

Figure S1. Flow chart showing the patients and respective lung function measurements included for the main analysis and the subgroup analysis.

N_{pat}: number of patients; N_{meas}: number of measurements; EM: electron microscopy

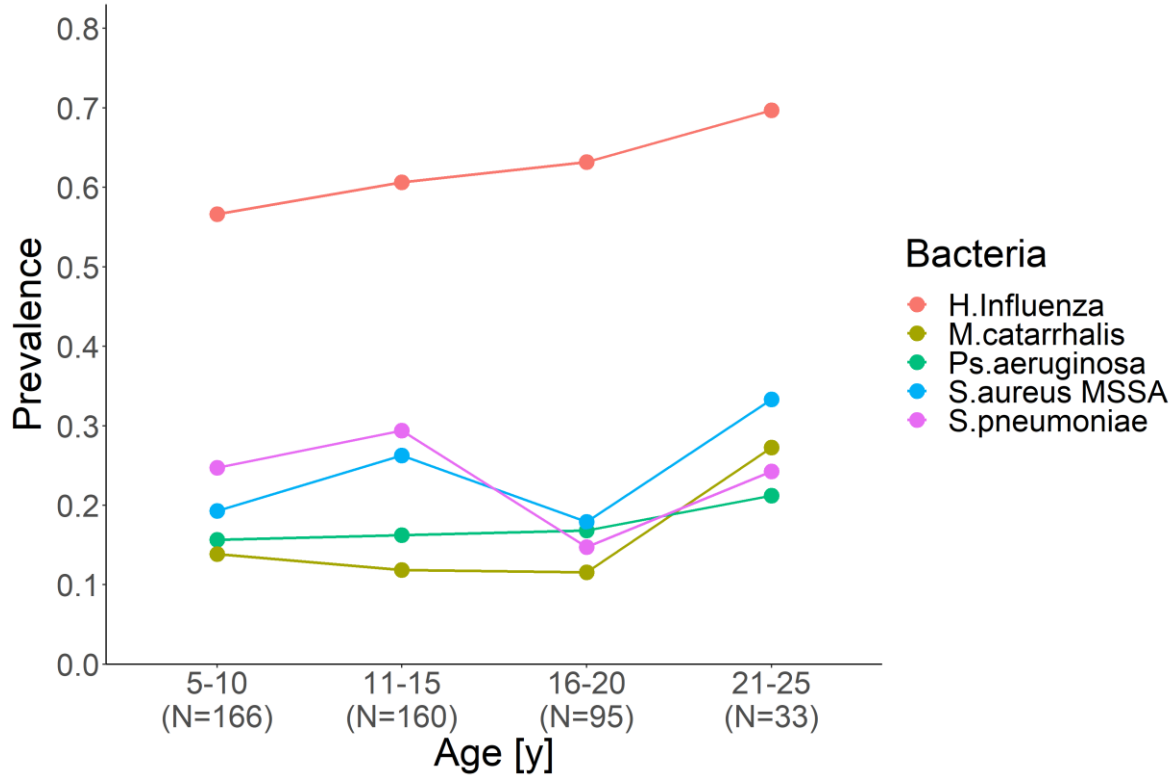


Figure S2. Cross-sectional prevalence of bacteria isolated from the respiratory tract in patients with primary ciliary dyskinesia (PCD) from the international PCD cohort.

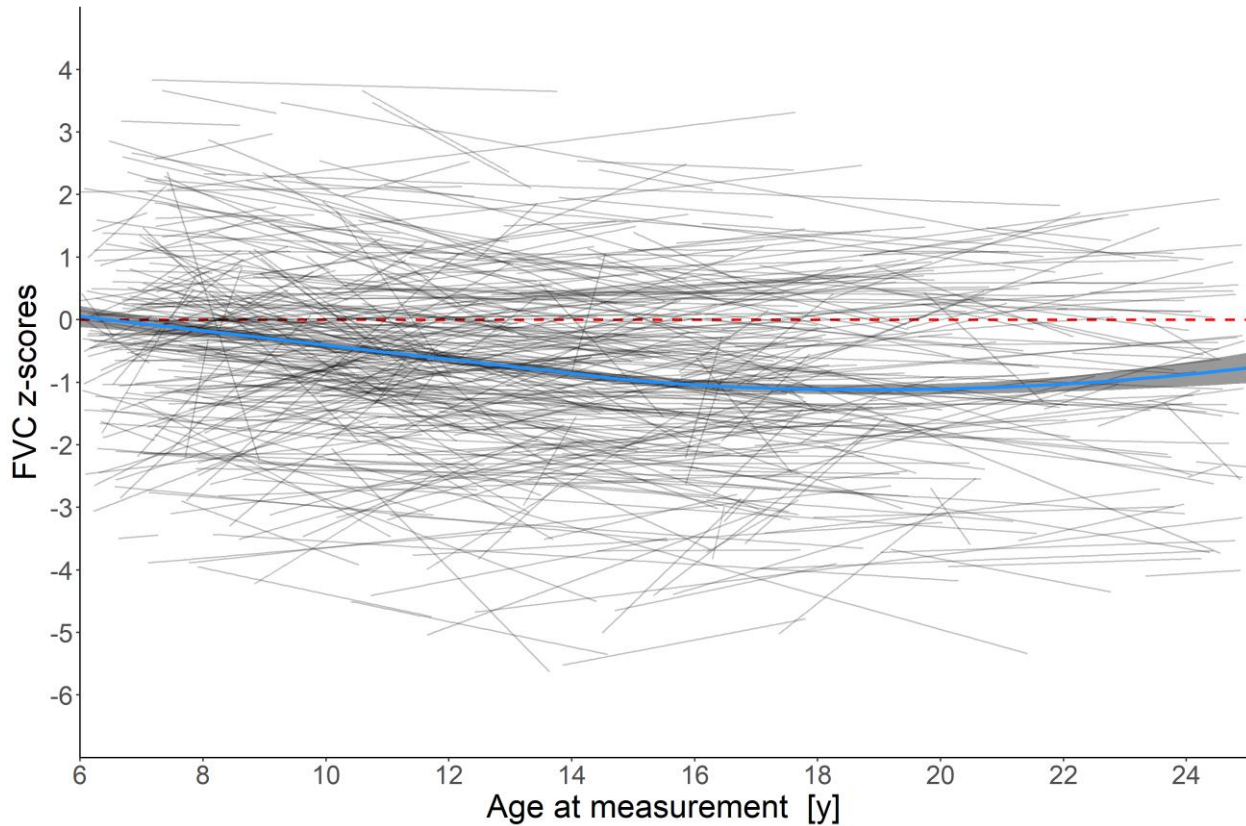


Figure S3. FVC trajectories during the lung growth period compared to Global Lung Function Initiative 2012 reference values.

FVC (Forced vital capacity) is presented as z-score. A loess curve (blue line) was used to display the trajectory over time of all measurements and is plotted with a 95% confidence interval (shaded bands). Grey lines represent the individual linear trajectories of each patient included in the study. The dashed line shows the mean z-score of the normal population

Table S1 FVC of patients with primary ciliary dyskinesia (PCD) from the international PCD cohort, compared to Global Lung Function Initiative 2012 reference values (linear mixed effects regression, adjusting for all covariates).

Variable	Estimate	FVC		p-value [¶]
		95% CI		
Intercept (Lung function at age 6 years for “reference patient”) [†]	-1.10	-2.07	-0.13	
Age at measurement	0.02	-0.07	0.11	
Country (Ref: Germany)				<0.01
Australia	0.06	-0.90	1.02	
Belgium	0.76	-0.10	1.62	
Cyprus	-0.82	-1.81	0.17	
Czech Republic	-0.73	-1.49	0.03	
Denmark	1.09	0.43	1.73	
France	0.80	-0.02	1.63	
Greece	1.09	-2.46	4.64	
Israel	0.36	-0.49	1.22	
Italy	0.52	-0.25	1.30	
Netherlands	2.98	2.16	3.81	
Norway	0.38	-0.59	1.36	
Poland	-0.01	-0.88	0.87	
Switzerland	0.52	-0.26	1.31	
Turkey	-1.78	-2.51	-1.05	
UK	-0.20	-1.05	0.65	
Sex (Ref: male)				0.79
Female	-0.11	-0.42	0.20	
Age at diagnosis	-0.02	-0.05	0.01	0.47
Diagnostic period	0.01	-0.02	0.04	0.49
Diagnostic certainty (Ref: definite PCD diagnosis)				0.30
Probable PCD diagnosis	-0.12	-0.52	0.29	
Clinical diagnosis only	0.33	-0.35	1.01	
Laterality defects (Ref: Situs solitus)				0.40
Situs Ambiguous	0.16	-0.83	1.15	
Situs Inversus	0.30	-0.05	0.64	
Situs Unknown	0.00	-0.74	0.72	
BMI	0.40	0.35	0.45	<0.01
Change of lung function over time				
Country (Ref: Germany)				<0.01
Australia	-0.05	-0.13	0.04	
Belgium	-0.10	-0.18	-0.02	
Cyprus	-0.04	-0.12	0.05	
Czech Republic	-0.02	-0.09	0.06	
Denmark	-0.05	-0.12	0.01	
France	-0.10	-0.18	-0.03	
Greece	-0.08	-0.41	0.25	
Israel	-0.09	-0.17	-0.01	
Italy	-0.09	-0.17	-0.02	
Netherlands	-0.26	-0.37	-0.16	
Norway	-0.07	-0.18	0.04	
Poland	-0.04	-0.14	0.06	

Switzerland	-0.06	-0.14	0.02	
Turkey	0.08	0.01	0.16	
UK	-0.05	-0.13	0.04	
Sex (Ref: male)				0.61
Female	0.01	-0.02	0.04	
Age at diagnosis	0.002	-0.001	0.005	0.24
Diagnostic period	-2.12	-0.003	0.003	0.99
Diagnostic certainty (Ref: definite PCD diagnosis)				0.21
Probable PCD diagnosis	-0.01	-0.05	0.03	
Clinical diagnosis only	-0.07	-0.14	0.01	
Laterality defects (Ref: situs solitus)				0.73
Situs Ambiguous	-0.004	-0.10	0.09	
Situs Inversus	-0.01	-0.04	0.02	
Situs Unknown	-0.04	-0.10	0.03	
BMI	0.01	-0.005	0.02	0.01

FVC: Forced vital capacity; BMI: body mass index

[¶] Likelihood ratio test p-value indicating whether the characteristic explains differences in FVC within the study population.

[†] The Intercept describes the FVC of a reference patient at 6 years, who is male, from Germany, with a BMI z-score of 0, diagnosed at age 6 years in 1978, with a definite PCD diagnosis. Categorical variables describe the change from the reference category, while continuous variables describe the change from the reference patient for each unit of increase. * Defined as hallmark PCD ultrastructural defect identified by electron microscopy findings or biallelic PCD causing gene mutation based on the ERS PCD diagnosis guidelines [14]. [#] Abnormal light or high frequency video microscopy finding and/or low (≤ 77 nl/min) nasal NO value. Change of lung function over time describes the change in the trajectory of FEV₁ per year increase, based on the reference category for categorical variables and for each unit of increase for continuous variables.

Table S2 FEV₁/FVC of patients with primary ciliary dyskinesia (PCD) from the international PCD cohort, compared to Global Lung Function Initiative 2012 reference values (linear mixed effects regression, adjusting for all covariates).

Variable	Estimate	FEV/FVC		p-value [¶]
		95% CI		
Intercept (FEV ₁ /FVC at age 6 years for “reference patient”) ⁺	-0.36	-1.28	0.56	
Age at measurement	-0.09	-0.18	0.01	
Country (Ref: Germany)				<0.01
Australia	-0.70	-1.61	0.20	
Belgium	-1.75	-2.58	-0.93	
Cyprus	-0.51	-1.45	0.42	
Czech Republic	-0.40	-1.12	0.31	
Denmark	-1.25	-1.86	-0.63	
France	-1.16	-1.95	-0.38	
Greece	-0.07	-3.45	3.31	
Israel	-0.50	-1.31	0.31	
Italy	-1.32	-2.06	0.31	
Netherlands	-1.88	-2.65	-1.11	
Norway	-1.16	-2.09	-0.24	
Poland	-1.59	-2.42	-0.76	
Switzerland	-0.42	-1.16	0.33	
Turkey	-0.39	-1.09	0.30	
UK	-1.60	-2.42	-0.77	
Sex (Ref: male)				0.06
Female	-0.05	-0.35	0.24	
Age at diagnosis	-0.001	-0.01	0.03	0.01
Diagnostic period	0.02	-0.01	0.05	0.04
Diagnostic certainty (Ref: definite PCD diagnosis)				0.02
Probable PCD diagnosis	0.17	-0.22	0.56	
Clinical diagnosis only	0.21	-0.45	0.88	
Laterality defects (Ref: Situs solitus)				0.70
Situs Ambiguous	-0.19	-1.18	0.81	
Situs Inversus	0.08	-0.25	0.40	
Situs Unknown	-0.01	-0.73	0.70	
BMI	-0.04	-0.08	0.01	0.20
Change of lung function over time				
Country (Ref: Germany)				<0.01
Australia	0.04	-0.05	0.13	
Belgium	0.21	-0.12	0.26	
Cyprus	0.16	0.07	0.26	
Czech Republic	0.09	0.01	0.17	
Denmark	0.05	-0.02	0.12	
France	0.11	0.02	0.19	
Greece	0.17	-0.16	0.50	
Israel	0.08	-0.01	0.16	
Italy	0.11	0.04	0.19	
Netherlands	0.18	0.07	0.22	
Norway	0.10	-0.01	0.22	
Poland	0.16	0.06	0.26	

Switzerland	0.03	-0.05	0.11	
Turkey	0.06	-0.01	0.14	
UK	0.10	0.02	0.19	
Sex (Ref: male)				0.17
Female	-0.02	-0.05	0.01	
Age at diagnosis	0.004	0.001	0.01	0.02
Diagnostic period	-0.004	-0.01	-0.001	0.01
Diagnostic certainty (Ref: definite PCD diagnosis)				0.20
Probable PCD diagnosis	-0.001	-0.04	0.04	
Clinical diagnosis only	0.07	-0.01	0.15	
Laterality defects (Ref: situs solitus)				0.41
Situs Ambiguous	0.05	-0.06	0.15	
Situs Inversus	-0.02	-0.06	0.01	
Situs Unknown	-0.01	-0.09	0.06	
BMI	0.01	-0.01	0.02	0.17

FEV₁: Forced expiratory volume in 1 second; FVC: Forced vital capacity; BMI: body mass index

[¶] Likelihood ratio test p-value indicating whether the characteristic explains differences in FEV₁/FVC within the study population.

[†] The Intercept describes the FEV₁/FVC of a reference patient at 6 years, who is male, from Germany, with a BMI z-score of 0, diagnosed at age 6 years in 1978, with a definite PCD diagnosis. Categorical variables describe the change from the reference category, while continuous variables describe the change from the reference patient for each unit of increase. * Defined as hallmark PCD ultrastructural defect identified by electron microscopy findings or biallelic PCD causing gene mutation based on the ERS PCD diagnosis guidelines [14]. [#] Abnormal light or high frequency video microscopy finding and/or low (≤ 77 nl/min) nasal NO value.

Change of lung function over time describes the change in the trajectory of FEV₁/FVC per year increase, based on the reference category for categorical variables and for each unit of increase for continuous variables.

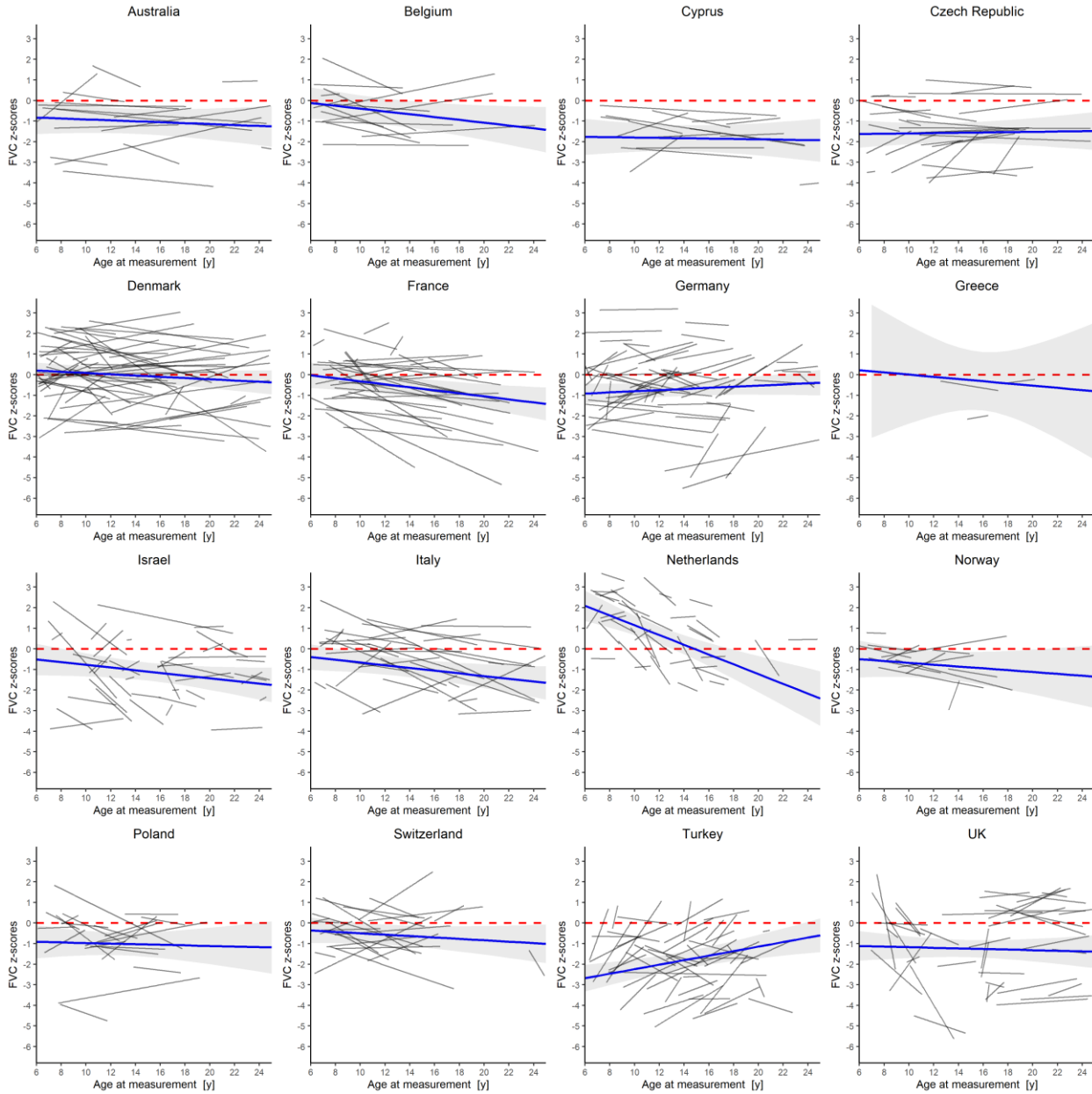


Figure S4. FVC trajectories of PCD patients in different countries compared to Global Lung Function Initiative (GLI) 2012 reference values.

Individual trajectories are shown as black lines, marginal effects (estimated regression line for subgroup) as blue lines, 95% confidence intervals as grey shaded areas. The dashed line shows the mean z-score of the normal population (GLI 2012). FVC: Forced vital capacity

Table S3. FEV₁ and FVC of patients with primary ciliary dyskinesia (PCD) from the international PCD cohort with available ultrastructural defect information compared to Global Lung Function Initiative 2012 reference values (N = 366).

Variable	FEV ₁			FVC			
	Estimate	95% CI	p-value	Estimate	95% CI	p-value	
Intercept (Lung function at age 6 years for “reference patient”) +	-1.27	-2.41	-0.13	-0.35	-1.54	0.83	
Age at measurement	-0.02	-0.12	0.08	-0.08	-0.18	0.03	
Country (Ref: Germany)							<0.01
Australia	-0.29	-1.30	0.71	-0.20	-1.24	0.84	
Belgium	-0.02	-0.92	0.87	0.66	-0.27	1.58	
Cyprus	-1.40	-2.36	-0.44	-1.14	-2.14	-0.14	
Czech Republic	-1.02	-1.80	-0.23	-0.90	-1.71	-0.09	
Denmark	0.53	-0.20	1.26	1.03	0.27	1.78	
France	0.74	-0.22	1.70	1.04	0.04	2.04	
Israel	0.63	-0.32	1.58	0.69	-0.29	1.68	
Italy	-0.43	-1.26	0.40	0.34	-0.52	1.21	
Netherlands	1.71	0.74	2.68	2.78	1.78	3.78	
Norway	-0.20	-1.20	0.81	0.27	-0.77	1.31	
Poland	-1.01	-2.04	0.02	-0.32	-1.40	0.75	
Switzerland	0.07	-0.79	0.93	0.07	-0.82	0.97	
Turkey	-1.04	-2.27	0.19	-1.24	-2.52	0.03	
UK	-1.02	-1.96	-0.08	-0.57	-1.55	0.40	
Sex (Ref: male)							0.08
Female	-0.05	-0.39	0.30	-0.28	-0.63	0.08	0.30
Age at diagnosis	-0.01	-0.04	0.03	-0.004	-0.04	0.03	0.15
Diagnostic period	0.02	-0.01	0.05	-0.01	-0.04	0.03	0.57
Laterality defects (Ref: Situs solitus)							0.81
Situs Ambiguous	0.25	-0.71	1.20	0.13	-0.86	1.12	
Situs Inversus	0.14	-0.25	0.53	0.04	-0.37	0.45	
Situs Unknown	-0.41	-1.23	0.41	-0.50	-1.35	0.36	
Ultrastructural defects (Ref: ODA)							0.01
Central Complex defect	-0.11	-0.67	0.45	-0.36	-0.94	0.22	
ODA/IDA	0.67	0.19	1.14	0.41	-0.08	0.90	
Microtubular disorganisation	-0.49	-1.15	0.17	-0.47	-1.16	0.22	
Non-diagnostic	0.36	-0.20	0.91	0.10	-0.48	0.68	
BMI	0.34	0.29	0.39	0.43	0.37	0.48	<0.01
Change of lung function over time							
Country (Ref: Germany)							<0.01
Australia	-0.03	-0.12	0.05	-0.02	-0.11	0.07	
Belgium	-0.01	-0.09	0.07	-0.07	-0.15	0.02	
Cyprus	0.05	-0.03	0.14	-0.02	-0.11	0.07	
Czech Republic	0.02	-0.05	0.10	-0.004	-0.08	0.07	
Denmark	-0.05	-0.12	0.02	-0.05	-0.12	0.02	
France	-0.10	-0.19	-0.02	-0.12	-0.21	-0.03	
Israel	-0.11	-0.20	-0.02	-0.11	-0.20	-0.01	
Italy	-0.06	-0.13	0.02	-0.08	-0.16	-0.004	

Netherlands	-0.17	-0.31	-0.03		-0.24	-0.38	-0.10	
Norway	-0.04	-0.15	0.06		-0.07	-0.19	0.04	
Poland	0.06	-0.06	0.17		-0.04	-0.16	0.09	
Switzerland	-0.02	-0.10	0.07		0.01	-0.07	0.10	
Turkey	0.01	-0.11	0.12		0.01	-0.11	0.13	
UK	0.01	-0.08	0.10		-0.01	-0.10	0.08	
Sex (ref: male)				0.11				0.20
Female	-0.03	-0.06	0.01		0.02	-0.01	0.06	
Age at diagnosis	0.003	-0.001	0.01	0.09	0.002	-0.002	0.005	0.33
Diagnostic period	-0.001	-0.004	0.002	0.50	0.002	-0.001	0.005	0.18
Laterality defects (Ref: Situs solitus)				0.99				0.87
Situs Ambiguous	0.01	-0.08	0.09		0.003	-0.09	0.09	
Situs Inversus	-0.004	-0.04	0.03		0.02	-0.02	0.05	
Situs Unknown	-0.01	-0.08	0.06		0.01	-0.07	0.08	
Ultrastructural defects (Ref: ODA)				0.04				0.18
Central Complex defect	0.03	-0.02	0.07		0.05	-0.001	0.10	
ODA/IDA	-0.05	-0.09	-0.01		-0.01	-0.05	0.04	
Microtubular disorganisation	0.01	-0.05	0.08		0.06	-0.01	0.12	
Non-diagnostic	-0.01	-0.06	0.05		-0.02	-0.08	0.04	
BMI	0.01	0.004	0.03	<0.01	0.01	0.00	0.02	0.04

[¶] Likelihood ratio test p-value indicating whether the characteristic explains differences in FEV₁ or FVC within the study population.

Adjusted for all variables of the full model, the full summary output is in the online supplement (Table S1).

+ The Intercept describes the FEV₁ and FVC of a reference patient 6 years, who is male, from Germany, with a BMI z-score of 0, diagnosed at birth (age = 0) in 1978, with a definite PCD diagnosis. Categorical variables describe the change from the reference category, while continuous variables describe the change from the reference patient for each unit of increase. Change of lung function over time describes the change in the trajectory of FEV₁ and FVC per year increase, based on the reference category for categorical variables and for each unit of increase for continuous variables.

FEV₁: Forced expiratory volume in 1 second; FVC: Forced vital capacity; ODA: outer dynein arm; IDA: inner dynein arm; BMI: body mass index

Table S4. FEV₁ of patients with primary ciliary dyskinesia (PCD) from the international PCD cohort compared to Global Lung Function Initiative 2012 reference values (linear mixed effects regression, adjusting for all covariates) for single countries with more than 30 patients

N: measurements, individuals	Denmark 1459, 59			France 340, 38			Germany 664, 60			Israel 239, 41		
	Estimate	95% CI	p-val	estimate	95% CI	p-val	Estimate	95% CI	p-val	Estimate	95% CI	p-val
Intercept	0.26	-1.18	1.71	-0.98	-2.12	0.17	-6.91	-11.43	-2.39	88.5	-41.6	218
Sex (Ref: male)			0.28			0.11			0.38			<0.01
Female	-0.28	-1.03	0.48	-0.73	-1.40	-0.06	0.56	-0.23	1.35	-0.65	-1.94	0.64
Age at diagnosis	-0.10	-0.19	0.02	0.04	-0.01	-0.10	0.08	0.69	-0.18	-0.30	-0.06	0.02
Diagnostic period	0.01	-0.05	0.07	0.85	0.01	-0.05	0.07	0.04	0.023	-0.07	0.39	0.02
Diagnostic certainty (Ref: definite)			0.23			0.70			0.46			0.02
Probable PCD	-0.08	-0.86	0.70	-	-	-	-0.49	-1.40	0.42	1.91	0.29	3.54
Clinical diagnosis	-0.24	-2.62	2.13	0.29	-0.60	1.17	-1.47	-3.25	0.31	0.63	-0.93	2.19
Laterality defects (Ref: situs solitus)			0.34			0.11			0.06			0.02
Situs Ambiguous	-	-	-	-	-	-	2.08	-0.99	5.14	-	-	-
Situs Inversus	-0.80	-1.62	0.02	1.11	0.19	2.04	1.26	0.31	2.21	0.90	-0.59	2.40
Situs Unknown	-0.09	-2.78	2.60	0.53	-0.21	1.27	-	-	-	-2.93	-5.27	-0.59
BMI	0.48	0.38	0.57	<0.01	0.15	0.00	0.29	0.02	0.42	0.31	0.53	<0.01
Change in FEV1 over time												
Sex (Ref: male)			0.28			0.64			0.54			0.39
Female	-0.3	-0.09	0.03	0.02	-0.07	0.11	-0.03	-0.11	0.06	-0.07	-0.21	0.08
Age at diagnosis	0.01	0.002	0.01	0.02	-0.003	-0.01	0.01	0.56	0.02	0.002	0.03	0.04
Diagnostic period	-0.001	-0.01	0.004	0.57	0.01	0.001	0.02	0.04	-0.01	-0.03	0.01	0.27
Diagnostic certainty (Ref: definite)			0.16			0.89			0.51			0.06
Probable PCD	-0.06	-0.13	0.003	-	-	-	0.06	-0.04	0.16	-0.21	-0.39	-0.03
Clinical diagnosis	-0.08	-0.31	0.16	0.01	-0.15	0.17	0.05	-0.13	0.22	0.04	-0.17	0.25
Laterality defects (Ref: situs solitus)			0.58			0.69			0.53			0.09
Situs Ambiguous	-	-	-	-	-	-	-0.13	-0.43	0.17	-	-	-
Situs Inversus	0.02	-0.05	0.09	0.02	-0.10	0.13	-0.04	-0.13	0.06	-0.12	-0.29	0.04
Situs Unknown	-0.08	-0.27	0.11	-0.03	-0.12	0.06	-	-	-	0.18	-0.07	0.43
BMI	0.004	-0.02	0.03	0.72	0.03	0.001	0.06	0.05	0.03	0.002	0.05	0.05

Models adjusted for age at measurement as a linear term and age at measurement as quadratic term

N: measurements, individuals	Italy 163, 32			Netherlands 114, 38			Turkey 329, 49			UK 167, 37		
	Estimate	95% CI	p-val	estimate	95% CI	p-val	Estimate	95% CI	p-val	Estimate	95% CI	p-val
Intercept	0.28	-1.98	2.53	-8.26	-20.7	4.13	-6.13	-13.37	1.11	4.18	-0.52	8.88

Sex (Ref: male)				0.58				0.04				0.60				0.81
Female	-0.30	-1.56	0.96		2.01	0.57	3.45		0.60	-0.54	1.74		-0.46	-1.94	1.01	
Age at diagnosis	-0.08	-0.20	0.04	0.15	-0.22	-0.70	0.26	0.02	-0.20	-0.41	0.02	<0.01	0.36	0.20	0.52	<0.01
Diagnostic period	-0.06	-0.15	0.02	0.23	0.28	-0.19	0.75	0.05	0.14	-0.10	0.38	0.04	-0.23	-0.38	-0.08	0.01
Diagnostic certainty (Ref: definite PCD)				<0.01				0.53				0.21				0.06
Probable PCD	0.27	-2.38	2.91		0.18	-1.46	1.83		-0.17	-1.71	1.38		0.74	-3.94	5.42	
Clinical diagnosis	-1.85	-4.78	1.09		1.55	-7.47	10.57		1.07	-0.58	2.73		7.64	2.36	12.92	
Laterality defects (Ref: situs solitus)				0.43				0.12				0.62				0.04
Situs Ambiguous	-	-	-		-0.09	-3.49	3.32		-	-	-		4.88	0.05	9.70	
Situs Inversus	0.84	-0.81	2.50		2.75	0.72	4.78		0.37	-0.67	1.41		0.68	-0.72	2.08	
Situs Unknown	-	-	-		6.78	-5.70	19.2		-	-	-		-4.34	-10.16	1.46	
BMI (continuous)	0.33	0.16	0.49	<0.01	0.32	0.01	0.64	0.05	0.28	0.12	0.44	<0.01	0.15	-0.12	0.43	<0.01
Change in FEV1 over time																
Sex (Ref: male)				0.31				0.04				0.40				0.52
Female	0.05	-0.04	0.15		-0.18	-0.34	-0.02		-0.05	-0.17	0.07		0.04	-0.07	0.14	
Age at diagnosis	0.01	0.001	0.02	0.06	0.06	-0.001	0.11	0.05	0.002	-0.03	0.03	0.91	-0.03	-0.05	-0.02	<0.01
Diagnostic period	0.001	-0.01	0.01	0.92	-0.06	-0.13	-0.001	0.05	-0.001	-0.03	0.03	0.99	0.02	0.01	0.04	<0.01
Diagnostic certainty (Ref: definite)				<0.01								0.12				0.03
Probable PCD	0.33	0.10	0.56		0.03	-0.20	0.25	0.97	0.09	-0.07	0.25		-0.03	-0.39	0.34	
Clinical diagnosis	0.66	0.30	1.01		0.03	-0.91	0.98		-0.10	-0.30	0.10		-0.44	-0.78	-0.09	
Laterality defects (Ref: situs solitus)				0.19				0.23				0.83				0.36
Situs Ambiguous	-	-	-		0.03	-0.38	0.44		-	-	-		-0.18	-0.48	0.11	
Situs Inversus	-0.09	-0.22	0.04		-0.23	-0.49	0.04		-0.01	-0.13	0.10		0.04	-0.07	0.14	
Situs Unknown	-	-	-		-0.86	-2.19	0.47		-	-	-		0.24	-0.26	0.74	
BMI	0.04	0.02	0.06	<0.01	0.01	-0.04	0.06	0.69	0.03	0.01	0.06	0.01	0.05	0.02	0.08	<0.01

Models adjusted for age at measurement as a linear term and age at measurement as quadratic term

Table S5 FEV₁ and FVC in patients with primary ciliary dyskinesia (PCD) from the international PCD cohort with available microbiological information compared to Global Lung Function Initiative 2012 reference values.

Characteristic	FEV1				FVC			
	Estimate	95% CI		p-value [¶]	Estimate	95% CI		p-value [¶]
Microbiology								
Any isolated pathogen	0.05	-0.26	0.36	0.07	-0.23	-0.58	0.13	0.01
Haemophilus influenzae	-0.15	-0.43	0.12	0.39	-0.28	-0.59	0.03	0.09
Moraxella catarrhalis	0.04	-0.38	0.47	0.55	0.17	-0.31	0.65	0.50
Pseudomonas aeruginosa	0.37	-0.22	0.96	0.39	0.43	-0.23	1.10	0.11
Streptococcus pneumoniae	-0.11	-0.45	0.23	0.96	-0.11	-0.50	0.28	0.67
Staphylococcus aureus	0.03	-0.37	0.42	0.28	-0.04	-0.50	0.41	0.48
Interactions with age at measurement								
Any isolated pathogen	-0.01	-0.03	0.01	0.38	0.01	-0.02	0.03	0.62
Haemophilus influenzae	0.01	-0.01	0.03	0.38	0.01	-0.01	0.04	0.19
Moraxella catarrhalis	0.0001	-0.03	0.03	1.00	-0.01	-0.04	0.03	0.62
Pseudomonas aeruginosa	-0.02	-0.06	0.02	0.29	-0.02	-0.07	0.02	0.37
Streptococcus pneumoniae	0.01	-0.02	0.03	1.00	0.01	-0.02	0.04	0.46
Staphylococcus aureus	0.003	-0.02	0.03	0.82	0.01	-0.02	0.04	0.65

[¶] Likelihood ratio test p-value indicating whether the characteristic explains differences in FEV₁ or FVC within the study population.

Table S6. Sensitivity analysis: FEV₁ of patients with primary ciliary dyskinesia (PCD) from the international PCD cohort compared to Global Lung Function Initiative 2012 reference values (linear mixed effects regression, adjusting for all covariates) excluding patients diagnosed the same year as first lung function measurement (n=356).

Variable	Estimate	FEV ₁ 95% CI		p-value [¶]
Intercept (Lung function at age 6 years for “reference patient”) ⁺	-1.10	-2.11	-0.09	
Age at measurement	-0.04	-0.13	0.05	
Country (Ref: Germany)				<0.01
Australia	-0.26	-1.30	0.77	
Belgium	-0.24	-1.09	0.61	
Cyprus	-1.05	-2.22	0.11	
Czech Republic	-1.16	-1.93	-0.40	
Denmark	0.22	-0.44	0.87	
France	-0.001	-0.84	0.84	
Greece	1.69	-1.93	5.30	
Israel	0.01	-0.87	0.89	
Italy	-0.19	-0.95	0.58	
Netherlands	1.67	0.84	2.51	
Norway	-0.40	-1.37	0.57	
Poland	-1.15	-2.04	-0.26	
Switzerland	-0.01	-0.80	0.78	
Turkey	-1.76	-2.48	-1.04	
UK	-1.24	-2.11	-0.36	
Sex (Ref: male)				0.28
Female	0.03	-0.28	0.34	
Age at diagnosis	-0.03	-0.06	0.01	0.14
Diagnostic period	0.02	-0.01	0.05	0.43
Diagnostic certainty (Ref: definite PCD diagnosis)				0.51
Probable PCD diagnosis	-0.05	-0.46	0.36	
Clinical diagnosis only	0.43	-0.24	1.10	
Laterality defects (Ref: situs solitus)				0.73
Situs Ambiguous	0.49	-0.50	1.48	
Situs Inversus	0.30	-0.06	0.66	
Situs Unknown	0.12	-0.62	0.86	
BMI	0.33	0.28	0.37	<0.01
Change of lung function over time [#]				
Country (Ref: Germany)				<0.01
Australia	-0.03	-0.12	0.06	
Belgium	0.02	-0.06	0.10	
Cyprus	0.06	-0.04	0.16	
Czech Republic	0.05	-0.02	0.13	
Denmark	-0.01	-0.07	0.05	
France	-0.03	-0.11	0.04	
Greece	-0.06	-0.39	0.28	
Israel	-0.04	-0.13	0.04	
Italy	-0.04	-0.11	0.04	
Netherlands	-0.16	-0.27	-0.05	
Norway	0.001	-0.11	0.11	
Poland	0.07	-0.03	0.17	
Switzerland	-0.01	-0.09	0.06	
Turkey	0.11	0.04	0.18	
UK	0.04	-0.05	0.12	
Sex (Ref: male)				0.20
Female	-0.02	-0.05	0.01	
Age at diagnosis	0.003	0.001	0.01	0.05

Diagnostic period	-0.001	-0.004	0.001	0.33
Diagnostic certainty (Ref: definite PCD diagnosis)				0.99
Probable PCD diagnosis	-0.002	-0.04	0.04	
Clinical diagnosis only	-0.003	-0.07	0.07	
Laterality defects (Ref: situs solitus)				0.64
Situs Ambiguous	-0.02	-0.12	0.08	
Situs Inversus	-0.02	-0.06	0.01	
Situs Unknown	-0.01	-0.08	0.06	
BMI	0.01	0.01	0.02	<0.01

FEV₁: Forced expiratory volume in 1 second; BMI: body mass index ¶ Likelihood ratio test p-value indicating whether the characteristic explains differences in FEV₁ within the study population. [†]The Intercept describes the FEV₁ of a reference patient at 6 years, who is male, from Germany, with a BMI z-score of 0, diagnosed at birth (age = 0) in 1978, with a definite PCD diagnosis. Categorical variables describe the change from the reference category, while continuous variables describe the change from the reference patient for each unit of increase. * Defined as hallmark PCD ultrastructural defect identified by electron microscopy findings or biallelic PCD causing gene mutation based on the ERS PCD diagnosis guidelines [14]. # Abnormal light or high frequency video microscopy finding and/or low (≤ 77 nl/min) nasal NO value. [#]Change in lung function over time are based on interaction terms between the characteristics (e.g. country, sex) and age. Change of lung function over time thus describes the change in the trajectory of FEV₁ per year increase, based on the reference category for categorical variables and for each unit of increase for continuous variables.