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The efficacy of a novel smart watch on medicine adherence and symptom control of allergic rhinitis patients: Pilot study

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ABSTRACT

Background: Allergic rhinitis (AR) is a common allergic airway disorder that is often poorly managed. There is an urgent need to enhance medication adherence in order to improve treatment outcomes in patients with AR. The efficacy of wearable smart watches in improving medication adherence is currently unclear.

Objectives: This study aimed to evaluate the efficacy of a novel smart watch in improving medication adherence and symptom control in patients with AR. The reliability of self-reported medication use was also investigated.

Methods: This randomized, open-label, parallel controlled, pilot study enrolled adult patients with AR caused by cypress pollen. Patients were randomized in a 1:2 ratio to an intervention group and control group. Smart watches were only distributed to patients in the intervention group. During the cypress pollen season, all patients were required to take oral antihistamines daily and use nasal corticosteroids and antihistamine eye drops as needed. Daily AR symptom scores and medication usage were recorded in both groups. The smart watch was able to identify medication-taking behaviors of patients via artificial intelligence (AI) and relay this information to physicians, who sent short message service reminders to patients who forgot to take oral antihistamines for more than 2 days.

Results: During the pollen season, the adherence rate to oral antihistamines in the intervention group ($n = 17$) was significantly higher than that in the control group ($n = 38$) (63.3% $\pm$ 28.5% versus 43.2% $\pm$ 30.2%, $P = 0.02$). The daily symptom score of the intervention group was lower than that of the control group (2.4 $\pm$ 1.1 versus 3.9 $\pm$ 1.0, $P < 0.001$). There was no significant difference in the on-demand medication score between the 2 groups (1.3 $\pm$ 0.4 versus 1.5 $\pm$ 0.5, $P = 0.13$). The consistency rate between self-reported nasal corticosteroid usage and the gold standard (ie, human observation of medication usage in the videos recorded by the smart watch) was 20.0% (0%, 53.7%), and the consistency rate between self-reported antihistamine eye drop usage and the gold standard was 24.3% (2.1%, 67.1%).

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Conclusions: This pilot study showed that the application of smart watches in patients with AR was associated with improved medication adherence and symptom control. Furthermore, the reliability of self-reported medication usage was limited.

Keywords: Allergic rhinitis, Smart devices, Medication adherence, Treatment outcome, Self-report

INTRODUCTION

Allergic rhinitis (AR) is a common allergic airway disorder that affects patients worldwide. The prevalence of AR in the 20- to 44-year-old age group has been reported to range from 11.8 to 46% across 15 countries.[1] Uncontrolled AR is known to reduce quality of life, as well as adversely affect performance at school and work.[2] Unfortunately, AR is often poorly managed. Indeed, a previous multicenter cross-sectional survey showed that 62% of patients with AR had a symptom visual analog scale (VAS) score higher than 5/10 in the previous month, thus indicating a lack of disease control.[3]

Non-adherence to prescribed medications is one of the most important reasons for the poor control of AR. It is a well-known fact that "drugs do not work in patients who do not take them."[4] Indeed, a cross-sectional study conducted in 8 schools in Colombia found that only 40% of 394 children with AR symptoms had adhered to their prescribed medication.[5] The large-scale real-world Mobile Airways Sentinel Network (MASK) study, which assessed medication adherence in 1195 AR patients using a mobile e-diary, reported that 11.28% of patients were adherent to their prescribed treatment and 4.23% were partly adherent.[6] These findings reflect an urgent need to enhance medication adherence in order to improve treatment outcomes in patients with AR.

In modern society, mobile and digital technologies have pervasively influenced every aspect of daily life, including the use of medical services. Smartphone applications allow doctors to monitor patients' health status, share scientific knowledge, and send medication reminders.[4] A mobile patient engagement application for patients with AR or asthma was shown to increase medication adherence and improve the quality of life.[7] A wide range of smart devices have been developed to improve medication adherence.[8,9] Among them, wearable smart watches enable continuous near-real time monitoring of physiological status, behavior verification, and the sending of messages and reminders. These features make smart watches potentially effective tools for enhancing medication adherence in patients.[10] Nevertheless, there is a lack of studies that have investigated the efficacy of smart watches in improving medication adherence and disease control in patients with AR.[11]

A novel smart watch developed by InHandPlus, Inc. is capable of automatically recording short videos of the medication-taking behaviors of patients and recognizing the type of medicine (tablets, nasal sprays, or eye drops) via artificial intelligence (AI) analysis. This information can be transferred directly to physicians, thus enabling them to identify patients with poor medication adherence and send short reminder messages.

This pilot study aimed to evaluate the efficacy of the novel smart watch in improving medication adherence and symptom control in patients with seasonal AR attributed to cypress pollen. Furthermore, the reliability of self-reported medication usage was evaluated via comparison with human observation of medication usage in the videos recorded by the smart watch.

MATERIALS AND METHODS

Patient recruitment

Sixty adult patients with AR attributed to cypress pollen, who were living in Beijing, were recruited from the outpatient Allergy Clinic of Peking Union Medical College Hospital. The inclusion criteria comprised the following: 1) patients with typical AR symptoms (including rhinorrhea, sneezing,

itchy nose, and itchy eyes) during the cypress pollen season (usually from early March to early April), but without symptoms in other seasons; 2) skin prick tests (Allergen Manufacturing Laboratory of Peking Union Medical College Hospital, Beijing, China) performed in Peking Union Medical College Hospital that showed a positive result (diameter of wheal was 3 mm larger than the negative control) for cypress pollen; 3) serum-specific immunoglobulin E (sIgE) tests conducted in Peking Union Medical College Hospital that were positive for cypress pollen (≥0.7 KUA/L) (ImmunoCAP, ThermoFisher Scientific Inc. Waltham, MA, USA); and 4) AR classified as moderate/severe according to the criteria of Allergic Rhinitis and its Impact on Asthma (ARIA) guideline[2] in the previous pollen season, which made the frequent use of oral antihistamines, nasal corticosteroids, and antihistamine eye drops necessary to relieve the symptoms. Exclusion criteria consisted of: 1) history of asthma, immunodeficiency, auto immune diseases, chronic infection, or tumor; and 2) pregnancy or lactation. The study protocol was approved by the Peking Union Medical College Hospital Ethics Committee (ZS-2507), and written informed consent was obtained from all patients.

Smart watch

The smart watch with AI was developed by InHandPlus, Inc. It is capable of monitoring specific behaviors (eg, taking pills, as well as using eye drops, inhalers, and nasal sprays) in real-world settings. The smart watch has a camera module that can record short 20-second videos of patients who are in the process of taking different medications. The camera module is in the sleep mode by default; activation requires the attachment of an electronic tag on each medication container (eg, pill bottle, dropper, spray bottle). This electronic tag transfers the signal to the smart watch, which activates the camera when the following 3 conditions are satisfied: 1) the movement of the medication container is detected by the electronic tag, which has a motion sensor; 2) some amount of light is detected by the light sensor of the electronic tag; and 3) the distance between the electronic tag and the smart watch is within 10–15 cm. The camera module returns to the sleep mode after recording the video, which is analyzed by AI. The AI system analyzes the full 20-second video, which shows the continuous movements of both hands required for taking the medication, from the initial opening to the closing of the medicine container. The ability of the AI system to provide the final output ("medication" or "no medication") for taking different kinds of medicine was acquired through thousands of trainings (Fig. 1). Furthermore, the smart watch can also directly detect the user's motion and steps through its motion sensor; these gesture data are used by the AI system as supplementary data to improve accuracy.

Study design

This randomized, open-label, parallel controlled, pilot study was conducted from early January to early April in 2021. Patients who met the inclusion and exclusion criteria were recruited by physicians in January and February, 2021. A research assistant with no clinical involvement in the study used a computer-generated random number list to allocate patients in a 1:2 ratio to the intervention and control groups; a block

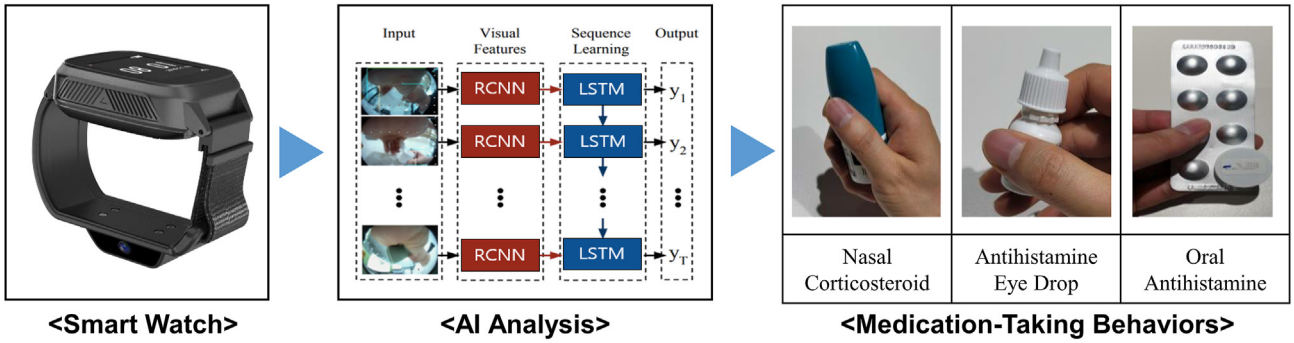

Fig. 1 Schematic diagram of working principle of the smart watch. AI, artificial intelligence

randomization method (block size of 6) was used. The research assistant sent the group allocation list to the physicians, who subsequently distributed the smart watches to patients in the intervention group. The intervention group was given detailed information and instruction videos that covered the following aspects of the smart watch: main working principle; activating conditions of the camera; range and duration of video recording; uploading of short videos and the location in which they were saved; and the fact that only authorized researchers could watch the videos. Patients in the control group were informed that there were 2 groups and that only the intervention group received a novel smart watch for monitoring medication use. Symptomatic medications, including oral antihistamines, nasal corticosteroids, and antihistamine eye drops were prescribed for both groups before the cypress pollen season.

During the cypress pollen season (from March 11 to April 8, 2021), all patients were required to take oral antihistamines daily, while nasal corticosteroids and antihistamine eye drops were to be used as needed. All patients recorded their AR symptom scores and daily medication usage in an online e-diary. The smart watches worn by patients in the intervention group automatically detected the medication-taking behaviors of patients and uploaded the data to the AI system, which relayed this information to physicians. Patients who had forgotten to take oral antihistamines for more than 2 days received short message service (SMS) reminders from the physicians. The follow-up period lasted from the time of randomization (March 1, 2021) to the end of the cypress pollen season (April 8, 2021).

Outcomes

At the end of the cypress pollen season, the primary outcomes (adherence rate to oral antihistamines, AR symptom score, and on-demand medication score reported by the patients) were compared between the intervention and control groups. All short videos recorded by the smart watches were double-checked by authorized researchers. Direct human observation of medication usage in videos served as the gold standard for comparison when determining the secondary outcomes (ie, the reliability of self-reported and AI-reported medication usage).

Primary outcomes

The adherence rate for oral antihistamines in each patient was calculated by dividing the number of days the patient used this medication (as self-reported via the e-diary) by the total number of days (29) in the cypress pollen season in 2021.

The total rhinoconjunctivitis symptom score (tRCSS)[12] was based on the daily evaluation of 6 typical rhinoconjunctivitis symptoms (itchy nose, sneezing, runny nose, blocked nose, itchy/red eyes, and watery eyes) on a four-point scale: 0, no symptoms; 1, minimal awareness of mild symptoms that are easily tolerated; 2, moderate symptoms that are bothersome but tolerable; and 3, severe symptoms that are hard to tolerate and interfere with daily activities and sleep. The daily tRCSS was calculated as the sum of all individual scores, ranging from 0 to 18.

The on-demand medication score (MS)[12,13] was determined via the self-reported daily intake of on-demand medication (including nasal corticosteroids and antihistamine eye drops). The score was calculated according to the following rules: nasal corticosteroid, 1 point per spray; antihistamine eye drop, 0.5 point per drop. The daily on-demand MS was the sum of the individual medication scores.

Secondary outcomes

The gold standard for the determination of medication usage was the direct human observation and double-checking of videos recorded by the smart watches. The consistency rate of self-reported drug usage was calculated by dividing self-reported medication intake by the intake as determined via the gold standard. The consistency rate of AI-reported drug usage was calculated by dividing the AI-reported medication intake by the intake as determined via the gold standard. The consistency rate between self-reported medication usage and the gold standard was calculated separately for oral antihistamine, nasal corticosteroid, and antihistamine eye drop.

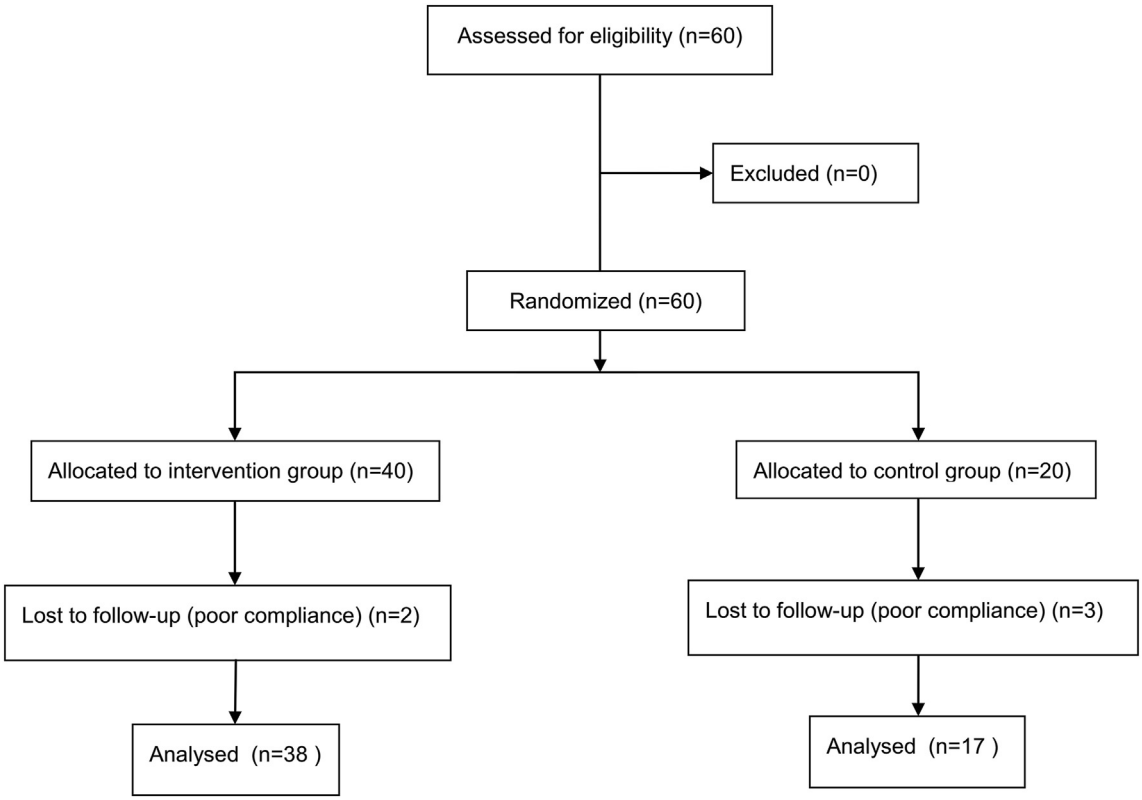

Fig. 2 Flow diagram of the study

Statistical analysis

All statistical analyses were performed with the Statistical Package for the Social Sciences software (ver. 23; SPSS Inc., Chicago, IL, USA). Qualitative data are presented as percentages. Quantitative data with a normal distribution are shown as mean and standard deviation; non-normally distributed data are presented as median and interquartile range. Comparisons of the sex ratio and proportion of patients with persistent AR between the intervention and control groups were performed with the Pearson $\chi 2$ test. Differences in age, adherence rate to oral antihistamines, tRCSS, and on-demand medication score between the two groups were compared using the *t*-test. The Mann–Whitney *U* test was used to compare the consistency rate of self-reported medication usage for different medicines. The level of statistical significance was set at $P < 0.05$.

RESULTS

Baseline condition

A total of 60 eligible patients were recruited from January 2021 to February 2021 and randomly allocated into the intervention group (n = 20) and control group (n = 40) (Fig. 2). Three patients in the intervention group and 2 patients in the control group were lost to follow-up due to poor compliance and lack of outcome indexes recording. Thus, 17 patients (aged 29–59 years) in the intervention group and 38 patients (29–67 years) in the control group completed the study and were included in the final analysis. There were no significant differences between groups in terms of age, sex, persistent AR, or rhinoconjunctivitis VAS scores in the previous pollen season (Table 1).

Comparison of adherence rates and symptom scores

During the pollen season, the adherence rate for oral antihistamines in the intervention group was significantly higher than that in the control group (63.3% ± 28.5% versus 43.2% ± 30.2%, $P = 0.02$). In contrast, the daily tRCSS of the intervention group was lower than that of the control group (2.4 ± 1.1 versus 3.9 ± 1.0 , $P < 0.001$) (Fig. 3). There was no significant difference in the on-demand medication score

Baseline features	intervention group (n = 17)	control group (n = 38)	*P* value
Age	41 ± 7	41 ± 10	0.97
Gender, female, n (%)	13 (76.5)	25 (65.8)	1.00
Persistent AR, n (%)	12 (70.6)	29 (76.3)	0.74
VAS in the previous pollen season	7.5 (6.0, 8.0)	7.8 (6.0, 9.0)	0.46

Table 1. Comparison of baseline features between the intervention group and the control group. *AR, allergic rhinitis; VAS, visual analogue scale*

between the two groups (1.3 ± 0.4 versus 1.5 ± 0.5, $P = 0.13$). However, during the middle term of the cypress pollen season (from March 17 to April 2), when the cypress pollen counts were relatively high, the on-demand medication score of the intervention group was significantly lower than that of the control group (1.1 ± 0.4 versus 1.8 ± 0.4, $P < 0.001$) (Fig. 4).

The consistency rate of self-reported and AI-reported medication usage with the gold standard

After watching the videos recorded by the smart watches, the researchers identified 310, 198, and 286 instances in which patients used oral antihistamines, nasal corticosteroids, and antihistamine eye drops, respectively. AI-reported medication usage was 100% consistent with the gold standard for all three medicines. The consistency rates between self-reported medication usage and the gold standard were 88.9% (69.2%, 100.0%), 20.0% (0%, 53.7%), and 24.3% (2.1%, 67.1%) for oral antihistamine, nasal corticosteroid, and antihistamine eye drop usage, respectively. The consistency rates for self-reported nasal corticosteroid and antihistamine eye drop usage were both significantly lower than that for oral antihistamine usage ($P < 0.001$).

DISCUSSION

This study evaluated the efficacy of a novel smart watch in improving medication adherence and symptom control in patients with seasonal AR. The results showed that patients who wore a smart watch (intervention group) had a higher medication adherence rate and lower symptom score than patients who did not wear a smart watch (control group). Furthermore, there was a lower need for additional medication use in the intervention group during the peak pollen season. The reliability of self-reported and AI-reported medication usage was evaluated by making comparisons to direct human observation of video recordings, which served as the gold standard. While AI-reported medication usage was in total agreement with the gold standard, the consistency rate of self-reported medication usage was much lower, particularly for nasal corticosteroids and antihistamine eye drops.

Although AR is not a life-threatening condition, it remains the most common allergic disorder[14] and is a significant risk factor for allergic asthma.[2] As mentioned previously, the large-scale real-world MASK survey[6] reported that treatment adherence is extremely poor among patients with AR. Medication non-adherence not only hinders the alleviation of AR symptoms, but also results in substantial healthcare costs[15] and a heavy societal burden due to frequent absenteeism (absence from work) and presenteeism (reduced working capacity at work).[16] Therefore, active measures should be taken to effectively increase treatment adherence in patients with AR. Previous studies have indicated the ability of mobile and digital technologies to improve adherence to AR treatment. For example, a daily SMS reminding patients to take their medication resulted in a higher self-reported medication adherence rate (60%) compared to that in a control group (28%); a greater VAS score was also observed in the SMS group.[17] Another study investigated the effects of an internet-based monitoring software (AllergyMonitorTM, AM), which required patients to complete an e-diary for AR symptoms and automatically sent an alert SMS to patients who failed to enter data for 2 consecutive days. It was found that this intervention increased the adherence rate for nasal corticosteroid use in children

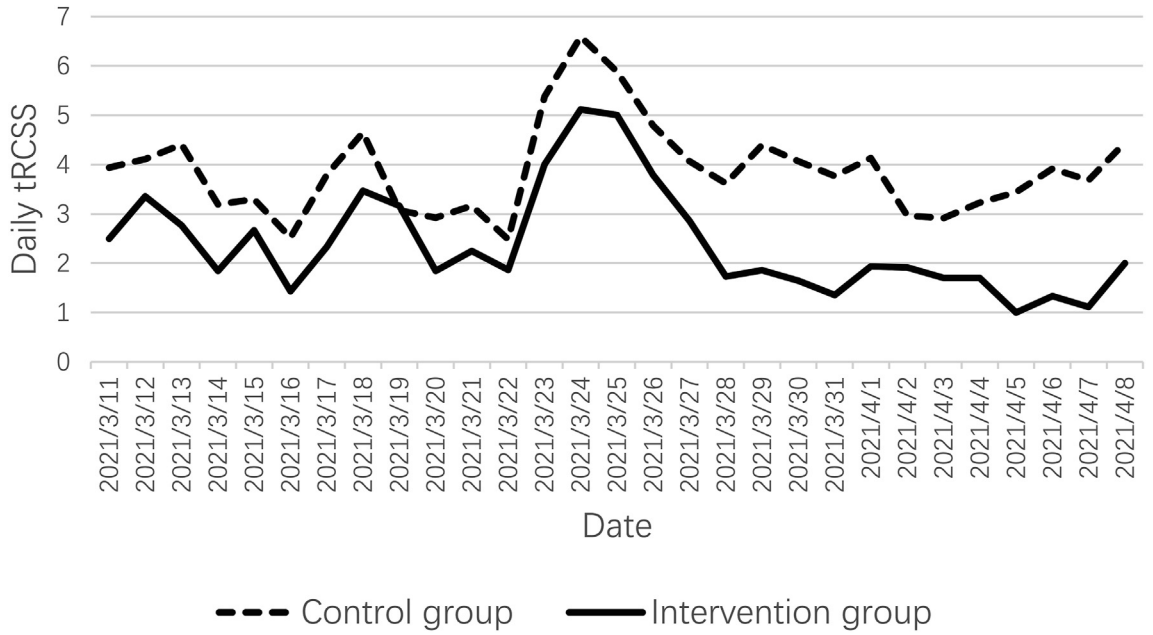

Fig. 3 Comparison of rhinoconjunctivitis symptom score between the intervention group and control group during the cypress pollen season. tRCSS, total rhinoconjunctivitis symptom score

with seasonal AR.[18] These results are consistent with the findings in our study.

The novelty of this pilot study is that a wearable smart watch was used to monitor medication-taking behavior by recording short videos and reporting the data to physicians in real time. In recent years, wearable smart devices have shown the potential to revolutionize disease prevention, detection, and treatment.[19] For example, a wearable heart rate belt electrocardiogram

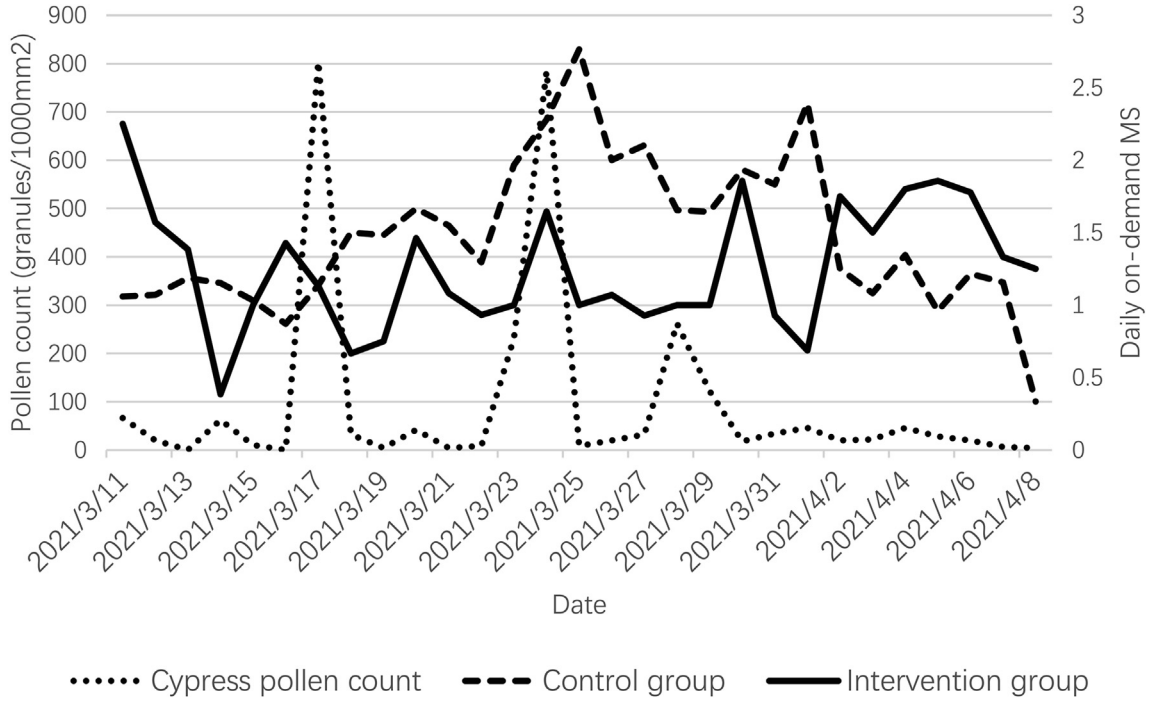

Fig. 4 Comparison of on-demand medication score between the intervention group and control group during the cypress pollen season. The cypress pollen count was measured through the gravity sedimentation method. MS, medication score

monitoring device was able to detect the occurrence of atrial fibrillation with a sensitivity and specificity of 100%.[20] In addition, a wearable smart watch that could reliably record the respiratory rate, heart rate, and oxygen saturation was successfully used to screen for the early deterioration of chronic obstructive pulmonary disease.[21,22] The smart watch used in this study also provided reliable information on medication usage that helped physicians to make appropriate decisions regarding individualized treatment and send reminders to specific patients with low adherence. Our study demonstrated the potential of wearable smart devices to improve medication adherence and symptom control in patients with AR. However, their application value in the long-term management of allergic disorders requires further investigation in studies with larger sample sizes.

Self-reported doses of symptomatic medications are widely used as indicators of the degree to which AR is appropriately controlled. This approach is also used to evaluate the efficacy of novel therapies for AR,[9] particularly allergen immunotherapy, which is the only immune-modifying and causal treatment available for patients with AR.[6] However, our comparison of self-reported medication usage in patients and usage as determined by direct human observation of recorded videos found that the reliability of self-reporting was poor. Self-reports of nasal corticosteroid and antihistamine eye drop use were significantly less reliable than those for oral antihistamine use. The reason for this finding is not clear. It is possible that patients tended to ignore medications intended for local application and paid more attention to orally ingested tablets. These results highlight the urgent need for the development of more reliable and objective tools for monitoring and measuring actual medicine usage, which is essential for high-quality clinical trials. The conventional method for evaluating medication usage involves weighing the unused medication, or counting the remaining tablets. While this method is objective and generally accurate, it may not be practical in all settings. Furthermore, this method does not reflect daily variations in medication usage. The novel smart watch with AI technology used in this pilot study demonstrated a high level of reliability as a monitoring tool for medication use, as it had a 100% consistency rate with direct human observation. Nevertheless, this study only analyzed the videos recorded by the smart watches, and it is acknowledged that patients may have forgotten to wear the watch in some instances. Furthermore, there was a risk of missing reports in cases where the electronic tag sensors malfunctioned, thereby failing to activate recording by the camera module. Thus, this smart watch still requires continuous improvement in order to enhance ease-of-use and provide an accurate evaluation of medication usage.

There were some limitations in our study. First, this open-label study had a relatively small sample size and was conducted at a single medical center. Therefore, the study results could not be directly extrapolated to the general population. This requires further studies with larger sample sizes. Second, patients in both the intervention and control groups were required to complete the e-diary every day during the cypress pollen season. As it has been shown that regular use of an e-diary alone can improve self-management and medication adherence,[18] the observed differences in these outcomes between the two groups in the present study may have been larger if the intervention group was compared with a less trained patient population in routine practice. Third, the use of an e-diary to record symptom scores may have been a source of recall bias. Fourth, although the adherence rate of the intervention group was higher than that of the control group, the mean adherence rate of the intervention group (63.3%) was much lower than 80%, which is usually considered to be the lower threshold of eligible adherence. As mentioned above, the adherence to AR treatment was extremely poor, and there is still much work to be done to further improve management of this condition. Fifth, in this study, we mainly focused on the adherence to prescribed oral antihistamines, while the use of nasal corticosteroids was decided by the patients themselves. Thus, the patients may have used the nasal corticosteroids intermittently; this would have hampered the achievement of best efficacy due to the delayed onset of action of corticosteroids.

Furthermore, the smart watches had some inherent limitations. For example, they needed to be recharged daily and a Wi-Fi connection was required to upload the videos to the AI system. Also, recording the videos at the patients' home could have possibly increased the stigma of being monitored and raised privacy concerns. Data collected by the smart watch should be anonymized in order to ensure privacy protection. This is essential if the watch is to be used in daily clinical practice.[23] The shortcomings of the watches should be rectified and their efficacy investigated in future clinical trials with larger sample sizes.

In conclusion, this pilot study showed that the application of smart watches in patients with AR was associated with improved medication adherence and symptom control. The reliability of self-reported medication usage was limited, thus highlighting the need for the development of novel objective tools for evaluating medication use.

Abbreviations
AI, artificial intelligence; AR, allergic rhinitis; ARIA, Allergic Rhinitis and its Impact on Asthma; MS, medication score; SIgE, specific immunoglobulin E; SMS, short message service; tRCSS, total rhinoconjunctivitis symptom score; VAS, visual analogue scale.

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Availability of data and materials
The data that support the findings of this study are available from the corresponding author, on special request.

Author contributions
We claim that we have directly participated in the planning, execution and analysis of the study. Kai Guan designed the project and guided the study. Lisha Li, Zixi Wang, Le Cui and Yingyang Xu contributed to the patient recruitment and follow-up communication. Lisha Li, Hwiwon Lee and Kai Guan contributed to the clinical data collection and statistical analyses. Lisha Li wrote the manuscript. Zixi Wang, Le Cui, Yingyang Xu, Hwiwon Lee, and Kai Guan revised the manuscript.

Ethics statement
Approval of the Peking Union Medical College Hospital Ethics Committee (ZS-2507) had been obtained. Written informed consents were obtained from all the patients.

Consent for publication
All contributing authors consent to this publication.

Declaration of competing interest
Author Hwiwon Lee reports that he has a patent METHOD FOR DETECTING EVENT OF OBJECT BY USING WEARABLE DEVICE AND MANAGEMENT SERVER OPERATING SAME issued to InHandPlus, Inc. Author Hwiwon Lee is employed by InHandPlus, Inc. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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