Long-term air pollution exposure is associated with increased severity of idiopathic pulmonary fibrosis in the IPF-PRO Registry

Coralynn Sack,[1] Daniel Wojdyla,[2] Maeve G MacMurdo,[3] Amanda Gassett,[1] Joel D Kaufman,[1] Ganesh Raghu,[1] Carrie A Redlich,[4] Peide Li,[5] Amy L Olson,[5] Thomas B Leonard,[5] Jamie L Todd,[2,6] Megan L Neely,[2,6] Laurie D Snyder,[2,6] Mridu Gulati,[4] on behalf of the IPF-PRO Registry investigators

[1]University of Washington, Seattle, WA, USA; [2]Duke Clinical Research Institute, Durham, NC, USA; [3]Cleveland Clinic, Cleveland, OH, USA; [4]Yale School of Medicine, New Haven, CT, USA; [5]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [6]Duke University Medical Center, Durham, NC, USA.

IPF-PRO™ ILD-PRO™

INTRODUCTION

- Exposure to air pollution has been associated with worse lung function,[1] faster decline in lung function[2] and increased mortality[3] in patients with IPF.

AIM

- To investigate the effects of long-term exposure to air pollution on disease severity and progression in patients in the IPF-PRO Registry.

METHODS

The IPF-PRO Registry

- Patients with IPF that was diagnosed or confirmed at the enrolling center in the previous 6 months were enrolled into the registry at 46 US sites between June 2014 and October 2018.[4]
- Patients were followed prospectively, with data collected as part of routine clinical care.

Exposure assessment

- Average pollution exposures (particulate matter with aerodynamic diameter <2.5 microns [$PM_{2.5}$], nitrogen dioxide [NO_2], ozone [O_3]) in the 5 years prior to enrollment at participants' home addresses were estimated using validated national spatio-temporal models.[5-7]

Analyses

- Associations between pollution exposure and physiologic measurements (FVC, DLco, supplemental oxygen use) and quality of life measurements (St. George's Respiratory Questionnaire [SGRQ], EuroQoL, Cough and Sputum Assessment Questionnaire (CASA-Q) cough domains) at enrollment were analyzed using multivariable regression models.
- Associations between pollution exposure and a composite outcome of mortality, lung transplant, or absolute decline in FVC % predicted ≥10% in the year after enrollment were analyzed using Cox proportional hazard regression models.
- Models were adjusted for potential individual-level and spatial confounders, including proxies for disease onset.

CONCLUSIONS

- Among patients in the IPF-PRO Registry, higher long-term exposure to $PM_{2.5}$ was associated with lower lung function and worse quality of life, but not with short-term disease progression. Further data are needed to investigate relationships between exposure to air pollutants and long-term outcomes.
- The reasons for the observed association between higher O_3 exposure and higher FVC at enrollment is uncertain, but may include confounding from co-pollutants, geographic factors, or comorbid conditions that contribute to disease presentation.

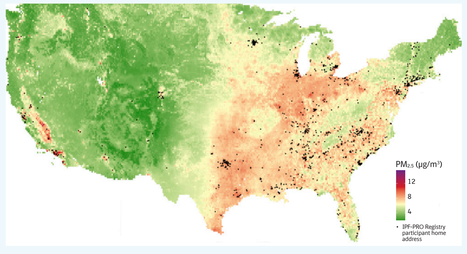
RESULTS

Patient characteristics at enrollment (N=835)

Age (years)	69.7 (7.7)
Male	632 (76)
Race/Ethnicity	
Non-Hispanic White	759 (92)
Hispanic	29 (3)
Black	11 (1)
Other	25 (3)
Smoking history	
Current	15 (2)
Past	545 (65)
Never	274 (33)
Months from symptom onset to new/confirmed diagnosis	15 (7, 32)
FVC % predicted	73.2 (17.5)
FEV_1 % predicted	78.3 (18.0)
DL_{CO} % predicted	42.9 (14.5)
Antifibrotic drug use	455 (54)

Data are mean (SD), median (Q1, Q3) or n (%) of patients with available data.

Exposure to $PM_{2.5}$



$PM_{2.5}$ exposure was positively correlated with mean 5-year NO_2 concentration

$PM_{2.5}$ exposure was negatively correlated with mean 5-year O_3 concentration

Associations between five-year average pollution concentrations and lung function or oxygen use at enrollment

FVC % predicted

	Base adjusted model* Difference in means‡ (95% CI)	p-value	Fully adjusted model† Difference in means‡ (95% CI)	p-value
$PM_{2.5}$	-3.37 (-5.31, -1.44)	<0.001	-2.86 (-4.97, -0.76)	0.008
NO_2	-0.19 (-1.48, 1.10)	0.769	-0.71 (-2.16, 0.75)	0.340
O_3	1.71 (0.41, 3.00)	0.010	1.57 (0.15, 2.98)	0.030

DL_{CO} % predicted

	Base adjusted model* Difference in means‡ (95% CI)	p-value	Fully adjusted model† Difference in means‡ (95% CI)	p-value
$PM_{2.5}$	-2.90 (-4.52, -1.28)	<0.001	-2.05 (-3.79, -0.30)	0.022
NO_2	0.63 (-0.42, 1.68)	0.241	0.11 (-1.09, 1.31)	0.857
O_3	1.51 (0.43, 2.58)	0.006	1.09 (-0.09, 2.26)	0.070

Supplemental oxygen use (at rest vs none/on exertion)

	Base adjusted model* Odds ratio‡ (95% CI)	p-value	Fully adjusted model† Odds ratio‡ (95% CI)	p-value
$PM_{2.5}$	1.22 (0.92, 1.62)	0.166	1.09 (0.78, 1.53)	0.623
NO_2	0.88 (0.72, 1.07)	0.204	1.04 (0.83, 1.31)	0.721
O_3	1.01 (0.84, 1.22)	0.886	1.07 (0.86, 1.35)	0.534

*Adjusted for age, sex, smoking status (ever/never), antifibrotic drug use and time since diagnosis.
†Adjusted for age, sex, smoking status (ever/ never), antifibrotic drug use, time since diagnosis, region, social vulnerability index at enrollment and site (random).
‡Estimated difference in means or odds ratio for 2 units higher $PM_{2.5}$, 4 units higher NO_2, 3 units higher O_3.

Associations between five-year average pollution concentrations and patient-reported outcomes at enrollment

SGRQ total score

	Base adjusted model* Difference in means‡ (95% CI)	p-value	Fully adjusted model† Difference in means‡ (95% CI)	p-value
$PM_{2.5}$	3.03 (0.94, 5.12)	0.005	2.25 (-0.05, 4.56)	0.055
NO_2	-1.14 (-2.54, 0.26)	0.110	-0.59 (-2.18, 0.99)	0.463
O_3	-0.50 (-1.92, 0.93)	0.494	0.38 (-1.17, 1.93)	0.632

EuroQoL score

	Base adjusted model* Difference in means‡ (95% CI)	p-value	Fully adjusted model† Difference in means‡ (95% CI)	p-value
$PM_{2.5}$	-0.04 (-0.06, -0.02)	0.001	-0.04 (-0.06, -0.01)	0.007
NO_2	-0.00 (-0.02, 0.01)	0.763	-0.01 (-0.03, 0.01)	0.347
O_3	0.02 (-0.00, 0.03)	0.066	0.01 (-0.01, 0.02)	0.410

CASA-Q cough impact

	Base adjusted model* Difference in means‡ (95% CI)	p-value	Fully adjusted model† Difference in means‡ (95% CI)	p-value
$PM_{2.5}$	-2.03 (-4.60, 0.53)	0.120	-1.14 (-3.81, 1.54)	0.405
NO_2	1.68 (-0.03, 3.39)	0.055	0.73 (-1.13, 2.59)	0.440
O_3	0.09 (-1.59, 1.77)	0.919	-0.42 (-2.14, 1.30)	0.631

CASA-Q cough symptoms

	Base adjusted model* Difference in means‡ (95% CI)	p-value	Fully adjusted model† Difference in means‡ (95% CI)	p-value
$PM_{2.5}$	-1.34 (-3.79, 1.11)	0.285	-0.35 (-2.95, 2.26)	0.794
NO_2	1.87 (0.17, 3.56)	0.031	0.79 (-1.07, 2.66)	0.404
O_3	-0.34 (-1.97, 1.28)	0.680	-0.64 (-2.33, 1.06)	0.460

*Adjusted for age, sex, smoking status (ever/ never), anti-fibrotic treatment and time since diagnosis.
†Adjusted for age, sex, smoking status (ever/ never), anti-fibrotic treatment, time since diagnosis, region, social vulnerability index at enrollment and site (random).
‡Estimated difference in mean for 2 units higher $PM_{2.5}$, 4 units higher NO_2, 3 units higher O_3.

Associations between air pollution and one-year outcome

- Within 1 year of enrollment, 181 patients (22%) patients had experienced the composite outcome.
- No associations were observed between exposure to $PM_{2.5}$, NO_2 or O_3 at enrollment and the composite outcome (hazard ratios 0.91 [95% CI: 0.70, 1.19], 0.95 [0.79, 1.14] and 1.02 [0.85, 1.22], respectively).

REFERENCES

1. Johannson KA et al. Chest 2018;154:119-125.
2. Zheng Q et al. Respirology 2023;28:916-924.
3. Sesé L et al. Ann Am Thorac Soc 2024;21:519-523.
4. O'Brien EC et al. BMJ Open Respir Res 2016;3:e000108.
5. Keller JP et al. Environ Health Perspect 2015;123:301-309.
6. Wang M et al. Atmos Environ 2015;123:79-87.
7. Young MT et al. Environ Sci Technol 2016;50:3686-3694.

ACKNOWLEDGEMENTS AND DISCLOSURES

The IPF-PRO/ILD-PRO Registry is supported by Boehringer Ingelheim Pharmaceuticals, Inc and run in collaboration with the Duke Clinical Research Institute and enrolling centers. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors did not receive payment for the development of this poster. Elizabeth Ng and Wendy Morris of Fleishman-Hillard, London, UK, provided editorial assistance, which was contracted and funded by Boehringer Ingelheim Pharmaceuticals, Inc. Boehringer Ingelheim was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations. Coralynn Sack reports payment from Boehringer Ingelheim Pharmaceuticals, Inc to her institution to generate the air pollution estimates for this project.

Scan QR code or visit URL for a device-friendly version of this poster.
https://www.usscicomms.com/respiratory/ATS2024/Sack

Scan QR code or visit URL for a webpage featuring BI-supported presentations at ATS 2024.
https://www.usscicomms.com/respiratory/ATS2024

IPF-PRO Registry enrolling centers: Albany Medical Center, Albany, NY; Baylor College of Medicine, Houston, TX; Baylor University Medical Center at Dallas, Dallas, TX; Cleveland Clinic, Cleveland, OH; Columbia University Medical Center/New York Presbyterian Hospital, New York, NY; Duke University Medical Center, Durham, NC; Froedtert & The Medical College of Wisconsin Community Physicians, Milwaukee, WI; Houston Methodist Lung Center, Houston, TX; Lahey Clinic, Burlington, MA; Loyola University Health System, Maywood, IL; Lynchburg Pulmonary Associates, Lynchburg, VA; Medical University of South Carolina, Charleston, SC; National Jewish Health, Denver, CO; NYU Medical Center, New York, NY; Piedmont Healthcare, Austell, GA; Pulmonary Associates of Stamford, Stamford, CT; PulmonIx LLC. Greensboro, NC; Renovatio Clinical, The Woodlands, TX; Salem Chest and Southeastern Clinical Research Center, Winston Salem, NC; South Miami Hospital, South Miami, FL; St. Joseph's Hospital, Phoenix, AZ; Stanford University, Stanford, CA; Temple University, Philadelphia, PA; The Oregon Clinic, Portland, OR; Tulane University, New Orleans, LA; UNC Chapel Hill, Chapel Hill, NC; University of Alabama at Birmingham, Birmingham, AL; University of California, Davis, Sacramento, CA; University of California Los Angeles, Los Angeles, CA; University of Chicago, Chicago, IL; University of Cincinnati Medical Center, Cincinnati, OH; University of Louisville, Louisville, KY; University of Miami, Miami, FL; University of Michigan, Ann Arbor, MI; University of Minnesota, Minneapolis, MN; University of Pennsylvania, Philadelphia, PA; University of Pittsburgh, Pittsburgh, PA; University of Virginia, Charlottesville, VA; UT Southwestern Medical Center, Dallas, TX; Vanderbilt University Medical Center, Nashville, TN; Vermont Lung Center, Colchester, VT; Wake Forest University, Winston Salem, NC; Washington University, St. Louis, MO; Weill Cornell Medical College, New York, NY; Wilmington Health and PMG Research, Wilmington, NC; Yale School of Medicine, New Haven, CT.

Poster developed for the American Thoracic Society International Conference, 2024.

SC-US-77472