## THE ECONOMIC COST DUE TO POOR DISEASE CONTROL IN ADULT PATIENTS WITH NEUTROPHILIC ASTHMA FROM THE GENERAL ITALIAN POPULATION

Lando V[1], Miotti J[1], Martinelli L[1], Calciano L[1], Tardivo S[2], Corsico A[3], Accordini S[1]

*1- Unit of Epidemiology and Medical Statistics, Department of Diagnostics and Public Health, University of Verona - Verona (Italy)*
*2- Unit of Hygiene and Preventive, Environmental and Occupational Medicine, Department of Diagnostics and Public Health, University of Verona - Verona (Italy)*
*3- Department of Internal Medicine and Therapeutics, University of Pavia - Pavia (Italy)*

### Introduction

Asthma is a complex inflammatory disease of the airways involving multiple genetic, environmental and lifestyle-related factors [1]. Airway inflammation is driven by the recruitment of inflammatory cells, i.e. eosinophils and/or neutrophils, produced in the bone marrow by myeloid stem cells [2]. Often, the neutrophilic endotype represents a severe form of the disease, characterised by frequent respiratory symptoms and hospital admissions, difficulty of treatment and poor prognosis [3]. The economic burden of asthma is significantly influenced by the extent of poor disease control, which increases the use of hospital services and causes loss of productivity and leisure time [4]. Cost-of-illness analysis [5] is an important decision-making tool to quantify the economic burden of a disease and to plan cost-containment policies, as information is collected at the individual level from representative samples of patients.

### Aim

To provide a real-life assessment of the economic cost generated by poor disease control in adult patients with neutrophilic asthma, identified from a random sample of the general population in Italy.

### Methods

A prevalence-based cost-of-illness study, which is a cross-sectional assessment of the economic impact of the disease over one year, regardless of the date of onset [6], was performed on adult subjects with current asthma and with low (<5000 cells/mm$^{-3}$; n=168, mean age 43.1 years, female 46.4%) or high (≥5000 cells/mm$^{-3}$; n=56, mean age 41.6 years, female 50.0%) blood neutrophils [7]. These patients were identified within the Gene Environment Interactions in Respiratory Diseases (GEIRD; 2008-2014) survey in Verona, Italy. GEIRD is an Italian population based (multi)case-control survey, where cases and controls were recruited through a two-stage screening process (postal questionnaire and clinical examination). Information on direct medical expenditures (number of emergency department visits and number of hospital admissions) and on loss of productivity and leisure time (number of lost working days and number of days with limited daily life activities, such as looking after the children, housework, studying) due to breathing problems in the past 12 months was collected by a clinical interview [4]. All costs were calculated from the societal perspective following the bottom-up approach based on 2013 rates, wages, and prices (obtained from official Italian sources). The mean annual cost per patient (with the 95%CI) was estimated separately by neutrophil level (high *vs* low) using a two-part model (first part: logistic regression; second part: gamma regression) [8] with robust standard errors. The 95% confidence limits of the mean survival time, considering cost as the "time" variable, was computed for the patients with non-zero costs to relax the distribution assumption of the conditional model, as it might be advantageous particularly for data with skewness and a heavy tail [9].

### Results

The mean annual cost per patient due to poor disease control was 156 (95%CI: 86-225) and 400 (95%CI: 82-719) euro for the asthmatic subjects with low or high blood neutrophils, respectively. The individual annual economic burden was 1,005 (95%CI: 735-1,275) euro for the 26/168 (15.5%) patients with non-zero costs and low blood neutrophils, whereas it was 2,241 (95%CI: 981-3,501) euro for the 10/56 (17.9%) patients with non-zero costs and high blood neutrophils. The 95% confidence limits of the mean survival time in the two groups of patients (low blood neutrophils, 739-1,272 euro; high blood neutrophils, 999-3,484 euro) were similar to the 95% confidence limits of the mean annual cost per patient obtained using the gamma model.

**Conclusion**

The individual annual cost due to poor disease control in adult patients with asthma from the general Italian population increases significantly with the level of blood neutrophils. Our real-world estimates may be policy relevant and can be used in combination with other information to develop a targeted perspective on healthcare of patients with endotype with treatment difficulties.

**Bibliography**

[1] Kauffmann F., Demenais F. Gene-environment interactions in asthma and allergic diseases: challenges and perspectives. J Allergy Clin Immunol., 2012; 130: 1229-40.

[2] Hammad H., Lambrecht B.N. The basic immunology of asthma. Cell., 2021 Mar 18; 184: 1469-85.

[3] Syabbalo N. Neutrophilic asthma: a complex phenotype of severe asthma. J Lung Pulm Respir Res., 2020; 7: 18-24.

[4] Accordini S., Corsico A.G., Braggion M., et al. The cost of persistent asthma in Europe: an international population-based study in adults. Int Arch Allergy Immunol., 2013; 160: 93-101.

[5] Akobundu E., Ju J., Blatt L., et al. Cost-of-Illness Studies. A Review of Current Methods. Pharmacoeconomics, 2006; 24: 869-90.

[6] Tarricone R. Cost-of-illness analysis. What room in health economics?. Health Policy, 2006; 77: 51-63.

[7] Nadif R., Siroux V., Boudier A., et al. Blood granulocyte patterns as predictors of asthma phenotypes in adults from the EGEA study. Eur Respir J., 2016; 48: 1040-51.

[8] Belotti F., Deb P., Manning W.G., et al. twopm: Two-Part Models. Stata Journal, 2015; 15: 3-20.

[9] Mihaylova B., Briggs A., O'Hagan A., et al. Review of statistical methods for analysing healthcare resources and costs. Health Econ., 2011; 20: 897-916.