

# **Inhalation adherence for asthma and COPD improved during the COVID-19 pandemic: a questionnaire survey at a university hospital in Japan**

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## **Author contributions**

E.F. and K.W. designed the study; E.F., K.W., S.N., E.Y., Y.S., K.S., S.O., I.T., and N. Hashimoto distributed and collected questionnaires; A.Y., M.M., and Y.N. performed study about PMC; E.F. and K.W. analyzed data and wrote manuscript; Y.N., N. Hamajima, and M.I supervised the study. All authors read and approved the final manuscript.

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## Background

Good adherence to an inhaled medication protocol is necessary for the management of asthma and chronic obstructive pulmonary disease (COPD), and several interventions to improve adherence have been reported. However, the impact of patient life changes and psychological aspects on treatment motivation is obscure. Here, we investigated changes in inhaler adherence during the COVID-19 pandemic and how lifestyle and psychological changes affected it.

## Methods

Seven-hundred sixteen adult patients with asthma and COPD who had visited Nagoya University Hospital between 2015 and 2020 were selected. Among them, 311 patients had received instruction at a pharmacist-managed clinic (PMC). We distributed one-time cross-sectional questionnaires from January 12 to March 31, 2021. The questionnaire covered the status of hospital visits, inhalation adherence before and during the COVID-19 pandemic, lifestyles, medical conditions, and psychological stress. The Adherence Starts with Knowledge-12 (ASK-12) was used to assess adherence barriers.

## Results

Four-hundred thirty-three patients answered the questionnaire. Inhalation adherence was significantly improved in both diseases during the COVID-19 pandemic. The most common reason for improved adherence was fear of infection. Patients with improved adherence were more likely to believe that controller inhalers could prevent COVID-19 from becoming more severe. Improved adherence was more common in patients with asthma, those not receiving counseling at PMC, and those with poor baseline adherence.

## Conclusions

Inhalation adherence for asthma and COPD improved in the COVID-19 pandemic. The patients seemed to realize the necessity and benefits of the

medication more strongly than before the pandemic, which motivated them to improve adherence.

Running head: Inhaler adherence improved during the COVID-19 pandemic

Keywords: inhalation adherence; asthma; COPD; COVID-19; pharmacist-managed clinic

## **Introductions**

Inhalers are the mainstay of drug therapy for asthma and chronic obstructive pulmonary disease (COPD). Appropriate controller inhaler technique and maintenance of good adherence are necessary to control symptoms, decrease mortality, and improve the quality of life (1). However, the percentage of patients with good adherence with controller inhaler medications has been reported to be particularly low, compared to about 50% for common chronic diseases (2, 3). Poor treatment adherence can be attributed to a variety of factors, including lifestyle, cost of treatment, and patients' attitudes toward the effects and side effects of inhaled medications, in addition to their understanding of the need for inhaler medications. In fact, several treatment adherence behavior models have shown the importance of treatment motivation, along with disease knowledge and behavioral skills (4). Furthermore, the formation of a partnership between health care professionals and patients to make treatment decisions, known as “shared decision making”, is considered an effective approach to improve adherence (5), and is also emphasized in the Global Initiative for Asthma guidelines (6).

In 2000, Nagoya University opened a pharmacist-managed clinic (PMC) as a comprehensive drug management service providing counseling on inhalation therapy for asthma and COPD patients. In addition to explaining inhalation methods, pharmacists at PMC provided education on pathophysiology, drug effects, and treatment needs, as well as motivational counseling, including monitoring symptoms, improving living conditions, and setting treatment goals. We have previously reported that PMC has improved understanding of the disease state, inhalation technique, drug adherence, and symptoms (7, 8).

Other reports have also shown that inhalation adherence can be improved by various interventions by healthcare providers, such as teaching inhalation techniques (9,

10), adherence education (11), and the use of reminders (12). However, it is not clear how the patient's own environment and its changes affect the patient's motivation for treatment. Past reports have not fully elucidated how patients' living environment and psychological status affect their willingness to be treated due to the heterogeneity of the studies (13).

The recent COVID-19 pandemic has drastically changed people's behavior, lifestyle, and psychological status (14, 15). In particular, it is assumed that patients with chronic respiratory diseases such as asthma and COPD are affected by anxiety and stress about infection (16, 17), which may have changed their motivation for treatment and adherence. Indeed, there have been several reports of changes in inhaler adherence in asthma and COPD patients in other countries due to the COVID-19 pandemic (18, 19), but the impact in Japan is unknown, and the reasons for the adherence changes and patient characteristics are not fully understood. In addition, it is unclear how motivating patients to treatment through PMC counseling affects adherence during the COVID-19 pandemic.

Investigating changes in inhaler adherence along with treatment motivation during the COVID-19 pandemic may provide interesting insights into the factors of adherence barriers. First, we conducted a questionnaire survey of patients with a history of hospital visits to determine how COVID-19 affected adherence to controller inhalers in patients with asthma and COPD. Secondly, we also investigated the reasons for changes in adherence and how lifestyle, psychological stress, and whether or not the patient had experienced counseling at PMC affected these changes.

## **Methods**

### ***Subjects***

Patients aged 20 years or older with "bronchial asthma" and "COPD" as disease name in their electronic medical record who visited the Respiratory Medicine Outpatient Clinic at Nagoya University Hospital from September 1, 2015 to August 31, 2020 were consecutively selected. Nagoya University Hospital, established by the National University Corporation, is one of the core regional medical facilities in Japan with 1,080 beds. Outpatient services are provided by respiratory specialists, and most patients are referred by local medical institutions. Of the selected patients, 831 for asthma and 670 for COPD, as shown in the upper part of Figure 1, we identified those who had visited the PMC on the advice of the physician. All patients were checked to ensure that the diagnoses were correct, and patients whose diagnoses were incorrect, who had died, who were not currently using inhaler, or who were considered unable to answer the self-administered questionnaire (e.g., dementia, poor general condition) were excluded. In this way, a total of 716 people were targeted for questionnaire distribution (Figure 1).

Questionnaires were distributed by mail or hand delivered between January 12, 2021, and March 31, 2021, and collected by mail until April 30, 2021. This period corresponds to the third to fourth wave of the COVID-19 epidemic in Japan (Supplementary Figure 1).

### ***Education and counseling for inhalation therapy at PMC***

PMC is a department within the hospital that provides counseling to asthma and COPD patients regarding inhalation therapy under the direction of their doctors.

Of patients who were eligible for survey distribution, we identified those who had experienced PMC counseling. More specifically, between September 1, 2015 and August 31, 2020, patients who requested counseling by a pharmacist on inhalation therapy support on the advice of a physician and who agreed to participate in the study at PMC, “Study of Symptoms, Adherence and Patient Satisfaction After Inhalation Instruction for Bronchial Asthma and COPD Patients” (2008- 0653-5).

Counseling on inhalation therapy at PMC according to this study protocol included: (a) inhalation method and dosage of inhalers, (b) pathophysiology and characteristics and necessity of inhalers, (c) how to improve the living environment to prevent attacks or acute exacerbations, (d) how to use a peak flow meter and asthma diary (if applicable), (e) monitoring of patient symptoms, and (f) establishment of treatment goals. After the consultation, the pharmacist again checked to see if the patient inhaled properly. Counseling at PMC took about 30 minutes per patient.

### ***Questionnaire***

The questionnaire contained 24 questions that include the status of hospital visits (whether the patient is attending the hospital, and whether the hospital is Nagoya University or not), experience of inhalation technique instruction, inhalation adherence, lifestyles, symptoms, psychological stress, and therapeutic drugs. A pilot test was conducted by three physicians to determine the answerability of the questions, the time required to answer the questions, and the validity of the questions. Questionnaires were distributed only once, in which patients responded to adherence in controller inhalers both before and during the COVID-19 pandemic. Symptoms were assessed by the Asthma Control Test (ACT) (20) for patients with asthma and COPD Assessment Test

(CAT) (21) for patients with COPD. To assess adherence, patients were asked to choose the number from 0 (0%) to 10 (100%) that was closest percentage of times they used their controller inhalers as prescribed. For the evaluation of their confidence in controller inhaler technique, patients were asked to choose the number closest to 10 for “completely confident” and 0 for “not confident at all.” These results were expressed as a percentage when multiplied by 10. For the assessment of psychological stress, respondents were asked to choose the number closest to the stress they were feeling on a scale of 0 to 10, with 0 being “no stress at all” and 10 being the “strongest conceivable stress”. Patients were asked to complete the questionnaire on their own, without an interview with a healthcare professional. The complete questionnaire is included in the supplementary materials.

#### ***Adherence Starts with Knowledge-12 (ASK-12)***

The ASK-12 questionnaire was used to assess inhalation adherence barriers. ASK-20 was developed by extracting 20 items from a list of 47 items that affect medication adherence (22). ASK-12 was developed as a simplified version of ASK-20 with 12 items more closely related to adherence (23). The Japanese version of ASK-12 has recently been developed, and its usefulness in evaluating adherence to inhaled medications by patients with asthma has been validated (24). All items in ASK-12 are as shown in Supplementary Table 1. Each questionnaire item is rated on a 5-point scale, with higher scores indicating greater barriers to adherence. Each item has a cutoff value for adherence barrier. In this study, respondents were asked to answer the ASK-12 questions about the controller inhaler they use.



### ***Ethical approval and informed consent***

The study was approved by the Ethics Committee of Nagoya University (approval number 2020-0445). We explained the study to the subjects by including a document describing the research along with the questionnaire, and we considered their consent to have been obtained by their response to the questionnaire.

### ***Statistical analysis***

Missing values were excluded from the analysis. The total scores of ACT, CAT, and ASK-12 were used only for those who responded to all items. Patients who started inhalation therapy on or after February 1, 2021, were excluded from the analysis for comparison of adherence before and after the COVID-19 pandemic. Patients with responses that contradicted each other were excluded from the analysis for both items. For example, if a patient reports that compliance "decreased" even though self-reports of the percentage of inhaler use were higher after the pandemic. (Questionnaire Q4-Q6)

Categorical variables were presented as numbers (%), while continuous variables were reported as the mean  $\pm$  standard deviation (SD). Between-group comparisons were made with Mann-Whitney U-test, chi-square test, or Fisher's exact test (if necessary) as appropriate. Comparison of inhalation adherence and psychological stress before and during the COVID-19 pandemic was analyzed by the Wilcoxon signed-rank test.

Relationship between ASK-12 total score and medication adherence was examined using spearman's correlation. All statistical analyses were performed using IBM SPSS statistics version 28.0 (SPSS Inc., Chicago, IL, USA). For all statistical analyses,  $p < 0.05$  was considered significant.

## **Results**

### ***Patient demographics and characteristics***

A total of 716 questionnaire participants were selected, of which 30 patients could not be reached due to death or change of address, and thus 686 were distributed. Of these, 433 patients answered, with a response rate of 63.1% (58.6% and 70.0% for asthma and COPD, respectively) (Figure 1). The characteristics of the respondents are shown in Table 1. At the time of the study, 52.1% of respondents were visiting our hospital for asthma and 41.9% for COPD. Patients visiting other hospitals accounted for 35.5% and 47.1%, respectively. The remaining patients were not visiting any hospital. The trigger for these patients' outpatient visits was preoperative evaluation in 36.0%, referral from another hospital due to worsening symptoms in 24.2%, referral from another department in 26.8%, and others in 12.9%. Patient characteristics for each of the main triggers for visit are shown in Supplementary Tables 2, 3. The self-reported inhalation adherence rate during the COVID-19 pandemic was 87.9% for asthma and 89.3% for COPD. Psychological stress felt before and after the COVID-19 pandemic was higher in patients with asthma than in patients with COPD. It was also significantly higher for both asthma and COPD than before the COVID-19 pandemic (asthma,  $p < 0.001$ , COPD,  $p < 0.001$ ).

### ***Change in inhalation adherence during COVID-19 pandemic***

Inhalation adherence was significantly improved in both asthma and COPD patients during the COVID-19 pandemic compared to before the pandemic (asthma:  $p = 0.030$ , COPD:  $p = 0.026$ ) (Table 2, Figure 2). Improved adherence was more common in patients with asthma, those not receiving counseling at PMC, those with poor

baseline adherence, and those with high stress prior to the COVID-19 pandemic (Table 3). In addition, non-smokers, those under 75 years of age, and patients with asthma who scored less than 20 or the full 25 points on the ACT tended to have increased adherence, although not significantly. A greater percentage of those with increased adherence reported sleeping less than before the pandemic compared to those without increased adherence (increased: 20.0%, not increased: 5%  $p = 0.006$ ) (Supplementary Table 4). We did not find significant association with changes in adherence to other lifestyles, although there was a trend toward increasing adherence in patients who spent more time outside the house.

### ***Reasons for the change in inhalation adherence during the COVID-19 pandemic***

Figure 3 shows the reasons for the change in inhalation adherence. For those whose adherence increased, the most common reason was anxiety about COVID-19 infection, and the second most common reason was concern about what people around the patients think about coughing. For those whose adherence decreased, the most common reason was improvement of symptoms. Figure 4 shows how patients thought the use of inhalers would affect COVID-19. Among all respondents, 25.9% believed that inhalers use would reduce the risk of COVID-19 infection, while only 3.1% believed it would increase the risk. Of all respondents, 37.0% of patients believed that the use of inhalers was effective in preventing COVID-19 from becoming more severe, with patients whose adherence improved from before the COVID-19 pandemic (55.9%) were significantly more likely to believe that than patients whose adherence did not increased (34.2%).

### ***ASK-12 analysis***

The mean ASK-12 total scores were 22.9 and 21.9 for asthma and COPD, respectively, and the ASK-12 total score was significantly negatively correlated with inhalation adherence (Supplementary Figure 2). ASK-12 has five options for each of the 12 questions regarding adherence barriers, and the cut-off value for determining whether a patient has a barrier to adherence was defined for each item. The percentage of patients who were judged to have adherence barriers for each question was compared between patients whose adherence improved during the COVID-19 pandemic and those whose adherence did not (Supplementary Table 1). Patients with increased adherence were significantly more likely to have adherence barriers in items “No. 1: I forget to take my medicines some of the time” and “No. 8: Have you taken a medicine more or less often than prescribed?” compared to patients whose adherence did not improve.

### **Discussion**

We investigated the effects of the COVID19 pandemic on inhalation adherence in asthma and COPD patients and found that inhalation adherence improved in both asthma and COPD. The main reasons for improved adherence were fear of infection and fear of what others would think of them for coughing. These results show that changes in inhalation adherence can be brought about by changes in environmental and psychological status. Improvements in inhalation adherence were more common in patients with asthma, in patients who had never received counseling at the PMC, and in patients with previously poor adherence. This suggests that improvements in adherence with the COVID-19 pandemic are more likely to occur in patients with remaining room

for improvement, and that these patients may be good candidates for treatment motivation through methods such as counseling at the PMC.

The improvement in inhalation adherence during the COVID-19 pandemic observed in this study is consistent with other reports. Inhaler adherence measured using electronic drug monitors in the United States (18) and obtained in a telephone survey of COPD patients in the United Kingdom (19) both improved during the pandemic. With regard to adherence in other diseases, adherence improved with continuous positive airway pressure (CPAP) treatment of sleep apnea syndrome (SAS) patients in France, especially in patients with low pre-pandemic adherence (25), which is similar to the results of this study. Several other reports have shown results that contradict the present study (26, 27). However, these reports evaluated prescription rates as adherence and did not rule out the possibility that the number of prescriptions decreased because patients refrained from seeing their physicians due to the lockdown or because their symptoms decreased. In this study, we directly asked patients in the questionnaire why they changed their inhaler adherence. The most significant reason for the increased adherence was “fear of infection” and the most significant reason for decreased adherence was “improvement of symptoms”. This showed that patients’ thoughts were strongly related to treatment adherence.

Patients who showed improved adherence in this study tended to believe that the use of inhalers had a positive health effect on COVID-19 infection. In Japan, cases of treatment response to ciclesonide inhalation were reported in the early stages of the pandemic (28). In addition, a statement was issued that inhaled steroids should not be reduced or stopped as this would induce attacks, increase the risk of emergency room visits and hospitalization, and consequently increase the risk of COVID-19 infection.

Therefore, increased awareness of the need for and effectiveness of treatment in asthma and COPD may have influenced improvements in adherence.

Many factors are intricately involved in medication adherence decision-making and behavior change, including not only individual skills and knowledge, but also social experiences and cultural perspectives. In recent years, various social-behavioral models have been proposed to conceptualize these complex pathways of adherence behavior and to achieve effective interventions (4). One of these theories, the information-motivation-behavioral (IMB) skills model, has been used to explain adherence to medications for human immunodeficiency virus and other diseases, and it is based on three major components: information, motivation (personal and social), and behavioral skills (29). We attempted to explain behavioral changes related to inhalation adherence and the impact of COVID-19 within the framework of the IMB model (Figure 5). The COVID-19 pandemic stimulated dissemination of a lot of health information, including the risks to infection and the importance of preventive actions. Hence it is possible that treatment beliefs, i.e., personal motivations, such as the need for and benefits of treatment in asthma and COPD patients may have affected adherence behavior. In addition, because so much information promoting health and preventing infection was reported daily, patients may have perceived these behaviors as some sort of social norm. Therefore, reducing symptoms such as coughing may have had a significant social motivation as well as a personal one (30).

Patients who improved adherence during the COVID-19 pandemic may have had lower treatment awareness, as characterized by higher adherence barriers related to “forgetfulness” in the ASK-12 analysis, and lower original adherence. In a report comparing adherence barriers between asthma and COPD patients using the ASK-20 (31), patients with asthma with mild disease had more “forgetfulness” barriers and may

have had less treatment awareness. Patients with these characteristics may be a particularly effective group for improving adherence by motivating them in the regular practice setting.

Increased adherence was less common in patients who received PMC counseling. Counseling at PMC has been effective in improving adherence, as well as improving understanding of disease and treatment in dementia (32) and patients with asthma (33), promoting smoking cessation in patients with COPD (34), and reducing anxiety about anticancer drug treatment (35). It is thought to be effective in comprehensively motivating patients to improve their health with a variety of methods. In this study, patients who experienced PMC counseling had significantly lower total ASK-12 scores than those who did not (experienced:  $21.1 \pm 5.2$ , not experienced:  $22.8 \pm 5.7$ ,  $p = 0.021$ , calculated by Mann-Whitney U test), suggesting that counseling had already removed some degree of the barriers to adherence. Those who experienced counseling at PMC in this study may have been less psychologically affected by the COVID-19 pandemic because they already had appropriate knowledge of the disease and its medications and had some motivation for self-management.

The patients in this study who improved their adherence during the COVID-19 pandemic period originally had the potential to improve their adherence with appropriate motivation even before the pandemic. Although many of these patients did not receive PMC counseling, actively encouraging these patients to participate in counseling may contribute to maintaining adherence.

Our study has several limitations. The assessment of inhalation adherence was based on patient self-report. The good degree of adherence in this study cannot rule out the involvement of social desirability bias and self-selection bias. However, adherence assessment based on prescription data may overestimate because patients may have

stockpiled prescription inhalers during the COVID-19 pandemic (36, 37). Furthermore, the inhalation adherence rate obtained in the study was significantly correlated with the ASK-12 total score in both asthma and COPD, suggesting some degree of reliability. In addition, adherence before the COVID-19 pandemic was based on past memory, and the fact that adherence was very high may indicate the presence of measurement error/recall bias. Therefore, the improvement in adherence due to the pandemic may have been small. The impact of lifestyle changes, such as going out and sleeping hours, on adherence was limited. It is presumed that the questionnaire in this study did not adequately capture the impact of lifestyle changes. Another reason may be that in Japan, strong behavioral restrictions such as lockdowns were not promulgated. Because counseling at PMC was based on the judgment of the attending physician and the patient's consent, some characteristics may be different from those of patients who did not receive counseling at PMC.

This was a study at a single institution. It is unclear whether the results of this study are generally applicable, especially since patients with a history of visiting a university hospital may have different characteristics than the general asthma/COPD population. However, no differences were found in this study when participants' adherence to inhalation was compared by reason for initiating hospital visit (Supplementary Tables 2, 3), suggesting that there were no significant differences in characteristics compared to patients at other facilities.

## **Conclusion**

During the COVID-19 pandemic, inhalation adherence improved in asthma/COPD patients, which may be due to changes in their personal and social



motivations. Such changes may have been limited in patients who were sufficiently motivated by counseling at PMC. In order to improve adherence, it may be effective to encourage patients to become more aware of the efficacy of the drug and the risk of not using the drug. In particular, motivating patients with asthma and those who have less communication with medical staff may bring about efficient improvement in adherence.

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### **Declaration of interest statement**

The authors declare no conflict of interest.

### **Data availability statement**

The data that support the findings of this study are available from the corresponding author, K.W., upon reasonable request.

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Table 1. Clinical characteristics of respondents

	Asthma	COPD	p value
	n = 242	n = 191	
Age, y	62.9 ± 16.2	74.3 ± 7.0	< 0.001
Male	86 (36.8)	164 (86.3)	< 0.001
Smoking status			< 0.001
current	17 (7.3) <sup>a</sup>	24 (13.3) <sup>a</sup>	
former	84 (35.9) <sup>b</sup>	156 (86.2) <sup>b</sup>	
never	133 (58.6) <sup>c</sup>	1 (0.6) <sup>c</sup>	
ACT score	22.0 ± 3.8	-	
CAT score	-	14.6 ± 8.2	
Psychological stress before the COVID-19 pandemic (scale of 0-10 points)	4.45 ± 2.73	3.60 ± 2.23	0.001
Psychological stress during the COVID-19 pandemic (scale of 0-10 points)	5.06 ± 2.69	4.20 ± 1.42	< 0.001
Current visit to our hospital	126 (52.1)	80 (41.9)	0.035
Current users of inhalers	198 (81.8)	156 (81.7)	0.970
Number of controller inhaler devices in use*			0.003
1 device	161 (83.4)	139 (93.9)	
2 devices	32 (16.6)	9 (6.1)	
Inhalation therapy counseling at PMC*	73 (30.2)	70 (36.6)	0.154
Inhaled corticosteroid dose (budesonide conversion)*			< 0.001
≤ 400	49 (24.7) <sup>d</sup>	20 (12.9) <sup>d</sup>	
< 400-800 µg	48 (24.2) <sup>e</sup>	12 (7.7) <sup>e</sup>	
> 800 µg	41 (20.7) <sup>f</sup>	5 (3.2) <sup>f</sup>	
non-ICS users	1 (0.5) <sup>g</sup>	92 (59.4) <sup>g</sup>	
unknown	59 (29.8) <sup>h</sup>	26 (16.8) <sup>h</sup>	
ASK-12 total score*	22.7 ± 5.69	21.5 ± 54.1	0.079
Confidence in inhalation procedure (%)*	83.8 ± 1.93	85.1 ± 1.79	0.710
Inhalation adherence before the COVID-19 pandemic (%)*	86.5 ± 1.92	88.0 ± 1.68	0.697
Inhalation adherence during the COVID-19 pandemic (%)*	87.9 ± 1.87	89.3 ± 1.44	0.922

Data are presented as mean ± standard deviation or number (%). P values were calculated using chi-square test or Fisher's exact test for categorical variables and Mann-Whitney U-test for continuous variables. Subgroups that were significantly different (p < 0.05) are indicated by the same lowercase superscript letter.

\*Analysis was conducted on current users of inhalers.

ACT, asthma control test; CAT, COPD assessment test; PMC, pharmacist-managed clinic; ICS, inhaled corticosteroid; ASK-12, adherence starts with knowledge

Table 2. Inhalation adherence rate before and during COVID-19 pandemic

	Before COVID-19 pandemic (%)	During COVID-19 pandemic (%)	p value
Asthma (n = 163)	86.5 ± 19.2	87.9 ± 18.7	0.030
COPD (n = 122)	88.0 ± 16.8	89.3 ± 14.4	0.026

Data are presented as mean ± standard deviation. P values were calculated using Wilcoxon matched-pairs signed-rank test.

COPD, chronic obstructive pulmonary disease.



Table 3. Characteristics of patients with increased adherence

Adherence compared to before the COVID-19 pandemic			Increased		Not increased	p value
			n = 36	n = 246		
Disease	asthma	n	27	138	0.032	
		%	75	56.1		
	COPD	n	9	108		
		%	25	43.9		
Sex	male	n	17	144	0.191	
		%	47.2	58.8		
	female	n	19	101		
		%	52.8	41.2		
Age	< 75	n	28	155	0.088	
		%	77.8	63.3		
	≥ 75	n	8	90		
		%	22.2	36.7		
Inhalation therapy counseling at the PMC	Experienced	n	6	97	0.008	
		%	16.7	39.4		
	Not experienced	n	30	149		
		%	83.3	60.6		
Current hospital visit	Nagoya University	n	21	137	0.765	
		%	58.3	55.7		
	others	n	15	109		
		%	41.7	44.3		
Smoking status	current	n	2	26	0.087	
		%	5.9	10.7		
	former	n	14	135		
		%	41.2	55.6		
	never	n	18	82		
		%	52.9	33.7		
ACT (Asthma)	< 20	n	5	17	0.075	
		%	26.3	15.7		
	20-24	n	5	59		
		%	26.3	54.6		
	25	n	9	32		
		%	47.4	29.6		
CAT (COPD)	< 19	n	6	62	0.669	
		%	85.7	71.3		
	≥ 20	n	1	25		
		%	14.3	28.7		
ASK-12	< 23	n	12	112	0.453	
		%	50	58		
	≥ 23	n	12	81		
		%	50	42		
Confidence in inhalation procedure (%)		mean	84.1	85.6	0.244	
		SD	14.8	18.7		
		n	34	244		

Adherence before COVID-19 pandemic (%)	mean	72.7	89.2	0.001 <sup>&lt;</sup>
	SD	24.7	16.2	
	n	35	243	
Adherence during COVID-19 pandemic (%)	mean	85.6	88.8	0.043
	SD	14.6	17.6	
	n	35	242	
Psychological stress before COVID-19 pandemic (selected one of 0-10 points)	mean	5.14	4.03	0.012
	SD	2.43	2.62	
	n	35	243	
Psychological stress during COVID-19 pandemic (selected one of 0-10 points)	mean	5.57	4.76	0.102
	SD	2.6	2.68	
	n	35	244	

P values were calculated using chi-square test, Fisher's exact test (categorical variables), or Mann-Whitney U-test (continuous variables).

PMC, pharmacist-managed clinic; COPD, chronic obstructive pulmonary disease; ACT, asthma control test; CAT, COPD assessment test, ASK-12, Adherence Starts with Knowledge-12.

Supplementary Table 1. Percentage of patients with barriers to adherence to each ASK-12 item of patients with and without improved adherence

	Adherence compared to before COVID-19 pandemic	Percentage of patients with adherence barriers (%)		p value
		Increased n = 36	Not increased n = 246	
ASK-1	I just forget to take my medicines some of time.	53.3	25.2	0.001
ASK-2	I run out of my medicines because I don't get refills on time.	8.0	8.2	1.000
ASK-3	Taking medicines more than once a day is inconvenient.	16.0	21.4	0.533
ASK-4	I feel confident that each one of my medicines will help me.	13.3	18.5	0.487
ASK-5	I know if I am reaching my health goals.	51.7	56.8	0.605
ASK-6	I have someone whom I can call with questions about my medicines.	22.6	24.2	0.848
ASK-7	My doctor/nurse and I work together to make decisions.	16.1	22.5	0.423
ASK-8	Have you taken a medicine more or less often than prescribed?	43.3	23.0	0.017
ASK-9	Have you skipped or stopped taking a medicine because you did not think it was working?	3.3	5.2	1.000
ASK-10	Have you skipped or stopped taking a medicine because it made you feel bad?	3.3	3.8	1.000
ASK-11	Have you skipped, stopped, not refilled, or taken less medicine because of the cost?	0.0	1.9	1.000
ASK-12	Have you not had medicine with you when it was time to take it?	25.8	12.1	0.052

P values were calculated using chi-square test or Fisher's exact test as appropriate.

ASK-12, Adherence Starts with Knowledge-12.

Supplementary Table 2. Characteristics by reason for visit (asthma)

	Preoperative evaluation	Symptom aggravation (from other hospitals)	Symptom aggravation (from other departments)	p value
	n = 74	n = 56	n = 68	
Age	59.4 ± 13.9 <sup>a</sup>	62.9 ± 17.2	65.9 ± 16.3 <sup>a</sup>	0.037
Male, n(%)	28 (37.8)	24 (42.9)	25 (36.8)	0.765
Smoking status (current/former/never)	9/34 <sup>a</sup> /26 <sup>b</sup> (13.0/49.3/37.7)	1/14 <sup>a</sup> /41 <sup>b</sup> (1.8/ 25.0/73.2)	3/24/40 (4.5/35.8/59.7)	< 0.001
ACT score	22.5 ± 3.4	21.7 ± 3.9	21.4 ± 4.2	0.209
Current visit to our hospital	11 (14.9) <sup>ab</sup>	35 (62.5) <sup>a</sup>	49 (72.1) <sup>b</sup>	< 0.001
Current users of inhalers	55 (74.3)	48 (85.7)	59 (86.8)	0.114
Number of controller inhaler devices in use*				0.762
1 device	42 (79.2)	40 (85.1)	47 (81.0)	0.743
2 devices	11 (20.8)	7 (14.9)	11 (19.0)	
Inhalation therapy counseling at PMC*	10 (18.2) <sup>a</sup>	15 (31.3)	23 (39.0) <sup>a</sup>	0.050
Inhaled corticosteroid dose (budesonide conversion)*				0.753
≤ 400 µg	15 (27.3)	8 (16.7)	13 (22.0)	
< 400–800 µg	13 (23.6)	12 (25.0)	18 (30.5)	
> 800 µg	11 (20.0)	15 (31.3)	12 (20.3)	
non-ICS users	1 (1.8)	0 (0.0)	0 (0.0)	
unknown	15 (27.3)	13 (27.1)	16 (27.1)	
ASK-12 total score*	22.3 ± 5.1	22.5 ± 5.7	22.5 ± 6.3	0.970
Confidence in inhalation procedure (%)*	85.2 ± 20.2	79.4 ± 21.1	82.6 ± 19.7	0.198
Inhalation adherence before COVID-19 pandemic (%)*	87.1 ± 21.9	83.8 ± 23.6	87.7 ± 15.5	0.480
Inhalation adherence during COVID-19 pandemic (%)*	89.2 ± 19.9	84.8 ± 23.4	87.8 ± 17.1	0.285
Psychological stress before COVID-19 pandemic (selected one of 0–10 points)	4.82 ± 2.56	4.27 ± 2.52	5.02 ± 2.99	0.376
Psychological stress during COVID-19 pandemic (selected one of 0–10 points)	5.65 ± 2.45	4.88 ± 2.64	5.53 ± 2.66	0.288

Data are presented as mean ± standard deviation or number (%). P values were calculated using chi-square test or Fisher's exact test for categorical variables and Mann-Whitney U-test for continuous variables. Subgroups that were significantly different ( $p < 0.05$ ) are indicated by the same lowercase superscript letter.

\*Current users of inhalers were included.

PMC, pharmacist-managed clinic; ACT, asthma control test; ICS, inhaled corticosteroid; ASK-12, adherence starts with knowledge-12.

Supplementary Table 3. Characteristics by reason for visit (COPD)

	Preoperative evaluation	Symptom aggravation (from other hospitals)	Symptom aggravation (from other departments)	p value
	n = 82	n = 49	n = 48	
Age	76.0 ± 6.5 <sup>ab</sup>	73.3 ± 6.3 <sup>a</sup>	72.8 ± 6.8 <sup>b</sup>	0.005
Male, n (%)	74 (90.2) <sup>a</sup>	44 (89.8)	36 (75.0) <sup>a</sup>	0.036
Smoking status (current/former/never)	11/65/1 (14.3/84.4/1.3)	11 <sup>a</sup> /37 <sup>b</sup> /0 (22.9/77.1/0.0)	2 <sup>a</sup> /43 <sup>b</sup> /0 (4.4/95.6/0.0)	0.045
CAT score	13.2 ± 8.4	14.6 ± 8.2	16.8 ± 7.8	0.079
Current visit to our hospital	13 (15.9) <sup>ab</sup>	32 (65.3) <sup>a</sup>	28 (58.3) <sup>b</sup>	< 0.001
Current users of inhalers	64 (78.0)	43 (87.8)	38 (79.2)	0.370
Number of controller inhaler devices in use*				
1 device	53 (93.0)	40 (95.2)	36 (94.7)	1.000
2 devices	4 (7.0)	2 (4.8)	2 (5.3)	
Inhalation therapy counseling at PMC*	20 (31.3)	20 (46.5)	16 (42.1)	0.248
Inhaled corticosteroid dose (budesonide conversion)*				0.059
≤ 400 µg	7 (11.1)	10 (23.3)	2 (5.3)	
< 400–800 µg	6 (9.5)	5 (11.6)	1 (2.6)	
> 800 µg	2 (3.2)	0 (0.0)	1 (2.6)	
non-ICS users	36 (57.1)	19 (44.2)	30 (78.9)	
unknown	12 (19.0)	9 (20.9)	3 (10.5)	
ASK-12 total score*	20.8 ± 5.0	21.9 ± 4.9	22.1 ± 6.0	0.579
Confidence in inhalation procedure (%)*	82.4 ± 18.6	90.2 ± 14.6	83.9 ± 20.2	0.065
Inhalation adherence before COVID-19 pandemic (%)*	86.1 ± 17.9	91.7 ± 14.2	88.4 ± 18.3	0.129
Inhalation adherence during COVID-19 pandemic (%)*	88.1 ± 13.7	92.2 ± 12.9	89.1 ± 17.5	0.199
Psychological stress before COVID-19 pandemic (selected one of 0-10 points)	3.38 ± 2.35	3.67 ± 2.35	3.84 ± 2.60	0.844
Psychological stress during COVID-19 pandemic (selected one of 0-10 points)	3.92 ± 2.62	4.44 ± 2.41	4.74 ± 2.51	0.354

Data are presented as mean ± standard deviation or number (%). P values were calculated using chi-square test or Fisher's exact test for categorical variables and Mann-Whitney U-test for continuous variables. Subgroups that were significantly different (p < 0.05) are indicated by the same lowercase superscript letter.

\*Current users of inhalers were included.

COPD, chronic obstructive pulmonary disease; PMC, pharmacist-managed clinic; CAT, COPD assessment test; ICS, inhaled corticosteroid; ASK-12, adherence starts with knowledge-12.

Supplementary Table 4. Lifestyle changes of people with increased adherence

Adherence compared to before the COVID-19 pandemic		Increased	Not increased	p value
Time spent outside the house	< 30 min	n 1 % 3.1	47 19.4	0.028*
	30 min–1 h	n 3 % 9.4	46 19.0	
	1–2 h	n 11 % 34.4	51 21.1	
	2–4 h	n 1 % 3.1	52 0.22	
	6–8 h	n 4 % 12.5	17 7.0	
	> 8 h	n 12 % 37.5	29 12.0	
	Changes in time spent outside the house	Increased by more than 2 hours	n 0 % 0.0	
Increased by 1–2 h		n 0 % 0.0	1 0.4	
No change		n 16 % 48.5	124 51.2	
Decreased by 1–2 hours		n 6 % 18.2	47 19.4	
Decreased by more than 2 hours		n 11 % 33.3	69 28.5	
Sleep duration		<5 hours	n 4 % 11.4	21 8.6
	5–6 hours	n 10 % 28.6	62 25.4	
	6–7 h	n 11 % 31.4	81 33.2	
	7–8 h	n 9 % 25.7	59 24.2	
	> 8 h	n 1 % 2.9	21 8.6	
	Changes in sleep time	Longer	n 3 % 8.6	13 5.3
No change		n 25 <sup>a</sup> % 71.4	219 <sup>a</sup> 89.4	
Shorter		n 7 <sup>b</sup> % 20.0	13 <sup>b</sup> 5.3	
Changes in family conversation time	Very increased	n 1 % 2.9	5 2.1	0.561*
	Slightly increased	n 5 % 14.7	25 10.3	
	No change	n 25 % 73.5	192 79.3	
	Slightly decreased	n 2 % 5.9	11 4.5	
	Very decreased	n 1 % 2.9	9 3.7	

As for the time spent outside the house, items 4–6 h were missed due to incomplete questionnaire design. Subgroups that were significantly different ( $p < 0.05$ ) are indicated by the same lowercase superscript letter.

\*Mann-Whitney U test †Fisher's exact test

## **Figure Caption**

### ***Figure 1: Selection of research subjects and flow of distribution and collection of questionnaires***

PMC, Pharmacist-managed Clinic; COPD, chronic obstructive pulmonary disease.

### ***Figure 2: Changes in adherence before and during COVID-19 pandemic in asthma and chronic obstructive pulmonary disease patients***

Adherence rates for inhalers improved significantly compared to before the COVID-19 pandemic (asthma:  $p = 0.030$ , COPD;  $p = 0.026$ , calculated by Wilcoxon signed-rank test).

Markers on dotted lines indicate patients with no change in adherence, while those above indicate patients with an increase and those below indicate patients with a decrease.

COPD, chronic obstructive pulmonary disease.

### ***Figure 3: Reasons for changes in inhalation adherence from before COVID-19 pandemic***

Participants were allowed multiple answers for each option. COPD, chronic obstructive pulmonary disease.

### ***Figure 4: Impressions of inhalers on COVID-19 infection***

Patients were asked how they thought the use of inhaled medications would affect COVID-19 infection. Increased, patients with improved adherence compared to before the COVID-19 pandemic; Not increased, patients with no change or decrease in adherence compared to before the COVID-19 pandemic. \* $p < 0.05$  as calculated by chi-square test.

***Figure 5: Information-motivation-behavioral skills (IMB) model adopted for inhaler adherence and impact of COVID-19 pandemic***

Shaded areas indicate the impact of the COVID-19 pandemic. Underlined areas indicate the factors that can be motivated by medical interventions. COPD, chronic obstructive pulmonary disease. (Modified from Fisher JD et al. 2006, p. 465)

***Supplementary Figure 1: Number of new cases of COVID-19 infection per day in Aichi Prefecture, Japan***

Questionnaires were distributed from the third to fourth waves of COVID-19 infection.

***Supplementary Figure 2: Relationships between ASK-12 score and inhalation adherence***

Spearman's correlation between ASK-12 total score and inhalation adherence during the COVID-19 pandemic both asthma and COPD. COPD, chronic obstructive pulmonary disease; ASK-12, Adherence Starts with Knowledge-12.



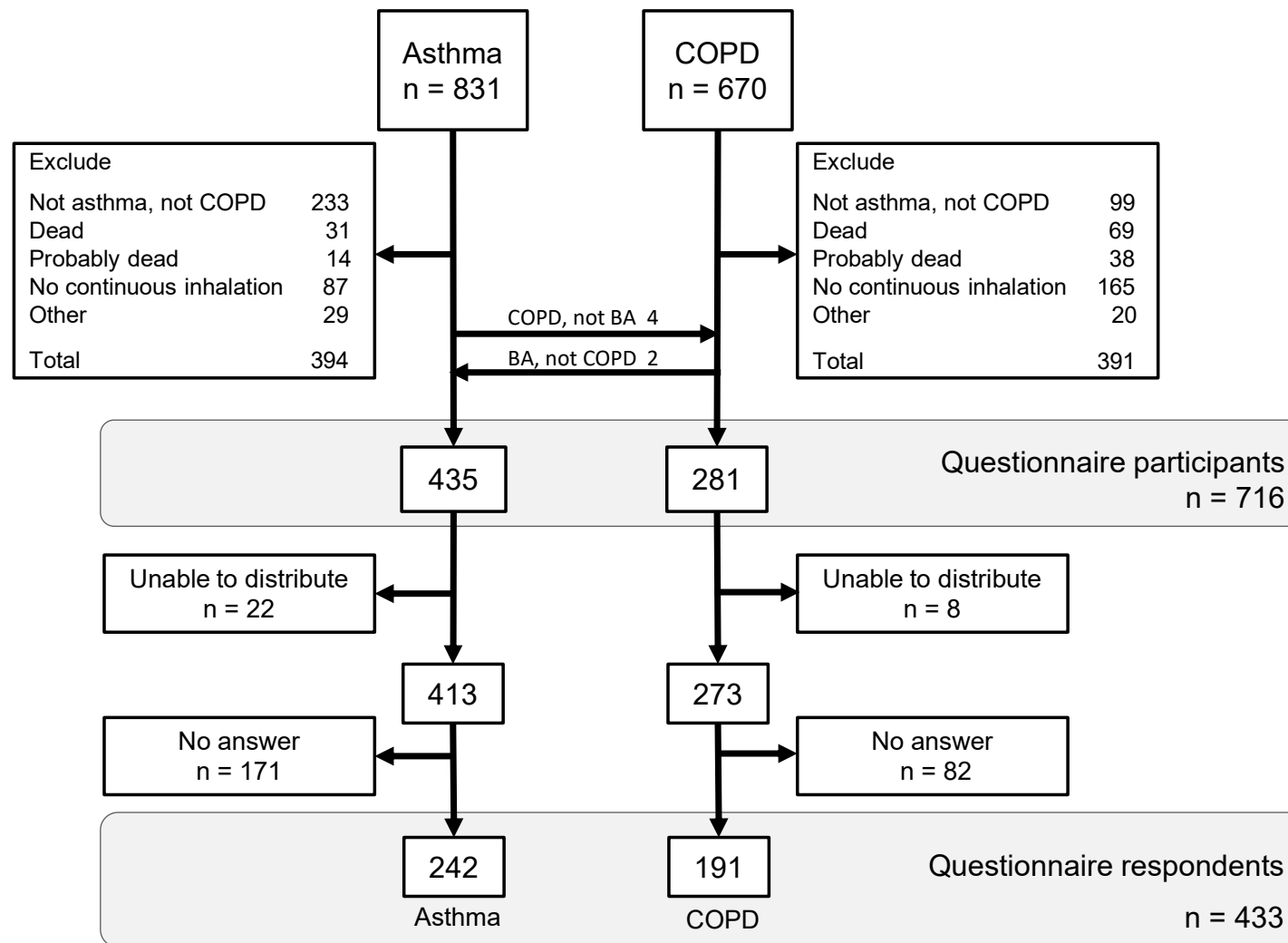


Fig.1

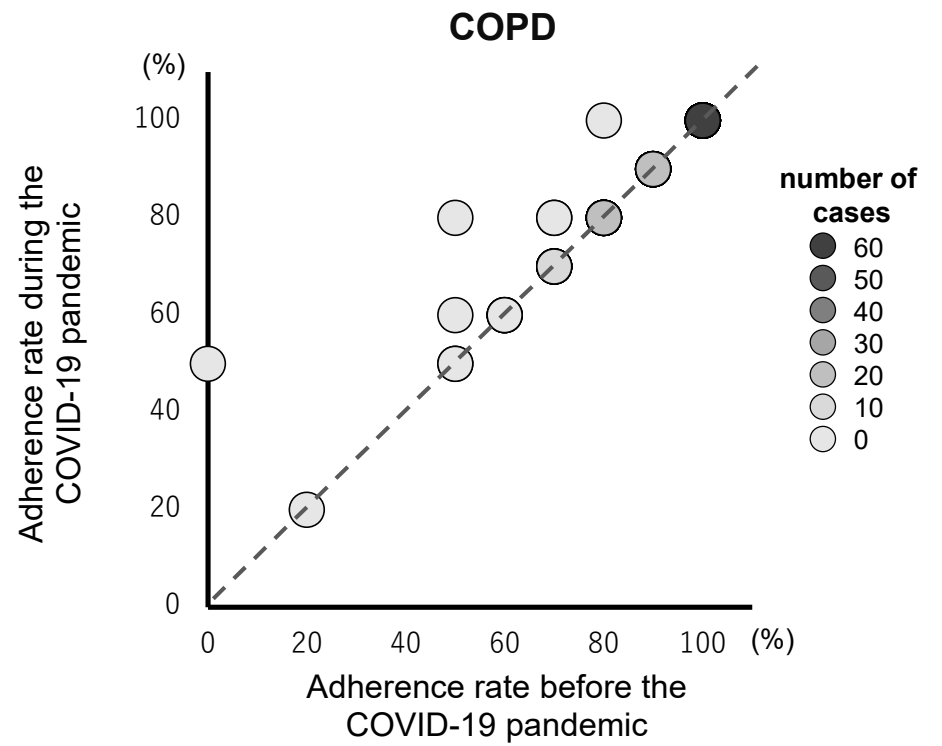
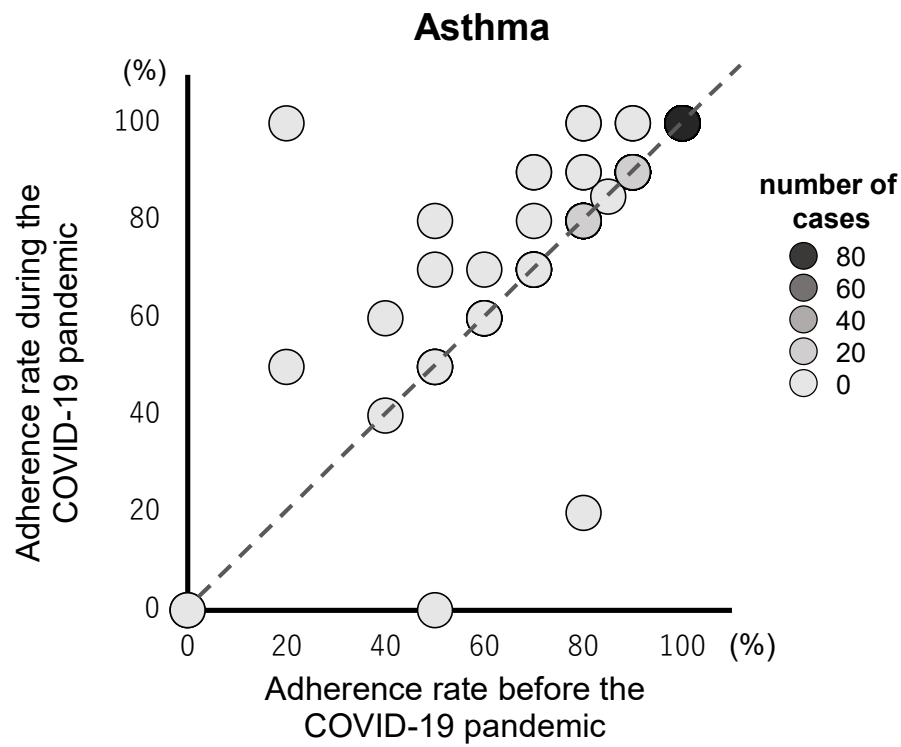
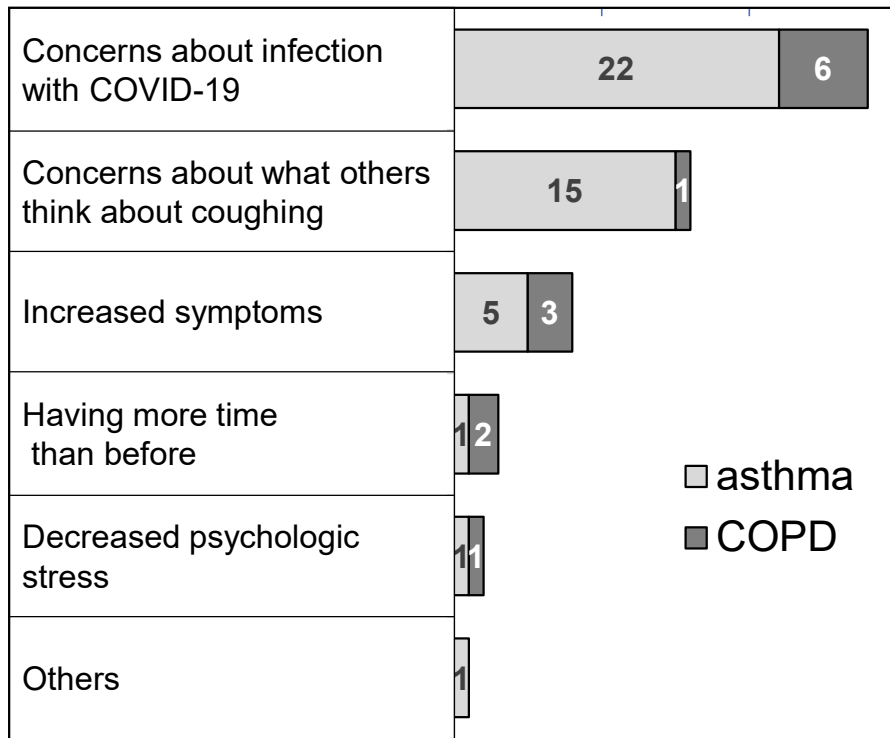


Fig.2

### Reasons for increased adherence (counts)

0 10 20 30



### Reasons for decreased adherence (counts)

0 1 2 3 4 5

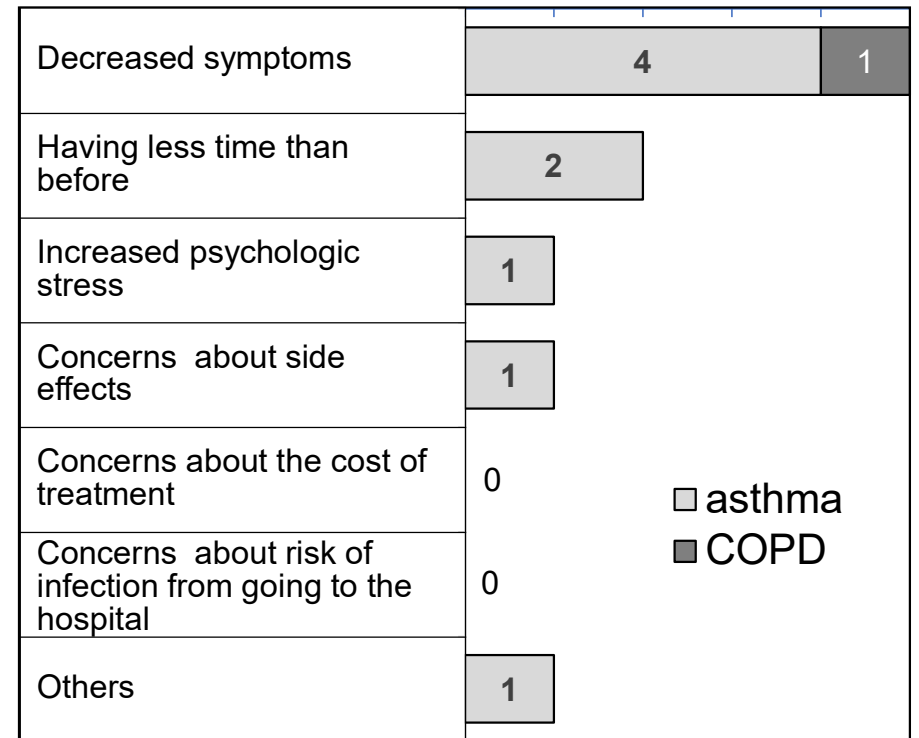


Fig.3

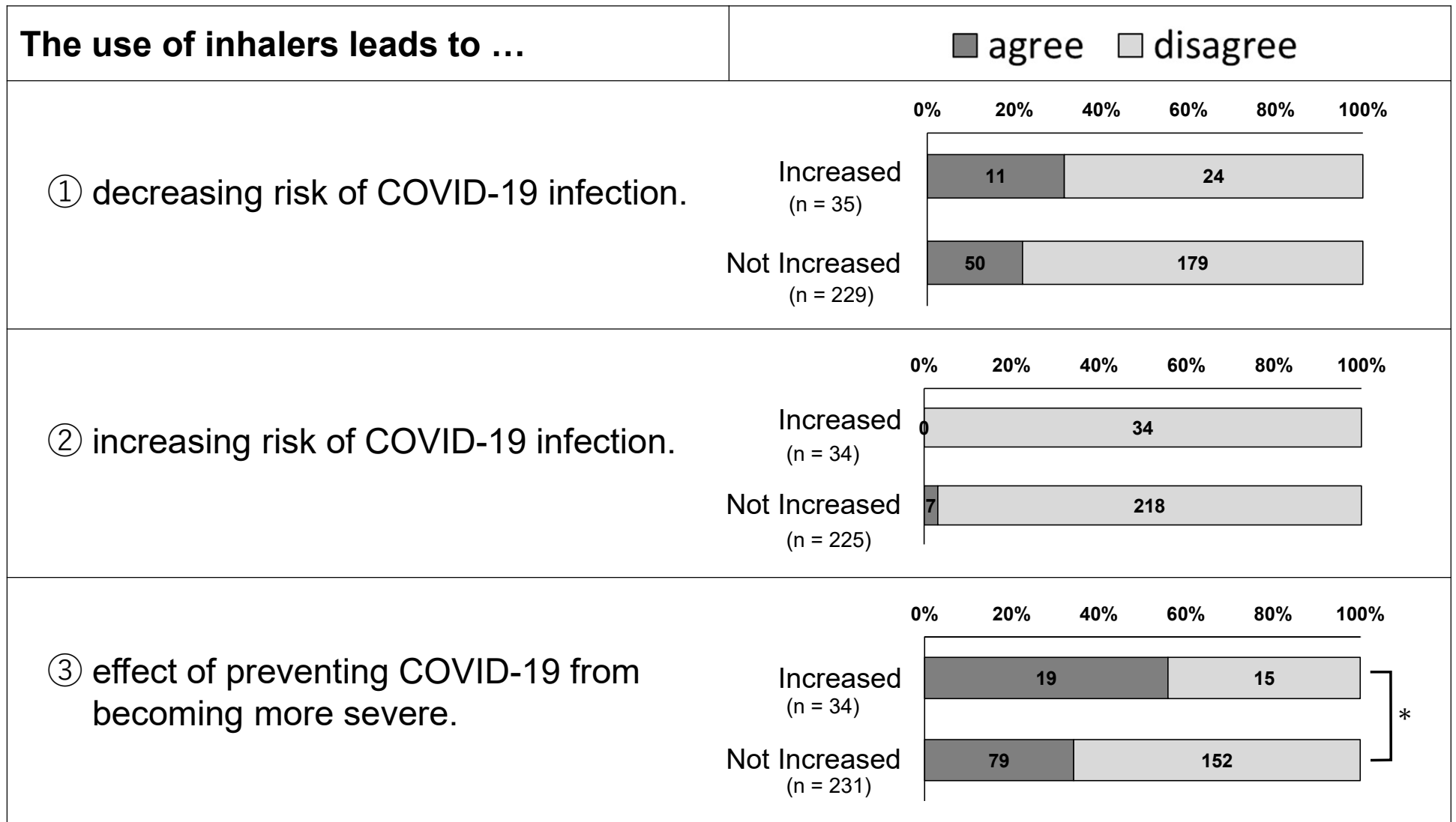


Fig.4

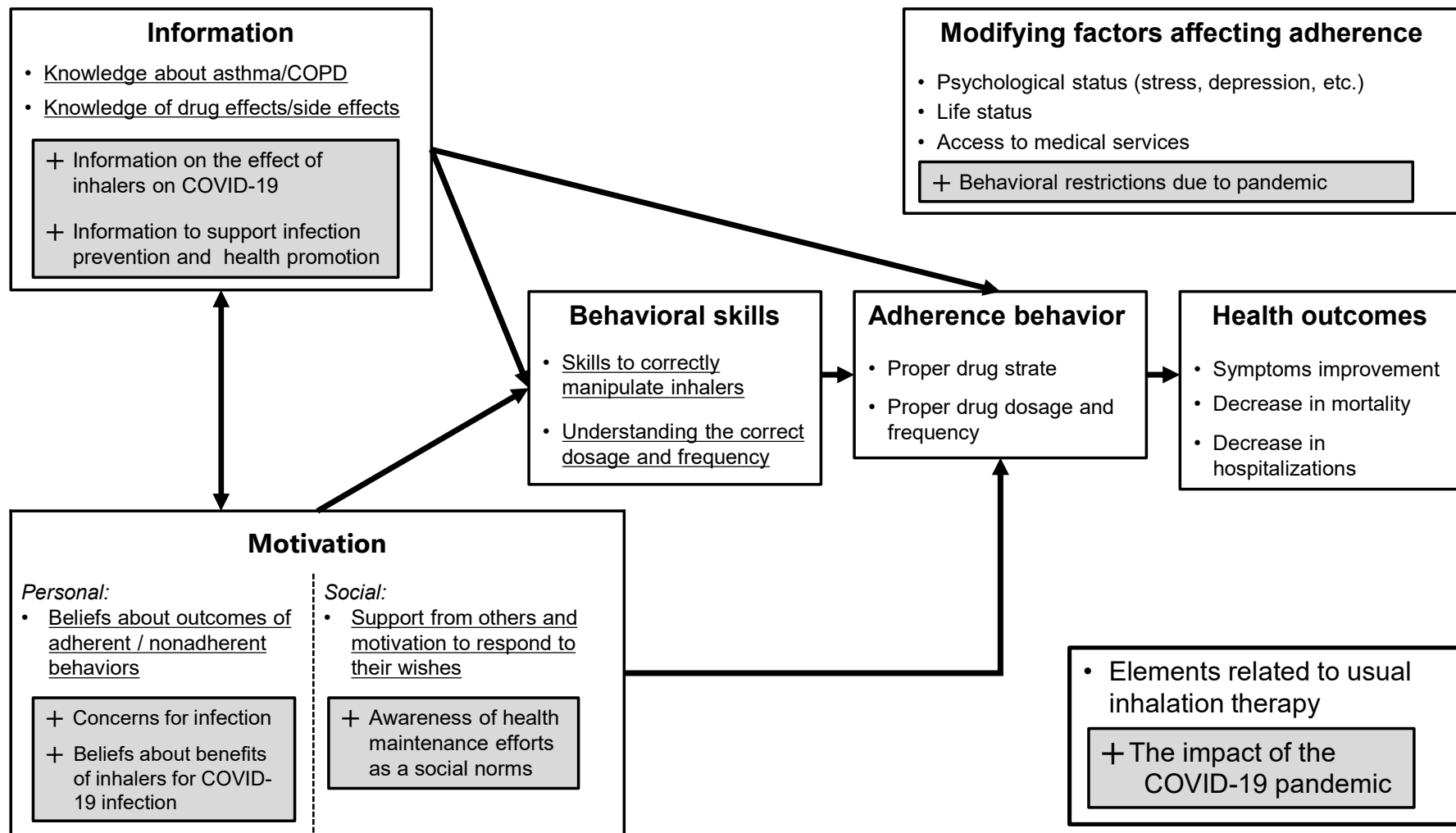
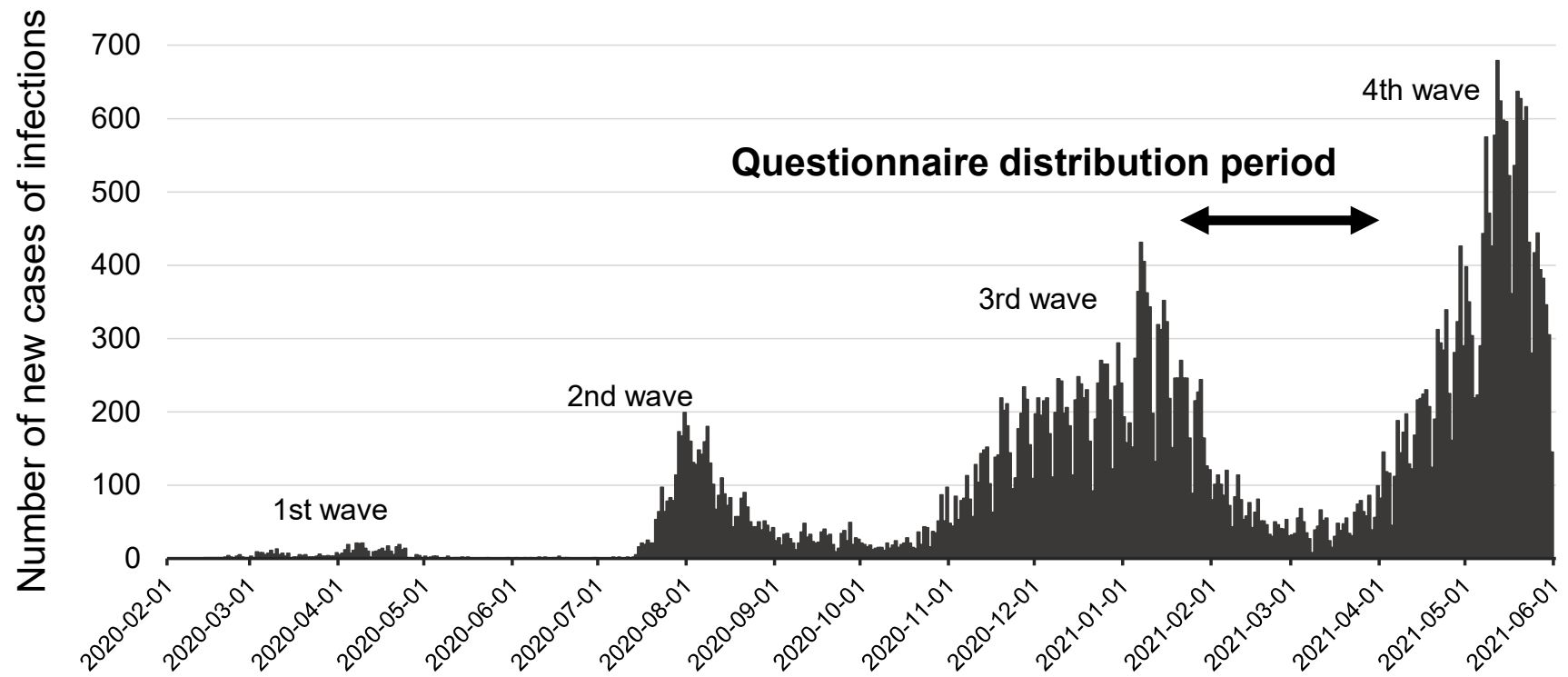
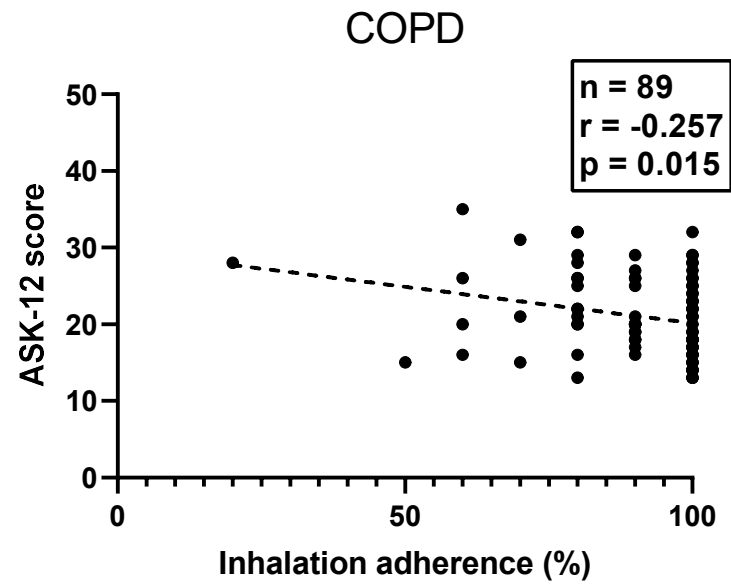
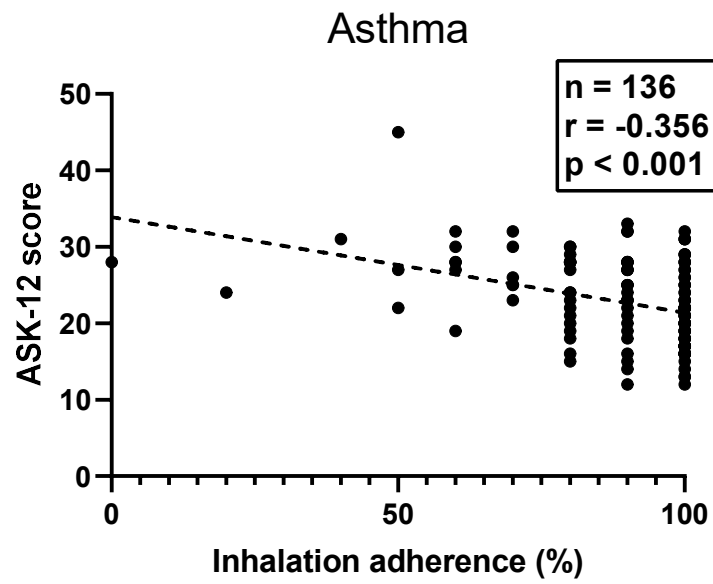


Fig.5



Supple Fig.1



Supple Fig.2

## Supplementary material: Questionnaire

Date of answer	year	month	day
Date of birth	year	month	day
Name	Age	years	Male· Female

Your current inhaled medication.

**Question 1:** Are you currently visiting a hospital or taking inhaled medication for treatment of bronchial asthma or COPD (chronic obstructive pulmonary disease)? Please circle the appropriate item.

- A. I have been going to the Nagoya University Hospital to receive prescriptions for inhalers.
- B. I have been going to hospitals other than Nagoya University Hospital to receive prescriptions for inhalers.
- C. I have been going to a hospital but have not been prescribed any inhalers.
- D. I am not consulting a physician.

In question 1,

If you answered "A" or "B", please answer all the questions on the second and subsequent pages.

If you answered "C" or "D", please answer from question 9 on page 4.



**Question 2:** Have you ever received inhalation instruction by a pharmacist?

Please circle the appropriate item.

1. I have received inhalation instruction at the pharmacist outpatient clinic of Nagoya University Hospital.
2. I have received inhalation instruction at places other than Nagoya University Hospital.
3. I have never received inhalation instruction.

**Question 3:** How confident are you in the operation and use of your usual inhalant? If "not at all confident" is 0 and "completely confident" is 10, please circle the number that best describes your level of confidence.

Not at all confident	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4 <input type="radio"/> 5 <input type="radio"/> 6 <input type="radio"/> 7 <input type="radio"/> 8 <input type="radio"/> 9 <input type="radio"/> 10	Completely confident
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**Question 4:** Currently, what percentage of your prescribed inhalation medications are you inhaling? If "I haven't inhaled any at all" is 0, "I'm inhaling about half" is 5, and "I'm inhaling all" is 10, please circle the closest number.

I haven't inhaled any	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4 <input type="radio"/> 5 <input type="radio"/> 6 <input type="radio"/> 7 <input type="radio"/> 8 <input type="radio"/> 9 <input type="radio"/> 10	I'm inhaling all
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**Question 5:** Before the pandemic of the new coronavirus (before February 2020), what percentage of your prescribed inhalation medications were you inhaling? If "I haven't inhaled any" is 0, "I'm inhaling about half" is 5, and "I'm inhaling all" is 10, please circle the closest number.

I haven't inhaled any	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4 <input type="radio"/> 5 <input type="radio"/> 6 <input type="radio"/> 7 <input type="radio"/> 8 <input type="radio"/> 9 <input type="radio"/> 10	I'm inhaling all
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About your lifestyle.

Please circle the number that applies to your situation.

<p><b>Question 9</b></p>	<p>Do you currently smoke ?</p>	<p>1. Currently smoke 2. Used to smoke but quit (<input type="checkbox"/> Less than 1 year ago. <input type="checkbox"/> More than 1 year ago.) 3. Never smoked</p>												
<p><b>Question 10</b></p>	<p>How much time do you spend away from home each day including private and work hours?</p>	<p>1. Less than 30 minutes    2. 30 minutes to 1 hour 3. 1 to 2 hours                    4. 2 to 4 hours 5. 6 to 8 hours                    6. 8 hours or more</p>												
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<p><b>Question 12</b></p>	<p>How long do you sleep each night?</p>	<p>1. Less than 5 hours    2. 5 to 6 hours 3. 6 to 7 hours            4. 7 to 8 hours 5. More than 8 hours</p>												
<p><b>Question 13</b></p>	<p><u>Compared to before the COVID-19 pandemic (before February 2020),</u> How has your average sleep time changed?</p>	<p>1. Increased 2. Decreased 3. No change</p>												
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<p><b>Question 16</b></p>	<p>How worried are you getting infected with COVID-19?</p>	<p>1. Very worried 2. Somewhat worried. 3. Not very worried. 4. Not worried at all.</p>												

About your medical condition

Please circle the number that applies to you.

<b>Question 17</b>	How many times did you catch a cold from April 2020 to the present?	1. 0 times 2. 1 to 3 times 3. 4 to 5 times 4. 6 or more times
<b>Question 18</b>	How many times did you visit a hospital (including emergency room) for an attack caused by asthma or COPD from April 2020 to the present?	1. 0 times 2. 1 to 3 times 3. 4 to 5 times 4. 6 or more times
<b>Question 19</b>	How many times were you hospitalized for an attack due to asthma or COPD from April 2020 to the present?	1. 0 times 2. 1 to 2 times 3. 4 to 5 times 4. 6 or more times

The stress you are feeling.

**Question 20** Currently, how much stress do you feel in your daily life? If no stress at all is 0, and the strongest stress you can feel is 10, please circle the closest number.

No stress at all	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4 <input type="radio"/> 5 <input type="radio"/> 6 <input type="radio"/> 7 <input type="radio"/> 8 <input type="radio"/> 9 <input type="radio"/> 10	Strongest stress
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**Question 21** Before the pandemic of the new coronavirus (before February 2020), how much stress did you feel in your daily life? If no stress at all is 0, and the strongest stress you can feel is 10, please circle the closest number.

No stress at all	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4 <input type="radio"/> 5 <input type="radio"/> 6 <input type="radio"/> 7 <input type="radio"/> 8 <input type="radio"/> 9 <input type="radio"/> 10	Strongest stress
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Your current treatment.

**Question 22** What medications are you currently using for asthma/COPD?

Please check boxes indicating the number of times you take inhalation medication.

<p><b>inhalers</b> <input type="checkbox"/> Adoair Diskus (100 • 250 • 500 • aerosol) <input type="checkbox"/> Relvar (100 • 200) <input type="checkbox"/> Symbicort Turbuhaler (budesonide/formoterol) <input type="checkbox"/> Flutiform <input type="checkbox"/> Spiriva <input type="checkbox"/> Spiolto <input type="checkbox"/> Onbrez <input type="checkbox"/> Ultibro <input type="checkbox"/> Other ( )</p> <p style="text-align: center;"><b>Inhalation times</b></p> <table border="1" style="margin-left: auto; margin-right: auto;"><tr><td style="width: 50px; height: 30px;"></td><td style="width: 50px; height: 30px;"></td></tr><tr><td style="text-align: center;">Times per day</td><td style="text-align: center;">Inhalations per time</td></tr></table>			Times per day	Inhalations per time
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**Question 23** While you were being treated for bronchial asthma and COPD during the COVID-19 pandemic,

- what do you think has changed compared to the past?
- what are your problems and concerns?

Also, please feel free to provide any comments or suggestions you may have about hospitals, medicines, things you have noticed, or things you would like to share.

( )

**Question 24** Finally, who filled out this questionnaire?

- Patient him/herself       Family member (relationship )

Thank you for taking the time to fill out the survey!

## Supplementary material: Questionnaire

Date of answer	year	month	day
Date of birth	year	month	day
Name	Age	years	Male· Female

Your current inhaled medication.

**Question 1:** Are you currently visiting a hospital or taking inhaled medication for treatment of bronchial asthma or COPD (chronic obstructive pulmonary disease)? Please circle the appropriate item.

- A. I have been going to the Nagoya University Hospital to receive prescriptions for inhalers.
- B. I have been going to hospitals other than Nagoya University Hospital to receive prescriptions for inhalers.
- C. I have been going to a hospital but have not been prescribed any inhalers.
- D. I am not consulting a physician.

In question 1,

If you answered "A" or "B", please answer all the questions on the second and subsequent pages.

If you answered "C" or "D", please answer from question 9 on page 4.

**Question 2:** Have you ever received inhalation instruction by a pharmacist?

Please circle the appropriate item.

1. I have received inhalation instruction at the pharmacist outpatient clinic of Nagoya University Hospital.
2. I have received inhalation instruction at places other than Nagoya University Hospital.
3. I have never received inhalation instruction.

**Question 3:** How confident are you in the operation and use of your usual inhalant? If "not at all confident" is 0 and "completely confident" is 10, please circle the number that best describes your level of confidence.

Not at all confident	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4 <input type="radio"/> 5 <input type="radio"/> 6 <input type="radio"/> 7 <input type="radio"/> 8 <input type="radio"/> 9 <input type="radio"/> 10	Completely confident
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**Question 4:** Currently, what percentage of your prescribed inhalation medications are you inhaling? If "I haven't inhaled any at all" is 0, "I'm inhaling about half" is 5, and "I'm inhaling all" is 10, please circle the closest number.

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**Question 5:** Before the pandemic of the new coronavirus (before February 2020), what percentage of your prescribed inhalation medications were you inhaling? If "I haven't inhaled any" is 0, "I'm inhaling about half" is 5, and "I'm inhaling all" is 10, please circle the closest number.

I haven't inhaled any	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4 <input type="radio"/> 5 <input type="radio"/> 6 <input type="radio"/> 7 <input type="radio"/> 8 <input type="radio"/> 9 <input type="radio"/> 10	I'm inhaling all
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About your lifestyle.

Please circle the number that applies to your situation.

<p><b>Question 9</b></p>	<p>Do you currently smoke ?</p>	<p>1. Currently smoke 2. Used to smoke but quit (<input type="checkbox"/> Less than 1 year ago. <input type="checkbox"/> More than 1 year ago.) 3. Never smoked</p>												
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