**Online only supplementary material**

**METHODS**

**Primary ciliary dyskinesia diagnosis**

The diagnostic criteria for PCD have evolved over many years [1]. Initially, diagnosis was based on the Kartagener triad [2] and transmission electron microscopy findings (EM).Then, light microscopy and, later, high frequency video microscopy (HVM) were introduced into the diagnostic algorithm. Recent recommendations include combining EM, HVM, nasal nitric oxide (nNO), and genetic testing [3], but availability of tests differs between countries [4] so not all PCD patients have been diagnosed according to current standards. Patients diagnosed years ago and patients who live in countries with limited resources are least likely to have been diagnosed according to these recommendations. The iPCD Cohort includes patients diagnosed since 1964, so we divided patients into three diagnostic subgroups based on the results of the tests available. The first subgroup included patients with definite PCD defined, based on recent guidelines of the ERS PCD Diagnostics Task Force [3], as hallmark EM findings and/or pathogenic biallelic PCD genetic mutations. The second subgroup, probable PCD, included patients with abnormal HVM findings and/or low nNO (we used a cut-off of 77nl/min [5]). The third subgroup included patients with clinical PCD diagnosis; these were patients for whom the PCD diagnostic algorithm had not yet been completed, or whose test results were negative or ambiguous. Patients in this latter group were followed up and treated as PCD at the collaborating centres based on a combination of several of the following features: situs anomalies, persistent cough, persistent rhinitis, chronic or recurrent upper or lower respiratory infections, and history of neonatal respiratory symptoms in term infants [3]. Other possible more common diseases such as cystic fibrosis and immunodeficiency were excluded.

**FEV1 and FVC**

We checked data quality to identify outliers and implausible values, and contacted data contributors to resolve any unclear issues. We used the Global Lung Function Initiative (GLI) reference values to calculate age, sex, ethnicity, and height-adjusted z-scores of forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) [6].

**Determinants of lung function**

We investigated the association of lung function with sex, age, country of residence, level of diagnostic certainty, organ laterality, BMI, and ultrastructural defect at time of lung function measurement. Despite having calculated age, height, and sex-specific z-scores, impairment of lung function might differ between male and female PCD patients. Analysis of different age groups helps to find whether PCD affects lung growth in children, or whether it accelerates lung function decline in adults. To facilitate comparison with available published cystic fibrosis (CF) data [7], we categorised patients into the same 12 age groups (6-9, 10-13, 14-17, 18-21, 22-25, 26-29, 30-33, 34-37, 38-41, 42-45, 46-49 and ≥50 years). Patients with situs inversus might have less severe disease because they are diagnosed and treated earlier, sometimes even before symptoms develop [4]. We categorised organ laterality into three groups (situs solitus totalis, situs inversus, and heterotaxia). BMI as an indicator of nutrition has been associated with lung function in many chronic respiratory diseases. We identified national growth references by contacting collaborating centres and searching the literature. For each centre, we chose one of the following methods to calculate z-scores based on national references: 1) an LMS approach using tables that contained L, M, and S parameters needed to generate exact z-scores [8]; 2) direct calculation via online national z-score or percentile growth calculators; or 3) interpolating exact z-scores from plotted percentile boundaries on growth curves. Available references for BMI were intended for use with children only. For paediatric patients aged <18 years, we calculated age- and sex-adjusted BMI z-scores based on available reference values, preferably national where they were available (the sources are listed in the online supplement, Table S1), and we defined underweight as a BMI z-score less than or equal to -1.96, and overweight as a BMI z-score ≥1.96. For patients aged ≥18 years we used the WHO international BMI classification for adults, which define underweight as BMI < 18.5 and overweight as BMI ≥ 25.0 [9]. Differences between countries could show ethnic variations, or differences in age at diagnosis or disease management. We categorised ultrastructural defects into non-diagnostic, dynein arm defects (outer and/or inner dynein arm defects), microtubular defects (central pair, tubulus disorganisation, tubular transposition and/or nexin link defect), and acilia.

**Table S1.** National references used for calculations of BMI z-scores

|  |  |  |
| --- | --- | --- |
| **Country**  | **Growth reference source** | **Year of publication** |
| **Australia** | Centre for Disease Control and Prevention [10] | 2000 |
| **Belgium** | Flemish growth study (Roelants et al.) [11] | 2009 |
| **Cyprus** | Growth curves for Greek children 0-5 years (Papadimitriou et al.) [12]Growth curves for Cypriot children 6-17 years (Savva et al.) [13] | 20002001 |
| **Denmark** | Danish growth references (Tinggaard et al.) [14] | 2014 |
| **France** | French references for Height (Sempé et al.) [15]French references for BMI (Rolland-Cachera et al.) [16] | 19791991 |
| **Germany** | KiGGS study [17] | 2006 |
| **Israel** | Centre for Disease Control and Prevention [10] | 2000 |
| **Italy** | Centre for Disease Control and Prevention [10] | 2000 |
| **Netherlands** | Fifth Dutch Growth Study [18] | 2009 |
| **Norway** | Growth charts for Norwegian children (Júlíusson et al.) [19] | 2009 |
| **Poland** | Growth references (Kulaga et al.) [20] | 2010 |
| **Serbia** | Not available\* | - |
| **Switzerland** | Swiss growth curves (Braegger et al.) [21] | 2011 |
| **Turkey** | Growth references for Turkish children (Neyzi et al.) [22] | 2006 |
| **United Kingdom** | Royal College of Paediatrics and Child Health [23,24] | 1990 |

\* No national growth references were available in Serbia, for which the WHO references are used instead. Table adapted from Goutaki et al. [25]

Patients <6 years old

(N=176)

 Data delivered and standardised by the time of analysis
(N=2667 from 21 centres)

April 2016

No lung function data contributed

by centre

(N=519)

 Data of patients ≥6 years old
(N=2491 from 19 centres)

Data from centres contributing lung function data
(N=1972 from 19 centres)

Insufficient information to calculate z-scores

(N=981)

Patients included in situs analysis

(N=860)

Patients included in main analyses

(N=991)

Patients included in analysis of BMI

 (N=920)

Patients included in age at diagnosis analysis

 (N=167)

Patients with definite PCD diagnosis

(N=611)

**Figure S1.** Flow chart showing the patients included for the different analyses performed.

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**Figure S2.** Study design on patient inclusion to assess the association of age at diagnosis with lung function.

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**Fig S3.** FEV1 and FVC in PCD patients aged 15 to 20 years by age of diagnosis compared to GLI 2012 reference values. FEV1 and FVC are presented as mean z-score (95%CI).



**Fig S4.** Associationof FEV1 of PCD patients with CF patients using GLI 2012 references values. FEV1 of PCD patients are presented as mean %predicted and 95%CI, and FEV1 of CF patients are presented as mean, without adjusting for other factors. The dashed line shows the mean of the normal population.

**Table S2.** Characteristics of PCD patients included in this study compared to those who were excluded

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Study Participants****(n=991)** | **Insufficient information on lung function****(n=981)** | **Comparison****with participants****p-value¶** | **No lung function data contributed****(n=519)** | **Comparison****with participants****p-value¶** |
|  | **n (%)** | **n (%)** |  | **n (%)** |  |
| **Sex** |  |  | 0.91 |  | 0.01 |
| Male | 487 (49) |  481 (49) |  | 290 (56) |  |
| Female | 504 (51) | 491 (50) |  | 228 (44) |
| Missing | 0 (0) | 9 (1) |  | 1 (0) |
| **Country of residence\*** |  |  | <0.001 |  | <0.001 |
| Australia | 34 (3) | 42 (4) |  | 0 (0) |  |
| Northern Europe | 306 (31) | 145 (15) |  | 0 (0) |
| Western Europe | 392 (40) | 731 (75) |  | 0 (0) |
| Eastern Europe | 74 (7) | 8 (1) |  | 0 (0) |
| Southern Europe | 42 (4) | 5 (1) |  | 0 (0) |
| Western Asia | 143 (14) | 50 (5) |  | 0 (0) |
| North America | 0 (0) | 0 (0) |  | 418 (81) |
| South America | 0 (0) | 0 (0) |  | 101 (19) |  |
| **Current age#**  |  |  | <0.001 |  | <0.001 |
| 6-9 years | 15 (2) | 213 (22) |  | 44 (8) |  |
| 10-19 years | 445 (45) | 354 (36) |  | 218 (42) |
| 20-29 years | 248 (25) | 146 (15) |  | 122 (24) |
| 30-39 years | 129 (13) | 100 (10) |  | 34 (7) |
| 40-49 years |  64 (6) | 70 (7) |  | 43 (8) |
| >50 years | 90 (9) | 76 (8) |  | 57 (11) |
| Missing | 0 (0) | 22 (2) |  | 1 (0) |  |

\* Based on the United Nations Statistics Division

¶ Chi-squared tests

# In April 2016

**Table S3.** FEV1 and FVC of PCD patients of the iPCD Cohort with available situs information compared to GLI 2012 references (N=860)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   |   | **FEV1** |  | **FVC** |
| **Characteristic** | **N** | **mean****z-score** | **95% CI** | **p-value**¶ |  **N** | **mean****z-score** | **95% CI** | **p-value**¶ |
| **Total** | 860 | -1.52 | -1.63 | -1.41 |  | 853 | -0.79 | -0.90 | -0.67 |  |
| **Sex** |  |  |  |  | 0.10 |  |  |  |  | 0.51 |
| Male | 417 | -1.47 | -1.62 | -1.32 |  | 413 | -0.75 | -0.90 | -0.60 |  |
| Female | 443 | -1.56 | -1.71 | -1.42 |  | 440 | -0.82 | -0.96 | -0.67 |  |
| **Age group** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| 6-9 years | 164 | -0.80 | -1.04 | -0.56 |  | 163 | -0.29 | -0.53 | -0.05 |  |
| 10-13 years | 188 | -1.05 | -1.28 | -0.83 |  | 187 | -0.50 | -0.72 | -0.27 |  |
| 14-17 years | 184 | -1.48 | -1.71 | -1.26 |  | 182 | -0.77 | -0.99 | -0.54 |  |
| 18-21 years | 85 | -1.58 | -1.91 | -1.25 |  | 85 | -0.63 | -0.96 | -0.30 |  |
| 22-25 years | 60 | -1.80 | -2.19 | -1.40 |  | 59 | -0.89 | -1.29 | -0.49 |  |
| 26-29 years | 42 | -2.29 | -2.76 | -1.82 |  | 41 | -1.32 | -1.80 | -0.84 |  |
| 30-33 years | 27 | -2.61 | -3.19 | -2.03 |  | 26 | -1.42 | -2.02 | -0.83 |  |
| 34-37 years | 23 | -2.75 | -3.37 | -2.12 |  | 24 | -1.76 | -2.38 | -1.15 |  |
| 38-41 years | 14 | -2.47 | -3.28 | -1.66 |  | 14 | -1.25 | -2.06 | -0.43 |  |
| 42-45 years | 14 | -3.24 | -4.05 | -2.42 |  | 14 | -2.74 | -3.55 | -1.92 |  |
| 46-49 years | 20 | -2.90 | -3.59 | -2.22 |  | 20 | -1.95 | -2.64 | -1.26 |  |
| ≥50 years | 39 | -2.41 | -2.90 | -1.92 |  | 38 | -1.48 | -1.97 | -0.98 |  |
| **Country** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| Australia | 34 | -1.79 | -2.31 | -1.27 |  | 34 | -1.17 | -1.69 | -0.65 |  |
| Belgium | 69 | -1.18 | -1.56 | -0.81 |  | 69 | -0.05 | -0.42 | 0.33 |  |
| Cyprus | 27 | -1.89 | -2.48 | -1.30 |  | 27 | -1.74 | -2.34 | -1.15 |  |
| Denmark | 72 | -1.21 | -1.57 | -0.86 |  | 72 | -0.19 | -0.55 | 0.16 |  |
| France | 11 | -1.36 | -2.28 | -0.45 |  | 11 | -0.85 | -1.78 | 0.07 |  |
| Germany | 104 | -1.21 | -1.51 | -0.91 |  | 99 | -0.64 | -0.95 | -0.33 |  |
| Israel | 85 | -1.57 | -1.89 | -1.24 |  | 82 | -1.09 | -1.43 | -0.76 |  |
| Italy | 35 | -1.45 | -1.97 | -0.93 |  | 35 | -0.67 | -1.20 | -0.15 |  |
| Netherlands | 65 | -0.50 | -0.88 | -0.12 |  | 65 | 0.67 | 0.29 | 1.05 |  |
| Norway | 14 | -1.36 | -2.17 | -0.56 |  | 14 | -0.79 | -1.60 | 0.03 |  |
| Poland | 74 | -1.93 | -2.29 | -1.57 |  | 74 | -0.98 | -1.34 | -0.61 |  |
| Serbia | 7 | -2.34 | -3.49 | -1.20 |  | 7 | -2.58 | -3.73 | -1.42 |  |
| Switzerland | 29 | -1.87 | -2.43 | -1.31 |  | 29 | -1.23 | -1.79 | -0.67 |  |
| Turkey | 29 | -1.91 | -2.51 | -1.31 |  | 29 | -1.65 | -2.25 | -1.04 |  |
| UK | 205 | -1.85 | -2.07 | -1.64 |  | 206 | -1.16 | -1.37 | -0.94 |  |
| **Diagnostic certainty** |  |  |  |  | 0.58 |  |  |  |  | 0.50 |
| Definite PCD diagnosis+ | 554 | -1.55 | -1.68 | -1.42 |  | 551 | -0.78 | -0.91 | -0.65 |  |
| Probable PCD diagnosis# | 195 | -1.58 | -1.80 | -1.35 |  | 191 | -0.88 | -1.11 | -0.65 |  |
| Clinical diagnosis only | 111 | -1.27 | -1.58 | -0.97 |  | 111 | -0.66 | -0.97 | -0.34 |  |
| **Situs anomalies** |  |  |  |  | 0.67 |  |  |  |  | 0.35 |
| Situs solitus totalis | 499 | -1.52 | -1.66 | -1.38 |  | 496 | -0.83 | -0.98 | -0.69 |  |
| Situs inversus  | 348 | -1.46 | -1.63 | -1.29 |  | 344 | -0.77 | -0.94 | -0.59 |  |
| Heterotaxia | 13 | -1.82 | -2.68 | -0.96 |   | 13 | -1.40 | -2.29 | -0.51 |   |

Mean z-scores (95%CI) for each group after adjusting for the remaining characteristics

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

+ Defined as hallmark PCD electron microscopy findings and/or biallelic gene mutation identified based on the ERS PCD Diagnostics Task Force guidelines [26]

# Abnormal light or high frequency video microscopy finding and/or low nasal NO value

**Table S4.** FEV1 and FVC of PCD patients of the iPCD Cohort with available BMI information compared to GLI 2012 references (N=927)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   |   | **FEV1** |  | **FVC** |
| **Characteristic** | **N** | **mean****z-score** | **95% CI** | **p-value**¶ | **N** | **mean****z-score** | **95% CI** | **p-value**¶ |
| **Total** | 927 | -1.47 | -1.58 | -1.37 |  | 924 | -0.73 | -0.84 | -0.62 |  |
| **Sex** |  |  |  |  | 0.08 |  |  |  |  | 0.31 |
| Male | 458 | -1.39 | -1.52 | -1.25 |  | 458 | -0.68 | -0.82 | -0.54 |  |
| Female | 469 | -1.56 | -1.69 | -1.42 |  | 466 | -0.78 | -0.92 | -0.65 |  |
| **Age group** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| 6-9 years | 182 | -0.76 | -0.97 | -0.54 |  | 181 | -0.19 | -0.41 | 0.04 |  |
| 10-13 years | 220 | -1.03 | -1.23 | -0.83 |  | 217 | -0.44 | -0.65 | -0.24 |  |
| 14-17 years | 207 | -1.42 | -1.63 | -1.22 |  | 210 | -0.70 | -0.90 | -0.49 |  |
| 18-21 years | 90 | -1.53 | -1.84 | -1.22 |  | 90 | -0.56 | -0.88 | -0.25 |  |
| 22-25 years | 54 | -1.75 | -2.16 | -1.35 |  | 53 | -0.85 | -1.27 | -0.44 |  |
| 26-29 years | 37 | -2.21 | -2.70 | -1.72 |  | 36 | -1.23 | -1.73 | -0.72 |  |
| 30-33 years | 25 | -2.84 | -3.43 | -2.25 |  | 25 | -1.84 | -2.45 | -1.24 |  |
| 34-37 years | 22 | -2.98 | -3.61 | -2.36 |  | 23 | -1.85 | -2.48 | -1.23 |  |
| 38-41 years | 15 | -2.72 | -3.48 | -1.97 |  | 15 | -1.53 | -2.31 | -0.75 |  |
| 42-45 years | 14 | -3.43 | -4.22 | -2.65 |  | 15 | -2.96 | -3.74 | -2.18 |  |
| 46-49 years | 20 | -3.03 | -3.70 | -2.36 |  | 19 | -2.04 | -2.75 | -1.34 |  |
| ≥50 years | 41 | -2.59 | -3.06 | -2.11 |  | 40 | -1.66 | -2.15 | -1.17 |  |
| **Country** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| Australia | 34 | -1.73 | -2.24 | -1.23 |  | 34 | -1.12 | -1.63 | -0.60 |  |
| Belgium | 69 | -1.14 | -1.50 | -0.78 |  | 69 | -0.03 | -0.40 | 0.34 |  |
| Cyprus | 25 | -1.73 | -2.33 | -1.13 |  | 25 | -1.53 | -2.14 | -0.91 |  |
| Denmark | 70 | -1.15 | -1.50 | -0.80 |  | 70 | -0.13 | -0.49 | 0.23 |  |
| France | 75 | -1.45 | -1.79 | -1.10 |  | 72 | -0.55 | -0.91 | -0.19 |  |
| Germany | 123 | -1.27 | -1.54 | -1.00 |  | 123 | -0.68 | -0.96 | -0.41 |  |
| Israel | 75 | -1.57 | -1.91 | -1.23 |  | 74 | -1.14 | -1.48 | -0.79 |  |
| Italy | 35 | -1.52 | -2.02 | -1.02 |  | 35 | -0.72 | -1.24 | -0.21 |  |
| Netherlands | 66 | -0.52 | -0.88 | -0.15 |  | 66 | 0.58 | 0.21 | 0.95 |  |
| Norway | 14 | -1.30 | -2.08 | -0.52 |  | 14 | -0.73 | -1.52 | 0.07 |  |
| Poland | 74 | -1.90 | -2.24 | -1.55 |  | 74 | -0.98 | -1.34 | -0.63 |  |
| Serbia | 7 | -2.39 | -3.49 | -1.29 |  | 7 | -2.70 | -3.83 | -1.57 |  |
| Switzerland | 40 | -1.72 | -2.18 | -1.26 |  | 40 | -0.97 | -1.44 | -0.49 |  |
| Turkey | 29 | -1.79 | -2.35 | -1.23 |  | 29 | -1.56 | -2.13 | -0.98 |  |
| UK | 191 | -1.77 | -1.98 | -1.55 |  | 192 | -1.09 | -1.31 | -0.87 |  |
| **Diagnostic certainty** |  |  |  |  | 0.45 |  |  |  |  | 0.54 |
| Definite PCD diagnosis+ | 574 | -1.50 | -1.62 | -1.37 |  | 574 | -0.73 | -0.86 | -0.60 |  |
| Probable PCD diagnosis# | 191 | -1.53 | -1.74 | -1.31 |  | 190 | -0.82 | -1.05 | -0.60 |  |
| Clinical diagnosis only | 162 | -1.33 | -1.58 | -1.09 |  | 160 | -0.64 | -0.89 | -0.38 |  |
| **BMI** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| Underweight | 59 | -2.54 | -2.92 | -2.16 |  | 60 | -1.94 | -2.33 | -1.55 |  |
| Normal | 752 | -1.48 | -1.58 | -1.37 |  | 750 | -0.74 | -0.85 | -0.63 |  |
| Overweight | 116 | -0.91 | -1.20 | -0.62 |   | 114 | -0.07 | -0.37 | 0.23 |   |

 Mean z-scores (95%CI) for each group after adjusting for the remaining characteristics

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

+ Defined as hallmark PCD electron microscopy findings and/or biallelic gene mutation identified based on the ERS PCD Diagnostics Task Force guidelines [26]

# Abnormal light or high frequency video microscopy finding and/or low nasal NO value; patients from Serbia were excluded from this analysis as there are no available national references

**Table S5.** FEV1 and FVC of PCD patients of the iPCD Cohort with a definite PCD diagnosis compared to GLI 2012 references (sensitivity analysis) (N=611)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   |  | **FEV1** |  | **FVC** |
| **Characteristic** | **N** | **mean** **z-score** | **95% CI** | **p-value**¶ | **N** | **mean z-score** | **95% CI** | **p-value**¶ |
| **Total** | 611 | -1.54 | -1.68 | -1.41 |  | 606 | -0.75 | -0.89 | -0.61 |  |
| **Sex** |  |  |  |  | 0.07 |  |  |  |  | 0.17 |
| Male | 301 | -1.35 | -1.52 | -1.17 |  | 299 | -0.72 | -0.90 | -0.54 |  |
| Female | 310 | -1.58 | -1.75 | -1.41 |  | 309 | -0.78 | -0.96 | -0.60 |  |
| **Age group** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| 6-9 years | 180 | -0.92 | -1.16 | -0.68 |  | 113 | -0.25 | -0.55 | 0.05 |  |
| 10-13 years | 118 | -1.04 | -1.31 | -0.76 |  | 136 | -0.45 | -0.72 | -0.18 |  |
| 14-17 years | 105 | -1.48 | -1.78 | -1.19 |  | 130 | -0.78 | -1.05 | -0.50 |  |
| 18-21 years | 51 | -1.56 | -1.98 | -1.13 |  | 63 | -0.56 | -0.96 | -0.17 |  |
| 22-25 years | 40 | -1.63 | -2.11 | -1.14 |  | 47 | -0.72 | -1.19 | -0.26 |  |
| 26-29 years | 30 | -2.10 | -2.65 | -1.54 |  | 28 | -1.13 | -1.73 | -0.53 |  |
| 30-33 years | 17 | -3.07 | -3.80 | -2.34 |  | 17 | -1.55 | -2.31 | -0.80 |  |
| 34-37 years | 14 | -3.08 | -3.88 | -2.28 |  | 16 | -2.01 | -2.79 | -1.23 |  |
| 38-41 years | 10 | -2.64 | -3.59 | -1.68 |  | 9 | -0.99 | -2.04 | 0.05 |  |
| 42-45 years | 12 | -3.47 | -4.35 | -2.60 |  | 9 | -3.07 | -4.12 | -2.02 |  |
| 46-49 years | 10 | -2.93 | -3.89 | -1.98 |  | 13 | -2.43 | -3.32 | -1.55 |  |
| ≥50 years | 24 | -2.18 | -2.80 | -1.56 |  | 27 | -1.37 | -1.98 | -0.77 |  |
| **Country** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| Australia | 31 | -1.86 | -2.40 | -1.32 |  | 31 | -1.11 | -1.67 | -0.55 |  |
| Belgium | 58 | -1.21 | -1.62 | -0.81 |  | 58 | 0.00 | -0.42 | 0.41 |  |
| Cyprus | 22 | -1.78 | -2.42 | -1.14 |  | 22 | -1.64 | -2.33 | -0.96 |  |
| Denmark | 45 | -0.95 | -1.41 | -0.50 |  | 45 | -0.21 | -0.67 | 0.25 |  |
| France | 46 | -1.27 | -1.72 | -0.83 |  | 46 | -0.50 | -0.97 | -0.04 |  |
| Germany | 58 | -1.36 | -1.76 | -0.97 |  | 55 | -0.66 | -1.08 | -0.23 |  |
| Israel | 50 | -1.34 | -1.77 | -0.91 |  | 49 | -0.91 | -1.35 | -0.46 |  |
| Italy | 33 | -1.25 | -1.78 | -0.73 |  | 33 | -0.61 | -1.16 | -0.06 |  |
| Netherlands | 35 | -0.21 | -0.72 | 0.29 |  | 35 | 0.90 | 0.38 | 1.43 |  |
| Norway | 12 | -1.44 | -2.30 | -0.58 |  | 12 | -0.78 | -1.68 | 0.12 |  |
| Poland | 28 | -2.20 | -2.77 | -1.63 |  | 28 | -1.30 | -1.89 | -0.71 |  |
| Serbia | 2 | -1.77 | -3.88 | 0.35 |  | 2 | -2.41 | -4.61 | -0.21 |  |
| Switzerland | 24 | -1.48 | -2.11 | -0.86 |  | 24 | -1.05 | -1.69 | -0.42 |  |
| Turkey | 7 | -2.31 | -3.45 | -1.18 |  | 7 | -2.28 | -3.45 | -1.10 |  |
| UK | 160 | -1.86 | -2.11 | -1.61 |   | 161 | -1.19 | -1.44 | -0.94 |   |

Mean z-scores (95%CI) for each group after adjusting for the remaining characteristics

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

+ Defined as hallmark PCD electron microscopy findings and/or biallelic gene mutation identified based on the ERS PCD Diagnostics Task Force guidelines [26]

# Abnormal light or high frequency video microscopy finding and/or low nasal NO value

**Table S6.** FEV1 and FVC of PCD patients of the iPCD Cohort using the latest available measurement instead of the earliest compared to GLI 2012 references (sensitivity analysis) (N=991)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   |   | **FEV1** |  | **FVC** |
| **Characteristic** | **N** | **mean** **z-score** | **95% CI** | **p-value**¶ | **N** | **mean** **z-score** | **95% CI** | **p-value**¶ |
| **Total** | 991 | -1.53 | -1.63 | -1.42 |  | 981 | -0.77 | -0.88 | -0.67 |  |
| **Sex** |  |  |  |  | 0.11 |  |  |  |  | 0.26 |
| Male | 487 | -1.45 | -1.59 | -1.31 |  | 483 | -0.71 | -0.85 | -0.56 |  |
| Female | 504 | -1.61 | -1.74 | -1.47 |  | 498 | -0.83 | -0.97 | -0.68 |  |
| **Age group** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| 6-9 years | 185 | -0.80 | -1.03 | -0.57 |  | 187 | -0.25 | -0.48 | -0.01 |  |
| 10-13 years | 237 | -1.12 | -1.32 | -0.92 |  | 232 | -0.53 | -0.74 | -0.31 |  |
| 14-17 years | 204 | -1.55 | -1.77 | -1.33 |  | 200 | -0.80 | -1.02 | -0.57 |  |
| 18-21 years | 107 | -1.54 | -1.84 | -1.25 |  | 107 | -0.64 | -0.95 | -0.33 |  |
| 22-25 years | 59 | -1.68 | -2.09 | -1.28 |  | 57 | -0.58 | -1.00 | -0.15 |  |
| 26-29 years | 45 | -2.24 | -2.70 | -1.77 |  | 44 | -1.20 | -1.69 | -0.71 |  |
| 30-33 years | 31 | -2.65 | -3.21 | -2.09 |  | 32 | -1.68 | -2.25 | -1.11 |  |
| 34-37 years | 27 | -2.82 | -3.42 | -2.23 |  | 26 | -1.74 | -2.36 | -1.11 |  |
| 38-41 years | 15 | -2.56 | -3.36 | -1.76 |  | 15 | -1.31 | -2.14 | -0.49 |  |
| 42-45 years | 20 | -3.15 | -3.85 | -2.46 |  | 20 | -2.54 | -3.26 | -1.83 |  |
| 46-49 years | 20 | -3.07 | -3.77 | -2.37 |  | 21 | -2.24 | -2.95 | -1.53 |  |
| ≥50 years | 41 | -2.39 | -2.88 | -1.90 |  | 40 | -1.38 | -1.89 | -0.87 |  |
| **Country** |  |  |  |  | <0.001 |  |  |  |  | <0.001 |
| Australia | 34 | -1.83 | -2.36 | -1.30 |  | 34 | -0.99 | -1.54 | -0.44 |  |
| Belgium | 69 | -1.18 | -1.56 | -0.81 |  | 69 | -0.07 | -0.46 | 0.32 |  |
| Cyprus | 27 | -1.67 | -2.28 | -1.07 |  | 27 | -1.62 | -2.24 | -0.99 |  |
| Denmark | 74 | -1.29 | -1.65 | -0.93 |  | 74 | -0.21 | -0.59 | 0.16 |  |
| France | 75 | -1.44 | -1.80 | -1.07 |  | 72 | -0.61 | -1.00 | -0.23 |  |
| Germany | 142 | -1.43 | -1.69 | -1.16 |  | 137 | -0.82 | -1.10 | -0.55 |  |
| Israel | 87 | -1.58 | -1.91 | -1.25 |  | 84 | -1.10 | -1.45 | -0.75 |  |
| Italy | 35 | -1.46 | -1.99 | -0.94 |  | 35 | -0.63 | -1.17 | -0.08 |  |
| Netherlands | 66 | -0.62 | -1.00 | -0.24 |  | 66 | 0.54 | 0.14 | 0.93 |  |
| Norway | 14 | -1.21 | -2.03 | -0.39 |  | 14 | -0.78 | -1.63 | 0.07 |  |
| Poland | 74 | -1.89 | -2.26 | -1.53 |  | 74 | -0.96 | -1.34 | -0.58 |  |
| Serbia | 7 | -2.08 | -3.25 | -0.92 |  | 7 | -2.35 | -3.56 | -1.14 |  |
| Switzerland | 40 | -1.61 | -2.10 | -1.12 |  | 40 | -0.77 | -1.27 | -0.26 |  |
| Turkey | 29 | -1.75 | -2.34 | -1.16 |  | 29 | -1.51 | -2.12 | -0.89 |  |
| UK | 218 | -1.85 | -2.06 | -1.64 |  | 219 | -1.13 | -1.35 | -0.91 |  |
| **Diagnostic certainty** |  |  |  |  | 0.71 |  |  |  |  | 0.78 |
| Definite PCD diagnosis+ | 611 | -1.55 | -1.68 | -1.42 |  | 608 | -0.77 | -0.90 | -0.63 |  |
| Probable PCD diagnosis# | 207 | -1.54 | -1.76 | -1.32 |  | 203 | -0.83 | -1.06 | -0.60 |  |
| Clinical diagnosis only | 173 | -1.43 | -1.68 | -1.18 |   | 170 | -0.70 | -0.97 | -0.44 |   |

Mean z-scores (95%CI) for each group after adjusting for the remaining characteristics

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# Abnormal light or high frequency video microscopy finding and/or low nasal NO value

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