Work productivity in rhinitis using cell phones

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Work productivity in rhinitis using cell phones: The MASK pilot study

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Short title: Work assessment in rhinitis with an App

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Abstract

Allergic rhinitis often impairs social life and performance. The aim of this cross-sectional study was to assess the impact of uncontrolled rhinitis assessed by visual analogue score (VAS) on work productivity using cell phone data collection.

A mobile phone app (*Allergy Diary,* Android and Apple stores*)* collects daily visual analogue scales (VAS) data for overall allergic symptoms (VAS-global measured), nasal (VAS-nasal), ocular (VAS-ocular), asthma symptoms (VAS-asthma) and work (VAS-work). A combined nasal-ocular score is calculated. *Allergy Diary* is available in 20 countries. The App includes the Work Productivity and Activity Impairment Allergic Specific Questionnaire (WPAI:AS) questionnaire in 6 EU countries. All consecutive users who filled the VAS-work from June 1 to October 31, 2016 were included in the study.

A total of 1,136 users filled in 5,818 days of VAS-work. Symptoms of allergic rhinitis were controlled (VAS-global<20) in approximately 60% of days. In users with uncontrolled rhinitis, approximately 90% had some work impairment and over 50% had severe work impairment (VAS-work>50). There was a significant correlation between VAS-global calculated and VAS-work (Rho=0.83, p<0.00001, Spearman rank test). In 144 users, there was a significant correlation between VAS-work and WPAI:AS (Rho=0.53, p<0.0001).

This pilot study not only provides proof-of-concept for data on the work impairment collected with the app but also provides data on the app itself, especially the distribution of responses for the VAS. This supports the interpretation that persons with rhinitis report both the presence and the absence of symptoms.

Abbreviations

AHA: Active and Healthy Aging

AR: allergic rhinitis

ARIA: Allergic Rhinitis and its Impact on Asthma

EIP: European Innovation Partnership

EQ-5D: Euroqol

ICT: information and communications technology

MACVIA: Contre les MAladies Chroniques pour un VIellissement Actif

MASK: MACVIA-ARIA Sentinel NetworK

VAS: visual analogue scale

VAS asthma: visual analogue scale for asthma

VAS-global calculated: visual analogue scale for global symptoms as an average of each specific score

VAS-global measured: visual analogue scale for global symptoms measured

VAS-nasal: visual analogue scale for nasal symptoms

VAS ocular: visual analogue scale for ocular symptoms

VAS-work: visual analogue scale for work impairment

WPAI:AS: Work Productivity and Activity Impairment Allergic Specific Questionnaire

Key words: App, ARIA, Rhinitis, work productivity, WPAIA:AS

Introduction

Allergic rhinitis (AR), one of the most common diseases in the world, affects over 25% of the European population (1). It exists in all age groups, often starts early in life and persists across the life cycle. AR often impairs social life, as well as school and work performance (1).

Uncontrolled allergic and non-allergic rhinitis has a significant impact on work productivity (2-12). The Work Productivity and Activity Impairment Allergic Specific Questionnaire (WPAI:AS) is used in many studies and has convincingly shown a significant negative effect on presenteeism in patients with moderate to severe AR (9, 10). Rhinitis may impact work productivity to a greater extent than other chronic diseases such as diabetes, hypertension, or asthma (11, 12). The treatment of AR improves work productivity over time (13-19). To date, however, studies have not collected data on productivity on a daily basis. Treatment of AR improves control and work productivity.

of AR control include symptom scores, patients' self-administered visual analogue scales (VAS), objective measures of nasal obstruction and patients' reported outcomes such as QOL or scores with several items (20, 21). VAS was found to be an appropriate measure of self-assessed rhinitis control (22) and offers fine nuances of judgment, easy handling, and good data quality. Also, it shows less distortion and bias than categorical scales. Moreover, continuous scores are well measured and statistically analysed by using VAS (23).

"Smart" devices and internet-based applications are already used in rhinitis (24-30). MASK-rhinitis (MACVIA-ARIA Sentinel NetworK for allergic rhinitis), an information and communications technology (ICT) system centred around the patient (31, 32), is one of the implementation tools of the B3 Action Plan of the European Innovation Partnership on Active and Healthy Ageing (EIP on AHA) (33, 34). A mobile phone app (*Allergy Diary)*, central to MASK-rhinitis belonging to the Région Occitanie (France) (35). Since June 2016, the App has included the WPAI:AS questionnaire (9, 10) in 6 EU countries and a daily VAS for work (VAS-work) in 20 countries. The *Allergy Diary* also collects daily VAS data for overall symptoms (VAS-global measured), nasal (VAS-nasal), ocular (VAS-ocular) and asthma symptoms (VAS-asthma).

Aims

The primary aim of this cross-sectional study was to assess the impact of uncontrolled rhinitis assessed by VAS on work productivity assessed by VAS in all 20 countries, and WPAI:AS in the six countries where only that it is available.

Methods

Setting

The App is freely available in 15 languages and 20 countries (Table 1 online).

Users

All consecutive users from June 1, 2016 to October 31, 2016 were included in the study. Some demographic characteristics such as age, sex, country and language were recorded. The *Allergy Diary* was used by people who downloaded it from the App store, Google Play, and other internet sources. A few users were clinic patients that were asked by their physicians to access the app. Due to anonymization (i.e. name and address) of data, no personal identifiers were gathered. None of the users was enrolled in a clinical study as we aimed to have a real life assessment. There was no specific advertisement or other recruitment campaign (35).

Allergy Diary

The *Allergy Diary* collects information on AR symptoms experienced (nasal and ocular), how symptoms impact users' lives, and type(s) of AR treatment used (Table 2 Online). Moreover, geolocalized users assess their daily symptom control using the touchscreen functionality on their smart phone to click on 5 consecutive VAS measures (VAS-global measured, VAS-nasal, VAS-ocular, VAS-asthma and VAS-work). The system is deployed in 20 countries and in 15 languages (translated and back-translated, culturally adapted and legally compliant). Daily AR treatments were also recorded.

Ethics

Terms of reference were translated into all relevant languages and customized according to each country's legislation to allow the use of the results for research purposes.

The data were anonymised (no name or address recorded) except for geolocalized data to the area-level (35). The European Commission's Article 29 Working Party states that geolocation information is personal data (http://ec.europa.eu/newsroom/just/item-detail.cfm?item_id=50083) and information can only be collected, shared, or stored with people's express consent. This is the case for MASK

because users have agreed to geolocation in the terms and reference for use of the App. Moreover, geolocation is optional and each user can allow it or not on his/her cell phone and geolocation if active can be disallowed at any time. Finally, geolocation is not used in the data mining process and the phone IP is not retained.

Formal Institutional Review Board review and approval was not required for this study.

Outcomes

Five VAS measurements (VAS-global measured, VAS-nasal, VAS-ocular, VAS-asthma and VAS-work, Table 1, Figure 1 online) and a calculated VAS-global calculated score (VAS-nasal + VAS-ocular divided by 2) were considered.

The WPAI:AS questionnaire was applied in the six languages where it is available (English, French, German, Italian, Spanish) (9, 10). The electronic form of the questionnaire was used according to the package obtained from Reilly and associates (www.reillyassociates.net/WPAI_General.html) (Table 3 online). The percentage of impairment while working due to allergy (Q4/10) was the outcome used in the study.

Biases

There are potential measurement biases when using apps since the information collected is usually restricted and less complete than when using lengthy paper or web-based questionnaires. A bias might be introduced because app users may be a selected subset and therefore are not fully representative of all patients with rhinitis. Higher education or specific age ranges might apply. The study was not meant to be representative of the general population.

Size of the study

In this exploratory pilot study, all registered users between June 1 and October 31, 2016 were included to obtain the best possible estimates for the specified time window. There were no exclusion criteria.

Statistical methods.

The proportion of users with baseline characteristics and the number of VAS days were described as percentages (for the full data set), by mean and standard deviation or median and interquartile range.

Some users reported VAS scores more than once per day. Before analysis, we proposed that if the same treatment was reported and the daily variation was under 30%, the highest VAS score would be used used. There were 1,042 days with multiple values and on only 70 days was the variation above

30%. We determined *post hoc* that this number was insufficient to impact the results and we used the highest value for the day.

Disease classification of users: We used Q1 and Q3 (Table 2 online) to define "allergic rhinitis", consistent with a previous study, showing that the impairment on activities was similar in subjects with Q1"yes" and Q1"no" + Q3"yes" (35).

- Users with AR included those who reported:
  - "I have AR" (Q1, Table 1 online).
  - And those who declared "I do not have AR" (Q1) BUT who ticked any rhinitis symptoms at Q3 (Table 1 online). Conjunctivitis symptoms were not considered as defining AR.
- Users with no AR were those who reported "No" for Q1 AND ticked no relevant symptom for Q3.

Independency of VAS questions was assessed using the Bland and Altman regression analysis (36).

A contingency table was made using cut-offs proposed by a previous consensus on AR control (22):

1. VAS score <20: fully productive at work or well-controlled AR.
2. VAS score 20-50: partly productive at work or partly controlled AR.
3. VAS score >50: Poorly productive at work or uncontrolled AR.

The mean square contingency coefficient Phi was computed.

Correlations including "allergic rhinitis" users were made using the Spearman rank test. Since there may be interactions between multiple observations for the same user, we first compared the first day of VAS and then separately, all days with VAS. The following correlations were made:

4. VAS-global calculated and VAS-work (co-primary end point).
5. VAS-global measured and VAS-work (co-primary end point).
6. VAS-nose and VAS-work.
7. VAS-ocular s and VAS-work.
8. VAS-asthma and VAS-work.

The statistically significant correlations were ascribed to "very strong" (Rho ranging from 0.80 to 1.00), "strong" (Rho 0.60 to <0.80) or "moderate" (Rho ranging from 0.40 to <0.60) (37).

Exploratory analyses: We used the Spearman rank test to correlate WPAI:AS with VAS-global calculated and VAS-work. However, WPAI:AS estimates work productivity during 7 days before

measurement and the App analysed events the day of WPAI:AS assessment and after. For this analysis, we selected Q4-WPAI and the baseline day of VAS.

Results

Users

A total of 1,120 users completed app responses on 5,889 days for VAS-work. There were 1,086 users who responded "Yes" to Q1 and 34 users responded "No" to Q1 but nonetheless ticked at least one nasal symptom (Q3). Only 16 users reported "no allergic rhinitis" making comparisons with "allergic rhinitis" impossible. There were 5,678 days of VAS-work filled-in by "allergic rhinitis" users. The number of users in Australia, Brazil, Canada, Mexico, and Switzerland was low since the App was introduced after September 2016. Among the 5,789 VAS-work days, all users filled in VAS-nasal and VAS-ocular, but 111 days were not filled in for VAS-global measured ("No" to Q1). The number of reported days per user ranged from one (608 users) to over 60 days (2-7 days: 121 users, 8-15 days: 52 users, >15 days: 40 users).

The phenotypic characteristics of the users are provided in Table 4 online.

The treatments received included a wide range of over-the-counter (OTC) and prescribed AR medications and there was no consistent pattern upon which to base any relevant comparisons.

VAS scores

The mean values for the first day reported and all reported days are similar (Table 2). In the 5,789 VAS days of "allergic rhinitis" users (Figure 2 online), VAS scores show that for 61% of days the symptoms of allergic rhinitis were well controlled (VAS-global measured or calculated < 20) (Table 1 and Figure 2 online). Uncontrolled rhinitis was observed for 39% of days. Few users reported uncontrolled asthma. VAS-work was <20 in 66% of days, between 20 and 50 in 20% of days and over 50 in 14% of days.

Independence between the VAS scores

The Bland and Altman regression analyses showed that all VAS measurements were independent ($p<0.05$ for all comparisons) and that therefore correlations could be estimated appropriately (Table 5 online, Figure 3 online).

Correlations between VAS scores for disease control

There was a highly significant correlation between VAS-global measured and VAS-global calculated for the first day of survey (N=1086, Rho=0.84, Figure 4a online) and for all days (N=5678, Rho=0.89, Figure 4b online)

Correlations between VAS scores for work and disease control

A contingency table was made using VAS score cut-offs of 20 and 50 (Table 3). Less than 20% days with controlled disease (VAS<20) were associated with work impairment. On the other hand, over 97% days with uncontrolled disease (VAS≥50) were associated with work impairment.

Using the Spearman rank correlation, there was a very strong correlation between VAS-work and VAS-global (measured or calculated), a strong correlation between VAS-work and VAS-ocular and a moderate correlation between VAS-work and VAS-asthma (Table 4, Figure 1 and Figure 5 online).

Correlations between VAS and WPAI:AS

There was a moderate correlation between Q4-WPAI:AS and VAS-work (N = 195, Rho = 0.45) and VAS-global measured (N = 195, Rho = 0.42) (Tables 2 and 4, Figure 6 online). Although numbers were small, when VAS work was >40, WPAI-AS was always impaired.

Discussion

A mobile phone app (*Allergy Diary,* Android and Apple stores*)* was used to collect daily visual analogue scales (VAS) data for allergic symptoms and work (VAS-work) in 20 countries. This pilot study not only provides proof-of-concept data on the work impairment collected using an app, but also provides data on the app performance itself. The distribution of answers of the VAS indicates that patients report adequately the absence of symptoms but also severe impairment. Most days with uncontrolled rhinitis were associated with impaired work. There was an association with WPAI:AS in a small data set (144 users).

Strengths and limitations

Smart devices and internet-based applications are already used in rhinitis (24-29) but none assessed work productivity. The strengths of the mobile technology include its wide acceptance and easy use, but there is a need to use appropriate questions and results should be assessed by pilot studies. This pilot study was based on 1,136 users who filled in 5,789 days of VAS allowing us to perform comparisons among outcomes, but not to make subgroup analyses.

We collected country, language, age, sex and date of entry of information with the App. We used very simple questions translated and back-translated into 15 languages. We did not check accuracy or the time taken to complete the survey. An additional bias may be introduced by countries with high versus low numbers of participants.

The App is not designed to compare AR patients with control subjects and this was not a clinical trial. Thus, as expected, over 98% users reported "AR" and we are unable to assess the responses of "non AR" users. On the other hand, there are many days with no symptoms in a sufficient number of persons with AR to allow comparisons between outcomes for those with more or less symptoms.

In this study, statistical hypothesis testing was carried out assessing differences in frequency distributions between groups as well as pairwise correlations. We used both the first observation for all users and multiple observations from the same individual, even though the latter are not independent observations from the same individual This can be addressed in future confirmatory analyses with a larger data sets using a repeated measures approach.

Medical treatments each participant used were recorded but we did not attempt to assess the effect of any treatment on VAS-work for two major reasons. Firstly, disease control is independent of treatment as shown in asthma or rhinitis (for review see (38, 39)) and correlations between disease control and work are likely to be treatment-independent. Secondly, there is no clear pattern of treatment among *Allergy Diary* users and the number of users is insufficient in the present study for an analysis of the impact of any specific treatment on work productivity. Such treatment effects may be amenable to study when more data are available.

Interpretation of the results and generalizability

Symptoms of AR are highly variable depending on allergen exposure and treatments received. Moreover, the duration of the use of the App was variable (from 1 day to over a month). We therefore compared results by day rather than by user. There were strong to very strong correlations between the overall control of rhinitis and work VAS. We used two methods to assess overall control

(measured and calculated from nasal and ocular symptoms) and the correlations were similar. In days with uncontrolled rhinitis, less than 11% were associated with no work impairment and over 50% were associated with severe work impairment.

We then attempted to correlate VAS with a validated questionnaire. However, the comparison between a 7-day instrument (WPAI:AS) and a single day of VAS may not be fully relevant and, since the WPAI:AS was only available in 6 languages, only 195 users were recorded. We may have used a 7-day prospective analysis, but WPAI:AS is relevant to the past 7 days. We found a significant correlation between Q4 (work productivity) and VAS-work or measured global VAS. The mean scores of Q4-WPAI:AS are relatively low by comparison to published studies and suggest that some rhinitis users may have a mild disease. This is confirmed by the VAS-nasal levels.

results of this pilot study confirm previous studies indicating that AR impacts work productivity (2-12). However, this is the first study using an App allowing a daily evaluation. Moreover, it shows the close relationship between work impairment and AR severity or control (9, 40). These results indicate that a simple VAS measurement of work status using an App can be a useful measure of daily work productivity. Such a tool is likely to be of great importance to assess the indirect costs incurred by AR and the benefits from therapeutic interventions. Moreover, the question on VAS-work can be used for other chronic diseases allowing comparisons of public health interest.

The economic impact of the loss of work productivity is an essential component to be considered as it has been estimated that the socioeconomic costs throughout the EU for undertreated allergic airways diseases are up to 100 b annually (41). The costs due to work impairment will be assessed using the *Allergy Diary* when data of more users will be available since EQ-5D (42) is included in the App.

Conclusions

This pilot study in a large number of users in 20 countries shows the impact of uncontrolled rhinitis in work and confirms previous data that consistently indicate such an effect using a variety of methods. The technology employed in this study is unique as it can provide data collected on a daily basis in a large sample and over a wide geographic, cultural and linguistic distribution. In summary, this novel technology allows researchers to assess potential new strategies assessing the burden of AR and potentially, its optimal management.

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Table 1: Study outcome measures

		Question	VAS score measured or calculated
1	**MASK**	VAS-global measured*	Overall, how much are your allergic symptoms bothering you today?
2		VAS-nasal	How much are your nose symptoms bothering you today?
3		VAS-ocular	How much are your eye symptoms bothering you today?
4		VAS-asthma	How much are your asthma symptoms bothering you today?
5		VAS-global calculated	VAS-nasal + VAS-ocular / 2
6		VAS-work**	How much are your allergic symptoms affecting your work today?
7	**WPAI:AS**	Q4-WPAI:AS***	During the past 7 days, how much did allergies affect your productivity while working?

*: The question was only applied to users reporting "Yes" to the question "Do you have AR?"), **:The question was applied to users who indicated that they had "worked today", **: with the question: "Are you currently employed (working or pay)?"

Table 2: VAS and Q4-WPAI:AS scores

	First day reported			All reported days		
	N	M ± sd	Median (25-75)	N	M ± sd	Median (25-75)
VAS-global measured	1086	32.4±27.3	24.1 (10-54.75)	5678	25.1 ± 26.1	15 (4-43)
VAS-global calculated	1120	26.8±23.8	19.2 (7.5-44)	5789	22.0 ± 23.2	13.0 (4-35)
VAS-nasal	1120	31.8±27.6	23.9 (9-52)	5789	25.6 ± 26.2	16 (4-44)
VAS-ocular	1120	21.8±26.0	11 (0-36)	5789	18.5 ± 24.6	7 (0-28)
VAS-asthma	1120	12.6±21.4	1 (0-16)	5789	12.0 ± 21.1	(0-14)
VAS-work	1120	21.2±22.8	13 (1-36)	5789	18.9 ± 22.8	10 (0-29)
Q4-WPAI:AS	195	29.7±27.2	19 (4.5-45)			

Table 3: Frequency distribution of VAS-global measured and VAS-work

VAS-global measured	VAS-work						Number
	<20		**20-50**		**>50**		
<20	3091	96.0%	111	3.4%	18	0.6%	3220
	80.4%		9.9%		2.2%		
20-50	571	44.2%	622	48.1%	101	7.8%	1294
	14.6%		55.3%		12.3%		
>50	126	10.8%	345	29.6%	693	59.6%	1164
	3.3%		30.7%		84.3%		
Not reported	55		46		10		111
Number	3843		1124		822		5789

Phi=0.86, P<0.0001

Table 4: Spearman rank correlations between VAS-work and VAS for disease control

	First day reported			**All days reported**		
Outcome	N	Rho	P value	N	Rho	P value
VAS-global measured	1086	0.76	p<0.0001	5678	0.83	p<0.0001
VAS-global calculated	1120	0.73	p<0.0001	5789	0.83	p<0.0001
VA-nasal	1120	0.69	p<0.0001	5789	0.80	p<0.0001
VAS-ocular	1120	0.61	p<0.0001	5789	0.70	p<0.0001
VAS-asthma	1120	0.45	p<0.0001	5789	0.56	p<0.0001
Q4-WPAI:AS	195	0.45	p<0.001			

Figure 1: Correlation between VAS-work and VAS-global calculated