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Title: Interactions between exposure to cigarette smoke and variations in the GSTM genotype for asthma quality of life

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Body: Background. Asthma is a heterogeneous condition and our hypothesis is that gene environment interactions explain some of the variation within the asthmatic population. Here we report on an interaction between exposure to second hand smoke (SHS, an oxidant stress) and variation in the gene coding for antioxidant protein GST-M for asthma outcomes. Methods Children with asthma were recruited from primary and secondary care across Scotland. A respiratory questionnaire and the Paediatric Asthma Quality of Life Questionnaire (PAQLQ) were completed and DNA collected. A subset underwent an assessment including spirometry and exhaled nitric oxide. Saliva was collected for cotinine analysis. Results From 894 children recruited, PAQLQ and DNA were obtained in 499 (56%). There were 88 children exposed to SHS. Compared to children null for GSTM who were not exposed to SHS, the overall PAQLQ score for exposed children null for GSTM was reduced (meaning worse quality of life) by a mean of -0.7 [95% CI -0.1, -1.3] p=0.020. Similar associations were present for domains of symptoms (mean difference -0.7 [-0.1, -1.3]) and emotions (mean difference -0.7 [-0.1, -1.2]) but not activities (mean difference -0.3 [95% CI -0.9, +0.3]). There were no differences in spirometry or exhaled nitric oxide between GSTM null children who were and were not exposed to SHS. Conclusion Our findings support the hypothesis that gene environment interactions are important to some of the heterogeneity of asthma. Whilst all children with asthma should avoid SHS exposure, parents of children null for GTSM (50% of all asthmatics) might be considered for specific intervention.