

# In Italy anti-asthmatic drug prescription is not always a reliable proxy of asthma

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We read with interest the article by Pitter et al. [1], in which an association was found between antibiotics therapy during the first year of life and an increased risk of subsequent treatment-required asthma. The association between early exposure to antibiotics and asthma is still debated, however, in our opinion the study by Pitter et al. has a relevant limitation. Healthcare databases can be a valuable tool for monitoring diseases, and in this regard strategies for estimating asthma prevalence have been developed, also in Italian context [2].

It is well known that in Italy anti-asthmatic drugs, in particular nebulised steroids, are commonly prescribed as symptomatic treatment of upper respiratory tract infections. An analysis of drugs prescribed by paediatricians found that, in 60 % of the cases, the reasons for prescribing nebulised steroids were cough, pharyngotonsillitis, rhinitis, otitis media and sinusitis [3]. This pattern of prescription is even more frequent in pre-school children. Moreover, independently of age, in Italy the number of non asthmatic children and adolescents treated with inhaled corticosteroids is ten times higher than in UK or in The Netherlands [4].

Thus, the criteria “at least two anti-asthmatic drug prescriptions within a period of 12 months” overestimates the number of children with asthma, and it is likely that many of them had respiratory tract infections only (false

positives). Also the choice to restrict to “at least two inhaled corticosteroids or combination of asthma drugs” did not reduce the risk of overestimation.

This bias is greater in children 13–35 months group, where an IRR of 2.07 was found. In this age group it should be considered also the presence of viral wheezing as a further confounding factor.

Anyway, it is likely that an overestimation exists also in children  $\geq 6$  years old, in which a current prevalence of asthma of 13.2 % was estimated, as well as in those  $\geq 13$  years old.

In order to identify asthmatic patients we previously proposed criteria different from those adopted by Pitter et al.: age  $\geq 6$  years AND at least one prescription of appropriate age formulation of anti-asthmatic drugs (i.e. metered dose inhalers, dry powder inhalers) [2]. Children who received nebulised formulation only were not considered as “potential asthmatics”. These criteria have been validated: the sensitivity was 0.91 (95 % CI 0.67–1.00), and the specificity was 0.98 (95 % CI 0.96–1.00) [5]. Using the above criteria we identified 2518 potential asthmatic (5.2 %) patients at 6 years of age in a cohort of 48,020 Italian children born in 2000–2001 living in the Lombardy Region. A total of 5036 non-asthmatic controls were randomly selected from the same cohort and matched (with a case–control 1:2 ratio) for gender, year of birth, and local health unit of residence. In all, 29 % of cases and 27 % of controls received at least one antibiotic drug prescription during the first 6 months of life (OR 1.13, 95 % CI 1.01–1.26,  $p = 0.02$ ) <http://pediatrics.aappublications.org/content/127/6/1125.comments>).

In our analysis, a statistically significant increased risk of asthma was found, but the magnitude was lower than that found in the study by Pitter et al. It is likely that the difference in magnitude is due to the overestimation of

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asthma cases in the study by Pitter and colleagues, as already discussed, thus, we would like to suggest to Pitter et al. to perform a sensitivity analysis excluding from the classification of asthmatic patients children who received only R03 drugs with a nebulised formulation, comparing and discussing new findings with previous ones published.

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