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Lung function before and after COVID-19 in young adults: A population-based study



Ida Mogensen, MD, PhD,^a Jenny Hallberg, PhD,^{a,b} Sophia Björkander, PhD,^a Likun Du, PhD,^c Fanglei Zuo, PhD,^c Lennart Hammarström, MD, PhD,^c Qiang Pan-Hammarström, MD, PhD,^c Sandra Ekström, PhD,^{d,e} Antonios Georgelis, PhD,^d Lena Palmberg, MD, PhD,^d Christer Janson, MD, PhD,^f Anna Bergström, PhD,^d Erik Melén, MD, PhD,^{a,b} and Inger Kull, PhD,^{a,b} on behalf of the BAMSE COVID-19 Study Group* *Stockholm, Huddinge, and Uppsala, Sweden*

Background: There is limited evidence on the long-term impact of mild-to-moderate coronavirus disease 2019 (COVID-19) on lung function among young adults.

Objectives: We aimed to assess whether COVID-19 has a negative impact on lung function in young adults and whether asthma, allergic sensitization, or use of inhaled corticosteroids (ICSs) modifies a potential association.

Methods: Participants from the population-based BAMSE (Barn, Allergi, Miljö, Stockholm, Epidemiologi) cohort with spirometry assessed before (2016-2019) and after onset of the COVID-19 pandemic (2020-2021) were included. Serum levels of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) receptor-binding domain-specific IgG, IgM, and/or IgA

(determined with ELISA) defined seropositivity. Mean change in lung function (ie, change in FEV₁, forced vital capacity [FVC], and FEV₁/FVC ratio expressed as percent of predicted [pp]) from before to after onset of the pandemic were compared between the seronegative and seropositive participants. In seropositive participants, change in lung function was assessed in relation to allergic sensitization and self-reported ICS use. **Results:** Of the 853 included participants, 29% (n = 243) were seropositive. There were no differences in change in lung function between the seronegative and seropositive participants (for mean change in FEV₁ pp [SD], seropositivity = 0.87% [4.79%] and seronegativity = 1.03% (4.76%) [*P* = .66] for difference using a *t* test; FVC pp (SD), seropositivity = 1.34% (4.44%) and seronegativity = 1.29% (4.27%) [*P* = .87]; and for FEV₁/FVC pp (SD), seropositivity = -0.25% (3.13%) and seronegativity = -0.13% (3.15%) [*P* = .61]). Similar results were observed among participants with asthma (n = 147 [17%]). Among seropositive participants, allergic sensitization or ICS use did not influence lung function.

Conclusion: We found no evidence of mild-to-moderate COVID-19 affecting lung function long term in a population-based cohort of young adults. Moreover, neither asthma nor allergic sensitization nor ICS use affected the results. (*J Allergy Clin Immunol Global* 2022;1:37-42.)

Key words: Asthma, COVID-19, Lung function

From ^athe Department of Clinical Science and Education Södersjukhuset, Karolinska Institutet, Stockholm; ^bthe Sachs' Children and Youth Hospital, Södersjukhuset, Stockholm; ^cthe Department of Biosciences and Nutrition, Karolinska Institutet, Huddinge; ^dthe Institute of Environmental Medicine, Karolinska Institutet, Stockholm; ^ethe Center for Occupational and Environmental Medicine, Region Stockholm; and ^fthe Department of Medical Sciences: Respiratory, Allergy, and Sleep Research, Uppsala University.

*The members of the BAMSE COVID-19 Study Group are as follows: Catarina Almqvist, Niklas Andersson, Natalia Ballardini, Anna Bergström, Sophia Björkander, Petter Brodin, Anna Castel, Sandra Ekström, Antonios Georgelis, Jenny Hallberg, Lennart Hammarström, Qiang Pan-Hammarström, Christer Janson, Maura Kere, Inger Kull, André Lauber, Alexandra Löfvquist, Erik Melén, Jenny Mjösberg, Ida Mogensen, Lena Palmberg, Göran Pershagen, Niclas Roxhed, and Jochen M. Schwenk.

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Corresponding author: Ida Mogensen, MD, PhD, Södersjukhuset, Jägargatan 20 -I, 118 83 Stockholm, Sweden. E-mail: ida.mogensen@ki.se.

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The coronavirus disease 19 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is primarily a respiratory disorder. The major effect on pulmonary function in the acute phase is a decreased diffusion capacity, and this is associated with severity of disease.¹⁻⁴ In hospitalized patients with severe disease, restrictive lung function impairment has been described.³⁻⁸ A difficulty, however, in evaluating the impact of COVID-19 on lung function measured with spirometry is the wide variability in lung function between individuals; specifically, the lung function of an individual with a habitually higher than average lung function can decline significantly before reaching a pathologic value. Whether spirometric lung function is also affected to an extent not reaching a clinically pathologic value is of interest both at a population level (for future public health consequences) and on an individual level (for better assessment of individual risks⁹ and follow-up measures).

Abbreviations used

AU:	Arbitrary unit
BAMSE:	Barn, Allergi, Miljö, Stockholm, Epidemiologi
BMI:	Body mass index
COVID-19:	Coronavirus disease 2019
FVC:	Forced vital capacity
ICS:	Inhaled corticosteroid
pp:	Percent of predicted
SARS-CoV-2:	Severe acute respiratory syndrome coronavirus 2

Although the abnormalities observed in the acute phase of severe COVID-19 are found to improve during the months after clearance of the infection,^{5,8,10,11} the extent of persistently affected lung function in a specific individual is unknown. The available follow-up studies are generally performed on clinic populations,^{5,8,10-12} where the patients have been in contact with a health care provider and have in most cases been hospitalized. However, post-COVID-19 symptoms have been reported to affect individuals independent of disease severity,¹³ and the degree to which lung function is affected by less severe disease is not known. The availability in our cohort of before- and after-COVID-19 measurements is therefore of great value to assess how COVID-19 disease affects spirometric lung function after recovery from mild-to-moderate COVID-19.

Nonsevere asthma is not a risk factor for hospitalization or severe COVID-19,^{14,15} but whether preexisting asthma influences changes in lung function related to mild or moderate COVID-19 is unknown. Further, use of inhaled corticosteroids (ICSs) may protect against more severe COVID-19.¹⁶ Similarly, allergic inflammation, which is often present in asthma, may protect against more severe COVID-19.¹⁷

The aim of this investigation was to assess whether mild-to-moderate COVID-19 has a negative impact on lung function in young adults and whether asthma modifies a potential association. Change in lung function from before to during the pandemic was compared between individuals who had COVID-19 (defined by the presence of SARS-CoV-2 antibodies in serum) and individuals who were seronegative for SARS-CoV-2. As a subanalysis, impact of allergic sensitization compared with no allergic sensitization and impact of ICS use compared with no ICS use were assessed in participants with positive serology.

METHODS

The examined population comes from the BAMSE (Barn, Allergi, Miljö, Stockholm, Epidemiologi) cohort, a Swedish population-based birth cohort that initially included 4089 children followed since infancy (1994-1996).¹⁸ For this investigation, the data analyzed were from an examination performed when the cohort members were 22 to 24 years of age (2016-2019)¹⁹ (referred to as the pre-COVID-19 examination) and an examination initiated after onset of the pandemic (2020-2021) (referred to as the COVID-19 examination).

The COVID-19 examination was done in 2 phases, the first of which was conducted a web-based questionnaire open from August to November 2020,²⁰ which all participants who had participated in the clinical examination at the pre-COVID-19 examination (n = 2270) were invited to complete. Thereafter, 1453 of the participants responding in the first phase were invited participate in to the second phase, which was conducted from October 2020 to June 2021, which consisted of a questionnaire and a clinical examination that included lung function assessment and measurements of antibodies against SARS-CoV-2 (n = 1028). After exclusion of participants with missing prebronchodilatory spirometry data from the pre-COVID-19 or COVID-19 examination,

insufficient blood samples, or vaccination against SARS-CoV-2, a total of 853 participants remained (Fig 1).

Lung function was measured (according to European Respiratory Society/American Thoracic Society guidelines²¹) by using a Vyaire Vyntus spirometer (Vyaire Medical, Chicago, Ill) at both examinations to determine FEV₁, forced vital capacity (FVC), and the ratio FEV₁/FVC. Measured values were expressed as percent of predicted (pp) using the Global Lung Initiative reference material.²² The change between examinations was calculated on an individual level as the lung function at the pre-COVID-19 examination subtracted from the lung function at the COVID-19 examination.

Previous COVID-19 was defined as seropositivity against SARS-CoV-2 and based on the presence of an anti-receptor-binding domain IgG level higher than 25.09 arbitrary units (AU)/mL, IgM level higher than 14.42 AU/mL, and/or IgA level higher than 2.61 AU/mL. Antibodies in serum were measured on the same day as performance of the spirometric examination. Antibody levels were determined by ELISA, as previously described in detail.^{23,24} Cutoff values for antibody positivity were determined on the basis of receiver operating characteristic curves with data from historical (prepan-demic) control samples and convalescent patients with COVID-19.²³

Asthma was considered present if the participant fulfilled the following criteria: a doctor's diagnosis of asthma (ever) and asthma symptoms and/or asthma medication use during the past year²⁵ at either of the 2 examinations.

Smoking was defined as present when a participant reported intermittent or daily use of cigarettes at the COVID-19 examination.

Allergic sensitization was assessed at the pre-COVID-19 examination and defined as an IgE level against common airborne allergens (Phadiatop mix, Thermo Fischer Scientific, Uppsala, Sweden) of 0.35kU/L or higher. Use of an ICS was self-reported at the COVID-19 examination covering the period from 4 weeks before the first COVID-19-questionnaire until the clinical examination. Participants were divided into the categories no use and as-needed/continuous use during this period.

Self-reported COVID-19 symptoms

The participants reported suspected symptoms of COVID-19 from onset of the pandemic to the time of the clinical examination. The group with antibodies against SARS-CoV-2 was divided into those with self-reported respiratory symptoms (cough or dyspnea) and those without such symptoms. The group was also divided into those reporting being bedbound at least 1 day during a suspected COVID-19 disease period and those who were not bedbound.

Study design and statistical analyses

The change in lung function from the pre-COVID-19 examination to the COVID-19 examination had a normal distribution for all lung function parameters. The change was compared between the seropositive group and the seronegative group by using *t* tests and linear regressions and thereafter in a multiple regression model adjusted for sex, body mass index (BMI), smoking (daily or intermittent), time between the examinations, and lung function at the pre-COVID-19 examination. These parameters were chosen as confounders having a potential association with the risk of getting infected by SARS-CoV-2^{26,27} and change in lung function.^{28,29} Further, to assess the impact of a presumably more recent infection, IgM-positive participants (regardless of seropositivity for other antibodies) were compared with the seronegative participants in a linear regression. Thereafter, the same analyses were done for the subgroup with asthma.

In the seropositive group, change in lung function was compared between the groups with and without allergic sensitization and the groups with and without self-reported ICS use.

As sensitivity analyses, stratifications were done for sex, elevated BMI (>25 kg/m²), and smoking (all at the COVID-19 follow-up) to assess the effect modification by these variables. Comparisons between change in lung function among seropositive participants reporting respiratory symptoms or having been bedbound and seronegative participants were done. Further, a lung function comparison between seropositive and seronegative participants was

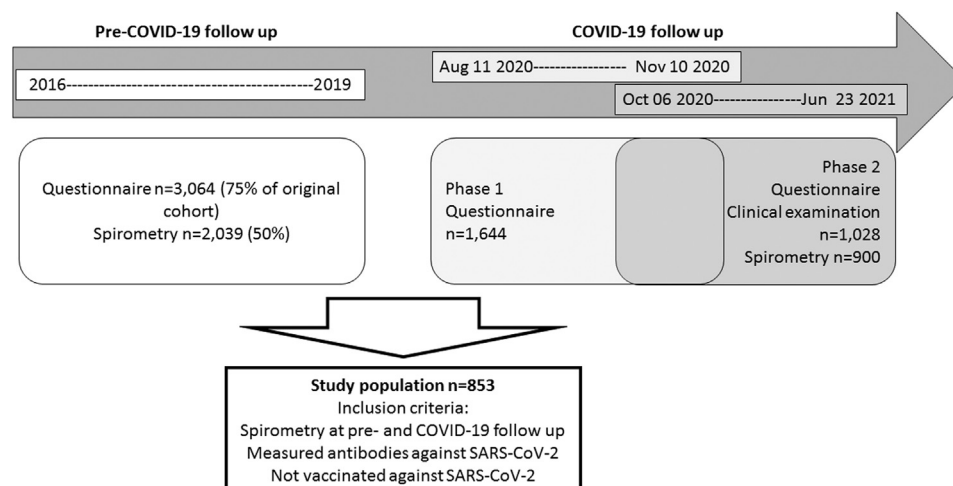


FIG 1. Flowchart of the study design and included population.

done with lung function measured in milliliters and as a ratio adjusted for height at the COVID-19 follow-up and sex.

A *P* value of .05 or less was considered statistically significant. Missing data were handled with complete cases. The statistical analyses were done with STATA statistical software, release 16.1 (StataCorp, College Station, Tex).

Ethical permission

The study was approved by the Swedish Ethical Review Authority (Dnr 2016/1380-31/2 and 2020-02922), and all participants provided written informed consent.

RESULTS

Characteristics in the pre-COVID-19 and COVID-19 examinations

Of the included population (*N* = 853), 17% (*n* = 147) fulfilled the criteria for asthma at 1 or both follow-ups. The mean period between the 2 examinations was 3.2 years (range 1.6-4.4 years). The prevalence of smoking decreased between the examinations. The mean FEV₁ and FVC expressed as pp increased (Table I). Compared with the whole cohort participating in the pre-COVID-19 examination, the study cohort had a lower prevalence of males (36% vs 44% [*P* < .001]) and a higher percentage of participants with a BMI of 25 or higher (20% vs 23% [*P* = .019]), but it did not differ from the standpoints of prevalence of current smokers, allergic sensitization, or lung function.

In total, 29% of the participants were seropositive (*n* = 243) and 71% were seronegative (*n* = 607) for SARS-CoV-2 antibodies. The majority of seropositive participants (81% [*n* = 196]) had SARS-CoV-2-specific IgG antibodies (Table I). Among those with positive serology, 149 (61%) reported respiratory symptoms (cough and/or dyspnea) and 121 (50%) reported being bedbound during the disease (with 22 of them [9%] reporting being bedbound for a week or more). Of the seropositive participants, 1 reported having been admitted to the hospital because of COVID-19. However, 36 participants (15%) reported no symptoms indicative of COVID-19. Hence, the majority of the participants had mild disease.

The prevalence of females was higher among the participants with asthma than among the participants without asthma (71% vs 62% [*P* = .031]). We found no significant differences in time

between the examinations, prevalence of smoking, or BMI between participants with and without asthma (data not shown).

Comparisons of characteristics between seropositive and seronegative groups

There were no significant differences between the seropositive and seronegative groups from the standpoints of time between the examinations, asthma prevalence, prevalence of allergic sensitization, smoking, or lung function at the COVID-19 examination (Table II). The seropositive subjects with asthma also did not differ from the seronegative subjects with asthma (see Table E1 in the Online Repository at www.jaci-global.org).

Change in lung function between the pre-COVID-19 and COVID-19 examinations

The crude linear regression analysis comparing change in lung function in the seropositive and seronegative groups did not reveal any significant differences (Fig 2, A). The mean changes in lung function in the seronegative versus seropositive groups were as follows: for FEV₁ pp (SD), 0.87% (4.79%) for seropositive participants versus 1.03% (4.76%) for seronegative participants (*P* = .66 [*t* test]); for FVC pp (SD), 1.34% (4.44%) for seropositive participants versus 1.29% (4.27%) for seronegative participants (*P* = .87); and for FEV₁/FVC pp (SD), -0.25% (3.13%) for seropositive participants versus -0.13% (3.15%) for seronegative participants (*P* = .61) (for presentation of the values in full, see Table E2 in the Online Repository at www.jaci-global.org). Adjustment for *a priori*-identified confounders (sex, BMI, smoking, time between the examinations, and lung function at the pre-COVID-19 examination) did not affect the estimates (Fig 2, A). When participants positive for SARS-CoV-2-specific IgM were compared with seronegative participants, similar results were found (Fig 2, A).

Among the participants with asthma (*n* = 147), no significant differences in lung function estimates were found between the seropositive (*n* = 38) and seronegative groups (*n* = 109) in the linear regression model (Fig 2, B). The estimates in the seropositive group showed a nonsignificant tendency toward a more obstructive pattern with a smaller increase in FEV₁ (*P* = .24) and a decrease in FEV₁/FVC (*P* = .16) compared with in the

TABLE I. Background and clinical characteristics at the pre-COVID-19 and COVID-19 examinations

Characteristic (N = 853)	Pre-COVID-19 examination (2016-2019)	COVID-19 examination (2020-2021)	Statistical comparison between before and after COVID-19 (P value)
Sex	310 (36%) males	310 (36%) males	
Age (y), median (IQR)	22.5 (22.2-22.8)	25.9 (25.1-26.4)	
BMI (kg/m ²), median (IQR)	22.1 (20.4-24.0)	22.6 (20.7-24.8)	<.001*
Asthma, no. (%)	103 (12%) [†]	123 (14%)	.015*
Seropositive, no. (%)		243 (29%) [†]	
IgG positive		196 (23%) [†]	
IgM positive		95 (11%)	
IgA positive		61 (7%)	
Current smoker, no. (%)	165 (19%) [‡]	103 (12%) [†]	<.001*
Allergic sensitization, no. (%)	358 (42%) [§]		
ICS use, no. (%)		74 (9%) [†]	
FEV ₁ (pp), mean (SD)	96.7% (9.8%)	97.7% (10.0%)	<.001**
FVC (pp), mean (SD)	99.2% (10.2%)	100.5% (10.5%)	<.001**
FEV ₁ /FVC (pp), mean (SD)	97.0% (6.9%)	96.9% (6.7%)	.14**

IQR, Interquartile range.

*Wilcoxon signed rank test; **paired *t* test.[†]n = 850.[‡]n = 851.[§]n = 846.**TABLE II.** Clinical characteristics among the seropositive and seronegative participants at the COVID-19 examination

Characteristic	Seronegative (n = 607)	Seropositive (n = 243)	P value
Time between examinations (y), mean (SD)	3.17 (0.61)	3.16 (0.60)	.71
Asthma, no. (%)	109 (18%)	38 (16%)	.42
Male sex, no. (%)	224 (37%)	86 (35%)	.70
BMI at the COVID-19 examination (kg/m ²), median (IQR)	22.5 (20.7-24.6)	22.8 (20.9-25.5)	.13
Allergic sensitization, no. (%)	262 (43%)	94 (39%)	.24
ICS use, no. (%)	50 (8%)	24 (10%)	.43
β ₂ agonist used on the day of spirometry, no. (%)	9 (1%)	3 (1%)	.87
Current smoker, no. (%)	69 (11%)	35 (14%)	.30
FEV ₁ (pp), mean (SD)*	97.7% (10.3%)	97.9% (9.4%)	.77
FVC (pp), mean (SD)*	100.1% (10.5%)	101.2% (10.6%)	.17
FEV ₁ /FVC (pp), mean (SD)*	97.1% (6.8%)	96.3% (6.6%)	.13

IQR, Interquartile range.

*At the COVID-19 examination.

estimates in the seronegative group (see Table E2). This tendency remained similar after adjustments for sex, BMI, smoking (daily or intermittent use), time between examinations, and lung function at the pre-COVID-19 examination.

Both FEV₁ pp and FVC pp in those participants with asthma and IgM antibodies (n = 13) did increase less than in the seronegative asthma group (n = 109), although none of the comparisons were statistically significant (FEV₁ P = .13; FVC P = .37; and FEV₁/FVC P = .32) (Fig 2, B). There was no interaction between asthma and seropositivity from the standpoint of change in lung function (all P > .10).

Allergic sensitization and ICS use in seropositive participants and change in lung function

In the analyses comparing change in lung function in seropositive participants with or without allergic sensitization or reported ICS use, the findings were no different between these exposures and change in lung function (Fig 3).

Self-reported COVID-19 symptoms and lung function

No difference in lung function was found between the 62% (n = 149) of seropositive participants with reported respiratory symptoms and the seronegative participants, although there was a trend for a higher increase in FVC (P = .068) than in the seronegative group (see Table E4 in the Online Repository at www.jaci-global.org). Assessment of the change in lung function in the 50% (n = 121) of seropositive participants reporting being bedbound during presumed COVID-19 did not reveal any differences in change in lung function from that in seronegative participants (see Table E4).

Sensitivity analyses

Stratification of the main analysis by sex, elevated BMI, or current smoking did not demonstrate any significant associations between seropositivity and change in lung function in these groups (see Table E3 in the Online Repository at www.jaci-global.org).

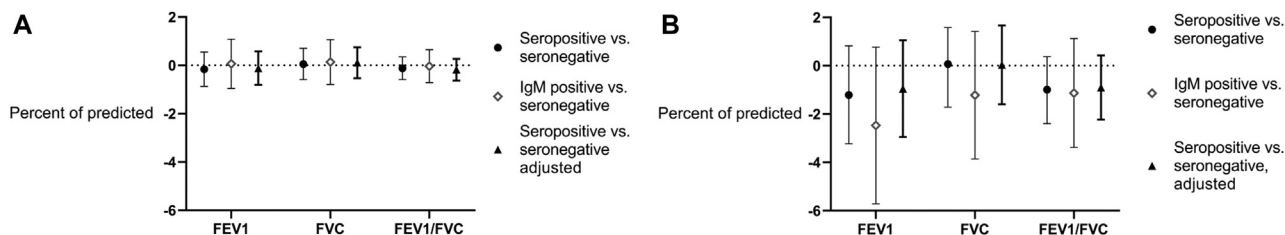


FIG 2. **A**, Regression coefficients and 95% CIs for the change in the seropositive group/IgM-positive group versus that in the seronegative group (reference group). **B**, Asthma group. Regression coefficients and 95% CIs for the change in the seropositive group/IgM-positive group versus that in the seronegative group (reference group) among participants with asthma. *Adjustments have been done for sex, BMI, current smoking, time between the examinations, and lung function at the pre-COVID-19 examination.

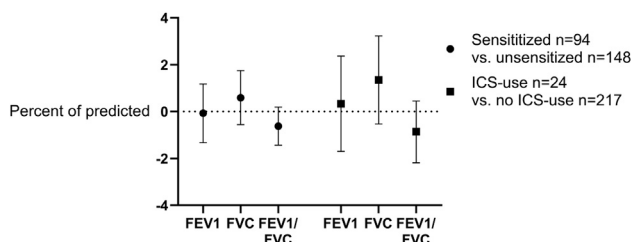


FIG 3. Regression coefficients and 95% CIs for the change in the seropositive participants with allergic sensitization versus that in participants without allergic sensitization (reference group), as well as for the seropositive participants with reported ICS use versus the participants without reported ICS use (reference group).

global.org). When the association between change in lung function was assessed in absolute values (expressed in milliliters or as a ratio) and seropositivity in a multiple regression adjusted for height and sex, the changes in lung function were no different between the groups with and without seropositivity (see Table E5 in the Online Repository at www.jaci-global.org).

DISCUSSION

In the present study based on the well-characterized population-based BAMSE birth cohort, we did not find evidence for a COVID-19-associated impairment in lung function in young adults with or without asthma. No association between allergic sensitization or ICS use and change in lung function was found in seropositive participants.

In the small group with IgM antibodies among the participants with asthma, the results suggested a possible spirometric worsening in proximity to the infection, with a nonsignificant lower change in pp lung function than in the seronegative group with asthma. A possible explanation for this finding could be an exacerbation of the asthma in proximity to the infection. Level of IgM against SARS-CoV-2 is commonly measurable in the first month(s) after the onset of COVID-19, but it then slowly declines in most cases, becoming absent after 6 months.²³ Viral respiratory infections, including those caused by coronaviruses, are common triggers for asthma exacerbations.³⁰ COVID-19 has, however, not been found to be a prominent trigger for asthma exacerbations. In children, Tosca et al³¹ did not find COVID-19 to affect lung function or asthma control. In adults, asthma exacerbations have in some cases been reported in association with COVID-19,^{32,33} although they are not seen on a

population level.³⁴ Our interpretation of the data would still be an effect on the asthma in proximity to the infection. This is also supported by the finding that the difference was reduced when analyzing the whole seropositive group with asthma (ie, when also including participants who had lost their IgM response). In addition to that, the potential differences found in our study are small and probably of limited clinical importance.³⁵

Presence of allergic sensitization was not found to affect the change in lung function in the seropositive group. Also, ICS use during the COVID-19 pandemic could not be linked to change in lung function. Earlier studies have found these factors to possibly protect against more severe COVID-19 disease.^{16,17} However, in our young cohort, most of the participants had mild disease, and a potential protective effect for less severe disease could be difficult to detect.

A major strength of our study is the unique availability of lung function measurements both recently before and after onset of the pandemic, with the potential to detect small changes in lung function among individuals with confirmed COVID-19 disease versus among nonaffected individuals. The majority of our participants had a mild disease,³⁶ reflecting the manifestations of COVID-19 seen in a population-based sample of young individuals. This does not however rule out the possibility that severe COVID-19 may influence lung function in young adults.

A weakness of our study is the lack of information on total lung capacity, thus not permitting conclusions regarding restrictive lung function impairment, even though the normal spirometry findings imply a significant restrictive impairment to be unlikely. Further, we used seropositivity as a marker for previous COVID-19 infection, thus not catching individuals for whom antibody responses were low or absent. Moreover, a decline in antibody levels could have occurred among participants infected early in the pandemic, with the study period reaching more than a year after onset of the pandemic. A decline in antibody levels has been found in approximately 2% of individuals on days 15 to 90 days after infection and 15% at 1 year after infection in Swedish data³⁷; other studies have found such a decline in 15% to 20% of infected individuals, albeit in populations older than ours.^{23,38} This would lead to a misclassification of some participants with a previous COVID-19 infection and potentially attenuate the results. A further limitation is the possibility of a nonresponse bias, although 50% of the invited population did participate in the clinical follow-up. However, the seropositivity rate is consistent with the official Swedish public health data, with a prevalence of 30% among those between 16 and 19 years of age and 18% among

those between 20 and 64 years in the unvaccinated population in late April to early May 2021.³⁷ A limitation for interpretation when having nonsignificant findings is the risk of a statistical-type error (ie, a sample size too small to detect significant differences). This could be the case in our study, especially in the group with asthma, which consisted of 146 individuals, 38 of whom were seropositive. However, the difference between the change in the seropositive asthma group and the change in the seronegative asthma group was small—less than 2% (Fig 2, B). Hence, a difference undetected because of small sample size is of unclear significance.

In conclusion, we found no evidence that COVID-19 results in impaired spirometric lung function in a population-based sample of young, healthy adults with mild-to-moderate disease. Further, we did not find any evidence indicating that participants with asthma are more susceptible to long-term lung function impairment. Allergic sensitization or recent ICS use did not significantly affect lung function among seropositive participants.

We thank the participants and their families participating in the BAMSE cohort and all staff involved in the study through the years.

Clinical implications: The finding that COVID-19 in young adults with a mainly mild case of disease does not affect spirometric lung function is reassuring for patients, health care providers, and public health management.

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