

# No long-term effect of past *Pneumocystis jirovecii* pneumonia on pulmonary function in people living with HIV



Patrick G.A. Oomen<sup>1</sup>, Inez Bronsveld<sup>2</sup>, Andy I.M. Hoepelman<sup>1</sup>, Berend J. van Welzen<sup>1</sup> and Tania Mudrikova<sup>1</sup>

<sup>1</sup>Department of Internal Medicine and Infectious Diseases, <sup>2</sup>Department of Pulmonary Diseases, University Medical Centre Utrecht, Utrecht, the Netherlands.

Contact: P.G.A.Oomen-2@umcutrecht.nl

## CONCLUSIONS

- Our study did not show an association between past *Pneumocystis jirovecii* pneumonia and persistent diffusion impairment in people living with HIV.
- Our findings suggest that *Pneumocystis jirovecii* pneumonia-related pulmonary damage recovers in the long-term or that, in the presence of pulmonary impairment from smoking or HIV infection, its contribution is marginal.

## Background

- *Pneumocystis jirovecii* pneumonia (PJP) is a common opportunistic infection in people living with HIV (PLWH) and advanced immunodeficiency, leading to severe hypoxemia due to diffusion capacity impairment.<sup>1,2</sup>
- The long-term consequences of past PJP are largely unknown.
- We aimed to assess the impact of past PJP on long-term diffusion capacity in PLWH with a history of advanced immunodeficiency.

## Methods

- **Design:** Prospective cross-sectional study.
- **Study group:** Adult PLWH with past PJP >1 year ago.
- **Control group:** Adult PLWH with a nadir CD4<sup>+</sup> count <200 cells/mm<sup>3</sup>, matched by age, sex at birth, time since HIV diagnosis and smoking status.
- **Pulmonary function test (PFT) (Table 1):**
  - One PFT in the period between 2016 and 2022, performed according to latest European Respiratory Society / American Thoracic Society standards using a Geratherm spirometer.<sup>3-6</sup>
- **Data:** Collected from electronic medical records; smoking habits and respiratory complaints registered at PFT.

Table 1. Different components of the study PFT with corresponding assessment and study outcome.

	Assessment	Outcome
Single-breath transfer factor for carbon monoxide (TLCO)	Diffusion capacity impairment	<b>Primary:</b> TLCO Z-score <b>Secondary:</b> Diffusion impairment (defined as TLCO Z-score <-1.645 yes/no)
Pre-bronchodilation spirometry	Obstructive impairment	<b>Secondary:</b> Forced expiratory volume in 1 s / forced vital capacity (FEV1/FVC) Z-score
Body plethysmography	Restrictive impairment	<b>Secondary:</b> Total lung capacity Z-score

## Statistical Analysis

- **Associations:** Multivariate linear regression and logistic regression using Firth's bias correction for small samples.<sup>7</sup>

## Results

- A total of 102 PLWH (including 51 with past PJP) were included in analysis (**Table 2**).
- Both groups were well matched in terms of age, sex at birth, time since HIV diagnosis and smoking status.

Table 2. Characteristics of PLWH according to PJP status at time of PFT.

	PJP+		PJP-		p-value
	n = 51	(IQR) / (%)	n = 51	(IQR) / (%)	
Age (years)	54.00	50.00 - 58.00	53.00	46.00 - 59.00	0.453
Sex at birth (male)	44	86.27	45	88.24	0.767
Time since HIV diagnosis (years)	10.00	6.00 - 17.00	11.00	7.00 - 17.00	0.245
Time since PJP (years)	10.00	5.00 - 16.00	-	-	-
Time since start antiretroviral therapy (years)	10.00	6.00 - 16.00	10.00	7.00 - 16.00	0.341
Smoking					0.834
- current	27	52.94	24	47.06	
- former	13	25.49	15	29.41	
- never	11	21.57	12	23.53	
Nadir CD4 <sup>+</sup> count (cells/mm <sup>3</sup> )	28.00	10.00-50.00	78.00	41.00-152.00	<b>&lt;0.001</b>
CD4 <sup>+</sup> at PFT <sup>a</sup>	478.00	372.75-559.75	537.00	392.50-691.75	0.120
VL <400 at PFT (cop/mL) <sup>*</sup>	51	100	51	100	-

## Mean Z-scores and rate of diffusion impairment between PJP+ and PJP-:

- TLCO Z-score (**Fig. 1**): -0.98 (1.11) vs. -0.92 (1.04), p=0.790
- Diffusion impairment: 14/51 (27.45%) vs. 12/51 (24.53%), p=0.650
- FEV1/FVC Z-score: -0.31 (1.08) vs. -0.28 (1.10), p=0.894
- TLC Z-score: -0.09 (1.04) vs. -0.01 (1.13), p=0.705
- **TLCO Z-scores and diffusion impairment:** No independent association was observed with past PJP. Only current (vs. never smoking) was associated with lower TLCO Z-scores and higher odds of diffusion impairment (**Table 3**).
- **FEV1/FVC and TLC Z-scores:** No independent association was observed with past PJP ( $\beta$  0.03; 95% CI -0.44 - 0.50 |  $\beta$  0.09; 95% CI -0.36 - 0.55). Only current (vs. never smoking) was associated with lower FEV1/FVZ and higher TLC Z-scores.

Table 3. Multivariate logistic and linear regression results for TLCO Z-scores and diffusion impairment (defined as TLCO Z-score <-1.645).

	TLCO Z-score			Diffusion impairment		
	$\beta$	95% CI	p-value	OR	95% CI	p-value
Past PJP (vs. no past PJP)	0.14	-0.30 - 0.57	0.545	1.00	0.36 - 2.75	0.997
Age at PFT (per year increase)	-0.02	-0.04 - 0.01	0.164	1.00	0.95 - 1.06	0.971
Male sex (vs. female sex)	0.21	-0.40 - 0.81	0.504	0.46	0.13 - 1.65	0.235
Time since HIV diagnosis (per year increase)	0.01	-0.02 - 0.04	0.454	1.02	0.95 - 1.09	0.648
Smoking						
- never	1		-	1		-
- former	-0.14	-0.63 - 0.36	0.597	1.68	0.51 - 5.74	0.396
- current	-1.10	-1.61 - -0.59	<b>&lt;0.001</b>	6.02	1.94 - 18.72	<b>0.002</b>
Nadir CD4 <sup>+</sup> count (per 5 cell/mm <sup>3</sup> increase)	0.02	0.00 - 0.04	0.061	0.97	0.93 - 1.02	0.195

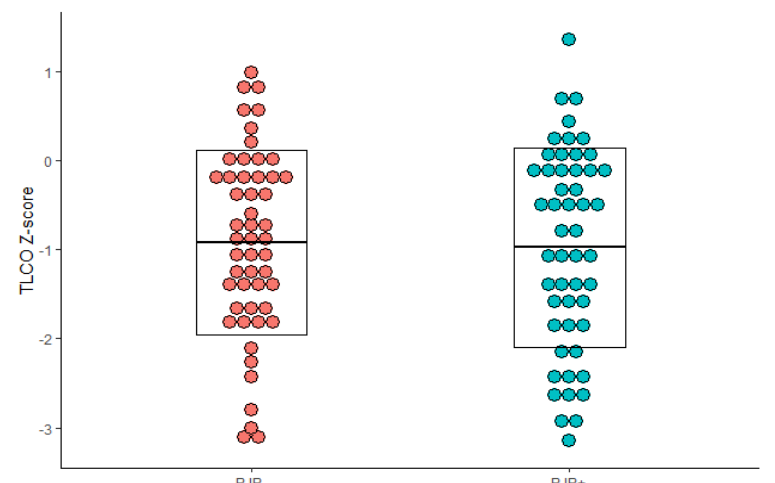


Figure 1. Dot plot of TLCO Z-score by PJP+ and PJP- group. Middle, upper and lower horizontal lines represent the mean ( $\pm$  standard deviation) TLCO Z-score.