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# Tosse em idade pediátrica: revisão bibliográfica e estudo piloto de prova de conceito da utilização de uma aplicação móvel para aquisição de sons da tosse em crianças

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## Resumo

**Introdução:** A tosse é o sintoma mais comum de apresentação clínica de doença respiratória na infância. O objetivo desta tese foi compreender a importância da tosse na doença respiratória pediátrica e estudar a utilização de uma aplicação móvel com um componente de aquisição de sons respiratórios, para recolha de sons de tosse em idade pediátrica.

**Métodos:** Pesquisa e revisão da literatura existente sobre os mecanismos, características, abordagem e tratamento da tosse em idade pediátrica. Posteriormente, realização de um estudo piloto de prova de conceito, realizado no Serviço de Pediatria do CHUP, numa população de crianças com doença respiratória com tosse em contexto ambulatorio ou de internamento. Foi realizada questionário estruturado, seguido da instalação e utilização da aplicação digital móvel AIRDOC, pelos cuidadores, para recolher os sons de tosse das crianças. O feedback sobre a aplicação foi recebido após uma semana de uso, por contacto telefónico. Os ficheiros de sons de tosse foram ouvidos posteriormente pelos investigadores.

**Resultados:** A abordagem e o tratamento da tosse em crianças assumem diferenças na apresentação aguda ou crónica, devendo ser realizada uma abordagem específica direcionada à patologia subjacente. A perceção parenteral da frequência e gravidade da tosse das crianças apresenta baixa fiabilidade, quando comparado a medidas mais objetivas desses parâmetros. No estudo piloto de prova de conceito, foram incluídas 7 crianças, com doença respiratória, com média de idade de 2,8 ( $\pm 1,5$ ) anos, sendo que 71% tinham um diagnóstico crónico e 29% um diagnóstico agudo. Todas as crianças foram recrutadas em contexto ambulatorio. Todos os participantes categorizaram sua tosse como paroxística. A maioria dos pacientes relatou que a tosse é intermitente e 4 dos participantes a descreveram como produtiva. O sintoma associado à tosse mais relatado foi o esternuto, e o uso de anti-histamínico foi declarado por 57% dos participantes. Os cuidadores demonstraram interesse no uso desta aplicação móvel. Foram relatados problemas no login e início do processo de gravação.

**Conclusões:** A tosse é um sintoma respiratório muito importante na caracterização da patologia respiratória em idade pediátrica. Pais e cuidadores de crianças com doenças respiratórias têm interesse em utilizar ferramentas de monitorização da tosse no ambulatorio, considerando este tipo de equipamento útil na gestão de doenças, para auxiliá-los no reconhecimento e autocontrole dos seus sintomas. A aplicação AIRDOC necessita de algumas reformulações em termos de programação para poder ser utilizada em ambiente real e de forma efetiva pelos cuidadores das crianças. Estudos posteriores serão fundamentais para ajustar esta ferramenta de saúde digital.

## **Abstract**

**Background:** Cough is the most common clinical presenting symptom of respiratory disease in childhood. The aim of this thesis was to understand the importance of cough in paediatric respiratory disease and to study the use of a mobile application with a respiratory sounds acquisition component to collect cough sounds in paediatric patients.

**Methods:** Research and review of existing literature on the mechanisms, characteristics, management, and treatment of paediatric cough. Subsequently, a pilot proof-of-concept study was carried out at the Paediatrics Service of CHUP, in a population of children with respiratory disease with cough in an outpatient or inpatient setting. A structured clinical interview was carried out, followed by the use of the AIRDOC application, by the caregivers, to collect the children's coughing sounds. Feedback on the application was received after one week of use, by telephone contact.

**Results:** The approach and treatment of cough in children assume differences in acute or chronic presentation, and a specific approach aimed at the underlying pathology should be taken. Parenteral perception of the frequency and severity of cough in children has low reliability when compared to more objective measurements of these parameters. In the pilot proof-of-concept study, 7 children with respiratory disease were included, with a mean age of 2.8 ( $\pm$  1.5) years, with 71% having a chronic diagnosis and 29% an acute diagnosis. All children were recruited in an outpatient setting. All participants categorized their cough as paroxysmal. Most patients reported that the cough is intermittent and 4 of the participants described it as productive. The most reported symptom associated with cough was sneezing, and the use of antihistamine medication was reported by 57% of the participants. Caregivers showed interest in the use of this mobile application. Problems in the login and initiation of the recording process were reported.

**Conclusions:** Cough is a very important respiratory symptom in the characterization of respiratory pathology in paediatric age. Parents and caregivers of children with respiratory diseases are interested in using cough monitoring tools, considering this type of equipment useful in disease management, to help them recognize and self-control their symptoms. The AIRDOC application needs some reformulation in terms of programming to be able to be used in a real environment and in an efficient way by the children's caregivers. Further studies will be essential to improve this digital health tool.

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## BIBLIOGRAPHIC REVIEW

Respiratory symptoms, such as cough, are among the most common presenting symptoms to general practitioners and paediatric primary care.<sup>1</sup> Cough is a common symptom of a wide spectrum of childhood respiratory disorders, from acute respiratory infections to asthma exacerbations.<sup>2,3</sup> Knowing the importance of this symptom in respiratory diseases, a review of the existing literature concerning the physiology, epidemiology, management, and treatment of cough in children was carried out. Through a computerized search in the *Pubmed* database, the following keywords were entered and searched: *Cough, respiratory sounds, child, mobile health, respiratory tract diseases*. Articles were selected and analysed in their entirety for the elaboration of this bibliographic review.

### Cough mechanisms

Cough is a natural process that is crucial for the protection of the airway, preventing aspiration and increasing and improving airway clearance. It can occur spontaneously or voluntarily.<sup>3,4</sup>

Cough can be separated into 3 physiologic phases. The first phase is called the inspiratory phase, consists of inhaling a variable amount of air that leads to the lengthening of the expiratory muscles and optimizes the length-tension relationship. The compressive phase, which takes place after inspiratory phase, begins with the closure of the glottis for a small amount of time.<sup>5</sup> The contraction of the expiratory muscles against this closed glottis originates an increase of the intrathoracic pressure while maintaining the lung volume. The third and final phase starts with the opening of the glottis, leading to a release of air that happens in 2 stages, a first very brief supramaximal expiratory flow followed by lower respiratory flows.<sup>6</sup> During this last phase, there is also a dynamic compression of the airways that, in combination with this high-velocity expulsion of air, is responsible for sweeping along airway debris and secretions, that are swept proximally by ciliary activity.<sup>7</sup>

Cough can also be divided into two different categories according to its mechanisms and location. The laryngeal cough (also referred to as “expiratory reflex”) and tracheobronchial cough. The laryngeal cough responds to mechanical stimuli, such as foreign materials, therefore it is important in the protection of the airways from airway aspiration.<sup>3</sup> The tracheobronchial cough can be voluntary, and even though it can also be mechanically stimulated, it is primarily stimulated by chemoreceptors in the lower airways, distal from the larynx. This type of cough is responsible for airway clearance and maintenance of the mucociliary apparatus.<sup>8</sup>

The cough pathway is composed of afferent and efferent arms. The terminations of vagal afferent nerves present in the airway, mucosa and submucosa have receptors and ion channels that detect and respond to noxious stimuli, either chemical or mechanical.<sup>4</sup> These cough and airway receptors mediated through the vagus nerve are relayed to the brainstem to the central cough generator, also responsible for the generation of the respiratory pattern. This system is capable of great plasticity and adaptation.<sup>9</sup>

An effective cough depends on the integrity of all these mechanisms, that culminate in the generation of this high-velocity expiratory flow, and the relationship between the air and the mucus in the airway.<sup>3,5</sup>

Cough can, therefore, be a result of excessive stimulation of this normal reflex, each happens, for example, after the inhalation of a foreign body.<sup>3,4</sup>

## Epidemiology

It is known that cough is very common among children. However, there is a scarcity of studies analysing the prevalence of cough in children worldwide.<sup>4</sup> The discrepancies in the definition of chronic cough in children and the subjective perception and reporting of the children's symptoms by the parents both influence the estimated prevalence of cough in children.<sup>10</sup> Few studies, show the prevalence of cough associated with a specific diagnosis. It was reported that the prevalence of cough in the previous 12 months could be as high as 30.9% in the overall Portuguese children, being 68.7% if there is a diagnosis of current asthma.<sup>11</sup>

## Classification of cough

Cough can be defined according to several criteria such as its duration, nature, quality, timing and even aetiology.

### Duration

For practical reasons, cough is divided into acute (< 3 weeks), subacute (3-8 weeks), and chronic (>8 weeks). However, there are no studies that can clearly define the moment a cough should be defined as chronic, in children. Acute recurrent cough is the term used to refer to more than 2 repeated episodes of cough a year that each last more than 7 days.<sup>2</sup>

### Nature

The distinction between dry and productive cough is also valid in children as it is in adults and has been proved reliable.<sup>1</sup> A "wet" cough normally implies an increase in the production of secretions or a problem in its clearance.<sup>2</sup> However, some defend the term "wet-moist" to be more appropriate

in children since they rarely expectorate sputum, even when they have secretions on their airway.<sup>12</sup>

### Quality

In terms of quality cough can be described as brassy, paroxysmal or staccato. A “brassy” or “barking cough” is suggestive of tracheal or glottic irritation and is associated with croup, tracheomalacia or habit cough. Normally children appear distressed with this type of cough. A paroxysmal type of cough is a major feature in pertussis syndromes, reason why the name “pertussis-like cough” is sometimes used. Although *Bordetella pertussis* is the most likely organism involved, this type of cough can also be caused by virus such as the adenovirus, syncytial virus, and parainfluenza virus and even by mycoplasma. A staccato cough in children, that is, essentially a cough that comes as a series of outbursts, is related with infection by *Chlamydia*.<sup>2</sup>

### Persistency

Cough can be present in a continuous manner, and in those cases, it is declared persistent, or it can be present in certain moments and absent in other, being referred to as an intermittent cough.<sup>2</sup>

### Timing

Regarding the timing of the cough, it can be considered nocturnal, if it's more pronounced during the night, diurnal, if it is more evidence during the day, or lack a specific pattern. These characteristics can be very helpful in the discrimination of different diagnosis since a specific timing of the cough can be more characteristic of a certain diagnosis.<sup>2</sup>

### Aetiology

Contrary to what happens in adults, cough in children can also be classified into a specific and non-specific cough. When the cough is present in combination with pointers that suggest an underlying aetiology, it is considered specific. Opposite to what happens in adults, where cough characteristics have little diagnostics value, paediatricians can recognize, in children, certain cough qualities that allow them to make a diagnostic association.<sup>13</sup>

### Management

#### Acute cough

A detailed history and clinical examination are important to help distinguish the cause of acute cough: acute respiratory infection, inhaled foreign body, seasonal allergic rhinitis, or the first presentation of a chronic disease.<sup>1</sup>

The most common cause of acute cough in children is a viral upper respiratory tract infection and most of these children will not need any investigation. However, because it can also be the presentation of a more serious problem, key questions should be asked to arrive at a specific clinical

diagnosis.<sup>2</sup>

The presence of coryzal symptoms is more suggestive of an upper respiratory infection. A sudden onset of cough in an otherwise healthy child should be seen as a possible result of an inhaled foreign body, which requires an urgent rigid bronchoscopy. In the presence of stridor with an associated “barking” or “croupy cough” diagnosis such as viral croup, recurrent spasmodic croup or bacterial croup should be investigated.<sup>2</sup>

Chest radiography in children with acute cough may be indicated in situations such as the presence of lower respiratory signs, a cough that is progressive in frequency and severity beyond 2 to 3 weeks and when there are features of an undiagnosed chronic respiratory disorder such as chest deformity, finger clubbing, overinflated chest.<sup>14</sup>

#### Subacute cough

Coughing that lasts more than 3 weeks in children is mostly related to a transient viral infection or infections pertussis-like. In these cases, it is normally recommended to keep the child in observation (3-8 weeks) and determine if more investigation is necessary after that period. When the cough progresses and becomes increasingly worst a chest radiography is usually indicated for the investigation of diagnosis such as: retained inhaled foreign body, lobar collapse secondary to mucus plug, tuberculosis or expanding neoplasm in the mediastinum.<sup>2</sup>

#### Chronic cough

In children, most chronic coughs are not caused by the same conditions that occur in adults. There are multiple causes of chronic cough. A systematic approach to chronic cough involves a careful and detailed history and thorough physical examination. It is important to address how and when the cough started, its nature and quality, if it is accompanied by other symptoms, presence of triggers and the existence of family history of respiratory disorders or symptoms or atopy, medications, or treatments the child has had, if the cough is present during the night and the exposure to environmental or cigarettes smoke.<sup>2,15</sup>

This can provide pointers that lead to specific diagnostic tests. One of the causes of chronic cough, habit cough, can be diagnosed by history and observation alone. Also named psychogenic cough or somatic cough disorder, this type of cough has a characteristic sound, frequently honking or barking and is absent during sleep. This absence of cough once asleep is useful to distinguish this habit cough from another type of chronic cough, *pertussis-like*, which is characterized by frequent spasms of coughing followed by nausea or vomiting. Other diagnoses such as asthma, cystic fibrosis, primary ciliary dyskinesia, or bronchiectasis are only confirmed after progressing to appropriate tests, and even therapeutic trials, based on the pointers obtained through the history.<sup>16</sup>

A pointer in the history that can suggest cystic fibrosis is the association with persistent productive cough, and its diagnosis requires the realization of the sweat test. Primary ciliary disorders should be considered in children with a history of recurrent pneumonia or pulmonary infiltrates and usually have an onset in the first few days-weeks of life.<sup>15</sup> A history of a cough associated with wheezing and that is triggered by exercise and cold air is very suggestive of asthma, and the presence of a strong family history of atopy or asthma makes this diagnosis even more likely.<sup>17</sup>

Therefore, chronic cough, unlike acute cough in children, will, in most cases require chest radiography in addition to the full clinical examination in order to reach a specific diagnosis. In children that are old enough to cooperate, spirometry and allergy testing can also be indicated. In some cases, like what happens with asthma, therapeutic trials are used to reach the diagnosis.<sup>15,18</sup>

### General considerations

Overall, the management of a child with cough, regardless of the cause, implies an assessment of possible exacerbation factors. One of the more documented associations is the increased risk of chronic cough in children exposed to tobacco smoke.<sup>12,13</sup> Though there are no randomized control trials that have investigated the effect of the cessation of the exposure on the children's cough when a child presents with chronic cough and has a history of tobacco smoke exposure, intervention options for cessation should be advised.<sup>19</sup>

The effect of the cough on the child and the parents should also be defined. It is known that cough generates a lot of anxiety, in both the child and the parents. One of the fears that are more commonly verbalized by parents of children with a cough is death from choking.<sup>1,2</sup> Moreover, many express concerns with a possible permanent damaged to the child's respiratory system caused by the cough, apart from the obvious concern of serious illness affecting their child.<sup>12</sup> For these reasons, the management of a child with cough must include education of the parents (and child, when appropriate) and addressing their expectations. Providing information about the condition of the child and the expected time of improvement of their cough could reduce the parent's anxiety, use of medication or the need for additional consultation.<sup>13</sup>

Paediatricians advocate that illnesses in children should be managed differently from adults and respiratory illnesses are not an exception.<sup>1,3</sup> Despite the similarities in the physiology of the respiratory system of children and adults, there are important differences between the two in the maturity of the airway, respiratory muscles and chest wall structure, respiratory control and reflexes and sleep-related characteristics. Because of these disparities, it is easy to understand that the aetiology factors of a cough in children are significantly different from the ones in adults and, therefore, its approach and treatment should also be distinct.<sup>12,13</sup>

## Treatment

Despite its high prevalence, cough in children is, very frequently, misdiagnosed and, therefore, treated inappropriately.<sup>2,3</sup>

In children, the treatment based on aetiology is defended. The empiric treatment frequently used in adults, is not recommended for the lack of evidence of the use of medication for symptomatic relief of cough in children.<sup>12</sup> If medication is used, it is essential that the child is evaluated, and that the medication is ceased if there is no effect within the time frame expected for the response.<sup>13,</sup>

For an aetiology-based treatment to be possible, a detailed clinical history is of key importance to identify pointers suggestive of an underlying respiratory or systemic illness. In young children, the clinical history is limited to the information provided by the parents and their perception of the symptoms. The reporting from parents of characteristics such as dry or wet cough is described to have good reliability.<sup>13</sup> However, recent evidence has shown that parenteral reporting of the frequency and severity of their child's cough has poor reliability, especially when it comes to nocturnal cough when compared to more objective measures of those parameters.<sup>20</sup>

## Ambulatory monitoring of cough and mobile health

Recently, to collect additional information about the symptoms of the patients, such as cough, especially during the night, new studies have been performed to access the possibility of objective and repeatable measurement of these symptoms using automated detection systems. Nocturnal breath monitors such as the Leo-Sound device have proved to be useful in the determination and assessment of these respiratory symptoms in children.<sup>21</sup>

Currently, in addition to these devices, mobile health has been the target of great development through smartphone applications, the so-called "apps".

Before the development of these applications, health interventions involving this type of technology were limited to sending voice or text messages.<sup>22</sup> However, more and more apps are emerging that can be used by people with the intention of creating healthy habits and behavioural changes in them. These applications can have a big impact in several important health-related domains, including chronic disease management, mental health and education and patient participation and empowerment.<sup>23</sup>

It is important that healthcare professionals learn about these applications and their current status, as well as their limitations and future directions.<sup>24</sup>

## PROOF-OF-CONCEPT PILOT STUDY

### Study aims

The general purpose of this study was to perform a proof of concept of the use of a mobile application with a component of acquisition of respiratory sounds, for the collection of sounds of cough.

More specifically, this study aimed to:

- i. Assess and improve coughing sound acquisition systems;
- ii. Constitute a database of coughing sounds useful for the development and validation of sound processing modules;
- iii. Test the feasibility of the mobile application (errors, sensors' ability to capture respiratory sounds in real-time, sound storage, among others);
- iv. Investigate the opinions of patients/caregivers on the potential of using a mobile application and

## Methods

### Study design and setting

This was an observational cross-sectional study with participants (from 0 to 17 years old, inclusive) diagnosed with respiratory diseases who present clinically with cough.

Eligible patients were invited to participate by the study researchers allocated to the Pediatric Department from Centro Hospitalar Universitário do Porto, in two settings: 1) hospitalized children, 2) outpatient children.

### Participants and data collection

The inclusion criteria for this study were: i) Age less than or equal to 17 years; ii) Medical diagnosis of acute or chronic respiratory disease that is clinically presented with cough; iii) Ability to use mobile applications.

Were excluded from the recruitment individuals (minors and their respective caregivers): 1) with infection by SARS-Cov-2, 2) whose state of health did not allow the collection without risk to the participant (contraindications for collecting breath sounds) and 3) that they were unable to perform the procedures required in the study. Recruitment was carried out for convenience, whenever the researchers were available.

Data were determined to be collected in 2 settings:

- Hospitalized children

After the identification of eligible patients at admission, the participants and caregivers / legal representatives were contacted and all information about the study was provided, as well as informed consent, as described below ('Ethical considerations'). Subsequently, a structured face-to-face clinical interview (see annex 1) was carried out by the researcher, with demographic variables (date of birth and sex), respiratory symptoms, the disease in question and preferences for using mobile applications being collected. Clinical interviews were answered by caregivers of participants up to 14 years old, inclusive. On the other hand, participants over 14 years old responded to the interview themselves, with the presence of the caregiver / legal representative. An anonymization code was provided to each participant, registering on the clinical interview sheet, which was later crossed with the code generated with the mobile application.

Then, an email was sent to the caregiver / legal representative, with the study information, informed consent, and the download link for the application to collect cough sounds. After the application was successfully downloaded, caregivers / legal representatives were instructed to

collect coughing sounds using a mobile application. This collection was made freely by the patients themselves, whenever they verified the occurrence of coughing episodes. The sounds were recorded in a validated, safe and anonymized database in accordance with the GDPR, as described below ('Ethical considerations').

The collection of cough sounds was carried out for 5 consecutive days, ending after that period.

After a week, the caregivers / legal representatives were contacted by phone to access their opinion on the application and to discuss eventual limitations and difficulties in its use.

- Ambulatory

After identifying the eligible participants in the clinic, the caregivers / legal representatives were contacted by phone and all information about the study was provided, as well as informed consent, as described below ('Ethical considerations'). Then, an email was sent to the caregiver / legal representative, with the study information, informed consent, and the download link for the application to collect cough sounds. After replying and sending a written consent email to participate in the study, the caregiver / legal representative was contacted again. A structured telephone clinical interview (see annex 1) was then carried out by the researcher, with demographic variables, respiratory symptoms, the disease in question and preferences for using mobile applications being collected. Clinical interviews were answered by caregivers of participants up to 14 years old, inclusive. On the other hand, participants over 14 years old responded to the interview themselves, with the presence of the caregiver / legal representative with the participant. An anonymization code was given to each participant, registering on the clinical interview sheet, which was subsequently crossed with the code generated with the mobile application.

Subsequently, after the application was successfully downloaded, caregivers / legal representatives were instructed to collect coughing sounds using a mobile application. This collection was made freely by the patients themselves, whenever they verified the occurrence of coughing episodes. The sounds were recorded in a database, safe and anonymous according to the GDPR, as described below ('Ethical considerations').

The collection of cough sounds was carried out for 5 consecutive days, ending after that period.

After a week, the caregivers / legal representatives were contacted by phone to access their opinion on the application and to discuss eventual limitations and difficulties in its use. Also, the cough sounds were listened by the researchers to assess if the recorded sounds were compatible with cough sounds.

## Mobile application

The AIRDOC mobile application: Intelligent mobile application for individualized support and monitoring of the function and Respiratory sounds of Chronic Obstructive Patients, (<http://cintesis.eu/en/portfolio-items/airdoc-aplicacao-movel-inteligente-para-suporte-individualized-and-monitoring-of-the-function-and-respiratory-sounds-of-chronic-obstructive-patients/>) is a prototype that includes respiratory sound recording modules (Figure 1). The device's own microphone is used to acquire sound records that are subsequently sent securely to a database stored on a protected server located at the University of Porto. The app is available in Portuguese and English.

Registration in the database requires the provision of an email and the definition of a user name (username) and password, which are then used for authentication (Figure 2). The module screen (Figure 1b) shows the user's pseudo-anonymization code in the database in the upper right corner.

After authentication, the free sound recording module can be accessed from the module screen by clicking on the respective button (Figure 1b). The module performs sound recording using the "GRAVAR" and "PARAR" buttons (Figure 3), allows you to hear the recorded sound immediately after recording using the "OUVIR" button, as well as add a note, writing in the available free field.

## Statistical analysis

Statistical analyses were performed using SPSS version 27 (SPSS IBM, New York, NY, USA). Continuous variables were described using mean, 25th centile (P25) and 75th centile (P75). Categorical variables were described using absolute and relative frequencies.

The respiratory sounds collected were analysed through pre-processing and processing techniques developed by the team.

## Ethical considerations

The provisions of the General Data Protection Regime were complied with by Law No. 58/2019, of August 8. The objectives and procedures of the study were explained by the researchers both to the adult legal guardian who authorized it and to the child or adolescent who participated, using age-appropriate language. Written informed consent in accordance with the Helsinki declaration and with detailed information was given to the legal guardian. According to Portuguese legislation, participants up to 14 years old, even, gave their consent, with the caregiver / legal guardian giving informed consent. Participants over 14 years of age gave consent, as well as their caregivers / legal representatives.

To guarantee the security and privacy of the personal and sensitive data of the participants in this study, pseudo-anonymization measures were adopted that guaranteed the physical separation between the data to be analysed from the identifying data, with encryption of the latter.

The pseudo-anonymization code used in the app was sent to the researcher to access the sound files on the server and to correspond with the other data collected in the study.

The AIRDOC mobile application allows the user to hear the sound record immediately after its collection and delete it if they do not want it to be sent to the server. Sending to a database is carried out securely and the server is protected in accordance with the GDPR. The system includes a security layer responsible for authentication and authorization, using OAuth 2.0 and an identity server with openID structure, to promote security and trust. Thus, the collection, storage and sending of data collected by the AIRDOC App comply with all the measures recommended in the legislation. There is a security management plan for GDPR compliance, and all necessary security and privacy measures and requirements have been implemented.

## Results

All the children were recruited in ambulatory setting. Seven children were included in this study, of which six were male and one female (table 1). The mean age of the participants was 2.8 ( $\pm$  1.5) years old. In terms of diagnostic characteristics, seventy-one per cent (71%) of the participants had a chronic diagnose and the remaining twenty-nine per cent (29%) had an acute diagnose. Two of the seven children had URTI, six were diagnosed with rhinitis, one was asthmatic, three had an asthma exacerbation, one was diagnosed with BPD and one had an alfa-1- antitrypsin deficiency. In terms of cough nature, four of the participants characterised the cough as wet and three reported the cough as being dry. All seven participants choose “paroxistic” to describe the cough’s quality. The majority of the patients (86%) reported the cough persistence as intermittent, while only fourteen per cent (14%) qualified the cough as persistent. Regarding the timing of the cough, fifty-seven per cent of the participants (57%) reported the cough had a nocturnal pattern, fourteen per cent (14%) associated the cough to exercise and twenty-nine per cent (29%) were not able to find a timing pattern. The duration of the cough was considered chronic in one of the participants, sub-acute in two, and acute in the remaining four participants.

Concerning the clinical characteristics (table 2), the most reported symptom associated with the cough was sneezing (86%), followed by rhinorrhoea (57%), nasal itching (29%), and wheezing. Dyspnoea and nasal obstruction were reported in a smaller number of participants (14%). As to the use of medication, none of the participants reported the use of cough inhibitors, inhaled  $\beta$ -agonists, inhaled steroids and nasal steroids were reported in forty-three per cent (43%) of the participants. Fifty-seven per cent (57%) of the participants declared the use of antihistamine medication.

In the matter of mobile technologies preferences (table 3), all the caregivers selected Facebook as one of the social networks they use. Five participants also selected Instagram and WhatsApp. The entirety of the caregivers stated the use of a smartphone and three affirmed the use of a table. When asked about the frequency of use of the smartphone or tablet regarding specific activities, the activity performed more frequently was the use of applications (mean of nine - several times per hour), followed by reading emails, being on the internet, listening to music and use of a social network (mean of seven - several times a day). The use of this devices to take photos, check the news and find information was selected as activities performed with moderate frequency (mean of six - once a day). The activities that were selected as being performed in these devices with little frequency were the recording of videos (mean of four – once a week), use of GPS (mean of two – once a month) and playing games (mean of one - never). Only one of the caregivers stated the download of health and fitness applications.

In terms of interest to use an application to monitor respiratory disease, record cough or send cough records to physician, all the options reported a mean of 5 ("I'm very interested") what translates a high level of interest from the caregivers to participate in this study.

Finally, regarding the feedback received from the participants by phone after a week of use of the application, the most reported problem was related to the login and initiation of the recording process. Caregivers stated that it took them too much time to initiate the app and that this negatively influenced their ability to record the sound on time. In the same direction, there were very few cough sounds recorded appropriately in the database.

## Discussion

This was a proof-of-concept pilot study that was not carried out under ideal conditions and that failed to achieve its objectives in their entirety. The conclusions that can be drawn are, therefore, still limited.

One of the limitations present since the beginning of the study was the lack of children that could be included in this study, especially hospitalized children. The main, and possibly only, reason was the current pandemic and the consequential outstanding reduction in acute respiratory diseases in children. As a matter of fact, in other ongoing study of the CHUP Pediatric Department, it was shown that there were only 2 cases of RSV bronchiolitis hospitalized in the last year.

The data and recordings collected were scarce due to the small sample included in the study, leading to a small database of coughing sounds useful for the development and validation of sound processing modules was not entirely possible. However, this study was able to highlight the importance of remote monitoring and showcase the various variables that must be optimized to make it possible.

In this study, all patients / caregivers demonstrated a very high interest in using a mobile application and its components to collect respiratory sounds to self-monitor and self-manage the respiratory disease. This type of monitoring is considered by them to be a very useful tool that they would contemplate purchasing and using in the future.

This study was able to test the mobile application, detect its errors and assess the sensors' ability to capture respiratory sounds in real-time.

As mentioned previously, the main problems reported in the use of the application were the difficulty in being able to record the sound of the cough when it appears unpredictably. It was reported by parents and caregivers that the time it took them to start the application and start recording was too long, often culminating in the impossibility of recording the sounds since when they were effectively ready to record the sound the child had already stopped coughing. This will be one of the main points to be optimized in the application. The time spent logging in and starting recording should be minimized.

An alternative to this problem will be the automatic activation of the microphone when the sound is detected. This option will be feasible in cases of nocturnal cough in which there is a smaller number of sounds capable of activating the system. An option of interesting exploration will be, for example, the implementation of the recording application in already existing infant surveillance systems, the baby monitors.

In addition to these systems, it would also be interesting to implement these recording systems in other types of equipment often used by patients or caregivers, such as smartwatches, which are often more quickly accessible than devices such as tablets or mobile phones.

Under the conditions it is currently in, this sound recording application will have greater applicability in cases of acute disorders, in which the coughing episodes will be more predictable and more frequent. In cases of chronic diseases, in which the predictability and frequency of coughing are lower, it will be more difficult to apply this type of device. An exception is, for example, the cough triggered by exercise, very typical of asthma, which is more predictable and, therefore, makes the use of this type of equipment easier.

## Conclusion

This study highlighted parents' interest in self-monitoring tools, alike this mobile application. This type of equipment was considered, by patients with respiratory pathology and their caregivers, to be an interesting and useful tool, with the potential to aid them control of their symptoms and in the early detection of periods of exacerbation of their disease.

Further studies and investigations need to be carried out to correct the limitations found in AIRDOC app to make possible its implementation and efficient use by patients and caregivers.

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Figures and Tables

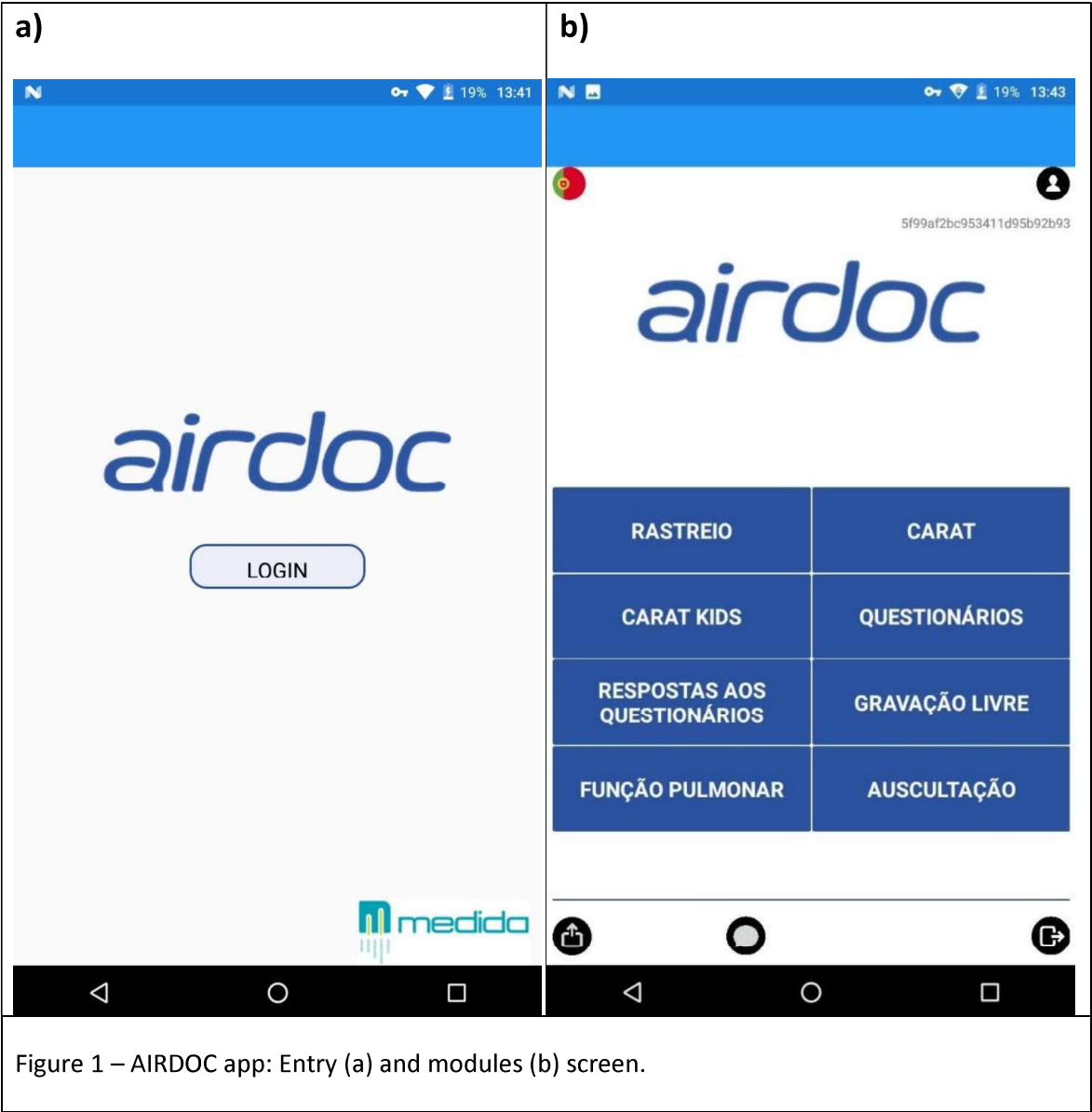


Figure 1 – AIRDOC app: Entry (a) and modules (b) screen.

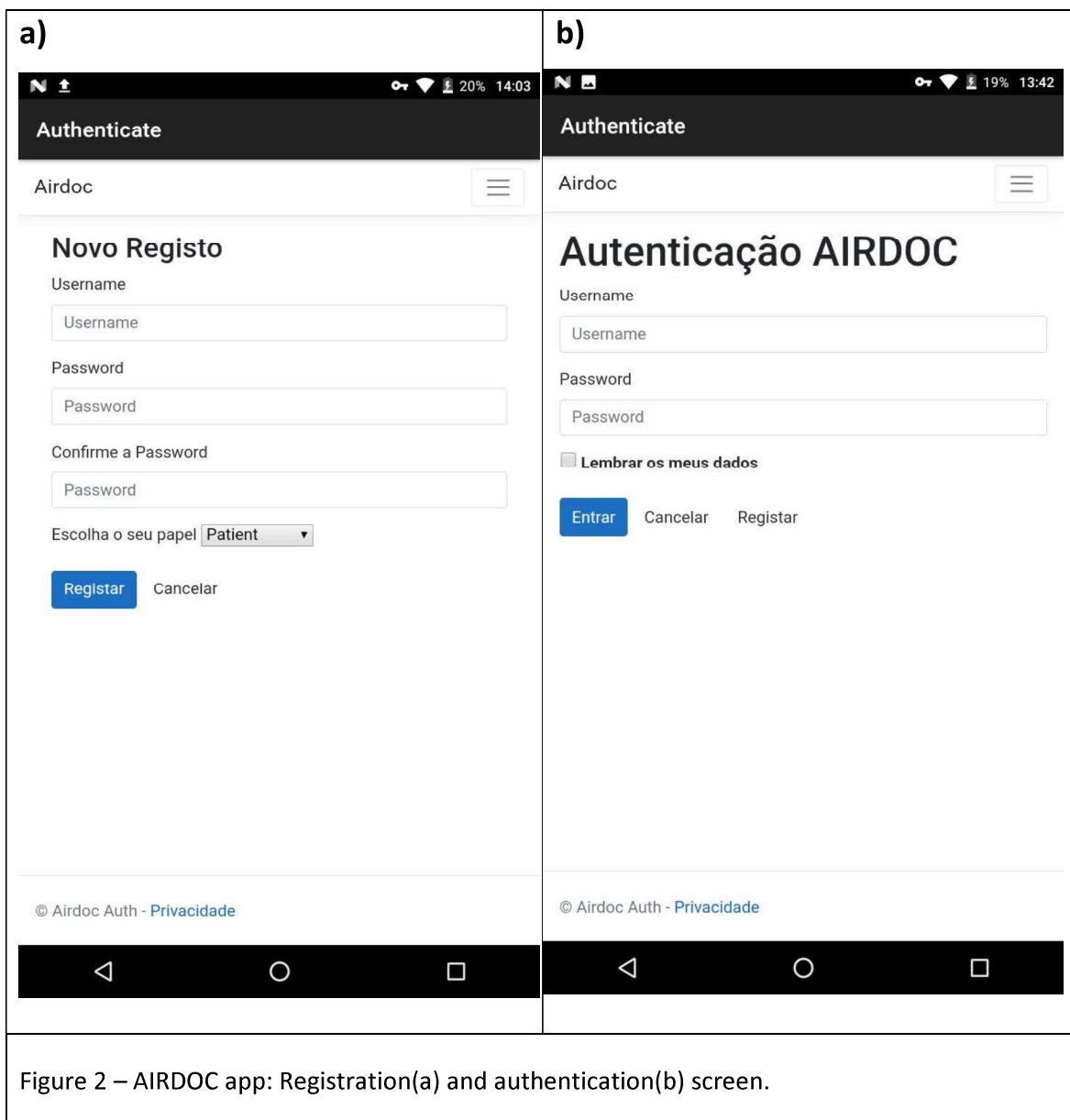


Figure 2 – AIRDOC app: Registration(a) and authentication(b) screen.

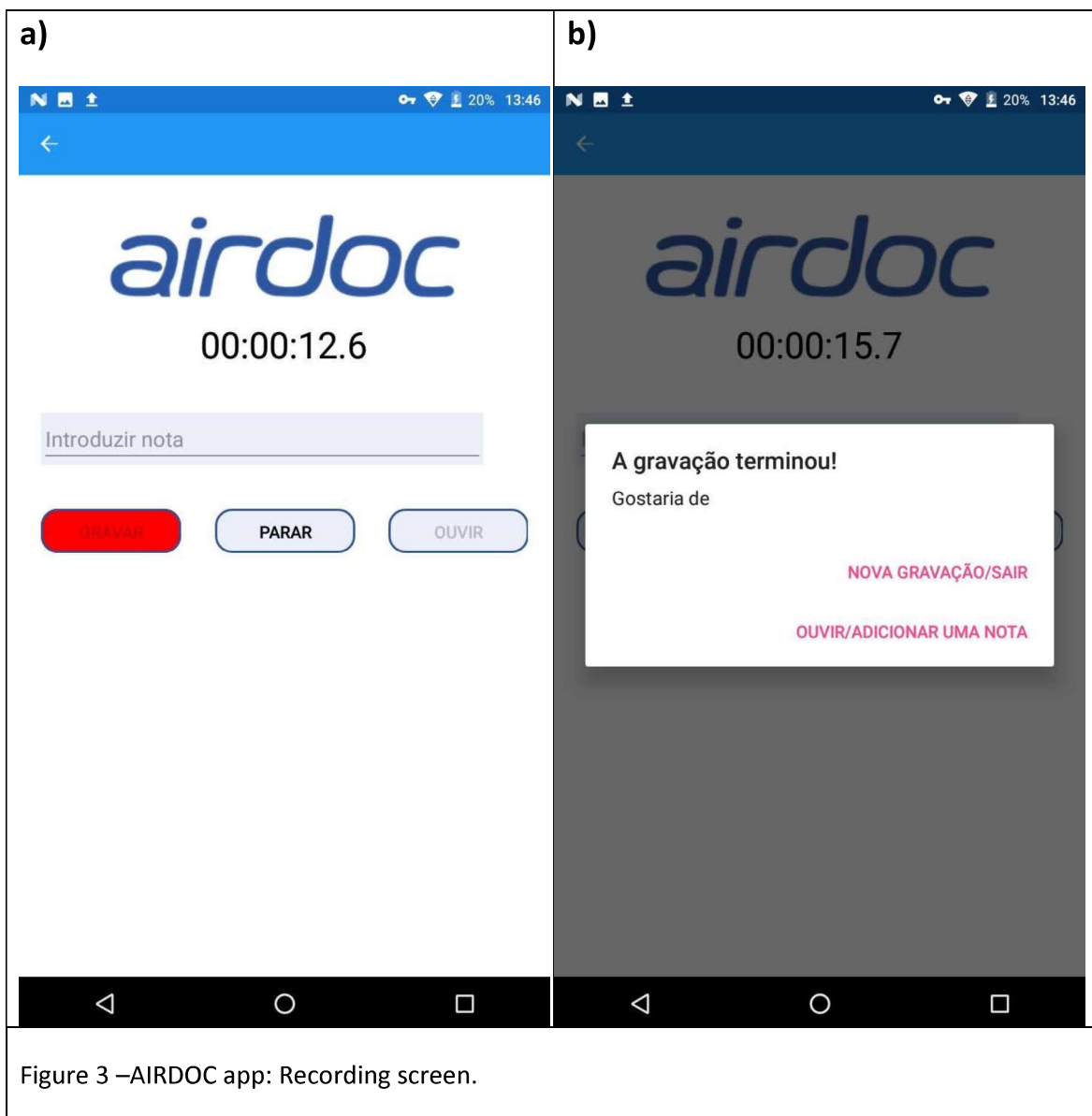


Figure 3 –AIRDOC app: Recording screen.

Table 1 – Participants and diagnostic characteristics.

|                                 | TOTAL     |
|---------------------------------|-----------|
| <b>Gender, n (%)</b>            |           |
| Female                          | 1 (14)    |
| Male                            | 6 (86)    |
| <b>Age (years)</b>              |           |
| Mean (SD)                       | 2.8 (1.5) |
| <b>Diagnostic type, n(%)</b>    |           |
| Acute                           | 2 (29)    |
| Chronic                         | 5 (71)    |
| <b>Specific diagnosis, n(%)</b> |           |
| URTI                            | 2 (29)    |
| Rhinitis                        | 6 (86)    |
| Asthma                          | 1 (14)    |
| Asthma exacerbation             | 3 (43)    |
| BPD                             | 1 (14)    |
| Alfa1-antitrypsin deficiency    | 1 (14)    |
| <b>Cough nature, n (%)</b>      |           |
| Dry                             | 3 (43)    |
| Wet                             | 4 (57)    |
| <b>Cough quality, n (%)</b>     |           |
| Paroxysmal                      | 7 (100)   |
| <b>Cough persistence, n (%)</b> |           |
| Persistent                      | 1 (14)    |
| Intermittent                    | 6 (86)    |
| <b>Cough timing, n (%)</b>      |           |
| Night                           | 4 (57)    |
| Exercise                        | 1 (14)    |
| No timing pattern               | 2 (29)    |
| <b>Cough duration, n (%)</b>    |           |
| Acute                           | 4 (57)    |
| Sub-acute                       | 2 (29)    |
| Chronic                         | 1 (14)    |

URTI: upper respiratory tract infection; BPD: bronchopulmonary dysplasia

Table 2 – Clinical and medication characteristics.

|                           | TOTAL  |
|---------------------------|--------|
| <b>Symptoms, n(%)</b>     |        |
| Wheezing                  | 1 (14) |
| Dyspnea                   | 1 (14) |
| Rhinorrhea                | 4 (57) |
| Sneezing                  | 6 (86) |
| Nasal obstruction         | 1 (14) |
| Nasal itching             | 2 (29) |
| <b>Medication, n (%)</b>  |        |
| Cough inhibitors          | 0 (0)  |
| Antihistamine             | 4 (57) |
| Inhaled $\beta$ -agonists | 3 (43) |
| Inhaled steroids          | 3 (43) |
| Nasal steroids            | 3 (43) |

Table 3 – Mobile technologies preferences of caregivers.

|                                                           | TOTAL    |
|-----------------------------------------------------------|----------|
| <b>Social networks, n(%)</b>                              |          |
| Facebook                                                  | 7 (100)  |
| Instagram                                                 | 5 (71)   |
| Whatsapp                                                  | 5 (71)   |
| <b>Mobile devices use, n (%)</b>                          |          |
| Smartphone                                                | 7 (100)  |
| Tablet                                                    | 3 (43)   |
| <b>Smartphone use scores, mean (P25-P75)</b>              |          |
| Emails                                                    | 7 (6-10) |
| GPS                                                       | 2 (1-3)  |
| Internet                                                  | 7 (6-7)  |
| Music                                                     | 7 (1-7)  |
| Photos                                                    | 6 (4-8)  |
| News                                                      | 6 (5-6)  |
| Videos                                                    | 4 (2-6)  |
| Any app                                                   | 9 (7-10) |
| Find information                                          | 6 (5-8)  |
| Play                                                      | 1 (1-2)  |
| Social networks                                           | 7 (6-10) |
| <b>Download of health &amp; fitness app, n (%)</b>        | 1 (14)   |
| <b>Willing to use an app to... [mean score (P25-P75)]</b> |          |
| Monitor respiratory disease                               | 5 (4-5)  |
| Record cough                                              | 5 (4-5)  |
| Send cough records to physician                           | 5 (4-5)  |

## Annexes

### Annex 1 – Interview

|                                                                 |                                                                                                                                                                                                                                                                                                                                                                          |                                                    |
|-----------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| <b>1. Contexto</b>                                              | Internamento <input type="checkbox"/> <sub>1</sub>                                                                                                                                                                                                                                                                                                                       | Ambulatório <input type="checkbox"/> <sub>1</sub>  |
| <b>2. Data de nascimento</b>                                    | ___ / ___ / _____                                                                                                                                                                                                                                                                                                                                                        |                                                    |
| <b>3. Sexo</b>                                                  | Feminino <input type="checkbox"/> <sub>1</sub>                                                                                                                                                                                                                                                                                                                           | Masculino <input type="checkbox"/> <sub>2</sub>    |
| <b>4. Tipo de diagnóstico atual</b>                             | Agudo <input type="checkbox"/> <sub>1</sub>                                                                                                                                                                                                                                                                                                                              | Crónico <input type="checkbox"/> <sub>2</sub>      |
| <b>5. Se Sim, na questão 3),<br/>Tipo de diagnóstico agudo:</b> | Infecção das vias aéreas superiores <input type="checkbox"/> <sub>1</sub><br>Bronquiolite aguda <input type="checkbox"/> <sub>2</sub><br>Pneumonia <input type="checkbox"/> <sub>3</sub><br>Croup <input type="checkbox"/> <sub>4</sub><br>Exacerbação de asma <input type="checkbox"/> <sub>5</sub><br>Outro <input type="checkbox"/> <sub>6</sub> Especificar _____    |                                                    |
| <b>6. Diagnóstico respiratório crónico:</b>                     | Asma <input type="checkbox"/> <sub>1</sub><br>Rinite <input type="checkbox"/> <sub>2</sub><br>Outro <input type="checkbox"/> <sub>3</sub> Especificar _____                                                                                                                                                                                                              |                                                    |
| <b>7. Sintomas respiratórios presentes atualmente:</b>          | Tosse <input type="checkbox"/> <sub>1</sub><br>Pieira <input type="checkbox"/> <sub>2</sub><br>Dispneia <input type="checkbox"/> <sub>3</sub><br>Rinorreia <input type="checkbox"/> <sub>4</sub><br>Esternutos <input type="checkbox"/> <sub>5</sub><br>Outro <input type="checkbox"/> <sub>6</sub> Especificar _____                                                    |                                                    |
| <b>8. Tipo de tosse: (exemplificar cada termo)</b>              |                                                                                                                                                                                                                                                                                                                                                                          |                                                    |
| <b>8.1 Natureza</b>                                             | Seca <input type="checkbox"/> <sub>1</sub>                                                                                                                                                                                                                                                                                                                               | Produtiva <input type="checkbox"/> <sub>2</sub>    |
| <b>8.2 Qualidade</b>                                            | Estridulosa <input type="checkbox"/> <sub>1</sub><br>Paroxística <input type="checkbox"/> <sub>2</sub><br>Stacatto <input type="checkbox"/> <sub>3</sub>                                                                                                                                                                                                                 |                                                    |
| <b>8.3 Persistência</b>                                         | Persistente <input type="checkbox"/> <sub>1</sub>                                                                                                                                                                                                                                                                                                                        | Intermitente <input type="checkbox"/> <sub>2</sub> |
| <b>8.4 Timing</b>                                               | Diurna <input type="checkbox"/> <sub>1</sub><br>Noturna <input type="checkbox"/> <sub>2</sub><br>Sem padrão diário <input type="checkbox"/> <sub>3</sub>                                                                                                                                                                                                                 |                                                    |
| <b>9. Duração da tosse:</b>                                     | Aguda (< 3 semanas) <input type="checkbox"/> <sub>1</sub><br>Sub-aguda (3-8 semanas) <input type="checkbox"/> <sub>2</sub><br>Crónica (> 8 semanas) <input type="checkbox"/> <sub>3</sub><br>Aguda recorrente (≥ 2 episódios/ano, > 7 dias) <input type="checkbox"/> <sub>4</sub>                                                                                        |                                                    |
| <b>10. Faz medicação?</b>                                       | Sim <input type="checkbox"/> <sub>1</sub>                                                                                                                                                                                                                                                                                                                                | Não <input type="checkbox"/> <sub>0</sub>          |
| <b>Se Sim, na questão 10:<br/>10.1 Qual(ais)?</b>               | Anti-tússico <input type="checkbox"/> <sub>1</sub><br>Anti-histamínico <input type="checkbox"/> <sub>2</sub><br>Broncodilatador inalado <input type="checkbox"/> <sub>3</sub><br>Corticoide inalado <input type="checkbox"/> <sub>4</sub><br>Corticoide sistémico <input type="checkbox"/> <sub>5</sub><br>Outro <input type="checkbox"/> <sub>6</sub> Especificar _____ |                                                    |

11. Usa as redes sociais?

Sim ☐<sub>1</sub>

Não ☐<sub>0</sub>

Se Sim na questão 11:

11.1 Qual(ais)?

Facebook ☐<sub>1</sub>

Instagram ☐<sub>2</sub>

Outra ☐<sub>3</sub>

Especificar: \_\_\_\_\_

12. Tem algum dispositivo móvel?

Sim ☐<sub>1</sub>

Não ☐<sub>0</sub>

Se Sim na questão 1:

12.1 Qual(ais)?

Smartphone (iPhone/Android) ☐<sub>1</sub> (telemóvel com características semelhantes às de um computador)

Tablet/iPad ☐<sub>2</sub>

Telemóvel (telemóvel simples essencialmente para realizar chamadas/mensagens escritas) ☐<sub>3</sub>

Se Smartphone/tablet na questão 12.1:

12.1.1 Com que frequência desempenha as atividades seguintes no *smartphone/tablet*?

|                                                                                   |                                | Nunca                                 | 1 vez<br>por<br>mês                   | Várias<br>vezes<br>por<br>mês         | 1 vez<br>por<br>sema-<br>na           | Várias<br>vezes<br>por<br>sema-<br>na | 1 vez<br>por<br>dia                   | Várias<br>vezes<br>por<br>dia         | 1 vez<br>por<br>hora                  | Várias<br>vezes<br>por<br>hora        | Const-<br>tante-<br>mente              |
|-----------------------------------------------------------------------------------|--------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|----------------------------------------|
|                                                                                   |                                |                                       |                                       |                                       |                                       |                                       |                                       |                                       |                                       |                                       |                                        |
| S<br>M<br>A<br>R<br>T<br>P<br>H<br>O<br>N<br>E<br>-<br>T<br>A<br>B<br>L<br>E<br>T | Ler os e-mails                 | <input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub> | <input type="checkbox"/> <sub>6</sub> | <input type="checkbox"/> <sub>7</sub> | <input type="checkbox"/> <sub>8</sub> | <input type="checkbox"/> <sub>9</sub> | <input type="checkbox"/> <sub>10</sub> |
|                                                                                   | Obter direções ou usar o GPS   | <input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub> | <input type="checkbox"/> <sub>6</sub> | <input type="checkbox"/> <sub>7</sub> | <input type="checkbox"/> <sub>8</sub> | <input type="checkbox"/> <sub>9</sub> | <input type="checkbox"/> <sub>10</sub> |
|                                                                                   | Navegar na internet            | <input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub> | <input type="checkbox"/> <sub>6</sub> | <input type="checkbox"/> <sub>7</sub> | <input type="checkbox"/> <sub>8</sub> | <input type="checkbox"/> <sub>9</sub> | <input type="checkbox"/> <sub>10</sub> |
|                                                                                   | Ouvir música                   | <input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub> | <input type="checkbox"/> <sub>6</sub> | <input type="checkbox"/> <sub>7</sub> | <input type="checkbox"/> <sub>8</sub> | <input type="checkbox"/> <sub>9</sub> | <input type="checkbox"/> <sub>10</sub> |
|                                                                                   | Tirar fotografias              | <input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub> | <input type="checkbox"/> <sub>6</sub> | <input type="checkbox"/> <sub>7</sub> | <input type="checkbox"/> <sub>8</sub> | <input type="checkbox"/> <sub>9</sub> | <input type="checkbox"/> <sub>10</sub> |
|                                                                                   | Verificar as notícias          | <input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub> | <input type="checkbox"/> <sub>6</sub> | <input type="checkbox"/> <sub>7</sub> | <input type="checkbox"/> <sub>8</sub> | <input type="checkbox"/> <sub>9</sub> | <input type="checkbox"/> <sub>10</sub> |
|                                                                                   | Gravar vídeo                   | <input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub> | <input type="checkbox"/> <sub>6</sub> | <input type="checkbox"/> <sub>7</sub> | <input type="checkbox"/> <sub>8</sub> | <input type="checkbox"/> <sub>9</sub> | <input type="checkbox"/> <sub>10</sub> |
|                                                                                   | Usar aplicações (qualquer uma) | <input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub> | <input type="checkbox"/> <sub>6</sub> | <input type="checkbox"/> <sub>7</sub> | <input type="checkbox"/> <sub>8</sub> | <input type="checkbox"/> <sub>9</sub> | <input type="checkbox"/> <sub>10</sub> |
|                                                                                   | Procurar informação            | <input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub> | <input type="checkbox"/> <sub>6</sub> | <input type="checkbox"/> <sub>7</sub> | <input type="checkbox"/> <sub>8</sub> | <input type="checkbox"/> <sub>9</sub> | <input type="checkbox"/> <sub>10</sub> |
|                                                                                   | Jogar                          | <input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub> | <input type="checkbox"/> <sub>6</sub> | <input type="checkbox"/> <sub>7</sub> | <input type="checkbox"/> <sub>8</sub> | <input type="checkbox"/> <sub>9</sub> | <input type="checkbox"/> <sub>10</sub> |
|                                                                                   | Acéder a redes sociais         | <input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub> | <input type="checkbox"/> <sub>6</sub> | <input type="checkbox"/> <sub>7</sub> | <input type="checkbox"/> <sub>8</sub> | <input type="checkbox"/> <sub>9</sub> | <input type="checkbox"/> <sub>10</sub> |

13. Já fez o *download* e usou aplicações móveis de saúde e *fitness*?

Sim ☐<sub>1</sub>

Não ☐<sub>0</sub>

13.1 Se Sim na questão 13, qual(ais)?

\_\_\_\_\_  
\_\_\_\_\_

14. Teria interesse em utilizar uma aplicação móvel nos seguintes contextos...

(em relação ao entrevistado ou ao representado, de acordo com a situação)

|                                         | Não tenho interesse<br>e é desadequado                                         | Não tenho<br>interesse                                                         | É indiferente                                                                  | Tenho<br>interesse                                                             | Tenho muito<br>interesse                                                       |
|-----------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| 14.1 Monitorizar a doença respiratória  | <input type="checkbox"/> <sub>1</sub><br><input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub><br><input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub><br><input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub><br><input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub><br><input type="checkbox"/> <sub>5</sub> |
| 14.2 Gravar e monitorizar a tosse       | <input type="checkbox"/> <sub>1</sub><br><input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub><br><input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub><br><input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub><br><input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub><br><input type="checkbox"/> <sub>5</sub> |
| 14.3 Enviar sons de tosse ao seu médico | <input type="checkbox"/> <sub>1</sub><br><input type="checkbox"/> <sub>1</sub> | <input type="checkbox"/> <sub>2</sub><br><input type="checkbox"/> <sub>2</sub> | <input type="checkbox"/> <sub>3</sub><br><input type="checkbox"/> <sub>3</sub> | <input type="checkbox"/> <sub>4</sub><br><input type="checkbox"/> <sub>4</sub> | <input type="checkbox"/> <sub>5</sub><br><input type="checkbox"/> <sub>5</sub> |