IMPACT OF RHINITIS ON WORK PRODUCTIVITY: A SYSTEMATIC REVIEW

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Authors' contribution

JB and OV contributed to the development of the bibliographic search strategy, the risk of bias assessment strategy and data extraction criteria. PD, DV, and JJ provided statistical expertise. JB and OV drafted the manuscript. All authors read, provided feedback and approved the final manuscript. OV acts as guarantor of the manuscript.

Highlight Box

1. What is already known about this topic?

   Information on the economic impact of allergic rhinitis on work productivity remains fragmented and therefore cannot be taken efficiently into account by the medical community and policy makers.

2. What does this article add to our knowledge?

   This systematic review confirms that rhinitis impacts at-work productivity more than absenteeism and provides a summary estimate that may serve as guidance for physicians and public health interventions.

3. How does this study impact current management guidelines?

   Physicians should draw more attention to the burden of allergic rhinitis on work productivity, and inform the patient of the possible occupational impacts of the condition and the benefits of treatment.

Key Words: Absenteeism; allergy; rhinitis; work productivity; presenteeism;

List of Abbreviations

AR:	Allergic rhinitis
ARIA:	Allergic Rhinitis and its Impact on Asthma
RCT:	Randomized controlled trial
SR:	Systematic review
WPAI:	Work Productivity and Activity Impairment questionnaire

T**ext word count:** 3,982 words

Abstract

Background: Allergic rhinitis (AR) is increasingly acknowledged as having a substantial socio-economic impact associated with impaired work productivity, although available information remains fragmented.

Objective: This systematic review summarizes recently available information to provide a quantitative estimate of the burden of AR on work productivity including lost work time (i.e. absenteeism) and reduced performance while working (i.e. presenteeism)

Methods: A Medline search retrieved original studies from 2005 to 2015 pertaining to the impact of AR on work productivity. A pooled analysis of results was carried out with studies reporting data collected through the validated Work Productivity and Activity Impairment (WPAI) questionnaire.

Results: The search identified 19 observational surveys and 9 interventional studies. Six studies reported economic evaluations. Pooled analysis of WPAI-based studies found an estimated 2.3% (95% CI, 0; 7.9%) missed work time and 32.5% (95% CI, 20.8; 44.1%) impairment in at-work performance due to AR. Economic evaluations indicated that indirect costs associated with lost work productivity are the principal contributor to the total AR costs and result mainly from impaired presenteeism. The severity of AR symptoms was the most consistent disease-related factor associated with a greater impact of AR on work productivity, although ocular symptoms and sleep disturbances may independently affect work productivity. Overall, pharmacologic treatment of AR showed a beneficial effect on work productivity.

Conclusions: This systematic review provides summary estimates of the magnitude of work productivity impairment due to AR and identifies its main determinant factors. This information may help guide both clinicians and health policy makers.

Abstract word count: 249 words

INTRODUCTION

Allergic rhinitis (AR) is a global public health issue due to its high prevalence and its adverse impacts on sleep, cognitive functioning, mood, and associated comorbid conditions, such as asthma and sinusitis, and ultimately on quality of life and work and school performance (1-3).

A number of reviews have highlighted the socioeconomic burden of AR in terms of impaired work productivity, including lost work time (i.e. absenteeism) and reduced performance while working (i.e. impaired presenteeism) (4-8). Blanc et al. (9) first reported that reduction in self-rated job effectiveness was more common in individuals with rhinitis (36%) than among those with asthma (19%) while absenteeism was similar in both conditions. US population-based surveys have provided estimates of the annual number of workdays missed because of AR ranging from 0.03 to 0.8 per employed individual (10-13). Goetzel et al. (14) combined data on work productivity impairment from three large-scale US surveys and concluded that 'allergy' (excluding asthma) was associated with an average 3.4% (range: 0.3%-9.0%) productivity loss due to work absence and an average 10.9% (range: 8.3%-14.5%) reduction in at-work performance. Even though an increasing number of studies of AR have included quantitative and validated measures of absenteeism and presenteeism (15), to our knowledge, no systematic review (SR) of this area has yet been conducted. Therefore, available information on the impact of AR on work productivity remains fragmented and cannot be efficiently taken into account to guide clinical practice and public health interventions.

This SR aimed to synthesize and critically analyze the available information pertaining to the burden of AR on work productivity both in terms of absenteeism and impaired presenteeism in order to derive summary quantitative estimates of these effects. The secondary aim of this SR was to identify the factors that may affect, either negatively or positively, these productivity impairments.

METHODS

Protocol

This SR was conducted according to the *Preferred Reporting Items for Systematic reviews and Meta-Analyses* (PRISMA) (*www.prisma-statement.org*) (16).

Eligibility criteria

We screened all original studies with an English abstract containing information on work productivity and/or indirect costs of rhinitis and published between January 2005 and December 2015. Case-series, review articles, and model-based economic evaluations were excluded. We did not consider studies published before 2005 as they have already been reviewed previously (4).

Information Sources and Search Strategy

The online database PubMed was searched using the following keywords: work [and] productivity [and] rhinitis; WPAI [and] rhinitis; productivity [and] rhinitis; and costs [and] work [and] rhinitis. Other databases were not searched, but we used the alternative strategy of sending the list of retrieved publications to an international panel of 11 experts in the field of allergy from 10 countries (Online Repository Table E1) asking them if they were aware of any other relevant published or unpublished data. In addition, the publications cited in the reference lists of the retrieved studies as well as review articles were carefully scrutinized to ensure that no original published data had been missed in the original search.

Selection of Studies

The 41 retrieved papers were screened for eligibility by two independent reviewers (JB and OV) followed by full text evaluation of the 35 articles that met the initial inclusion criteria (see Online Repository Figure 1). Twelve studies were excluded due to methodological issues or missing data (Online Repository Table E2). This process left 23 remaining studies (17-39). The expert panel feed-back identified four additional studies that were included in the

analysis (40-43). Another three relevant publications were retrieved through the analysis of citations lists (44-46).

Data Collection Process

The data from the 30 included studies were extracted in a standardized manner and verified by two authors (OV and JB) using a list of predefined variables (Online Repository Table E3). Authors were contacted whenever possible to obtain additional information unavailable in the original publication (30, 36, 41, 43).

Assessment of the Quality of Selected Studies

The studies were classified into three categories: 1) observational surveys; 2) interventional studies; and 3) economic evaluations of the impact of AR on work productivity. Bias in the observational surveys was evaluated using the Newcastle-Ottawa Quality scale for assessing the quality of cohort studies in meta-analyses (*www.ohri.ca/programs/clinical_epidemiology/oxford.htm*). The risk of bias in randomized controlled trials (RCT) was assessed using the descriptive Cochrane Collaboration's 'Risk of bias' tool (47).

Data Analysis

Data of studies using the Work Productivity and Activity Impairment (WPAI)-Allergy Specific (AS) instrument were pooled to estimate the magnitude of the work productivity impairment related to AR. The WPAI-AS was selected as the outcome measure for this pooled analysis because it has been extensively validated in a large variety of health disorders (15, 48, 49) (*http://www.reillyassociates.net/WPAI_References.html*) and was the most commonly used instrument in the retrieved studies. The WPAI instrument produces three outcome measures of work disability: 1) the work time missed due to a specific health condition (i.e. absenteeism); 2) the productivity impairment while working due to the specific health condition (i.e., impaired presenteeism); and 3) the overall work impairment which is the sum

of absenteeism and impaired presenteeism (15, 48). These metrics are expressed as percentages (from 0% to 100%), with higher percentages indicating greater impairment. These were reported as non-integer summary values with a measure of variability for the distribution (e.g., a mean and standard deviation [SD] or a median and interquartile range) that varied among the studies.

Baseline pre-intervention data that were reported separately by treatment vs. control group in RCTs contributed separately to the pooled estimate and, whenever possible, stratified data by the pattern of AR (i.e. seasonal/intermittent vs. persistent) or disease severity (mild vs. moderate-to-severe) also contributed separately to the overall pooled estimates.

For each WPAI metric (absenteeism, presenteeism, and overall productivity impairment), the overall or subsets of pooled estimates of the mean value with its corresponding 95% confidence interval (95% CI) were calculated by weighting for the variance of each contributing value included in the estimate using a fixed effect approach. Since individual studies reported either standard error (SE), or standard deviation (SD) or interquartile range (IQR), the variance of each reported metric was derived by applying the following formulae as appropriate: $V=n*SE^2$, $V=SD^2$ or $V=(IQR/1.35)^2$, assuming normal distributions. Pooling was not possible for absenteeism in persistent and mild AR because only a single study/stratum was applicable. We also excluded from the pooled analyses data for the stratum of observations for the placebo group in one interventional study (31) because it reported an extreme variance estimate that could not be verified. Pooled analyses were performed with arithmetic calculations of spreadsheet-entered data.

A pooled analysis of the effects of treatment interventions on work productivity could not be conducted because data were not collected using the WPAI-AS (32) or were not appropriately reported (31, 33, 37-39).

RESULTS

The 30 selected studies included 19 observational surveys (17-23, 25-30, 40, 41, 43-46) and 9 interventional studies (31-39). Six studies reported economic evaluations (18, 24, 32, 41-43), among which three were also identified among the observational surveys (18, 41, 43) and one among interventional studies (32).

Characteristics of Observational Surveys

The surveyed populations, diagnostic criteria and reported outcomes of the 19 observational surveys are summarized in Table 1 and Online Repository Table E4. The criteria and results of quality assessment are detailed in Online Repository Table E5.

Populations

The participants with AR were recruited from various population sources (Online Repository Table E4). Six studies compared AR individuals with referent groups without AR derived from the same population (18, 21, 22, 25, 44, 46), but adjustment for confounding demographic characteristics and multimobidity was performed in only two studies (25, 46).

Characteristics of Allergic Rhinitis

The diagnosis of AR was documented using various criteria as detailed in Online Repository Table E4. Ascertainment of allergen sensitization through skin-prick tests and/or serum specific IgE antibodies was used as a diagnostic criterion in only three surveys (25, 40, 43) and reported to be present in 41% to 55% of the AR participants in three other studies (17, 19, 26).

Five observational surveys provided the proportion of participants with moderate/severe AR (61% to 93%) (Table 1) (17, 21, 25, 30, 43). Work productivity was reported separately for mild and moderate/severe AR in only two studies (17, 43). Eleven studies reported the duration of AR symptoms (17, 22, 23, 26-30, 40, 43, 45). The proportion of persistent AR among these studies ranged from 0% to 72%. Data on work productivity were provided separately for persistent and intermittent AR in only two studies (17, 43).

Outcomes

Seven surveys collected data on the impact of AR on work productivity using validated instruments (Table 1): the WPAI instrument either in its specific version for allergic diseases (WPAI-AS) (17, 19, 30, 43) or in its generic version (25), the Stanford Presenteeism Scale (SPS) (44), and the Work Productivity Short Inventory questionnaire (WPSI) (18). The recall periods assessed by these questionnaires were seven days, four weeks, and 12 months, respectively. In one prospective cohort study of AR participants recruited in a random sample of specialized clinics in Spain, the WPAI-AS questionnaire was administered quarterly over a one-year period (43). The remaining observational surveys collected information on the impact of AR on work productivity using diverse non-validated instruments.

Characteristics of Interventional Studies

Populations

Eight of the nine interventional studies (Table 2 and Online Repository Table E6) were randomized controlled trials (RCTs) evaluating the effects of AR medications on work productivity (31-33, 35-39). One study was a pragmatic, investigator-randomized design and compared the treatment of AR based on the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines with a "free-choice" strategy (34). For two studies that failed to provide the number of enrolled participants who were currently employed, work and school productivity impairments could not be differentiated (35, 36). Quality assessment of interventional studies is presented in Online Repository Table E7.

Characteristics of Allergic Rhinitis

Sensitization to relevant allergens was ascertained in all AR participants, although the tested allergens were not detailed in four studies (33, 35, 36, 38). Five RCTs evaluated participants with “seasonal AR” (31, 33, 37, 39) and one RCT included participants with “intermittent AR” (35). Symptom severity at baseline was categorized according to a symptom score in six

RCTs and to the ARIA grades in one study (34), and was not specified in one study (33). The majority (n=7) of the nine RCTs enrolled participants with moderate-to-severe AR at baseline (Online Repository Table E6) (31, 32, 35-39).

Outcomes

The impact of AR on work productivity was assessed using the WPAI-AS questionnaire in eight RCTs (Table 2).

Absenteeism

Seven observational surveys reported that 3 to 30% of participants "missed work time due to AR" (22, 23, 26, 27, 29, 40, 45), but failed to provide any quantitative estimate of absenteeism (Table 1). Six observational surveys provided quantitative estimates of missed work time expressed as an absolute number of hours or days lost over variable intervals of time (Table 1) (18, 20, 21, 30, 41, 44). These estimates ranged from 0.8 to 9.9 workdays lost per year. The Medical Expenditure Panel Survey (MEPS) estimated a 0.6 incremental workday missed per year in participants with AR after controlling for socio-demographic characteristics, smoking, and multimorbidity (46).

The pooled analysis of six WPAI-based studies (1,666 participants) provided an overall pooled estimate of 2.3% (95% CI, 0; 7.9%) missed work time due to AR (Table 3) (19, 25, 31, 37, 39, 43).

Presenteeism

Seven observational surveys reported that 10% to 50% of participants with AR experienced "work limitation" related to AR (Table 2) (22, 23, 26-28, 30, 45). Seven observational surveys assessed quantitatively the impact of AR on work productivity using various non-validated indices (18, 23, 26, 27, 29, 30, 41) (Table 2).

The pooled analysis of impaired presenteeism included eight studies using the WPAI-AS instrument (4,563 participants) and provided an estimated 32.5% (95%CI, 20.8; 44.1%) impairment in work performance due to AR (Table 3) (17, 19, 25, 31, 34, 37, 39, 43).

Overall Work Productivity

The pooled analysis of 11 studies using the WPAI-AS questionnaire (6536 participants) found an estimated 35.5% (95% CI, 25.2; 45.8%) impairment in overall work productivity due to AR (Table 3) (17, 19, 25, 31, 33-37, 39, 43).

Disease-Related Factors Impacting Work Productivity

The severity of AR symptoms (17, 19, 21, 22, 25, 30, 41, 43) was the most consistent disease-related factor associated with a greater impact of AR on work productivity. The pooled analysis of WPAI questionnaire-based studies retrieved in this SR showed a trend toward greater impairment in overall work productivity impairment in moderate/severe AR (38.5% [95%CI, 27.0; 49.9]) as compared to mild AR (14.2% [95%CI, 0; 31.7]), although the difference was not significant (Table 3).

Two studies reported that ocular symptoms (conjunctivitis) in addition to nasal symptoms were associated with a more detrimental effect on work productivity (20) or ‘professional effectiveness’ (22). One of these studies also documented an independent adverse effect of sleep disturbance and low health-related quality of life on work productivity (20).

Impact of Pharmacologic Treatment

Overall, RCTs reported a beneficial effect of the pharmacologic treatment of AR on work productivity (31-39) (Table 4). One study showed that treatment based on ARIA guidelines significantly improved absenteeism and presenteeism as compared with a “free-choice” treatment (34).

Comparison with Other Health Conditions

A formal comparison of the work impairment due to AR with other chronic diseases could not be performed because the SR identified only three relevant surveys that used different outcome measures. Using the Stanford Presenteeism Scale, Collins et al. (44) found that the mean work time missed (0.9 hour [95% CI: 0.7-1.1]) in the last four weeks and work performance impairment (18.2% [95% CI: 17.5-18.8%]) related to AR were similar to those attributed to asthma, arthritis, diabetes, heart and circulatory problems, and musculoskeletal disorders. Lamb et al. (18) reported that the estimated mean total productivity loss per employee during the last year, including the number of days missed and the number of unproductive hours, was significantly higher for AR compared to ten other chronic conditions, including high stress, migraine, depression, arthritis/rheumatism, anxiety disorders, respiratory infections, hypertension, diabetes, asthma, and coronary heart disease. Using the generic WPAI, de la Hoz et al. (25) found that absenteeism was similar in AR (adjusted mean ± SE, 4.6±1.1%) compared to diabetes (4.2±1.7%) and hypertension (2.1±1.5%) but significantly lower than in symptomatic depression (31.7±2.6%). AR was associated with a significantly higher overall loss of productivity (adjusted mean ± SE, 26.6±1.8%) than hypertension (8.8±2.5%) and diabetes (16.7±2.8%) but it was lower than in symptomatic depression (59.5±4.3%).

Economic Evaluations

Six studies assessed the economic costs of lost work productivity related to AR (Table 5) (18, 24, 32, 41-43). Overall, these economic evaluations indicated that the costs of impaired presenteeism were 2.2 to 18.7-fold higher than those of absenteeism, while the total costs of lost productivity (i.e. absenteeism *plus* impaired presenteeism) were 3.2 to 13.5-fold higher than the direct medical costs. The indirect costs resulting from lost work productivity represented 76% to 93% of the total AR costs.

A Swedish population-based questionnaire survey (42) showed that the cost of moderate-to-severe persistent AR was four-fold higher than mild persistent AR. A prospective 1-year

cohort study found that the mean indirect costs resulting from presenteeism were approximately 1.9-fold higher in moderate/severe AR compared to mild AR and 2.3-fold higher in participants with persistent AR compared to those with intermittent AR (43). The cost of absenteeism did not differ according to the severity or duration of AR symptoms. In persistent AR, the costs of absenteeism and presenteeism due to AR were significantly reduced in participants treated with levocetirizine as compared with placebo (32).

DISCUSSION

Summary of Evidence

The pooled analysis of WPAI-based studies identified in this SR showed that AR is associated with a substantial adverse impact on the productivity at work (i.e. presenteeism) with an estimated 32.5% (95%CI, 20.8; 44.1%) impairment, while the impact on absenteeism was minimal (2.3% [95% CI, 0; 7.9%]). These figures are similar to previous estimates of absenteeism, while estimates of impaired productivity at work are higher than those reported in previous US surveys that used various instruments to quantify the impact of AR on work productivity (10-14). The estimates derived in this SR are however in line with those reported by two recently published WPAI-based studies conducted in Asian healthcare settings which documented mean (SD) overall productivity impairment due to AR of 32 (26)% and 40 (29)%) (50, 51).

Overall, this SR indicated that the level of impaired productivity due to AR is at least similar to that reported in many other chronic diseases (18, 25, 44). The recent Asian studies cited previously further confirm that overall work productivity is more impaired by rhinitis than asthma (20 [25]% vs. 33 [30]%) and COPD (17 [27]% vs. 15 [23]%) (50, 51). In addition, our pooled estimate of the overall productivity impairment due to AR (35.5% [95% CI, 25.2; 45.8%]) is in line with the mean (range) percentage impairment provided by a recent SR of WPAI-based studies in various chronic health disorders: depression (29%; 15-43%); chronic obstructive pulmonary disease (31%; 19-42%); irritable bowel syndrome and constipation

(36%; 21-51%); and arthritis (45%; 21-69%) (49). However, in this SR, the studies on asthma and “allergies” were pooled together and included only two studies on rhinitis (17, 48). Nevertheless, the impact of seasonal or intermittent AR is likely to be of more limited duration than other chronic diseases.

This SR confirmed that more severe AR symptoms are associated with a more detrimental impact on work productivity (17, 19, 21, 22, 25, 30, 41, 43). These findings are further substantiated by a recent study showing a correlation between the WPAI-AS score and the overall intensity of AR symptoms assessed using a visual analogue scale (VAS) (52). In addition, this SR indicated that associated conjunctivitis and sleep disturbances could have detrimental effect on work productivity independently from nasal symptoms (20, 22). The aggravating role of ocular symptoms was further substantiated by an observational survey of AR patients recruited by primary care physicians and specialists which, however, was not eligible for inclusion in this SR because detailed WPAI questionnaire data were not reported (53). This study demonstrated that ocular symptoms were associated with a greater impact on absenteeism and productivity while at work, even after adjustment for the severity of nasal symptoms. A number of observational surveys in this SR reported on sleep problems related to AR (17, 19-21, 23, 26, 27, 40, 45), but they failed to investigate the specific impact of sleep disorders on work productivity, with the exception of the study by Szeinbach et al. (20). These findings – if further confirmed – may have clinical implications since ocular symptoms and sleep disturbances are highly prevalent among patients with AR and are often underestimated by health care providers (1, 54, 55). Greater awareness of these symptoms and their potential effects may help physicians to identify subjects with an increased risk of impaired work productivity and to target their treatment in order to reduce the work and economic impact of AR.

Although a formal meta-analysis of the effects of pharmacological treatment of AR was not appropriate to the retrieved data, the RCTs identified through this SR showed an overall beneficial effect of oral antihistamines and nasal sprays on work productivity. These findings

are in line with a critical review of studies published before 2003 showing that treatment with non-sedating antihistamines reduces the productivity losses due to AR (56).

Earlier population-based studies conducted in the US provided a wide range of estimates of the indirect costs of AR, ranging from 7% (11) to 25% (10) of the total costs. Unfortunately, few studies have assessed both absenteeism and presenteeism (6). The current SR indicates that: 1) the indirect costs associated with lost work productivity are the principal component of the total AR costs and result mainly from the costs of presenteeism and 2) the indirect costs of AR appear to be greater or similar to those resulting from many other chronic diseases traditionally considered as being more important from a medical perspective.

Limitations

Several methodological weaknesses of this SR should be considered for interpreting the estimates of the burden of AR on work productivity. First, the pooled estimates of the impact of AR on work productivity were derived from a limited number of studies based on the validated WPAI instrument. Most observational surveys used non-validated measures of at-work productivity and most reports of the effects of pharmacological interventions presented data in a form that could not be utilized in a pooled analysis. The findings from these non-WPAI studies were only descriptively assessed and summarized. Second, IgE sensitization to aeroallergens was not systematically documented in the majority of observational surveys. Thus, the findings derived from these surveys are likely to be relevant not only to AR, but also to other forms of rhinitis.

Third, most available studies had a substantial, though unquantifiable, potential for bias toward the selection of participants with more severe AR. The AR subjects participating in population or patient panels (21-23, 26-30, 41) and ‘convenience’ samples surveys (18, 45) might be those who were more prone to report a higher impact of the disease. Individuals who seek primary healthcare (17, 19, 25, 40, 43) or managed care (20) are unlikely to

accurately represent the whole population of individuals suffering from AR. Only five of the 19 observational surveys provided information on the severity of AR (17, 21, 25, 30, 43), and data on work productivity impairment associated with mild AR was available in only two studies (17, 43). Moderate-to-severe AR seemed to be over-represented in observational surveys as compared with existing population-based data (e.g. 29%-40% (54, 57)); the proportion of participants with moderate/severe AR ranged from 61% to 93% in the five surveys that provided this information (17, 21, 25, 30 , 43). In addition, RCTs are inherently affected by a selection bias toward more severe and/or symptomatic AR since, in these studies, only participants with a moderate to severe disease were enrolled.

Studies based on self-reporting may be affected by recall failure and attribution bias (e.g. confusion about whether AR is the cause of the work impairment). Few available studies attempted to disentangle the impact of AR from that resulting from comorbid conditions, particularly asthma and rhinosinusitis, although these conditions may increase the adverse impact on work productivity (58, 59). Only two observational surveys took into account the potential confounding demographic characteristics and comorbidities in the analysis of their results (25, 46).

A major limitation of our pooled analysis results from the fact that the impact of seasonal AR cannot be estimated on an annual time framework. The WPAI-AS questionnaire is one of the best validated tools to assess absenteeism and presenteeism in AR (15, 48). The WPAI-AS questionnaire is applied for a seven-day recall period in an attempt at minimizing the recall bias. However, most studies evaluating specifically individuals with seasonal AR were interventional studies based on the WPAI-AS which were conducted during the relevant pollen season and failed to provide information on the total duration of the symptomatic period (31, 33, 37, 39) while work impairment has been significantly correlated with outdoor pollen and mould levels in individuals with AR (60, 61). Apps running on smartphone devices can help gather real time information on daily work performance and AR symptoms over longer periods of time and, accordingly, should further reduce recall bias and make it

possible to estimate more accurately the cumulative impact of seasonal and intermittent AR on work productivity (62).

Conclusion

This SR indicates that AR is substantially impairing at-work productivity (presenteeism) but only minimally absenteeism, although further studies assessing daily work productivity and severity of symptoms at the same time over prolonged periods and comparing with other chronic diseases are needed to better characterize the impact of AR. Nevertheless, the findings of this SR should increase the awareness of the medical community on the impact of AR on work productivity and provide an evidence-base to assist healthcare payers and policy-makers implementing interventions to reduce the socioeconomic burden of AR.

Table 1. Observational surveys: Summary findings

Reference	Working AR adults	Severity of AR	Duration of AR	Questionnaire instrument	Work time missed (absenteeism)	Impairment in at-work productivity (presenteeism)
Collins, 2005 (44)	1,472	NA	NA	SPS	Mean (95% CI) missed work-time: 0.9 h (0.7-1.1) in the last 4 wk (estimate: 9.9 d/yr)¥	Mean (95% CI) work impairment: 18.2 (17.5-18.8)
Bousquet, 2006 (17)	84	Mild	IAR	WPAI-AS	0	Median (IQR) % work impairment: 20 (10-30)
	66	Mild	PAR		0	Median (IQR) % work impairment: 20 (0-40)
	894	M/S	IAR		0	Median (IQR) % work impairment: 40 (20-70)
	1,107	M/S	PAR		0	Median (IQR) % work impairment: 40 (20-62)
Lamb, 2006 (18)	4,524	NA	NA	WPSI	Average missed work time: 3.6 d/yr	Unproductive work due to AR: 2.3 h/d when experiencing Sx
Stull, 2007 (19)	301	NA	NA	WPAI-AS	Mean (SD) % missed work time: 6.8 (14.6)	Mean (SD) % work impairment: 40.0 (26.9)
Szeinbach, 2007 (20)	577	NA	NA	10-point scale	Average missed work time:1 h/wk (range: 0-32h) (estimate: 5.5 d/yr)¥	NA
Valovirta, 2008 (45)	2,287	NA (AA: 42%)	PAR: 62%	Non-validated	Taking time off work in the past yr due to AR: 26%	Work affected (unable to concentrate): average 49%
Meltzer, 2009 (21)	3,831	M/S: 66%	NA	Non-validated	• Mean (SD) entire workdays missed due to AR: 0.4 (2.0) past 4 wk (estimate: 4.4 d/yr)* vs. 0.2 (1.5) for non-AR (estimate: 2.2 d/yr)¥ • Mean (SD) partial workdays missed due to AR: 0.3 (1.9) past 4 wk vs. 0.1 (1.4) for non-AR	NA
Van Cauwenberge, 2009 (22)	600	NA	SAR: 59%	Non-validated	Absence from work, late arrival or early departure: 27%, average 6 h work missed per symptomatic wk	Moderate or considerable effect of AR on concentration: 31%
Neffen, 2010 (23)	1,088†	NA	SAR: 62%	Non-validated	Missed work because of AR (past 12 mo): 20%	Interference with work performance: 33%; 30% point decrease in work productivity related to AR
de la Hoz, 2012 (25)	134	M/S: 61%*	NA	WPAI-Generic	Adjusted mean (SE): 4.6 (1.1)%	Adjusted mean (SE): 23.5 (1.6)%
Katelaris, 2011 (26)	1,043†	NA	SAR: 66%	Non-validated	Missed work because of AR (past 12 mo): 25%	Interference with work performance: 50%; 25% point decrease in work productivity related to AR
Demoly, 2011 (40)	702†	NA (AA: 22%)	SAR: 51%	Non-validated	Sick leave at the time of physician visit: 5.1% for an average of 4.5 days	NA
Bhattacharyya, 2012 (46)	NA	NA	NA	Not detailed	Mean (SE) incremental workdays lost/yr: 0.6 (0.4) vs. non-AR participants	Proportion (SE) of participants with work limitation: 13.9 (1.0)% vs. 10.4 (0.3) in non-AR participants; adjusted OR: 1.43 (95%CI: 1.2–1.7)
Keith, 2012 (28)	1,001†	NA (AA: 27%)	SAR: 51%	3-point scale	NA	Reduced productivity during the allergy season: 2% very troublesome, 8% moderately troublesome

Meltzer, 2012 (27)	2,500†	NA (AA: 32%)	PAR: 56%	Non-validated	Missed work because of AR during the past 12 mo: 30%	Interference with work performance : 42%; 23% point decrease in work productivity related to AR
Bielory, 2014 (29)	962	NA	SAR: 78%	100-point scale	Missed work because of AR (unknown period of time assessed): 3%	Reduced productivity by 26% points (from 91 to 65) when allergy Sx at their worst vs. no Sx
Jantunen, 2014 (41)	636	NA	NA	100-point scale	Mean (SD) missed work time: 0.8 (5.1) days/yr	Mean (SD) % reduction in work productivity: 15.2 (14.5) % when Sx
Price, 2015 (30)	691	M/S: 75% (AA: 30%)	SAR: 100%	Categorical scale of impairment from 10% to 100%	Mean (SD) missed work time: 4.1 (16.4) days/yr in M/S AR vs. 2.5 (7.7) days/yr in mild AR	• Decreased work performance >50% in 32.8% of M/S AR vs. 12.2% of mild AR • Decreased work performance on mean (SD) 37.7 (53.0) days/yr in M/S AR vs. 21.0 (29.9) days/yr in mild AR.
Colas, 2016 (43)	241	Mild	Na	WPAI-AS	Mean (SD) % missed work time: 0.8 (1.6) (n=18)	Mean (SD) % work impairment: 8.9 (11.7) (n=18)
		M/S	Na		Mean (SD) % missed work time: 1.9 (6.0) (n=223)	Mean (SD) % work impairment: 16.9 (17.1) (n=199)
		Na	IAR		Mean (SD) % missed work time: 1.6 (4.4) (n=64)	Mean (SD) % work impairment: 8.3 (8.8) (n=56)
		Na	PAR		Mean (SD) % missed work time: 1.9 (6.2) (n=177)	Mean (SD) % work impairment: 19.0 (18.0) (n=161)

Legend: AA: associated asthma; AR: allergic rhinitis; PAR = persistent AR; SAR = seasonal AR; M/S = moderate/severe AR; Sx: symptoms; SPS: Stanford Presenteeism Scale; WPAI-AS: Work Productivity and Activity Impairment questionnaire-Allergy Specific; WPSI: Work Productivity Short Inventory

* Severity assessed using the Clinical Global Impression (CGI) generic scale

† Unknown working status

¥ Estimate based on a 8-hour work day, 5 workdays per week and 220 workdays per year

Table 2. Interventional studies: Work productivity impairment at baseline assessment

Reference	Duration of AR	Severity of AR	Intervention group	No. of participants	% work time missed (absenteeism)*	% impairment in at-work productivity (presenteeism)*	% overall work impairment*
Okubo, 2005 (31)	SAR	M/S	Fexofenadine	79	Mean (SD): 1.1 (4.5)	Mean (SD) : 39.1 (27.6)	Mean (SD): 39.4 (27.9)
			Placebo	89	Mean (SD): 0.3 (1.7)	Mean (SD): 36.6 (25.8)	Mean (SD): 36.7 (25.9)
Fairchild 2007 (33)	SAR	M/S	Olopatadine NS 0.6%	293	NA	NA	Mean (SD) : 48.5 (24.7)
			Olopatadine NS 0.4%	303	NA	NA	Mean (SD): 45.0 (26.3)
			Placebo	297	NA	NA	Mean (SD): 44.1 (25.2)
Bousquet, 2009 (34)	PAR : 62%	M/S : 72%	ARIA guidelines	339	0	Median (IQR) : 30 (20-50)	Median (IQR) : 30 (20-50)
			Free-choice	342	0	Median (IQR) : 30 (10-50)	Median (IQR) : 30 (10-50)
Bousquet, 2009 (35)	IAR	M/S	Desloratadine	262†	NA	NA	Mean (SEM): 46.4 (2.4)
			Placebo	256†	NA	NA	Mean (SEM): 41.4 (2.3)
Bousquet, 2010 (36)	PAR	M/S	Desloratadine	301†	NA	NA	Mean (SEM): 48.0 (2.4)
			Placebo	261†	NA	NA	Mean (SEM) : 47.0 (2.3)
Mansfield, 2010 (37)	SAR	M/S	Levocetirizine	235	Mean (SD): 4.5 (12.9)	Mean (SD): 51.8 (24.2)	Mean (SD): 52.9 (24.9)
			Placebo	233	Mean (SD): 3.5 (9.8)	Mean (SD): 49.0 (24.2)	Mean (SD): 49.9 (24.6)
Meltzer, 2010 (38)	PAR	M/S	Mometasone NS	20	Mean (range): 4.7 (0-33.3)	Mean (range): 5.9 (2.0-9.0)	NA
			Placebo	9	Mean (range): 4.4 (0-20.0)	Mean (range): 5.9 (3.0-9.0)	NA
Segall, 2010 (39)	SAR	M/S	Levocetirizine	216	Mean (SD): 3.8 (11.2)	Mean (SD) : 51.6 (24.1)	Mean (SD): 52.5 (24.6)
			Placebo	227	Mean (SD): 3.3 (9.4)	Mean (SD): 49.3 (24.0)	Mean (SD): 50.1 (24.3)

Legend: AR: allergic rhinitis; IAR = intermittent AR; PAR = persistent AR; SAR = seasonal AR; M = mild AR; M/S = moderate/severe AR; NA = not available; NS: nasal spray.

* Assessed using the Work Productivity and Activity Impairment-Allergy Specific (WPAI-AS) questionnaire

† Unknown working status

Table 3. Pooled analysis of the impact of rhinitis on work productivity: Estimates weighted for variance

Study Type	Absenteeism, %*				Impaired presenteeism, %*				Overall work productivity impairment, %*			
	N studies (reference)	N strata	N participants	Mean % (95% CI)	N studies (reference)	N strata	N participants	Mean % (95% CI)	N studies (reference)	N strata	N participants	Mean % (95% CI)
All studies	6 (19, 25, 31, 37, 39, 43)	8	1666	2.3 (0; 7.9)	8 (17, 19, 25, 31, 34, 37, 39, 43)	15	4563	32.5 (20.8; 44.1)	11 (17, 19, 25, 31, 33-37, 39, 43)	22	6535	35.5 (25.2; 45.8)
By study design:												
Observational	3 (19, 25, 43)	3	676	2.8 (0; 12.5)	4 (17, 19, 25, 43)	7	2803	23.9 (8.1;39.8)	4 (17, 19, 25, 43)	7	2802	25.0 (9.6; 40.4)
Interventional	3 (31, 37, 39)	5	990	2.2 (0; 8.9)	4 (31, 34, 37, 39)	8	1760	42.6 (25.3; 59.9)	7 (31, 33-37, 39)	15	3733	44.0 (30.2; 57.9)
By disease pattern:												
IAR/SAR	4 (31, 37, 39, 43)	6	1054	1.9 (0; 7.2)	5 (17, 31, 37, 39, 43)	9	2113	24.3 (12.6; 36.0)	7 (17, 31, 33, 35, 37, 39, 43)	14	3523	30.2 (19.1; 41.4)
PAR	1 (43)	1	NA	NA	3 (17, 34, 43)	5	2015	25.9 (4.5; 47.2)	4 (17, 34, 36, 43)	7	2522	29.5 (9.3; 49.7)
By disease severity:												
Mild AR	1 (43)	1	NA	NA	2 (17, 43)	3	168	13.8 (0; 31.0)	2 (17, 43)	3	168	14.2 (0; 31.7)
M/S AR	5 (25, 31, 37, 39, 43)	7	1347	2.2 (0; 7.9)	7 (17, 25, 31, 34, 37, 39, 43)	12	4094	35.5 (22.0; 49.1)	10 (17, 25, 31, 33-37, 39, 43)	19	6066	38.5 (27.0; 49.9)

Legend: AR: allergic rhinitis; IAR: intermittent AR; NA: not appropriate; PAR: persistent AR; SAR: seasonal AR; M/S: moderate/severe AR.
* Assessed using the Work Productivity and Activity Impairment-Allergy Specific (WPAI-AS) questionnaire

Table 4. Interventional studies: Impact of treatment on work productivity

Reference	Duration of AR	Severity of AR	Intervention group	N participants	Impact on missed worktime (absenteeism)	Impact on at-work productivity (presenteeism)	Impact on overall work impairment
Okubo, 2005 (31)	SAR	M/S	Fexofenadine	79	NA	Mean difference vs. baseline: • Treated = -5.6% • Placebo = +3.2%	Mean difference vs. baseline: • Treated = -5.5% • Placebo = +3.4%
			Placebo	89			
Bousquet, 2005 (32)	PAR	M/S	Levocetirizine	186	Mean (95%CI) no. of missed work days/mo: • Treated = 0.2 (0.1-0.3) • Placebo = 0.4 (0.3-0.8)	Mean (95% CI) work impairment, d/mo: • Treated = 0.7 (0.5-0.9) • Placebo =1.0 (0.8-1.3)	Mean (95% CI) total work days lost, days per mo: • Treated = 0.9 (0.7-1.1) • Placebo = 1.49 (1.2-2.0)
			Placebo	196			
Fairchild 2007 (33)	SAR	M/S	Olo 0.6%	293	NA	NA	Mean difference vs. baseline: • Olo 0,6% = -15.2% • Olo 0,4% : -13.0% • Placebo : -7.4%
			Olo 0.4%	303			
			Placebo	297			
Bousquet, 2009 (34)	PAR : 62%	M/S : 72%	ARIA	339	Missed % work time: • ARIA group = 0 • Free-choice group = 0	Median (IQR) difference vs. baseline: • ARIA group = -20 (-35; 0)% • Free choice group = -10 (-30; 0)%	Median (IQR) difference vs. baseline: • ARIA group = -20 (-40; 0)% • Free choice group = -10 (-30; 0)%
			Free-choice	342			
Bousquet, 2009 (35)	IAR	M/S	Desloratadine	262	NA	NA	Mean (SEM) difference vs. baseline: • Treated = -15.0 (2.8)% • Placebo = -5.7 (2.7)%
			Placebo	256			
Bousquet, 2010 (36)	PAR	M/S	Desloratadine	301	NA	NA	Mean (SEM) difference vs. baseline: • Treated = -15.9 (2.8)% • Placebo = -11.9 (2.7)%
			Placebo	261			
Mansfield, 2010 (37)	SAR	M/S	Levocetirizine	235	Mean (SD) % work time missed at baseline and endpoint: • Treated = 4.5 (12.9); 1.2 (4.9) • Placebo = 3.5 (9.8); 2.3 (8.8) Mean (95% CI) % difference vs. placebo at endpoint: -1.4 (-2.6; -0.2)	Mean (SD) % work impairment at baseline and endpoint: • Treated = 51.8 (24.2); 37.8 (21.4) • Placebo = 49.0 (24.2); 40.9 (24.1) Mean (95% CI) % difference vs. placebo at endpoint: -4.6 (-8.3; -0.9)	Mean (SD) % impairment in overall work productivity: • Treated = 52.9 (24.9); 38.2 (21.8) • Placebo = 49.9 (24.6); 40.9 (24.1) Mean (95% CI) % difference vs. placebo at endpoint: -4.4 (-8.2; -0.6)
			Placebo	233			
Meltzer, 2010 (38)	PAR	M/S	Mometasone	20	Mean difference vs. baseline: • Treated = -2.2% • Placebo = +5.8%	Mean difference vs. baseline: •Treated = -1.9% • Placebo = -0.1%	NA
			Placebo	9			
Segall, 2010 (39)	SAR	M/S	Levocetirizine	216	NA	NA	Adjusted mean difference between groups = -4.44%
			Placebo	227			

Legend: AR: allergic rhinitis; IAR = intermittent AR; PAR = persistent AR; SAR = seasonal AR; M/S = moderate/severe AR; NA: not available; Olo: Olopatadine nasal spray;

Table 5. Estimated costs of lost work productivity due to rhinitis

Reference	Study design	Monetary unit (year)	Average daily wage[¥]	Cost of absenteeism, mean per patient per yr	Cost of presenteeism, mean per patient per yr	Total cost of lost work productivity, mean per patient per yr	Direct medical costs, mean per patient per yr
Bousquet, 2005 (32)	RCT of levocetirizine vs. placebo (6 mo), 5 EU countries; 2001-2002	€ (2002)	106.76				
	Levocetirizine group			153.96	589.20 (3.8)*	743.16 (3.4)†	218.16
	Placebo group			406.80	948.12 (2.3)*	1,354.92 (13.5)†	100.44
Lamb, 2006 (18)	Survey of 8,267 US employees (WPSI, 12 mo); 2001-2002	US$ (2002)	274.00	182.99	409.56 (2.2)*	592.58	NA
Kim, 2010 (24)	Population survey based on Korean NHIC data; 2007	US$ (2009)	82.51	11.53	NA	NA	49.10
Jantunen, 2014 (41)	Nationwide questionnaire panel survey, Finland ; 2013	€ (2011)	141.00	111.40	511.80 (4.6)*	623.20	NA
Cardell, 2016 (42)	Questionnaire-based survey of a random population sample, Sweden; 2014	€ (2014)	NA	78.0	672.8 (8.6)*	750.8 (3.6)†	210.3
Colas, 2016 (43)	Questionnaire-based survey of 498 AR participants recruited in a national random sample of 101 specialized clinics; follow-up of 12 mo; Spain; 2009	€ (2010)	NA	90.19	1,682.71 (18.7)*	1,772.90 (3.2)†	553.80

Legend: NHIC: National Health Insurance Corporation; RCT: randomized controlled trial; WPSI: Work Productivity Short Inventory questionnaire.

* Cost of presenteeism/cost of absenteeism ratio

† Total cost of lost productivity/direct medical cost ratio;

[¥] National average of workers' daily wage used by investigators to calculate the cost components of AR.

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