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**Title:** Nocturnal gastroesophageal reflux, asthma and symptoms of obstructive sleep apnea: A longitudinal, general population study

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**Body:** Background Nocturnal gastroesophageal reflux (nGER) is associated with asthma and obstructive sleep apnea (OSA) in observational studies, but prospective epidemiological studies are lacking. Our aim was to investigate whether nGER is a risk factor for onset of asthma, respiratory and OSA symptoms in a prospective population based study. Methods We invited 2640 randomly selected subjects from Iceland, Sweden and Belgium for two evaluations with a nine years interval (participation rate 66.7%). They participated in a structured interview, answered a questionnaire regarding respiratory symptoms, sleep and nGER, underwent spirometry and a methacholine challenge. Blood samples were analyzed for specific IgE. Results Subjects with persistent nGER (n = 123) had an increased risk of asthma at follow-up after 9 years, independent of gender, age, location, smoking history, BMI at baseline and change in BMI [OR (95% CI): 2.3 (1.1-4.9)]. Persistent nGER was also independently related to the onset of various respiratory symptoms (OR (95% CI): 3.0 (1.6-5.6)). The risk of developing symptoms of OSA was increased in subjects with new onset of nGER and persistent nGER [OR (95% CI): 2.2 (1.3-1.6) and 2.0 (1.0-3.7), respectively]. No significant independent association was found between nGER and lung function or bronchial responsiveness. Conclusions Persistent nocturnal gastroesophageal reflux contributes to the development of asthma and respiratory symptoms. The risk of new onset of OSA symptoms is also higher among subjects with nGER. These findings further support the conclusion that nGER may play a causative role in the genesis of respiratory symptoms and diseases.

