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**Title:** Novel asthma definition for epidemiological studies

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**Body:** Background: The best definition of asthma for epidemiological studies is still debated. In clinics the absence and occurrence of wheeze between episodes is used to classify the syndrome into episodic and unremitting (multitrigger) wheeze, respectively. The latter should be treated with anti-inflammatory agents whereas for episodic wheeze treatment should only be initiated within episodes. These concepts have not been evaluated in population based studies. Methods: The multi-centre PASTURE birth cohort enrolled 1133 children and followed them up to age 6 years. A doctor's diagnosis of asthma ever was assessed at age 6. Unremitting wheeze was defined as wheezy children with symptoms between episodes from age 1-6. Moreover, we performed a Latent Class Analysis (LCA) to identify wheezing phenotypes over time. Results: LCA identified four classes which were very similar to those found in other studies (ALSPAC, PIAMA). Unremitting wheeze was better represented in the intermediate, late onset and persistent classes than a doctor's diagnosis of asthma:

% of affected children in respective wheeze-class

children with...	transient	intermediate	late onset	persistent
...dr. diagnosis of asthma	11.3%	29.1%	42.9%	56.2%

...unremitting wheeze	39.6%	67.3%	81.6%	90.0%
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Unremitting wheeze was also significantly associated with atopy ( $p=0.0007$ ), with risk alleles on the asthma locus 17q21 (rs7216389,  $p=0.0003$ ) and with reduced lung function ( $FEV_1$ ;  $p=0.0009$ ). Interestingly, 58% of children with unremitting wheeze had not been labelled as 'asthma' but still showed significant reductions in lung function and significant associations with the chromosome 17 risk allele. Conclusion: Unremitting wheeze is a useful parameter also in population based studies.