Serum Respiratory Virus Antibodies: Predictor of Reduced One-Second Forced Expiratory Volume (FEV₁) in Norwegian Adults

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Background. The purpose of this cross-sectional study was to investigate whether the presence of serum respiratory virus antibodies was associated with reduced one-second forced expiratory volume (FEV₁) in adults.

Methods. From a stratified random sample of 18–73 year old adults, we performed measurements of serum complement fixing virus antibodies against influenza type A and B, parainfluenza type 1, 2, and 3, respiratory syncytial virus and adenovirus on 82% (n = 1239).

Results. In the crude data, subjects having five of the seven virus antibodies had significantly lower lung function, given as sex-, age- and height-standardized residuals of FEV₁ (SFEV₁), compared with those without. After adjusting in addition for smoking habits, lifetime smoking consumption and season, the lung function levels were significantly lower in subjects with influenza type B and respiratory syncytial virus antibodies compared to those without (P < 0.01). Increasing influenza and respiratory syncytial virus antibody titres and increasing numbers of virus antibodies, respectively, were related to progressively lower lung function. Subjects with respiratory symptoms but without obstructive lung disease had lower antibody levels than subjects with obstructive lung disease, but higher levels than asymptomatic subjects. In a final multiple linear regression analysis adjusting in addition for respiratory symptom and disease status as well as for the other respiratory virus antibodies, the presence of respiratory syncytial virus antibodies was a significant predictor for reduced SFEV₁ (regression coefficient: -0.226; SE = 0.112; P = 0.04). The magnitude of the effect on lung function remained after excluding subjects reporting symptoms of respiratory infection within 3 weeks prior to the examination (regression coefficient: -0.252; SE = 0.218; P = 0.25).

Conclusions. This cross-sectional community study indicates that respiratory syncytial virus infection or re-infection is an independent predictor for reduced lung function in adults of a wide age range.

Keywords: population survey, virus antibodies, smoking, lung function, obstructive lung disease, environment

Healthy people may experience an impairment in bronchial airflow1-4 as well as increased bronchial reactivity5 in conjunction with respiratory viral infections. Respiratory viruses may also cause airflow impairment and exacerbations of asthma.6-10 However, little information is available on the possible association between respiratory virus antibody levels and impaired lung function in adults from a general population. The aim of the present report of this cross-sectional community study in Norwegian adults11,12 was to investigate whether the presence of serum respiratory virus antibodies was associated with reduced lung function in adults of a wide age range and if so, we wanted to examine if this relationship was influenced by sex, age, smoking habit, season and respiratory symptom and disease status. The present survey included information on subjects with obstructive lung disease, respiratory symptoms without clinical disease as well as asymptomatic subjects, giving us the possibility of examining whether these relationships were modified by respiratory symptom and disease status.

MATERIAL AND METHODS

Study Design

The survey was a two-phased cross-sectional study performed in the city of Bergen, Norway and 11 surrounding municipalities. The target population had at 1 January 1985, a total of 298 110 inhabitants, of which 205 478 were aged 15–70 years. A random sample of
3740 people in this age group was sent a postal questionnaire in 1985 and altogether 3370 (90%) responded.

The responders were categorized according to respiratory symptoms and environmental exposures into two strata with 1108 and 2261 subjects in each. Random samples were drawn from the first stratum \((n = 1007, 91\%)\) and from the second stratum \((n = 505, 22\%)\) using a random number generator. In the second phase of the study, these 1512 subjects were invited to a lung health examination between April 1987 and August 1988, and 1275 subjects appeared (84%). Subjects born on the first day in every month were invited and examined first, thereafter those born on the second day and so forth.

Attenders to the second phase of the study answered a standardized questionnaire and underwent spirometric tests and blood examinations. They were, without knowledge of serum virus antibody results, post hoc classified into four mutually exclusive categories by respiratory symptoms and disease status in 1987–1988. Obstructive lung disease included subjects with bronchial asthma (category 1) and chronic obstructive lung disease (COLD) (category 2). Category 3 included subjects with respiratory symptoms, but without a diagnosis of bronchial asthma or chronic obstructive lung disease. Category 4 contained subjects without respiratory symptoms or disease. The lung function level of subjects in the initial two strata within each of the four categories, respectively, did not differ significantly, and these two strata were therefore combined in the statistical analyses.

Bronchial asthma was diagnosed in those with a history of attacks of shortness of breath at rest, and with wheezing in the chest changing in severity over short periods of time, either spontaneously or after treatment. At least one typical attack had to have occurred within the previous 6 months. Chronic obstructive lung disease was diagnosed in those with a history of chronic cough; phlegm when coughing; breathlessness or wheezing, or both; and a ratio of \(FEV_1\) to \(FVC\) of <0.7. The diagnostic criteria were thus based on a combination of clinical physiological investigations and clinical judgement and have been used in previous reports of the present survey as well as in a previous Norwegian survey. The following respiratory symptoms were assessed; morning cough, cough during the day, chronic cough, phlegm when coughing, breathlessness when walking uphill, attacks of breathlessness and wheezing. Acute respiratory infection was assessed by answering the following question: Have you had symptoms of respiratory infection within the last 3 weeks? The survey was approved by the Regional Committee of Medical Research Ethics.

**Smoking Habit**

Non-smokers were subjects who had never smoked daily. Ex-smokers were subjects who had smoked daily and given it up. Smokers were those who smoked daily at the time of the study. Amount of lifetime smoking was assessed as pack-years. The answers on smoking habit were validated by carboxyhaemoglobin measurements of venous blood samples with an OSM3 Hemoximeter, Radiometer, Denmark.

**Blood Sampling**

Serum virus antibodies against influenza virus types A and B, parainfluenza virus types 1, 2 and 3, respiratory syncytial virus and adenoviruses were analysed by the complement fixation test using antigens obtained from the Department of Virology, National Institute of Public Health, Oslo. A titre of 1 : 8 or more diluted was considered positive (described in results as >8), indicating a recent or past infection/re-infection.

Of those with complete examinations, 492 subjects were examined in the winter months from October through March, while 747 subjects were examined in the summer months from April through September.

**Spirometry**

The forced vital capacity (FVC) and the forced expiratory volume in one second (\(FEV_1\)) were measured with Gould 2100 pulmonary function laboratory equipment (SensorMedics BV, Bilthoven, the Netherlands). The highest \(FEV_1\) measurement was used in the analysis. Age- sex- and height-standardized residuals of \(FEV_1\) (SFEV1) were calculated by dividing the residual (observed \(FEV_1\) minus predicted) by the residual standard deviation (543 ml in men and 403 ml in women) taken from the regression equation of a Norwegian reference population.

**Statistical Analysis**

Differences in prevalences between groups were tested by \(\chi^2\) test. Differences in mean values between groups were tested by one-way analysis of variance. Multiple linear regression analysis was performed in order to evaluate factors of importance for prediction of lung function level. Categorical variables were introduced to the equations using dummy variable technique. In the multivariate analysis season was scored as a trend variable with six levels going from the summer months July/June (1) to the winter months December/January (6). Regression coefficients were compared between groups by analysis of covariance. The statistical analyses were performed with the BMDP package.
Table 1 The presence of serum respiratory virus antibodies* by respiratory symptom and disease status in Norwegian adults

<table>
<thead>
<tr>
<th>Respiratory symptom and disease status</th>
<th>Parainfluenza virus</th>
<th>Influenza virus</th>
<th>Respiratory syncytial virus</th>
<th>Adenovirus</th>
<th>Any virus antibodyb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>type 1 %</td>
<td>type 2 %</td>
<td>type 3 %</td>
<td></td>
<td>%</td>
</tr>
<tr>
<td>Obstructive lung disease (n = 101)c</td>
<td>11</td>
<td>25</td>
<td>14</td>
<td>63</td>
<td>27</td>
</tr>
<tr>
<td>Symptomatic subjectsd (n = 545)c</td>
<td>7</td>
<td>13</td>
<td>7</td>
<td>46</td>
<td>24</td>
</tr>
<tr>
<td>Asymptomatic subjectsd (n = 591)c</td>
<td>7</td>
<td>8</td>
<td>7</td>
<td>36</td>
<td>18</td>
</tr>
</tbody>
</table>

* Complement fixing antibody titre of 1 : 8 or more diluted.

b Chi-square test between respiratory symptom and disease status groups; P < 0.01

c The sum of subjects with virus antibodies is higher than the number of subjects in the study population because each subject may have more than one virus antibody.

d Without obstructive lung disease.

RESULTS

Respiratory Virus Antibodies and Respiratory Symptom and Disease Status

Of the 1512 subjects invited, 1239 (82%) answered the questionnaire, and had acceptable FEV₁ recordings as well as respiratory virus antibody measurements. Of the 689 virus antibody positive subjects in the study population, 263 subjects had only one of the seven examined antibodies, while 426 (62%) had two or more. This indicates that combinations of infections or re-infections are predominant in this adult population. The percentages of subjects with serum antibodies against the seven viruses by respiratory symptom and disease status are given in Table 1. Subjects with respiratory symptoms but without obstructive lung disease had lower antibody levels than subjects with obstructive lung disease, but higher levels than asymptomatic subjects.

When excluding subjects reporting symptoms of acute respiratory infection within 3 weeks prior to the examination, indicating a recent infection or re-infection, we observed rates of antibody positivity at similar levels to those in the total material.

Respiratory Virus Antibodies and Lung Function

The sex- age- and height-standardized residuals of forced expiratory volume in one second (SFEV₁) were estimated for subjects with antibodies against each of the seven respiratory virus antibodies and compared with the SFEV₁ for those without any of these (Figure 1). Subjects having any of these virus antibodies had lower lung function than those without. This was statistically significant for those with influenza virus types A and B, respiratory syncytial virus and parainfluenza virus types 1 and 2 antibodies. After adjustment for smoking habit, lifetime smoking consumption and season in a one-way analysis of covariance, respiratory syncytial virus (P < 0.01) and influenza virus type B (P < 0.01) remained significant predictors of impaired lung function, while influenza type A was of borderline significance (P = 0.08) (Table 2).

Performing the same analyses for subjects with influenza virus type A antibodies only (n = 160), influenza virus type B antibodies only (n = 32) and respiratory syncytial virus antibodies only (n = 33), the SFEV₁ differences between those with and those without virus antibodies were still approximately of the same magnitude as after adjustment in the analysis for all subjects having that specific antibody.

Number of Respiratory Virus Antibodies and SFEV₁

Increasing number of respiratory virus antibodies were related to progressively reduced lung function (Figure 2). Also when adjusting for smoking habit, lifetime smoking consumption and season, we observed a significant relationship between numbers of virus antibodies (0,1,2,3) and SFEV₁ (regression coefficient: −0.084; SE = 0.032; P < 0.01). There was no significant variation of this relationship by respiratory symptom and disease status (P = 0.39).

Respiratory Syncytial Virus and Influenza Type B Antibodies and SFEV₁

In analyses of covariance stratified by sex, age, smoking habit and season of the year, respectively (Table 3), we observed that the relationship between the presence of respiratory syncytial virus antibodies and impaired
Subjects without any respiratory serum virus antibody

Subjects with respiratory serum antibodies against Parainfluenza virus type 1, type 2, type 3, Influenza virus type A, type B, Respiratory syncytial virus, Adenovirus

Subjects (n) 560 89 145 98 528 266 163 290

P-values

<0.01<br>0.17<br><0.01<br><0.01<br><0.01<br>0.19

**FIGURE 1** Sex-, age- and height-standardized residuals (mean, standard error) of forced expiratory volume in one second (SFEV) in Norwegian adults by presence of serum respiratory virus antibodies (n = 1239)

* Significance probabilities for each respiratory virus antibody comparing subjects with that specific virus antibody to those without any virus antibody.

**TABLE 2** Sex-, age- and height-adjusted residuals of forced expiratory volume in one second (SFEV) in Norwegian adults with or without seven respiratory virus antibodies after adjusting for smoking habit, lifetime smoking consumption and season (n = 1239)

<table>
<thead>
<tr>
<th>Virus antibodies</th>
<th>n</th>
<th>SFEV (mean ± SE)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without any</td>
<td>560</td>
<td>-0.28 ± 0.05</td>
<td></td>
</tr>
<tr>
<td>Parainfluenza virus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>type 1</td>
<td>89</td>
<td>-0.47 ± 0.14</td>
<td>0.17</td>
</tr>
<tr>
<td>type 2</td>
<td>145</td>
<td>-0.47 ± 0.11</td>
<td>0.22</td>
</tr>
<tr>
<td>type 3</td>
<td>98</td>
<td>-0.39 ± 0.13</td>
<td>0.44</td>
</tr>
<tr>
<td>Influenza virus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>type A</td>
<td>528</td>
<td>-0.47 ± 0.06</td>
<td>0.08</td>
</tr>
<tr>
<td>type B</td>
<td>266</td>
<td>-0.54 ± 0.08</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td>163</td>
<td>-0.61 ± 0.10</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>290</td>
<td>-0.39 ± 0.08</td>
<td>0.30</td>
</tr>
</tbody>
</table>

* Two-tailed significance probabilities comparing subjects with each specific virus antibody to those without any.

* Unadjusted mean value.

Lung function was stronger for women than for men. Furthermore, this relationship tended to be weakened by increasing age. Never-smokers appeared to have a stronger relationship between the presence of virus antibodies and reduced lung function level than smokers. Finally the association between virus antibodies and low lung function was more overt in winter months compared with summer months. Tests of equality of slopes showed that there was no significant variation across the categories of the abovementioned stratification variables either for respiratory syncytial virus or for influenza virus type B antibodies. There was, however, a significant variation for respiratory syncytial virus antibodies between males and females (P < 0.01).

Furthermore, we observed a dose-response relationship between respiratory syncytial virus antibody titres (<8 (n = 1074), 8–16 (n = 119), 16–32 (n = 38), ≥32 (n = 6)) and impaired lung function in the crude data as well as after adjustment for sex, age, smoking habit, lifetime smoking consumption as well as season, in a regression analysis (regression coefficient: -0.218; SE = 0.078; P < 0.01). The same relationship was
Number of serum respiratory virus antibodies

SFEV

0

-0.5

-1.0

Subjects (n) 560 283 176 240

FIGURE 2 Sex-, age- and height-standardized residuals (mean, standard error) of forced expiratory volume in one second (SFEV) in Norwegian adults by numbers of serum respiratory virus antibodies (n = 1239)

TABLE 3 Sex-, age- and height-adjusted residuals of forced expiratory volume in one second (SFEV) in Norwegian adults with specific respiratory virus antibodies compared with those without any stratified by sex, age, smoking habits and season after adjustments in analyses of covariancea (n = 1239)

<table>
<thead>
<tr>
<th>Stratifying variables</th>
<th>Without any respiratory virus antibody (titre &lt; 1 : 8)</th>
<th>Respiratory syncytial virus antibodies (titre of 1 : 8 or more diluted)</th>
<th>Influenza type B virus antibodies (titre of 1 : 8 or more diluted)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n  Mean SFEV ± SE</td>
<td>n  Mean SFEV ± SE  Pb</td>
<td>n  Mean SFEV ± SE  Pb</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>278  -0.47 ± 0.08</td>
<td>91  -0.50 ± 0.13  0.81</td>
<td>136  -0.56 ± 0.12  0.51</td>
</tr>
<tr>
<td>Women</td>
<td>282  -0.10 ± 0.07</td>
<td>72  -0.77 ± 0.15  &lt;0.01</td>
<td>130  -0.52 ± 0.11  &lt;0.01</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–34</td>
<td>219  -0.08 ± 0.08</td>
<td>60  -0.49 ± 0.16  0.02</td>
<td>101  -0.18 ± 0.16  0.81</td>
</tr>
<tr>
<td>35–54</td>
<td>195  -0.23 ± 0.10</td>
<td>53  -0.53 ± 0.09  0.13</td>
<td>94   -0.37 ± 0.14  0.05</td>
</tr>
<tr>
<td>55–73</td>
<td>146  -0.67 ± 0.11</td>
<td>50  -0.90 ± 0.18  0.27</td>
<td>71   -0.99 ± 0.17  0.11</td>
</tr>
<tr>
<td>Smoking habits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smokers</td>
<td>334  -0.06 ± 0.06</td>
<td>81  -0.48 ± 0.13  &lt;0.01</td>
<td>138  -0.30 ± 0.10  0.04</td>
</tr>
<tr>
<td>Ex-smokers</td>
<td>106  -0.47 ± 0.15</td>
<td>31  -0.65 ± 0.27  0.58</td>
<td>43    -0.46 ± 0.23  0.81</td>
</tr>
<tr>
<td>Smokers</td>
<td>120  -0.69 ± 0.12</td>
<td>51  -0.93 ± 0.19  0.28</td>
<td>85   -1.02 ± 0.15  0.09</td>
</tr>
<tr>
<td>Season of the yearb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Winter months</td>
<td>161  -0.33 ± 0.11</td>
<td>89  -0.70 ± 0.10  0.02</td>
<td>152  -0.51 ± 0.11  0.24</td>
</tr>
<tr>
<td>Summer months</td>
<td>399  -0.26 ± 0.06</td>
<td>74  -0.54 ± 0.15  0.11</td>
<td>144  -0.59 ± 0.12  0.01</td>
</tr>
<tr>
<td>Total</td>
<td>560  -0.28 ± 0.06</td>
<td>163 -0.61 ± 0.10  &lt;0.01</td>
<td>266  -0.54 ± 0.08  &lt;0.01</td>
</tr>
</tbody>
</table>

* Adjusted for lifetime smoking consumption as well as sex, age, smoking habits and season, respectively in one-way analyses of covariance.

b Two-tailed significance probabilities comparing subjects with respiratory syncytial virus antibodies and influenza virus type B antibodies, respectively with those without any respiratory virus antibody.

c Winter months – October through March; Summer months – April through September.
in a final multiple linear regression analysis after adjusting for sex, age, smoking habit, lifetime smoking consumption, season, respiratory symptom and disease status and the presence of the other virus antibodies. No interaction terms remained significant at the 0.05 level in the final model. When excluding subjects reporting having symptoms of respiratory infections within the last 3 weeks prior to the examination (n = 344) the magnitude of the effect of respiratory syncytial virus antibodies on lung function remained (regression coefficient: -0.252; SE = 0.218; P = 0.25). Having influenza virus type B antibodies (regression coefficient: -0.160; SE = 0.098; P = 0.10) was not a significant predictor of reduced lung function in the final model.

DISCUSSION
This cross-sectional study showed in the crude data that subjects having five of the seven examined virus antibodies had significantly lower lung function, given as sex-, age- and height-standardized residuals of forced expiratory volume in one second (SFEV₁), than those without. The presence of respiratory syncytial virus antibodies, reflecting recent or past infections/re-infections, was associated with impaired lung function in adults in the crude data as well as after adjustment for possible confounders in a multiple linear regression analysis. If subjects with symptoms of respiratory infection within 3 weeks prior to the examination were excluded, the magnitude of the effect on lung function still remained.

Selection bias may affect the results in cross-sectional community studies. However, the subjects in this survey were selected from the community regardless of their respiratory infection status. Furthermore, the attenders and the non-attenders were comparable with respect to important environmental exposures.¹²

Recall bias is unlikely to have influenced our results since both the exposure status (specific virus antibodies) and the outcome variable (lung function) were based on objective measurements. Self-reported smoking status may be an actual confounder. However, using the smoking status from the carboxyhaemoglobin measurements in the final analysis revealed basically the same results.

The classification of the patients as infected or re-infected with a specific respiratory virus may be subject to many sources of error. Firstly, the sensitivity of the serological analysis for infection is less than 100%. Secondly, the patients were not examined for rhinoviruses and coronaviruses causing common colds, because tests for these antibodies are not generally available. Such infections may therefore have been present in subjects without any of the examined antibodies. Subjects may thus have been misclassified, and the difference between the two groups may have been underestimated. The fact that 60% of virus-positive subjects have virus antibodies against more than one virus type may on the other hand tend to overestimate the true relationship. However, the magnitude of the effect of lung function between those with only one specific virus antibody compared with those without was at the same level as after adjustment in the multivariate analyses. Furthermore, in the final multiple linear regression analysis we have adjusted for the presence of all the other respiratory virus antibodies. These adjustments could result in overcorrection of the covariables, since there was a considerable overlap between the seven examined virus antibodies. Despite this possible overadjustment, respiratory syncytial virus antibodies remained independently associated with impaired lung function.

We observed a dose-response relationship between increasing virus antibody titres for respiratory syncytial virus antibodies as well as for influenza virus types A and B, but not for the parainfluenza viruses and
adenoviruses. This may indicate that these virus infections may be related to impaired lung function in a causal way, while the other virus infections might not.

A decrease in lung function during an acute respiratory infection or after previous respiratory illnesses has been observed in adults. Our results provide support that this relationship is not only limited to periods of acute infections, but also to periods without.

The relationship between the presence of respiratory syncytial virus antibodies and impaired lung function did not differ significantly by sex in the final analysis of our study. Although there was no significant interaction between the presence of respiratory virus antibodies and sex versus lung function impairment\(^1\), the effects on lung function tended to be greater in women than in men. Sex differences may be due to inherently different susceptibility, different smoking behaviour as well as differences in environmental and occupational exposure. Furthermore, women have smaller lungs and larger airways than men of comparable size.\(^2\) Since airway size may influence smoke distribution and lung size may be related to impaired lung function, mechanical factors may favour an increased sensitivity of females to cigarette smoking. Even though we have adjusted for smoking status as well as lifetime smoking consumption it may be incomplete. Finally, hormonal factors may influence epithelial cell function and there are also possible sex differences in inflammatory responses, atopy and airways' responsiveness.

Pattenmore et al.\(^8\) have suggested that subjects with obstructive lung disease may get more virus infections than those without, which is in agreement with our observations. Our results also indicate that symptomatic but non-diseased subjects may get more infections than asymptomatic subjects.

In our study the association between the presence of respiratory syncytial virus antibodies and impaired lung function did not differ significantly by respiratory symptom and disease status. This may indicate that respiratory virus infections or re-infections and impaired lung function may affect wider populations than only those with obstructive lung disease.

We did not observe a significant association between the presence of respiratory virus antibodies other than respiratory syncytial virus and lung function, although antibodies to influenza virus types A and B were more prevalent than respiratory syncytial virus antibodies. However, the magnitude of the effect on lung function for influenza virus type B (regression coefficient: \(-0.160, SE = 0.098; P = 0.10\)) and influenza virus type A (regression coefficient: \(-0.082, SE = 0.045; P = 0.18\)) antibodies should thus not be overlooked as possible predictors of impaired lung function.

The presence of adenovirus antibodies did not predict impaired lung function in this survey. However persistent and latent viral infections have been suggested to play a role in the pathology of asthma in children.\(^22,29\) In our survey we have examined adenovirus as a group, but these possible effects may be limited to some of the more than 40 serotypes of adenoviruses. Furthermore, there may be differences between children undergoing growth and adults in a more stable phase of lung function level or in a decline phase.

The decrement in ventilatory function may be due to respiratory tract infections affecting the epithelium of the airways, damaging the cilia, or temporarily increasing the mucus and thus eventually producing obstruction.\(^30\) Increased bronchial reactivity,\(^5\) parenchymal damage, interstitial changes and necrosis with oedema and infiltrates are further consequences of respiratory infections.\(^7\)

A cross-sectional study cannot highlight whether decreased pulmonary function was a result of past virus infections or these infections were more likely to occur in subjects with poor lung function. The latter has been proposed in children\(^31\) and in adults.\(^22\) Only longitudinal studies from childhood to adulthood can answer these questions. However, it is plausible to suggest that lung function might be influenced by viral infections during lung growth and during decline in adult life.

This study indicates that past or present respiratory syncytial virus infections and re-infections predicts impaired lung function. If so, avoiding respiratory viral infections and re-infections may have both preventive and therapeutic implications for achieving optimal lung function in adults of a wide age range.

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