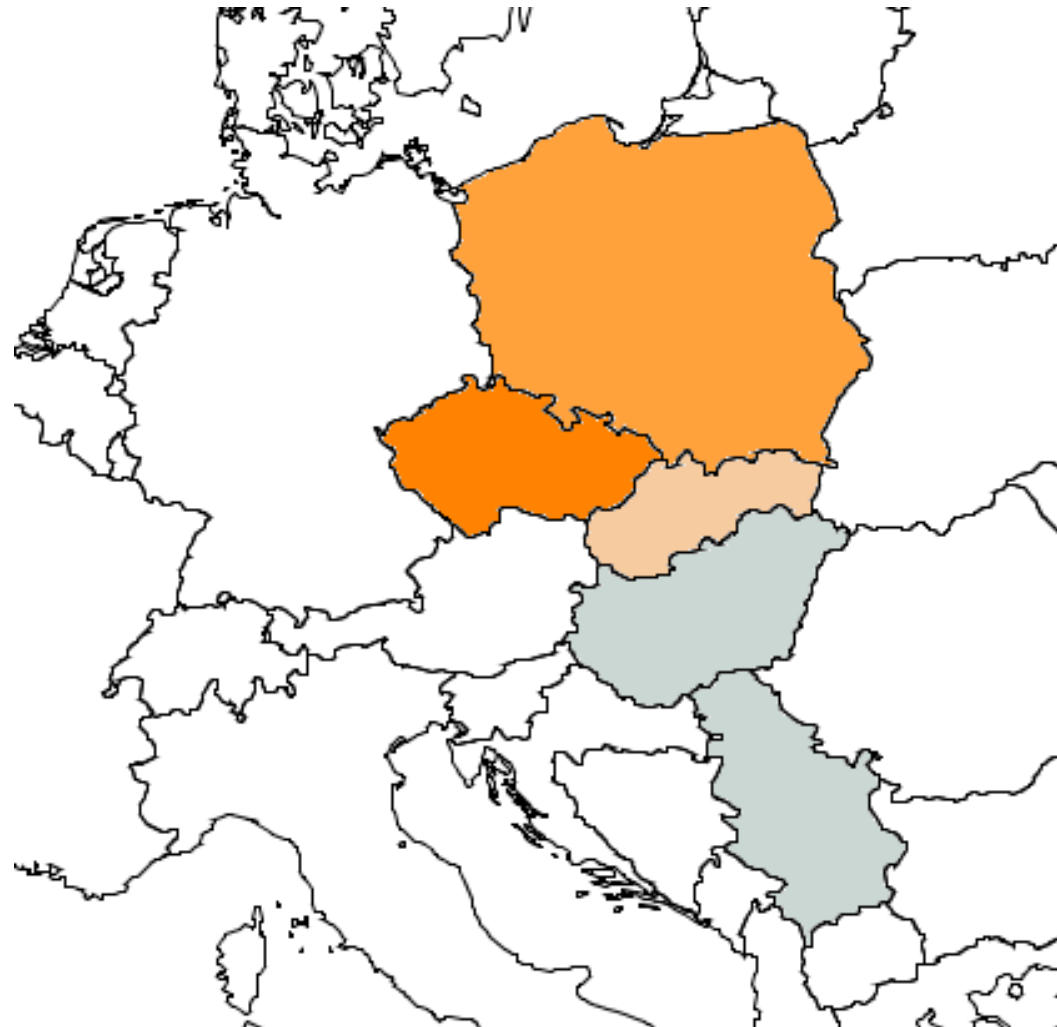
I. Basic descriptions



Representation of countries in EMPIRE registry

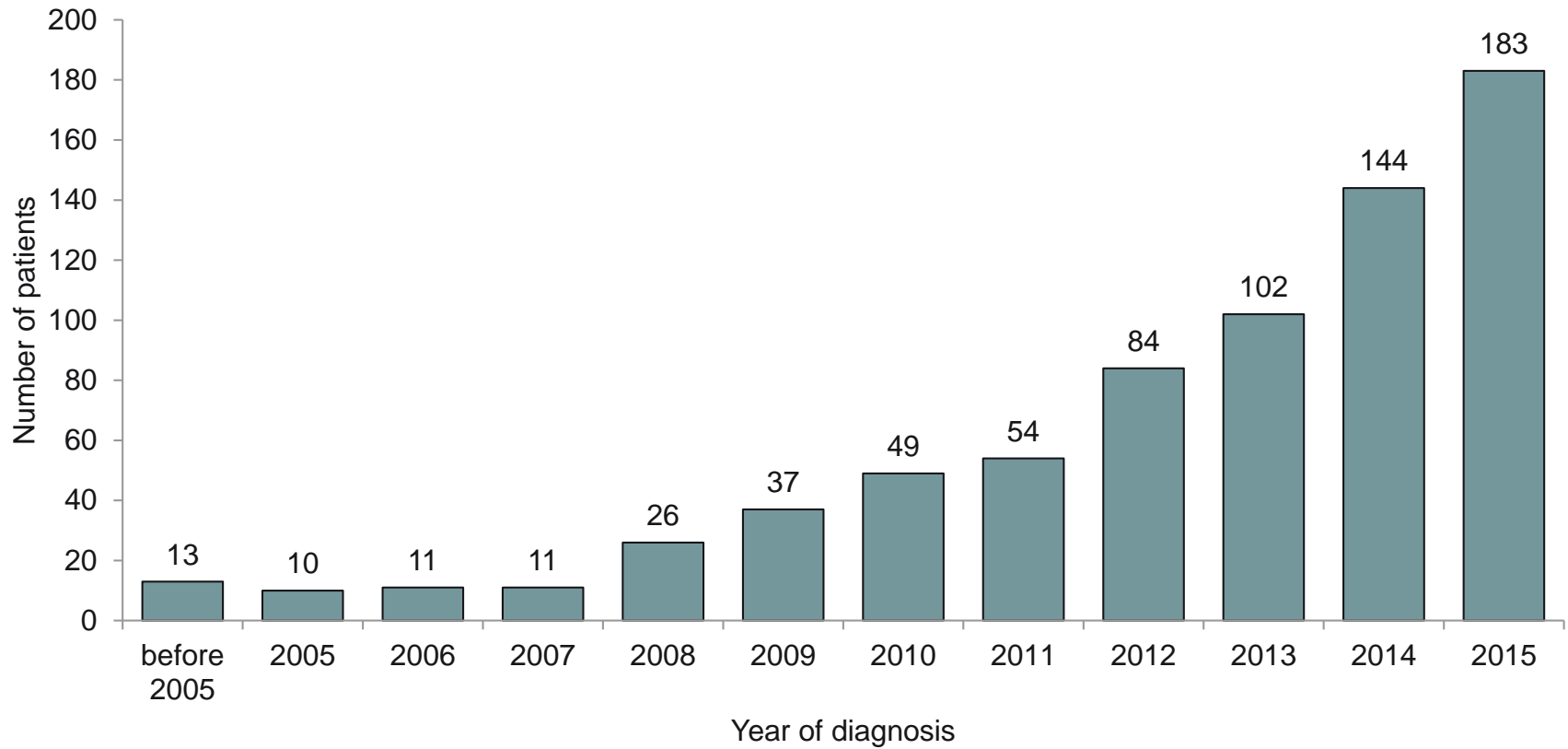
N = 724

	N (%)
Czech Republic	512 (70.7 %)
Poland	107 (14.8 %)
Slovakia	54 (7.5 %)
Hungary	37 (5.1 %)
Serbia	14 (1.9 %)



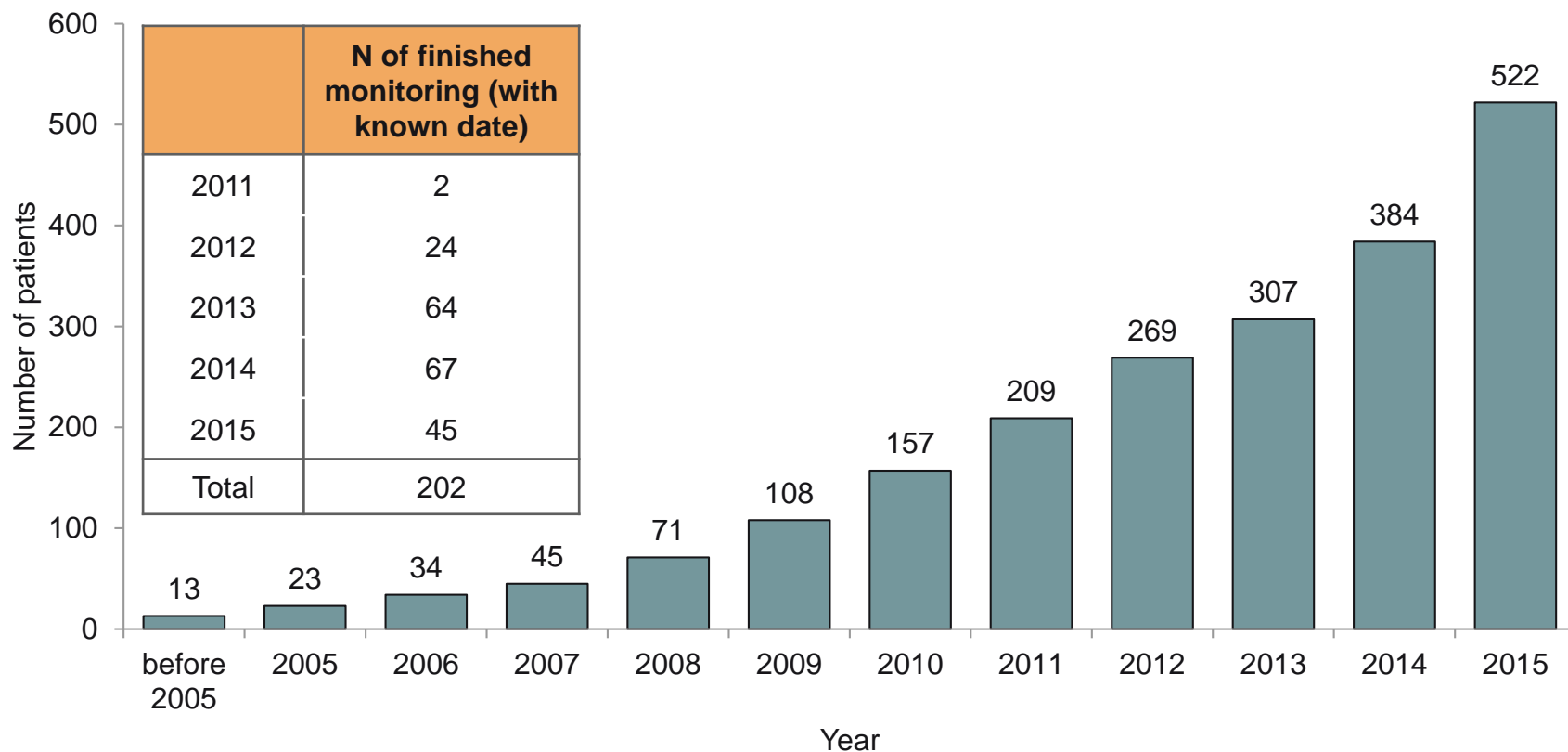
Number of newly diagnosed patients

N = 724



Number of monitored patients

N = 724



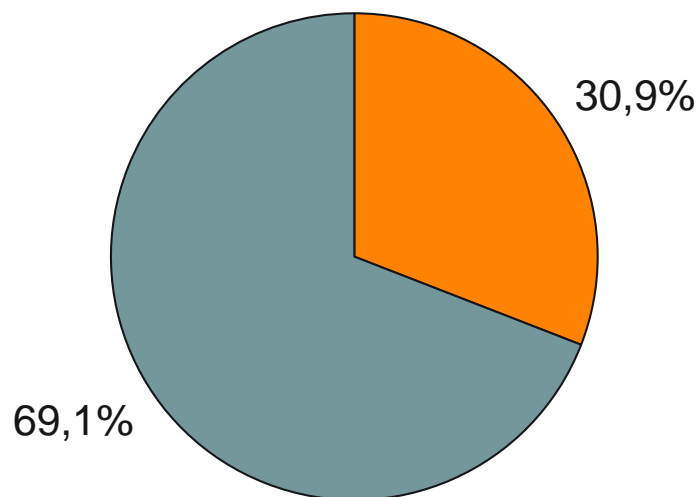
The number of monitored patients in the registry EMPIRE is reduced in a given year by the number of patients with ended follow-up (death, lung transplantation, patients lost from follow-up, etc.).



Demographic characteristics of patients

N = 724

Sex



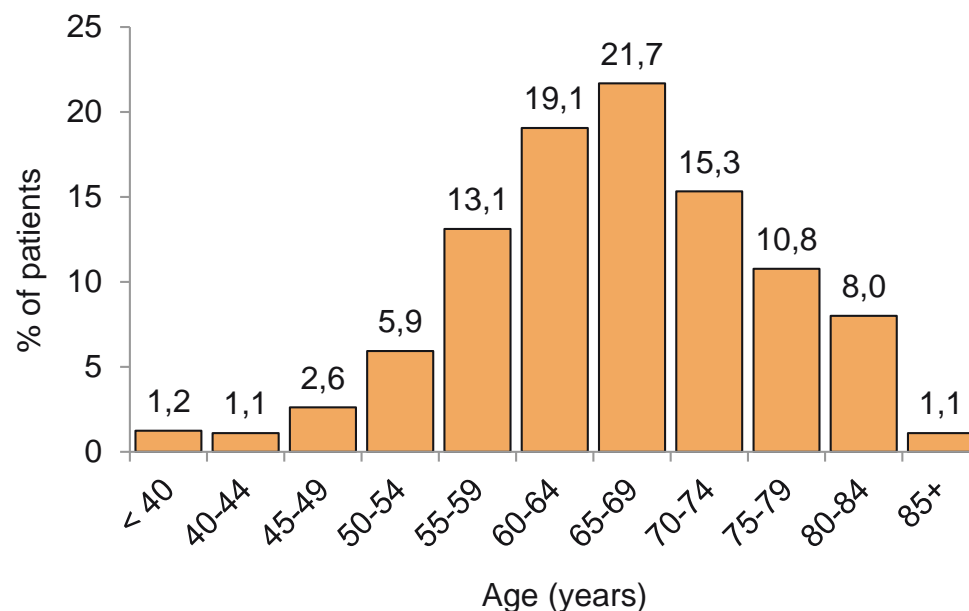
Women

N = 224

Men

N = 500

Age at diagnosis



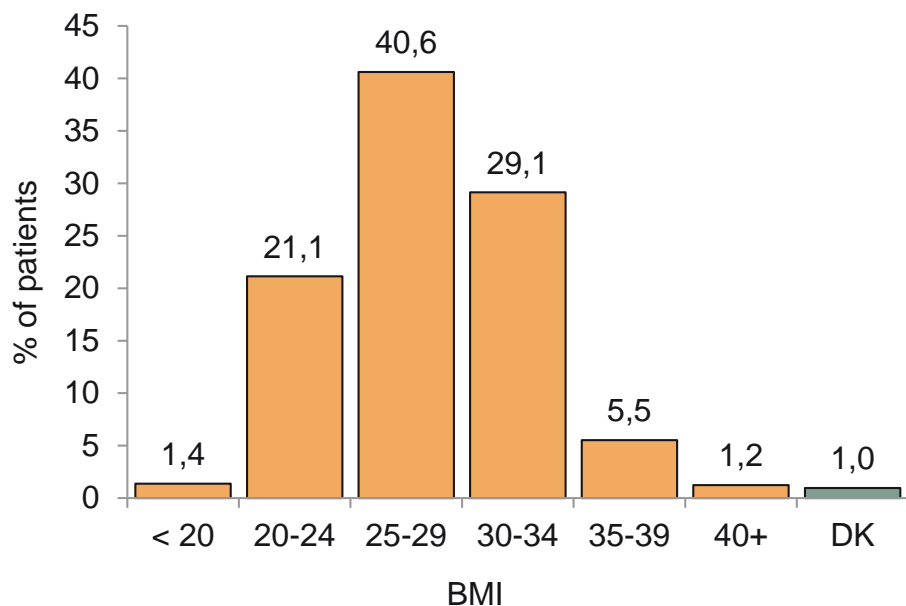
	Median (5.-95. percentile)	Mean (SD)
Age at diagnosis	66.7 (50.1 – 81.7)	66.3 (9.8)



Demographic characteristics of patients

N = 724

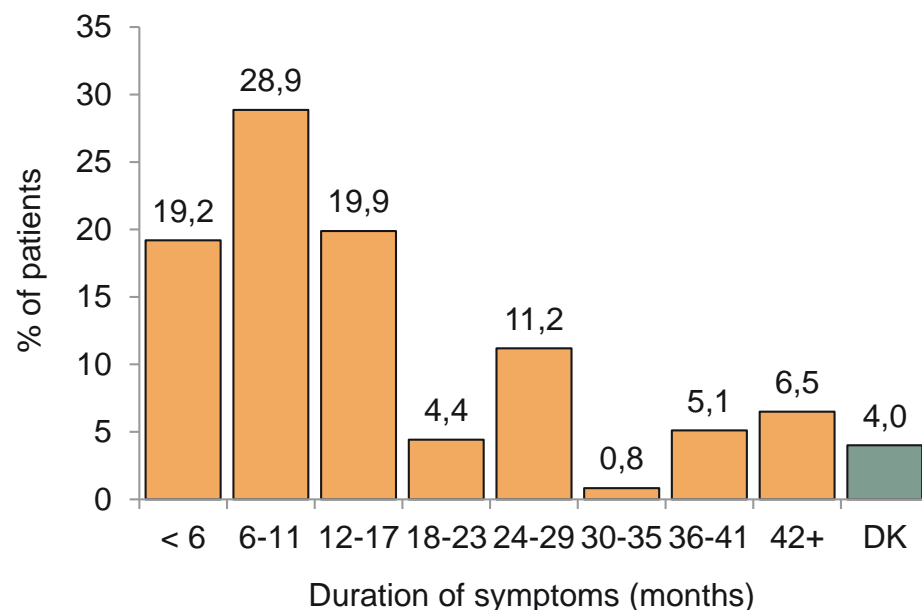
BMI



	Median (5.-95. percentile)	Mean (SD)
BMI	28.4 (22.0 – 35.6)	28.5 (4.4)

No information about BMI in 7 patients.

Duration of symptoms at diagnosis



	Median (5.-95. percentile)	Mean (SD)
Duration of symptoms	11.0 (2.0 – 48.0)	15.6 (17.5)

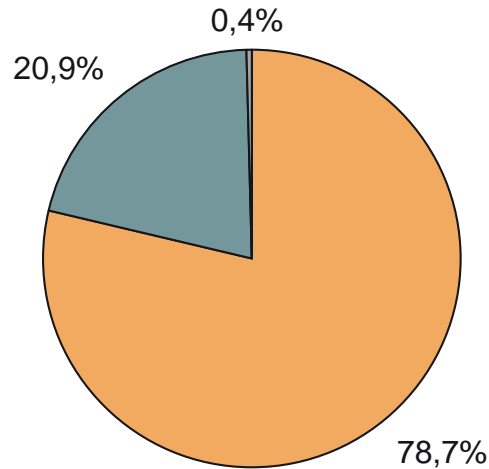
No information about duration of symptoms at diagnosis in 29 patients.



Other characteristics of patients

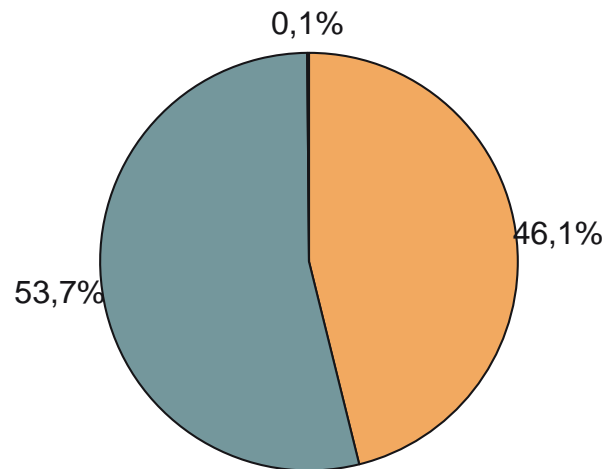
N = 724

HRCT



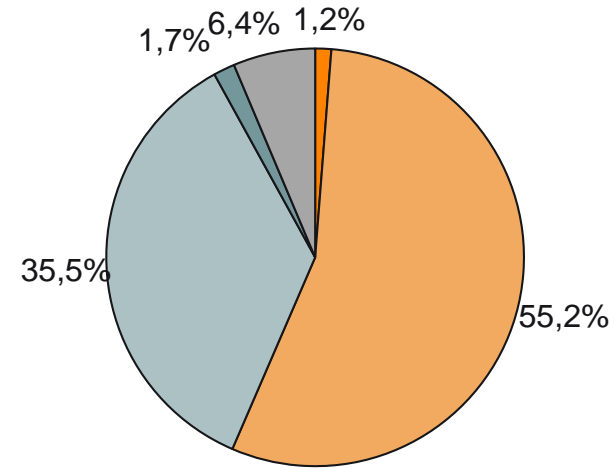
- Typical (N = 570)
- Atypical (N = 151)
- DK (N = 3)

Smoking



- Non-smoker (N = 334)
- Smoker (N = 389)
- DK (N = 1)

NYHA

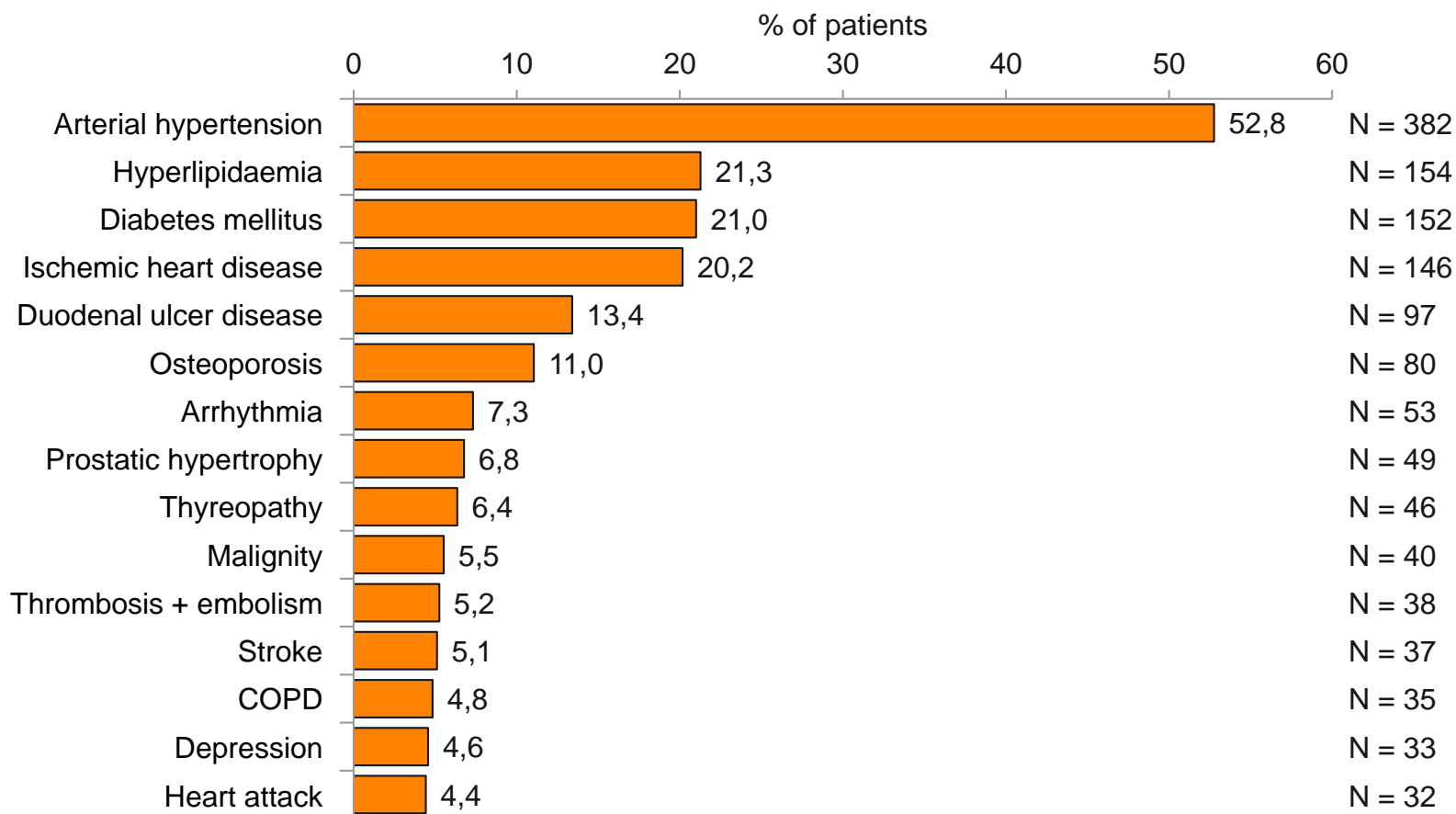


- I (N = 9)
- II (N = 400)
- III (N = 257)
- IV (N = 12)
- DK (N = 46)



Comorbidities

N = 724



The graph shows the 15 most common comorbidities.
More comorbidities can occur in one patient .



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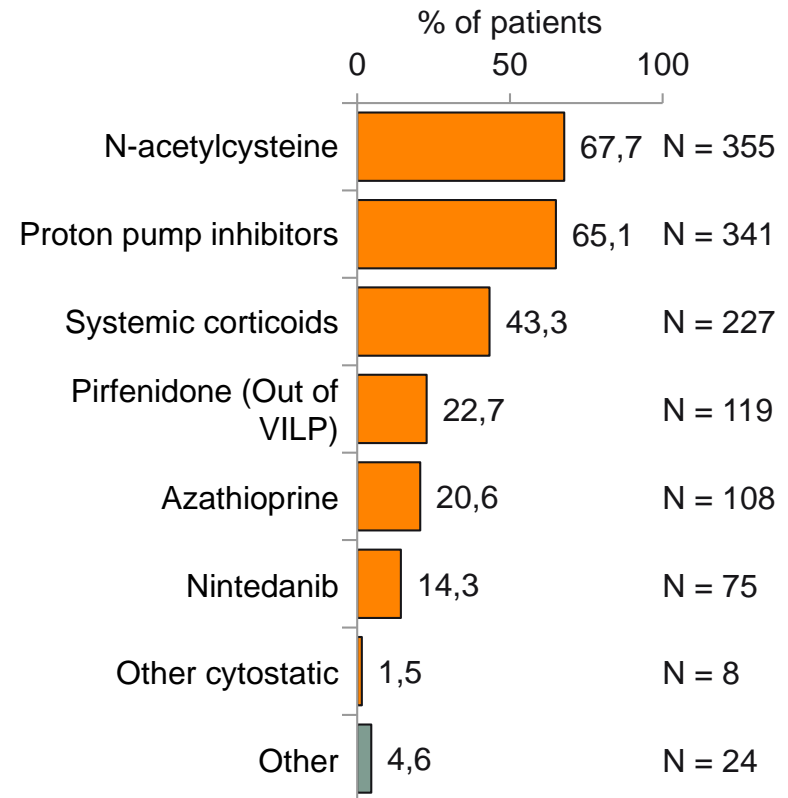
Treatment

N = 724

Treatment	Valid N	N (%)
Pharmacological treatment	N = 643	524 (81.5 %)
Rehabilitation	N = 636	231 (36.3 %)
Oxygen therapy	N = 638	170 (26.6 %)
Lung transplantation	N = 636	89 (14.0 %)
Clinical Study	N = 637	55 (8.6 %)



N = 524



1 patient could have more types of treatments during follow up.

1 patient with pharmacological treatment could use more drugs during follow up.

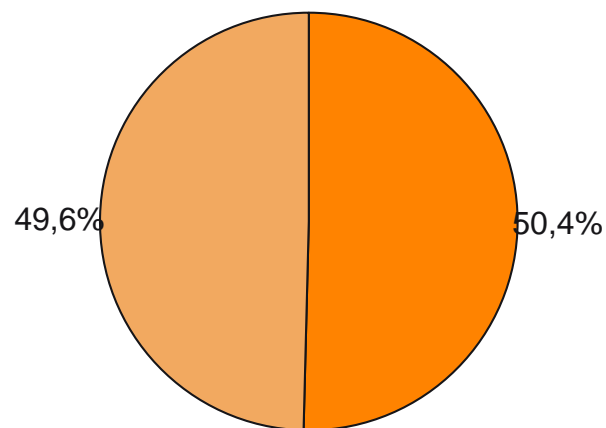


Pharmacological treatment – pirfenidone (out of VILP)

N = 119

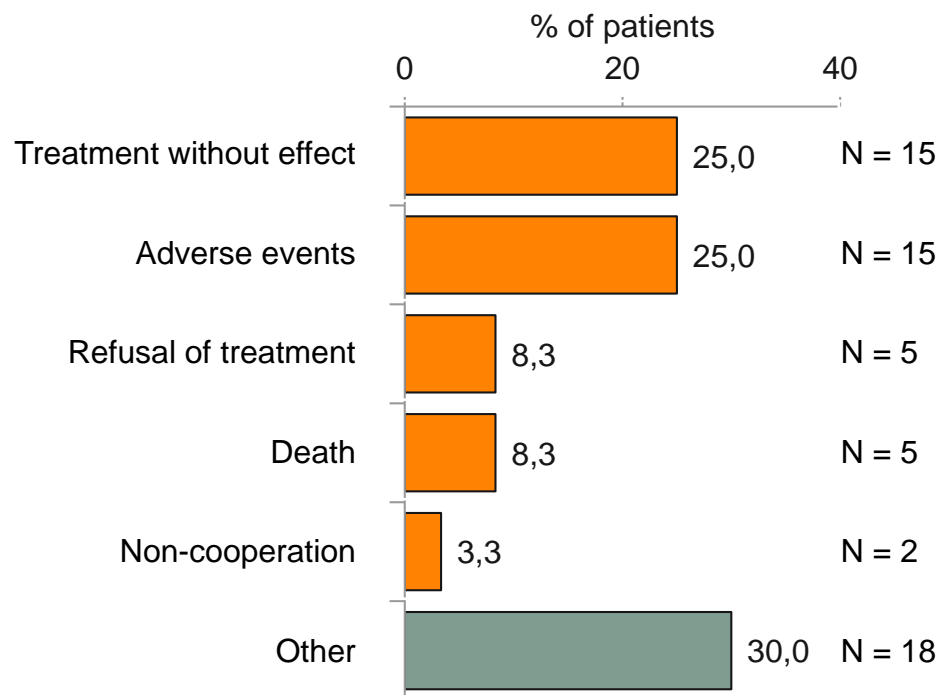
114 patients were treated by pirfenidone once, 5 patients used it twice.

Pirfenidone at diagnosis (year)



- Yes – same year (N = 60)
- No – other year (N = 59)

Termination of treatment (N = 60)

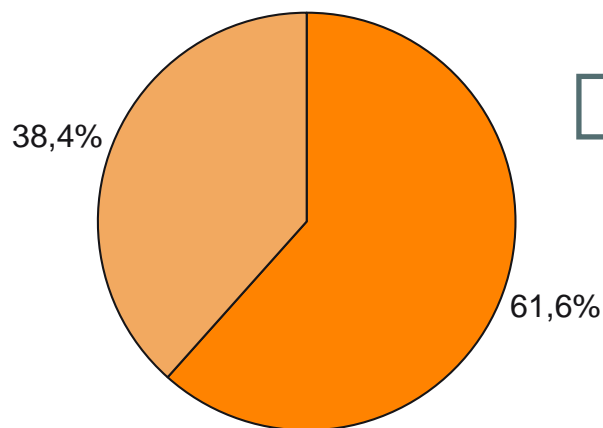




Pharmacological treatment – pirfenidone (VILP)

Pirfenidone at diagnosis (year)
- VILP

N = 211

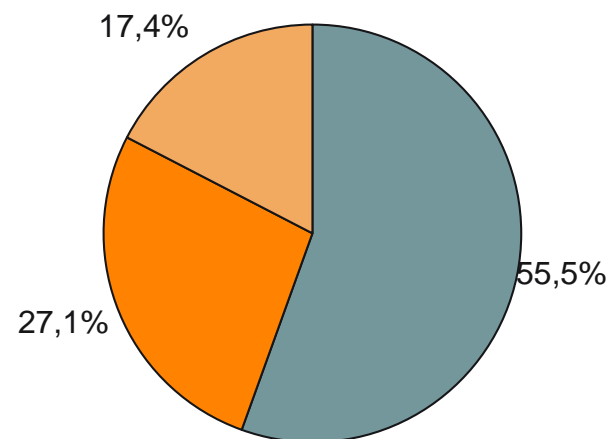
(Only Czech patients)






-  Yes – same year (N = 130)
-  No – other year (N = 81)

Treated by pirfenidone
(overall)

N = 546*



-  No, without pirfenidone (N = 303)
-  Yes, in diagnosis year (N = 148)
-  Yes, in other year (N = 95)

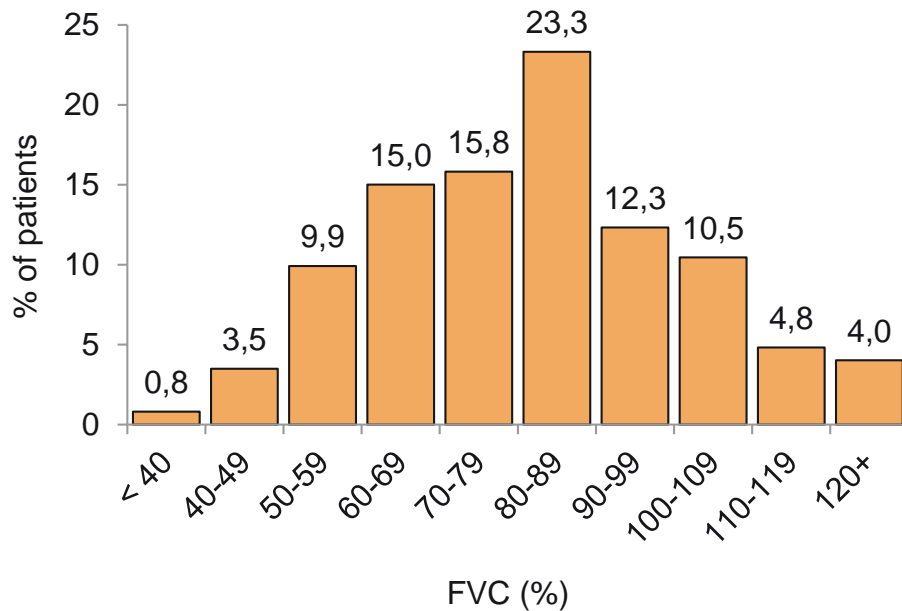
Connection with non-VILP

* We can determine treatment by pirfenidone.

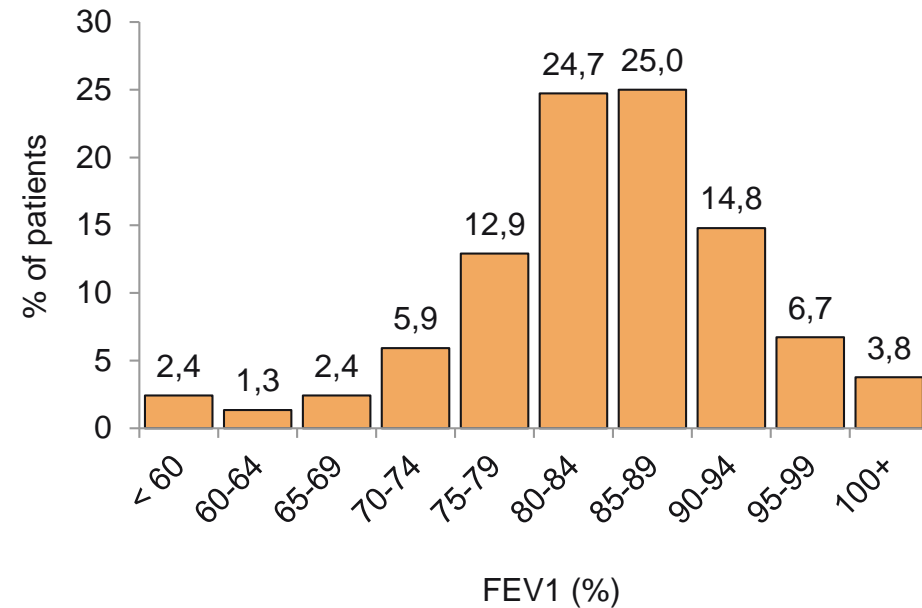


Functional parameters at diagnosis (± 1 month)

FVC (%)
(N = 373)



FEV1 (%)
(N = 372)



	Median (5.-95. percentile)	Mean (SD)
FVC (%)	81.8 (51.2 – 116.4)	82.0 (20.2)

No information about FVC (%) in 351 patients.

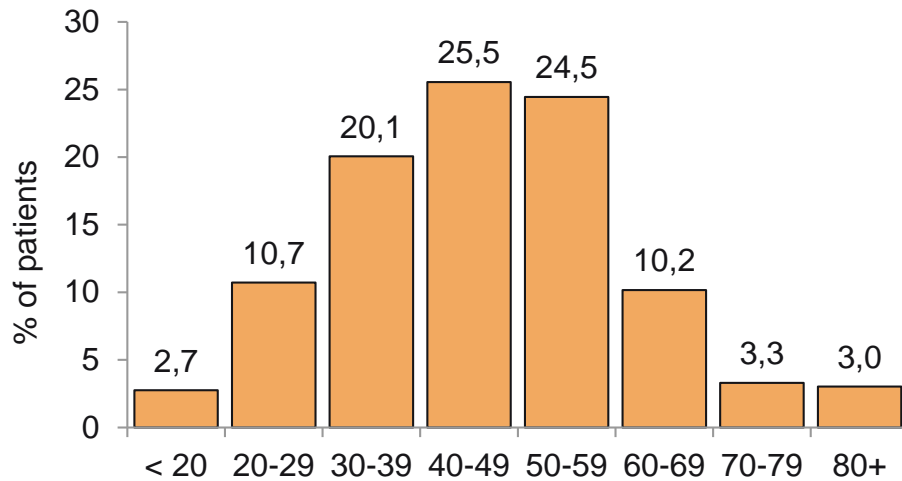
	Median (5.-95. percentile)	Mean (SD)
FEV1 (%)	85.0 (68.2 – 99.0)	84.6 (10.0)

No information about FEV1 (%) in 352 patients.



Functional parameters at diagnosis (± 1 month)

TLCO (%)
(N = 364)

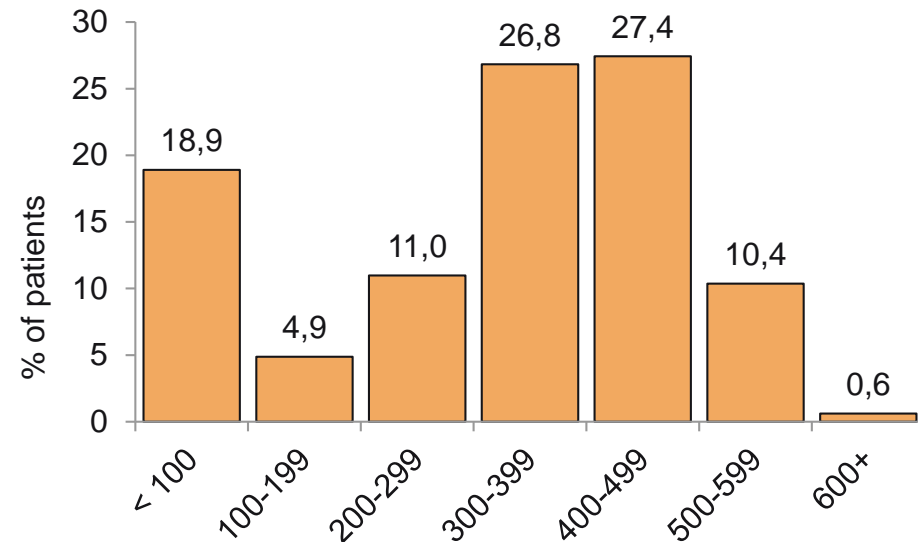


TLCO (%)

	Median (5.-95. percentile)	Mean (SD)
TLCO (%)	46.6 (21.4 – 71.4)	46.7 (15.6)

No information about TLCO (%) in 360 patients.

6MWT (m)
(N = 164)



6MWT (m)

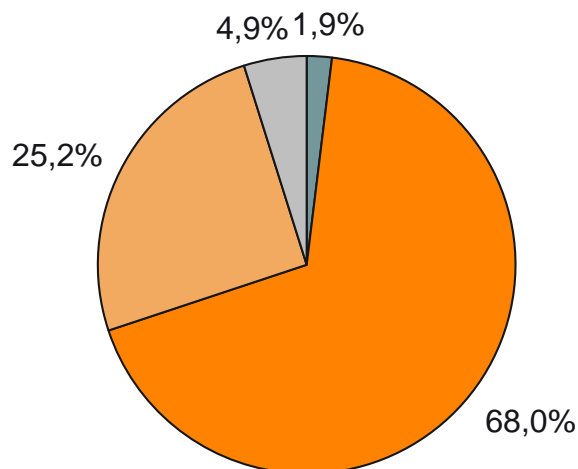
	Median (5.-95. percentile)	Mean (SD)
6MWT (m)	360.0 (0.0 – 540.0)	307.3 (178.3)





No information about 6MWT (m) in 560 patients.



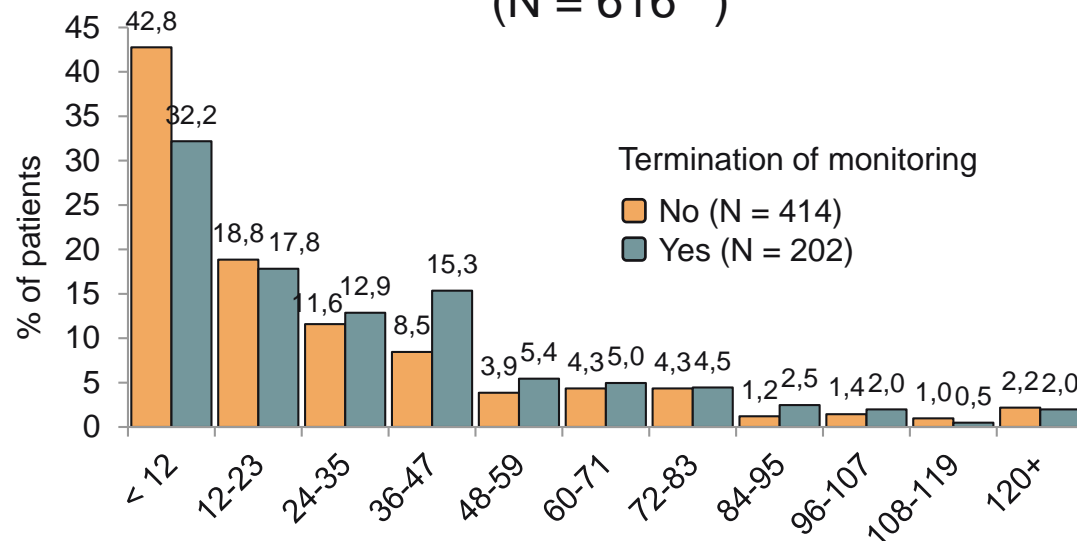
Termination of monitoring, length of follow-up

Reasons of termination
(N = 206*)



-  Lung transplantation (N = 4)
-  Death (N = 140)
-  Lost of patient (N = 52)
-  Other (N = 10)

Length of follow-up
(N = 616**)



Length of follow-up (months)

Termination of monitoring	Median (5.-95. percentile)	Mean (SD)
No	16.3 (0.0 – 93.0)	28.1 (35.9)
Yes	23.5 (0.2 – 90.5)	31.8 (29.1)

* Number of patients with termination of monitoring.

** Number of patients with known follow-up.



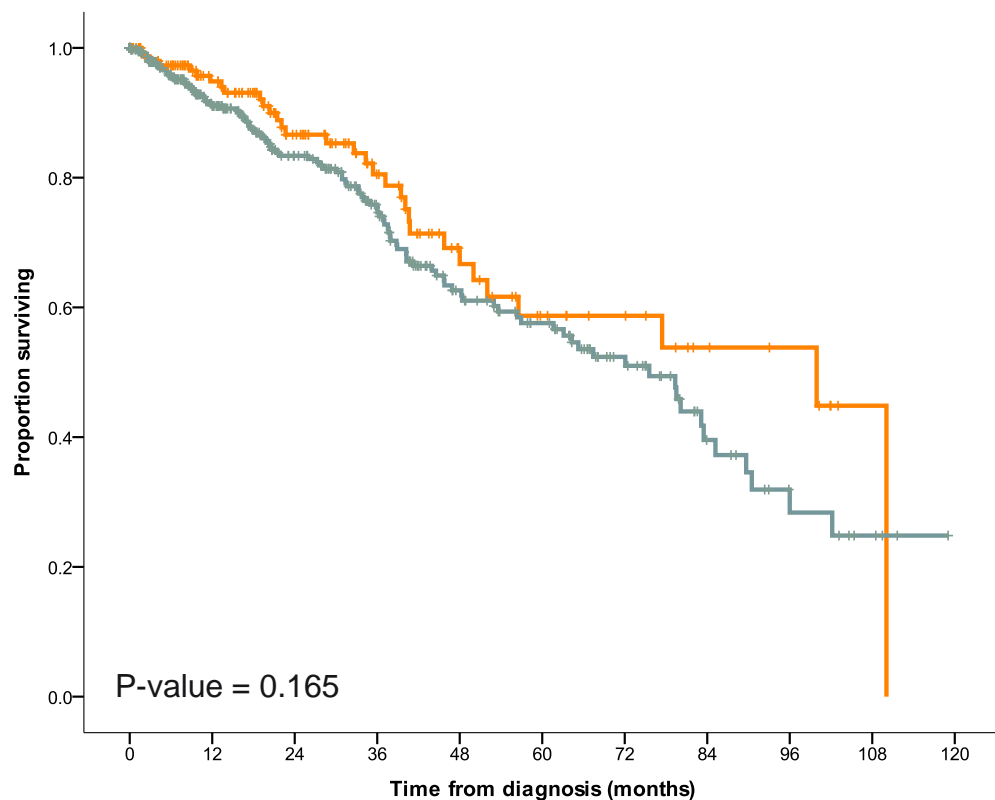
II. Long-term survival

Overall survival is shown for patients with follow up less than 120 months using the Kaplan-Meier estimate of survival function (testing the statistical significance of differences between the two groups is done by Log Rank test).

Log Rank test compares the survival distributions of two samples.



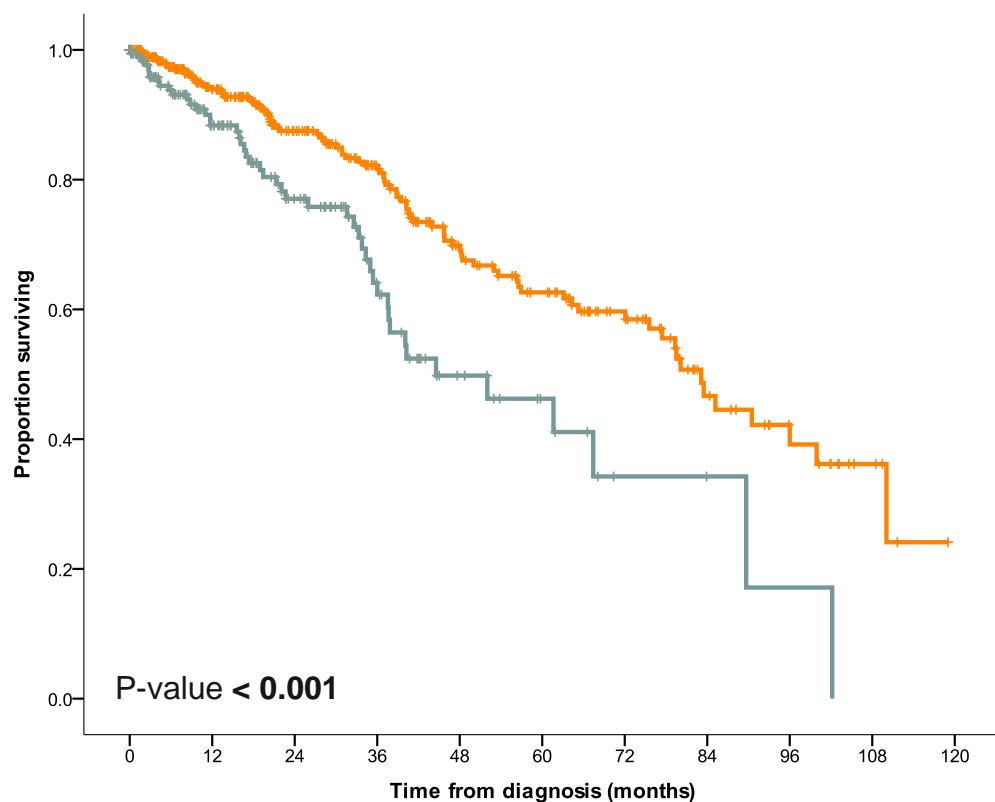
Long-term survival – sex



Sex	N deaths	Median survival (95% CI)	1 year survival (95% CI)	2 years survival (95% CI)	5 years survival (95% CI)
Women	32 (17.7 %)	99.9 (35.8 – 164.1)	0.948 (0.911 - 0.986)	0.866 (0.802 - 0.931)	0.587 (0.453 - 0.721)
Men	104 (24.6 %)	75.6 (63.0 – 88.2)	0.910 (0.879 - 0.942)	0.834 (0.789 - 0.878)	0.576 (0.501 - 0.651)



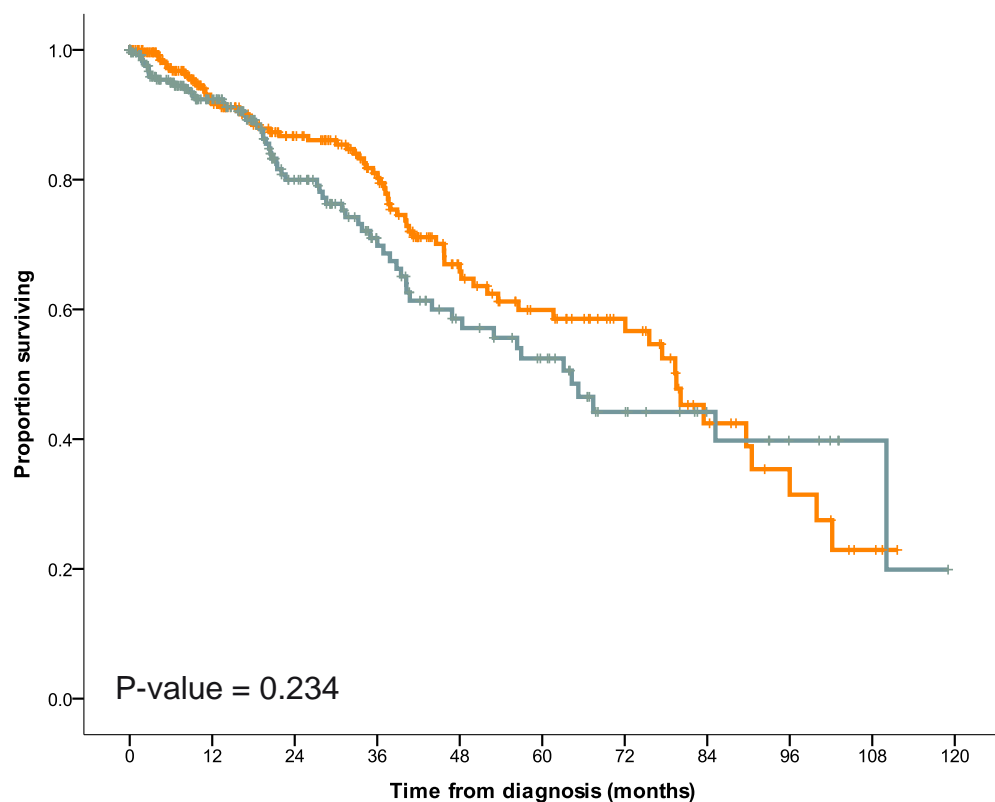
Long-term survival – age at diagnosis



Age	N deaths	Median survival (95% CI)	1 year survival (95% CI)	2 years survival (95% CI)	5 years survival (95% CI)
< 70	88 (22.1 %)	83.1 (76.2 – 90.1)	0.939 (0.912 - 0.966)	0.875 (0.835 - 0.915)	0.626 (0.552 - 0.701)
≥ 70	48 (23.4 %)	44.6 (25.2 – 63.9)	0.883 (0.831 - 0.936)	0.770 (0.693 - 0.848)	0.462 (0.328 - 0.596)



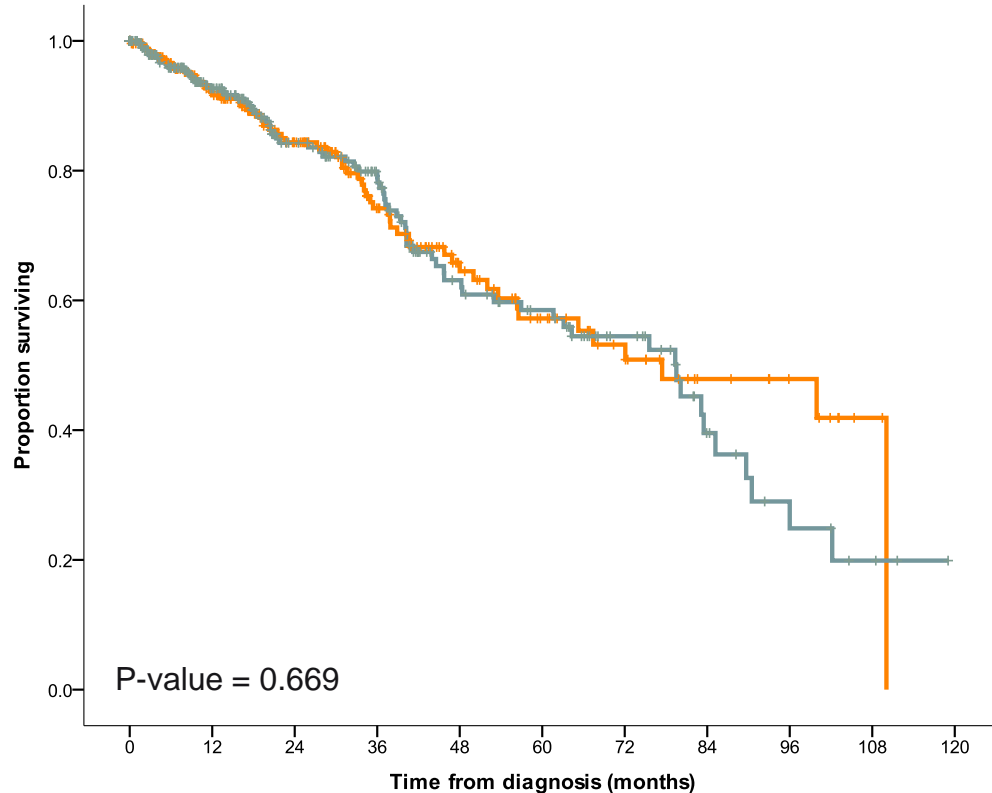
Long-term survival – duration of symptoms



Duration of symptoms (months)	N deaths	Median survival (95% CI)	1 year survival (95% CI)	2 years survival (95% CI)	5 years survival (95% CI)
< 12	71 (24.0 %)	79.5 (70.4 - 88.6)	0.917 (0.880 - 0.953)	0.867 (0.821 - 0.914)	0.599 (0.510 - 0.688)
≥ 12	63 (21.8 %)	64.3 (50.6 - 78.0)	0.924 (0.889 - 0.959)	0.800 (0.737 - 0.863)	0.524 (0.421 - 0.627)



Long-term survival – smoking



Smoking

- No (N = 270)*
- Yes (N = 333)*

* Only for patients with known follow-up < 120 months.

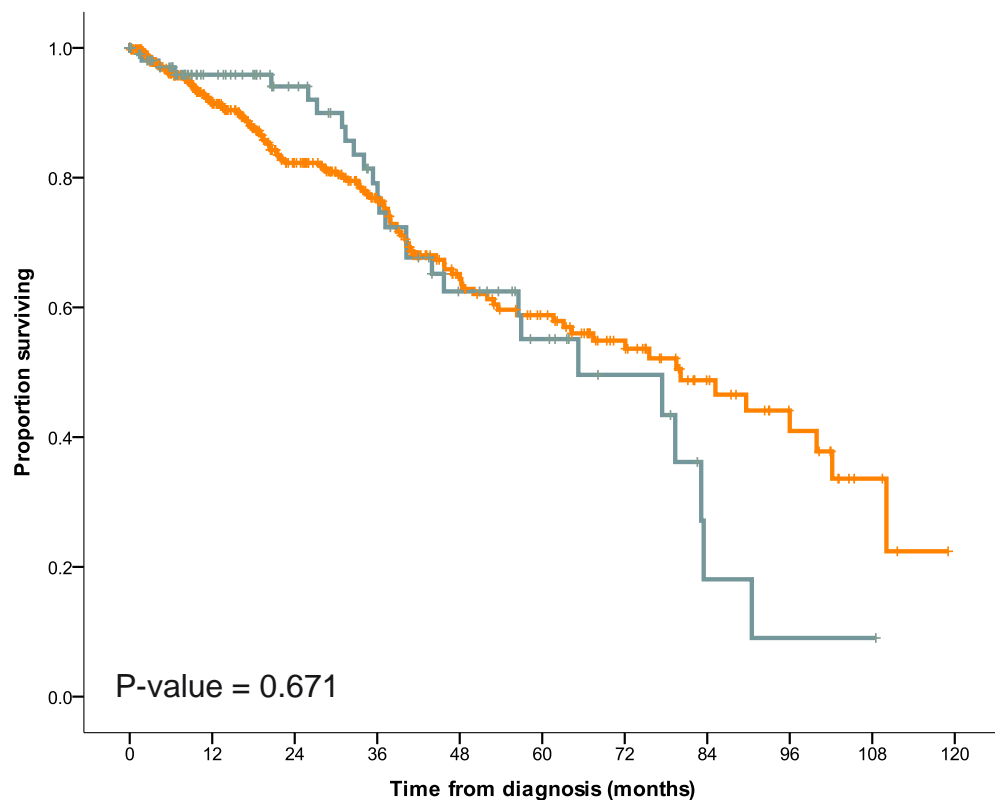
Long-term survival is illustrated by Kaplan-Meier estimate of survival function.

Statistical significance of difference between groups is tested by Log Rank test.

Smoking	N deaths	Median survival (95% CI)	1 year survival (95% CI)	2 years survival (95% CI)	5 years survival (95% CI)
No	62 (23.0 %)	77.4 (46.9 - 108.0)	0.916 (0.879 - 0.953)	0.844 (0.791 - 0.896)	0.572 (0.475 - 0.669)
Yes	74 (22.2 %)	79.5 (63.3 - 95.7)	0.927 (0.894 - 0.960)	0.843 (0.791 - 0.894)	0.585 (0.496 - 0.674)



Long-term survival – HRCT



HRCT

Typical (N = 481)*

Atypical (N = 122)*

* Only for patients with known follow-up < 120 months.

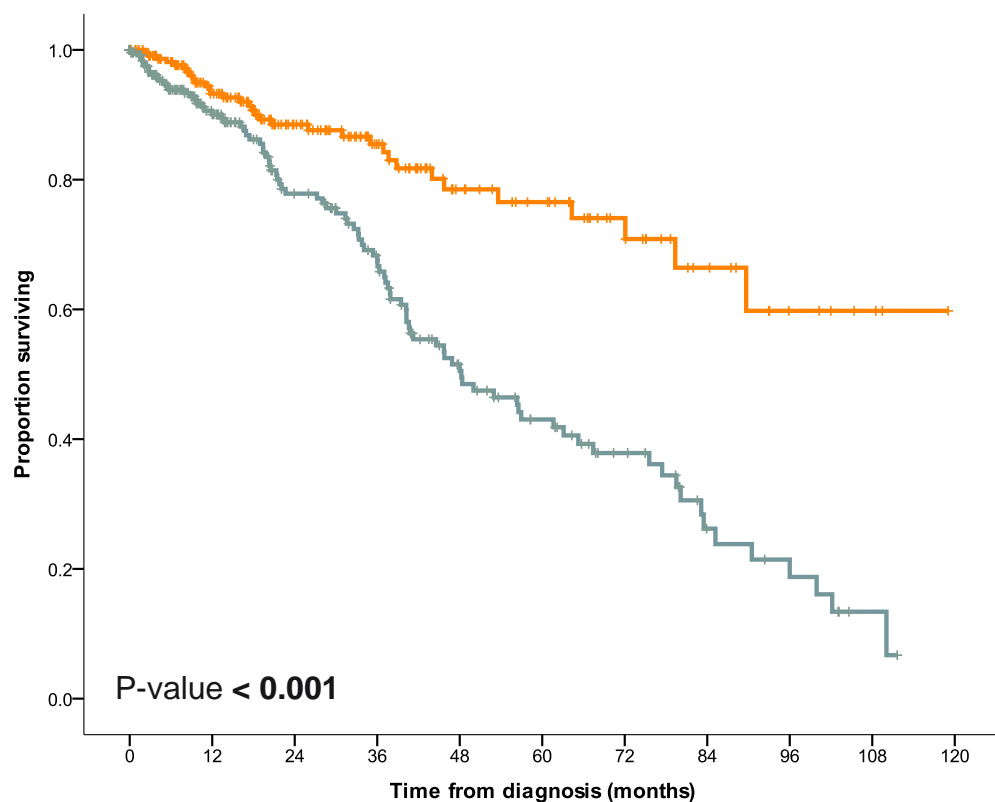
Long-term survival is illustrated by Kaplan-Meier estimate of survival function.

Statistical significance of difference between groups is tested by Log Rank test.

HRCT	N deaths	Median survival (95% CI)	1 year survival (95% CI)	2 years survival (95% CI)	5 years survival (95% CI)
Typical	109 (22.7 %)	80.1 (61.1 - 99.1)	0.914 (0.885 - 0.942)	0.823 (0.780 - 0.865)	0.588 (0.516 - 0.660)
Atypical	27 (22.1 %)	65.2 (34.7 - 95.8)	0.959 (0.919 - 0.998)	0.941 (0.888 - 0.993)	0.551 (0.394 - 0.708)



Long-term survival – treatment by pirfenidone



* Only for patients with known follow-up < 120 months.

Long-term survival is illustrated by Kaplan-Meier estimate of survival function.

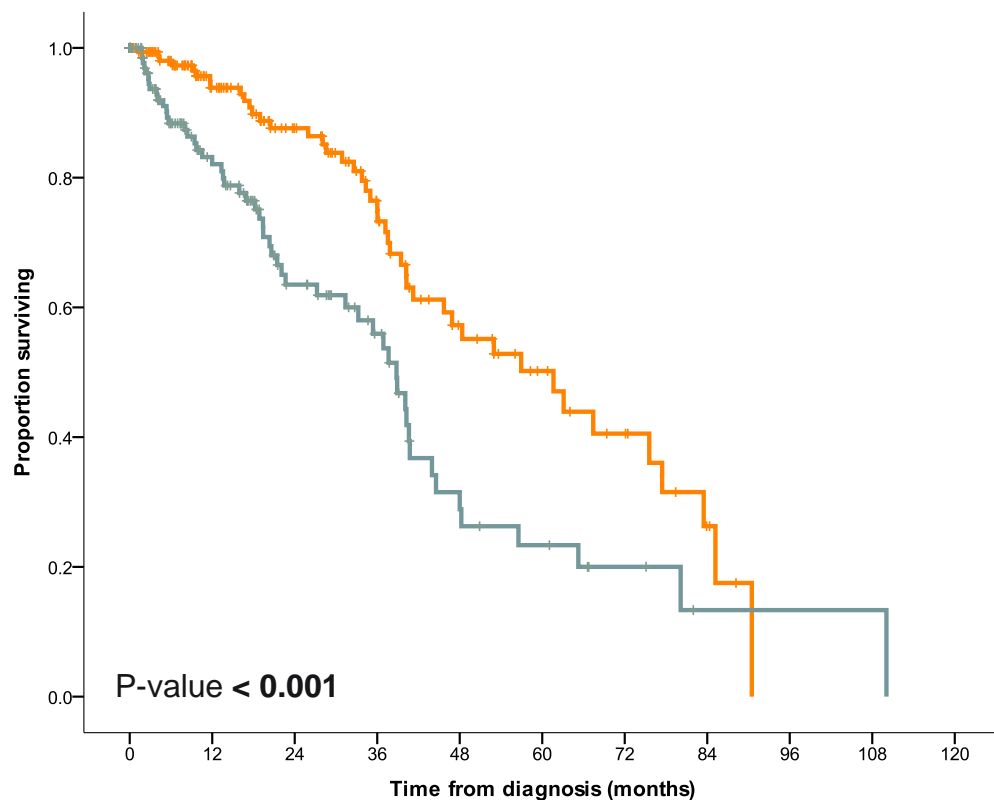
Statistical significance of difference between groups is tested by Log Rank test.

** Treatment by pirfenidone in any year.

Pirfenidone	N deaths	Median survival (95% CI)	1 year survival (95% CI)	2 years survival (95% CI)	5 years survival (95% CI)
Yes	33 (14.0 %)	-	0.933 (0.897 - 0.968)	0.885 (0.837 - 0.933)	0.765 (0.679 - 0.852)
No	94 (34.9 %)	48.2 (36.2 - 60.2)	0.900 (0.860 - 0.941)	0.778 (0.715 - 0.842)	0.430 (0.340 - 0.521)



Long-term survival – FVC (%) at diagnosis



* Only for patients with known follow-up < 120 months.

Long-term survival is illustrated by Kaplan-Meier estimate of survival function.

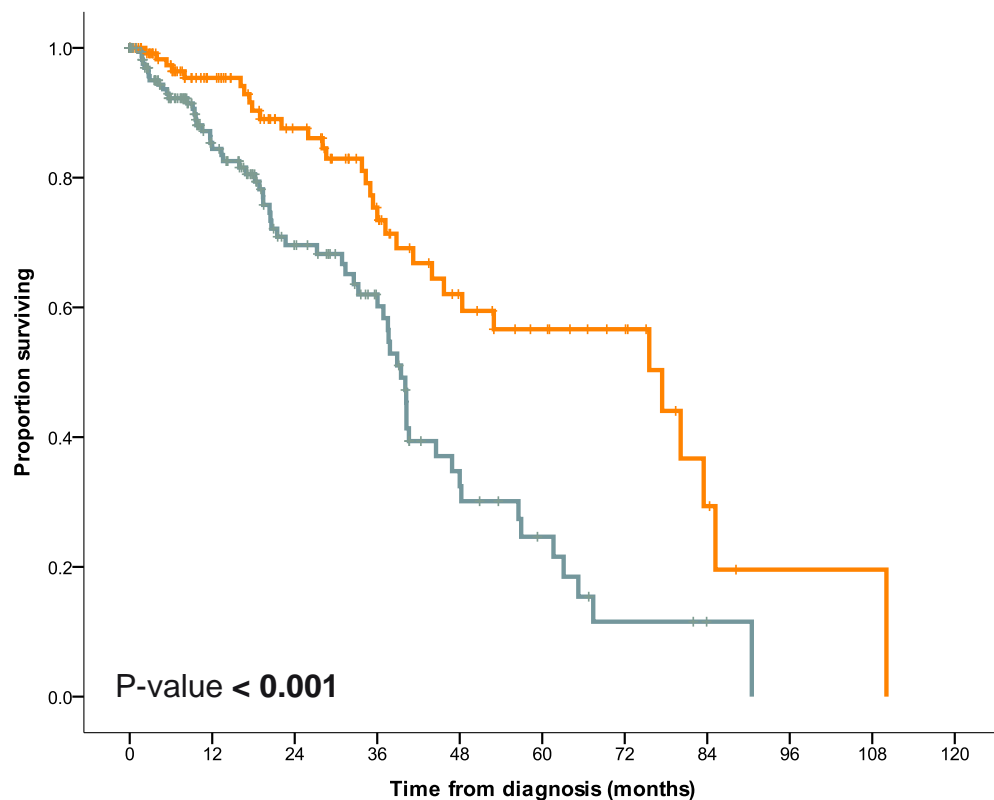
Statistical significance of difference between groups is tested by Log Rank test.

** ± 1 month

FVC (%)	N deaths	Median survival (95% CI)	1 year survival (95% CI)	2 years survival (95% CI)	5 years survival (95% CI)
≥ 80	44 (22.1 %)	61.6 (43.8 - 79.4)	0.939 (0.897 - 0.980)	0.876 (0.814 - 0.938)	0.502 (0.372 - 0.631)
< 80	54 (33.1 %)	38.8 (33.8 - 43.8)	0.821 (0.749 - 0.893)	0.635 (0.532 - 0.738)	0.233 (0.107 - 0.360)



Long-term survival – TLCO (%) at diagnosis



* Only for patients with known follow-up < 120 months.

Long-term survival is illustrated by Kaplan-Meier estimate of survival function.

Statistical significance of difference between groups is tested by Log Rank test.

** ± 1 month

TLCO (%)	N deaths	Median survival (95% CI)	1 year survival (95% CI)	2 years survival (95% CI)	5 years survival (95% CI)
≥ 50	32 (21.6 %)	77.4 (40.9 - 114.0)	0.954 (0.914 - 0.993)	0.876 (0.806 - 0.946)	0.566 (0.428 - 0.705)
< 50	62 (30.1 %)	39.5 (37.4 - 41.5)	0.844 (0.782 - 0.907)	0.696 (0.606 - 0.786)	0.246 (0.125 - 0.368)

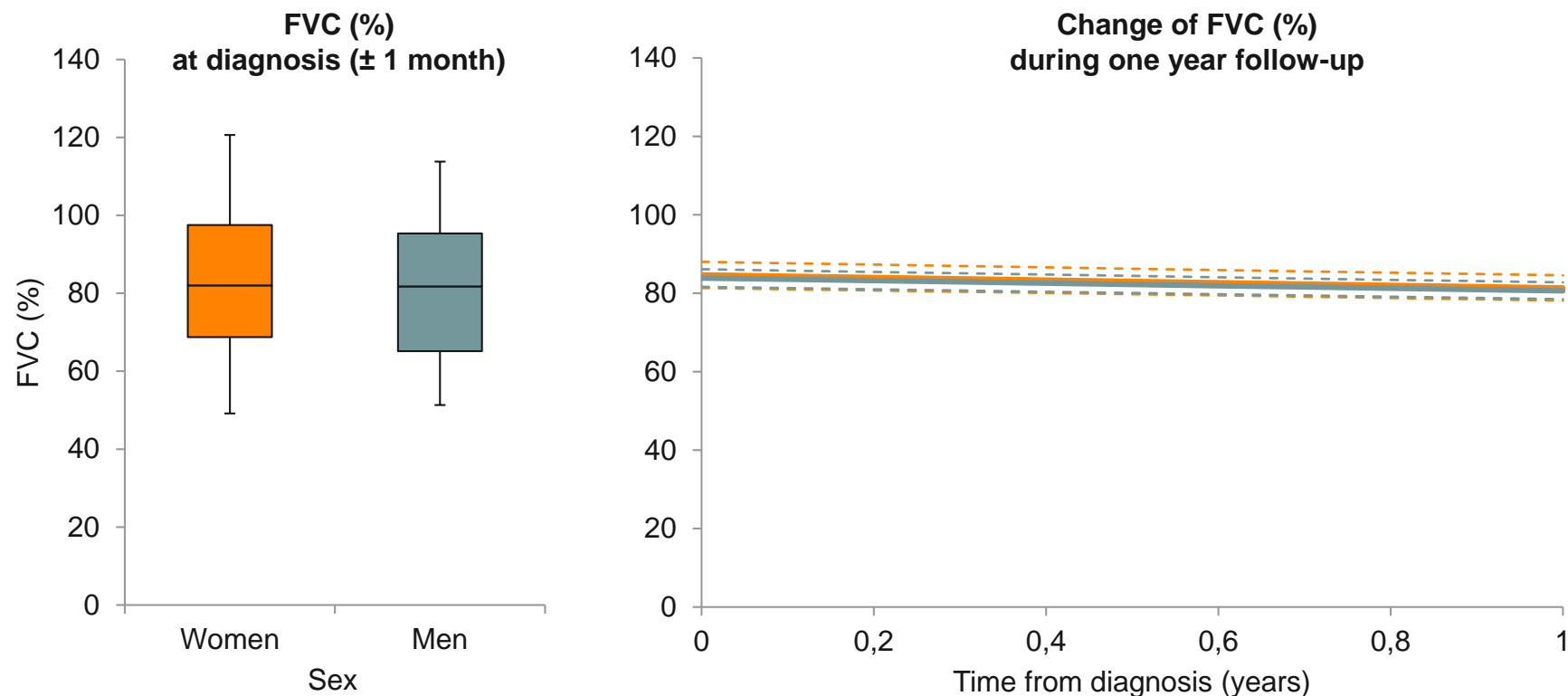


III. Change of FVC (%) and TLCO (%) during follow-up

The primary aim of the analysis is comparing the annual decline of lung functions during follow-up between two groups. Testing the statistical significance of differences at diagnosis between two groups is done by Mann-Whitney test. To estimate the annual change of FVC and TLCO is used a linear regression model with mixed effects.



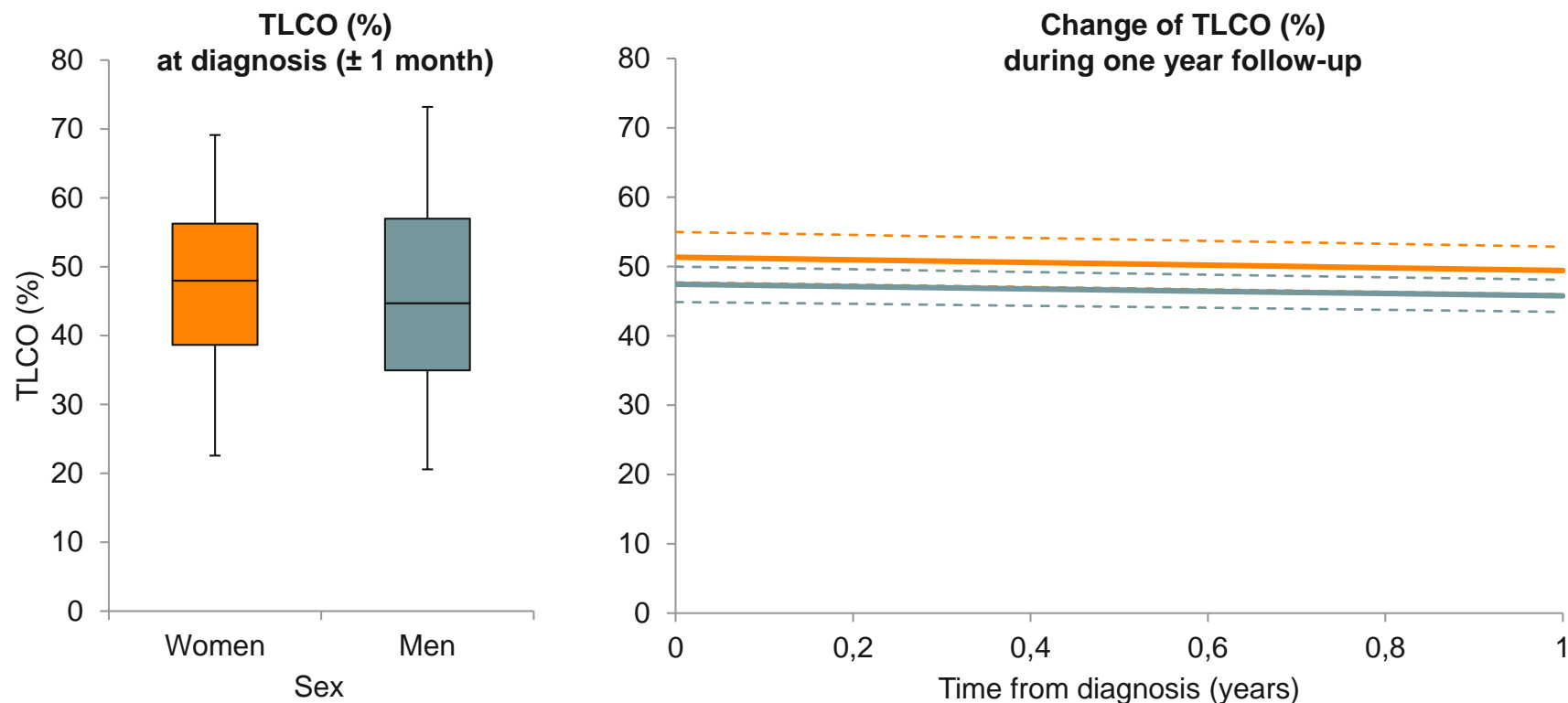
Annual change of FVC (%) – sex



Sex	FVC (%) at diagnosis (± 1 month)			Annual change of FVC (%)	
	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
Women	N = 119	82.0 (49.2 - 120.6)	0.241	-3.326 (-4.293; -2.360)*	0.903
Men	N = 254	81.8 (51.3 - 113.8)		-3.253 (-3.934; -2.573)*	



Annual change of TLCO (%) – sex

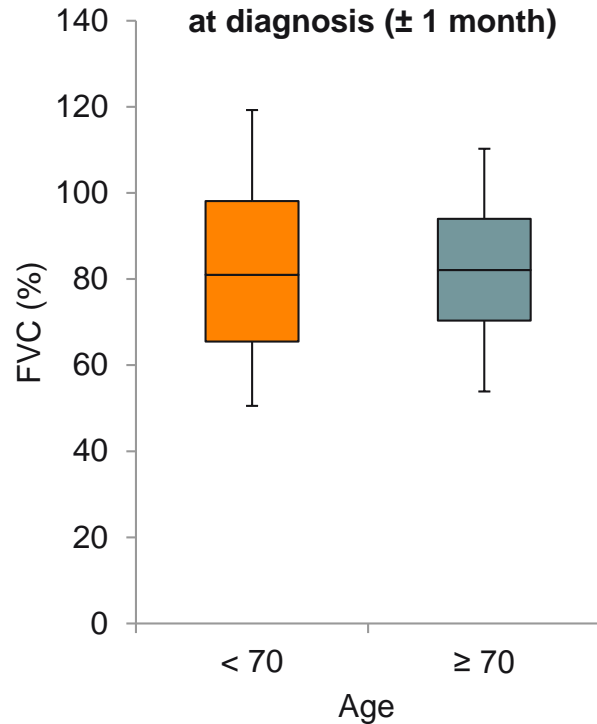


Sex	TLCO (%) at diagnosis (± 1 month)			Annual change of TLCO (%)	
	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
Women	N = 116	48.0 (22.6 - 69.1)	0.171	-1.926 (-2.770; -1.082)*	0.660
Men	N = 251	44.7 (20.6 - 73.2)		-1.670 (-2.441; -0.899)*	

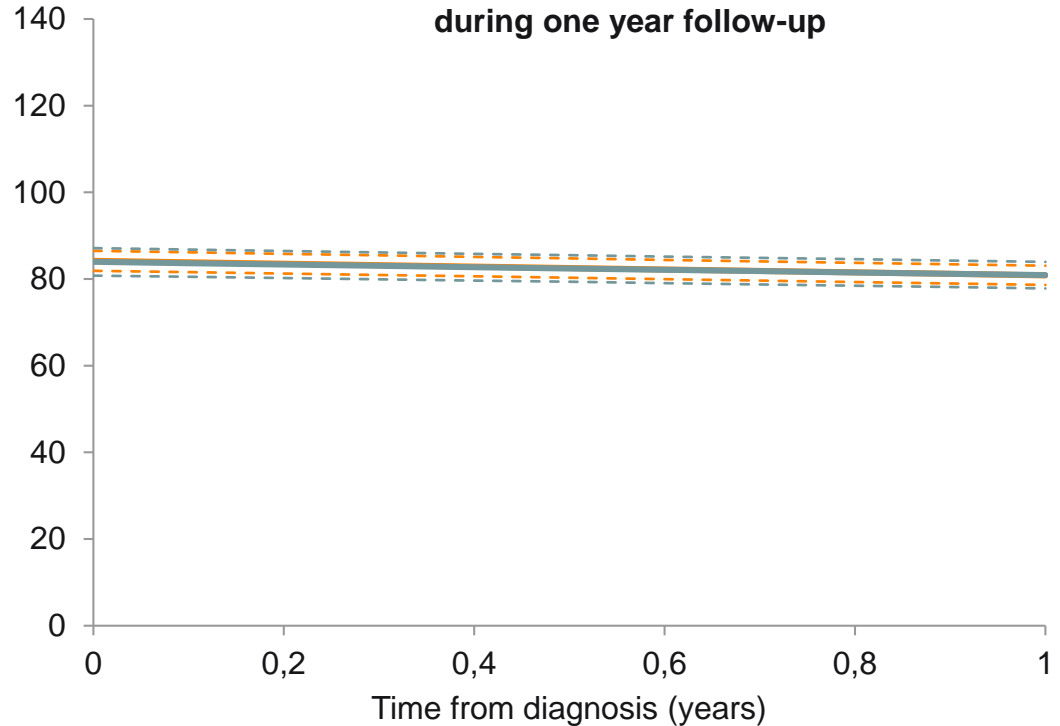


Annual change of FVC (%) – age at diagnosis

**FVC (%)
at diagnosis (± 1 month)**



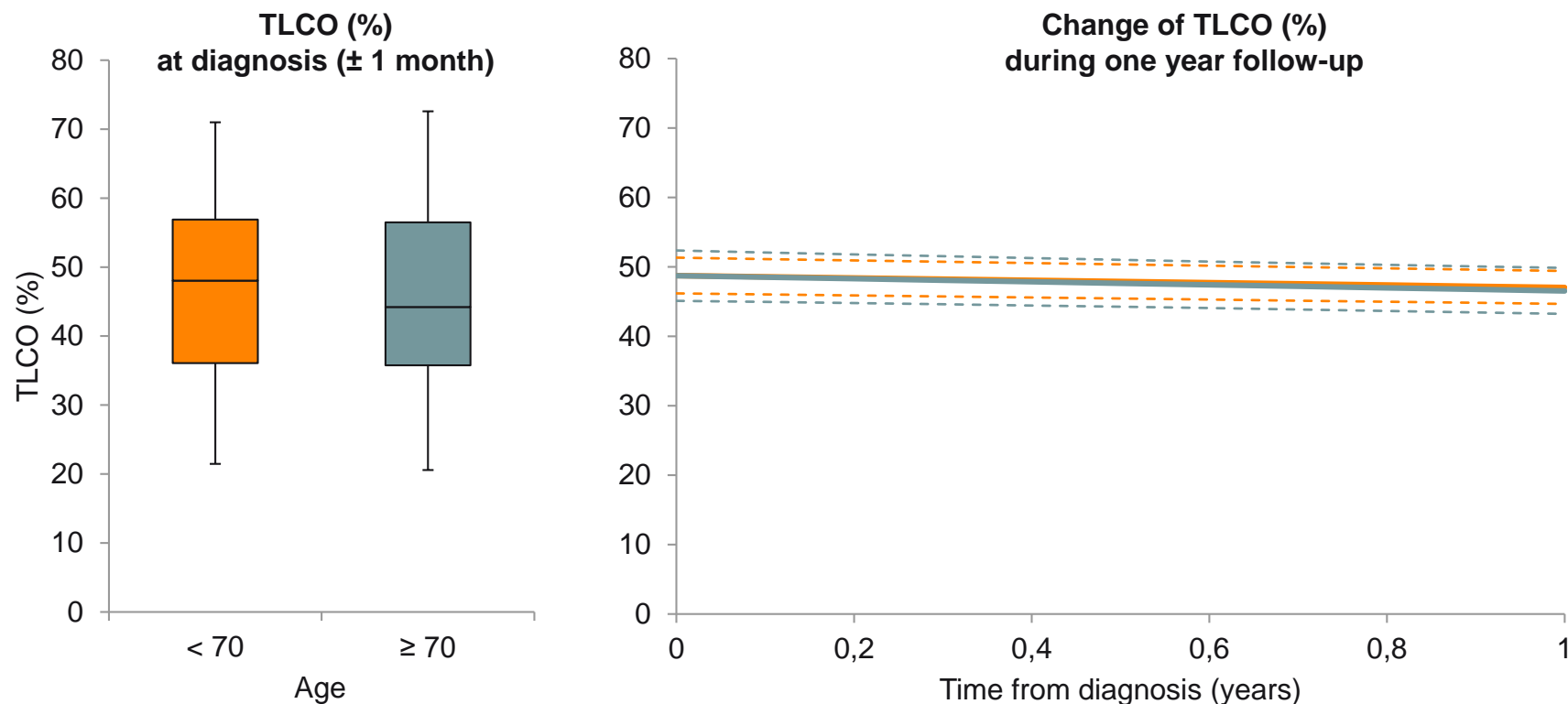
**Change of FVC (%)
during one year follow-up**



Age	FVC (%) at diagnosis (± 1 month)			Annual change of FVC (%)	
	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
< 70	N = 228	81.0 (50.5 - 119.3)	0.780	-3.352 (-3.995; -2.708)*	0.655
≥ 70	N = 145	82.1 (53.9 - 110.3)		-3.060 (-4.171; -1.948)*	



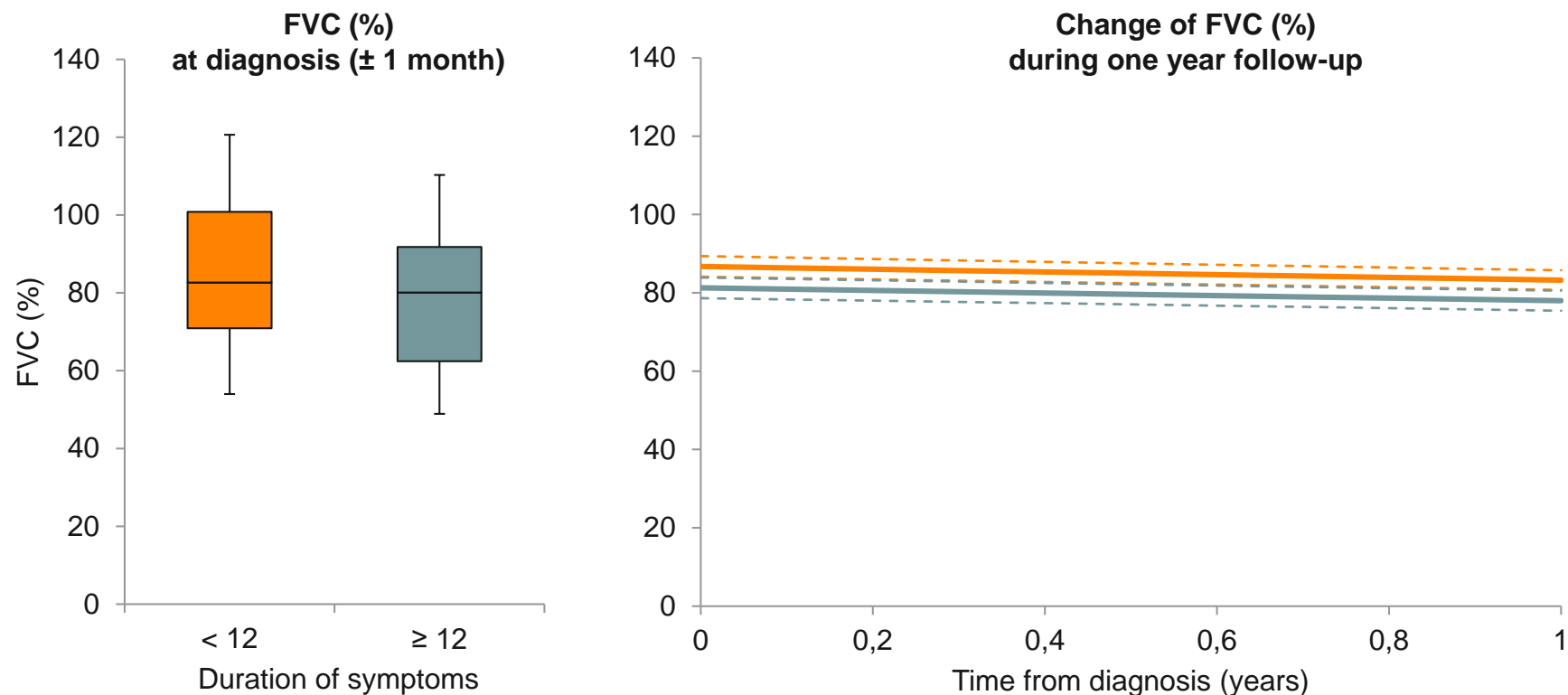
Annual change of TLCO (%) – age at diagnosis



TLCO (%) at diagnosis (± 1 month)				Annual change of TLCO (%)	
Age	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
< 70	N = 224	48.0 (21.5 - 71.0)	0.448	-1.705 (-2.320; -1.091)*	0.562
≥ 70	N = 143	44.2 (20.6 - 72.6)		-2.195 (-3.735; -0.655)*	



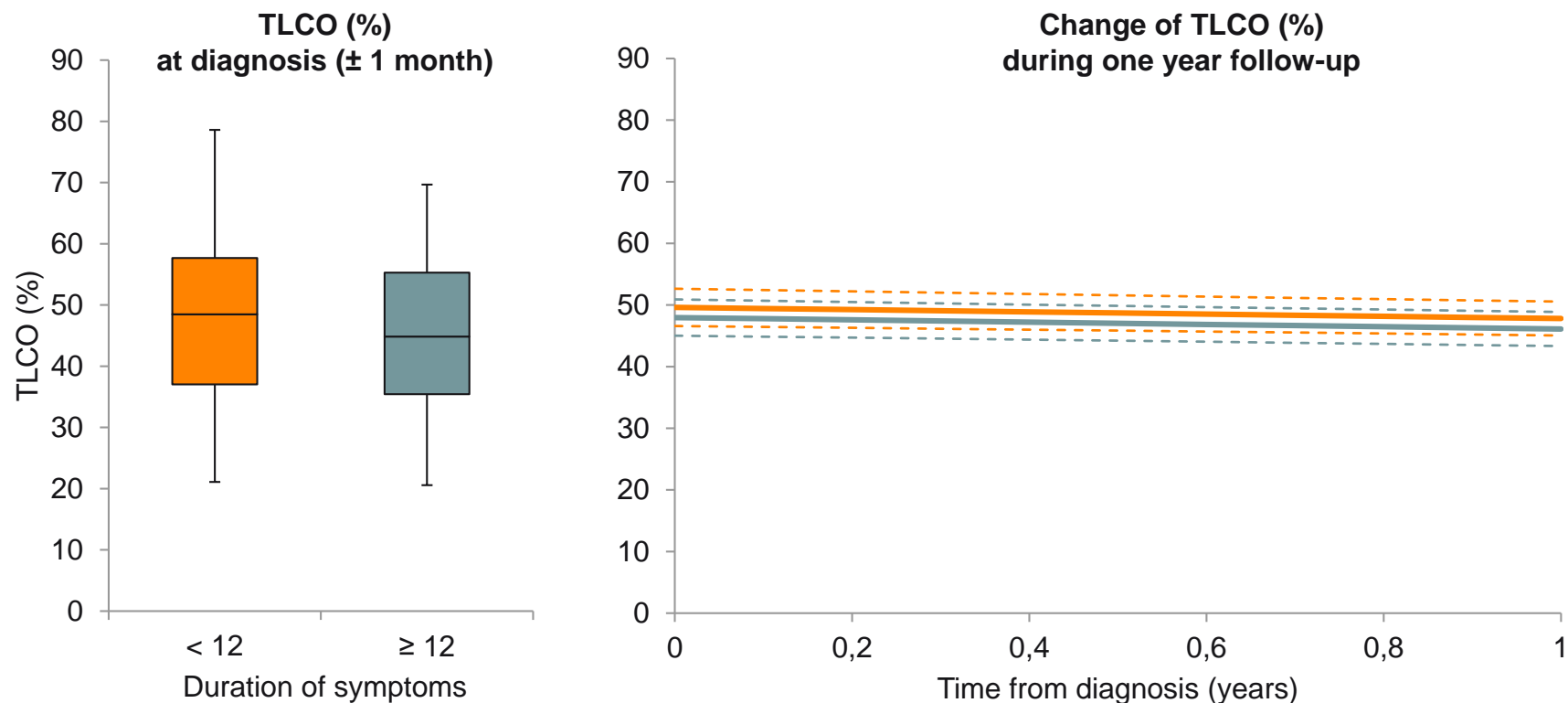
Annual change of FVC (%) – duration of symptoms



FVC (%) at diagnosis (± 1 month)		Annual change of FVC (%)			
Duration of symptoms	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
< 12	N = 169	82.7 (54.0 - 120.6)	0.002	-3.481 (-4.238; -2.725)*	0.726
≥ 12	N = 200	80.1 (48.9 - 110.3)		-3.280 (-4.123; -2.436)*	



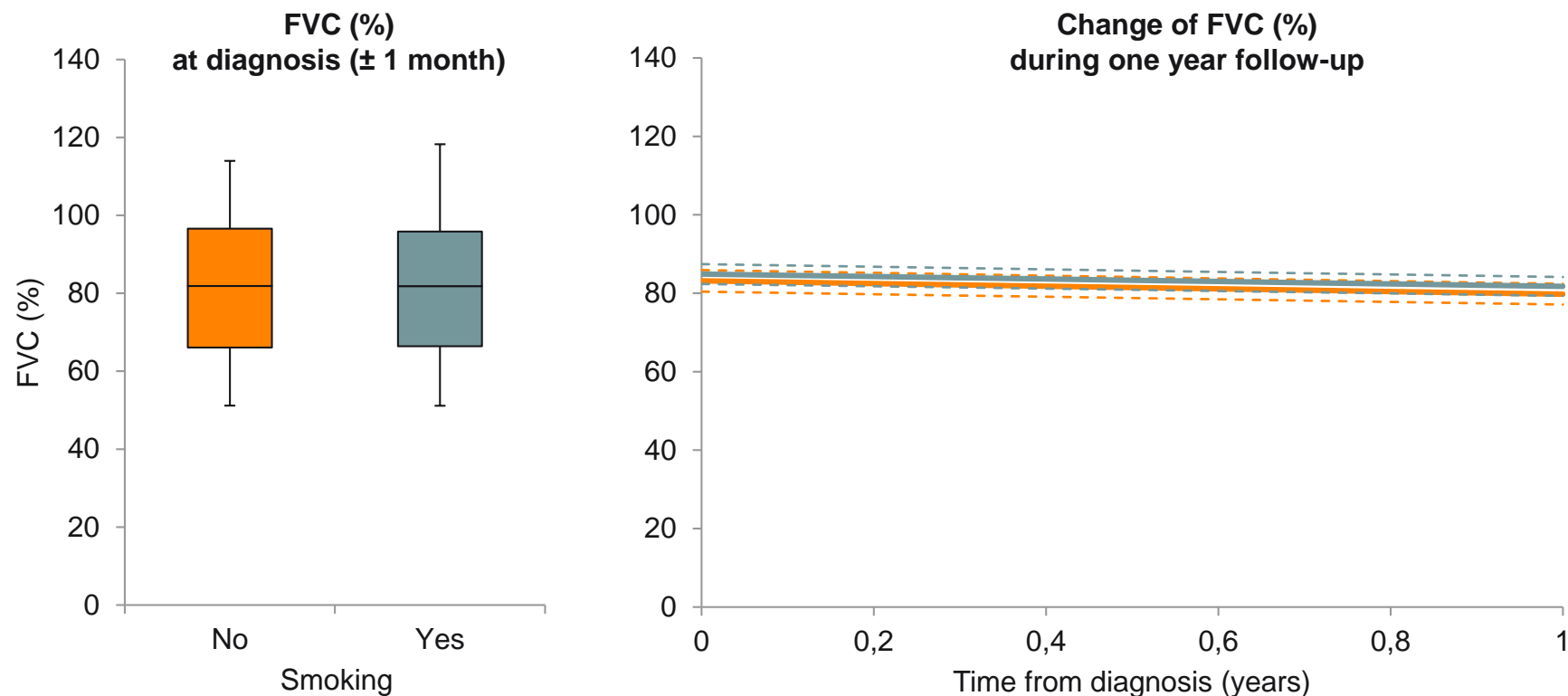
Annual change of TLCO (%) – duration of symptoms



TLCO (%) at diagnosis (± 1 month)				Annual change of TLCO (%)	
Duration of symptoms	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
< 12	N = 168	48.5 (21.1 - 78.6)	0.072	-1.813 (-2.654; -0.972)*	0.936
≥ 12	N = 196	44.8 (20.6 - 69.7)		-1.861 (-2.667; -1.054)*	



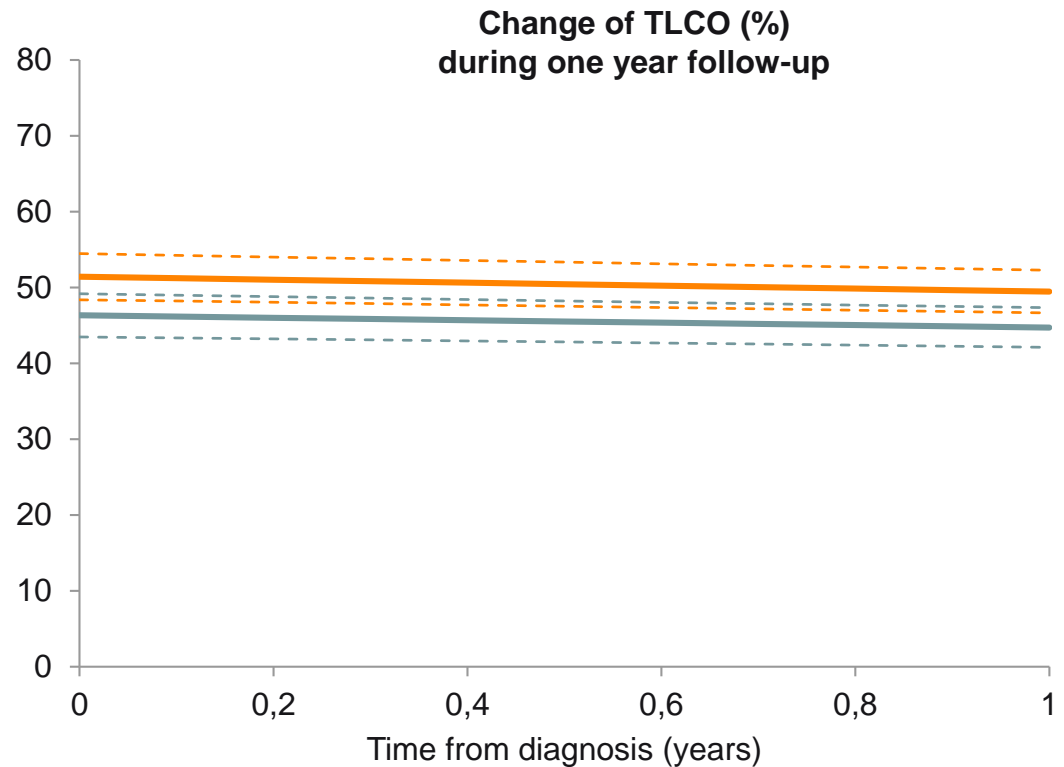
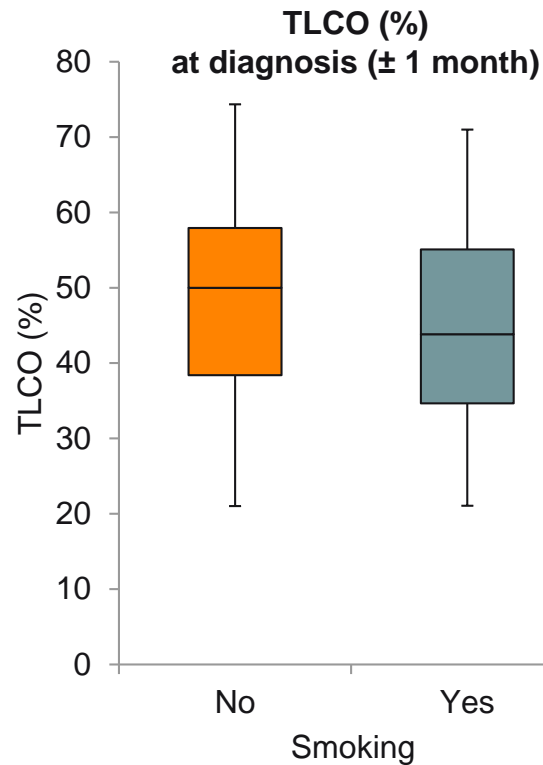
Annual change of FVC (%) – smoking



FVC (%) at diagnosis (± 1 month)				Annual change of FVC (%)	
Smoking	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
No	N = 157	81.9 (51.2 - 114.0)	0.996	-3.394 (-4.172; -2.616)*	0.667
Yes	N = 216	81.8 (51.1 - 118.3)		-3.151 (-3.946; -2.355)*	



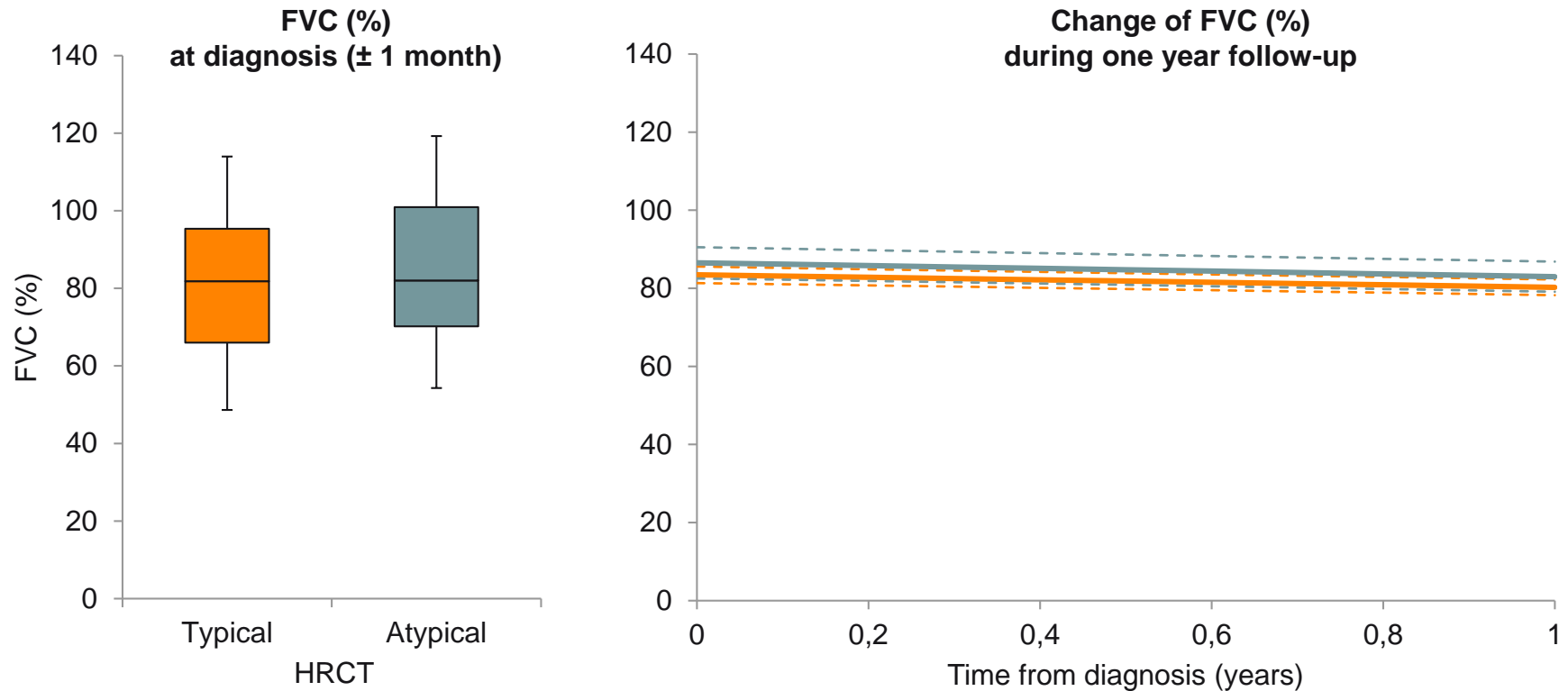
Annual change of TLCO (%) – smoking



Smoking	TLCO (%) at diagnosis (± 1 month)			Annual change of TLCO (%)	
	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
No	N = 155	50.0 (21.0 - 74.4)	0.006	-1.961 (-2.730; -1.193)*	0.546
Yes	N = 212	43.8 (21.1 - 71.0)		-1.606 (-2.467; -0.746)*	



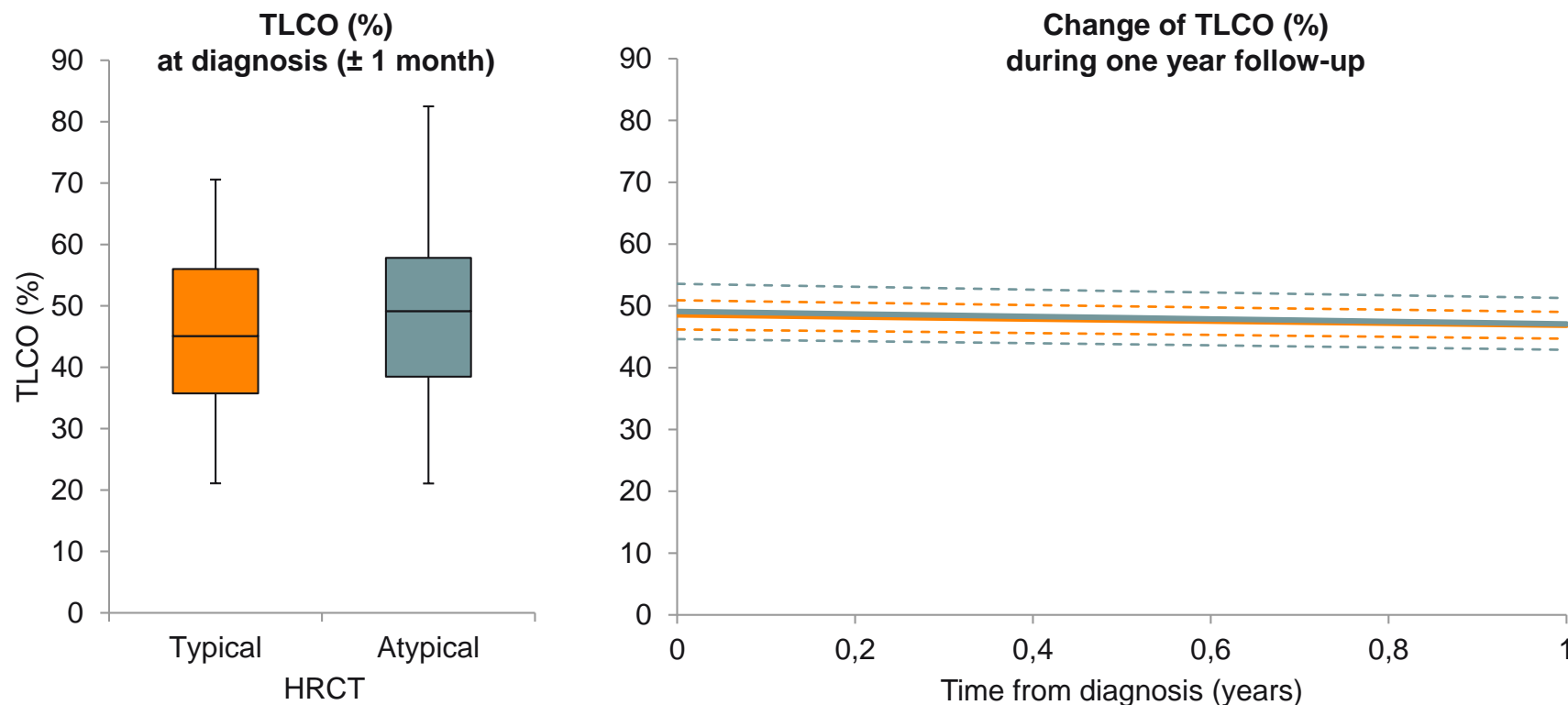
Annual change of FVC (%) – HRCT



HRCT	FVC (%) at diagnosis (± 1 month)			Annual change of FVC (%)	
	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
Typical	N = 289	81.8 (48.7 - 114.0)	0.289	-3.200 (-3.824; -2.576)*	0.613
Atypical	N = 84	82.0 (54.3 - 119.3)		-3.552 (-4.770; -2.333)*	



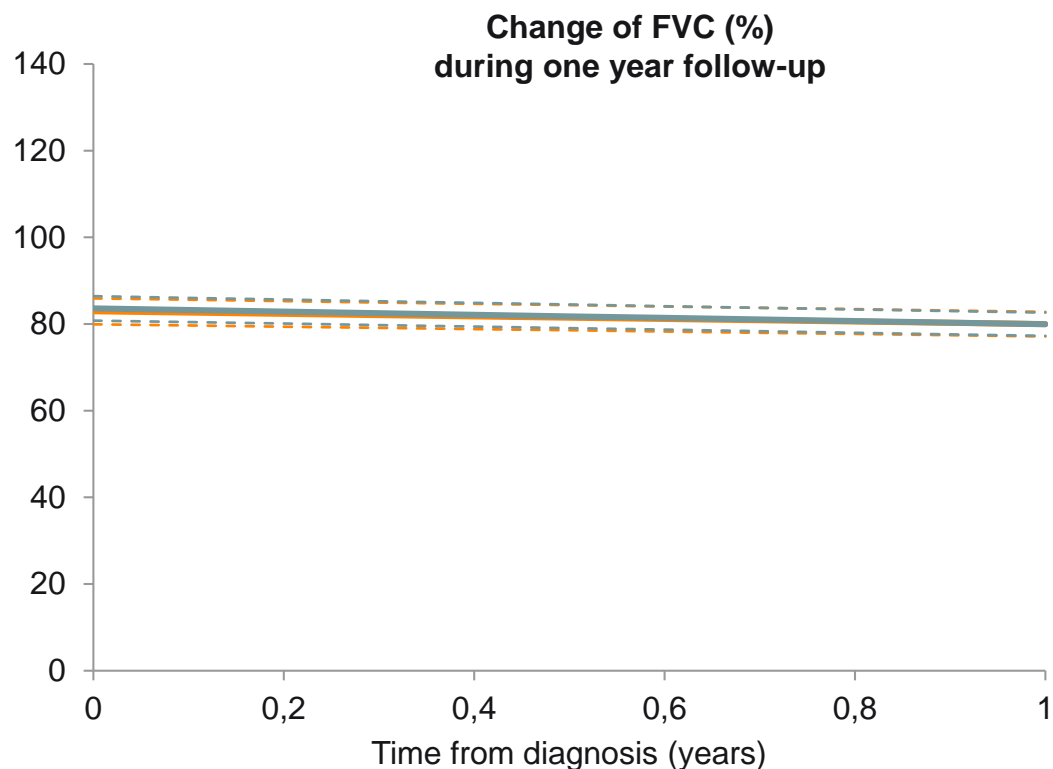
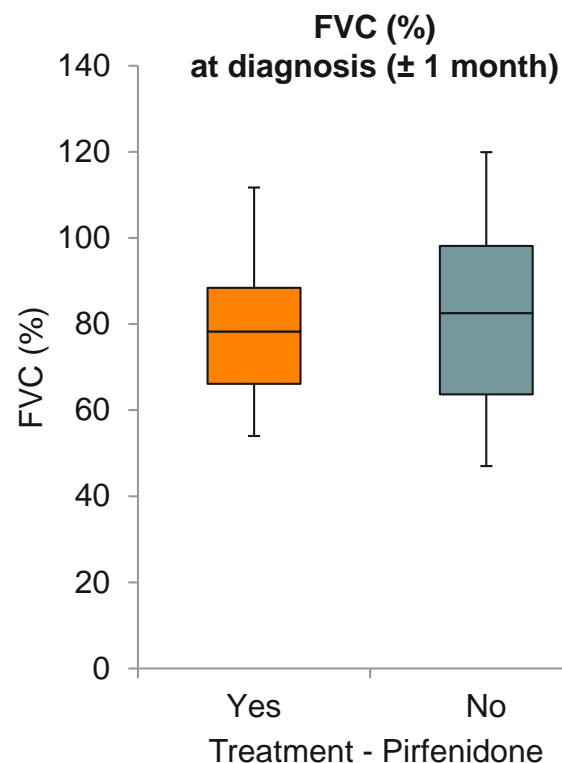
Annual change of TLCO (%) – HRCT



HRCT	TLCO (%) at diagnosis (± 1 month)			Annual change of TLCO (%)	
	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
Typical	N = 284	45.1 (21.1 - 70.6)	0.141	-1.689 (-2.339; -1.040)*	0.637
Atypical	N = 83	49.2 (21.1 - 82.5)		-2.010 (-3.175; -0.845)*	



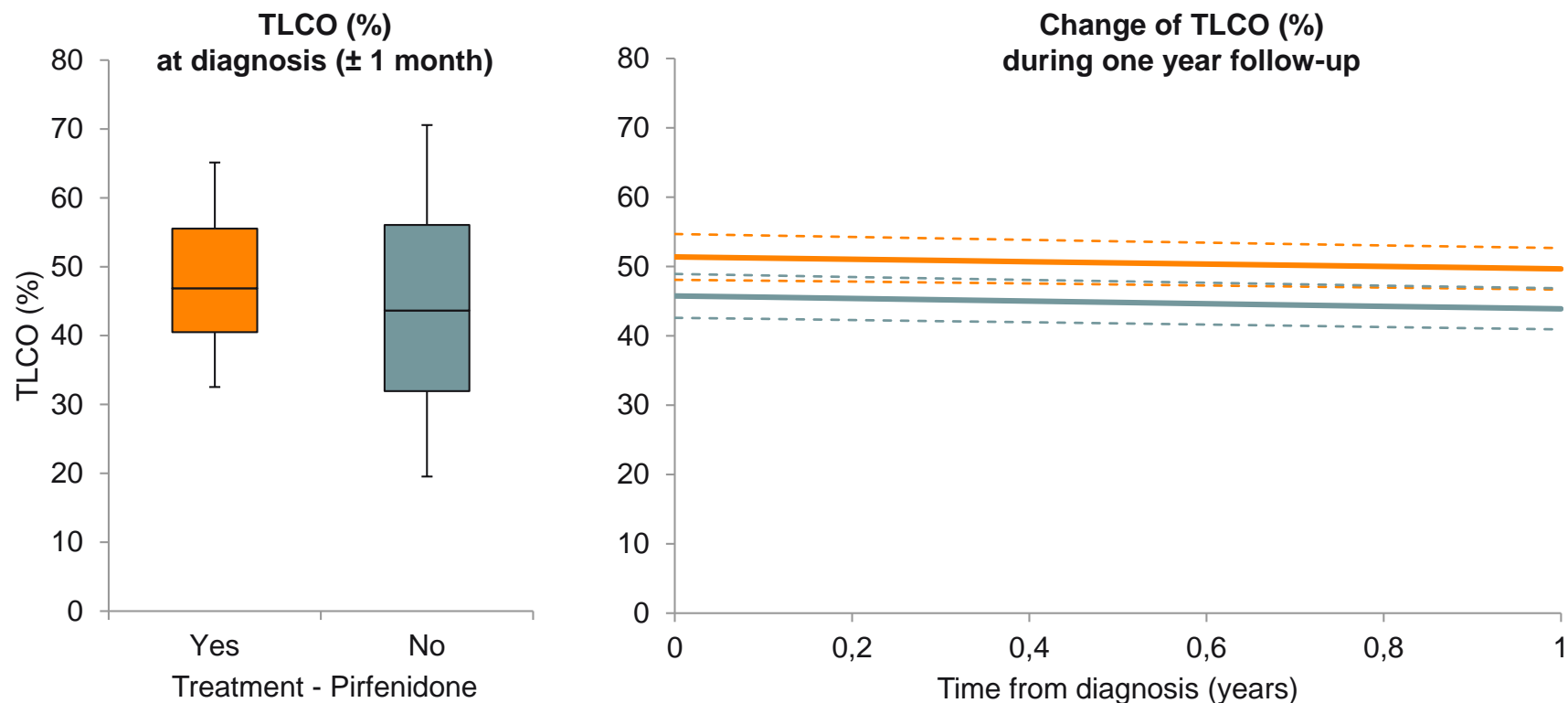
Annual change of FVC (%) – pirfenidone



Treatment - Pirfenidone	FVC (%) at diagnosis (± 1 month)			Annual change of FVC (%)	
	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
Yes	N = 141	78.3 (54.0 - 111.7)	0.285	-2.957 (-3.753; -2.161)*	0.228
No	N = 180	82.5 (47.0 - 120.0)		-3.664 (-4.497; -2.830)*	



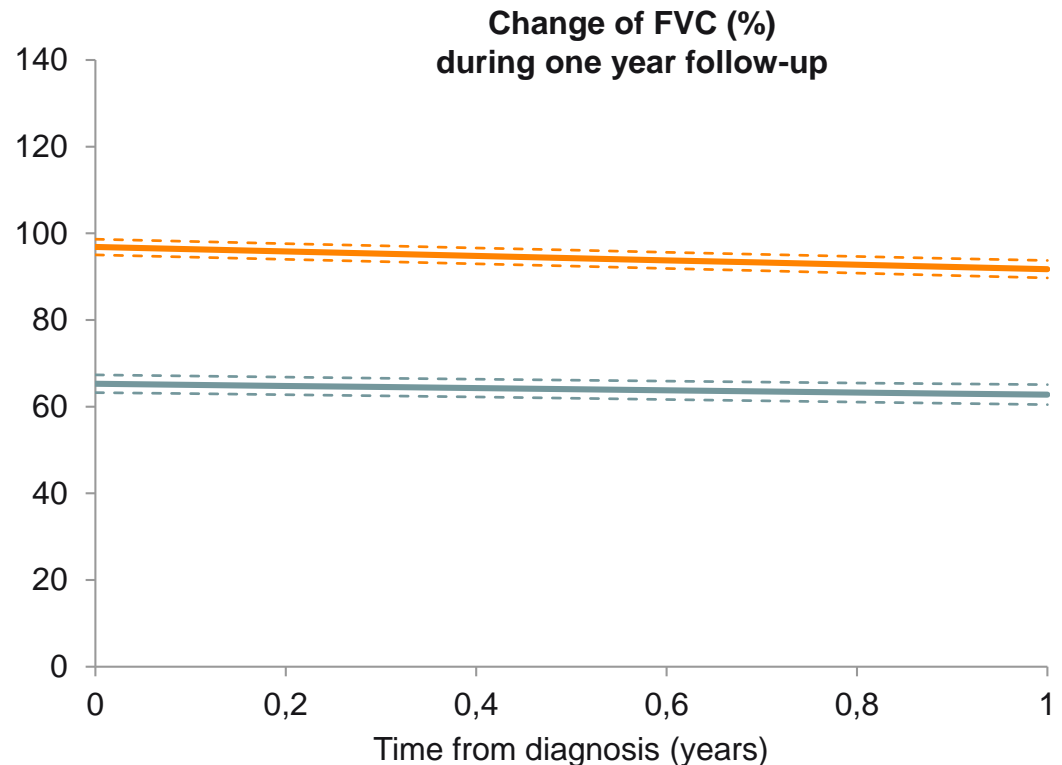
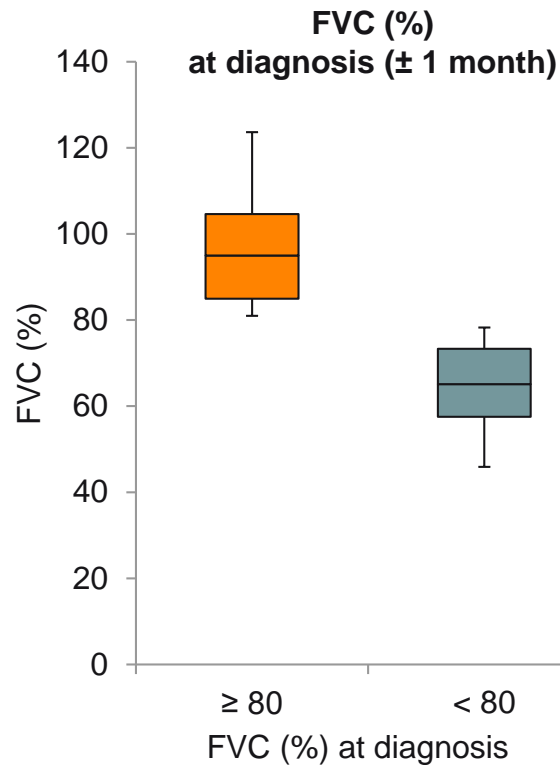
Annual change of TLCO (%) – Pirfenidone



Treatment - Pirfenidone	TLCO (%) at diagnosis (± 1 month)			Annual change of TLCO (%)	
	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
Yes	N = 140	46.9 (32.5 - 65.1)	0.013	-1.722 (-2.631; -0.814)*	0.804
No	N = 176	43.6 (19.5 - 70.6)		-1.875 (-2.670; -1.081)*	



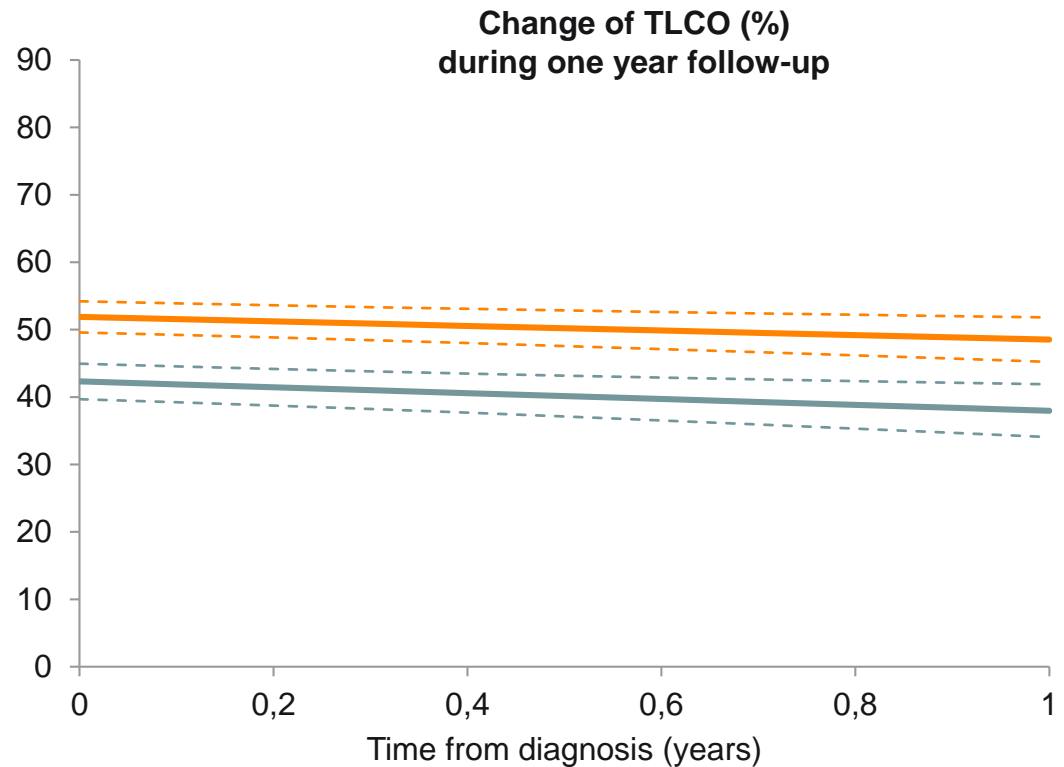
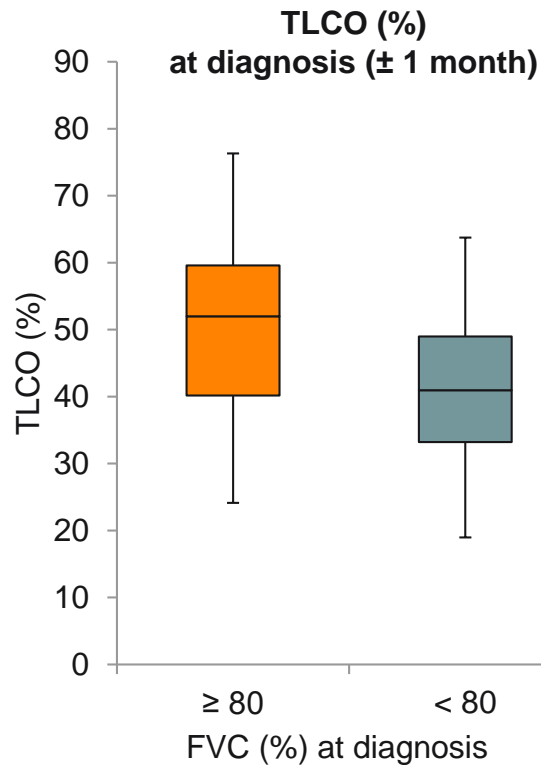
Annual change of FVC (%) – FVC (%) at diagnosis



FVC (%) at diagnosis (± 1 month)		Annual change of FVC (%)			
FVC (%) at diagnosis	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
≥ 80	N = 205	95.0 (81.0 - 123.7)	< 0.001	-5.118 (-6.152; -4.084)*	0.003
< 80	N = 168	65.1 (45.9 - 78.3)		-2.527 (-3.828; -1.226)*	



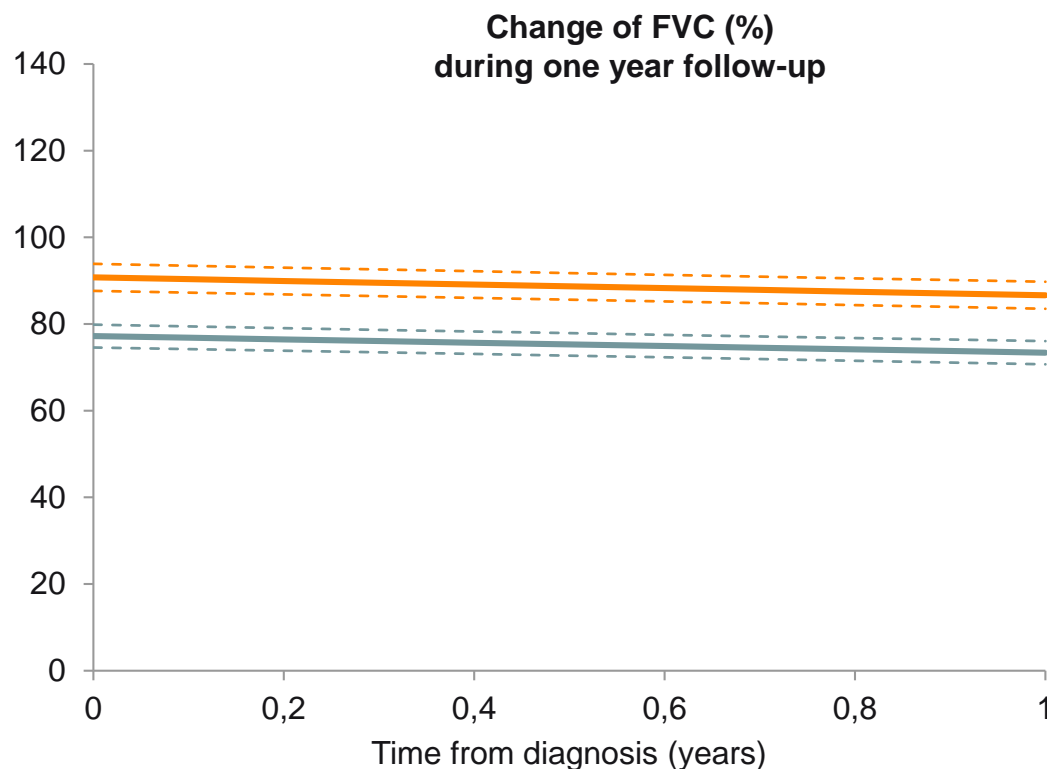
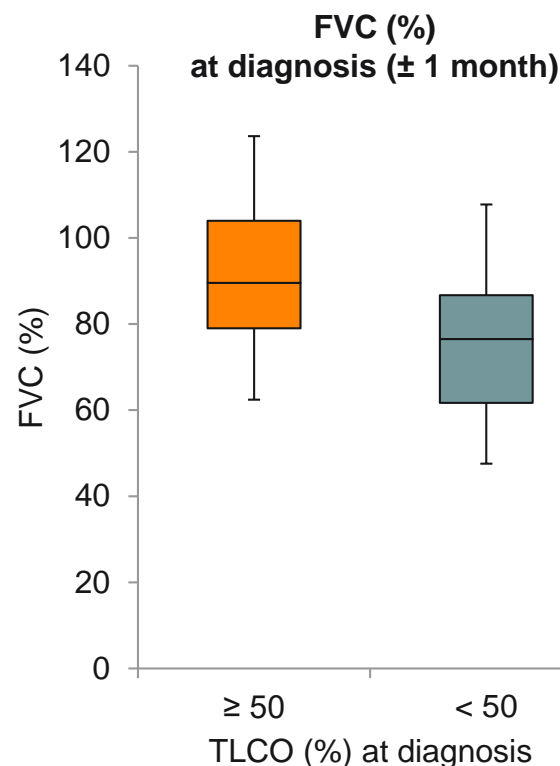
Annual change of TLCO (%) – FVC (%) at diagnosis



TLCO (%) at diagnosis (± 1 month)				Annual change of TLCO (%)	
FVC (%) at diagnosis	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
≥ 80	N = 202	52.0 (24.1 - 76.3)	< 0.001	-3.386 (-5.566; -1.206)*	0.593
< 80	N = 165	40.9 (19.0 - 63.8)		-4.352 (-7.154; -1.550)*	



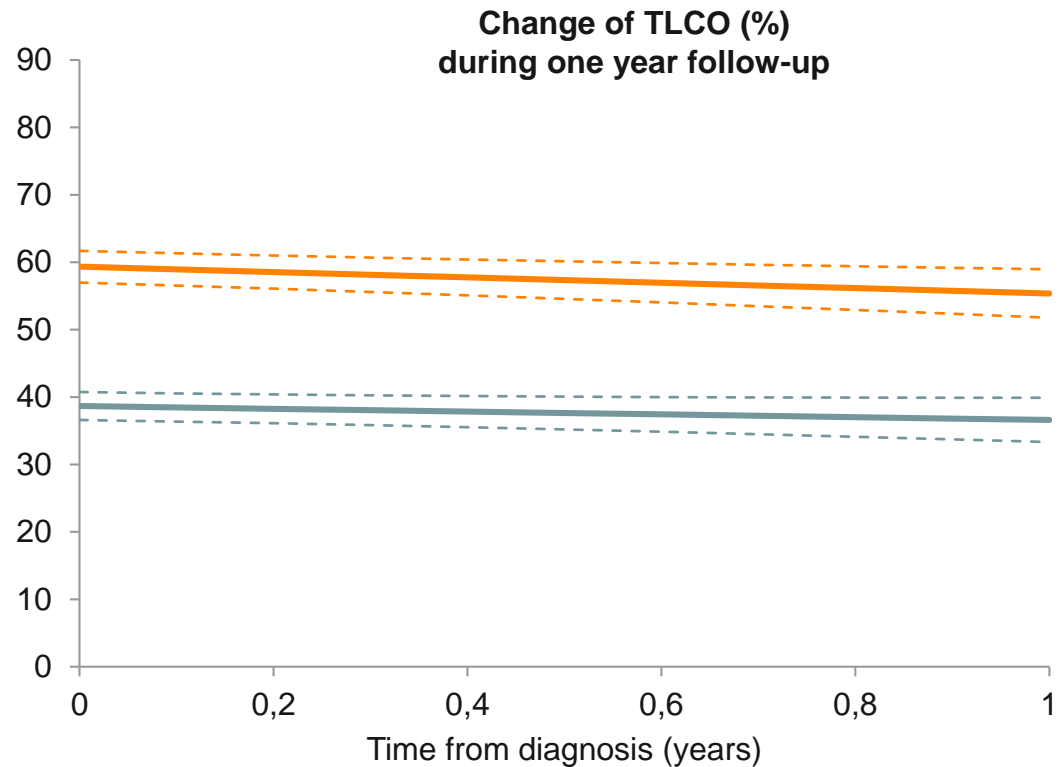
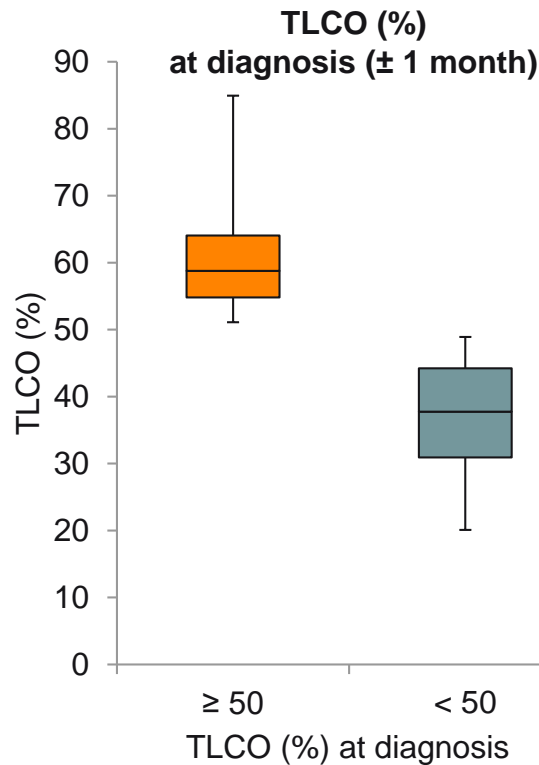
Annual change of FVC (%) – TLCO (%) at diagnosis



FVC (%) at diagnosis (± 1 month)		Annual change of FVC (%)			
TLCO (%) at diagnosis	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
≥ 50	N = 149	89.6 (62.4 - 123.7)	< 0.001	-4.119 (-5.221; -3.018)*	0.719
< 50	N = 215	76.5 (47.6 - 107.8)		-3.832 (-4.967; -2.696)*	



Annual change of TLCO (%) – TLCO (%) at diagnosis



TLCO (%) at diagnosis (± 1 month)				Annual change of TLCO (%)	
TLCO (%) at diagnosis	Valid N	Median (5.-95.percentile)	P-value	Estimate (95% CI)	P-value
≥ 50	N = 149	58.8 (51.1 - 84.9)	< 0.001	-3.972 (-6.403; -1.540)*	0.289
< 50	N = 215	37.7 (20.1 - 48.9)		-2.059 (-4.629; 0.510)	





EMPIRE
(IPF)

**Thank you for attendance on the
3rd international SC meeting**