# original research e of a Digital Asthma

# Factors Affecting Usage of a Digital Asthma Monitoring Application by Old-Age Asthmatics Living in Inner Central Portugal

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**Purpose:** To analyse factors affecting the ability to use the digital asthma monitoring application Mask-Air<sup>®</sup> in old-age individuals living in inland Portugal.

**Patients and Methods:** In this observational study, patients with medically confirmed asthma who agreed to participate were interviewed and subdivided into Non-users Group: those who could not use the application and Users Group: those who could. Sociodemographic and psychological data, comorbidities, and asthma status were compared between groups. Assessment of reasons for refusal was based on a 6-item questionnaire.

**Results:** Among the 72 sequentially recruited patients (mean  $age\pmSD 73.26\pm5.43$  yrs; 61 women; 11 men), 44 (61.1%; mean  $age\pmSD 74.64\pm5.68$  yrs; 38 women; 6 men)) were included in Non-users Group and 28 (38.9%; mean  $age\pmSD 71.11\pm4.26$  yrs; 23 women; 5 men) in Users Group. Non-users Group patients were significantly older, had lower socioeconomic level, and more frequently had severe asthma (25% vs 3.6%; Odds ratio=0.08 (95% CI=0.01-0.81; p=0.033)) and diabetes (32.6% vs 7.4%; Odds ratio=0.17 (95% CI=0.03-0.80; p=0.025)) than Users Group. The main reasons for not using the App were "Lack of required hardware" (n=35) and "Digital illiteracy" (n=26), but lack of interest to use the App among those who had conditions to use it was uncommon.

**Conclusion:** Most old-age asthmatics living in Beira Interior either lack a smartphone or digital skills, which are significant obstacles to implementing app-based monitoring studies.

**Plain Language Summary:** This study was done to see whether it was possible to use a mobile phone application (App) to help old-age asthmatics living in inner Central Portugal better monitor and self-manage their disease.

The researchers interviewed a group of 72 patients with proven asthma who agreed to participate in the study. This group was subdivided into two subgroups: Non-users Group (44 patients) included those who could not use the App because they did not have a smartphone; Users Group (28 patients) included those who had all the conditions to use the App. Patients were helped to download

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the App (called MASK-Air), were given a thorough explanation about it, and about how it should be used on a daily basis to monitor their asthma symptoms.

The researchers found that patients in Non-users Group were significantly older, had worse socioeconomic conditions, and more often had severe asthma and diabetes. They also discovered that the main reasons for not using the App were lack of a smartphone and not knowing how to use a smartphone.

These results show that lacking a smartphone and not knowing how to use digital tools are frequent situations in old-age asthmatics living in inner Central Portugal, and these may be obstacles for patients in monitoring their own asthma symptoms.

Keywords: asthma, mHealth, digital literacy, disease monitoring, old-age

### Introduction

Asthma has significant morbidity.<sup>1–3</sup> Many patients with more severe asthma experience disease exacerbations, which are associated with lower quality of life and increased disease costs.<sup>3</sup> Low health literacy levels, low socioeconomic status or poor accessibility to healthcare may further compound this situation.<sup>3,4</sup> This is especially relevant in old-age patients, who may also more frequently be isolated, have lower symptom awareness, and poor adherence to medication.<sup>3</sup>

Mobile Health (mHealth) may be a useful adjunct to monitor asthma, and this may be particularly beneficial in oldage individuals and those with more severe disease.<sup>4</sup> MASK-Air (Mobile Airways Sentinel Network) is a flexible e-platform for allergic diseases and asthma, which includes an application (App) which is available for free in Android and iOS systems, and has been validated in multiple parameters.<sup>5-7</sup> It is operational in 29 countries and 19 languages (including Portuguese), and more than 60,000 patients have been registered to use the App. Besides the app, the supporting system also provides other components, namely to support healthcare professionals in shared decisionmaking. After having downloaded the app to their smartphones from the internet, patients need to answer the daily monitoring questionnaire, comprising (i) a set of visual analogue scales with questions on asthma, rhinitis and conjunctivitis symptoms, as well as (ii) questions on daily medication use<sup>5-7</sup> MASk-Air is a Good Practice of DGSanté regarding the digital transformation of health.<sup>8</sup> MASK-Air App aims to reduce the global burden of asthma and rhinitis, allowing better decision-making by doctors and patients.<sup>8</sup> However, usage of digital approaches by old-age individuals remains variable, as low digital literacy, poor education level, low socioeconomic status, and cognitive deficits may be obstacles.<sup>9,10</sup> This may explain why, when the App was validated, only 5% of all the daily data collected was from patients aged over 65 years.<sup>11</sup> In spite of this aspect, a MASK-air study comparing <65 and  $\geq 65$ -year-old users, results suggested that patients of up to at least 75 years can be included in MASK-air-based monitoring of disease, without any significant effect on reliability of results, although this issue should be addressed in a larger sample of patients in this age range.<sup>12</sup>

A recent study performed in Puglia, Italy, showed that old age asthmatics, even with a lower education level, could use the MASK-Air *App* on their smart device after a short training session.<sup>9</sup> However, this study did not fully evaluate factors associated with not being able to use the *App*. Furthermore, old age patients living in inland, rural areas, who frequently have a lower socioeconomic status than those living in larger seaside cities, may more frequently have lower health and digital literacy.<sup>13,14</sup> Although they may be helped by younger close relatives regarding digital literacy and using smartphones, it is important to ascertain factors hindering these aspects. Thus, our study aimed to analyse factors affecting acceptance and capacity to use Mask-Air in old-age asthmatic patients from various places in Beira Interior, an aged and sparsely populated area of inner Central Portugal.

## **Material and Methods**

### Study Type and Design

Observational study was performed at Centro Hospitalar Universitário Cova da Beira (CHUCB), Covilhã, between July and December 2022. All patients who agreed to participate were interviewed and subdivided into 2 groups (A and B). Non-users Group included patients who could not use the MASK-Air App, whereas Users Group included those who could use it.

### Study Sample

Since there were no previous studies on digital literacy and capacity to use an App on a smartphone for monitoring health parameters by old-age individuals in inner Central Portugal, we decided to carry out this pilot study with a minimum of 70 patients. Old-age asthmatics were sequentially recruited at the Pulmonology and Immunoallergology outpatient clinics of CHUCB.

Patients were referred from various healthcare centres throughout the whole of inner Central Portugal (districts of Guarda and Castelo Branco). Inclusion criteria were being at least 65 years-old; having medically confirmed asthma;<sup>15</sup> being regularly seen at outpatient clinics; and willingness to participate in the study. Exclusion criteria included significant cognitive deficits or Chronic Obstructive Pulmonary Disease.

### Characterisation of the Study Sample

Validated questionnaires were used to characterise factors that might affect acceptance of the *App*: a) *Sociodemographics*: gender, age, marital status, education, hobbies, housing type, co-inhabitants, Graffar scale,<sup>16</sup> b) *Psychological aspects*: Geriatric Depression Scale,<sup>17</sup> Brief Symptom Inventory,<sup>18</sup> c) *Comorbidities and other health aspects*: Atopic and non-atopic comorbidities, smoking history; d) *Asthma control*: CARAT questionnaire.<sup>19,20</sup> Assessment of reasons for refusal to use the *App* was based on a 6-item questionnaire.<sup>9</sup> Digital literacy was qualitatively assessed by directly asking the patients whether they had ever used a smartphone, a computer or a tablet, and, in case they had, by directly asking them to show how to find, download and use an *App*.

### Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences<sup>®</sup> (SPSS<sup>®</sup>) version 28.0. Categorical variables were described using absolute frequencies and percentages and quantitative variables using means, standard deviations, and maximum and minimum levels. Associations between accepting to use MASK-Air and potential factors affecting such acceptance were evaluated using univariable and multivariable logistic regression models. Multivariable regression models were initially built considering age, gender, and variables with P<0.2 resulting from univariate logistic regression models. A stepwise selection variables method, based on the likelihood ratio, was then applied (significance level at 5% for a variable entering and 10% for its removal). Exponentials of logistic regression models were interpreted as odds ratio (OR). P<0.05 was considered to be statistically significant.

### Ethical Aspects

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committees of the University of Beira Interior (Reference number: CE-UBI-Pj-2022-034-ID1337) and of CHUCB (Reference number: 25/2022, dated 2022/06/03). Written informed consent was obtained from all patients. Data were recorded, in a semi-anonymized form, in a computer with encrypted access, to which only the study coordinator had access. MASK-Air follows the General Data Protection Regulation.

## Results

Seventy-four elderly asthmatics were sequentially recruited. Only two patients (both female; 67 and 72-year-old) declined to participate; these patients did not have a smartphone, and their clinical and sociodemographic features were similar to those of patients who accepted to participate in the study. Thus, only 72 patients were entered into the study. Most recruited patients were female (84.7% in the global sample; 86.4% in the Non-users Group; 82.1% in the Users Group). Regarding language, all patients were native Portuguese speakers. Most of the 72 volunteers (Table 1) were not able to use the *App* and were included in Non-users Group (n=44; 61.1%). Non-users Group patients were older, had lower schooling, fewer hobbies, and a lower sociodemographic status (higher Graffar Scale class) than Users Group patients.

Most individuals had GINA Steps 2 or 3 asthma, but only half of them had controlled symptoms (Table 2). Non-users Group had a significantly higher percentage of patients with Steps 4 and 5 (severe) asthma. There were no significant differences in rhinitis symptom control (Table 2) or prevalence (Table 3) between groups. Diabetes was also significantly

Table I Sociodemographic C	Characterisation
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Variables	Total n=72	Non-Users Group n=44	Users Group n=28	uOR (95% CI) Reference: A	P <sup>a</sup>
Age (years)					
Mean (SD)	73.26 (5.43)	74.64 (5.68)	71.11 (4.26)	0.87 (0.78-0.97)	0.009
Min-Max	65–93	65–93	65-80	0.07 (0.70 0.77)	0.007
Gender Male, n (%)	( 5.3)	6 (13.6)	5 (17.9)	1.38 (0.38–5.03)	0.628
Marital Status, n (%)					
Single	7 (9.7)	4 (9.1)	3 (10.7)	I	0.766
Married	45 (62.5)	28 (63.3)	17 (60.7)	0.81 (0.16-4.07)	0.797
Divorced	5 (6.9)	2 (4.5)	3 (10.7)	2.00 (0.19-20.61)	0.560
Widower	15 (20.8)	10 (22.7)	5 (17.9)	0.67 (0.11-4.21)	0.666
Schooling, n (%)					
≤ 4 years	52 (72.2)	37 (84.1)	15 (53.6)	I	0.023
5-9years	13 (18.1)	4 (9.1)	9 (32.1)	5.55 (1.48-20.81)	0.011
> 9 years	7 (9.7)	3 (6.8)	4 (14.3)	3.29 (0.66–16.50)	0.148
	/ (7./)	3 (0.0)	т (14.3)	3.27 (0.00-10.30)	0.140
Hobbies, n (%)	F7 (70 2)		2( (02.0)	F 4F (1 12 24 40)	0.025
Yes	57 (79.2)	31 (70.5)	26 (92.9)	5.45 (1.13–26.40)	0.035
No	15 (20.8)	13 (29.5)	2 (7.1)	I	
Type of housing, n (%)					
House	50 (69.4)	33 (75.0)	17 (60.7)	1.94 (0.70–5.38)	0.203
Flat	22 (30.6)	11 (25.0)	11 (39.3)	I	
Co-habitants, n (%)					
Yes	55 (76.4)	33 (75.0)	22 (78.6)	1.22 (0.39-3.79)	0.728
No	17 (23.6)	11 (25.0)	6 (21.4)	I	
Graffar Scale					
Mean (SD)	17.14 (2.11)	17.66 (2.21)	16.32 (1.66)	0.71 (0.54-0.93)	0.014
Min-Max	11–23	11–23	12–19	(,	
	(IV)	(IV)	(III)		
GDS					
Normal	42 (58.3)	26 (59.1)	16 (57.1)	I	0.872
Slightly depressed	27 (37.5)	15 (34.1)	12 (42.9)	1.30 (0.49–3.47)	0.600
• / /		. ,		1.50 (0.17-5.17)	0.000
Severely depressed	3 (4.2)	3 (6.8)	0 (0.0)	-	-
BSI Global		10.07 (10.00)	22.07 (12.02)		0.100
Mean (SD)	19.63 (12.65)	18.07 (12.30)	22.07 (13.03)	1.03 (0.99–1.07)	0.192
Min-Max	I-49	I-49	3–48		
BSI Somatisation					
Mean (SD)	7.50 (5.53)	6.50 (4.91)	9.07 (6.15)	1.09 (1.00–1.19)	0.058
Min-Max	0–22	0–17	0–22		
BSI Depression					
Mean (SD)	4.46 (4.31)	4.00 (4.22)	5.18 (4.43)	1.07 (0.95-1.19)	0.260
Min-Max	0–17	0–17	0–16		
BSI Anxiety					
Mean (SD)	7.67 (4.63)	7.57 (4.52)	7.82 (4.88)	1.01 (0.91-1.12)	0.820

Variables	Total	Non-Users	Users	uor (95% CI)	P <sup>a</sup>
		Group	Group	Reference: A	
GINA 2022 Classification, n (%)					
Mild (Step 1)	11 (15.3)	5 (11.4)	6 (21.4)	I	0.097
Moderate (Steps 2 and 3)	49 (68.I)	28 (63.6)	21 (75.0)	0.63 (0.17–2.33)	0.484
Severe (Steps 4 and 5)	12 (16.7)	11 (25.0)	l (3.6)	0.08 (0.01–0.81)	0.033
Asthma, n (%)					
Controlled (CARAT $\geq$ 16)	34 (47.2)	19 (43.2)	15 (53.6)	I	0.390
Not controlled	38 (52.8)	25 (56.8)	13 (46.4)	0.66 (0.25–1.71)	
Rhinitis, n (%)					
Controlled rhinitis (CARAT > 8)	21 (42.0)	11 (42.3)	10 (41.7)	I	0.963
Not controlled rhinitis	29 (58.0)	15 (57.7)	14 (58.3)	1.03 (0.33–3.16)	

#### Table 2 Asthma and Rhinitis Characterisation

Abbreviations: uOR, unadjusted odds ratio; CI, confidence interval; "Wald's test.

Variables	Total n (%)	Non-Users Group n (%)	Users Group n (%)	uOR (95% CI) Reference: A	P <sup>a</sup>
Atopic Comorbidities, n (%)	57 (79.2)	32 (72.7)	25 (89.3)	3.13 (0.80–12.29)	0.103
Allergic Rhinitis, n (%)	49 (86.0)	25 (78.1)	24 (96.0)	6.72 (0.77–58.79)	0.085
Allergic Conjunctivitis, n (%)	16 (28.1)	7 (21.9)	9 (36.0)	2.01 (0.62-6.47)	0.243
Chronic Rhinosinusitis, n (%)	19 (33.3)	12 (37.5)	7 (28.0)	0.65 (0.21–2.00)	0.452
Non-Atopic Comorbidities, n (%)	70 (97.2)	43 (97.7)	27 (96.4)	0.63 (0.04–10.46)	0.746
Obesity, n (%)	19 (27.5)	11 (25.6)	8 (30.8)	1.29 (0.44-3.80)	0.641
Pulmonary Thromboembolism, n (%)	I (I.4)	I (2.3)	0 (0.0)	-	-
Cancer, n (%)	4 (5.7)	3 (7.0)	I (3.7)	0.51 (0.05-5.20)	0.572
Hypertension, n (%)	53 (75.7)	33 (76.7)	20 (74.1)	0.87 (0.28-2.64)	0.800
Diabetes Mellitus, n (%)	16 (22.9)	14 (32.6)	2 (7.4)	0.17 (0.03-0.80)	0.025
GERD, n (%)	25 (35.7)	13 (30.2)	12 (44.4)	1.85 (0.68-5.02)	0.229
Dyslipidaemia, n (%)	43 (61.4)	26 (60.5)	17 (63.0)	1.11 (0.41–3.00)	0.834
Cardiac Insufficiency, n (%)	17 (24.3)	13 (30.2)	4 (14.8)	0.40 (0.12–1.39)	0.151
Other, n (%)	16 (22.9)	11 (25.6)	5 (18.5)	0.66 (0.20-2.17)	0.495

Table 3	Atopic and	Non-Atopic	Comorbidities
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Abbreviations: uOR, unadjusted odds ratio; CI, confidence interval; <sup>a</sup>Wald's test.

more prevalent in Non-users Group. In fact, all patients with concurrent severe asthma and diabetes and most patients with concurrent moderate asthma and diabetes were in this Group (Table S1)

Multivariable analysis showed that age, Graffar scale and having diabetes mellitus were significantly associated with accepting to use MASK-Air, with the odds of being able to use the *App* decreasing 17% for each year of age, 31% for each higher point in Graffar Scale, and 87% if the patient was diabetic (Table 4).

Figure 1 shows the most frequent reasons given by 44 patients (Non-users Group) for not using MASK-Air. Overall, reasons indicating lack of possibility to use MASK-Air ("Lack of required technology"; "Digital illiteracy"; being unable to read or write; Total n=65 reasons) were much more frequent than reasons indicating not wanting to use the App ("Lack of interest"; "Distrust"; Total n=6 reasons) (Figure 1A). More specifically, reasons or combinations of reasons given by these 44 patients (Non-users Group) were "Lack of required technology + digital illiteracy" (n=14); "Lack of required technology" (n=14), "Digital illiteracy" (n=8) and "Lack of required technology + Digital illiteracy + Being unable to read or write" (n=4) (Figure 1B). Less frequent combinations were as follows: "Lack of interest + lack of required technology" (n=2), "Lack of interest" (n=2), "Distrust" (n=1) and "Lack of required technology + distrust" (n=1).

Variables	Total n=70	Non-Users Group n=43	Users Group n=27	aOR (95% CI) Reference: A	P <sup>a</sup>
Age (years) Mean (SD) Min-Max	73.17 (5.40) 65–93	74.47 (5.63) 65–93	71.11 (4.34) 65–80	0.83 (0.73–0.95)	0.005
Graffar Scale Mean (SD) Min-Max	17.10 (2.11) 11–23	17.60 (2.21) 11–23	16.30 (1.68) 12–19	0.69 (0.50–0.96)	0.027
Diabetes mellitus, n (%)	16 (22.9)	14 (32.6)	2 (7.4)	0.13 (0.02–0.71)	0.019

Table 4 Adjusted Odds Ratio for Being Able to Use Mask-Air

**Notes**: Assessment of the logistic model: Assessment of the logistic model: Likelihood ratio test: P<0.001; Hosmer-Lemeshow test: p=0.834; Cox & Snell R<sup>2</sup>=0.266; Nagelkerke R<sup>2</sup>=0.361; AUC=0.803 (95% CI 0.701–0.905, P<0.001); Sensitivity=81.5% and specificity=67.4% for probability cut-off 0.3311;

Among the 28 patients who were able to use the App (Users Group), that is, those who had a smartphone and minimal digital skills, only 3 (10.7%) did not want to use it, due to "Lack of interest".

### Discussion

We showed that most elderly individuals living in central inner Portugal, many of whom have severe asthma, could not use a digital monitoring *App*, due to lack of possibility rather than lack of interest. Main reasons for not using the *App* were lack of a smartphone and/or digital skills. In addition, the poorer, the less educated, and the older patients were, the less likely were they to use Mask-Air.



**Figure I** Reasons for not using MASK-Air App by Non-users Group asthmatics. Most frequent reasons given by Non-users Group (44 patients) for not using MASK-air; these results show lack of possibility to use the App versus not wanting to use the App (**A**). Venn diagram showing specific reasons and combinations of reasons given by Non-users Group (44 patients) for not using MASK-Air App (**B**).

Notes: \*Isolated "Digital illiteracy" (n=8); \*\*isolated "Lack of required technology" (n=4); <sup>§</sup>isolated "Lack of interest" (n=2); <sup>#</sup>isolated "Distrust" (n=1).

Abbreviations: aOR, adjusted odds ratio for age, gender, and variables with P<0.2 from Tables I, 2 e 3; CI, confidence interval; <sup>a</sup>Wald's test.

Most patients lacked adequate digital technology and/or digital skills. This was also found in the Puglia study, in which almost 40% of 174 volunteers had to be excluded mostly due to these two reasons.<sup>9</sup> However, in our study, this problem was even more prevalent, not only due to lack of a smartphone but particularly regarding low digital literacy levels. This is in agreement with a study on digital literacy in adults from 28 European countries, which showed that the percentage of use of internet for health-related information was lower in Portugal than in Italy, namely in the old-age patients.<sup>21</sup>

In our study, the more aged, the poorer, and the less educated patients were, the less likely were they to use MASK-Air App. This is in agreement with most studies, but not all, on digital literacy in old-age patients. For example, the Pew Research Center 2014 Report showed that in the US, older, less affluent patients are more frequently digitally disconnected.<sup>22</sup> A Greek study also found that older ages and a lower education level were predictors of low eHealth literacy.<sup>23</sup> In addition, a recent systematic review and meta-analysis also showed that increasing age and lower socioeconomic status had a negative effect on digital health literacy, particularly among older adults.<sup>24</sup> This may translate into lower capacity to use mobile Apps, as suggested by a study performed in post-discharge acute coronary syndrome patients in which acceptance to use a monitoring App significantly dropped in those 75 years-old and older in comparison with younger patients.<sup>25</sup> In any case, in our study, although patients who could use the App had a higher level of schooling, it was still low. This suggests that, independently of schooling, in the appropriate context (having a smartphone and minimal digital literacy), elderly individuals tend to accept using mHealth approaches. However, it should be borne in mind that supplying access to digital hardware and promoting digital literacy does not ensure that older patients will be willing to use an App to monitor their disease. Nevertheless, it should be highlighted that, in our sample, of those who lacked the required technology, only 3 patients (6.8%) would possibly never use the App, due to "Lack of interest" (n=2), or "distrust" (n=1). Even among the 31 patients who were able to use the App, only 3 (9.7%) did not want to use it. Thus, we might expect that around 8% of patients, even when given a smartphone and digital training might still not want to use the App.

We also found that significantly more patients were diabetic in Non-users Group than in Users Group. Although this may have occurred by chance, this finding is in line with the data from the Pew Research Center 2014 Report which showed that older patients who also tend to have more significant health problems and co-morbidities, are less frequently digital users.<sup>22</sup> Also, in a study carried out in Spain, involving 116 COPD patients, which focused on compliance with and utility of a smartphone app for detecting disease exacerbations, those who were active smokers, with a higher dyspnoea score, and had associated co-morbidities such as depression and obesity, had lower overall compliance and duration of compliance in recording data on the *App*.<sup>26</sup> It is also possible that type 2 diabetes mellitus and asthma are reciprocal risk factors and this may be more relevant in more severe disease.<sup>27</sup> This was the case in our study, since a high proportion of patients with more severe asthma in Non-users Group had diabetes and, in fact, all patients with concurrent severe asthma and diabetes were in this Group.

In our study, severe asthma was significantly more prevalent in Non-users Group (those who could not use the *App*) than in Users Group (those who could use it). Although this may have been biased because of the low sample size, this observation still potentially implies that a high proportion of old-age patients with severe asthma cannot be adequately monitored using mHealth in Beira Interior (inner Central Portugal). This is important, because although all patients in our study had a written asthma management plan, they may not fully follow it and need to be more frequently seen at checked regarding this aspect. This would be in line with the need for old-age asthmatic patients to be more frequently checked in terms of their asthma inhaler technique, as we have previously shown.<sup>28</sup> However, accessibility to healthcare in inner Central Portugal is not homogeneous and can be relatively low. Furthermore, patients with severe asthma tend to have a worse quality of life and worse symptom control, culminating in a greater need for hospital visits, when compared with those with mild or moderate asthma.<sup>29</sup> In fact, as recently shown by a study analysing asthma data in Portugal, there is a high rate of hospital admissions due to asthma exacerbations per 1000 inhabitants with asthma, in Beira Interior.<sup>30</sup>

This study has several limitations including the small patient sample and the fact that it only involved patients from Beira Interior. In addition, digital health literacy was not analysed using a validated tool such as the 16-item Mobile Device Proficiency Questionnaire (MDPQ-16).<sup>31–33</sup> It also has strengths: there are few mHealth studies in older adults, and it is the first to more thoroughly evaluate factors affecting the capacity to use mHealth in elderly asthmatics.

# Conclusion

Most elderly asthmatics living in inland Portugal either lack a smartphone or digital skills, which are obstacles to implementing *App*-based monitoring studies and may contribute to inequities in the application of digital approaches to asthma management. Supplying access to digital hardware and promoting digital literacy are needed to adequately evaluate the potential benefits of mHealth in old-age asthmatics living in inland Portugal.

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### **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

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