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1 Title: **Is it about what comes in or what goes out?: a reply to Sesé *et al.*, 2021**

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18 Keywords: Low-income; idiopathic pulmonary fibrosis; proxy variable; health; living
19 conditions; mediators

20

1 We read with interest the recent manuscript « low income and outcome in idiopathic pulmonary
2 fibrosis (IPF): an association to uncover » by Sesé and colleagues (1). The authors compared
3 the survival of 200 patients selected from the French national prospective cohort COFI
4 according to their income, low *versus* high income (using a threshold of 18170 euros / year).
5 With an average follow-up of 33.8 ± 22.7 months, low-income was significantly associated
6 with worse overall survival after adjustment in a multivariate model. Occupational exposure
7 was not independently associated with survival. Exposure to fine particles was not included in
8 the model probably for multi collinearity issue with occupational exposure.

9

10 The World Health Organization (WHO) defines social determinants of health as “the
11 conditions, in which people are born, grow, work, live, and age, and the wider set of forces and
12 systems shaping the conditions of daily life”. Evaluation of health should address both social
13 and behavioural causes (2). Living conditions are conditioned by how much people can afford
14 for food, accommodation, transportation, healthcare... and is complex to measure. Individuals
15 with restricted consumption budgets are confronted with deprivation, inability to acquire or
16 consume certain goods, to reach a certain level of comfort or finally to honor certain compulsory
17 expenses. Insufficient outcome (what goes out) results from insufficient income (what comes
18 in) but reflects a minor aspect of poverty and needs to be complemented by non-monetary
19 indicators based on living conditions. In 2019, according to the French national institute of
20 statistics and economic studies (INSEE), 11% to 13% of the French population was considered
21 poor based on non-monetary indicators.

22 Low-income families have altered life conditions including reduced access to healthcare (3).
23 Not only health access plays a role in health in general, environmental and occupational
24 exposures have their own contribution.

1 The relationship between economically disadvantaged households and health environmental
2 conditions has been widely reported (4–6). Low-income households often bear a higher
3 exposure to environmental pollution than high-income households. Air pollution is associated
4 with increased death from lung cancer and cardiopulmonary disease and the development of
5 fibrotic interstitial lung diseases (7,8). In addition, poor housing leads to exposure to lead,
6 molds, moisture, dust mites, and rodents, associated with the increased rate of chronic diseases
7 such as asthma, obesity and diabetes (4,9). Over 50% of low-income housing had at least 3
8 exposure-related problems (10).

9 Furthermore, low-income results from low-wages occupations which are associated with higher
10 occupational exposure risks (11). Burgard and Lin clearly described the correlation between
11 “bad Jobs” and “bad Health” (12). Interestingly, occupational risks were reported to be involved
12 in the development of IPF. Second-hand smoke, breathable dust, asbestos, silica, wood dust,
13 metal dust or fumes vapours, gases, dust or fumes were risk factors independently associated
14 with IPF (13,14). Air pollution plays a major role in both the natural history of IPF and lung
15 function (15,16). The involvement of metal dust remains controversial (13,17). The
16 predominant cause of death in patients with IPF is acute exacerbation of idiopathic pulmonary
17 fibrosis that accounts for 40% mortality (18–20). Exposure to fine particles and air pollution
18 were observed as risk factors for acute exacerbation of IPF (21–23).

19

20 In summary, low-income is a strong health determinant that often includes poor environmental
21 and occupational conditions. In other words, low-income is a driver of several behavioural and
22 social mediators that directly affect the outcome. Consequently, the question may be is low-
23 income a directly relevant variable associated with IPF survival? Or is low-income a proxy
24 variable, with close correlation to living conditions? Consequently, the association between

1 low-income and reduced survival in IPF should be interpreted with caution and warrants further
2 studies to uncover unobservable or immeasurable variables linked to environment and
3 occupational exposure in IPF in addition to path analysis to correctly interpret the association
4 observed. As a result, assessment of both environmental and occupational exposures, by means
5 of questionnaires, has to be systematically implemented.

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