# Direct and indirect costs of allergic and non-allergic rhinitis in the Netherlands 

To the Editor,
Chronic rhinitis is a symptomatic inflammation of nasal mucosa that lasts at least 12 weeks per year. Both allergic (AR) and non-allergic (NAR) rhinitis are highly prevalent: they affect about $30 \%$ and $10 \%$ of population, respectively. ${ }^{1}$ About $30 \%$ of patients with chronic rhinitis have a mixed form, and several endotypes of chronic rhinitis have been described. ${ }^{2}$ Considering the high prevalence and the impact on general well-being, ${ }^{3}$ chronic rhinitis has a significant financial impact due to direct costs (medications, healthcare visits etc) and indirect costs (absenteeism and presenteeism). To our knowledge, no data on financial costs of non-allergic rhinitis are currently available.

In order to estimate direct and indirect costs of allergic and non-allergic rhinitis in the Netherlands, we performed a cross-sectional study in patients with allergic and non-allergic rhinitis visiting their family doctors and the patients of the Department of Otorhinolaryngology of Amsterdam UMC, location AMC, in the Netherlands (secondary/tertiary healthcare facility). Details on the materials and methods are given in the online repository (App S1).

Questionnaires were obtained from 512 participants with rhinitis and 23 healthy controls. By the nature of these questionnaires, direct costs and absenteeism were not disease-specific, whereas presenteeism was. The characteristics of the study population are presented in Table 1. The baseline characteristics of the control group were comparable to the chronic rhinitis groups.

Total costs of chronic rhinitis were $€ 5042$ patient/year ( $€ 5258$ patient/year of NAR, € $£ 827$ patient/year of AR). Direct costs were $€ 1043$ patient/year vs $€ 793$ in controls. As the direct costs were not disease-specific, the most expensive component was daycare procedures (such as grommets placement, immunotherapy and gastroscopy). In the (relatively small) control group, average direct costs were dominated by specialist visits and hospital admission by some subjects. Indirect costs in the chronic rhinitis group were €3999 patient/year: $€ 1329$ for absenteeism, $€ 2390$ for (disease-specific) presenteeism and $€ 280$ for unpaid work (Table 2). On average, absenteeism costs were increased fourfold in rhinitis patients compared with controls, while presenteeism costs were increased eightfold. As such, the average total costs in rhinitis patients were increased with around $€ 3650$ patient/year, mainly due to a significant increase in presenteeism costs. Indeed, presenteeism costs were the highest component in all employed subgroups, except for those with mild rhinitis and those currently smoking.

According to the Central Bureau of Statistics, each year 5\% of the Dutch population are seeking medical care due to allergic rhinitis complaints, which is about 730000 patients of 16 years and older.

Costs of these patients alone are around $€ 3.5-€ 4.0$ billion a year ( $€ 750$ million due to direct, $€ 3$ billion due to indirect costs). Chronic rhinosinusitis (CRS) costs per patient are even higher than chronic rhinitis costs. In the Netherlands, CRS costs were found to be $€ 7160$ patient/year ( $€ 1501$ for direct and $€ 5659$ for indirect costs). ${ }^{4}$ But due to a lower prevalence, total annual costs of CRS are lower than those of chronic rhinitis, corresponding to $€ 2$ billion annually.

The presented data could also be used as an estimation of the true costs of chronic rhinitis in the Netherlands. The current numbers could be an overestimation: the study included patients seeking medical care, mainly suffering from moderate/severe rhinitis, while in the general population, the proportion of mild chronic rhinitis cases is higher. ${ }^{5}$ As such, the average costs per patient in the general population are probably lower. Indeed, compared to the TOTALL study conducted in Sweden, rhinitis costs in our study were higher: $€ 5042$ vs $€ 961$ patient/year for total costs, while the same trends could be observed with presenteeism being the most expensive component. ${ }^{6}$ The TOTALL study included participants with self-reported allergic rhinitis, leading to $62 \%$ of the sample having mild rhinitis (compared to $11 \%$ in our study). Indeed, in studies including patients seeking medical care, the costs were higher: in Germany, in 2003 the total costs of allergic rhinitis (excluding productivity costs) were estimated to be around $€ 1.543$ patient/year. ${ }^{7}$ Ten years after, the direct costs of AR patients in Germany were estimated to be $€ 1546$ patient/year. ${ }^{8}$

Of course, other factors contributed largely to the found differences such as inclusion of NAR, reference prices and general healthcare expenditures. Still, if we would assume the same $62 \%$ of rhinitis patients to be mild in the Dutch population, the average costs would be $€ 3761$ patient/year. Assuming a prevalence of chronic rhinitis of $30 \%$, the total costs in the general population would be at least $€ 19.6$ billion.

On the other hand, there are several factors that could lead to underestimation of the costs. First, the last update of the used reference standard is based on prices of 2014, negating inflation of costs between 2015 and 2020. Second, for the calculation of medication costs we used a price of only one package of each reported medication at the lowest price reported by the Pharmacotherapeutic Compass of the Dutch National Healthcare Institute. Moreover, the participants only reported medication that they were currently using. We would estimate that both factors combined would give a $10 \%$ rise of the costs, meaning on average €4137 patient/year, or $€ 21.6$ billion annually in the Netherlands.

TABLE 1 Characteristics of the participants

|  | NAR N = 159 | AR N = 350 | Total rhinitis $\mathrm{N}=512^{\text {a }}$ | Controls $\mathrm{N}=23$ |
| :---: | :---: | :---: | :---: | :---: |
| Primary care patient | 84 (53\%) | 288 (82\%) | 375 (73\%) | $\mathrm{n} / \mathrm{a}$ |
| Secondary/tertiary care patient | 75 (47\%) | 62 (18\%) | 137 (27\%) | n/a |
| Age | $44.9 \pm 17.7$ | $37.3 \pm 13.7$ | $40.0 \pm 15.4$ | $43.1 \pm 15.6$ |
| Gender |  |  |  |  |
| Male | 52 (33\%) | 128 (36\%) | 182 (35\%) | 5 (22\%) |
| Female | 106 (66\%) | 219 (63\%) | 326 (64\%) | 18 (78\%) |
| No answer | 1 (1\%) | 3 (1\%) | 4 (1\%) | 0 |
| Education |  |  |  |  |
| No education | 1 (0.5\%) | 1 (0.5\%) | 2 (0.5\%) | 0 |
| Primary education | 1 (0.5\%) | 6 (2\%) | 7 (1.5\%) | 1 (4.5\%) |
| Lower secondary education | 27 (17\%) | 46 (13\%) | 74 (15\%) | 2 (9\%) |
| Upper secondary education | 61 (38.5\%) | 139 (39.5\%) | 201 (40\%) | 5 (22\%) |
| Bachelor or equivalent | 43 (27\%) | 100 (28\%) | 144 (28\%) | 7 (30\%) |
| Master or equivalent | 15 (10\%) | 39 (11\%) | 54 (10\%) | 7 (30\%) |
| Other | 10 (6\%) | 16 (5\%) | 26 (5\%) | 1 (4.5\%) |
| Unknown | 1 (0.5\%) | 3 (1\%) | 4 (1\%) | 0 |
| Present employment |  |  |  |  |
| Student | 23 (14\%) | 49 (14\%) | 72 (14\%) | 1 (4\%) |
| Paid employment | 80 (50\%) | 222 (63\%) | 304 (59\%) | 16 (70\%) |
| Self-employed | 16 (10\%) | 26 (7\%) | 42 (8\%) | 2 (9\%) |
| Housewife | 8 (5\%) | 19 (5\%) | 28 (6\%) | 0 |
| Unemployed | 4 (3\%) | 10 (3\%) | 14 (3\%) | 0 |
| Disabled | 4 (3\%) | 9 (3\%) | 13 (2\%) | 0 |
| Pension | 22 (14\%) | 10 (3\%) | 32 (6\%) | 4 (17\%) |
| Other | 2 (1\%) | 3 (1\%) | 5 (1\%) | 0 |
| Unknown |  | 2 (1\%) | 2 (1\%) | 0 |
| ARIA classification |  |  |  |  |
| Mild | 26 (16\%) | 31 (9\%) | 57 (11\%) | $\mathrm{n} / \mathrm{a}$ |
| Moderate/severe | 123 (78\%) | 304 (87\%) | 430 (84\%) | n/a |
| Unknown | 10 (6\%) | 15 (4\%) | 25 (5\%) | $\mathrm{n} / \mathrm{a}$ |
| QoL VAS | $71.0 \pm 18.8$ | $74.1 \pm 19.1$ | $73.1 \pm 19.0$ | $85 \pm 12.6$ |
| CARAT nasal domain | $6.5 \pm 3.0$ | $6.3 \pm 3.0$ | $6.3 \pm 3.0$ | $\mathrm{n} / \mathrm{a}$ |
| Controlled CARAT, nasal domain, N | 56 (40\%) | 109 (37\%) | 165 (38\%) | $\mathrm{n} / \mathrm{a}$ |
| Blocked nose |  |  |  |  |
| (Almost) every day | 68 (43\%) | 115 (33\%) | 183 (36\%) | n/a |
| More than 2 d a week | 34 (21\%) | 64 (18\%) | 100 (19\%) | $\mathrm{n} / \mathrm{a}$ |
| 1 or 2 d a week | 26 (16\%) | 105 (30\%) | 131 (26\%) | n/a |
| Never | 31 (20\%) | 62 (18\%) | 94 (18\%) | $\mathrm{n} / \mathrm{a}$ |
| CARAT pulmonary domain | $13.3 \pm 3.5$ | $13.3 \pm 3.8$ | $13.2 \pm 3.7$ | n/a |
| Controlled CARAT, pulmonary domain, N | 42 (28\%) | 108 (32\%) | 150 (30\%) | $\mathrm{n} / \mathrm{a}$ |
| CARAT total | $20.0 \pm 5.2$ | $20.0 \pm 5.5$ | $20.0 \pm 5.4$ | n/a |
| Presence of asthma/pulmonary complaints | 37 (26\%) | 91 (28\%) | 129 (27\%) | 2 (10\%) |
| Diagnosed asthma | 16 (11\%) | 73 (22\%) | 89 (19\%) | 1 (4\%) |
| Smoking status |  |  |  |  |
| Current smoker | 30 (19\%) | 53 (15\%) | 84 (17\%) | 3 (13\%) |

TABLE 1 (Continued)

|  | NAR N = 159 | AR N = 350 | Total rhinitis $\mathrm{N}=512^{\text {a }}$ | Controls $\mathrm{N}=23$ |
| :---: | :---: | :---: | :---: | :---: |
| Former smoker | 39 (25\%) | 64 (18\%) | 104 (21\%) | 7 (30\%) |
| Never smoked | 87 (56\%) | 230 (66\%) | 318 (62\%) | 13 (57\%) |
| Allergy type |  |  |  |  |
| Grass/tree pollen |  | 303 (89\%) |  |  |
| House dust mite |  | 184 (54\%) |  |  |
| Other |  | 133 (39\%) |  |  |
| Immunotherapy use |  |  |  |  |
| SCIT |  | 30 (9\%) |  |  |
| SLIT |  | 15 (4\%) |  |  |

Abbreviations: AR, allergic rhinitis; ARIA, Allergic Rhinitis and its Impact on Asthma; CARAT, Control of Allergic Rhinitis and Asthma Test; NAR, nonallergic rhinitis; SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy; VAS, visual analogue scale.
${ }^{\text {a }}$ The total number of rhinitis patients is higher than the sum of AR and NAR patients, because in three patients, no allergy test data were available. Their answers were used for calculation of costs in the "Total rhinitis" group.

TABLE 2 Subgroup analyses of patients with chronic rhinitis, mean costs per individual/year, €

|  | N | Direct costs | Indirect costs: absenteeism | Indirect costs: presenteeism | Indirect costs: unpaid work | Total costs ${ }^{\text {a }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Controls | 23 | 793 | 330 | 285 | 0 | 1408 |
| All rhinitis | 512 | 1043 | 1329 | 2390 | 280 | 5042 |
| NAR | 159 | 1110 | 1374 | 2195 | 580 | 5258 |
| AR | 350 | 1001 | 1252 | 2429 | 145 | 4827 |
| Primary patient | 375 | 621 | 1408 | 2118 | 72 | 4218 |
| Secondary/tertiary patient | 137 | 2200 | 1113 | 3135 | 850 | 7298 |
| Gender |  |  |  |  |  |  |
| Male | 182 | 1197 | 1866 | 3146 | 175 | 6384 |
| Female | 326 | 959 | 1045 | 1997 | 342 | 4343 |
| Age subgroups |  |  |  |  |  |  |
| 16-18 | 4 | 259 | 853 | 0 | 0 | 1112 |
| 18-29 | 155 | 1066 | 1202 | 2011 | 309 | 4588 |
| 30-44 | 150 | 740 | 1324 | 2325 | 431 | 4821 |
| 44-65 | 159 | 934 | 1837 | 3079 | 163 | 6013 |
| 65+ | 36 | 2294 | 0 | 1243 | 112 | 3649 |
| Education |  |  |  |  |  |  |
| No education | 2 | 1776 | 0 | 0 | 420 | 2196 |
| Primary education | 7 | 4987 | 2726 | 542 | 0 | 8256 |
| Lower secondary education | 74 | 892 | 238 | 1347 | 95 | 2572 |
| Upper secondary education | 201 | 1073 | 1608 | 2634 | 95 | 5410 |
| Bachelor or equivalent | 144 | 884 | 1797 | 2808 | 502 | 5991 |
| Master or equivalent | 54 | 919 | 887 | 2234 | 442 | 4482 |
| Other | 26 | 1455 | 534 | 2302 | 782 | 5043 |

TABLE 2 (Continued)

|  | N | Direct costs | Indirect costs: absenteeism | Indirect costs: presenteeism | Indirect costs: unpaid work | Total costs ${ }^{\text {a }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Employment status |  |  |  |  |  |  |
| Student | 72 | 1320 | 525 | 1202 | 306 | 3353 |
| Paid employment | 304 | 703 | 1884 | 3007 | 160 | 5754 |
| Self-employed | 42 | 947 | 1377 | 5045 | 308 | 7677 |
| Housewife | 28 | 1613 | 0 | 262 | 2052 | 3927 |
| Unemployed | 14 | 849 | 0 | 0 | 0 | 849 |
| Disabled | 13 | 3657 | 0 | 0 | 65 | 3722 |
| Pension | 32 | 2276 | 0 | 118 | 42 | 2436 |
| Other | 5 | 1165 | 2427 | 0 | 0 | 4072 |
| ARIA classification |  |  |  |  |  |  |
| Mild | 57 | 970 | 1443 | 242 | 0 | 2655 |
| Moderate/severe | 430 | 1041 | 1389 | 2804 | 333 | 5566 |
| Diagnosed with asthma | 89 | 1506 | 470 | 1511 | 242 | 3728 |
| Self-reported asthma/ pulmonary complaints | 129 | 1391 | 651 | 2456 | 255 | 4753 |
| No self-reported asthma/ pulmonary complaints | 345 | 950 | 1586 | 2489 | 303 | 5328 |
| Smoking status |  |  |  |  |  |  |
| Current smoker | 84 | 1382 | 2613 | 1702 | 598 | 6294 |
| Former smoker | 104 | 967 | 1293 | 3286 | 126 | 5674 |
| Never smoked | 318 | 990 | 1026 | 2310 | 252 | 4578 |

Abbreviations: AR, allergic rhinitis; ARIA, Allergic Rhinitis and its Impact on Asthma; NAR, non-allergic rhinitis.
${ }^{\text {a}}$ Total direct costs are different from a sum of costs presented in the table due to rounding up of the numbers.

Since the largest portion of costs is rhinitis-related presenteeism, one could argue that these costs could possibly be reduced by appropriate management of chronic rhinitis. Indeed, two thirds of participants had uncontrolled nasal complaints (CARAT score) and more than a half had nasal congestion on more than 2 days a week. Currently, a lot of patients are not being treated according to the guidelines and often self-medicate. ${ }^{9}$ Possibly, if the patients will receive care according to the guidelines, their complaints, and consequently presenteeism, could be reduced. Future prospective studies evaluating costs of patients receiving the treatment according to the guidelines are needed.

To our knowledge, this is the first study to report costs of NAR. Future studies are needed to understand the costs of chronic rhinitis (especially of non-allergic rhinitis) in the general population.

## CONCLUSION

The costs of both allergic and non-allergic rhinitis are high, with presenteeism being the most expensive component.

## ACKNOWLEDGMENTS

Dr Avdeeva reports grants from ALK, from Allergy Therapeutics, from Mylan BV, during the conduct of the study. Dr Reitsma reports grants from ALK, from Allergy Therapeutics, from Mylan BV, during the conduct of the study. Dr Fokkens reports grants from ALK, from Allergy Therapeutics, from Mylan BV, during the conduct of the study.

## CONFLICTS OF INTEREST

This study was helped with an educational grant of MEDA, ALK and Allergy Therapeutics.

Klementina S. Avdeeva
Sietze Reitsma
Wytske J. Fokkens

Department of Otorhinolaryngology, Amsterdam UMC, Location
Academic Medical Centre, Amsterdam, The Netherlands

Correspondence
Klementina S. Avdeeva, KNO research, Amsterdam UMC,
location Academic Medical Centre, Meibergdreef 9, 1105 AZ
Amsterdam, The Netherlands.
Email: k.avdeeva@amsterdamumc.nl

## ORCID

Klementina S. Avdeeva (iD https://orcid.org/0000-0002-3910-4371 Wytske J. Fokkens (iD https://orcid.org/0000-0003-4852-229X

## REFERENCES

1. Reitsma S, Subramaniam S, Fokkens WWJ, Wang Y. Recent developments and highlights in rhinitis and allergen immunotherapy. Allergy. 2018;73(12):2306-2313.
2. Meng Y, Lou H, Wang Y, et al. Endotypes of chronic rhinitis: a cluster analysis study. Allergy. 2019;74(4):720-730.
3. Segboer CL, Terreehorst I, Gevorgyan A, Hellings PW, van Drunen CM, Fokkens WJ. Quality of life is significantly impaired in nonallergic rhinitis patients. Allergy. 2018;73(5):1094-1100.
4. Lourijsen ES, Fokkens WJ, Reitsma S. Direct and indirect costs of adult patients with chronic rhinosinusitis with nasal polyps. Rhinology. 2020;58(3):213-217.
5. Wang XD, Zheng M, Lou HF, et al. An increased prevalence of self-reported allergic rhinitis in major Chinese cities from 2005 to 2011. Allergy. 2016;71(8):1170-1180.
6. Cardell L-O, Olsson P, Andersson M, et al. TOTALL: high cost of allergic rhinitis-a national Swedish population-based questionnaire study. NPJ Prim Care. Respir Med. 2016;26:15082-.
7. Schramm B, Ehlken B, Smala A, Quednau K, Berger K, Nowak D. Cost of illness of atopic asthma and seasonal allergic rhinitis in Germany: 1-yr retrospective study. Eur Respir J. 2003;21(1):116-122.
8. Tesch F, Domdey A, Sydendal Grand T, et al. Healthcare costs associated with allergic rhinitis, asthma allergy immunotherapy. Eur Ann Allergy Clin Immunol. 2019. http://www.eurannallergyimm.com/cont/online-first /757/original-articlebrhealthcare-costs-associated-with-allergic-rhini tis-3500allasp1.pdf. [Epub ahead of print].
9. Bousquet J, Devillier P, Arnavielhe S, et al. Treatment of allergic rhinitis using mobile technology with real-world data: the MASK observational pilot study. Allergy. 2018;73(9):1763-1774.

## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

# Is time to remove parabens from standard patch test batteries? Retrospective study of 10461 patients 

To the Editor
Parabens are para-hydroxybenzoic acid esters that have been used for almost 100 years as preservatives in cosmetics, drugs, and foods. ${ }^{1}$ Sensitization to parabens was first described in the 1940s, and these compounds were subsequently included in the standard patch test batteries. Data based on weak scientific evidence have attributed parabens with carcinogenic, infertility, and endocrine disruption effects. Genuine phobia toward these compounds, adoption of "paraben-free" labeling on cosmetic products, and European regulations were introduced. ${ }^{2}$ Parabens are currently regarded as weakly sensitizing compounds, with sensitization rates of under $1 \%{ }^{3}$ However, only few studies have assessed the current situation after those changes.

We sought to describe the rate of sensitization to parabens in a large series of patients and to analyze the relationship between the European regulations and the changes in incidence. As a secondary objective, their clinical-epidemiological characteristics were evaluated.

A retrospective observational study including patients sensitized to parabens seen in the Department of Dermatology of a Spanish Hospital between January 1980 and June 2019. The study data were compiled from the skin allergy database of the Department.

Patch testing was performed according to International Contact Dermatitis Research Group guidelines, with readings taken on days 2 and 4. Positive patch test reactions to parabens ( $16 \%$ in petrolatum) were recorded. A descriptive statistical analysis of all variables included in the MOAHLFA index was performed. The chi-squared test was used for statistical testing. The SPSS version 26.0 statistical package (IBM, Armonk, NY, USA) was used throughout. Statistical significance was considered for $P<.05$.

Patch tests were performed in 10461 patients. Sensitization to parabens was established in 60 patients ( $0.57 \%$ ). In 31 cases, sensitization was of current relevance ( $51.7 \%$ ), being more frequent methylparaben (37.5\%), propylparaben (37.5\%), benzylparaben (12.5\%), and butylparaben ( $37.5 \%$ ). In 7 cases, sensitization was past relevance ( $11.7 \%$ ) and in 22 of unknown relevance ( $36.7 \%$ ). The mean incidence of sensitization was $0.58 \%$. It was higher in the early period between 1980 and 2002 ( $0.75 \%$ ), and then decreased to $0.33 \%$ between 2003 and 2018 (Figure 1).

Allergic contact dermatitis affected mainly the hands (19.3\%), legs (18.5\%), face (13.4\%), and arms (10.1\%), while $11.8 \%$ of the patients presented with generalized involvement (three or more affected body regions). Sensitization was iatrogenic in $59.6 \%$ of the cases, due to cosmetics in $26.9 \%$, occupational in $7.7 \%$, and attributable to

