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## **Doctoral thesis summary**

**The impact of e-medicine in the management of  
patients with bronchial asthma**

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## **Introduction**

Asthma is a chronic condition of the respiratory tract that affects more than 334 million people of all ages in all parts of the world and is expected to increase by 100 million more by 2025. (1)

It negatively affects different areas of patients' quality of life due to long-term treatment and multiple exacerbations. Asthma is a growing cause of morbidity and mortality and imposes a significant burden on patients, families and healthcare systems, thus it is known as the third leading cause of hospitalization among children. (2)

According to asthma management guidelines, educating the patient with an emphasis on increasing knowledge about adherence and treatment to medication is essential.

Some problems, such as non-adherence to medication and lack of information related to self-management, have led to patients' unwillingness to engage in disease management activities.

Due to the poor implementation of self-management programs and their underutilization, the need for new and innovative methods of self-management has emerged.

IT interventions, such as e-medicine applications, have the potential to improve the results of self-management by providing support (information, education and alarms) to the patient. Estimates show that more than one billion people will use m-medicine applications on smartphones by 2018. Moreover, these applications have a multifunctional media for communicating information, exchanging experiences and collecting data, being easy to individualize, cost effective and accessible to all. Thus, these interventions have the potential to improve the self-management of patients with chronic diseases. (3)

Several studies have been conducted evaluating the effect of m-medicine applications on self-management of asthma patients, but all of these studies reported different results. For example, one study showed that self-management interventions transmitted through the mobile phone application improved lung function, quality of life, asthma symptoms and reduced the use of emergency medication and exacerbations. (4)

However, another study showed that the use of mobile applications does not have a significant impact on asthma control, self-management, quality of life and the number of hospitalizations and exacerbations. (5)

Several review studies have been conducted on IT interventions to promote adherence and self-management of asthma patients. In 2013, such a study was conducted to evaluate the effect of mobile phone applications on the self-management of asthma patients. Only two randomized controlled

trials were included in that paper, and in the end, due to the small number of studies performed in this field, no clear and definitive results were found. (6)  
(7)

In 2014, a meta-review was conducted to evaluate the effectiveness of digital and online interventions on self-management outcomes in asthma patients. This study demonstrated the positive impact of these interventions on self-management, including on quality of life and adherence to treatment. (6)

Another review study was conducted in 2016 which included 12 studies with a wide range of IT interventions that focused on the characteristics of these assessments (education, monitoring/electronic journal, action plans, alarms, asthma control). This review showed that the most effective interventions had multiple characteristics, but the effects on the health outcomes of asthma patients were inconsistent. (8)

To our knowledge, to date, no studies have been conducted to investigate the adherence and self-management of asthma in patients with mobile phone applications.

Starting from the above-mentioned facts, I set out to evaluate first of all the inhalation technique of asthma patients and to determine what types of errors are made more often, all with the help of an application on the mobile phone. Secondly, I aimed to see what effect the mobile application has on self-management and disease control of asthmatic patients in Romania.

## **Study objectives**

- Evaluation of the inhalation technique in patients with asthma using the application
- Determining the types of errors in inhalation technique using the application
  - Determination of handling errors of inhalation devices
  - Determination of critical errors in inhalation technique
  - Evaluating the effectiveness of the application on the mobile phone in self-management of the disease of patients with asthma
- Evaluation of disease control using the mobile phone application of patients with asthma
  - Determining the number of uses of emergency medication for patients with asthma after the intervention of the application
  - Determining the number of exacerbations of patients with asthma after the intervention of the application

- Determining the number of hospitalizations of patients with asthma after the intervention of the application

### **Study 1 - Inhaler technique errors in Romanian patients with asthma - a multicenter study**

The main types of errors in inhalation technique are "critical" and "non-critical" errors. "Critical" errors significantly reduce the proper delivery of medication to the lungs. "Non-critical" errors result in a partial reduction in the concentration of the drug in the lungs.

In recent documents, GINA stressed the importance of assessing and correcting inhalation technique before climbing the asthma treatment level. Video education has become increasingly used in recent years, but few studies have investigated the effectiveness of video instructions on the correct inhalation technique.

Considering these aspects, we aimed in this paper to evaluate and improve the inhalation technique in patients with asthma with the help of an mobile phone application. In addition, we evaluated the types of errors and their number in inhalation techniques.

This was a multicenter observational study that was conducted over a period of 1 year. To evaluate the errors of the inhalation technique we adopted a design with the subject together. One of the advantages of the design of this study is that only a small number of participants are needed and the chance of discovering differences between repeated evaluations increases. Patients were randomly selected and assigned also randomly to evaluate the inhaler. Although we included patients who had previously received inhalation medication, none of them had experience with the mobile phone application.

We chose to analyze the following medical devices: turbuhaler, diskus, pMDI and SMI because they are the most prescribed inhaler devices for asthma patients in Romania.

The technique was divided into handling errors and inhalation errors. A critical error was considered when preventing the patient from completely inhaling the medication from the device. A non-critical error was considered when administering the suboptimal drug even though the patient inhaled some of the medication. The steps were marked with "1" if the technique was correct and "0" if it was incorrect. The same doctor evaluated the technique at each medical visit.

After the first evaluation, patients downloaded the application to their mobile phone and were encouraged to use it each time to remind them of the correct inhalation technique. Patients were recalled every 3 months for

evaluation and treatment. Inhalation technique was assessed at each medical visit.

## **Results**

Data were analyzed using SPSS v.17 software (SPSS Inc., Chicago, IL, USA). Graphics were generated using GraphPad Prism v8.0.2. the value of 0.05 was considered the statistically significant threshold and a confidence level of 0.95 was considered for estimating the intervals.

To evaluate the errors recorded by the Turbuhaler device, we considered a sample of 25 people, 12 men and 13 women. At the first evaluation, a total number of 7.00 errors, the average 6.00 (5.00-6.00) were noted, and after 3 months, a maximum number of 3.00 errors, the median of 2.00 (2.00-2.00) errors were noted, while no errors were observed after 6 months. When we considered only the critical errors, at the first evaluation, we noticed a maximum number of 4.00 errors, median (3.00-4.00), while after 3 and 6 months, the number decreased to 2 errors, median 0.00 (0.00-1.00) respectively 0 errors.

In connection with the error evaluation for the Diskus device, a number of 14 individuals were considered 9 men and 5 women. The total number of errors decreased from the first evaluation (10.00 errors median 6.00 (6.00-7.00) errors) to the evaluation from 3 months (maximum number of 5.00 errors, median 2.00 (2.00-2.00) errors) and to 6 months (only one error).

When we tested the errors of the pMDI device, we considered a group of 26 individuals, 13 men and 13 women. At the first evaluation we noticed a total number of 9.00 errors, median 7.00 (6.00-8.00) errors. After 3 months, we noticed a total number of 3.00 errors, the median 2.00 (1.00-2.00) errors, while after 6 months, we observed a single error. When we considered only the critical errors, we noticed a number of 5.00 errors, median 3.5 (3.00-4.00) at the first evaluation, while after 3 and 6 months, the number decreased to only two errors, median 1.00 (0.00- 1.00) errors, respectively zero errors.

When we evaluated the inhalation technique with the SMI device, we considered a group of 10 individuals, 6 men and 4 women. We noticed a number of 11 errors, the median 7.00 (5.00-8.00) errors at the first evaluation. After 3 months, we observed a total of 7 errors, the median 3.00 (2.00-4.00) errors, while at 6 months, we noticed a single error, the median 0.50 (2.00-4.00) errors. When we considered only the critical errors, we noticed a number of 6.00 errors, the median 5.00 (3.00-5.00) at the first evaluation, while at the evaluations at 3 and 6 months, the number

decreased to 3 errors, the median 2.00 (1.00-2.00) errors, respectively to a single error.

### **Conclusions**

The results of this study show that the video instructions provided by a specific application on the mobile phone can improve the inhalation technique of patients with asthma.

### **Study 2 - The efficacy of a mobile phone application to improve adherence to treatment and self-management in people with chronic respiratory disease in Romanian population - a pilot study**

There is ample evidence for effective self-management in asthma but there are important challenges in their implementation. These obstacles arise due to the lack of information of the patient regarding the disease and the inhalation technique and on the other hand due to the health care providers who do not have the time, skills or motivation to offer self-management education to the patients. (9)

Significant improvements have been made in the last three decades in adherence to the treatment of asthma patients through the Internet and other electronic means. (10)

The conclusions of the last World Asthma Awareness Campaign in Romania showed that asthma treatment is deficient; only 13.5% of the studied patients known to have asthma were treated. (11)

Although nowadays there are many applications on the mobile phone to improve medical services, there is no special application for asthmatic patients in Romania. In Romania, asthma remains underdiagnosed, and in many cases, poorly treated. Thus, the objective of this study was to observe the effect of a mobile phone application on self-management and disease control in the Romanian population.

### **Results**

This was a non-randomized controlled pragmatic study. For a period of six months we included patients who were diagnosed with asthma and wanted to participate in this study. According to the study design, at the T<sub>0</sub> visit (which was considered the baseline value) patients were evaluated and educated on how to use the correct inhalation technique.

At this point, all patients received an action plan that was explained face to face and shown the inhalation technique, then the patients were divided into two groups. The division was made according to the patient's desire to use or not the application on the mobile phone.

The first group included 54 patients who received only drug treatment and the second group, which was composed of 39 patients, received drug treatment plus the application on the mobile phone.

The included patients were recalled every three months for a full year for evaluation and treatment ( $T_1$  to  $T_4$ ). The number of exacerbations and the ACT questionnaire were recorded. At each recall, patients completed the questionnaire that is used to assess symptoms.

The median ACT score at the initial assessment was 18.00 (17 - 19.00). Most patients (85.18%) used emergency medication. In addition, more than half of the patients (53.66%) had severe exacerbations that required hospitalization, while 46.34% of patients had mild-to-moderate exacerbations that did not require hospitalization.

At baseline, all patients in the application group experienced exacerbations, while 85% of patients in the control group who did not use the application experienced exacerbations. At the first evaluation ( $T_1$ ), after 3 months, the ACT score of patients who used the application was significantly higher than that of patients who did not use it (Mann-Whitney U test,  $p < 0.001$ ). Similarly, at the other evaluations ( $T_2$ ,  $T_3$ ,  $T_4$ ), we noticed that the ACT score was significantly higher in the case of asthmatic patients who used the application compared to the control group (Mann-Whitney U test,  $p < 0.001$ ). When we compared the number of uses of emergency medication between the two groups, we noticed significant differences at the first evaluation ( $T_1$ ; Pearson Chi-Square  $X^2(1)=23,626$ ,  $p < 0.001$ ), at the second evaluation ( $T_2$ ; Pearson Chi-Square  $X^2(1)=9,445$ ,  $p = 0.002$ ), to the third ( $T_3$ ; Pearson Chi-Square  $X^2(1)=9,136$ ,  $p=0.003$ ), and to the last ( $T_4$ ; Pearson Chi-Square  $X^2(1)=5.836$ ,  $p=0.016$ ). When we consider the number of exacerbations, at the first  $T_1$  evaluation, we noticed that significantly fewer patients who used the application showed exacerbations, 10.30% vs. 46.30%.

## **Conclusions**

This study indicates that smartphone apps are an effective way to improve asthma control and self-management if used continuously. We observed significant positive effects in disease control and frequency of exacerbations. Pneumocontrol is an application that could be useful to improve asthma results for our population.

## **Final conclusions**

After conducting the two studies we observed:

1. In the study in which we analyzed the inhalation technique using a mobile phone application, we noticed that the total number of errors decreased from the first assessment to three to six months for all medical devices.

2. Regarding the inhalation technique with the Turbuhaler device, we noticed that the total number of errors decreased from the first evaluation to the one from 3 months and 6 months.

3. At the first evaluation 7 errors were recorded and after 3 months the maximum number of errors was reduced to 3 while after 6 months no errors were observed.

4. Regarding critical errors, 4 errors were recorded at the first evaluation, at 3 months the number of errors decreased to 2 errors and after 6 months no errors were observed.

5. We did not observe statistically significant differences between the number of errors related to handling or inhalation, in the case of male patients vs. female, 53.3% vs. 46.7%.

6. Regarding the inhalation technique with the Diskus device, we noticed at the first evaluation a number of 10 errors, at 3 months the number of errors decreased to 5 and at 6 months this number decreased to a single error.

7. Regarding critical errors, 6 errors were recorded at the first evaluation, at 3 months the number decreased to 3 errors and at 6 months it decreased to a single error.

8. We did not notice significant differences between the number of errors in the case of men vs. women, when we considered the techniques of handling and inhalation. At the same time, we did not notice significant differences between the number of errors in patients in different age groups.

9. Regarding the inhalation technique with the pMDI device, we noticed a number of 9 errors, after 3 months the number decreased to 3 errors while after 6 months this number decreased to a single error.

10. Regarding the number of critical errors, we noticed 5 errors at the first evaluation, at 3 months the number decreased to 2 errors and at 6 months no critical errors were found.

11. We noticed that the number of errors recorded in the case of patients grouped by sex, that men had significantly more errors compared to women in the handling techniques "Does not have lips sealed to the device", 76.9% vs. 23.1%.



12. We did not notice significant differences between the number of errors in the case of men vs. women when I considered other handling and inhalation techniques.

13. When we compared the number of errors in the case of patients aged 20-40 years vs. those aged between 41-62 years, we noticed significant differences between the number of errors in the handling technique "Do not remove/open the lid", 16.7% vs. 83.3%.

14. Regarding the inhalation technique with the SMI device, we noticed 11 errors at the first evaluation, at 3 months the number decreased to 7 errors and after six months only one error was recorded.

15. Regarding the number of critical errors, at the first evaluation we noticed 6 errors, at 3 months the number decreased to 3 errors and after 6 months we recorded a single error.

16. We did not notice significant differences between the number of errors in the case of men vs. women when it comes to handling and inhalation techniques. Moreover, we did not find significant differences between these errors when different age groups were taken into account.

17. In the study in which we evaluated the effect of the application on the mobile phone on self-management and disease control, the average ACT score at the initial evaluation was 18 points and most patients (85.18%) used emergency medication.

18. We observed that more than half of the patients (53.66%) presented severe exacerbations that required hospitalization, while 46.34% of patients presented mild-moderate exacerbations that did not require hospitalization.

19. At the first evaluation ( $T_1$ ), after 3 months, the ACT score of patients who used the application was significantly higher than that of patients who did not use it ( $p < 0.001$ ).

20. When we compared the number of uses of emergency medication between the two groups, we noticed significant differences at all moments of the evaluation.

21. When we considered the number of exacerbations, at the first  $T_1$  evaluation, we noticed that significantly fewer patients who used the application had exacerbations, 10.30% vs. 46.30%.

22. At the second evaluation, we did not notice significant differences between the two groups when we evaluated the number of exacerbations, 12.8% vs. 14.8%.

23. On the third evaluation, we noticed that in the group that used the application there were significantly fewer patients with exacerbation 2.6% vs. 16.7%.

24. At the last assessment, no significant differences were found between the two groups 10.3% vs. 24.1%.

25. We observed significant differences between the ACT score of the patients in the group that used the application and the control group, stratified by gender. ACT  $T_1$  score for male patients who did not use the vs. those who used the app was 19 vs. 21 and in the case of female patients, the scores were 20 vs. 22 ( $p < 0.001$ ).

26. ACT  $T_2$  for male patients who did not use the application vs. those who used it was 22 vs. 23 ( $p < 0.001$ ), and in the case of female patients, the scores were 20 vs. 23.50 ( $p < 0.001$ ).

27. ACT  $T_3$  score of male patients who did not use the application vs. those who used the app was 22 vs. 23 ( $p < 0.001$ ) and in the case of female patients, the scores were 21 vs. 23.50 ( $p < 0.001$ ).

28. We observed significant differences between ACT  $T_4$  scores of male patients who did not use the application vs. those who used the application 21 vs. 24 ( $p < 0.001$ ) as well as in the case of female patients, 21 vs. 23 ( $p < 0.001$ ).

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