



**HAL**  
open science

## Meta-analysis of 20 genome-wide linkage studies evidenced new regions linked to asthma and atopy.

Emmanuelle Bouzigon, Paola Forabosco, Gerard H. Koppelman, William O. C. M. Cookson, Marie-Hélène Dizier, David L. Duffy, David M. Evans, Manuel A. R. Ferreira, Juha Kere, Tarja Laitinen, et al.

### ► To cite this version:

Emmanuelle Bouzigon, Paola Forabosco, Gerard H. Koppelman, William O. C. M. Cookson, Marie-Hélène Dizier, et al.. Meta-analysis of 20 genome-wide linkage studies evidenced new regions linked to asthma and atopy.: Asthma and atopy genome linkage scan meta-analyses. *European Journal of Human Genetics*, 2010, 18 (6), pp.700-6. 10.1038/ejhg.2009.224 . inserm-00748654

**HAL Id: inserm-00748654**

**<https://inserm.hal.science/inserm-00748654>**

Submitted on 5 Nov 2012

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

**Meta-analysis of 20 genome-wide linkage studies evidenced new regions linked to asthma and atopy**

Emmanuelle Bouzigon<sup>1,2</sup>, Paola Forabosco<sup>3,4</sup>, Gerard H. Koppelman<sup>5</sup>, William O. C. M. Cookson<sup>6</sup>, Marie-Hélène Dizier<sup>7,8</sup>, David L. Duffy<sup>9</sup>, David M. Evans<sup>10</sup>, Manuel A. R. Ferreira<sup>9</sup>, Juha Kere<sup>11</sup>, Tarja Laitinen<sup>12</sup>, Giovanni Malerba<sup>13</sup>, Deborah A. Meyers<sup>14</sup>, Miriam Moffatt<sup>6</sup>, Nicholas G. Martin<sup>9</sup>, Mandy Y Ng<sup>15</sup>, Pier Franco Pignatti<sup>13</sup>, Mathias Wjst<sup>16,17</sup>, Francine Kauffmann<sup>8,18</sup>, Florence Demenais<sup>1,2</sup>, Cathryn M. Lewis<sup>3,15</sup>

(1) INSERM, U946, Paris, France, (2) Université d'Evry, Evry, France (3) King's College London, Department of Medical and Molecular Genetics, London, UK, (4) Istituto di Genetica delle Popolazioni-CNR, Alghero, Italy, (5) Department of Pediatric Pulmonology and Pediatric Allergology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands, (6) National Heart Lung Institute, Imperial College, London, UK, (7) INSERM, U535, Villejuif, France, (8) Univ Paris-Sud, IFR69, Villejuif, France, (9) Queensland Institute of Medical Research, Royal Brisbane Hospital, Brisbane, Australia, (10) Department of Social Medicine, University of Bristol, Bristol, UK, (11) Department of Biosciences and Nutrition, Karolinska Institute, Stockholm, Sweden, (12) Departments of Pulmonary Medicine and Medical Genetics, University of Helsinki, Helsinki, Finland, (13) Department of Mother and Child, and Biology-Genetics, Section of Biology and Genetics, University of Verona, Verona, Italy, (14) Center for Human Genomics, Wake Forest University, Winston Salem NC, USA, (15) King's College London, MRC SGDP Centre, Institute of Psychiatry, London, UK, (16) Institute of Experimental Pneumology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany, (17) Institute of Genetic Medicine, EURAC research, Bozen, Italy, (18) INSERM, U780, Villejuif, France

**Corresponding author:**

Emmanuelle Bouzigon,  
INSERM U946,  
Fondation Jean Dausset-CEPH,  
27 rue Juliette Dodu,  
75010 Paris - France  
Tel: +33 1 53725023 / Fax: +33 1 53725049  
E-mail: [emmanuelle.bouzigon@inserm.fr](mailto:emmanuelle.bouzigon@inserm.fr)

**Running title:** Asthma and atopy genome linkage scan meta-analyses

**Abstract**

Asthma is a common disorder that arises from a heterogeneous combination of environmental and genetic factors. In the context of GA2LEN (Global Allergy and Asthma European Network), we carried out meta-analyses of almost all genome-wide linkage screens conducted to date in 20 independent populations from different ethnic origin ( $\geq 3,024$  families with  $\geq 10,027$  subjects), for asthma, atopic asthma, bronchial hyper-responsiveness and five atopy-related traits (total IgE level, positive skin test response [SPT] to at least one allergen or to House Dust Mite, quantitative score of SPT [SPTQ] and eosinophils). We used the rank-based Genome Scan Meta-Analysis method to assess the strongest evidence for linkage within bins of traditionally 30cM width, and explored how these results were affected by bin definition. Meta-analyses were conducted in all studies and repeated in families of European ancestry. Genome-wide evidence for linkage was detected for asthma in two regions (2p21-p14 and 6p21) in European families ascertained through two asthmatic sibs. One region reached genome-wide significance level in all families (3p25.3-q24 for SPT) and three additional in European families (2q32-q34 for eosinophils, 5q23-q33 for SPTQ and 17q12-q24 for SPT). Tests of heterogeneity showed consistent evidence of linkage for SPTQ with 3p11-3q21 while between-study heterogeneity was detected for asthma with 2p22-p13 and 6p21, and for atopic asthma with 1q23-q25. This large-scale meta-analysis provides an important resource of information that can be used to prioritize further fine mapping studies but also to be integrated with genome-wide association studies to increase power and to better interpret outcomes of these studies.

**Keywords:** asthma, atopy, meta-analysis, linkage scan

## INTRODUCTION

Asthma is a complex and heterogeneous disease resulting from many genetic and environmental factors, with a wide spectrum of clinical manifestations.<sup>1</sup> Asthma is associated with intermediate biological and physiological phenotypes, including traits related to atopy and inflammation (total serum immunoglobulin E levels (IgE), specific IgE and skin test reactivity to common aero-allergens, and eosinophilia) and those related to lung function (forced expiratory volume in one second, and airway responsiveness).

Considerable efforts have been made over the past ten years to map the chromosomal location of genes potentially involved in the development of asthma. To date, 20 independent research groups have conducted genome-wide linkage scans, mainly for asthma and atopy-related phenotypes, in 24 different populations around the world.<sup>2</sup> These scans have led to the identification of eight genes by positional cloning but also to a large number of genomic regions that may harbour susceptibility genes.<sup>3</sup> However, many of these regions did not show strong evidence for linkage in individual studies and/or have not been replicated across studies. Lack of replication may derive from discrepancies in phenotype definition across studies, differences in family ascertainment schemes, differences in analytical methods, insufficient power to detect linkage and genetic heterogeneity of the disease.

Meta-analysis, combining results of genome-wide linkage screens, is one approach that can improve the information available from a series of under-powered studies. Thus, meta-analysis can be a powerful tool not only for strengthening the evidence of previously detected linkage regions but also for identifying novel regions where the genetic effect is too small to be detected in a single study. Meta-analysis cannot completely overcome the problem of genetic heterogeneity but can identify regions implicated in a subset of the pooled studies. Regions highlighted in meta-analysis of linkage can be useful to prioritize future gene localization studies, whether these are based on positional cloning or on follow-up of genome-wide association (GWA) studies. Moreover, it has been shown that taking into account prior linkage information in computing false-discovery rate can improve the power of GWA studies.<sup>4</sup> Recently, a meta-analysis of nine genome scans conducted in families of European-ancestry for asthma and three asthma-associated phenotypes (IgE, positive skin test response and bronchial hyper-responsiveness) identified several regions with suggestive evidence of linkage, but failed to reach genome-wide significance level.<sup>5</sup>

In the context of GA2LEN (Global Allergy and Asthma European Network, <http://www.ga2len.net/index.cfm?CFID=393465&CFTOKEN=35235253>), we conducted a collaborative meta-analysis of 20 genome-wide linkage scans conducted worldwide for the most studied phenotypes across studies: asthma, atopic asthma, bronchial hyper-responsiveness and five atopy-related phenotypes, using the Genome Scan Meta-Analysis method.<sup>6</sup> The inclusion of populations with different genetic ancestry allowed us to identify common genetic regions underlying the pathogenesis of asthma across populations and to evaluate the variability of linkage findings by formally testing for genetic heterogeneity between studies.<sup>7</sup> We also explored the robustness of our results by using different bin width definitions for the GSMA method.

## MATERIALS AND METHODS

### Study inclusion criteria

We identified 24 genome-wide linkage studies performed for asthma or asthma-associated phenotypes, using PubMed searches (last search updated January 2009, using the following keywords: "asthma", "atopy", "BHR", "IgE", "eosinophils", "skin tests", "genome search", "genome scan") and examining reference lists of papers in asthma genetics. Results were limited to English language papers. Searching was performed by the first author (EB) and the inclusion of data and decision strategy were mainly reviewed by the statistical genetic group (EB, PF, FD and CML). We excluded linkage studies of candidate regions, which considered only short regions of the genome. Linkage studies which overlapped in samples, or were extended versions of previous publications were identified, and only independent studies were included. Where studies had performed a two-stage analysis, genotyping more markers in targeted regions in stage 2, only stage 1 results were used, as GSMA requires a uniform distribution of markers and families across the genome.

Among the 24 eligible genome-wide linkage (GWL) scans, 20 were included in the present study. The four excluded studies, included two studies focusing on specific regions (positional cloning studies) that mentioned in their publication that they conducted genome-wide linkage study *but for whom no genome-wide results were published*,<sup>8,9</sup> one analysed only specific IgE which was not one of our phenotypes examined in the present paper<sup>10</sup> and one had no data available.<sup>11</sup> As described in Table 1, for 12 studies, we obtained data on marker maps and, for each phenotype, genome-wide linkage statistics (eg, LOD or NPL scores and/or p-values) from investigators<sup>12-20</sup> or from a website ([http://www.springerlink.com/content/8660v8526j362846/MediaObjects/439\\_2006\\_285\\_MOESM2\\_ESM.xls](http://www.springerlink.com/content/8660v8526j362846/MediaObjects/439_2006_285_MOESM2_ESM.xls)).<sup>21</sup> For seven studies, results were presented as chromosomal graphs from multipoint linkage analysis, and linkage scores were extracted using the digitising program Engauge Digitiser

(v.2.14, © Mark Mitchell, 2002, <http://digitizer.sourceforge.net/>) which converts curves into (x,y) co-ordinates.<sup>22-32</sup> Finally, for one study, we used data extracted from published tables, where only peak linkage statistics were shown.<sup>33,34</sup>

### Phenotypes analysed

Eight phenotypes were considered by this meta-analysis: asthma, atopic asthma, bronchial hyper-responsiveness (BHR), a positive skin prick test response to at least one allergen (SPT) or specifically to House Dust Mite (SPT to HDM), a quantitative measure of positive skin test response to allergens (SPTQ, corresponding to the proportion of positive skin prick tests), total serum immunoglobulin E levels (IgE) and eosinophil counts (EOS). Asthma definition was based on a physicians' diagnosis in six studies, on standardised questionnaires in four studies, or on self reporting and/or doctor diagnosed combined with different traits (bronchial hyper-responsiveness (BHR) and/or asthma therapy and/or hospitalization for asthma) in five studies. Finally, asthma was based on a decision algorithm in the Dutch study.<sup>15</sup> Atopic asthma phenotype was defined by adding to the previous definitions of asthma the presence of positive SPT (7 studies) and/or specific IgE (1 study). BHR definition was based on methacholine (4 studies) or histamine challenge tests (2 studies).

### Genome Search Meta-Analysis

Results from individual GWL scans were combined using the genome scan meta-analysis (GSMA) method.<sup>6,35</sup> The GSMA method is a rank-based analysis assessing the strongest evidence for linkage within bins of fixed width, traditionally 30 cM, giving a total of 118 bins on the autosomes using the Marshfield map. For each study, the maximum evidence for linkage achieved within a bin was noted (e.g. maximum LOD or NPL or minimum p-value). When partial data were available, the bins with no result given were all assigned a rank equal to the median of the unused ranks. Bins were then ranked and ranks were summed across studies. Statistical evidence for linkage within the bin was assessed from this summed rank (SR) using permutation tests available in the GSMA software.<sup>36</sup> In order to explore how the meta-analysis results could be affected by bin definition, we repeated the analyses using 20cM (giving a total of 173 bins) and 40cM (87 bins) bin widths, and shifted 30cM bins obtained by moving bin boundaries by 15cM.<sup>37</sup> By applying Bonferroni correction for multiple testing on the basis of 118 bins, a p-value of 0.05/118=0.00042 is necessary for genome-wide evidence of linkage, and a p-value of 1/118=0.0084 for suggestive evidence of linkage. Corresponding p-values were calculated for other bin sizes.

For each phenotype, the meta-analysis was performed for all studies, and repeated for the sub-sample including only families with European ancestry (EUR). Initially, only linkage screens with genome-wide results were analysed, then genome scans with partial results were added. Meta-analyses of the different traits were performed both unweighted (assuming equal contribution from each study) and weighted by study size, using as weighting factor the square root of the number of affected individuals (binary traits) or phenotyped subjects (quantitative traits).

### Testing for between-scan heterogeneity

In bin reaching the 5% threshold, we tested for heterogeneity 1) between ALL studies and 2) between EUR studies, using the Q statistic proposed by Zintzaras and Ioannidis.<sup>7</sup> For bin  $j$ ,

$$Q = \sum_{i=1}^N w_i (R_{i,j} - R_j)^2 \quad \text{where } w_i \text{ is the weight of study } i, R_{i,j} \text{ the rank of study } i \text{ in bin } j \text{ and } R_j$$

the mean rank for bin  $j$ . The statistical significance of the heterogeneity metric was tested using Monte Carlo permutations, i.e. by randomly reassigning the ranks to bins within each study, and recalculating each heterogeneity statistic. High between-study heterogeneity was defined as the proportion of simulated bins with Q-statistics exceeding the observed value, indicating large differences in relative rank of a bin between studies. Conversely, low heterogeneity was defined as the percentage of simulated bins below the observed value, corresponding to consistent linkage evidence across studies. High or low between-study heterogeneity were based on one-sided tests ( $p < 0.05$  for left or right-sided testing, respectively). Since the distribution of the heterogeneity statistic depends on the summed rank statistic,<sup>7</sup> the observed heterogeneity statistic was only compared to simulated bins with similar SR values ( $\pm 2$ ). Heterogeneity tests were performed using HEGESMA software.<sup>38</sup>

## RESULTS

In total, our meta-analysis included genome linkage scan results on asthma and atopy-related phenotypes from 20 different studies (including more than 3,000 families). The genome screens were carried out in families with different geographical and ethnic origin: Europe, United States (families of European, African American or Hispanic American origin), Australia, Japan,

China and Costa-Rica (Table 1). Families were mainly ascertained through at least one asthmatic subject, with some additional affected individuals available. All linkage analyses, except two, were multipoint non-parametric, using a range of programs (e.g. Mapmaker/Sibs, GeneHunter, Solar, MLB-GH, Merlin) reflecting the family structures, and the date of the analysis.

The main results from weighted ( $p_{SR,W}$ ) and unweighted ( $p_{SR,U}$ ) meta-analyses (30cM bin width) conducted in the entire set of studies (ALL families) and in European-ancestry (EUR) families are shown in Tables 2 and S1. Figures 1 and S1 illustrate results for all bins (ALL and EUR analyses). Exhaustive meta-analysis results (eight phenotypes) are presented in Tables S2-S10.

### **Asthma and atopic asthma**

Meta-analysis of asthma was performed in 16 asthma GWL studies of which 14 scans had complete results (2,053 families with 5,425 affected individuals). Suggestive evidence for linkage occurred in two bins: bin 4\_7 ( $p_{SR,W}=0.007$ ) and bin 5\_5 ( $p_{SR,W}=0.003$ ) in ALL families. Moreover, whatever the strategy used (different bin width, inclusion of two scans with partial results), suggestive evidence for linkage was consistently detected on chromosome 4 between 182 and 200cM and chromosome 5 between 139 and 141cM. When restricting the analysis to studies including families ascertained through at least two asthmatic sibs, suggestive evidence for linkage was observed on bin 2\_3 ( $p_{SR,W}=0.002$ ) and bin 6\_2 ( $p_{SR,W}=0.004$ ), that both reached genome-wide significance level ( $p_{SR,W}<0.0002$ ) in EUR families. Varying bin widths (Figure S2) supported these results and defined two linked regions of less than 20cM: 2p21-p14 (63.4-82.8 cM) and 6p21.31-p21.1 (49.5-65.1 cM). Genetic heterogeneity ( $p_{SR,W}\geq 0.975$ ) between studies was detected in ALL families for bin 2\_3 and in families ascertained through two asthmatic sibs for bin 6\_2.

Overall, data for atopic asthma consisted of 618 families with 1,276 atopic asthmatic offspring from six studies. Suggestive evidence for linkage was detected on chromosome 17q in ALL families and when analyses were restricted to EUR families (bin 17\_3,  $p_{SR,W}=p_{SR,U}=0.001$ ). Analyses with different bin width definitions consistently detected the 17q region at a suggestive evidence level ( $p_{SR,W}$  varying from 0.0004 to 0.001 for ALL families and from 0.0006 to 0.002 in the EUR sample), delineating a linked region of 18cM between 63 and 81cM. Suggestive evidence for linkage was also obtained for two other regions: 1p (125-145cM,  $p_{SR,W}=0.006$ ) and 1q (271cM-pter,  $p_{SR,W}=0.005$ ) in EUR families. For the 1q region, there was nominally significant evidence for genetic heterogeneity between studies ( $p_{SR,W} \geq 0.98$ ) both for ALL and EUR families.

### **Bronchial hyper-responsiveness**

Meta-analysis for BHR was carried out on six scans including 391 EUR families (1,397 affected subjects). Suggestive evidence for linkage was observed on chromosome 6 (bin 6\_3,  $p_{SR,W}=0.006$ ). Varying bin allowed defining a linked region of 13cM between 65 and 78cM.

### **IgE levels**

The meta-analysis of 13 genome-wide linkage scans with available data for IgE included 2,471 families, corresponding to 8,076 subjects. Suggestive evidence for linkage was obtained in ALL families on chromosome 6p for bin 6\_2 ( $p_{SR,W}=0.005$ ;  $p_{SR,U}=0.003$ ). Suggestive evidence for linkage was consistently detected for 6q region using different bin widths and/or when adding the Australian population-based scan with partial results ( $p_{SR}$  between 0.001 and 0.01). When restricting the study to EUR families, no region reached the suggestive significance threshold.

### **SPT phenotypes**

Together, the data for SPT consisted of 1,264 families (3,255 atopic subjects) from nine scans. Genome-wide evidence for linkage was observed in ALL families for chromosome 3q (bin 3\_6,  $p_{SR,W}=0.0001$  and  $p_{SR,U}=0.0003$ ) and in EUR families for two adjacent bins on chromosome 17q: bin 17\_2 ( $p_{SR,W}=p_{SR,U}=0.00006$ ) and bin 17\_3 ( $p_{SR,W}=0.00009$ ;  $p_{SR,U}=0.0001$ ). Analyses using different bin widths supported the evidence for linkage across a broad region of chromosome 17q in EUR families and of chromosome 3q ( $p_{SR,W}$  varying from 0.0001 to 0.004 in ALL families and from 0.0005 to 0.01 in EUR families), defining two large regions of at least 40cM between 124-166cM for chromosome 3 and 43-86cM for chromosome 17 (Figure S2).

The meta-analysis for SPT to HDM included eight scans with a total of 548 families (1,030 affected subjects). Weighted analysis identified a single region with suggestive evidence for linkage: bin 11\_4 (90-118 cM,  $p_{SR}=0.007$ ).

Meta-analysis for a quantitative score of SPT (SPTQ) was performed on four scans including only EUR families (715 families with 1,561 offspring). Suggestive evidence for linkage was observed for two bins: bin 5\_5 ( $p_{SR} \leq 0.003$ ) and bin 3\_6 ( $p_{SR} \leq 0.007$ ). Analyses using different bin widths (Figure S2) delineated a minimal region of approximately 28cM on chromosome 5q23.1-q33.1 with genome-wide evidence for linkage (128-156cM,  $p_{SR}=0.0002$ ). Genetic heterogeneity

between studies was detected for bin 21\_1 ( $p_{SR,W}=0.975$ ). Conversely, bin 3\_5 showed consistent evidence for linkage across studies ( $p_{SR,W} \leq 0.001$ ).

### Eosinophils

The data for EOS included six genome-wide linkage scans with 1,285 EUR families, corresponding to 3,534 subjects. Genome-wide evidence for linkage occurred on 2q31.1-q34 region whatever the strategy used for bin 2\_7 (181-210 cM,  $p_{SR}=5.10^{-5}$ ), with suggestive evidence for linkage in the adjacent bin 2\_8 (210-241 cM,  $p_{SR}=0.0006$ ). Varying bin widths supported these results and defined a linked region of 15cM between 194 and 210 cM (2q32.3-q34) (Figure S2).

### DISCUSSION

This meta-analysis of 20 genome linkage scans conducted for asthma, BHR and five atopy-related phenotypes has identified several chromosomal regions that are likely to harbour genes involved in asthma. This study has provided genome-wide evidence for linkage to five regions in European families: 2p21-p14 and 6p21 with asthma, 2q31.1-q34 with EOS, 5q23.1-q33.1 with SPTQ, 17p12-q25 with SPT and to one region in all families: 3p25.3-q24 with SPT. Interestingly, the 17q region was found associated with several phenotypes (IgE, EOS, SPT to HDM, asthma and atopic asthma) suggesting that this region may harbour several susceptibility genes with potential pleiotropic effects. Tests of heterogeneity indicated consistent evidence for linkage of SPTQ with 3p11-3q21 region and between-study heterogeneity for asthma for 2p21-p14 and 6p21 regions, and for atopic asthma for 1q23-q25 region.

We can first compare our results to those of the recent GSMA performed by Denham *et al.*<sup>5</sup> Whereas the main phenotypes (asthma, SPT, IgE and BHR) have been examined by both meta-analyses, the present study explored in more details the atopic dimension of asthma (atopic asthma, polysensitization, positive skin test to HDM and eosinophils) and included all genome-wide scans conducted to date. There are a number of consistencies in the results of the two meta-analyses. Regions identified at a suggestive significance level by Denham *et al.* were detected in the present study with at least the same significant level, and three of them reached the genome-wide significance (chromosomes 6 with asthma, 3 and 17 with SPT) in our meta-analysis. Moreover, we identified additional regions with genome-wide or suggestive evidence of linkage: 2p21-p14, 4q34.3-qter and 5q31.1-5q31.2 regions for asthma. The differences of identified regions and of significance levels were likely due in part to differences in population included in the two meta-analyses. Indeed Denham *et al.*<sup>5</sup> selected nine genome-wide-scans conducted in European-ancestry families, whereas we gathered 20 genome scans performed in different ethnic populations including European, Hispanic, Asian and African American subjects. This strategy allowed searching for common genetic region across populations and also for genetic heterogeneity between studies. We also included two unpublished European studies but sensitivity analyses showed that these two data sets did not influence our findings. There are also methodological differences; we used only scans with full data in our primary analysis, and then added those with partial data and used different bin definitions in order to conduct sensitivity analyses. We also performed heterogeneity tests and evidenced genetic heterogeneity between studies in four linkage regions.

In this study, we performed GSMA on genome-wide scans for asthma-related phenotypes using the traditional 30cM bin width definition that allows having at least two bins of equal width on the smallest chromosomes. However, peak linkage scores in individual studies may map to adjacent bins, and dilute the evidence for linkage in the GSMA, reducing both power and precision. In order to evaluate the consistency of our results, we repeated the analyses using two additional bin widths of 20cM and 40cM and using a shifted 30cM bin.<sup>37</sup> Significant results were obtained consistently for regions identified at genome-wide or suggestive significance levels (2p and 6p with asthma, 2q with EOS, 17q with atopic asthma, 3q and 17q regions with SPT and 6p with IgE). These analyses strengthened the evidence for linkage to 5q region for SPTQ and identified new regions for atopic asthma (1p22-p13, 1q23-q25) and SPT (1p34-p22). Moreover these analyses allowed us to delineate chromosomal regions of interest to be further investigated.

Regarding asthma, our meta-analysis allowed identification of a novel region (2p21-p14). Looking at the contribution to 2p locus among all studies individually, six scans only showed weak evidence of linkage to this locus ( $p \geq 0.01$ ). This suggests that the genetic effect mediating the linkage may be too weak to be identified by any of the individual scans and highlights the importance of conducting meta-analysis to identify such candidate region. Moreover, between-study heterogeneity was significantly high. Such heterogeneity may be due to difference in family ascertainment but also may reflect the intrinsic complexity of the disease architecture or differences in asthma definition across studies. Indeed, asthma genetic research is hampered by the lack of a gold standard for case-definitions and linkage studies are sensitive to the misclassification of individuals leading to reduction of statistical power. Interestingly, analysis of different bin widths delineated a chromosomal region (63-83cM) which overlaps a locus identified

for severe asthma in German families<sup>39</sup> and is located at 10cM from a linkage signal detected in the French EGEA study for an asthma severity score.<sup>40</sup>

For SPT, the strongest evidence of linkage in the analysis of all families arose in the 3p25.3-q24 region. This evidence fell when restricting the analysis to European ancestry families, suggesting that this region may harbour a major susceptibility gene being involved in all populations. Indeed, among the nine genome scans included in the meta-analysis, two had suggestive evidence for linkage, five scans having LOD >0.70. This region has been reported linked to various atopy (IgE, Specific IgE, EOS) and lung function phenotypes<sup>17,19,23,34,41,42</sup> and it harbours *COL29A1* gene recently found associated to atopic dermatitis<sup>43</sup> as well as genes encoding pattern recognition receptors (TLR9) and chemokine receptors (CCR3, CCR5).

The most significant result for SPT obtained from GSMA in families of European ancestry was the 17p12-q25 region. Significant or suggestive linkage to this region was detected in four studies (French, Dutch, Australian twin and GAIN)<sup>14,17,20,24</sup> but not in the other ones, confirming the ability of GSMA to detect linkage in the presence of heterogeneity. Interestingly, evidence for linkage of the 17q region was less significant when considering the whole sample including African American and Hispanic American families from CSGA study, suggesting that susceptibility gene(s) included in that region may play a more important role in Caucasian populations. Recently, the first GWA study conducted for asthma in European children, identified strong association of the disease with 17q21 locus that harbors *GSDML* and *ORMDL3* genes.<sup>44</sup> These genes are located at the boundary between 17\_2 and 17\_3 bins. Further studies have shown that the 17q21 genetic variants are more strongly associated with early-onset asthma but did not show association with atopy.<sup>45</sup> It remains to be investigated whether polymorphisms at 17q21 locus account fully or partially for the observed linkage in this region. Moreover, bins on chromosome 17 were detected linked to various atopy phenotypes by the present meta-analysis and linkage signals in this region have been also reported for asthma by previous studies,<sup>12,14,17,20,34,46</sup> suggesting that this region is likely to harbor several susceptibility genes, a few of them with pleiotropic effects on correlated phenotypes.

The 5q23.1-q33.1 region provided genome-wide evidence for linkage to SPTQ in different analyses. This linkage was supported by three scans with LOD >1.2, the fourth having a modest signal in that region. The 5q region was also identified by the asthma analysis, this linkage signal being mainly supported by the three smallest studies (Japanese, Australian twins, and Hispanic families from CSGA study) and the Dutch genome scan. This region was first reported linked to IgE and BHR by candidate linkage studies, and then detected with asthma, suggesting that this region may harbour several genes.<sup>3</sup> Candidate genes are present within this region, including *ADRB2* gene and the Interleukin gene cluster.<sup>3</sup> Moreover, this region includes *CYFIP2* gene found associated with atopic asthma by positional cloning.<sup>47</sup>

Genome-wide evidence for linkage was detected on 2q32-q34 for eosinophils. This region has been reported linked to IgE and lung function<sup>12,41</sup> and harbours several candidate genes including genes involved in T-cell signalling (ICOS, CD28 and CTLA-4) and apoptosis (CASP8). Moreover, this region includes several SNPs recently found associated with eosinophils by a GWA study.<sup>48</sup>

Suggestive evidence was also observed on chromosome 6p22-p21 for IgE and asthma. No individual study showed strong evidence for linkage with IgE (LOD > 2.0) in this region, but six had nominally significant LOD scores (LOD > 0.70). This 6p region was mainly detected linked to asthma and atopy-related phenotypes.<sup>14,18,23,25,30,49</sup> This chromosomal region includes the MHC region and in particular the HLA-G locus found associated with asthma and bronchial hyperresponsiveness in an isolated population not included in the present analysis and replicated in Dutch families included in the present meta-analysis.<sup>50</sup>

Genome-wide association studies have successfully identified novel genes contributing to common complex diseases but which however explain a small proportion of heritability of disease.<sup>51</sup> It is more and more admitted now that genetic susceptibility to complex diseases as asthma includes a wide spectrum of genetic variation from rare alleles with strong effects to common alleles with modest effects.<sup>52</sup> Current GWA studies have power to identify mainly common variants while linkage analysis can detect different types of genetic factors within one locus or several loci including rare variants segregating in families. Therefore, our meta-analysis provides an important resource of information that can be used not only to prioritize further fine mapping studies in regions of interest but also to be integrated with GWAs to increase power<sup>4</sup> and to better interpret the outcomes of these studies.

## ACKNOWLEDGMENTS

We thank all the patients who participated in the different studies. We also thank Professors William Cookson and Pier Franco Pignatti and the EGEA cooperative group for providing unpublished results. The work was supported by the European Commission as part of the Ga2len project, Global Allergy and Asthma European Network (contract n° FOOD-CT-2004-506378) and GABRIEL, a multidisciplinary study to identify the genetic and environmental causes of asthma in the European Community (contract n° 01896 under the Integrated Programme LSH-2004-1.2.5-1

Post genomic approaches to understand the molecular basis of asthma (aiming at a preventive or therapeutic control). This research was funded by a grant from the UK MRC to Cathryn M Lewis (G0400960). The Finnish study was supported by Academy of Finland and Sigrid Jusélius Foundation. The Dutch family study was supported by grants from the Netherlands Asthma Foundation (AF 95.09 and 98.48) and the US National Institute of Health.

## REFERENCES

- 1 Wenzel SE: Asthma: defining of the persistent adult phenotypes. *Lancet* 2006; **368**: 804-813.
- 2 Steinke JW, Rich SS, Borish L: 5. Genetics of allergic disease. *J Allergy Clin Immunol* 2008; **121**: S384-387.
- 3 Vercelli D: Discovering susceptibility genes for asthma and allergy. *Nat Rev Immunol* 2008; **8**: 169-182.
- 4 Roeder K, Bacanu SA, Wasserman L, Devlin B: Using linkage genome scans to improve power of association in genome scans. *Am J Hum Genet* 2006; **78**: 243-252.
- 5 Denham S, Koppelman GH, Blakey J *et al*: Meta-analysis of genome-wide linkage studies of asthma and related traits. *Respir Res* 2008; **9**: 38.
- 6 Wise LH, Lanchbury JS, Lewis CM: Meta-analysis of genome searches. *Ann Hum Genet* 1999; **63**: 263-272.
- 7 Zintzaras E, Ioannidis JP: Heterogeneity testing in meta-analysis of genome searches. *Genet Epidemiol* 2005; **28**: 123-137.
- 8 Van Eerdewegh P, Little RD, Dupuis J *et al*: Association of the ADAM33 gene with asthma and bronchial hyperresponsiveness. *Nature* 2002; **418**: 426-430.
- 9 Balaci L, Spada MC, Olla N *et al*: IRAK-M is involved in the pathogenesis of early-onset persistent asthma. *Am J Hum Genet* 2007; **80**: 1103-1114.
- 10 Kurz T, Altmueller J, Strauch K *et al*: A genome-wide screen on the genetics of atopy in a multiethnic European population reveals a major atopy locus on chromosome 3q21.3. *Allergy* 2005; **60**: 192-199.
- 11 Ober C, Cox NJ, Abney M *et al*: Genome-wide search for asthma susceptibility loci in a founder population. The Collaborative Study on the Genetics of Asthma. *Hum Mol Genet* 1998; **7**: 1393-1398.
- 12 Wjst M, Fischer G, Immervoll T *et al*: A genome-wide search for linkage to asthma. German Asthma Genetics Group. *Genomics* 1999; **58**: 1-8.
- 13 Xu J, Postma DS, Howard TD *et al*: Major genes regulating total serum immunoglobulin E levels in families with asthma. *Am J Hum Genet* 2000; **67**: 1163-1173.
- 14 Koppelman GH, Stine OC, Xu J *et al*: Genome-wide search for atopy susceptibility genes in Dutch families with asthma. *J Allergy Clin Immunol* 2002; **109**: 498-506.
- 15 Meyers DA, Postma DS, Stine OC *et al*: Genome screen for asthma and bronchial hyperresponsiveness: interactions with passive smoke exposure. *J Allergy Clin Immunol* 2005; **115**: 1169-1175.
- 16 Laitinen T, Daly MJ, Rioux JD *et al*: A susceptibility locus for asthma-related traits on chromosome 7 revealed by genome-wide scan in a founder population. *Nat Genet* 2001; **28**: 87-91.
- 17 Bouzigon E, Dizier MH, Krahenbuhl C *et al*: Clustering patterns of LOD scores for asthma-related phenotypes revealed by a genome-wide screen in 295 French EGEA families. *Hum Mol Genet* 2004; **13**: 3103-3113.
- 18 Daniels SE, Bhattacharya S, James A *et al*: A genome-wide search for quantitative trait loci underlying asthma. *Nature* 1996; **383**: 247-250.
- 19 Evans DM, Zhu G, Duffy DL, Montgomery GW, Frazer IH, Martin NG: Major quantitative trait locus for eosinophil count is located on chromosome 2q. *J Allergy Clin Immunol* 2004; **114**: 826-830.
- 20 Ferreira MA, O'Gorman L, Le Souef P *et al*: Robust estimation of experimentwise P values applied to a genome scan of multiple asthma traits identifies a new region of significant linkage on chromosome 20q13. *Am J Hum Genet* 2005; **77**: 1075-1085.
- 21 Pillai SG, Chiano MN, White NJ *et al*: A genome-wide search for linkage to asthma phenotypes in the genetics of asthma international network families: evidence for a major susceptibility locus on chromosome 2p. *Eur J Hum Genet* 2006; **14**: 307-316.
- 22 Hakonarson H, Bjornsdottir US, Halapi E *et al*: A Major Susceptibility Gene for Asthma Maps to Chromosome 14q24. *Am J Hum Genet* 2002; **71**.
- 23 Haagerup A, Bjerke T, Schiøtz PO, Binderup HG, Dahl R, Kruse TA: Asthma and atopy - a total genome scan for susceptibility genes. *Allergy* 2002; **57**: 680-686.
- 24 Webb BT, van den Oord E, Akkari A *et al*: Quantitative linkage genome scan for atopy in a large collection of Caucasian families. *Hum Genet* 2007; **121**: 83-92.



- 25 Xu J, Meyers DA, Ober C *et al*: Genomewide screen and identification of gene-gene interactions for asthma-susceptibility loci in three U.S. populations: collaborative study on the genetics of asthma. *Am J Hum Genet* 2001; **68**: 1437-1446.
- 26 Colilla S, Nicolae D, Pluzhnikov A *et al*: Evidence for gene-environment interactions in a linkage study of asthma and smoking exposure. *J Allergy Clin Immunol* 2003; **111**: 840-846.
- 27 Mathias RA, Freidhoff LR, Blumenthal MN *et al*: Genome-wide linkage analyses of total serum IgE using variance components analysis in asthmatic families. *Genet Epidemiol* 2001; **20**: 340-355.
- 28 Blumenthal MN, Langefeld CD, Beaty TH *et al*: A genome-wide search for allergic response (atopy) genes in three ethnic groups: Collaborative Study on the Genetics of Asthma. *Hum Genet* 2004; **114**: 157-164.
- 29 Blumenthal MN, Ober C, Beaty TH *et al*: Genome scan for loci linked to mite sensitivity: the Collaborative Study on the Genetics of Asthma (CSGA). *Genes Immun* 2004; **5**: 226-231.
- 30 Yokouchi Y, Nukaga Y, Shibasaki M *et al*: Significant evidence for linkage of mite-sensitive childhood asthma to chromosome 5q31-q33 near the interleukin 12 B locus by a genome-wide search in Japanese families. *Genomics* 2000; **66**: 152-160.
- 31 Xu X, Fang Z, Wang B *et al*: A genomewide search for quantitative-trait loci underlying asthma. *Am J Hum Genet* 2001; **69**: 1271-1277.
- 32 Teerlink CC, Camp NJ, Bansal A *et al*: Significant evidence for linkage to chromosome 5q13 in a genome-wide scan for asthma in an extended pedigree resource. *Eur J Hum Genet* 2009; **17**: 636-643.
- 33 Cledon JC, Soto-Quiros ME, Avila L *et al*: Significant linkage to airway responsiveness on chromosome 12q24 in families of children with asthma in Costa Rica. *Hum Genet* 2007; **120**: 691-699.
- 34 Raby BA, Soto-Quiros ME, Avila L *et al*: Sex-specific linkage to total serum immunoglobulin E in families of children with asthma in Costa Rica. *Hum Mol Genet* 2007; **16**: 243-253.
- 35 Levinson DF, Levinson MD, Segurado R, Lewis CM: Genome scan meta-analysis of schizophrenia and bipolar disorder, part I: Methods and power analysis. *Am J Hum Genet* 2003; **73**: 17-33.
- 36 Pardi F, Levinson DF, Lewis CM: GSMA: software implementation of the genome search meta-analysis method. *Bioinformatics* 2005; **21**: 4430-4431.
- 37 Hermanowski J, Bouzigon E, Forabosco P, Ng MY, Fisher SA, Lewis CM: Meta-analysis of genome-wide linkage studies for multiple sclerosis, using an extended GSMA method. *Eur J Hum Genet* 2007; **15**: 703-710.
- 38 Zintzaras E, Ioannidis JP: HEGESMA: genome search meta-analysis and heterogeneity testing. *Bioinformatics* 2005; **21**: 3672-3673.
- 39 Altmuller J, Seidel C, Lee YA *et al*: Phenotypic and genetic heterogeneity in a genome-wide linkage study of asthma families. *BMC Pulm Med* 2005; **5**: 1.
- 40 Bouzigon E, Siroux V, Dizier MH *et al*: Scores of asthma and asthma severity reveal new regions of linkage in EGEA study families. *Eur Respir J* 2007; **30**: 253-259.
- 41 Postma DS, Meyers DA, Jongepier H, Howard TD, Koppelman GH, Bleecker ER: Genomewide screen for pulmonary function in 200 families ascertained for asthma. *Am J Respir Crit Care Med* 2005; **172**: 446-452.
- 42 Wilk JB, DeStefano AL, Arnett DK *et al*: A genome-wide scan of pulmonary function measures in the National Heart, Lung, and Blood Institute Family Heart Study. *Am J Respir Crit Care Med* 2003; **167**: 1528-1533.
- 43 Soderhall C, Marenholz I, Kerscher T *et al*: Variants in a novel epidermal collagen gene (COL29A1) are associated with atopic dermatitis. *PLoS Biol* 2007; **5**: e242.
- 44 Moffatt MF, Kabesch M, Liang L *et al*: Genetic variants regulating ORMDL3 expression contribute to the risk of childhood asthma. *Nature* 2007; **448**: 470-473.
- 45 Bouzigon E, Corda E, Aschard H *et al*: Effect of 17q21 variants and smoking exposure in early-onset asthma. *N Engl J Med* 2008; **359**: 1985-1994.
- 46 A genome-wide search for asthma susceptibility loci in ethnically diverse populations. The Collaborative Study on the Genetics of Asthma (CSGA). *Nat Genet* 1997; **15**: 389-392.
- 47 Noguchi E, Yokouchi Y, Zhang J *et al*: Positional Identification of an Asthma Susceptibility Gene on Human Chromosome 5q33. *Am J Respir Crit Care Med* 2005.
- 48 Gudbjartsson DF, Bjornsdottir US, Halapi E *et al*: Sequence variants affecting eosinophil numbers associate with asthma and myocardial infarction. *Nat Genet* 2009; **41**: 342-347.
- 49 Wjst M: Specific IgE--one gene fits all? German Asthma Genetics Group. *Clin Exp Allergy* 1999; **29**: 5-10.
- 50 Nicolae D, Cox NJ, Lester LA *et al*: Fine mapping and positional candidate studies identify HLA-G as an asthma susceptibility gene on chromosome 6p21. *Am J Hum Genet* 2005; **76**: 349-357.
- 51 Maher B: Personal genomes: The case of the missing heritability. *Nature* 2008; **456**: 18-21.
- 52 Hardy J, Singleton A: Genomewide association studies and human disease. *N Engl J Med* 2009; **360**: 1759-1768.

Table 1. Characteristics of individual genome-wide linkage scans included in the present study.

Population	Origin	Family ascertainment	Data*	Results	Asthma	No. of affected or phenotyped subjects						
						Atopic Asthma	IgE	SPT	STP HDM	SPTQ	EOS	BHR
German <sup>12,39</sup>	EUR	≥ 2 asthmatic sibs	RD, G	Full	413	268	465		99		221	96
Dutch <sup>13-15</sup>	EUR	1 asthmatic parent	RD	Full	368		1,136	327	224		1,136	446
Finnish <sup>16</sup>	EUR	≥ 1 asthmatic	RD	Full	185							
Icelandic <sup>22</sup>	EUR	≥ 2 asthmatic relatives	G	Full	596							
French (EGEA) <sup>17</sup>	EUR	≥ 1 asthmatic	RD	Full	237	176*	707	370	181*	703	699	191
Danish <sup>23</sup>	EUR	≥ 2 atopic sibs	G	Partial	78	78	90					
British**	EUR	≥ 1 asthmatic sib	RD	Full	163		359				341	
Italian**	EUR	≥ 1 asthmatic sib	RD	Full	88	88		148	82			98
Australian <sup>18</sup>	EUR	Population	RD	Partial			203				203	
Australian twins <sup>19,20</sup>	EUR	≥ 1 asthmatic twin	RD	Full	68		387	230	138		934	98
GSK <sup>21,24</sup> – All together	EUR	≥ 2 asthmatic sibs	Web, G	Full	1,422	560						
- GAIN***							770	482		482		
- Minnesota							148	108		108		468
- Denmark								268		268		
Utah <sup>32</sup>	EUR	≥ 2 asthmatics	G	Full	693							
CSGA <sup>† 25-29</sup> – All		≥ 2 asthmatic sibs	G	Full				1,322				
- Euro-Americans	EUR				466		924		210			
- African Americans	Non-EUR				350		171		66			
- Hispanic-Americans	Non-EUR				91		558		30			
Japanese <sup>30</sup>	Non-EUR	≥ 2 asthmatic sibs	G	Full	106	106						
Chinese <sup>31</sup>	Non-EUR	≥ 2 asthmatic sibs	G	Full			1,506					
Costa-Rican <sup>33,34</sup>	Non-EUR	≥ 1 asthmatic sib	T	Partial	101		652					
Total of subjects												
ALL studies					5,425	1,276	8,076	3,255	1,030	1,561	3,534	1,397
EUR studies					4,777	1,170	5,189	1,933	934	1,561	3,534	1,397

SPT: defined by at least one positive skin prick test response, SPT HDM: positive skin prick test response to House Dust Mite, SPTQ: quantitative measure of positive skin test response to allergens, EOS: eosinophil counts, BHR: bronchial-hyperresponsiveness

\* RD: raw data available; G: data extracted from published graphs; Web: data available online; T: published table

\*\* Unpublished results

\*\*\* IgE results for GAIN and Minnesota groups were included separately; Atopy results were included separately for GAIN, Minnesota and Denmark families respectively

† Asthma and IgE were analysed separately in families from European, African-American and Hispanic American origin

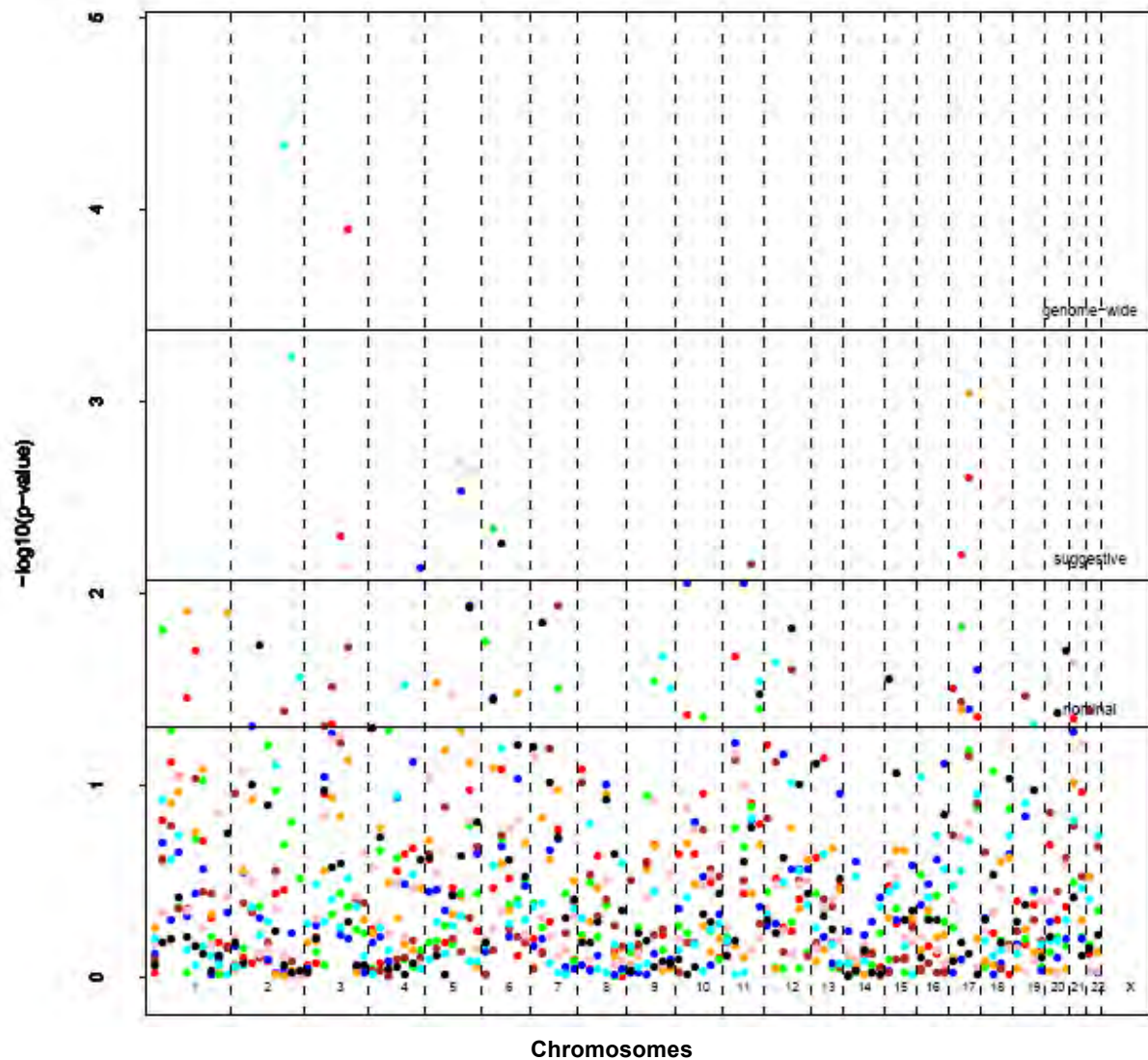
Table 2. Summary of chromosomal regions with suggestive evidence of linkage for at least one phenotype, for weighted (W) and unweighted (U) analysis of all groups with complete data sets using 30 cM bin widths.

Interval			Asthma (14 studies)		Atopic asthma (5 studies)		IgE (11 studies)		SPT (8 studies)		SPT to HDM (8 studies)		SPTQ (4 studies)		Eosinophils (7 studies)		BHR (6 studies)	
Chr	Bin*	(cM)	W	U	W	U	W	U	W	U	W	U	W	U	W	U	W	U
1	1_5	117-145			0.01	<b>0.008</b>			0.04	0.03								
2	2_3	60-90	<b>0.002*</b>	<b>0.003*</b>														
	2_7	181-209									0.04	0.04			<b>0.00005</b>	<b>0.00006</b>		
	2_8	210-240													<b>0.0006</b>	<b>0.0007</b>		
3	3_5	115-144							<b>0.005</b>	<b>0.008</b>			0.05 <b>(0.0007)</b>	0.04 <b>(0.001)</b>				
	3_6	144-171							<b>0.0001</b>	<b>0.0003</b>	0.02	0.03	<b>0.007</b>	<b>0.006</b>				
4	4_7	182-qter	<b>0.007</b> 0.02*	<b>0.004</b> 0.02*														
5	5_5	113-141	<b>0.003</b>	<b>0.0007</b>	0.05	0.03							<b>0.002</b>	<b>0.003</b>				
	5_6	141-169	0.01	<b>0.0003</b>													0.01	0.03
6	6_2	33-65	0.04 <b>0.004*</b> <b>(0.98)</b>	0.05 0.02* <b>(0.98)</b>	n.s.	0.04	<b>0.004</b>	<b>0.003</b>									0.03	n.s.
	6_3	65-97							n.s.	0.01							<b>0.006</b>	0.01
7	7_4	92-121					0.03	0.03			0.01	<b>0.008</b>						
11	11_4	90-118									<b>0.007</b>	<b>0.008</b>						
17	17_2	32-64			0.04	0.04	0.01	0.01	<b>0.006</b>	<b>0.0005</b>	0.04	0.02						
	17_3	64-96	0.04 0.02*	0.01 0.01*	<b>0.0009</b>	<b>0.001</b>	n.s.	0.04	<b>0.002</b>	<b>0.0004</b>								
20	20_3	69-qter															0.02	<b>0.008</b>

**Bold, underlined p-value:** genome wide evidence for linkage ( $p_{SR} < 0.0004$ ). **Bold p-value:** suggestive evidence for linkage ( $p_{SR} < 0.0081$ ). n.s., non-significant. Significant heterogeneity p-values for the high-ranking bins are shown in parentheses.

\* Results obtained in families ascertained through at least two asthmatic sib

**Figure 1. Meta-analysis results for genome-wide linkage scans of asthma and asthma-related phenotypes in ALL families.**



Minus Log<sub>10</sub> P-value of weighted summed ranks (vertical axis) are plotted against the bin location (horizontal axis), with a single point plotted for each bin. Thresholds for genome-wide, suggestive and nominal significance are shown. Each phenotype is represented with a different colour: Asthma (blue), atopic asthma (orange), BHR (black), IgE (green), SPT (red), SPT to HDM (brown), SPTQ (magenta) and eosinophils (cyan).

**Supplementary information**

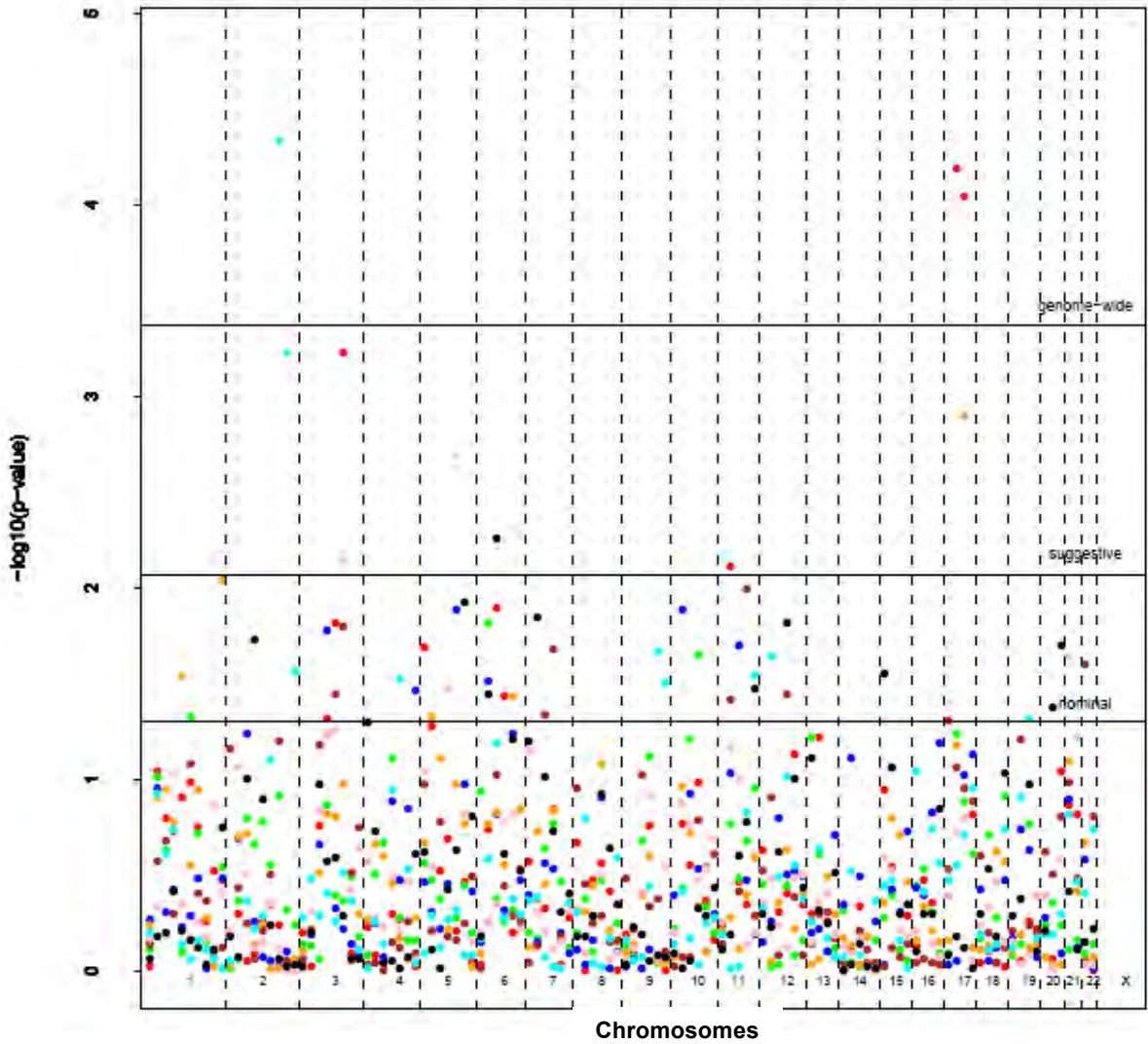
**Table S1.** Summary of chromosomal regions with suggestive evidence of linkage for at least one phenotype, for weighted (W) and unweighted (U) analysis of EUR families with complete data sets using 30 cM bin widths.

Interval			Asthma (11 studies)		Atopic asthma (4 studies)		IgE (8 studies)		SPT (7 studies)		SPT to HDM (6 studies)		SPTQ (4 studies)		Eosinophils (7 studies)		BHR (6 studies)	
			W	U	W	U	W	U	W	U	W	U	W	U	W	U	W	U
1	1_10	263-qter			0.009 <b>(0.99)</b>	0.04 <b>(0.99)</b>												
2	2_3	60-90	<b>0.0001*</b>	<b>0.0002*</b>														
	2_7	181-209													<b>0.00005</b>	<b>0.00006</b>		
	2_8	210-240													<b>0.0006</b>	<b>0.0007</b>		
3	3_5	115-144						0.02	0.02	0.04	n.s.	0.05 <b>(0.0007)</b>	0.04 <b>(0.001)</b>					
	3_6	144-171						<b>0.0006</b>	<b>0.001</b>	0.02	0.03	<b>0.007</b>	<b>0.006</b>					
5	5_5	113-141	0.01	<b>0.004</b>								<b>0.002</b>	<b>0.003</b>					
6	6_2	33-65	0.03 <b>0.0002*</b>	0.03 <b>0.0002*</b>			0.02	0.01									0.03	n.s.
	6_3	65-97						0.01	<b>0.005</b>								<b>0.006</b>	0.01
11	11_2	31-59	n.s.	0.02					<b>0.008</b>	0.01	0.04	n.s.						
17	17_2	32-64					0.05	0.04	<b>0.00006</b>	<b>0.00006</b>								
	17_3	64-96			<b>0.001</b>	<b>0.001</b>			<b>0.00009</b>	<b>0.0001</b>								
20	20_3	69-qter															0.02	<b>0.008</b>

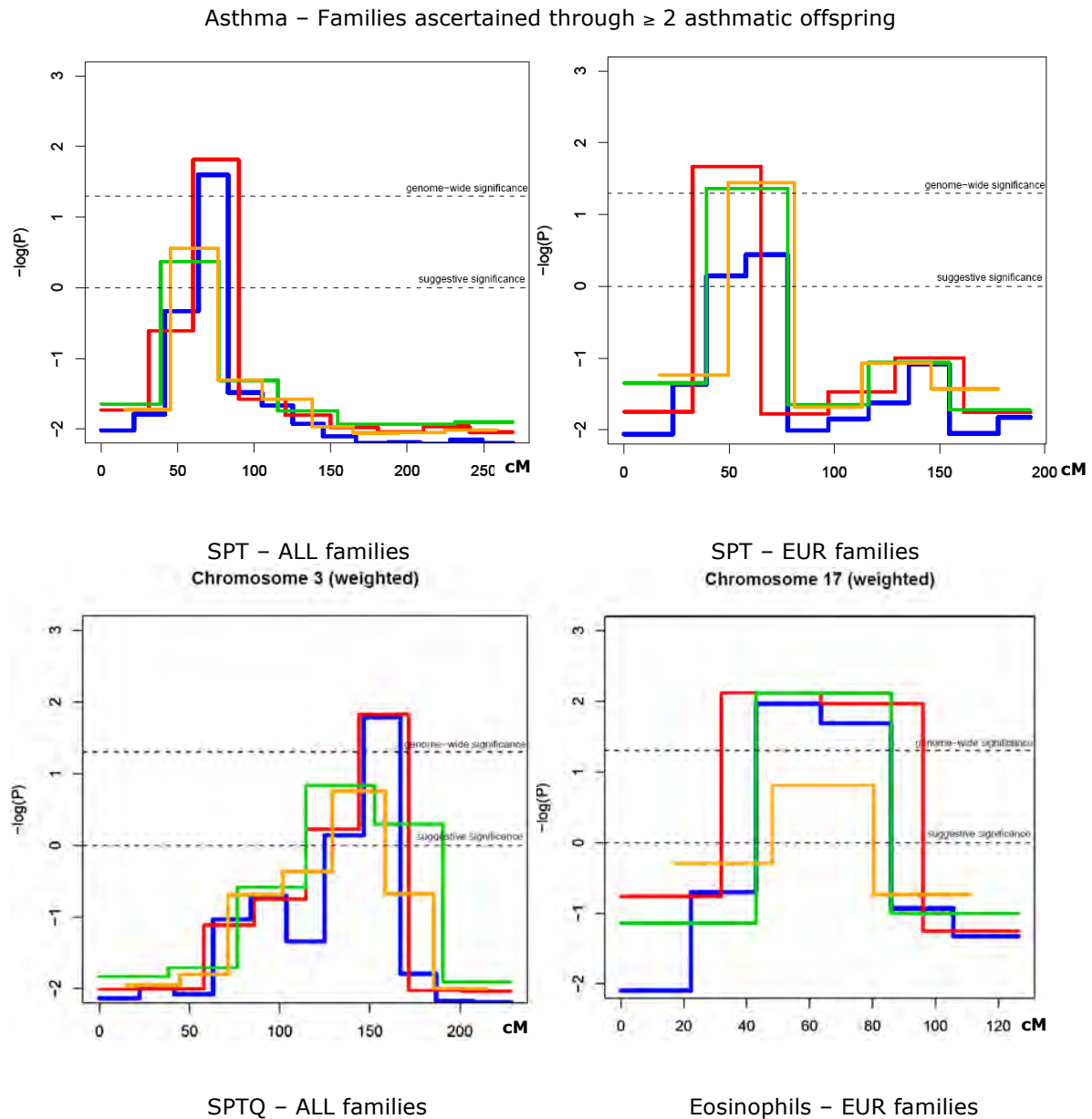
**Bold, underlined p-value:** genome wide evidence for linkage ( $p_{SR} < 0.0004$ ). **Bold p-value:** suggestive evidence for linkage ( $p_{SR} < 0.0081$ ). n.s., non-significant p-value. Significant heterogeneity p-values for the high-ranking bins are shown in parentheses.

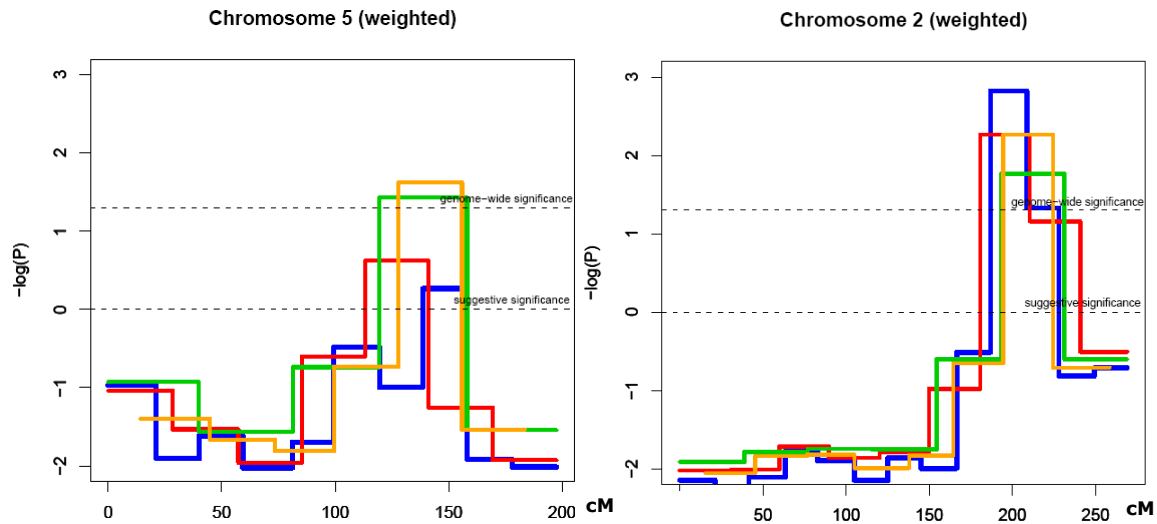
\* Results obtained in families ascertained through at least two asthmatic sib

**Figure S1. Meta-analysis results for genome-wide linkage scans of asthma and asthma-related phenotypes in EUR families.** Minus Log10 P-value of weighted summed ranks (vertical axis) are plotted against the bin location (horizontal axis), with a single point plotted for each bin. Thresholds for genome-wide, suggestive and nominal significance are shown. Each phenotype is represented with a different colour: Asthma (blue), atopic asthma (orange), BHR (black), IgE (green), SPT (red), SPT to HDM (brown), SPTQ (magenta) and eosinophils (cyan).



**Figure S2.** Graphical representation of GSMA results for (A) Asthma on chromosomes 2 and 6, (B) SPT on chromosome 3 and (C) SPTQ on chromosome 5 in all families, and for (D) SPT on chromosome 17 and for (E) Eosinophils on chromosome 2 in EUR families using different bin widths (30cM: red, 20cM: blue, 40cM: green and shifted 30cM: orange). The Y-axis is the log base 10 of the  $p_{SR}$ -values, multiplied by the total number of bins, to give a consistent definition for genome-wide and suggestive significance for all bin widths. Summed rank p-values ( $p_{SR}$ ) are shown below.





**ASTHMA – EUR families**

Bins	20 cM	30 cM	40 cM	Shifted 30 cM
2_1	0.602706	0.455889	0.508594	0.447703
2_2	0.355438	0.0343457	<b>0.00490574</b>	<b>0.00232712</b>
2_3	0.0124277	<b>0.00012966</b>	0.23436	0.171826
2_4	<b>0.000146</b>	0.320053	0.639269	0.319432
2_5	0.175226	0.539203	0.977632	0.784737
2_6	0.267725	0.804967	0.974831	0.964088
2_7	0.484977	0.932297	0.916795	0.9543
2_8	0.734367	0.773844		0.871937
2_9	0.923041	0.936984		0.602412
2_10	0.902734			
2_11	0.94812			
2_12	0.826757			
2_13	0.915678			

**ASTHMA – EUR families**

Bins	20 cM	30 cM	40 cM	Shifted 30 cM
6_1	0.661381	0.477187	0.255724	0.14605
6_2	0.134567	<b>0.000182203</b>	<b>0.000501149</b>	<b>0.000305932</b>
6_3	<b>0.00414566</b>	0.511347	0.509584	0.408985
6_4	<b>0.00209248</b>	0.249578	0.132503	0.0999897
6_5	0.586121	0.0848516	0.604471	0.226728
6_6	0.406747	0.48106		0.44825
6_7	0.241771			
6_8	0.0695104			
6_9	0.65155			
6_10	0.385023			

**SPT – ALL families**

Bins	20 cM	30 cM	40 cM	Shifted 30 cM
3_1	0.787257	0.866925	0.773626	0.761441
3_2	0.553405	0.856138	0.586427	0.536833
3_3	0.695441	0.110956	0.0440758	0.0416957
3_4	0.0627104	0.0480601	<b>0.00166666</b>	0.0196508
3_5	0.029663	0.00506017	0.00579999	<b>0.00147881</b>



3_6	0.126775	<b>0.000126271</b>	0.934444	0.0402474
3_7	<b>0.00418844</b>	0.898714		0.843498
3_8	<b>0.00009479</b>	0.929387		0.643905
3_9	0.358244			
3_10	0.8597			
3_11	0.896064			

---

**SPT – EUR families**

Bins	20 cM	30 cM	40 cM	Shifted 30 cM
17_1	0.724555	0.0490915	0.158422	0.0168737
17_2	0.0291717	<b>0.00006440</b>	<b>0.00008850</b>	<b>0.00129491</b>
17_3	<b>0.00006242</b>	<b>0.00009152</b>	0.115113	0.0460584
17_4	<b>0.00011849</b>	0.152141		0.132959
17_5	0.0495046			
17_6	0.122111			

---

**SPTQ – ALL families**

Bins	20 cM	30 cM	40 cM	Shifted 30 cM
5_1	0.0538254	0.0920016	0.0975194	0.212429
5_2	0.468106	0.288533	0.4258	0.390574
5_3	0.240483	0.768559	0.0628091	0.549827
5_4	0.610827	0.0339813	<b>0.000428735</b>	0.0454466
5_5	0.28633	<b>0.00202542</b>	0.400587	<b>0.000202542</b>
5_6	0.0175578	0.152522		0.290625
5_7	0.0572231	0.716802		0.332078
5_8	<b>0.00312081</b>			
5_9	0.474419			
5_10	0.596975			

---

**Eosinophils – EUR families**

Bins	20 cM	30 cM	40 cM	Shifted 30 cM
2_1	0.800712	0.882872	0.93634	0.963922
2_2	0.976729	0.866164	0.696284	0.578744
2_3	0.737347	0.437771	0.637594	0.559819
2_4	0.341067	0.614413	0.64901	0.82369
2_5	0.452666	0.519191	0.0457413	0.57003
2_6	0.808758	0.0804101	<b>0.000197701</b>	0.0379398
2_7	0.416617	<b>0.0000457627</b>	0.0458275	<b>0.000045763</b>
2_8	0.568533	<b>0.00058644</b>		0.0431711
2_9	0.0188133	0.0272127		0.0720821
2_10	<b>0.00000867052</b>			
2_11	<b>0.000271676</b>			
2_12	0.0377231			
2_13	0.0296682			

**Supplementary information**

**Table S2. Results for Asthma in A) ALL families and B) EUR families, for weighted and unweighted GSMA, using 30 cm bins.**

Pos: position, with 1 assigned to bin with highest summed rank and most significant  $p_{SR}$

SR: summed rank

$p_{SR}$ : summed rank p-value. The nominal probability that a bin would achieve or exceed the observed summed rank under the null hypothesis of no linkage in the bin.

$p_{OR}$ : ordered rank p-value. The probability that the  $k$ th highest summed rank achieves or exceeds an observed summed rank under the null hypothesis of no linkage in the bin.

**A. ALL families**

<b>Asthma</b>									
UNWEIGHTED ANALYSIS					WEIGHTED ANALYSIS				
BIN	Posn	SR	$p_{SR}$	$p_{OR}$	BIN	Posn	SR	$p_{SR}$	$p_{OR}$
1_1	83	744	0.757288	0.984402	1_1	85	732.561	0.761132	0.954305
1_2	33	932	0.219404	0.0170983	1_2	25	951.501	0.199857	0.386961
1_3	40	904	0.289165	0.0463954	1_3	60	828.961	0.509933	0.580042
1_4	37	911.5	0.269677	0.069593	1_4	28	939.259	0.225207	0.382962
1_5	45	879	0.359353	0.260174	1_5	56	838.151	0.483877	0.69663
1_6	43	881	0.353549	0.40106	1_6	47	878.176	0.373729	0.228077
1_7	30	935	0.212413	0.0760924	1_7	37	915.72	0.278385	0.126387
1_8	102	674.5	0.894409	0.931807	1_8	118	550.296	0.981229	0.0925907
1_9	59	808.5	0.57545	0.9985	1_9	91	705.341	0.817531	0.975202
1_10	66	798.5	0.605625	0.968503	1_10	54	844.135	0.467104	0.694331
2_1	98	685.5	0.877271	0.982802	2_1	83	757.887	0.701566	0.536146
2_2	76	779.5	0.661843	0.786621	2_2	38	910.83	0.290392	0.157884
2_3	25	970.5	0.140652	0.00349965	2_3	9	1062.21	0.0495983	0.107389
2_4	68	797.5	0.608717	0.909209	2_4	58	832.267	0.500476	0.686231
2_5	91	702.5	0.847402	0.9991	2_5	92	702.859	0.822252	0.966303
2_6	105	632.5	0.94397	0.9986	2_6	108	606.599	0.949703	0.980402
2_7	101	683.5	0.880498	0.890111	2_7	107	616.921	0.94095	0.977002
2_8	67	797.5	0.608717	0.952205	2_8	68	798.053	0.595961	0.810019
2_9	112	591	0.97327	0.972803	2_9	113	585.193	0.964393	0.766823
3_1	96	692.5	0.865496	0.988801	3_1	102	640.03	0.917387	0.9951
3_2	58	810	0.570817	0.999	3_2	65	816.185	0.545833	0.487551
3_3	12	1037.5	0.0537635	0.0135986	3_3	16	1019.22	0.0917398	0.0377962
3_4	11	1041	0.0508084	0.0214979	3_4	11	1056.95	0.0537652	0.0316968
3_5	53	846	0.459353	0.69853	3_5	69	795.627	0.602477	0.789321
3_6	71	791	0.628302	0.866613	3_6	76	782.886	0.636866	0.454755
3_7	118	495	0.997022	0.70143	3_7	104	627.244	0.931066	0.9954
3_8	117	549.5	0.988654	0.60464	3_8	111	599.682	0.9548	0.857514
4_1	77	779.5	0.661843	0.686031	4_1	79	772.487	0.664348	0.486251
4_2	60	807.5	0.578438	0.996	4_2	71	787.451	0.624648	0.845015
4_3	85	735	0.77887	0.989801	4_3	93	694.5	0.837553	0.982602
4_4	22	987	0.11363	0.00209979	4_4	20	1000.96	0.115703	0.0170983
4_5	34	919.5	0.249447	0.10039	4_5	42	893.824	0.33274	0.242776
4_6	16	1019	0.0719881	0.00259974	4_6	14	1033.1	0.0760482	0.0319968
4_7	3	1161.5	0.00435	0.0130987	4_7	2	1164.32	0.00742288	0.215778
5_1	49	866.5	0.396578	0.30337	5_1	46	883.289	0.360182	0.174783
5_2	41	899.5	0.301327	0.0623938	5_2	44	887.094	0.350273	0.246675

5_3	47	868.5	0.390512	0.446155	5_3	53	849.101	0.453167	0.617738
5_4	57	819	0.543138	0.989901	5_4	48	876.672	0.377738	0.181282
5_5	2	1227.5	0.000714406	0.00289971	5_5	1	1204.15	0.00291695	0.29507
5_6	1	1258.5	0.000282203	0.0330967	5_6	5	1142.58	0.011739	0.00849915
5_7	21	990	0.109077	0.00289971	5_7	30	936.448	0.231163	0.239176
6_1	55	831	0.506075	0.947505	6_1	84	739.051	0.74637	0.929007
6_2	10	1044	0.0482864	0.040096	6_2	7	1083.98	0.0351093	0.10399
6_3	19	1005.5	0.0878728	0.00129987	6_3	26	946.971	0.209102	0.390761
6_4	88	714.5	0.824025	0.9994	6_4	73	786.309	0.627776	0.687131
6_5	29	936.5	0.208979	0.106489	6_5	17	1018.84	0.0922059	0.0174983
6_6	65	798.5	0.605625	0.984602	6_6	43	892.478	0.336279	0.190181
7_1	95	695.5	0.860207	0.992601	7_1	82	757.931	0.70146	0.655734
7_2	52	847.5	0.454771	0.750625	7_2	75	784.215	0.633341	0.526547
7_3	13	1034.5	0.0564347	0.00739926	7_3	27	942.829	0.217775	0.392261
7_4	17	1012.5	0.0792626	0.00269973	7_4	24	955.264	0.192329	0.393661
7_5	110	610	0.961925	0.976802	7_5	99	653.419	0.900925	0.9971
7_6	106	623.5	0.95162	0.999	7_6	100	651.523	0.903352	0.995
8_1	97	690.5	0.868965	0.982402	8_1	98	670.116	0.877624	0.982602
8_2	93	700	0.852109	0.9969	8_2	103	633.536	0.924532	0.9954
8_3	82	754.5	0.730721	0.926007	8_3	87	722.363	0.783387	0.973603
8_4	36	917.5	0.254439	0.0426957	8_4	18	1012.3	0.100376	0.0184982
8_5	115	574.5	0.980653	0.814619	8_5	116	554.179	0.979847	0.560044
8_6	104	666.5	0.905759	0.89781	8_6	101	641.32	0.915854	0.9975
9_1	108	616.5	0.957261	0.9955	9_1	114	585.006	0.964516	0.591241
9_2	107	617	0.956879	0.9986	9_2	109	604.648	0.951164	0.958404
9_3	111	599	0.968921	0.979902	9_3	115	554.359	0.979773	0.793321
9_4	87	728.5	0.793815	0.988701	9_4	86	729.056	0.768972	0.954605
9_5	90	707	0.838866	0.9992	9_5	96	687.486	0.849804	0.946605
9_6	89	708.5	0.835985	0.9996	9_6	89	710.446	0.807553	0.986201
10_1	50	859	0.419542	0.50175	10_1	52	851.913	0.445365	0.627037
10_2	6	1079	0.025989	0.0729927	10_2	4	1155.42	0.00897796	0.0188981
10_3	42	881.5	0.352079	0.50205	10_3	23	974.533	0.157141	0.089791
10_4	72	785.5	0.644587	0.919208	10_4	40	905.012	0.304668	0.136686
10_5	109	611.5	0.960919	0.991001	10_5	97	676.545	0.867701	0.978002
10_6	73	782	0.654696	0.928007	10_6	55	841.476	0.474537	0.683832
11_1	46	876.5	0.366778	0.244676	11_1	78	775.396	0.656759	0.50185
11_2	9	1066	0.0330051	0.00909909	11_2	12	1049.4	0.0602161	0.0308969
11_3	5	1082.5	0.0243432	0.148185	11_3	3	1155.57	0.00895338	0.0850915
11_4	23	983.5	0.119079	0.00159984	11_4	22	976.451	0.153877	0.127587
11_5	56	830.5	0.507667	0.914709	11_5	51	855.437	0.435495	0.607939
12_1	44	881	0.353549	0.291971	12_1	66	816.002	0.546358	0.374463
12_2	51	852.5	0.439455	0.662434	12_2	64	821.837	0.530068	0.385961
12_3	15	1025	0.0657144	0.00309969	12_3	13	1038.91	0.0699491	0.0378962
12_4	27	969.5	0.142422	0.00069993	12_4	34	918.103	0.272724	0.339266
12_5	26	970	0.141503	0.00149985	12_5	36	916.289	0.277051	0.189581
12_6	35	917.5	0.254439	0.0780922	12_6	35	916.705	0.276055	0.270873
13_1	78	777.5	0.667765	0.652135	13_1	81	761.017	0.693809	0.664334
13_2	48	867	0.395018	0.390461	13_2	72	786.87	0.626227	0.773323
13_3	94	699.5	0.853048	0.992401	13_3	95	688.419	0.848218	0.969703
13_4	31	934	0.214689	0.0493951	13_4	19	1003.14	0.112566	0.030097
14_1	92	701.5	0.849309	0.9981	14_1	67	805.491	0.575627	0.671533
14_2	70	794	0.61928	0.864914	14_2	32	926.036	0.254157	0.316268

14_3	99	685	0.878042	0.964304	14_3	70	791.972	0.61251	0.805719
14_4	74	782	0.654696	0.873113	14_4	62	826.202	0.517752	0.448155
14_5	62	803	0.591928	0.994101	14_5	49	873.949	0.385071	0.173783
15_1	116	567.5	0.983312	0.687931	15_1	105	627.178	0.931136	0.986501
15_2	79	777	0.669199	0.550345	15_2	59	829.137	0.509419	0.688031
15_3	80	773.5	0.679201	0.576042	15_3	61	828.884	0.510138	0.461754
15_4	54	833	0.499826	0.955804	15_4	33	923.161	0.260765	0.289071
16_1	39	906.5	0.28264	0.0528947	16_1	50	858.144	0.428053	0.626337
16_2	24	977	0.129719	0.00249975	16_2	41	896.009	0.327116	0.279672
16_3	32	933.5	0.215858	0.0277972	16_3	31	930.655	0.243746	0.292771
16_4	8	1066	0.0330051	0.0291971	16_4	15	1031.49	0.0777279	0.0171983
17_1	114	586.5	0.975479	0.849615	17_1	112	588.422	0.962426	0.863114
17_2	75	779.5	0.661843	0.862714	17_2	90	709.356	0.809732	0.977802
17_3	4	1115	0.0126822	0.0574943	17_3	8	1075.58	0.0402567	0.0848915
17_4	7	1070.5	0.0304737	0.0527947	17_4	6	1103.73	0.0249313	0.0588941
18_1	69	796.5	0.61173	0.872613	18_1	57	835.344	0.491796	0.683932
18_2	113	587.5	0.975032	0.939906	18_2	117	551.584	0.980773	0.319868
18_3	86	732	0.785809	0.989401	18_3	94	690.061	0.845355	0.982802
18_4	18	1007	0.0860194	0.00259974	18_4	29	936.908	0.230189	0.333667
19_1	64	802.5	0.593488	0.978302	19_1	80	767.983	0.676083	0.534947
19_2	14	1030	0.0607127	0.00389961	19_2	21	981.416	0.145496	0.124188
19_3	38	909.5	0.27483	0.0563944	19_3	45	884.784	0.356203	0.219578
19_4	103	668.5	0.903041	0.938206	19_4	106	622.751	0.935532	0.981402
20_1	81	756	0.726916	0.945905	20_1	63	825.13	0.520842	0.373163
20_2	84	742	0.762258	0.980202	20_2	88	716.752	0.795048	0.980502
20_3	63	803	0.591928	0.987901	20_3	74	785.212	0.630721	0.615938
21_1	20	1005	0.0885245	0.00049995	21_1	10	1057.89	0.0529813	0.0708929
21_2	61	805	0.585865	0.9962	21_2	77	782.403	0.638145	0.354765
22_1	28	941.5	0.197876	0.0872913	22_1	39	907.025	0.299716	0.165483
22_2	100	683.5	0.880498	0.943106	22_2	110	600.571	0.954214	0.931607

**B. EUR families**

**Asthma**

		UNWEIGHTED ANALYSIS			WEIGHTED ANALYSIS				
BIN	Posn	SR	p <sub>SR</sub>	p <sub>OR</sub>	BIN	Posn	SR	p <sub>SR</sub>	p <sub>OR</sub>
1_1	50	663.5	0.468146	0.963404	1_1	64	639.313	0.54643	0.624038
1_2	16	795.5	0.105983	0.128987	1_2	15	804.692	0.112382	0.315368
1_3	37	709	0.314837	0.580842	1_3	58	656.561	0.4919	0.561244
1_4	66	631.5	0.579679	0.816118	1_4	47	693.603	0.376465	0.263774
1_5	68	624	0.60558	0.890311	1_5	69	623.387	0.596528	0.724128
1_6	58	644.5	0.534756	0.957804	1_6	61	648.751	0.516677	0.559244
1_7	28	751	0.196944	0.0819918	1_7	39	708.235	0.33288	0.60104
1_8	106	504	0.910292	0.771523	1_8	118	404.09	0.982193	0.10229
1_9	71	620.5	0.617433	0.768923	1_9	88	559.269	0.776556	0.908209
1_10	49	664	0.466331	0.978102	1_10	38	709.437	0.329484	0.673333
2_1	102	523	0.878967	0.785121	2_1	76	604.674	0.652927	0.689531
2_2	57	645.5	0.53121	0.972603	2_2	27	757.35	0.204153	0.215878
2_3	30	739.5	0.226366	0.182682	2_3	8	847.533	0.0581906	0.371463
2_4	78	594.5	0.701544	0.947005	2_4	65	638.196	0.54997	0.550945
2_5	99	534.5	0.856674	0.812219	2_5	98	526.467	0.848909	0.823418
2_6	105	505	0.908787	0.851315	2_6	107	498.356	0.897509	0.413959

2_7	109	494.5	0.923579	0.588841	2_7	112	452.791	0.95182	0.670133
2_8	98	539	0.847321	0.80112	2_8	93	550.375	0.797718	0.70373
2_9	117	419.5	0.983633	0.410259	2_9	117	415.136	0.977217	0.219178
3_1	96	552.5	0.817079	0.625337	3_1	103	509.528	0.879687	0.686231
3_2	69	621.5	0.614072	0.890811	3_2	75	606.452	0.647748	0.732727
3_3	25	761	0.17343	0.0891911	3_3	28	751.25	0.218391	0.286371
3_4	2	914.5	0.00971525	0.314269	3_4	3	911.408	0.0167873	0.316668
3_5	43	699.5	0.345126	0.290271	3_5	55	662.239	0.473747	0.670233
3_6	75	611.5	0.647374	0.720628	3_6	70	621.399	0.602687	0.69543
3_7	113	476.5	0.94481	0.332767	3_7	84	578.225	0.72786	0.776022
3_8	110	491	0.928109	0.514349	3_8	97	533.737	0.834477	0.748125
4_1	59	644	0.536473	0.929207	4_1	63	642.333	0.537027	0.611939
4_2	61	640.5	0.548605	0.905709	4_2	68	633.858	0.563665	0.379262
4_3	85	580.5	0.74379	0.845215	4_3	99	523.054	0.855631	0.805219
4_4	12	815	0.0773669	0.165483	4_4	19	793.497	0.131028	0.138286
4_5	31	737	0.233107	0.166183	4_5	42	705.885	0.339768	0.329967
4_6	17	785.5	0.123234	0.237776	4_6	20	786.665	0.143346	0.182082
4_7	6	871.5	0.0264296	0.0794921	4_7	6	877.021	0.0341195	0.19918
5_1	41	702.5	0.335481	0.389461	5_1	44	705.167	0.341854	0.162084
5_2	46	677.5	0.419359	0.889311	5_2	57	656.72	0.491389	0.677232
5_3	65	632.5	0.576287	0.860014	5_3	72	618.685	0.610886	0.579642
5_4	56	649.5	0.517222	0.955604	5_4	45	702.29	0.3504	0.165783
5_5	1	945.5	0.00429152	0.40186	5_5	2	922.825	0.0129441	0.458254
5_6	3	887	0.0188542	0.384362	5_6	14	808.672	0.106125	0.350865
5_7	39	704	0.330718	0.566443	5_7	50	690.673	0.385323	0.10379
6_1	47	668.5	0.450662	0.980102	6_1	82	584.19	0.711486	0.778622
6_2	10	857	0.0356432	0.0049995	6_2	5	882.273	0.0307839	0.288571
6_3	4	886	0.0192771	0.188181	6_3	22	781.349	0.153547	0.124688
6_4	73	618	0.625821	0.664534	6_4	56	659.842	0.481428	0.659634
6_5	21	769	0.155863	0.233277	6_5	7	848.317	0.0574364	0.536246
6_6	64	634.5	0.56937	0.873113	6_6	40	706.046	0.339295	0.570143
7_1	51	662	0.473412	0.952405	7_1	52	684.103	0.405326	0.126087
7_2	72	619	0.62247	0.730527	7_2	81	586.782	0.704288	0.790821
7_3	15	797	0.103551	0.189681	7_3	31	729.478	0.273257	0.709029
7_4	18	782	0.129636	0.214579	7_4	32	722.217	0.293205	0.836316
7_5	84	585.5	0.729115	0.783622	7_5	74	609.25	0.639403	0.732427
7_6	104	512.5	0.897028	0.809019	7_6	95	545.598	0.808669	0.619038
8_1	74	617	0.629167	0.591141	8_1	89	558.762	0.777725	0.854715
8_2	92	558	0.803809	0.862014	8_2	110	474.407	0.92969	0.546345
8_3	70	621	0.615711	0.838216	8_3	80	590.57	0.693775	0.768823
8_4	38	707	0.321101	0.552145	8_4	17	797.149	0.124812	0.257474
8_5	116	432.5	0.977828	0.510849	8_5	116	416.777	0.976319	0.459654
8_6	81	592	0.709371	0.836616	8_6	94	548.924	0.801132	0.634737
9_1	107	497	0.920224	0.80082	9_1	113	443.764	0.959257	0.660934
9_2	93	557	0.806233	0.80292	9_2	102	519.108	0.863036	0.548645
9_3	115	451	0.966692	0.436356	9_3	114	421.438	0.973895	0.820718
9_4	88	575	0.759217	0.747325	9_4	90	558.702	0.777861	0.769323
9_5	87	575.5	0.757843	0.821018	9_5	100	521.456	0.858714	0.742926
9_6	103	520	0.884318	0.747725	9_6	104	509.527	0.879688	0.544346
10_1	42	700.5	0.341946	0.362564	10_1	51	684.856	0.402937	0.180182
10_2	7	866	0.0297644	0.0469953	10_2	1	922.885	0.0129263	0.80182
10_3	35	722	0.275433	0.265273	10_3	16	800.399	0.119353	0.29967

10_4	63	639	0.553711	0.809419	10_4	33	721.513	0.295168	0.769123
10_5	111	487	0.933041	0.447455	10_5	91	551.096	0.796021	0.869313
10_6	80	593	0.706255	0.883312	10_6	60	651.241	0.508871	0.566143
11_1	60	643	0.539905	0.90291	11_1	85	573.342	0.740763	0.820018
11_2	5	880	0.0219424	0.107589	11_2	12	817.913	0.0927635	0.407359
11_3	8	859.5	0.0339101	0.0327967	11_3	4	903.331	0.0199712	0.19778
11_4	36	710.5	0.310107	0.633037	11_4	41	705.894	0.33974	0.447555
11_5	91	563.5	0.789909	0.808519	11_5	77	603.774	0.655582	0.607239
12_1	62	639.5	0.552033	0.871813	12_1	83	583.736	0.712789	0.69713
12_2	45	679	0.414106	0.911509	12_2	67	634.818	0.560667	0.458454
12_3	26	755	0.18737	0.133287	12_3	23	778.833	0.158463	0.0978902
12_4	29	740.5	0.223649	0.247775	12_4	35	714.946	0.31352	0.784322
12_5	34	729.5	0.253721	0.127287	12_5	34	718.81	0.302812	0.756324
12_6	48	668.5	0.450662	0.961804	12_6	37	712.469	0.320769	0.666233
13_1	82	590	0.715593	0.820818	13_1	73	610.118	0.63678	0.79572
13_2	53	656.5	0.492747	0.958404	13_2	71	620.316	0.605968	0.625737
13_3	100	530	0.865698	0.821318	13_3	92	551.087	0.796045	0.784322
13_4	52	657.5	0.489226	0.973503	13_4	26	760.599	0.196839	0.226377
14_1	79	593.5	0.704687	0.922008	14_1	54	670.353	0.448193	0.422358
14_2	33	733.5	0.242517	0.107589	14_2	11	829.098	0.0782669	0.292171
14_3	67	627.5	0.593507	0.865613	14_3	36	712.74	0.319936	0.761024
14_4	94	555	0.811117	0.764824	14_4	78	602.354	0.65981	0.547445
14_5	97	551	0.820671	0.550345	14_5	66	636.459	0.555499	0.505349
15_1	118	400.5	0.989786	0.281472	15_1	109	475.081	0.928839	0.685531
15_2	55	652	0.508455	0.952105	15_2	48	692.132	0.380872	0.219378
15_3	76	599	0.687589	0.958004	15_3	59	654.215	0.4994	0.549645
15_4	40	702.5	0.335481	0.511049	15_4	25	764.778	0.187472	0.210979
16_1	19	774.5	0.144477	0.30147	16_1	46	696.117	0.368822	0.273373
16_2	27	754	0.189744	0.089591	16_2	53	683.329	0.407649	0.0872913
16_3	14	797.5	0.10278	0.29577	16_3	21	782.697	0.150928	0.176082
16_4	9	857.5	0.0353076	0.0128987	16_4	9	841.303	0.0644033	0.334067
17_1	112	484.5	0.936044	0.337466	17_1	111	464.129	0.941053	0.609539
17_2	90	565	0.786037	0.852515	17_2	105	507.023	0.883841	0.470653
17_3	11	836.5	0.0528322	0.0267973	17_3	13	816.058	0.0953643	0.306169
17_4	20	774	0.145462	0.206979	17_4	10	831.807	0.0749906	0.380562
18_1	44	687.5	0.385325	0.726627	18_1	49	691.978	0.381347	0.136786
18_2	95	553.5	0.814689	0.707229	18_2	106	499.307	0.896082	0.542046
18_3	77	597.5	0.692256	0.944806	18_3	87	563.749	0.765497	0.889111
18_4	24	762	0.17113	0.132987	18_4	43	705.422	0.341086	0.243076
19_1	54	656.5	0.492747	0.924608	19_1	79	596.883	0.675835	0.657034
19_2	13	808.5	0.0861965	0.174883	19_2	24	767.305	0.182068	0.248875
19_3	23	763.5	0.167714	0.182882	19_3	29	743.91	0.236211	0.418158
19_4	89	567.5	0.779487	0.866813	19_4	101	521.358	0.858892	0.622638
20_1	83	587	0.724595	0.822918	20_1	62	645.629	0.526605	0.583342
20_2	108	495	0.922887	0.723728	20_2	108	478.127	0.92516	0.759224
20_3	101	529	0.867664	0.746925	20_3	96	542.859	0.814843	0.587341
21_1	32	735	0.238446	0.140386	21_1	18	795.295	0.127927	0.188681
21_2	86	579.5	0.746574	0.792221	21_2	86	566.384	0.758759	0.90011
22_1	22	769	0.155863	0.144286	22_1	30	732.552	0.265276	0.714129
22_2	114	475	0.946391	0.20098	22_2	115	418.764	0.975308	0.676232

**Table S3. Results for Asthma in A) ALL families and B) EUR families ascertained through at least two asthmatic sibs, for weighted and unweighted GSMA, using 30 cM bins.**

Pos: position, with 1 assigned to bin with highest summed rank and most significant  $p_{SR}$

SR: summed rank

$p_{SR}$ : summed rank p-value. The nominal probability that a bin would achieve or exceed the observed summed rank under the null hypothesis of no linkage in the bin.

$p_{OR}$ : ordered rank p-value. The probability that the  $k$ th highest summed rank achieves or exceeds an observed summed rank under the null hypothesis of no linkage in the bin.

**A. ALL families**

<b>Asthma in families ascertained through at least two asthmatic sibs</b>									
UNWEIGHTED ANALYSIS					WEIGHTED ANALYSIS				
BIN	BIN	Posn	SR	$p_{SR}$	$p_{OR}$	BIN	Posn	SR	$p_{SR}$
1_1	98	277.5	0.826217	0.49855	1_1	99	263.568	0.83512	0.505049
1_2	38	399	0.312345	0.414859	1_2	40	390.557	0.364663	0.874213
1_3	29	421.5	0.225016	0.261274	1_3	53	362.028	0.477218	0.890711
1_4	2	546.5	0.0100407	0.339166	1_4	3	553.742	0.0130017	0.188181
1_5	13	482	0.0685288	0.0323968	1_5	18	465.109	0.12748	0.185381
1_6	21	449.5	0.137886	0.0718928	1_6	17	466.648	0.124027	0.244376
1_7	34	406.5	0.281786	0.463954	1_7	22	454.844	0.152953	0.114889
1_8	110	223	0.946336	0.843916	1_8	118	178.628	0.978264	0.0634937
1_9	83	303.5	0.735724	0.915908	1_9	92	286.527	0.765557	0.356064
1_10	56	351	0.52897	0.983002	1_10	46	372.428	0.43571	0.972203
2_1	84	303.5	0.735724	0.852015	2_1	62	346.49	0.540165	0.764324
2_2	32	410.5	0.266016	0.481252	2_2	12	474.162	0.10746	0.669033
2_3	1	574	0.00338898	0.335866	2_3	1	597.39	0.00205932	0.220078
2_4	35	405.5	0.285918	0.40096	2_4	32	413.7	0.279643	0.685631
2_5	51	373	0.426561	0.478252	2_5	58	352.893	0.514413	0.850415
2_6	102	269.5	0.849864	0.341766	2_6	108	227.502	0.918527	0.650035
2_7	95	283.5	0.807199	0.594641	2_7	106	234.563	0.904876	0.69773
2_8	46	386	0.367737	0.253175	2_8	55	358.102	0.493256	0.880212
2_9	101	269.5	0.849864	0.476352	2_9	105	239.6	0.894324	0.655934
3_1	91	288.5	0.790453	0.815318	3_1	94	275.861	0.799403	0.607739
3_2	43	392	0.341666	0.248075	3_2	35	405.716	0.308172	0.725327
3_3	22	447.5	0.14322	0.0593941	3_3	20	455.921	0.150159	0.258574
3_4	61	340.5	0.577339	0.990201	3_4	56	357.242	0.496802	0.839216
3_5	108	237.5	0.923439	0.738326	3_5	115	187.111	0.971604	0.565243
3_6	78	308.5	0.715994	0.985401	3_6	89	291.716	0.748134	0.474953
3_7	118	163.5	0.99157	0.360264	3_7	107	231.873	0.910257	0.651635
3_8	116	197.5	0.973458	0.369463	3_8	111	220.422	0.930831	0.39786
4_1	94	286	0.798848	0.59824	4_1	69	336.751	0.579132	0.478452
4_2	63	338.5	0.586377	0.979002	4_2	59	350.548	0.523933	0.860114
4_3	82	305	0.729763	0.927307	4_3	75	322.425	0.635666	0.563944
4_4	48	383	0.381234	0.213479	4_4	27	434.788	0.209949	0.289571
4_5	72	318	0.677054	0.9956	4_5	72	327.986	0.613825	0.617838
4_6	12	485.5	0.0629737	0.039896	4_6	5	534.755	0.0240652	0.135686
4_7	5	532	0.0164822	0.0349965	4_7	6	533.552	0.0249686	0.0578942
5_1	73	317.5	0.679244	0.992201	5_1	73	326.408	0.620064	0.584042
5_2	44	390	0.350281	0.247075	5_2	60	347.94	0.534361	0.875012
5_3	37	400	0.308269	0.479952	5_3	61	347.244	0.537154	0.825417
5_4	70	319	0.672764	0.9988	5_4	64	344.471	0.548283	0.648435
5_5	19	463	0.105035	0.0129987	5_5	19	462.128	0.134651	0.171383

5_6	4	540.5	0.0123576	0.0478952	5_6	14	472.518	0.111027	0.432557
5_7	16	469.5	0.0913025	0.0350965	5_7	29	432.956	0.215532	0.154185
6_1	49	381.5	0.387945	0.19938	6_1	65	344.274	0.549071	0.532647
6_2	6	530	0.0176466	0.00959904	6_2	2	582.092	0.00435932	0.0907909
6_3	74	315	0.689572	0.994301	6_3	70	334.777	0.587	0.468453
6_4	89	289.5	0.787047	0.919708	6_4	47	369.951	0.445474	0.975702
6_5	30	418.5	0.235808	0.291171	6_5	24	453.3	0.157123	0.0437956
6_6	57	348	0.54262	0.990601	6_6	52	364.692	0.466554	0.872413
7_1	113	214.5	0.956973	0.60304	7_1	97	269.163	0.819338	0.528647
7_2	59	342	0.57044	0.9961	7_2	82	307.407	0.692397	0.530047
7_3	23	439.5	0.166106	0.161484	7_3	50	368.25	0.45227	0.892811
7_4	71	319	0.672764	0.9965	7_4	98	267.858	0.823009	0.448555
7_5	111	220	0.950237	0.787321	7_5	101	256.242	0.854708	0.554845
7_6	93	287.5	0.793887	0.649735	7_6	83	306.916	0.694248	0.430257
8_1	103	259.5	0.876576	0.641136	8_1	88	292.631	0.745058	0.552045
8_2	114	214.5	0.956973	0.40246	8_2	114	203.103	0.955214	0.354465
8_3	97	279.5	0.820082	0.536046	8_3	102	255.104	0.857653	0.466653
8_4	25	433.5	0.184502	0.184782	8_4	15	472.199	0.111701	0.307369
8_5	112	215	0.956383	0.760724	8_5	116	185.268	0.973172	0.354565
8_6	106	247	0.90513	0.70283	8_6	95	272.907	0.808265	0.617338
9_1	77	311	0.705919	0.982802	9_1	81	309.678	0.684032	0.530947
9_2	115	204.5	0.967368	0.444456	9_2	113	203.301	0.954996	0.556044
9_3	100	270	0.848526	0.588741	9_3	109	226.85	0.9197	0.512249
9_4	66	322.5	0.657703	0.9999	9_4	76	322.4	0.63576	0.436556
9_5	87	293.5	0.77286	0.935506	9_5	85	299.949	0.719477	0.550745
9_6	86	298	0.756454	0.883212	9_6	93	279.129	0.789241	0.580942
10_1	99	271	0.845642	0.668333	10_1	100	256.753	0.853415	0.667033
10_2	26	431	0.192551	0.182882	10_2	23	453.345	0.157002	0.0850915
10_3	41	395.5	0.327005	0.271773	10_3	28	434.226	0.21166	0.20338
10_4	64	331	0.620249	0.9987	10_4	34	407.247	0.302663	0.761824
10_5	105	254	0.889701	0.579142	10_5	90	288.607	0.758706	0.505449
10_6	50	376.5	0.410708	0.372263	10_6	38	392.035	0.358944	0.936406
11_1	60	341.5	0.572749	0.993701	11_1	96	270.073	0.81661	0.617538
11_2	58	344.5	0.559019	0.9957	11_2	54	361.978	0.477435	0.819018
11_3	39	398.5	0.314527	0.327567	11_3	30	422.067	0.25128	0.524048
11_4	24	437.5	0.17221	0.143786	11_4	41	388.259	0.373556	0.870513
11_5	10	504	0.0388101	0.00659934	11_5	13	473.755	0.108316	0.535346
12_1	47	386	0.367737	0.166083	12_1	68	341.311	0.560946	0.337666
12_2	76	312	0.701888	0.988601	12_2	87	292.748	0.744673	0.670433
12_3	8	507.5	0.0351059	0.0387961	12_3	11	483.285	0.0894465	0.49945
12_4	17	467	0.0963618	0.0274973	12_4	33	412.314	0.284522	0.635436
12_5	11	493.5	0.0515372	0.019898	12_5	21	455.256	0.151871	0.180382
12_6	7	511.5	0.0313144	0.0575942	12_6	7	501.927	0.0590186	0.574843
13_1	88	291.5	0.779966	0.927607	13_1	103	250.995	0.867981	0.49505
13_2	85	298.5	0.754643	0.927007	13_2	110	222.506	0.927419	0.49775
13_3	107	240	0.918834	0.787821	13_3	117	179.763	0.977425	0.227777
13_4	15	471	0.0883304	0.0579942	13_4	16	467.947	0.121084	0.322868
14_1	69	321.5	0.662079	0.9993	14_1	51	366.475	0.459428	0.882412
14_2	90	289.5	0.787047	0.859914	14_2	49	368.604	0.450873	0.933307
14_3	104	254	0.889701	0.713729	14_3	80	310.129	0.682348	0.627837
14_4	42	392.5	0.339652	0.328467	14_4	66	343.943	0.550417	0.428857
14_5	45	386.5	0.365606	0.334667	14_5	48	369.215	0.448439	0.958004
15_1	79	307.5	0.719917	0.979302	15_1	63	345.392	0.544527	0.710229
15_2	96	282	0.812036	0.539246	15_2	71	329.733	0.607015	0.640636



15_3	40	395.5	0.327005	0.381762	15_3	26	436.591	0.204396	0.325267
15_4	68	321.5	0.662079	0.9995	15_4	42	386.466	0.380545	0.859114
16_1	75	312	0.701888	0.9958	16_1	84	304.325	0.703821	0.445855
16_2	36	401.5	0.302123	0.510749	16_2	43	380.801	0.402422	0.945205
16_3	54	358.5	0.493906	0.933407	16_3	37	392.172	0.358415	0.968803
16_4	18	463.5	0.103932	0.0268973	16_4	25	444.975	0.179943	0.134687
17_1	109	227.5	0.939828	0.859314	17_1	91	287.059	0.763821	0.455554
17_2	67	322.5	0.657703	0.9997	17_2	77	319.015	0.648788	0.505849
17_3	3	544.5	0.0107627	0.127787	17_3	4	544.773	0.0175474	0.140986
17_4	9	507	0.0355771	0.0123988	17_4	10	484.216	0.0877787	0.629437
18_1	53	367	0.454368	0.632637	18_1	31	420.025	0.258072	0.493651
18_2	117	193.5	0.976514	0.212979	18_2	112	216.06	0.937703	0.362064
18_3	92	288	0.792119	0.738226	18_3	79	311.487	0.67726	0.678332
18_4	52	370.5	0.438073	0.521748	18_4	44	376.934	0.417851	0.968803
19_1	65	330	0.624707	0.9981	19_1	74	324.224	0.628665	0.584542
19_2	33	410	0.267896	0.382762	19_2	57	355.293	0.504667	0.839216
19_3	62	339	0.584061	0.989501	19_3	86	298.406	0.724926	0.50285
19_4	80	307.5	0.719917	0.956604	19_4	78	318.55	0.650569	0.409059
20_1	20	451.5	0.132674	0.089791	20_1	8	494.004	0.0709949	0.642336
20_2	31	412.5	0.258374	0.493051	20_2	45	376.18	0.420823	0.951205
20_3	28	427.5	0.20413	0.131687	20_3	39	391.815	0.359802	0.89781
21_1	14	476	0.0788491	0.0486951	21_1	9	491.397	0.0753211	0.559844
21_2	27	428	0.202291	0.193281	21_2	36	404.015	0.314442	0.694831
22_1	55	357	0.500914	0.925407	22_1	67	343.595	0.5518	0.327967
22_2	81	305.5	0.727899	0.954605	22_2	104	247.479	0.87646	0.49865

## B) EUR families

### Asthma in families ascertained through at least two asthmatic sibs

UNWEIGHTED ANALYSIS					WEIGHTED ANALYSIS				
BIN	Posn	SR	P <sub>SR</sub>	P <sub>OR</sub>	BIN	Posn	SR	P <sub>SR</sub>	P <sub>OR</sub>
1_1	41	197	0.383631	0.934807	1_1	69	164.978	0.574419	0.40346
1_2	7	262.5	0.0818194	0.906309	1_2	20	232.268	0.21049	0.966503
1_3	21	226.5	0.217349	0.953205	1_3	50	186.578	0.450081	0.887511
1_4	5	266.5	0.071916	0.962004	1_4	4	283.948	0.0431305	0.79652
1_5	20	227	0.214814	0.972103	1_5	19	234.552	0.199986	0.961704
1_6	31	213	0.289057	0.879912	1_6	23	226.839	0.236194	0.966703
1_7	24	222.5	0.237944	0.930207	1_7	18	235.466	0.195999	0.974603
1_8	118	52.5	0.987552	0.20478	1_8	118	53.8899	0.987634	0.205379
1_9	102	115.5	0.852038	0.371763	1_9	89	142.849	0.696016	0.0164984
1_10	28	216.5	0.269762	0.918008	1_10	29	222.537	0.257235	0.734927
2_1	90	141	0.728052	0.124588	2_1	51	185.559	0.455889	0.867713
2_2	4	276.5	0.0502389	0.889511	2_2	3	289.164	0.0343457	0.816418
2_3	1	343	0.00021271	0.0248975	2_3	1	345.064	0.00012966	0.0152985
2_4	38	202.5	0.349968	0.886511	2_4	37	210.252	0.320053	0.661034
2_5	36	205	0.335141	0.90181	2_5	63	171.157	0.539203	0.643836
2_6	89	142	0.722363	0.147585	2_6	102	121.102	0.804967	0.0129987
2_7	111	94.5	0.920157	0.210779	2_7	109	86.3286	0.932297	0.748625
2_8	98	127.5	0.799572	0.146985	2_8	97	127.539	0.773844	0.0389961
2_9	109	98	0.910973	0.347765	2_9	110	84.4452	0.936984	0.69533
3_1	84	148.5	0.685963	0.208879	3_1	88	143.167	0.694951	0.0361964
3_2	37	203.5	0.344166	0.905509	3_2	44	192.095	0.418423	0.976202

3_3	66	171	0.547609	0.389461	3_3	41	196.921	0.390965	0.971703
3_4	29	214	0.283478	0.944106	3_4	36	212.526	0.308218	0.609839
3_5	112	91	0.928009	0.194981	3_5	113	80.4967	0.94576	0.341066
3_6	97	129	0.793053	0.165783	3_6	91	139.025	0.716705	0.0269973
3_7	86	145	0.705629	0.236276	3_7	66	168.359	0.554626	0.488551
3_8	92	139	0.739188	0.0823918	3_8	86	146.141	0.678774	0.0344966
4_1	81	150.5	0.674134	0.383762	4_1	43	195.552	0.39884	0.936906
4_2	65	171.5	0.544389	0.465553	4_2	47	189.676	0.432274	0.935106
4_3	82	150.5	0.674134	0.271073	4_3	83	151.221	0.651434	0.0284972
4_4	32	211	0.300468	0.89661	4_4	27	224.006	0.249975	0.847615
4_5	94	135.5	0.759341	0.10109	4_5	81	152.281	0.645724	0.0747925
4_6	12	252	0.112286	0.742526	4_6	7	273.096	0.0656762	0.709729
4_7	14	242	0.147876	0.916208	4_7	12	248.304	0.14288	0.975902
5_1	78	153.5	0.656052	0.490751	5_1	75	157.748	0.615277	0.266073
5_2	69	168	0.566451	0.30047	5_2	93	136.323	0.730078	0.0168983
5_3	73	164	0.591707	0.19878	5_3	95	134.084	0.741682	0.00989901
5_4	83	149.5	0.680471	0.241076	5_4	62	173.899	0.523767	0.541546
5_5	59	181	0.484672	0.337166	5_5	39	200.118	0.373673	0.971603
5_6	68	169	0.559947	0.323168	5_6	67	167.099	0.56212	0.472853
5_7	57	183.5	0.468561	0.348265	5_7	45	191.934	0.419379	0.953505
6_1	26	219	0.255995	0.936006	6_1	55	181.848	0.477187	0.728227
6_2	2	343	0.00021271	0.00029997	6_2	2	343.82	0.0001822	0.00019998
6_3	43	195.5	0.393271	0.892311	6_3	58	176.005	0.511347	0.825717
6_4	46	193	0.408917	0.812019	6_4	26	224.076	0.249578	0.913109
6_5	13	251	0.115488	0.657634	6_5	9	265.704	0.0848516	0.731227
6_6	55	184	0.465118	0.548545	6_6	56	181.213	0.48106	0.664134
7_1	58	181	0.484672	0.456254	7_1	54	184.458	0.462127	0.630737
7_2	103	113.5	0.860131	0.361964	7_2	100	124.897	0.787259	0.0118988
7_3	40	202	0.353136	0.755124	7_3	68	166.592	0.565396	0.393761
7_4	113	88.5	0.937415	0.19868	7_4	114	76.5307	0.956153	0.376562
7_5	44	195.5	0.393271	0.819118	7_5	46	191.56	0.421582	0.923308
7_6	62	176.5	0.513255	0.381862	7_6	52	185.131	0.458344	0.808019
8_1	52	186	0.452577	0.724528	8_1	64	171.152	0.539239	0.516548
8_2	116	72.5	0.967315	0.220778	8_2	116	66.7854	0.969026	0.256074
8_3	85	146	0.700163	0.275972	8_3	96	130.091	0.761201	0.0256974
8_4	22	223	0.235071	0.978702	8_4	13	247.355	0.14648	0.958104
8_5	115	73	0.966513	0.416258	8_5	117	65.501	0.974892	0.174383
8_6	64	172.5	0.538545	0.50075	8_6	65	168.656	0.552882	0.59694
9_1	48	191.5	0.41818	0.720428	9_1	72	158.634	0.609901	0.559444
9_2	88	144.5	0.709101	0.107089	9_2	103	119.114	0.813815	0.0134987
9_3	101	122	0.825757	0.151685	9_3	106	100.369	0.89032	0.435356
9_4	67	169	0.559947	0.446255	9_4	79	153.523	0.639011	0.151585
9_5	74	162	0.604106	0.241776	9_5	92	137.764	0.722632	0.019598
9_6	105	109.5	0.874872	0.330267	9_6	107	97.6101	0.899585	0.452655
10_1	104	112.5	0.863776	0.291771	10_1	105	111.458	0.847509	0.0552945
10_2	27	218	0.261495	0.918608	10_2	24	226.727	0.236714	0.938406
10_3	18	236	0.172756	0.837116	10_3	14	246.623	0.149313	0.932207
10_4	54	184.5	0.462201	0.630037	10_4	32	216.24	0.289179	0.809119
10_5	96	129.5	0.789543	0.223978	10_5	73	158.137	0.612438	0.471753
10_6	51	187.5	0.44318	0.711829	10_6	40	196.978	0.390629	0.988101
11_1	107	108	0.879937	0.161984	11_1	108	92.7762	0.914239	0.571043
11_2	76	158.5	0.626106	0.30117	11_2	80	153.365	0.639914	0.0915908
11_3	63	175.5	0.519407	0.347165	11_3	48	188.653	0.43782	0.918408
11_4	72	164.5	0.588527	0.256674	11_4	90	141.73	0.702272	0.0142986

11_5	17	237	0.168398	0.876912	11_5	34	215.083	0.294907	0.667033
12_1	87	144.5	0.709101	0.182282	12_1	99	126.769	0.777704	0.010399
12_2	93	138.5	0.742892	0.0576942	12_2	101	122.985	0.795653	0.0108989
12_3	16	237.5	0.166367	0.922108	12_3	25	224.326	0.248389	0.951105
12_4	15	238	0.164153	0.949805	12_4	38	206.393	0.340163	0.811519
12_5	11	253	0.109141	0.810919	12_5	16	243.073	0.163363	0.911709
12_6	8	262.5	0.0818194	0.813219	12_6	6	273.656	0.0643347	0.825617
13_1	108	104	0.893995	0.228577	13_1	104	114.8	0.833311	0.0331967
13_2	114	88	0.93789	0.0930907	13_2	111	82.9182	0.940913	0.609339
13_3	117	70.5	0.969647	0.0994901	13_3	115	67.3062	0.968502	0.475652
13_4	45	194.5	0.399416	0.80302	13_4	28	223.825	0.250821	0.763024
14_1	30	213.5	0.286266	0.917308	14_1	33	215.985	0.290362	0.720228
14_2	19	229	0.204922	0.969603	14_2	11	250.684	0.133945	0.976502
14_3	42	196.5	0.386867	0.905809	14_3	35	213.171	0.3048	0.688131
14_4	70	165.5	0.582651	0.406259	14_4	94	135.333	0.735137	0.0118988
14_5	95	134.5	0.764595	0.0811919	14_5	85	146.742	0.675348	0.0549945
15_1	91	140.5	0.731472	0.0891911	15_1	57	179.755	0.489211	0.662234
15_2	77	157	0.635101	0.309569	15_2	49	187.746	0.443593	0.89821
15_3	25	221	0.245596	0.924608	15_3	17	241.593	0.169683	0.894111
15_4	49	191	0.421439	0.650235	15_4	30	219.494	0.27238	0.811919
16_1	60	180	0.490793	0.30137	16_1	82	151.544	0.649899	0.0541946
16_2	61	178.5	0.500313	0.318568	16_2	60	174.548	0.519597	0.726627
16_3	23	222.5	0.237944	0.965003	16_3	21	231.737	0.212994	0.945305
16_4	10	255	0.102986	0.842716	16_4	15	245.652	0.152972	0.89941
17_1	100	125.5	0.809637	0.0892911	17_1	78	153.905	0.636877	0.218578
17_2	106	108	0.879937	0.274473	17_2	98	126.848	0.777304	0.0242976
17_3	6	266	0.0731025	0.913409	17_3	8	273.085	0.0656966	0.530647
17_4	33	210.5	0.303154	0.855114	17_4	31	219.291	0.273326	0.722828
18_1	9	258	0.0942372	0.844916	18_1	10	252.028	0.129114	0.984602
18_2	75	159.5	0.61992	0.329067	18_2	84	150.63	0.654926	0.0193981
18_3	80	153.5	0.656052	0.254675	18_3	59	175.497	0.51403	0.759424
18_4	99	125.5	0.809637	0.162484	18_4	71	159.753	0.603968	0.60144
19_1	56	184	0.465118	0.419758	19_1	77	156.092	0.624697	0.176382
19_2	50	188.5	0.437269	0.745225	19_2	74	157.897	0.614244	0.370663
19_3	47	193	0.408917	0.714629	19_3	70	163.59	0.582614	0.40116
19_4	34	206.5	0.326385	0.944406	19_4	42	195.991	0.396229	0.963804
20_1	3	282.5	0.0397627	0.888911	20_1	5	281.553	0.0476008	0.709229
20_2	71	165.5	0.582651	0.289371	20_2	87	144.264	0.688632	0.0407959
20_3	79	153.5	0.656052	0.368263	20_3	76	156.463	0.62239	0.248675
21_1	35	206	0.329431	0.919808	21_1	22	229.501	0.223563	0.953005
21_2	39	202.5	0.349968	0.812719	21_2	53	184.741	0.460696	0.735826
22_1	53	184.5	0.462201	0.741026	22_1	61	174.51	0.519823	0.606739
22_2	110	97	0.914624	0.263274	22_2	112	82.5794	0.942154	0.452655

**Table S4. Results for Atopic asthma in A) ALL families and B) EUR families, for weighted and unweighted GSMA, using 30 cM bins.**

Pos: position, with 1 assigned to bin with highest summed rank and most significant  $p_{SR}$

SR: summed rank

$p_{SR}$ : summed rank p-value. The nominal probability that a bin would achieve or exceed the observed summed rank under the null hypothesis of no linkage in the bin.

$p_{OR}$ : ordered rank p-value. The probability that the  $k$ th highest summed rank achieves or exceeds an observed summed rank under the null hypothesis of no linkage in the bin.

**A. ALL families**

Atopic asthma									
UNWEIGHTED ANALYSIS					WEIGHTED ANALYSIS				
BIN	Posn	SR	$p_{SR}$	$p_{OR}$	BIN	Posn	SR	$p_{SR}$	$p_{OR}$
1_1	63	285	0.5668	0.913009	1_1	64	284.9	0.558714	0.781222
1_2	44	331	0.3345	0.10129	1_2	34	356.1	0.242866	0.0555944
1_3	18	392	0.1106	0.0445955	1_3	19	392.9	0.124635	0.0846915
1_4	26	367	0.1861	0.122288	1_4	15	398.9	0.109631	0.272973
1_5	2	476	0.0079	0.235676	1_5	2	471.5	0.0124398	0.436356
1_6	28	364	0.1967	0.0806919	1_6	24	376	0.173477	0.151185
1_7	13	404	0.0842	0.149185	1_7	12	410.8	0.083255	0.243376
1_8	58	307	0.4526	0.10169	1_8	55	302.2	0.478239	0.733727
1_9	83	246	0.7461	0.961804	1_9	102	194.4	0.894234	0.936406
1_10	8	421	0.0539	0.286971	1_10	3	470.8	0.0127949	0.183782
2_1	96	218	0.8501	0.950805	2_1	104	188.6	0.907514	0.922708
2_2	55	315	0.4148	0.0428957	2_2	41	345.5	0.284995	0.0124988
2_3	21	382	0.139	0.0735926	2_3	18	394.5	0.12044	0.114789
2_4	98	212	0.8663	0.951105	2_4	89	237.3	0.762357	0.685131
2_5	85	243	0.7607	0.957204	2_5	76	260.6	0.668033	0.857114
2_6	115	151	0.9749	0.656934	2_6	116	127.2	0.986075	0.777822
2_7	116	135	0.9863	0.785121	2_7	117	118.5	0.990274	0.678932
2_8	110	176	0.9458	0.842016	2_8	112	170	0.942198	0.457754
2_9	109	178	0.9419	0.887811	2_9	111	171.4	0.939891	0.585841
3_1	70	275	0.6166	0.844316	3_1	74	262.6	0.659301	0.912609
3_2	78	260	0.6875	0.872313	3_2	73	263.3	0.656402	0.944206
3_3	25	368	0.1825	0.164584	3_3	40	346	0.283173	0.0248975
3_4	22	381	0.1406	0.0418958	3_4	17	395.8	0.117152	0.161584
3_5	37	346	0.2675	0.060494	3_5	20	384.8	0.146822	0.219878
3_6	14	402	0.0875	0.10249	3_6	9	415.8	0.0735804	0.521748
3_7	117	126	0.9905	0.692731	3_7	113	165.8	0.948415	0.40436
3_8	74	267	0.6526	0.865913	3_8	61	295.4	0.509959	0.454155
4_1	80	255	0.7077	0.89821	4_1	67	276.1	0.598799	0.909109
4_2	30	363	0.2022	0.0343966	4_2	22	378.5	0.165883	0.251075
4_3	54	317	0.4049	0.0370963	4_3	44	336.3	0.323789	0.0445955
4_4	79	258	0.6967	0.879112	4_4	57	298.9	0.493369	0.709629
4_5	67	277	0.6039	0.925207	4_5	77	256.7	0.684577	0.917208
4_6	59	304	0.4706	0.173983	4_6	83	244.3	0.734955	0.914609
4_7	17	393	0.1092	0.0882912	4_7	47	332	0.342477	0.0255974
5_1	19	384	0.132	0.143886	5_1	25	368.7	0.197475	0.333467
5_2	4	434	0.0364	0.650935	5_2	4	447.6	0.029622	0.475152
5_3	12	404	0.0842	0.258474	5_3	8	419.6	0.0668771	0.555444
5_4	50	322	0.3776	0.0608939	5_4	54	302.9	0.474976	0.79612

5_5	3	437	0.0335	0.794921	5_5	7	429.3	0.0513872	0.40246
5_6	11	417	0.0595	0.0605939	5_6	10	414.8	0.0754084	0.385661
5_7	94	223	0.8342	0.949605	5_7	100	199.1	0.882665	0.955304
6_1	61	296	0.5112	0.481052	6_1	75	261.2	0.665372	0.89891
6_2	6	429	0.0429	0.391261	6_2	11	411.6	0.0818118	0.353765
6_3	33	358	0.2209	0.0182982	6_3	38	352.1	0.258594	0.00969903
6_4	69	276	0.6089	0.850715	6_4	52	308.2	0.450156	0.69753
6_5	7	424	0.0489	0.343466	6_5	5	444.4	0.0328144	0.337466
6_6	47	325	0.3629	0.127287	6_6	26	367.2	0.202799	0.293771
7_1	107	186	0.9287	0.905109	7_1	101	197.8	0.885919	0.934407
7_2	15	398	0.0962	0.111189	7_2	21	383.7	0.150033	0.163584
7_3	16	396	0.1019	0.0908909	7_3	36	355	0.247374	0.0169983
7_4	10	419	0.0564	0.0943906	7_4	14	400.5	0.105686	0.343266
7_5	84	245	0.7525	0.956104	7_5	80	247.2	0.7237	0.972503
7_6	27	364	0.1967	0.138186	7_6	43	338.2	0.3158	0.0470953
8_1	90	233	0.7993	0.945105	8_1	72	263.9	0.653686	0.961504
8_2	51	318	0.3999	0.149485	8_2	62	293.1	0.520747	0.491551
8_3	43	332	0.3298	0.126087	8_3	48	331.5	0.344833	0.0148985
8_4	36	347	0.2633	0.080292	8_4	16	397.9	0.111916	0.191381
8_5	108	183	0.9343	0.886611	8_5	92	230.5	0.786984	0.676632
8_6	72	271	0.6333	0.845215	8_6	79	249.5	0.714083	0.968503
9_1	87	238	0.7804	0.966603	9_1	99	202.2	0.874766	0.955804
9_2	68	277	0.6039	0.877012	9_2	91	232.1	0.781247	0.710029
9_3	34	352	0.2427	0.0606939	9_3	39	348.4	0.273341	0.020098
9_4	29	363	0.2022	0.0662934	9_4	29	365.2	0.209812	0.10439
9_5	103	204	0.8893	0.816918	9_5	109	174.2	0.93522	0.79862
9_6	95	219	0.847	0.968603	9_6	107	184.2	0.916667	0.756324
10_1	111	173	0.9496	0.777222	10_1	108	176.4	0.931375	0.854915
10_2	52	318	0.3999	0.0891911	10_2	27	367.1	0.203102	0.191881
10_3	66	280	0.589	0.889711	10_3	46	334	0.333532	0.0261974
10_4	91	232	0.801	0.910309	10_4	63	287.3	0.547676	0.751025
10_5	93	225	0.8258	0.951905	10_5	84	242.7	0.74146	0.90191
10_6	76	266	0.6598	0.770823	10_6	71	266.5	0.64221	0.951405
11_1	49	324	0.3704	0.0654935	11_1	65	284.3	0.561128	0.70273
11_2	73	271	0.6359	0.785021	11_2	78	252.4	0.702171	0.957804
11_3	82	250	0.7317	0.938306	11_3	93	228.7	0.793304	0.648635
11_4	35	350	0.2529	0.0743926	11_4	50	325.3	0.371851	0.0363964
11_5	53	317	0.4022	0.0566943	11_5	28	366.1	0.206551	0.147285
12_1	45	328	0.3511	0.170483	12_1	56	299.4	0.491171	0.787421
12_2	102	204	0.8893	0.89731	12_2	105	188.5	0.907733	0.853415
12_3	24	373	0.1658	0.0915908	12_3	45	335	0.329578	0.0381962
12_4	9	420	0.0554	0.179982	12_4	23	377.9	0.167485	0.171483
12_5	41	335	0.3185	0.175482	12_5	51	310.6	0.439187	0.663734
12_6	38	345	0.274	0.0513949	12_6	35	355.5	0.245377	0.0339966
13_1	86	240	0.7705	0.962804	13_1	95	215.1	0.838083	0.936706
13_2	60	297	0.5034	0.493551	13_2	82	245.1	0.7321	0.944206
13_3	20	384	0.1333	0.090091	13_3	30	363.7	0.215233	0.0846915
13_4	42	333	0.3252	0.161284	13_4	49	330.1	0.350711	0.0119988
14_1	100	210	0.8734	0.89831	14_1	90	233.9	0.77478	0.734427
14_2	105	192	0.9158	0.923908	14_2	97	212.4	0.846106	0.880012
14_3	114	158	0.9683	0.682232	14_3	115	152.1	0.965916	0.40316
14_4	88	234	0.7956	0.981302	14_4	86	240.2	0.750921	0.847315

14_5	118	116	0.9939	0.473853	14_5	118	114	0.992036	0.372763
15_1	81	252	0.7209	0.925007	15_1	59	298	0.497538	0.522548
15_2	46	325	0.3629	0.19958	15_2	31	362.4	0.219879	0.0641936
15_3	23	374	0.1625	0.130787	15_3	32	362.1	0.220685	0.0354965
15_4	64	282	0.579	0.931107	15_4	58	298.1	0.497322	0.645135
16_1	89	234	0.7956	0.963704	16_1	81	245.4	0.730951	0.969603
16_2	57	307	0.4526	0.167083	16_2	53	306.8	0.456844	0.673533
16_3	56	308	0.4502	0.224578	16_3	69	271.5	0.619965	0.931607
16_4	48	324	0.3678	0.0986901	16_4	68	275.4	0.602177	0.871413
17_1	101	208	0.8789	0.880612	17_1	94	225.4	0.804845	0.690931
17_2	5	432	0.0386	0.490951	17_2	6	437.9	0.0401118	0.326667
17_3	1	510	0.0014	0.156384	17_3	1	520.8	0.0009127	0.10299
17_4	75	266	0.6573	0.830817	17_4	70	267.9	0.636159	0.961104
18_1	97	213	0.8634	0.970703	18_1	96	213.4	0.843193	0.919108
18_2	99	210	0.8734	0.945805	18_2	98	202.8	0.873157	0.976702
18_3	39	341	0.2915	0.0985901	18_3	37	353.2	0.254353	0.0159984
18_4	32	362	0.204	0.00889911	18_4	33	356.9	0.240024	0.0845915
19_1	112	168	0.9565	0.764824	19_1	103	190.6	0.90309	0.944106
19_2	65	281	0.5868	0.925707	19_2	66	281.5	0.574203	0.766023
19_3	77	263	0.6738	0.828917	19_3	85	241.4	0.746454	0.876912
19_4	92	228	0.8171	0.952505	19_4	88	238.6	0.757378	0.732727
20_1	104	193	0.9148	0.959504	20_1	110	173.5	0.936417	0.681932
20_2	113	167	0.9578	0.619738	20_2	114	163.9	0.951149	0.278372
20_3	106	186	0.9287	0.956804	20_3	106	185	0.915063	0.843716
21_1	31	362	0.204	0.0186981	21_1	13	403.7	0.0983338	0.359864
21_2	71	271	0.6333	0.906609	21_2	60	296.7	0.503721	0.489951
22_1	40	339	0.3003	0.10129	22_1	42	341.7	0.300903	0.0272973
22_2	62	285	0.5668	0.951705	22_2	87	240	0.751882	0.770023

## B. EUR families

Atopic asthma									
UNWEIGHTED ANALYSIS					WEIGHTED ANALYSIS				
BIN	Posn	SR	P <sub>SR</sub>	P <sub>OR</sub>	BIN	Posn	SR	P <sub>SR</sub>	P <sub>OR</sub>
1_1	68	220.5	0.598413	0.834617	1_1	66	223.277	0.575455	0.782222
1_2	15	318	0.125508	0.542346	1_2	15	323.179	0.125536	0.540946
1_3	8	333	0.0850898	0.849515	1_3	14	327.161	0.114198	0.491751
1_4	43	274	0.304805	0.0188981	1_4	22	310.422	0.166672	0.265473
1_5	2	374	0.0216805	0.751325	1_5	3	372.124	0.0287669	0.69773
1_6	51	260	0.377378	0.0294971	1_6	39	281.903	0.281423	0.0467953
1_7	14	319.5	0.120896	0.605239	1_7	13	327.459	0.113342	0.623838
1_8	62	231	0.539479	0.752425	1_8	62	231.515	0.532972	0.672933
1_9	110	141	0.922065	0.39826	1_9	115	112.08	0.962221	0.314669
1_10	3	358.5	0.0384076	0.869813	1_10	2	397.775	0.00907965	0.293771
2_1	107	150.5	0.898208	0.428557	2_1	109	131.601	0.928252	0.679432
2_2	33	282.5	0.263796	0.330567	2_2	29	300.802	0.202273	0.0608939
2_3	31	284.5	0.25454	0.439356	2_3	26	303.712	0.191178	0.160084
2_4	100	168	0.843351	0.50475	2_4	84	192.097	0.726767	0.764824
2_5	73	212.5	0.641584	0.842816	2_5	67	223.019	0.576682	0.694831
2_6	113	116	0.965508	0.794621	2_6	116	95.468	0.980692	0.60184
2_7	117	109.5	0.972707	0.141686	2_7	117	93.9611	0.981925	0.352265
2_8	106	153.5	0.889729	0.431757	2_8	107	143.848	0.899592	0.452455

2_9	98	169	0.839922	0.70483	2_9	101	153.712	0.871821	0.807219
3_1	101	167.5	0.845247	0.39996	3_1	93	174.278	0.801131	0.752025
3_2	71	214.5	0.631046	0.892511	3_2	70	215.636	0.614241	0.835716
3_3	24	298	0.196369	0.450655	3_3	41	276.242	0.307299	0.0872913
3_4	25	298	0.196369	0.324768	3_4	19	314.097	0.154192	0.451855
3_5	37	278	0.285245	0.182782	3_5	20	313.736	0.155382	0.338166
3_6	19	314	0.138163	0.212079	3_6	11	329.489	0.107816	0.805319
3_7	114	115.5	0.966067	0.628737	3_7	106	147.86	0.888849	0.410159
3_8	77	207	0.670388	0.79642	3_8	60	235.713	0.511237	0.60204
4_1	72	213	0.638698	0.888211	4_1	65	229.603	0.542786	0.446855
4_2	38	277.5	0.28777	0.130787	4_2	32	296.653	0.2185	0.030097
4_3	36	279.5	0.277985	0.19538	4_3	35	288.917	0.250503	0.0553945
4_4	58	239.5	0.491863	0.566443	4_4	44	266.611	0.353456	0.278872
4_5	69	220	0.600844	0.774723	4_5	77	201.625	0.682508	0.905109
4_6	86	188.5	0.760362	0.912109	4_6	103	152.026	0.876966	0.642236
4_7	41	276.5	0.29264	0.0293971	4_7	61	233.009	0.525239	0.686731
5_1	18	315	0.134999	0.281572	5_1	30	298.104	0.212668	0.0715928
5_2	5	344	0.061794	0.89821	5_2	5	357.797	0.0476754	0.705629
5_3	11	328.5	0.0959516	0.614439	5_3	7	341.516	0.0783525	0.885611
5_4	67	222	0.589916	0.837216	5_4	68	216.391	0.610477	0.925107
5_5	10	330.5	0.0909872	0.680932	5_5	10	330.189	0.105898	0.881512
5_6	23	299	0.192422	0.522148	5_6	24	308.843	0.172246	0.136986
5_7	116	113.5	0.968528	0.254075	5_7	114	113.849	0.959564	0.461154
6_1	91	183.5	0.782516	0.724528	6_1	97	169.708	0.818406	0.508249
6_2	17	315.5	0.133302	0.389461	6_2	23	309.087	0.171386	0.214079
6_3	7	338.5	0.0725499	0.809419	6_3	18	315.459	0.149719	0.518448
6_4	47	268	0.335298	0.0143986	6_4	40	281.845	0.281671	0.0222978
6_5	4	350	0.05115	0.894011	6_5	4	365.29	0.0369771	0.665433
6_6	29	287	0.243115	0.523248	6_6	16	317.047	0.144557	0.706529
7_1	92	183.5	0.782516	0.606239	7_1	89	182.913	0.766443	0.736326
7_2	16	317	0.128664	0.455254	7_2	25	304.2	0.189303	0.233277
7_3	27	297.5	0.198393	0.153285	7_3	45	266.24	0.355307	0.20438
7_4	9	333	0.0850898	0.731427	7_4	17	316.569	0.146127	0.60084
7_5	83	195.5	0.72782	0.860314	7_5	80	198.021	0.699612	0.835616
7_6	42	275	0.299881	0.0249975	7_6	50	256.49	0.404091	0.281772
8_1	64	226	0.567521	0.861514	8_1	57	241.514	0.481184	0.535446
8_2	49	266	0.345791	0.00759924	8_2	58	239.152	0.493574	0.593341
8_3	48	266	0.345791	0.0161984	8_3	46	265.359	0.35957	0.162184
8_4	22	299	0.192422	0.647935	8_4	9	339.102	0.083677	0.711029
8_5	96	180.5	0.795	0.287571	8_5	72	213.396	0.625694	0.776822
8_6	70	217	0.617338	0.849015	8_6	81	196.916	0.704727	0.80492
9_1	74	210.5	0.652413	0.864314	9_1	96	170.549	0.815271	0.590341
9_2	57	241	0.483012	0.559544	9_2	83	192.559	0.724633	0.832017
9_3	52	249	0.437978	0.528047	9_3	49	256.82	0.402476	0.373163
9_4	32	284.5	0.25454	0.319368	9_4	36	288.872	0.250689	0.0282972
9_5	94	182.5	0.786809	0.418358	9_5	105	148.435	0.887358	0.535546
9_6	99	168.5	0.841793	0.619438	9_6	108	138.745	0.912518	0.536546
10_1	105	161.5	0.865439	0.20088	10_1	100	156.74	0.862409	0.79512
10_2	26	297.5	0.198393	0.243376	10_2	12	328.79	0.109669	0.705529
10_3	45	268.5	0.332827	0.0484952	10_3	27	303.575	0.191694	0.0986901
10_4	81	198	0.715571	0.893911	10_4	54	245.217	0.461914	0.622738
10_5	108	146	0.909849	0.486951	10_5	95	174.138	0.801734	0.514649

10_6	59	237.5	0.503208	0.607539	10_6	64	229.822	0.541742	0.557044
11_1	54	246.5	0.452319	0.485951	11_1	71	214.249	0.621305	0.820118
11_2	50	264	0.356243	0.00879912	11_2	63	230.844	0.53647	0.60304
11_3	80	198	0.715571	0.942006	11_3	92	179.188	0.781833	0.59964
11_4	39	277.5	0.28777	0.0757924	11_4	51	255.706	0.408194	0.230977
11_5	60	235	0.516949	0.679732	11_5	37	287.129	0.258272	0.0265973
12_1	44	271.5	0.317568	0.0274973	12_1	56	242.082	0.478314	0.620538
12_2	104	162.5	0.862248	0.270573	12_2	104	148.586	0.886875	0.670233
12_3	40	277	0.290099	0.0463954	12_3	53	248.9	0.442896	0.461854
12_4	12	328.5	0.0959516	0.462854	12_4	33	292.23	0.236442	0.0674933
12_5	66	223.5	0.581864	0.840116	12_5	69	216.38	0.61053	0.871613
12_6	61	234.5	0.520118	0.607039	12_6	48	258.838	0.392267	0.349765
13_1	112	123	0.955651	0.749625	13_1	113	123.462	0.94415	0.312069
13_2	93	183	0.784385	0.509049	13_2	102	153.339	0.872873	0.710129
13_3	34	282.5	0.263796	0.218678	13_3	42	272.356	0.325827	0.162284
13_4	65	225	0.573171	0.836616	13_4	59	236.514	0.507008	0.661534
14_1	90	186.5	0.769293	0.659034	14_1	76	202.766	0.67731	0.921808
14_2	97	177	0.809112	0.368763	14_2	86	187.983	0.744658	0.776022
14_3	109	141	0.922065	0.560844	14_3	110	130.508	0.930704	0.566743
14_4	78	204.5	0.683298	0.840716	14_4	75	204.703	0.667993	0.915808
14_5	118	82.5	0.991975	0.375262	14_5	118	84.5299	0.987732	0.217778
15_1	75	209	0.660088	0.860014	15_1	52	249.349	0.440654	0.560544
15_2	30	286	0.247653	0.463854	15_2	21	311.89	0.161532	0.308969
15_3	13	321	0.116643	0.677732	15_3	28	302.482	0.195838	0.0731927
15_4	46	268	0.335298	0.030497	15_4	43	268.44	0.344538	0.271673
16_1	88	187.5	0.764814	0.812619	16_1	79	198.3	0.698248	0.89561
16_2	56	244	0.466133	0.438556	16_2	55	244.348	0.466436	0.564344
16_3	55	246.5	0.452319	0.361864	16_3	73	212.812	0.628521	0.708729
16_4	63	230	0.545123	0.715628	16_4	82	194.743	0.714821	0.818518
17_1	84	191.5	0.746744	0.929707	17_1	78	199.414	0.693006	0.915408
17_2	6	340	0.0695728	0.884012	17_2	6	347.38	0.0662084	0.850915
17_3	1	423	0.00153644	0.167283	17_3	1	427.933	0.00127119	0.140486
17_4	102	167	0.846815	0.29557	17_4	88	184.442	0.759989	0.760524
18_1	89	187	0.766799	0.741126	18_1	91	181.695	0.771596	0.570543
18_2	76	207.5	0.668137	0.852315	18_2	87	187.538	0.746679	0.694731
18_3	35	282.5	0.263796	0.137986	18_3	34	290.85	0.242301	0.0546945
18_4	28	289	0.234298	0.521048	18_4	38	284.457	0.270097	0.0362964
19_1	103	163	0.860453	0.369363	19_1	94	174.202	0.801472	0.638436
19_2	79	200.5	0.703564	0.927607	19_2	74	209.662	0.644083	0.791921
19_3	82	197.5	0.71811	0.848515	19_3	90	182.114	0.769856	0.672433
19_4	95	180.5	0.795	0.408659	19_4	85	191.336	0.730054	0.69843
20_1	87	188.5	0.760362	0.852015	20_1	99	158.941	0.855279	0.806919
20_2	111	127	0.94948	0.774623	20_2	111	126.365	0.938835	0.565443
20_3	115	114.5	0.967386	0.446555	20_3	112	125.673	0.940463	0.418158
21_1	21	307	0.162226	0.317168	21_1	8	339.903	0.0818948	0.821418
21_2	53	247	0.44924	0.566743	21_2	47	260.607	0.383475	0.346065
22_1	20	307.5	0.160346	0.413459	22_1	31	297.858	0.213711	0.0420958
22_2	85	189.5	0.75591	0.933107	22_2	98	161.101	0.848225	0.818418



**Table S5. Results for total IgE in A) ALL families and B) EUR families, for weighted and unweighted GSMA, using 30 cM bins.**

Pos: position, with 1 assigned to bin with highest summed rank and most significant  $p_{SR}$

SR: summed rank

$p_{SR}$ : summed rank p-value. The nominal probability that a bin would achieve or exceed the observed summed rank under the null hypothesis of no linkage in the bin.

$p_{OR}$ : ordered rank p-value. The probability that the  $k$ th highest summed rank achieves or exceeds an observed summed rank under the null hypothesis of no linkage in the bin.

**A. ALL families**

		IgE							
		UNWEIGHTED ANALYSIS				WEIGHTED ANALYSIS			
BIN	Posn	SR	$p_{SR}$	$p_{OR}$	BIN	Posn	SR	$p_{SR}$	$p_{OR}$
1_1	108	504.5	0.909357	0.479252	1_1	97	528.763	0.855192	0.933907
1_2	3	892.5	0.0167144	0.311369	1_2	3	905.045	0.0157644	0.283272
1_3	10	836	0.053633	0.0708929	1_3	10	845.851	0.0523084	0.0631937
1_4	35	712	0.306162	0.690331	1_4	50	675.022	0.430839	0.662534
1_5	97	544	0.83647	0.768023	1_5	114	463.684	0.948145	0.227977
1_6	16	793	0.110502	0.181482	1_6	25	757.816	0.192894	0.281172
1_7	29	758	0.180852	0.0105989	1_7	15	809.642	0.0952414	0.10419
1_8	90	567	0.780631	0.79672	1_8	74	616.372	0.62376	0.514549
1_9	115	455	0.963707	0.351265	1_9	117	430.507	0.973173	0.150585
1_10	72	624.5	0.603411	0.466053	1_10	44	689.088	0.385558	0.734627
2_1	111	477	0.94387	0.670233	2_1	110	489.177	0.919361	0.343866
2_2	81	594	0.702665	0.771123	2_2	84	589.182	0.706513	0.487751
2_3	42	701.5	0.339252	0.329567	2_3	55	667.721	0.454981	0.40306
2_4	53	656	0.494013	0.958504	2_4	49	675.446	0.429426	0.749525
2_5	26	769	0.156265	0.00929907	2_5	11	836.846	0.0614906	0.0757924
2_6	18	785	0.124393	0.156684	2_6	16	802.597	0.105891	0.128687
2_7	13	799	0.100735	0.39786	2_7	27	752.734	0.205027	0.225977
2_8	33	738.5	0.229493	0.0391961	2_8	21	774.819	0.155745	0.236076
2_9	45	690	0.376804	0.49595	2_9	32	713.119	0.311468	0.952105
3_1	93	549	0.825205	0.945905	3_1	106	497.372	0.908133	0.747125
3_2	85	587	0.724092	0.618738	3_2	91	573.22	0.751155	0.278572
3_3	107	508.5	0.903307	0.522048	3_3	99	520.452	0.870973	0.933807
3_4	67	631.5	0.5795	0.716128	3_4	56	662.894	0.470893	0.508349
3_5	68	628	0.591488	0.758224	3_5	42	693.012	0.373131	0.784022
3_6	49	669.5	0.446764	0.89891	3_6	51	673.752	0.435088	0.607239
3_7	34	713	0.30314	0.755224	3_7	65	632.104	0.572679	0.828317
3_8	76	619.5	0.620337	0.244076	3_8	67	627.095	0.589213	0.822818
4_1	109	490.5	0.928354	0.678632	4_1	109	492.597	0.914675	0.414059
4_2	24	771.5	0.150994	0.0277972	4_2	29	747.489	0.217637	0.176882
4_3	11	832.5	0.0571516	0.0447955	4_3	9	846.605	0.0515762	0.128487
4_4	19	783.5	0.127205	0.107389	4_4	30	739.399	0.238314	0.330267
4_5	87	580	0.744575	0.670033	4_5	92	550.793	0.807576	0.890111
4_6	95	548.5	0.826359	0.834417	4_6	104	502.024	0.90128	0.858714
4_7	57	645.5	0.530974	0.968703	4_7	85	584.356	0.720411	0.564844
5_1	89	567.5	0.779263	0.860314	5_1	79	600.758	0.672131	0.60184
5_2	61	635	0.567509	0.977102	5_2	78	607.429	0.651629	0.428057
5_3	69	627.5	0.593201	0.673233	5_3	60	641.715	0.540771	0.911609
5_4	60	641.5	0.544949	0.931107	5_4	81	598.389	0.679268	0.461354

5_5	41	701.5	0.339252	0.442856	5_5	40	693.13	0.372741	0.918108
5_6	23	772	0.149938	0.0515948	5_6	23	770.349	0.16521	0.154685
5_7	38	702.5	0.336031	0.744726	5_7	39	694.009	0.369936	0.943706
6_1	5	859	0.0343534	0.381162	6_1	4	898.958	0.0180703	0.151885
6_2	1	962.5	0.00257966	0.263774	6_2	1	954.974	0.00462966	0.426057
6_3	28	759.5	0.177351	0.0175982	6_3	26	757.496	0.193632	0.189581
6_4	50	661	0.476552	0.979802	6_4	48	676.548	0.425788	0.79962
6_5	56	647	0.525711	0.976402	6_5	45	685.82	0.395898	0.751225
6_6	47	680	0.410398	0.721928	6_6	33	711.801	0.315416	0.930107
7_1	52	656.5	0.49227	0.974903	7_1	46	680.641	0.412424	0.832117
7_2	74	622.5	0.610253	0.329967	7_2	63	636.86	0.556939	0.844716
7_3	27	763.5	0.168207	0.0152985	7_3	12	833.109	0.0654355	0.0536946
7_4	6	858	0.0350432	0.212979	7_4	6	872.917	0.0313398	0.143786
7_5	32	739	0.228206	0.0693931	7_5	38	695.055	0.366733	0.963304
7_6	100	531.5	0.862587	0.784922	7_6	95	537.351	0.83771	0.925807
8_1	64	634.5	0.569267	0.870213	8_1	70	619.908	0.612419	0.806219
8_2	43	700	0.344088	0.281072	8_2	34	708.704	0.32479	0.934907
8_3	77	618	0.625343	0.205979	8_3	71	618.89	0.615655	0.750525
8_4	54	656	0.494013	0.925507	8_4	47	677.267	0.423427	0.859014
8_5	118	349.5	0.997696	0.757924	8_5	118	387.564	0.990271	0.29957
8_6	113	469.5	0.951363	0.471753	8_6	112	485.401	0.924183	0.151485
9_1	84	588	0.721104	0.685531	9_1	89	573.736	0.749749	0.49795
9_2	63	634.5	0.569267	0.925507	9_2	64	635.606	0.561074	0.79912
9_3	14	798	0.102385	0.286771	9_3	17	797.804	0.113499	0.126587
9_4	7	849	0.0419788	0.207779	9_4	5	876.904	0.0289313	0.247775
9_5	98	538	0.849527	0.822418	9_5	86	580.229	0.732068	0.605439
9_6	104	515.5	0.89188	0.742726	9_6	107	496.275	0.909664	0.636336
10_1	59	642.5	0.54143	0.952705	10_1	61	640.976	0.5433	0.866413
10_2	62	635	0.567509	0.956204	10_2	69	624.263	0.598546	0.740826
10_3	17	786	0.122575	0.227477	10_3	22	773.751	0.158038	0.164484
10_4	4	866	0.0297491	0.475252	10_4	8	855.385	0.0440356	0.126287
10_5	73	622.5	0.610253	0.442456	10_5	66	631.588	0.574365	0.756324
10_6	102	524.5	0.876067	0.750425	10_6	93	550.578	0.808083	0.822118
11_1	66	632	0.577786	0.793321	11_1	72	616.853	0.622168	0.722128
11_2	15	794	0.108863	0.262374	11_2	24	768.332	0.169498	0.118788
11_3	25	770	0.154186	0.0174983	11_3	28	750.663	0.210045	0.186881
11_4	12	823	0.0675864	0.0668933	11_4	18	787.689	0.131015	0.232277
11_5	8	849	0.0419788	0.0945905	11_5	7	860.407	0.040072	0.172583
12_1	31	742	0.220347	0.0723928	12_1	36	697.656	0.358539	0.982202
12_2	105	514	0.894464	0.654835	12_2	100	513.516	0.883037	0.952005
12_3	112	472.5	0.948488	0.593941	12_3	105	500.802	0.903058	0.782622
12_4	71	625	0.601757	0.562544	12_4	59	649.06	0.516538	0.775222
12_5	110	487.5	0.932194	0.59964	12_5	111	486.48	0.922799	0.258374
12_6	82	591.5	0.71037	0.762824	12_6	88	574.028	0.748943	0.607639
13_1	44	691	0.373545	0.566343	13_1	41	693.087	0.372887	0.857914
13_2	37	704	0.331266	0.785821	13_2	53	669.087	0.45041	0.582942
13_3	96	548	0.827499	0.757624	13_3	103	503.303	0.899333	0.911109
13_4	92	550	0.822926	0.967903	13_4	108	493.634	0.913269	0.549945
14_1	94	548.5	0.826359	0.90401	14_1	96	533.919	0.844815	0.918908
14_2	101	530	0.865463	0.717428	14_2	113	467.261	0.944703	0.328067
14_3	70	627	0.594897	0.588641	14_3	87	580.057	0.732557	0.491351
14_4	103	524.5	0.876067	0.625437	14_4	98	523.788	0.864847	0.943506

14_5	86	583.5	0.734554	0.644836	14_5	68	626.143	0.592439	0.770323
15_1	91	558	0.803835	0.918808	15_1	94	545.471	0.819862	0.853815
15_2	48	675	0.427645	0.817518	15_2	52	670.278	0.446493	0.642636
15_3	116	442.5	0.972174	0.338966	15_3	115	451.238	0.95897	0.251875
15_4	117	377.5	0.994559	0.871113	15_4	116	430.998	0.972897	0.358664
16_1	21	777	0.139849	0.0824918	16_1	31	718.49	0.295784	0.917408
16_2	36	706.5	0.323319	0.793521	16_2	57	656.004	0.493645	0.70463
16_3	39	702	0.337628	0.659934	16_3	43	691.084	0.379264	0.759324
16_4	88	573	0.764277	0.80012	16_4	58	649.526	0.515067	0.841416
17_1	78	608	0.658368	0.531147	17_1	62	638.57	0.551325	0.865013
17_2	2	908	0.0115458	0.39886	17_2	2	907.679	0.0148195	0.533447
17_3	9	845.5	0.0449305	0.0579942	17_3	13	832.471	0.0661076	0.0233977
17_4	20	780.5	0.132902	0.0882912	17_4	19	787.192	0.131946	0.151985
18_1	106	510.5	0.900146	0.617038	18_1	102	503.552	0.898941	0.956604
18_2	22	774.5	0.144835	0.0643936	18_2	14	816.605	0.0855745	0.0872913
18_3	80	595.5	0.698095	0.809019	18_3	77	609.135	0.646318	0.476852
18_4	30	743	0.217787	0.109289	18_4	20	785.871	0.134376	0.10429
19_1	83	591.5	0.71037	0.656434	19_1	80	600.167	0.673931	0.506949
19_2	99	532.5	0.860636	0.855314	19_2	76	613.649	0.632275	0.39616
19_3	55	651.5	0.509921	0.957004	19_3	37	696.133	0.363353	0.975402
19_4	114	463.5	0.956813	0.40056	19_4	101	511.538	0.886365	0.929107
20_1	65	633.5	0.572643	0.825817	20_1	90	573.677	0.749922	0.376462
20_2	51	659.5	0.481783	0.972103	20_2	75	615.085	0.627815	0.452055
20_3	58	645	0.53268	0.950305	20_3	83	592.36	0.697364	0.478252
21_1	40	702	0.337628	0.538446	21_1	35	708.584	0.325158	0.884912
21_2	75	621.5	0.613644	0.266273	21_2	73	616.617	0.622975	0.623838
22_1	79	596	0.696533	0.871813	22_1	82	596.355	0.685398	0.427357
22_2	46	681.5	0.405317	0.763824	22_2	54	668.168	0.453471	0.50075

## B. EUR families

		IgE							
		UNWEIGHTED ANALYSIS				WEIGHTED ANALYSIS			
BIN	Posn	SR	p <sub>SR</sub>	p <sub>OR</sub>	BIN	Posn	SR	p <sub>SR</sub>	p <sub>OR</sub>
1_1	93	406.5	0.76326	0.221578	1_1	95	397.627	0.783013	0.248675
1_2	5	622.5	0.0636847	0.909509	1_2	9	604.818	0.0971609	0.873113
1_3	22	557	0.201506	0.776622	1_3	28	547.557	0.23628	0.544846
1_4	47	507	0.37381	0.226477	1_4	47	503.705	0.389192	0.431757
1_5	84	427	0.692824	0.288471	1_5	98	390.855	0.802719	0.183582
1_6	2	658	0.0283856	0.874713	1_6	3	641.037	0.0471305	0.944606
1_7	19	564	0.181768	0.841216	1_7	21	562.785	0.191591	0.760924
1_8	91	411.5	0.746911	0.225777	1_8	85	420.476	0.709054	0.40176
1_9	99	394	0.802152	0.105089	1_9	102	387.3	0.812622	0.0274973
1_10	48	504	0.385473	0.260874	1_10	33	530.816	0.290798	0.718828
2_1	116	302.5	0.967526	0.237576	2_1	116	284.931	0.976346	0.452255
2_2	54	490.5	0.43918	0.30327	2_2	53	493.258	0.429764	0.285171
2_3	24	549.5	0.223944	0.833017	2_3	16	575.33	0.159231	0.870213
2_4	52	492.5	0.431193	0.423558	2_4	26	553.088	0.219479	0.551645
2_5	46	507	0.37381	0.330167	2_5	17	572.511	0.166046	0.852915
2_6	37	522	0.316929	0.608139	2_6	32	533.75	0.280776	0.69783
2_7	6	617.5	0.0705974	0.886611	2_7	12	592.159	0.121157	0.845715
2_8	61	479	0.486452	0.168583	2_8	57	479.763	0.482957	0.559644

2_9	78	441	0.639945	0.270273	2_9	68	456.27	0.575829	0.555744
3_1	65	455.5	0.582406	0.907609	3_1	86	414.419	0.729905	0.582842
3_2	69	453	0.59257	0.672733	3_2	89	411.777	0.738522	0.336166
3_3	106	367.5	0.871179	0.173383	3_3	108	366.743	0.864608	0.0233977
3_4	31	533.5	0.276237	0.745425	3_4	15	584.692	0.136996	0.721628
3_5	60	479.5	0.484369	0.232377	3_5	48	499.731	0.404487	0.530847
3_6	55	489.5	0.443289	0.247275	3_6	54	493.19	0.430045	0.19518
3_7	20	559	0.195722	0.886211	3_7	36	521.122	0.324541	0.808519
3_8	74	444.5	0.626416	0.549445	3_8	77	432.416	0.666231	0.745825
4_1	101	382.5	0.834376	0.245875	4_1	105	377.922	0.837523	0.0230977
4_2	29	541.5	0.249264	0.612539	4_2	35	523.951	0.314603	0.79632
4_3	18	564.5	0.180404	0.90111	4_3	25	555.217	0.213127	0.583042
4_4	7	612	0.0789126	0.878212	4_4	8	616.55	0.0780355	0.761024
4_5	73	445.5	0.62239	0.616838	4_5	64	467.503	0.531737	0.405559
4_6	88	413.5	0.740276	0.481552	4_6	81	425.513	0.691296	0.634337
4_7	64	461.5	0.558113	0.772623	4_7	80	425.758	0.69041	0.735426
5_1	45	507	0.37381	0.452255	5_1	31	534.59	0.278022	0.769423
5_2	30	536	0.267717	0.750525	5_2	38	517.324	0.338108	0.774023
5_3	50	494	0.425167	0.585941	5_3	50	495.738	0.420056	0.511749
5_4	40	517.5	0.333519	0.478252	5_4	45	509.487	0.367201	0.357964
5_5	59	485.5	0.459713	0.0944906	5_5	63	468.23	0.528833	0.491551
5_6	33	530	0.288393	0.684432	5_6	42	511.925	0.358063	0.590041
5_7	67	454.5	0.586435	0.80252	5_7	74	440.883	0.634943	0.670733
6_1	15	568	0.170968	0.971603	6_1	11	594.762	0.115911	0.876312
6_2	1	696.5	0.00989491	0.70473	6_2	1	686.949	0.0152229	0.852315
6_3	49	494.5	0.423238	0.674233	6_3	51	495.584	0.42059	0.39726
6_4	72	447	0.616515	0.654935	6_4	66	462.904	0.549777	0.420958
6_5	68	454	0.588482	0.730527	6_5	58	479.743	0.483045	0.437056
6_6	62	476	0.498756	0.206879	6_6	65	467.452	0.531933	0.292071
7_1	76	444	0.628322	0.338066	7_1	73	442.389	0.629063	0.70363
7_2	83	427	0.692824	0.405059	7_2	79	429.897	0.675534	0.653535
7_3	43	511	0.358189	0.467353	7_3	27	549.632	0.229836	0.577542
7_4	21	558	0.198593	0.840016	7_4	18	570.907	0.170167	0.807019
7_5	41	514	0.346685	0.544646	7_5	40	515.049	0.34651	0.665933
7_6	96	401.5	0.779247	0.127687	7_6	90	406.324	0.755954	0.461054
8_1	79	440.5	0.641861	0.194481	8_1	76	439.157	0.641406	0.524448
8_2	58	487.5	0.451428	0.0941906	8_2	52	494.197	0.42605	0.351965
8_3	87	422.5	0.709154	0.187581	8_3	97	392.567	0.797826	0.221878
8_4	35	526.5	0.300769	0.620338	8_4	39	517.267	0.338317	0.669433
8_5	118	248.5	0.993468	0.454155	8_5	117	271.26	0.983819	0.418758
8_6	82	430.5	0.679931	0.345265	8_6	67	457.475	0.571173	0.611239
9_1	80	436	0.65918	0.29927	9_1	92	403.269	0.76576	0.359564
9_2	105	376.5	0.849836	0.0725927	9_2	107	369.543	0.858018	0.030297
9_3	28	544	0.241152	0.616138	9_3	23	556.578	0.209167	0.761624
9_4	13	587	0.125113	0.785421	9_4	7	617.857	0.0760533	0.848515
9_5	113	320	0.950513	0.453055	9_5	110	344.894	0.908349	0.187381
9_6	111	349.5	0.907593	0.0912909	9_6	111	343.007	0.911614	0.125287
10_1	75	444.5	0.626416	0.425557	10_1	71	447.733	0.608794	0.662134
10_2	57	488	0.44944	0.140886	10_2	46	508.397	0.371283	0.29997
10_3	10	604	0.0919728	0.69583	10_3	6	627.88	0.0622762	0.79652
10_4	4	645	0.0388593	0.70333	10_4	2	671.875	0.022644	0.772023
10_5	77	441.5	0.63801	0.352665	10_5	56	485.636	0.459604	0.343866

10_6	94	406	0.764921	0.153085	10_6	75	439.644	0.639586	0.620238
11_1	66	455	0.584441	0.860514	11_1	72	444.296	0.622005	0.722728
11_2	14	580	0.140982	0.863214	11_2	19	570.901	0.170187	0.70173
11_3	38	520	0.324284	0.59554	11_3	37	520.288	0.327483	0.748525
11_4	12	598	0.102898	0.593541	11_4	24	555.711	0.211724	0.684332
11_5	11	601	0.0971711	0.637036	11_5	10	596.927	0.111615	0.917108
12_1	32	532	0.281398	0.70423	12_1	41	512.251	0.35689	0.691131
12_2	115	305	0.965366	0.394161	12_2	114	315.652	0.95007	0.264074
12_3	114	314	0.957045	0.405859	12_3	113	324.581	0.939236	0.230677
12_4	56	488.5	0.447414	0.19788	12_4	43	511.624	0.359195	0.479952
12_5	103	377	0.848569	0.212479	12_5	104	380.763	0.830293	0.0287971
12_6	81	430.5	0.679931	0.469253	12_6	83	425.018	0.692989	0.413759
13_1	8	610	0.082105	0.812319	13_1	5	628.962	0.0608974	0.891111
13_2	23	556	0.204402	0.69943	13_2	29	544.744	0.24507	0.553045
13_3	89	413	0.741921	0.380862	13_3	96	395.428	0.789521	0.227377
13_4	70	450	0.604499	0.718428	13_4	91	405.316	0.759178	0.383562
14_1	53	491.5	0.435174	0.361964	14_1	59	478.51	0.487972	0.383362
14_2	107	367	0.872275	0.10349	14_2	112	336.219	0.922779	0.142686
14_3	109	360	0.887307	0.0790921	14_3	115	314.004	0.951905	0.140086
14_4	117	262.5	0.989586	0.649435	14_4	118	264.353	0.986806	0.20128
14_5	97	399.5	0.785439	0.108489	14_5	82	425.138	0.692596	0.526747
15_1	63	467.5	0.533694	0.559344	15_1	61	469.216	0.524866	0.671133
15_2	36	526	0.302533	0.522648	15_2	49	499.246	0.406399	0.434857
15_3	104	377	0.848569	0.124688	15_3	94	397.868	0.782281	0.355064
15_4	112	320	0.950513	0.642636	15_4	109	358.545	0.88237	0.0491951
16_1	27	548	0.22855	0.552645	16_1	44	511.32	0.360371	0.374963
16_2	16	566.5	0.174997	0.958204	16_2	34	529.625	0.294843	0.657934
16_3	42	511.5	0.356288	0.562644	16_3	60	476.108	0.497604	0.39986
16_4	110	355.5	0.896435	0.0792921	16_4	100	388.251	0.809953	0.09989
17_1	98	396	0.796281	0.126187	17_1	103	386.997	0.813515	0.0128987
17_2	3	645	0.0388593	0.867913	17_2	4	631.057	0.0583516	0.944406
17_3	9	605.5	0.089372	0.794721	17_3	14	588.053	0.129669	0.741226
17_4	17	566	0.176368	0.924708	17_4	30	543.956	0.247597	0.464454
18_1	95	404	0.771322	0.131387	18_1	78	430.356	0.673926	0.742026
18_2	34	527.5	0.297186	0.690131	18_2	22	560.235	0.198642	0.738326
18_3	86	424.5	0.701997	0.20048	18_3	62	469.121	0.525238	0.559744
18_4	26	548	0.22855	0.677932	18_4	13	592.09	0.121275	0.742226
19_1	92	406.5	0.76326	0.327867	19_1	106	376.121	0.842055	0.0138986
19_2	100	390.5	0.812198	0.113989	19_2	87	413.462	0.73302	0.50185
19_3	25	549.5	0.223944	0.734027	19_3	20	570.688	0.170716	0.582042
19_4	108	362.5	0.882034	0.107689	19_4	99	390.586	0.80344	0.113189
20_1	51	493.5	0.427167	0.485751	20_1	69	455.636	0.578308	0.463754
20_2	39	519.5	0.326189	0.50035	20_2	55	489.659	0.443833	0.252675
20_3	44	509.5	0.364123	0.430157	20_3	70	454.666	0.582075	0.39606
21_1	90	413	0.741921	0.268673	21_1	93	399.085	0.778604	0.422758
21_2	85	425.5	0.698345	0.253475	21_2	84	422.099	0.703329	0.442156
22_1	102	380	0.840898	0.223678	22_1	101	387.737	0.811424	0.0553945
22_2	71	449	0.608544	0.659634	22_2	88	412.981	0.734572	0.40006

**Table S6. Results for SPT in A) ALL families and B) EUR families, for weighted and unweighted GSMA, using 30 cM bins.**

Pos: position, with 1 assigned to bin with highest summed rank and most significant  $p_{SR}$

SR: summed rank

$p_{SR}$ : summed rank p-value. The nominal probability that a bin would achieve or exceed the observed summed rank under the null hypothesis of no linkage in the bin.

$p_{OR}$ : ordered rank p-value. The probability that the  $k$ th highest summed rank achieves or exceeds an observed summed rank under the null hypothesis of no linkage in the bin.

**A. ALL families**

		SPT							
		UNWEIGHTED ANALYSIS				WEIGHTED ANALYSIS			
BIN	Posn	SR	$p_{SR}$	$p_{OR}$	BIN	Posn	SR	$p_{SR}$	$p_{OR}$
1_1	105	325	0.944356	0.9979	1_1	111	302.4	0.955557	0.872113
1_2	18	587	0.12513	0.160584	1_2	24	584.4	0.152112	0.0276972
1_3	16	592.5	0.113698	0.216378	1_3	15	625.6	0.0757287	0.0123988
1_4	26	569.5	0.166628	0.0251975	1_4	18	615.1	0.0919389	0.00529947
1_5	8	658.5	0.0281864	0.00969903	1_5	8	661.8	0.0353406	0.0382962
1_6	9	652	0.0331161	0.00889911	1_6	5	684.3	0.0201941	0.0763924
1_7	31	564.5	0.179795	0.00119988	1_7	27	566.7	0.195745	0.128487
1_8	55	481	0.478751	0.732227	1_8	56	477.8	0.491436	0.782522
1_9	63	471.5	0.517738	0.330067	1_9	70	429.3	0.667365	0.9976
1_10	82	413.5	0.74041	0.965503	1_10	74	421	0.695702	0.9969
2_1	91	379.5	0.841725	0.9983	2_1	96	359.9	0.864699	0.988101
2_2	86	398	0.789868	0.993901	2_2	89	386.6	0.799695	0.973803
2_3	103	329	0.939173	0.9996	2_3	95	363.1	0.857733	0.988601
2_4	94	368.5	0.868285	0.9987	2_4	88	387.4	0.797537	0.984502
2_5	77	439.5	0.646248	0.474653	2_5	91	375.1	0.829255	0.993001
2_6	48	502	0.393779	0.373063	2_6	49	510.1	0.373751	0.080192
2_7	51	485.5	0.460321	0.881812	2_7	47	515.4	0.355383	0.0722928
2_8	110	313.5	0.957223	0.955404	2_8	115	273.2	0.978769	0.768923
2_9	116	276.5	0.983827	0.707629	2_9	113	291.2	0.965949	0.80092
3_1	88	393.5	0.803334	0.990601	3_1	97	358.9	0.866925	0.978202
3_2	104	328	0.940514	0.9987	3_2	93	363.8	0.856138	0.9981
3_3	28	566.5	0.174472	0.010199	3_3	21	604.2	0.110956	0.0029997
3_4	10	642	0.0417669	0.0130987	3_4	12	648.1	0.0480601	0.00419958
3_5	4	705	0.00765847	0.0120988	3_5	3	730.1	0.00506017	0.0190981
3_6	1	788.5	0.00026356	0.030497	3_6	1	813.3	0.00012627	0.0148985
3_7	96	360.5	0.885647	0.9995	3_7	104	342.8	0.898714	0.835116
3_8	100	343	0.918283	0.9997	3_8	107	323.9	0.929387	0.910409
4_1	67	463	0.552589	0.346565	4_1	62	455.9	0.572535	0.969903
4_2	98	354.5	0.897735	0.999	4_2	94	363.4	0.856865	0.994501
4_3	106	324.5	0.944957	0.9955	4_3	109	316.4	0.939465	0.858414
4_4	40	512	0.354587	0.765623	4_4	38	538.2	0.279148	0.0739926
4_5	49	497	0.413709	0.540146	4_5	32	554.9	0.228495	0.0665933
4_6	32	551.5	0.217286	0.0310969	4_6	30	560.6	0.21259	0.0705929
4_7	99	346	0.913342	0.9996	4_7	103	344.1	0.896286	0.893311
5_1	14	618.5	0.0696974	0.0142986	5_1	36	548.9	0.246093	0.0217978
5_2	23	577	0.148069	0.0439956	5_2	46	516.4	0.351815	0.10169
5_3	56	480	0.482912	0.681132	5_3	71	428.7	0.669335	0.9959
5_4	37	527.5	0.297071	0.323968	5_4	44	518.7	0.343834	0.176482

5_5	54	482	0.474677	0.784922	5_5	50	509.3	0.376547	0.0528947
5_6	33	551	0.218796	0.0163984	5_6	19	606.1	0.107405	0.0143986
5_7	83	407	0.761864	0.989301	5_7	64	451.9	0.587015	0.964104
6_1	107	322	0.947904	0.991501	6_1	117	264.7	0.98332	0.394761
6_2	29	566.5	0.174472	0.00389961	6_2	45	517.5	0.348178	0.140086
6_3	6	684	0.0142678	0.00559944	6_3	17	620.1	0.0839448	0.00509949
6_4	30	566	0.175797	0.00229977	6_4	39	529.5	0.307409	0.240476
6_5	87	398	0.789868	0.983802	6_5	82	396.6	0.77131	0.9992
6_6	59	477.5	0.493091	0.459854	6_6	68	431.2	0.66091	0.9997
7_1	47	503	0.389842	0.437456	7_1	67	437.7	0.638066	0.9969
7_2	79	426	0.696582	0.875112	7_2	79	402.9	0.752811	0.9993
7_3	57	480	0.482912	0.566043	7_3	58	471.5	0.514695	0.846815
7_4	25	574.5	0.154068	0.0159984	7_4	26	575.9	0.172247	0.0385961
7_5	112	300.5	0.968993	0.943006	7_5	116	265.6	0.98287	0.670833
7_6	73	443.5	0.630708	0.724528	7_6	90	381.9	0.812037	0.982502
8_1	21	584.5	0.130661	0.0381962	8_1	16	620.4	0.0834059	0.0116988
8_2	114	289.5	0.97672	0.871713	8_2	106	330.8	0.919015	0.883912
8_3	34	547.5	0.229718	0.0206979	8_3	34	552.6	0.234984	0.0329967
8_4	45	505	0.382019	0.570843	8_4	53	496.5	0.422921	0.20438
8_5	70	454	0.589343	0.509949	8_5	76	410.8	0.728609	0.9996
8_6	118	240	0.995136	0.552845	8_6	118	210.6	0.997483	0.737926
9_1	69	456	0.581096	0.513549	9_1	75	415.8	0.712632	0.9988
9_2	80	417	0.728386	0.977402	9_2	77	409.2	0.733543	0.9995
9_3	36	532	0.281175	0.233577	9_3	37	547.5	0.250207	0.0127987
9_4	24	577	0.148069	0.0184982	9_4	28	562.6	0.206777	0.153085
9_5	85	399	0.786882	0.997	9_5	66	444.3	0.614424	0.985201
9_6	108	318	0.952452	0.987801	9_6	100	350.1	0.884857	0.963404
10_1	42	508	0.370213	0.754725	10_1	31	555.2	0.227846	0.118288
10_2	15	601	0.0975465	0.130087	10_2	9	652.7	0.0434415	0.0484952
10_3	38	518.5	0.3299	0.670033	10_3	33	553.6	0.232184	0.049595
10_4	17	589.5	0.119799	0.192781	10_4	22	603.2	0.112803	0.00089991
10_5	53	483.5	0.468617	0.811019	10_5	41	524.5	0.324001	0.239676
10_6	84	400.5	0.782323	0.9971	10_6	86	389.7	0.79125	0.9951
11_1	76	441	0.640528	0.512949	11_1	84	396.4	0.772045	0.993901
11_2	5	690	0.0120432	0.0108989	11_2	6	682.4	0.0212457	0.030397
11_3	44	505	0.382019	0.691231	11_3	48	512.2	0.366523	0.0884912
11_4	35	544.5	0.239333	0.0231977	11_4	23	596.9	0.12508	0.00359964
11_5	41	510	0.362425	0.760024	11_5	25	580.3	0.161696	0.0307969
12_1	13	621	0.0662076	0.0241976	12_1	13	635.9	0.0618127	0.0135986
12_2	46	503.5	0.387906	0.529147	12_2	40	529.4	0.30762	0.152985
12_3	62	472	0.515731	0.417958	12_3	61	459.6	0.558918	0.954705
12_4	50	486	0.458317	0.917908	12_4	63	453.4	0.581586	0.971203
12_5	20	585	0.129473	0.0672933	12_5	51	503.4	0.397829	0.128187
12_6	78	430.5	0.680077	0.806419	12_6	83	396.4	0.771748	0.9971
13_1	58	479	0.486988	0.493351	13_1	35	551	0.239785	0.0247975
13_2	12	624	0.0622703	0.0357964	13_2	14	627.7	0.0726788	0.0218978
13_3	74	443	0.632649	0.636736	13_3	69	429.7	0.665989	0.9998
13_4	68	456	0.581096	0.627737	13_4	43	520.6	0.337212	0.19698
14_1	113	296	0.972313	0.905209	14_1	92	368.3	0.845818	0.9973
14_2	97	354.5	0.897735	0.9998	14_2	102	344.2	0.896178	0.945905
14_3	65	466	0.540372	0.409659	14_3	85	394.8	0.776581	0.990801
14_4	109	317	0.953565	0.970203	14_4	110	313.5	0.943072	0.80162

14_5	115	277.5	0.983369	0.876412	14_5	101	346.8	0.891355	0.957904
15_1	39	513.5	0.348897	0.79552	15_1	42	520.8	0.336666	0.288271
15_2	61	474	0.50751	0.423658	15_2	59	468.1	0.527359	0.879612
15_3	89	391.5	0.809104	0.989201	15_3	87	387.8	0.796307	0.993301
15_4	66	466	0.540372	0.291371	15_4	60	465.9	0.535437	0.872813
16_1	92	378	0.845565	0.997	16_1	105	334.4	0.913075	0.90311
16_2	60	475.5	0.50133	0.455954	16_2	73	422	0.692199	0.9981
16_3	71	452	0.597263	0.49865	16_3	81	399.4	0.763383	0.9988
16_4	101	338	0.926281	0.9997	16_4	108	321.7	0.932434	0.866913
17_1	7	681.5	0.0153195	0.00079992	17_1	7	666.2	0.031833	0.0630937
17_2	3	775	0.00051949	1.00E-04	17_2	4	723	0.00640508	0.00619938
17_3	2	781.5	0.00038475	0.00159984	17_3	2	748.8	0.0025339	0.0327967
17_4	11	638	0.0457872	0.00879912	17_4	10	652.1	0.0440161	0.0178982
18_1	95	367	0.871759	0.9983	18_1	98	355.1	0.874886	0.979102
18_2	72	446	0.620822	0.706129	18_2	65	448.5	0.599395	0.974903
18_3	102	331.5	0.935758	0.9999	18_3	99	352.2	0.880792	0.974803
18_4	111	306	0.964374	0.959304	18_4	114	291.1	0.965959	0.624338
19_1	64	469.5	0.525957	0.324068	19_1	52	502.3	0.401825	0.0985901
19_2	90	381	0.837906	0.9986	19_2	72	424.3	0.684616	0.9987
19_3	52	485.5	0.460321	0.813819	19_3	54	496.3	0.423481	0.132987
19_4	75	441.5	0.638588	0.60184	19_4	78	408.8	0.734588	0.9988
20_1	43	505.5	0.380053	0.771823	20_1	29	562.4	0.207551	0.0931907
20_2	81	416	0.731853	0.965603	20_2	57	472.8	0.510138	0.876512
20_3	27	569	0.167839	0.0120988	20_3	55	494.6	0.429599	0.116188
21_1	22	583.5	0.132847	0.0226977	21_1	11	650.9	0.0451932	0.00739926
21_2	19	586.5	0.126228	0.0971903	21_2	20	604.6	0.110185	0.00839916
22_1	93	374	0.855415	0.998	22_1	80	399.8	0.762049	0.9995
22_2	117	252	0.992514	0.778822	22_2	112	297.5	0.960258	0.832617

## B. EUR families

SPT									
UNWEIGHTED ANALYSIS					WEIGHTED ANALYSIS				
BIN	Posn	SR	p <sub>SR</sub>	p <sub>OR</sub>	BIN	Posn	SR	p <sub>SR</sub>	p <sub>OR</sub>
1_1	106	286	0.928538	0.953505	1_1	108	261.696	0.955974	0.992101
1_2	18	527	0.110872	0.0526947	1_2	14	540.718	0.0901779	0.126687
1_3	25	497.5	0.185899	0.19788	1_3	24	509.632	0.158686	0.0530947
1_4	34	475.5	0.25769	0.163184	1_4	30	499.731	0.185965	0.00719928
1_5	14	551	0.0677042	0.00829917	1_5	19	523.188	0.125617	0.0939906
1_6	16	537	0.0912609	0.0327967	1_6	17	532.889	0.104916	0.060294
1_7	26	496.5	0.18885	0.144486	1_7	28	502.357	0.178471	0.0171983
1_8	59	415	0.505328	0.633437	1_8	67	403.838	0.55136	0.323968
1_9	41	457.5	0.325439	0.254875	1_9	40	464.621	0.302508	0.114089
1_10	70	399.5	0.573136	0.284872	1_10	43	455.07	0.338929	0.212679
2_1	81	365.5	0.712403	0.867013	2_1	78	384.541	0.631519	0.174283
2_2	77	384	0.638627	0.364164	2_2	60	415.167	0.503229	0.482852
2_3	109	274.5	0.945491	0.917608	2_3	97	297.33	0.90141	0.9998
2_4	91	317.5	0.86454	0.9999	2_4	88	333.464	0.812761	0.9964
2_5	55	425.5	0.459526	0.468653	2_5	69	401.981	0.559108	0.219178
2_6	51	430	0.440049	0.673633	2_6	53	427.914	0.44925	0.557444
2_7	71	397.5	0.581705	0.286871	2_7	70	398.286	0.574801	0.30067
2_8	100	299.5	0.904362	0.9965	2_8	104	284.494	0.924781	0.987301



2_9	114	222	0.987795	0.989001	2_9	112	214.174	0.98917	1
3_1	79	379.5	0.65708	0.384462	3_1	79	383.063	0.637427	0.152085
3_2	111	257	0.965053	0.962304	3_2	109	260.922	0.956818	0.980202
3_3	32	479.5	0.243733	0.188181	3_3	27	503.296	0.175851	0.029797
3_4	11	562	0.0528144	0.0245975	3_4	9	569.586	0.0483737	0.0873913
3_5	7	602	0.0184212	0.00429957	3_5	6	612.65	0.0153559	0.00529947
3_6	3	679.5	0.00109322	0.00019998	3_6	3	695.247	0.00059322	0.00019998
3_7	89	331.5	0.826931	0.9988	3_7	89	330.872	0.820446	0.9965
3_8	90	329	0.834033	0.9987	3_8	85	342.99	0.783411	0.994101
4_1	68	404	0.553493	0.252375	4_1	73	394.267	0.591349	0.19578
4_2	92	313.5	0.874032	1	4_2	90	328.081	0.828448	0.9966
4_3	103	293.5	0.915673	0.982302	4_3	99	296.022	0.903935	0.999
4_4	57	420	0.483261	0.564444	4_4	59	415.277	0.502777	0.60064
4_5	75	392	0.60496	0.168883	4_5	65	405.65	0.543724	0.452855
4_6	35	470.5	0.275649	0.263474	4_6	39	465.989	0.297404	0.140386
4_7	107	282	0.934811	0.947105	4_7	111	253.693	0.964279	0.956504
5_1	6	604.5	0.0171415	0.010499	5_1	7	602.899	0.0203763	0.00669933
5_2	10	563	0.0516322	0.0543946	5_2	11	565.228	0.0534593	0.0278972
5_3	36	466	0.292415	0.374363	5_3	41	464.107	0.304495	0.0744926
5_4	31	480	0.241989	0.262574	5_4	31	492.606	0.207104	0.0267973
5_5	74	392.5	0.602835	0.238376	5_5	75	387.412	0.619701	0.328867
5_6	48	441	0.393142	0.364364	5_6	45	453.642	0.344479	0.111789
5_7	96	307	0.888753	0.9999	5_7	96	297.695	0.900684	1
6_1	95	308	0.886492	0.9999	6_1	107	274.288	0.940264	0.971703
6_2	19	523	0.119706	0.059694	6_2	29	500.305	0.184364	0.0142986
6_3	4	640.5	0.00525169	0.0019998	6_3	5	618.781	0.01275	0.0118988
6_4	13	552	0.0662135	0.0221978	6_4	8	580.715	0.0369008	0.050395
6_5	83	364	0.718032	0.752125	6_5	80	382.084	0.64126	0.116088
6_6	38	463.5	0.301958	0.278172	6_6	38	466.748	0.29465	0.189681
7_1	28	489	0.212131	0.209779	7_1	34	474.213	0.267721	0.265873
7_2	61	412	0.518333	0.578542	7_2	50	434.24	0.422967	0.548245
7_3	54	425.5	0.459526	0.589041	7_3	57	422.586	0.471901	0.39806
7_4	23	507.5	0.15783	0.0935906	7_4	21	515.334	0.144193	0.108489
7_5	105	286.5	0.927733	0.978202	7_5	106	275.576	0.938386	0.985801
7_6	52	429.5	0.442212	0.587041	7_6	64	409.969	0.525234	0.316868
8_1	29	483.5	0.230138	0.330967	8_1	32	490.549	0.213439	0.0217978
8_2	115	205.5	0.993225	0.993301	8_2	117	193.793	0.994961	0.885011
8_3	37	465.5	0.294351	0.288771	8_3	44	454.436	0.341376	0.156784
8_4	40	459.5	0.317445	0.261174	8_4	35	471.666	0.276759	0.276372
8_5	49	440	0.397414	0.309369	8_5	47	443.412	0.385066	0.370863
8_6	112	226	0.985992	0.9991	8_6	113	212.047	0.989934	0.9994
9_1	62	410.5	0.524951	0.550345	9_1	81	378.01	0.657469	0.182482
9_2	86	356	0.747299	0.80352	9_2	87	335.596	0.806402	0.9972
9_3	44	446.5	0.370242	0.523948	9_3	49	440.601	0.396613	0.30057
9_4	21	512	0.146127	0.129887	9_4	26	504.09	0.173617	0.0464954
9_5	99	302.5	0.898235	0.9968	9_5	98	296.806	0.902455	0.9995
9_6	113	225	0.986471	0.9967	9_6	116	195.601	0.994581	0.978002
10_1	72	394	0.596592	0.369763	10_1	76	385.489	0.62767	0.325067
10_2	27	490	0.208901	0.271873	10_2	25	504.969	0.171161	0.0735926
10_3	46	443	0.384808	0.489851	10_3	36	470.438	0.281184	0.226677
10_4	20	516.5	0.134702	0.10489	10_4	16	533.318	0.104058	0.109489
10_5	66	405.5	0.546768	0.382662	10_5	51	431.089	0.436123	0.610639

10_6	82	364	0.718032	0.843916	10_6	83	368.139	0.695324	0.444856
11_1	60	413	0.513952	0.635936	11_1	71	395.285	0.587185	0.352265
11_2	5	621	0.0102576	0.00369963	11_2	4	633.845	0.0077644	0.00929907
11_3	45	443	0.384808	0.608639	11_3	46	452.788	0.347722	0.079792
11_4	53	427.5	0.450932	0.585341	11_4	54	427.364	0.451552	0.474253
11_5	73	394	0.596592	0.262274	11_5	62	410.583	0.522645	0.521048
12_1	22	509	0.153857	0.125387	12_1	33	483.33	0.236643	0.0719928
12_2	65	407	0.540222	0.412259	12_2	72	395.061	0.588104	0.251975
12_3	56	421	0.478939	0.624438	12_3	58	416.49	0.497661	0.645235
12_4	43	449.5	0.357795	0.465253	12_4	48	441.814	0.391572	0.343366
12_5	9	571	0.0425805	0.0416958	12_5	13	550.124	0.0744889	0.0619938
12_6	58	416.5	0.49866	0.658934	12_6	55	426.72	0.454405	0.39506
13_1	78	380	0.6551	0.479252	13_1	61	414.633	0.505506	0.39626
13_2	15	550	0.0691576	0.00359964	13_2	12	559.391	0.0609855	0.0289971
13_3	69	401	0.566673	0.307169	13_3	68	402.091	0.558648	0.308169
13_4	87	354	0.754424	0.790021	13_4	82	372.638	0.678258	0.326967
14_1	116	198	0.995026	0.983202	14_1	114	205.596	0.991998	0.9983
14_2	97	305.5	0.891925	0.999	14_2	103	287.489	0.91971	0.989701
14_3	42	452	0.347603	0.442856	14_3	56	424.474	0.463917	0.410959
14_4	104	287	0.926932	0.990801	14_4	100	294.934	0.906096	0.9973
14_5	117	186.5	0.996889	0.950905	14_5	115	196.379	0.99441	0.9962
15_1	30	480.5	0.240261	0.353165	15_1	18	527.746	0.115454	0.0784922
15_2	47	442	0.388963	0.426457	15_2	37	469.07	0.286181	0.193881
15_3	88	333.5	0.821152	0.9994	15_3	92	317.876	0.855403	0.9993
15_4	64	409	0.531407	0.40246	15_4	63	410.394	0.523434	0.40286
16_1	84	364	0.718032	0.650435	16_1	84	355.113	0.742754	0.90341
16_2	39	461.5	0.309641	0.270573	16_2	42	456.243	0.334292	0.258574
16_3	50	438	0.405755	0.30457	16_3	52	430.101	0.440208	0.548045
16_4	101	298	0.907209	0.992301	16_4	105	282.027	0.92866	0.979402
17_1	8	592	0.0245483	0.00419958	17_1	10	568.942	0.0490915	0.040296
17_2	1	727.5	6.02E-05	0.00709929	17_2	1	729.039	6.44E-05	0.00759924
17_3	2	718.5	0.00011356	0.00019998	17_3	2	724.101	9.15E-05	1.00E-04
17_4	17	530.5	0.103612	0.0548945	17_4	23	512.163	0.152141	0.0593941
18_1	93	312.5	0.87636	0.9998	18_1	102	288.058	0.918742	0.9955
18_2	80	367	0.706637	0.885711	18_2	86	340.883	0.790153	0.993101
18_3	108	280.5	0.937036	0.908409	18_3	101	292.592	0.910475	0.9958
18_4	110	269.5	0.951832	0.908009	18_4	110	254.417	0.963568	0.981102
19_1	85	356.5	0.745495	0.862714	19_1	91	326.688	0.832345	0.993801
19_2	102	295.5	0.911989	0.988701	19_2	95	298.429	0.899203	1
19_3	63	410	0.5271	0.459354	19_3	66	404.048	0.550473	0.427657
19_4	67	405	0.548993	0.29937	19_4	74	390.632	0.606517	0.270773
20_1	76	387.5	0.623916	0.286871	20_1	77	384.68	0.630909	0.257174
20_2	94	310	0.882007	0.9999	20_2	93	308.32	0.878153	1
20_3	12	555	0.0619338	0.0309969	20_3	15	540.218	0.0911025	0.0714929
21_1	33	479.5	0.243733	0.115688	21_1	20	518.724	0.13606	0.108589
21_2	24	503.5	0.168798	0.113589	21_2	22	512.288	0.151811	0.108089
22_1	98	304	0.895126	0.9985	22_1	94	305.004	0.88562	0.9999
22_2	118	175	0.998177	0.80272	22_2	118	171.006	0.998168	0.80242

**Table S7. Results for SPT to HDM in A) ALL families and B) EUR families, for weighted and unweighted GSMA, using 30 cM bins.**

Pos: position, with 1 assigned to bin with highest summed rank and most significant  $p_{SR}$

SR: summed rank

$p_{SR}$ : summed rank p-value. The nominal probability that a bin would achieve or exceed the observed summed rank under the null hypothesis of no linkage in the bin.

$p_{OR}$ : ordered rank p-value. The probability that the  $k$ th highest summed rank achieves or exceeds an observed summed rank under the null hypothesis of no linkage in the bin.

**A. ALL families**

		SPT to HDM								
		UNWEIGHTED ANALYSIS					WEIGHTED ANALYSIS			
BIN	Posn	SR	$p_{SR}$	$p_{OR}$	BIN	Posn	SR	$p_{SR}$	$p_{OR}$	
1_1	94	400.5	0.782112	0.349665	1_1	96	384.629	0.816413	0.611039	
1_2	37	531.5	0.284574	0.181582	1_2	33	545.648	0.24582	0.132387	
1_3	23	564.5	0.181457	0.357164	1_3	23	574.793	0.164182	0.150085	
1_4	42	524	0.311101	0.0691931	1_4	53	491.031	0.439317	0.414959	
1_5	46	511	0.359711	0.169283	1_5	54	489.06	0.446846	0.40116	
1_6	15	608.5	0.0852457	0.0419958	1_6	16	608.394	0.0941618	0.0462954	
1_7	30	550.5	0.222003	0.146185	1_7	44	511.607	0.361945	0.40076	
1_8	33	543	0.245843	0.134487	1_8	45	508.97	0.371513	0.417158	
1_9	91	404	0.771049	0.562344	1_9	91	395.119	0.787058	0.772523	
1_10	82	417.5	0.726186	0.907109	1_10	82	419.031	0.711558	0.779422	
2_1	20	579	0.144287	0.19668	2_1	18	598.721	0.111563	0.0564944	
2_2	50	497	0.414488	0.425357	2_2	50	498.69	0.410042	0.364564	
2_3	49	497.5	0.412494	0.518548	2_3	55	486.028	0.458672	0.448655	
2_4	93	403	0.774243	0.363364	2_4	93	390.261	0.800932	0.743826	
2_5	83	416	0.731346	0.884712	2_5	77	431.714	0.666999	0.753025	
2_6	38	531.5	0.284574	0.111489	2_6	36	534.041	0.283153	0.262974	
2_7	7	649.5	0.0353932	0.106789	2_7	9	648.899	0.0415779	0.0366963	
2_8	81	417.5	0.726186	0.950305	2_8	99	379.846	0.828991	0.410259	
2_9	116	262	0.989097	0.869913	2_9	117	242.119	0.992939	0.80112	
3_1	114	274.5	0.984155	0.968203	3_1	114	298.712	0.964224	0.582442	
3_2	71	437.5	0.653232	0.979202	3_2	69	443.06	0.624996	0.950105	
3_3	8	634	0.0502415	0.219878	3_3	10	641.175	0.0491389	0.0423958	
3_4	5	661	0.0264907	0.193181	3_4	5	662.069	0.0306229	0.288071	
3_5	16	602	0.0964525	0.059694	3_5	11	630.622	0.0613508	0.0758924	
3_6	6	654.5	0.0312745	0.149685	3_6	3	680.33	0.0193441	0.405959	
3_7	59	479	0.487632	0.378962	3_7	47	503.2	0.392917	0.481352	
3_8	76	422	0.71051	0.9953	3_8	51	498.277	0.411581	0.276572	
4_1	99	376.5	0.848472	0.712429	4_1	109	327.707	0.931654	0.737826	
4_2	103	359.5	0.886821	0.788121	4_2	106	331.646	0.926138	0.938906	
4_3	117	234.5	0.995591	0.910309	4_3	118	214.928	0.997431	0.736026	
4_4	98	392	0.807199	0.235976	4_4	98	383.138	0.820376	0.409159	
4_5	104	355	0.895777	0.79702	4_5	94	388.888	0.80473	0.691231	
4_6	89	409.5	0.753236	0.553845	4_6	72	436.092	0.650905	0.952805	
4_7	75	429	0.685144	0.978602	4_7	92	391.702	0.796819	0.791921	
5_1	43	523	0.314698	0.0492951	5_1	31	551.58	0.227688	0.124088	
5_2	70	439	0.647473	0.982802	5_2	83	418.034	0.714891	0.719028	
5_3	18	589.5	0.120756	0.119488	5_3	20	589.47	0.130452	0.0766923	
5_4	85	415	0.734741	0.750925	5_4	70	439.292	0.639061	0.968203	

5_5	90	408.5	0.756554	0.476852	5_5	86	409.564	0.74267	0.750125
5_6	57	486	0.458974	0.229677	5_6	58	475.232	0.500793	0.690031
5_7	27	556.5	0.204138	0.209679	5_7	29	557.418	0.210472	0.118188
6_1	111	313.5	0.956175	0.881712	6_1	116	275.706	0.980107	0.578242
6_2	79	419.5	0.719293	0.977902	6_2	84	413.652	0.729489	0.789421
6_3	24	560	0.194122	0.417758	6_3	27	567.128	0.183883	0.0592941
6_4	80	418.5	0.722782	0.966603	6_4	63	459.613	0.561755	0.878812
6_5	67	456	0.580963	0.739926	6_5	68	443.181	0.624528	0.972903
6_6	95	399	0.786577	0.29717	6_6	73	433.881	0.659114	0.950605
7_1	100	368.5	0.867337	0.841216	7_1	104	340.004	0.91292	0.949205
7_2	73	433.5	0.668301	0.976902	7_2	88	404.728	0.757965	0.732927
7_3	11	623	0.063616	0.0953905	7_3	12	628.215	0.0643906	0.0490951
7_4	1	702.5	0.00836864	0.642036	7_4	2	698.694	0.0117551	0.405759
7_5	68	453	0.593205	0.782822	7_5	66	450.701	0.596284	0.935106
7_6	55	491	0.438697	0.20078	7_6	49	500.245	0.404067	0.39816
8_1	22	566.5	0.176002	0.40216	8_1	17	606.461	0.097355	0.0305969
8_2	34	543	0.245843	0.0773923	8_2	37	531.326	0.292257	0.267573
8_3	62	473	0.512233	0.369963	8_3	57	478.6	0.487645	0.623338
8_4	47	502.5	0.392632	0.478652	8_4	46	503.264	0.392679	0.60054
8_5	56	489.5	0.444623	0.170283	8_5	61	464.191	0.543945	0.874713
8_6	63	467	0.53655	0.60284	8_6	81	424.886	0.691247	0.627737
9_1	45	512	0.355812	0.216678	9_1	41	524.425	0.316163	0.156784
9_2	86	415	0.734741	0.645435	9_2	79	426.978	0.683911	0.753525
9_3	61	473	0.512233	0.489951	9_3	34	541.088	0.26012	0.189381
9_4	88	410.5	0.749853	0.624138	9_4	67	446.779	0.611052	0.960104
9_5	87	415	0.734741	0.525747	9_5	64	458.083	0.567712	0.862714
9_6	107	336.5	0.927511	0.888611	9_6	101	358.306	0.879144	0.881212
10_1	108	336	0.928247	0.807719	10_1	110	315.941	0.946821	0.851615
10_2	65	460	0.564975	0.746425	10_2	76	433.163	0.661759	0.790321
10_3	60	473.5	0.510072	0.581542	10_3	78	430.888	0.67002	0.690031
10_4	29	552	0.217559	0.179282	10_4	25	571.34	0.172968	0.0872913
10_5	41	529	0.293325	0.0351965	10_5	35	536.302	0.275634	0.271473
10_6	54	493	0.430677	0.20198	10_6	39	527.877	0.304173	0.210579
11_1	53	494	0.426584	0.249975	11_1	74	433.683	0.659863	0.913709
11_2	21	575	0.15395	0.212179	11_2	14	620.86	0.0744237	0.0279972
11_3	40	531	0.286403	0.0384962	11_3	42	523.914	0.317954	0.106589
11_4	2	702.5	0.00836864	0.257674	11_4	1	715.602	0.00714237	0.583842
11_5	66	456	0.580963	0.825017	11_5	60	466.122	0.536394	0.881612
12_1	17	594.5	0.110601	0.10389	12_1	22	581.227	0.14871	0.089791
12_2	13	617.5	0.0712864	0.0460954	12_2	15	619.846	0.0758432	0.0131987
12_3	69	447	0.616839	0.909409	12_3	87	408.12	0.747286	0.70343
12_4	3	675	0.0184669	0.374063	12_4	4	670.006	0.0252271	0.347365
12_5	28	554	0.211619	0.20238	12_5	40	524.958	0.314363	0.227277
12_6	78	420	0.717571	0.987801	12_6	90	395.781	0.785138	0.840116
13_1	58	481	0.479377	0.380262	13_1	75	433.278	0.66134	0.863014
13_2	35	538	0.262419	0.132187	13_2	48	502.196	0.396702	0.413959
13_3	48	500.5	0.400597	0.467753	13_3	52	492.353	0.434316	0.463554
13_4	105	349	0.906932	0.834917	13_4	102	346.966	0.900905	0.962004
14_1	118	225.5	0.996825	0.684332	14_1	115	280.138	0.977592	0.734527
14_2	115	266	0.987705	0.950405	14_2	107	330.429	0.927882	0.890911
14_3	77	420.5	0.715743	0.994601	14_3	85	411.226	0.737312	0.785321
14_4	74	432.5	0.672036	0.965603	14_4	89	400.818	0.769903	0.772323

14_5	101	365	0.875207	0.841516	14_5	103	341.843	0.909903	0.968303
15_1	109	321.5	0.947445	0.933307	15_1	111	311.51	0.951813	0.817218
15_2	102	362.5	0.88059	0.810619	15_2	97	384.352	0.817139	0.493751
15_3	92	404	0.771049	0.439356	15_3	95	384.852	0.815814	0.721428
15_4	52	495.5	0.420515	0.278672	15_4	62	461.234	0.555416	0.89511
16_1	106	345	0.913952	0.826317	16_1	108	329.767	0.928828	0.817518
16_2	97	395.5	0.797092	0.216578	16_2	100	368.073	0.857809	0.724128
16_3	112	304.5	0.964604	0.89711	16_3	112	304.604	0.958811	0.80462
16_4	113	304	0.965064	0.788121	16_4	113	304.169	0.959242	0.653935
17_1	19	579.5	0.143057	0.286171	17_1	26	567.788	0.182088	0.0922908
17_2	4	673.5	0.0192042	0.177682	17_2	7	654.034	0.0369847	0.124988
17_3	10	623.5	0.0629313	0.176382	17_3	13	623.082	0.0712432	0.0458954
17_4	31	550.5	0.222003	0.0853915	17_4	19	592.014	0.125017	0.0926907
18_1	36	537.5	0.263995	0.0856914	18_1	30	551.858	0.226857	0.192181
18_2	51	496	0.418484	0.362464	18_2	56	483.515	0.46836	0.466653
18_3	110	318	0.951438	0.908709	18_3	105	335.389	0.920311	0.947905
18_4	84	415	0.734741	0.842116	18_4	80	426.72	0.68481	0.659034
19_1	72	437	0.655188	0.966003	19_1	65	454.095	0.583109	0.909109
19_2	12	619	0.0691254	0.0787921	19_2	6	656.829	0.0346237	0.214979
19_3	64	462	0.556821	0.753825	19_3	59	474.617	0.503192	0.60464
19_4	96	398	0.789637	0.228777	19_4	71	437.517	0.645661	0.964404
20_1	14	611	0.0811787	0.0580942	20_1	21	585.167	0.139824	0.0843916
20_2	44	517.5	0.334773	0.107289	20_2	43	511.835	0.361073	0.514849
20_3	39	531.5	0.284574	0.0637936	20_3	32	548.153	0.238174	0.143386
21_1	25	559.5	0.195531	0.317868	21_1	24	574.598	0.164709	0.0864914
21_2	26	558	0.199875	0.262774	21_2	38	529.193	0.299594	0.255674
22_1	9	623.5	0.0629313	0.308569	22_1	8	648.943	0.0415373	0.0931907
22_2	32	549.5	0.224997	0.059794	22_2	28	558.342	0.207918	0.167283

## B. EUR families

		SPT to HDM							
		UNWEIGHTED ANALYSIS				WEIGHTED ANALYSIS			
BIN	Posn	SR	P <sub>SR</sub>	P <sub>OR</sub>	BIN	Posn	SR	P <sub>SR</sub>	P <sub>OR</sub>
1_1	71	326.5	0.639588	0.938706	1_1	82	305.504	0.723565	0.887311
1_2	45	382.5	0.381923	0.577042	1_2	33	410.367	0.266988	0.376562
1_3	35	400.5	0.303746	0.663034	1_3	29	426.543	0.208975	0.10419
1_4	53	367	0.452998	0.617038	1_4	55	355.013	0.507038	0.952005
1_5	49	375	0.41607	0.578042	1_5	51	367.605	0.44983	0.787821
1_6	15	478.5	0.0735525	0.00949905	1_6	14	474.786	0.0837626	0.0731927
1_7	34	401.5	0.299719	0.724828	1_7	47	379.899	0.394353	0.505249
1_8	44	384	0.375123	0.59984	1_8	50	370.526	0.436465	0.732627
1_9	97	266	0.861379	0.961704	1_9	97	269.216	0.847336	0.884612
1_10	86	296.5	0.762999	0.924508	1_10	86	296.961	0.75585	0.878512
2_1	14	479	0.0727533	0.0225977	2_1	13	482.822	0.069683	0.0349965
2_2	46	381	0.388723	0.553045	2_2	45	385.497	0.369542	0.391461
2_3	66	340.5	0.576189	0.782022	2_3	64	341.038	0.570954	0.888311
2_4	102	261	0.874563	0.729427	2_4	101	262.445	0.865899	0.725527
2_5	74	322	0.659522	0.913209	2_5	72	328.921	0.625155	0.763024
2_6	36	398.5	0.311973	0.664834	2_6	38	397.939	0.316937	0.488451
2_7	9	492.5	0.0524305	0.138686	2_7	11	486.907	0.0632186	0.0920908
2_8	100	263.5	0.868026	0.849315	2_8	103	255.42	0.883472	0.742826

2_9	118	138	0.997562	0.746725	2_9	118	142.101	0.996769	0.679032
3_1	108	250.5	0.899169	0.30327	3_1	104	253.198	0.888655	0.69603
3_2	70	334.5	0.603676	0.70153	3_2	70	329.098	0.624406	0.90011
3_3	7	501	0.0421237	0.207479	3_3	12	485.28	0.0656872	0.0531947
3_4	12	483	0.0661389	0.0569943	3_4	9	490.454	0.0579406	0.216678
3_5	11	489	0.0572228	0.0481952	3_5	6	508.371	0.0361813	0.237576
3_6	4	514.5	0.0287534	0.445855	3_6	2	535.544	0.0159551	0.575542
3_7	43	384	0.375123	0.716028	3_7	37	400.366	0.306903	0.468053
3_8	31	409	0.269807	0.665533	3_8	28	435.4	0.180293	0.0210979
4_1	101	262.5	0.870644	0.787721	4_1	113	234.268	0.927036	0.0925907
4_2	110	245.5	0.9098	0.20368	4_2	111	240.151	0.916153	0.170283
4_3	117	154.5	0.994901	0.883312	4_3	117	153.777	0.994608	0.873613
4_4	76	321	0.663955	0.811919	4_4	80	307.266	0.716365	0.940406
4_5	94	279	0.823366	0.891511	4_5	87	296.538	0.757436	0.822118
4_6	63	343.5	0.562377	0.887511	4_6	60	345.044	0.552606	0.964304
4_7	82	310	0.710454	0.773923	4_7	93	280.907	0.811975	0.863014
5_1	17	467	0.0952008	0.0245975	5_1	19	463.637	0.10594	0.0160984
5_2	59	355	0.509096	0.689031	5_2	68	330.53	0.618033	0.955604
5_3	25	439.5	0.164227	0.0424958	5_3	27	439.36	0.168324	0.0141986
5_4	83	309	0.714387	0.719028	5_4	75	321.459	0.657795	0.838216
5_5	72	325.5	0.643949	0.917408	5_5	78	311.519	0.699314	0.941506
5_6	61	347	0.546226	0.894011	5_6	63	342.058	0.5663	0.912209
5_7	48	377.5	0.404514	0.531547	5_7	40	396.194	0.324137	0.346565
6_1	114	222.5	0.948585	0.233877	6_1	116	197.073	0.973451	0.368963
6_2	51	373.5	0.422922	0.429057	6_2	62	343.147	0.561324	0.932907
6_3	10	491	0.0544788	0.0816918	6_3	17	468.384	0.0961042	0.0261974
6_4	47	380.5	0.390911	0.456054	6_4	44	386.461	0.365407	0.458254
6_5	50	374	0.420747	0.519348	6_5	59	351.588	0.522572	0.839716
6_6	75	321.5	0.661725	0.869313	6_6	61	344.11	0.556853	0.950905
7_1	96	266.5	0.859952	0.979702	7_1	105	244.975	0.906664	0.835216
7_2	77	320.5	0.666025	0.741926	7_2	85	297.808	0.752795	0.909009
7_3	5	510	0.0327084	0.341466	7_3	8	499.374	0.0460339	0.148185
7_4	1	537.5	0.0138305	0.822318	7_4	3	527.104	0.0209864	0.459754
7_5	78	320	0.668362	0.663434	7_5	76	317.978	0.672614	0.889111
7_6	54	364	0.466895	0.691831	7_6	52	367.336	0.451042	0.707929
8_1	23	442.5	0.155511	0.0793921	8_1	21	461.054	0.111491	0.00419958
8_2	29	411	0.26204	0.778722	8_2	43	388.798	0.35515	0.428957
8_3	68	337	0.592381	0.773823	8_3	65	340.353	0.574036	0.845315
8_4	62	346.5	0.548457	0.843416	8_4	57	352.712	0.517526	0.923408
8_5	84	304.5	0.732342	0.825217	8_5	79	307.904	0.713819	0.962504
8_6	67	339.5	0.580777	0.737426	8_6	77	313.847	0.689825	0.937906
9_1	39	395	0.326862	0.507449	9_1	41	394.773	0.330012	0.312769
9_2	64	343	0.564832	0.838716	9_2	67	333.033	0.606827	0.945005
9_3	21	453	0.127255	0.0270973	9_3	16	468.807	0.0952906	0.0535946
9_4	57	358	0.495	0.727827	9_4	53	363.475	0.468555	0.809619
9_5	56	362.5	0.473881	0.550545	9_5	49	373.505	0.423114	0.671633
9_6	91	284	0.807383	0.937906	9_6	92	284.86	0.798823	0.817918
10_1	112	231	0.936067	0.339766	10_1	114	218.995	0.950186	0.256474
10_2	105	253	0.89371	0.644736	10_2	98	268.999	0.84795	0.808919
10_3	99	263.5	0.868026	0.915008	10_3	100	265.204	0.85853	0.734627
10_4	24	442	0.156985	0.0466953	10_4	26	440.646	0.164634	0.019798
10_5	41	391.5	0.34188	0.484652	10_5	34	405.089	0.287867	0.566243

10_6	38	395.5	0.324714	0.606539	10_6	31	415.507	0.247643	0.339566
11_1	69	336.5	0.594538	0.69803	11_1	81	306.091	0.721132	0.923208
11_2	8	493.5	0.0510949	0.233877	11_2	7	506.313	0.0382534	0.142986
11_3	52	371	0.434411	0.471453	11_3	46	382.012	0.384903	0.493551
11_4	2	537.5	0.0138305	0.49645	11_4	1	548.616	0.0101144	0.715928
11_5	60	351	0.527833	0.810819	11_5	58	351.755	0.521861	0.90001
12_1	42	389.5	0.350684	0.492051	12_1	36	401.221	0.303319	0.541946
12_2	18	461.5	0.106974	0.0368963	12_2	22	455.642	0.124196	0.00779922
12_3	89	296	0.764913	0.714929	12_3	95	271.925	0.839588	0.938506
12_4	3	532	0.0167644	0.319468	12_4	5	508.629	0.0359152	0.425457
12_5	37	397	0.318432	0.640236	12_5	48	376.558	0.409262	0.59954
12_6	95	276	0.832492	0.89701	12_6	94	273.613	0.834596	0.953305
13_1	73	323	0.655038	0.931607	13_1	84	305.219	0.724633	0.733827
13_2	55	363	0.471578	0.643236	13_2	56	353.699	0.513015	0.943306
13_3	58	355.5	0.50663	0.767623	13_3	54	356.601	0.499814	0.957704
13_4	98	265	0.864037	0.938406	13_4	96	269.312	0.847054	0.934007
14_1	115	212.5	0.960765	0.289471	14_1	108	241.588	0.913355	0.549045
14_2	107	253	0.89371	0.359764	14_2	91	286.266	0.794004	0.848815
14_3	65	342.5	0.567089	0.779122	14_3	71	329.048	0.624622	0.838516
14_4	87	296.5	0.762999	0.870113	14_4	90	288.313	0.786971	0.864014
14_5	106	253	0.89371	0.50095	14_5	110	240.653	0.915173	0.279072
15_1	116	204.5	0.968898	0.258674	15_1	115	207.754	0.96347	0.347965
15_2	92	283.5	0.809019	0.89961	15_2	89	293.725	0.767832	0.750325
15_3	93	281	0.81719	0.905009	15_3	99	265.936	0.856487	0.809419
15_4	81	310.5	0.708355	0.834917	15_4	83	305.486	0.723632	0.812319
16_1	111	242	0.91674	0.180082	16_1	112	238.44	0.919403	0.109389
16_2	103	260.5	0.875778	0.621838	16_2	102	259.305	0.873896	0.722728
16_3	109	250.5	0.899169	0.180682	16_3	109	241.43	0.91366	0.39896
16_4	104	254	0.891403	0.737526	16_4	106	243.895	0.908859	0.755624
17_1	32	407.5	0.275572	0.624438	17_1	35	403.144	0.295543	0.551545
17_2	13	481.5	0.0685677	0.0339966	17_2	15	472.794	0.0874635	0.0492951
17_3	20	458.5	0.113805	0.0131987	17_3	20	461.272	0.111017	0.0109989
17_4	27	423.5	0.215952	0.368563	17_4	23	452.967	0.130811	0.00789921
18_1	33	402.5	0.295571	0.774123	18_1	32	414.33	0.251977	0.287171
18_2	79	317	0.681355	0.721928	18_2	73	327.543	0.631367	0.734627
18_3	113	230	0.937733	0.212679	18_3	107	242.75	0.911073	0.662134
18_4	90	285	0.804007	0.959904	18_4	88	295.877	0.759899	0.758824
19_1	85	297	0.761215	0.956004	19_1	69	329.12	0.62431	0.944506
19_2	22	448	0.140223	0.0422958	19_2	10	487.88	0.0617076	0.156684
19_3	80	312	0.702211	0.855714	19_3	66	340.094	0.57519	0.772923
19_4	88	296	0.764913	0.813419	19_4	74	326.18	0.637263	0.705429
20_1	28	417	0.239435	0.593741	20_1	30	416.759	0.243065	0.393661
20_2	40	392.5	0.337518	0.540546	20_2	39	397.49	0.31879	0.385561
20_3	26	436.5	0.173293	0.0488951	20_3	25	443.166	0.15736	0.0215978
21_1	16	467.5	0.0941126	0.0470953	21_1	18	464.12	0.104893	0.0311969
21_2	30	410.5	0.263899	0.70213	21_2	42	394.355	0.331802	0.226477
22_1	6	502.5	0.0403305	0.332867	22_1	4	521.087	0.0252805	0.344766
22_2	19	458.5	0.113805	0.0339966	22_2	24	443.204	0.157263	0.0468953

**Table S8. Results for SPTQ in EUR families, for weighted and unweighted GSMA, using 30 cM bins.**

Pos: position, with 1 assigned to bin with highest summed rank and most significant  $p_{SR}$

SR: summed rank

$p_{SR}$ : summed rank p-value. The nominal probability that a bin would achieve or exceed the observed summed rank under the null hypothesis of no linkage in the bin.

$p_{OR}$ : ordered rank p-value. The probability that the  $k$ th highest summed rank achieves or exceeds an observed summed rank under the null hypothesis of no linkage in the bin.

		SPTQ							
		UNWEIGHTED ANALYSIS			WEIGHTED ANALYSIS				
BIN	Posn	SR	$p_{SR}$	$p_{OR}$	BIN	Posn	SR	$p_{SR}$	$p_{OR}$
1_1	92	187.5	0.765904	0.360964	1_1	81	203.274	0.676513	0.417158
1_2	32	278	0.283357	0.730627	1_2	56	244.23	0.464329	0.413759
1_3	62	236.5	0.506553	0.29607	1_3	78	207.139	0.657374	0.507149
1_4	16	316.5	0.128913	0.458754	1_4	12	334.402	0.092866	0.40316
1_5	30	280.5	0.271246	0.787621	1_5	53	247	0.449534	0.568643
1_6	60	241	0.480952	0.19518	1_6	84	202.405	0.680547	0.154785
1_7	72	217	0.616673	0.654535	1_7	65	226.807	0.556461	0.642336
1_8	81	203	0.690815	0.626337	1_8	83	202.681	0.679138	0.226277
1_9	24	292.5	0.217247	0.761724	1_9	16	317.137	0.140731	0.648035
1_10	52	254	0.407767	0.147985	1_10	45	258.486	0.389801	0.682132
2_1	91	188	0.763801	0.447255	2_1	74	212.878	0.62833	0.579542
2_2	20	300	0.186794	0.80452	2_2	10	336.48	0.0879287	0.632437
2_3	63	235.5	0.51225	0.263074	2_3	33	274.069	0.313339	0.923408
2_4	90	189.5	0.756776	0.474453	2_4	93	184.784	0.761029	0.194081
2_5	76	211	0.649203	0.635736	2_5	90	194.579	0.717643	0.0638936
2_6	74	216	0.622202	0.487451	2_6	50	248.036	0.444177	0.825117
2_7	108	150	0.902972	0.358964	2_7	98	180.881	0.777956	0.0288971
2_8	117	94.5	0.988617	0.607139	2_8	117	82.4966	0.992852	0.79792
2_9	118	71	1	1	2_9	118	69.5116	1	1
3_1	113	119	0.964857	0.783122	3_1	114	111.292	0.966832	0.650435
3_2	87	195	0.730445	0.459254	3_2	60	238.015	0.49687	0.391461
3_3	36	269.5	0.325096	0.819318	3_3	17	315.761	0.145169	0.579142
3_4	8	337	0.0748381	0.707929	3_4	6	350.884	0.0585703	0.738326
3_5	4	355.5	0.0420957	0.767323	3_5	5	352.443	0.0557906	0.839016
3_6	2	402	0.00573728	0.142286	3_6	2	401.768	0.0073144	0.209179
3_7	54	248	0.441278	0.332367	3_7	42	260.869	0.377767	0.836616
3_8	26	289	0.232394	0.733927	3_8	25	293.167	0.228146	0.787121
4_1	18	304.5	0.169805	0.80152	4_1	28	283.512	0.269611	0.918608
4_2	67	230	0.543894	0.233977	4_2	62	231.44	0.531777	0.652535
4_3	66	231	0.538105	0.264174	4_3	68	218.277	0.600749	0.863014
4_4	51	255	0.402239	0.171883	4_4	36	272.752	0.319478	0.755524
4_5	78	208.5	0.662111	0.575842	4_5	71	214.019	0.622413	0.825817
4_6	49	257	0.391173	0.231277	4_6	40	267.342	0.34559	0.652235
4_7	97	179.5	0.800031	0.246775	4_7	107	152.516	0.87865	0.149285
5_1	14	323.5	0.108285	0.390161	5_1	11	334.76	0.0920016	0.548145
5_2	17	315.5	0.132019	0.365363	5_2	29	279.348	0.288533	0.963404
5_3	88	190.5	0.751972	0.654935	5_3	97	183.108	0.768559	0.0294971
5_4	7	344	0.0607457	0.607339	5_4	4	367.328	0.0339813	0.592441



5_5	1	414	0.00277203	0.282072	5_5	1	421.505	0.00202542	0.213279
5_6	10	329.5	0.0922516	0.70333	5_6	18	313.564	0.152522	0.562844
5_7	73	216	0.622202	0.612139	5_7	89	194.759	0.716802	0.106789
6_1	77	209	0.659725	0.663734	6_1	77	210.909	0.638028	0.340766
6_2	39	266	0.343056	0.737526	6_2	64	226.911	0.555873	0.744326
6_3	38	268	0.332751	0.709729	6_3	54	246.113	0.454279	0.514149
6_4	33	276	0.293062	0.742826	6_4	21	308.94	0.168252	0.408559
6_5	45	260.5	0.372007	0.425557	6_5	19	313.019	0.154352	0.455554
6_6	56	248	0.441278	0.142686	6_6	69	216.265	0.611076	0.876312
7_1	6	347	0.0553237	0.670133	7_1	9	344.659	0.0704406	0.453955
7_2	83	202	0.695923	0.450655	7_2	59	238.429	0.494636	0.483052
7_3	79	205	0.68067	0.719428	7_3	73	213.59	0.624588	0.650035
7_4	94	187	0.768359	0.182482	7_4	99	179.022	0.785841	0.0262974
7_5	101	174.5	0.818557	0.0920908	7_5	88	195.275	0.714358	0.157884
7_6	58	245	0.458146	0.140086	7_6	57	240.23	0.485122	0.594041
8_1	44	261	0.369552	0.512549	8_1	58	238.677	0.493322	0.592741
8_2	95	181.5	0.791944	0.364664	8_2	102	171.57	0.814845	0.0374963
8_3	37	269	0.32773	0.755524	8_3	61	232.87	0.524166	0.669533
8_4	22	298	0.194724	0.689531	8_4	34	273.505	0.316015	0.884212
8_5	106	153.5	0.892754	0.481252	8_5	105	157.501	0.863538	0.178382
8_6	110	144	0.918005	0.327667	8_6	100	172.422	0.811686	0.107189
9_1	98	179	0.802159	0.173383	9_1	109	146.193	0.896846	0.153985
9_2	103	163	0.861893	0.393061	9_2	95	184.106	0.763898	0.080192
9_3	64	233.5	0.523801	0.29557	9_3	43	258.721	0.388521	0.854615
9_4	19	303.5	0.173514	0.744426	9_4	14	322.967	0.123213	0.642436
9_5	107	152	0.89709	0.405259	9_5	106	154.465	0.87276	0.178682
9_6	43	261.5	0.36671	0.589241	9_6	30	279.258	0.288951	0.931807
10_1	53	249.5	0.432465	0.327267	10_1	76	211.538	0.635053	0.420558
10_2	15	323	0.109708	0.279572	10_2	15	319.412	0.133638	0.670433
10_3	31	280	0.273795	0.718328	10_3	22	307.899	0.171924	0.335966
10_4	46	260	0.374968	0.347265	10_4	39	269.23	0.336397	0.647135
10_5	42	262.5	0.361365	0.641836	10_5	31	278.264	0.29354	0.911509
10_6	23	294.5	0.208804	0.759224	10_6	24	298.365	0.207215	0.626037
11_1	55	248	0.441278	0.227077	11_1	63	227.013	0.555277	0.830417
11_2	3	367	0.028233	0.673333	11_2	8	344.779	0.0701991	0.624638
11_3	11	325	0.10422	0.753625	11_3	13	331.613	0.0998686	0.387761
11_4	96	180.5	0.796125	0.306969	11_4	92	190.573	0.735803	0.0673933
11_5	93	187	0.768359	0.278972	11_5	75	211.707	0.634264	0.542146
12_1	41	263	0.358779	0.721028	12_1	52	247.438	0.447308	0.661534
12_2	57	246	0.45253	0.164384	12_2	38	269.834	0.333325	0.718128
12_3	84	201.5	0.698099	0.361064	12_3	66	223.01	0.576253	0.787921
12_4	99	178.5	0.803979	0.111789	12_4	94	184.115	0.763849	0.136486
12_5	27	284	0.254954	0.878612	12_5	37	270.826	0.328645	0.769723
12_6	29	281.5	0.266576	0.830117	12_6	35	272.824	0.319176	0.841816
13_1	100	178	0.805835	0.070393	13_1	85	197.494	0.704029	0.326767
13_2	48	257.5	0.388228	0.30147	13_2	51	247.665	0.446098	0.749625
13_3	50	255.5	0.399297	0.228377	13_3	46	257.004	0.397545	0.669333
13_4	71	218.5	0.608149	0.655734	13_4	79	207.109	0.657496	0.386961
14_1	104	161.5	0.866948	0.339766	14_1	96	183.88	0.7648	0.0430957
14_2	70	219.5	0.602831	0.69623	14_2	101	172.227	0.812559	0.0616938
14_3	47	259	0.380283	0.307769	14_3	82	203.27	0.676548	0.29677
14_4	115	108	0.977127	0.724828	14_4	115	101.717	0.976328	0.69683

14_5	116	97	0.985571	0.760224	14_5	116	99.8614	0.979328	0.552045
15_1	34	274	0.302632	0.756924	15_1	26	286.591	0.256017	0.933807
15_2	28	281.5	0.266576	0.90181	15_2	32	277.154	0.29874	0.887811
15_3	80	204	0.685699	0.675132	15_3	70	215.368	0.61561	0.843816
15_4	85	198	0.715685	0.49575	15_4	80	204.696	0.669425	0.437156
16_1	75	215.5	0.624811	0.405759	16_1	72	213.947	0.622794	0.736426
16_2	35	273	0.307634	0.715728	16_2	44	258.602	0.389128	0.780022
16_3	82	202	0.695923	0.576142	16_3	91	194.045	0.720173	0.0392961
16_4	109	149.5	0.903673	0.235476	16_4	104	160.032	0.855222	0.179782
17_1	25	289	0.232394	0.831217	17_1	47	256.332	0.400984	0.60174
17_2	12	325	0.10422	0.609039	17_2	23	303.564	0.18753	0.447055
17_3	13	323.5	0.108285	0.534247	17_3	20	310.797	0.161802	0.437456
17_4	86	197	0.720748	0.441956	17_4	108	148.033	0.891964	0.19798
18_1	65	232	0.53248	0.29927	18_1	67	222.761	0.577498	0.70153
18_2	59	243	0.469487	0.166183	18_2	55	244.268	0.464114	0.537046
18_3	40	264	0.353537	0.759324	18_3	41	267.189	0.346309	0.544946
18_4	89	190	0.754482	0.566643	18_4	87	196.844	0.706913	0.164784
19_1	69	228.5	0.552278	0.145885	19_1	86	197.175	0.705429	0.239276
19_2	112	125.5	0.95461	0.729127	19_2	112	126.387	0.940486	0.415958
19_3	102	173	0.824527	0.0781922	19_3	103	165.817	0.836126	0.0932907
19_4	68	229.5	0.546554	0.169083	19_4	49	254.801	0.40889	0.466053
20_1	61	237	0.503921	0.371863	20_1	48	256.067	0.402255	0.49995
20_2	114	119	0.964857	0.59534	20_2	113	111.292	0.966832	0.820018
20_3	21	299	0.19075	0.747325	20_3	27	285.487	0.260857	0.914109
21_1	9	330.5	0.0897923	0.79882	21_1	3	377.654	0.0229602	0.525547
21_2	5	350.5	0.0494339	0.732027	21_2	7	349.586	0.0609254	0.608539
22_1	105	155	0.88817	0.551645	22_1	110	131.909	0.931526	0.579942
22_2	111	126.5	0.952521	0.825917	22_2	111	127.608	0.938809	0.556944

**Table S9. Results for Eosinophils in EUR families, for weighted and unweighted GSMA, using 30 cM bins.**

Pos: position, with 1 assigned to bin with highest summed rank and most significant  $p_{SR}$

SR: summed rank

$p_{SR}$ : summed rank p-value. The nominal probability that a bin would achieve or exceed the observed summed rank under the null hypothesis of no linkage in the bin.

$p_{OR}$ : ordered rank p-value. The probability that the  $k$ th highest summed rank achieves or exceeds an observed summed rank under the null hypothesis of no linkage in the bin.

Eosinophils									
UNWEIGHTED ANALYSIS					WEIGHTED ANALYSIS				
BIN	Posn	SR	$p_{SR}$	$p_{OR}$	BIN	Posn	SR	$p_{SR}$	$p_{OR}$
1_1	74	275.5	0.610314	0.320168	1_1	72	267.582	0.642548	0.909309
1_2	13	394	0.105122	0.475352	1_2	16	390.886	0.120194	0.310069
1_3	26	357.5	0.219932	0.552145	1_3	27	352.841	0.24459	0.774523
1_4	23	364	0.195768	0.569243	1_4	23	369.223	0.184825	0.405559
1_5	70	281.5	0.580344	0.373363	1_5	85	249.723	0.722291	0.590041
1_6	98	215	0.858779	0.911309	1_6	104	204.913	0.878557	0.532447
1_7	88	244	0.754782	0.69513	1_7	83	255.536	0.697405	0.480052
1_8	92	230.5	0.807072	0.891611	1_8	93	234.547	0.783082	0.486651
1_9	94	226.5	0.821248	0.873313	1_9	102	210.653	0.862547	0.544246
1_10	118	127	0.990842	0.328367	1_10	117	135.229	0.985109	0.462354
2_1	95	225	0.826526	0.848315	2_1	105	203.324	0.882872	0.463454
2_2	105	197.5	0.905098	0.816518	2_2	103	209.415	0.866164	0.466153
2_3	73	278	0.597893	0.268573	2_3	53	309.68	0.437771	0.389561
2_4	83	263	0.670891	0.146185	2_4	71	273.497	0.614413	0.732727
2_5	54	309.5	0.438447	0.289671	2_5	61	293.113	0.519191	0.589541
2_6	11	398.5	0.0944889	0.588141	2_6	11	408.22	0.0804101	0.333667
2_7	1	549.5	5.76271e-05	0.00679932	2_7	1	553.277	4.57627e-05	0.00539946
2_8	2	521	0.000692372	0.00219978	2_8	2	525.025	0.00058644	0.00169983
2_9	8	433.5	0.0365313	0.0474953	2_9	5	446.445	0.0272127	0.20358
3_1	61	297.5	0.499537	0.312669	3_1	65	290.119	0.534059	0.321968
3_2	43	324	0.366682	0.59604	3_2	37	332.739	0.329159	0.765723
3_3	57	303	0.471417	0.392761	3_3	62	292.928	0.520139	0.483352
3_4	30	347.5	0.260016	0.640236	3_4	45	318.799	0.393711	0.727627
3_5	63	292.5	0.524906	0.428157	3_5	67	286.607	0.551333	0.321068
3_6	33	336.5	0.307967	0.884812	3_6	35	336.693	0.311772	0.759024
3_7	32	338	0.301235	0.893911	3_7	50	311.137	0.430735	0.662234
3_8	96	222	0.836815	0.864014	3_8	92	235.461	0.779577	0.561444
4_1	111	172	0.952616	0.826817	4_1	116	141.795	0.980544	0.594241
4_2	71	281.5	0.580344	0.266073	4_2	68	285.959	0.554495	0.259974
4_3	90	235	0.790379	0.889011	4_3	88	246.56	0.735658	0.413859
4_4	16	379	0.145992	0.724728	4_4	15	393.47	0.11359	0.339566
4_5	9	411	0.0690847	0.430857	4_5	7	443.277	0.0300966	0.0483952
4_6	44	323.5	0.369103	0.507849	4_6	33	341.255	0.292079	0.726727
4_7	103	198	0.903887	0.945805	4_7	107	191.926	0.91015	0.643836
5_1	85	248.5	0.736008	0.772123	5_1	94	225.082	0.816853	0.829317
5_2	53	310	0.435898	0.368263	5_2	60	293.883	0.515372	0.656534
5_3	80	265.5	0.659046	0.29987	5_3	90	240.21	0.761199	0.536846
5_4	59	302	0.476511	0.237276	5_4	66	287.938	0.544733	0.350065

5_5	46	321	0.381278	0.442056	5_5	56	300.708	0.481861	0.667033
5_6	99	214.5	0.860309	0.855014	5_6	95	218.79	0.837458	0.928607
5_7	109	181.5	0.937639	0.832917	5_7	96	217.723	0.840794	0.89711
6_1	78	272.5	0.625079	0.120488	6_1	80	258.934	0.682362	0.621638
6_2	15	379	0.145992	0.829817	6_2	29	348.386	0.262485	0.784522
6_3	6	444	0.0260847	0.0724928	6_3	10	416.361	0.0653974	0.209279
6_4	55	307.5	0.448615	0.307469	6_4	64	290.925	0.530072	0.383062
6_5	51	313.5	0.418403	0.366063	6_5	48	312.93	0.422032	0.764724
6_6	72	279	0.592967	0.312869	6_6	58	295.407	0.507917	0.771823
7_1	40	327	0.352301	0.739426	7_1	52	309.823	0.437106	0.511149
7_2	49	318.5	0.39351	0.260074	7_2	47	313.785	0.417845	0.809419
7_3	107	185	0.931357	0.922508	7_3	100	214.994	0.849422	0.606439
7_4	116	139	0.984856	0.737926	7_4	112	164.058	0.958337	0.79672
7_5	117	137	0.985987	0.49855	7_5	115	149.327	0.974336	0.643736
7_6	65	288	0.547853	0.519348	7_6	54	308.614	0.443056	0.345565
8_1	60	300	0.486775	0.262474	8_1	57	298.802	0.49118	0.677032
8_2	25	361.5	0.204744	0.444056	8_2	20	376.549	0.161124	0.429557
8_3	108	184	0.933162	0.871513	8_3	108	187.432	0.919818	0.669533
8_4	106	197	0.906282	0.715028	8_4	111	168.02	0.95295	0.829117
8_5	84	252.5	0.718778	0.660334	8_5	78	259.836	0.678369	0.782922
8_6	42	324.5	0.364317	0.680032	8_6	28	349.622	0.257551	0.826017
9_1	82	263.5	0.668482	0.20288	9_1	84	254.296	0.702785	0.436156
9_2	100	212	0.86763	0.846115	9_2	106	197.641	0.897059	0.564444
9_3	101	211	0.870458	0.781322	9_3	98	215.174	0.848861	0.822918
9_4	27	357	0.221841	0.449855	9_4	41	325.937	0.360166	0.732427
9_5	5	456	0.0172102	0.0435956	9_5	3	453.534	0.0215627	0.477052
9_6	4	458.5	0.0157093	0.10209	9_6	8	441.708	0.0316974	0.0206979
10_1	81	265	0.661419	0.223478	10_1	86	249.547	0.723049	0.477652
10_2	37	329.5	0.340416	0.875212	10_2	43	320.649	0.385051	0.821418
10_3	86	244.5	0.752752	0.855714	10_3	77	260.769	0.674145	0.832517
10_4	110	173	0.951194	0.90081	10_4	109	177.095	0.939019	0.849915
10_5	68	283.5	0.570433	0.476852	10_5	70	282.724	0.57023	0.243776
10_6	50	316.5	0.403359	0.277772	10_6	63	291.592	0.526768	0.457154
11_1	89	240	0.770855	0.788221	11_1	76	264.996	0.654717	0.707229
11_2	115	146.5	0.979843	0.79782	11_2	118	131.832	0.987016	0.20128
11_3	112	168	0.958003	0.790921	11_3	113	158.112	0.965464	0.791721
11_4	36	335	0.31474	0.69503	11_4	18	379.911	0.150814	0.534747
11_5	3	460.5	0.0145805	0.242876	11_5	6	444.602	0.0288534	0.10489
12_1	62	297	0.502116	0.236976	12_1	55	303.364	0.468741	0.60194
12_2	7	434.5	0.0353864	0.10229	12_2	4	451.535	0.0230864	0.285871
12_3	41	326	0.357104	0.694931	12_3	36	334.066	0.323257	0.79552
12_4	12	395	0.102747	0.585641	12_4	13	399.812	0.098472	0.359864
12_5	24	362.5	0.201102	0.520848	12_5	31	343.267	0.283684	0.825917
12_6	52	311.5	0.428377	0.382462	12_6	49	312.175	0.425691	0.70303
13_1	69	282.5	0.575414	0.424958	13_1	69	285.283	0.557792	0.19718
13_2	31	346.5	0.264134	0.575842	13_2	26	357.044	0.228373	0.679732
13_3	87	244	0.754782	0.79882	13_3	81	258.822	0.682875	0.508349
13_4	104	197.5	0.905098	0.90141	13_4	99	215.124	0.849026	0.727927
14_1	97	219.5	0.84484	0.862614	14_1	101	210.752	0.862248	0.669433
14_2	48	319.5	0.388568	0.30487	14_2	34	339.475	0.299607	0.719628
14_3	102	202.5	0.892872	0.923308	14_3	97	217.598	0.841211	0.826617
14_4	113	164	0.962999	0.741526	14_4	110	169.123	0.951346	0.905309

14_5	56	306.5	0.453679	0.270173	14_5	51	310.756	0.432532	0.563844
15_1	47	321	0.381278	0.319168	15_1	42	324.948	0.364773	0.680432
15_2	38	328	0.347556	0.863714	15_2	38	331.607	0.334358	0.728227
15_3	66	286.5	0.555478	0.50235	15_3	82	257.16	0.69034	0.49965
15_4	114	151.5	0.975865	0.855614	15_4	114	150.092	0.973698	0.815918
16_1	21	366.5	0.186967	0.69633	16_1	12	403.375	0.0905779	0.364864
16_2	58	302.5	0.473925	0.316468	16_2	44	319.745	0.389265	0.777322
16_3	19	374	0.161605	0.568343	16_3	24	369.206	0.184866	0.283072
16_4	28	354.5	0.231643	0.471953	16_4	30	345.335	0.274963	0.824918
17_1	35	335.5	0.312474	0.769523	17_1	39	330.81	0.337901	0.667733
17_2	39	327.5	0.349915	0.805619	17_2	32	342.951	0.285	0.746325
17_3	29	349	0.253788	0.674033	17_3	25	365.94	0.195976	0.322268
17_4	18	375.5	0.156847	0.626637	17_4	14	394.597	0.110762	0.430657
18_1	76	274	0.617824	0.208079	18_1	74	266.041	0.649724	0.837316
18_2	67	284.5	0.565463	0.527147	18_2	91	236.856	0.774162	0.606439
18_3	77	273	0.622644	0.174183	18_3	87	247.647	0.7312	0.475952
18_4	22	366	0.188668	0.588341	18_4	21	370.152	0.181646	0.619338
19_1	93	226.5	0.821248	0.930507	19_1	89	241.817	0.754862	0.572043
19_2	20	373.5	0.163245	0.462254	19_2	17	389.327	0.124219	0.248975
19_3	10	410	0.070883	0.306069	19_3	9	427.112	0.0488983	0.0942906
19_4	91	230.5	0.807072	0.941506	19_4	79	259.406	0.680297	0.70453
20_1	75	275	0.612825	0.248575	20_1	73	266.556	0.647386	0.887811
20_2	79	268.5	0.644672	0.225277	20_2	75	265.68	0.651386	0.769323
20_3	64	292	0.527442	0.345365	20_3	59	295.017	0.509844	0.69663
21_1	17	376.5	0.153691	0.711829	21_1	19	379.063	0.153363	0.438956
21_2	34	336	0.310251	0.832117	21_2	40	328.676	0.347477	0.678932
22_1	45	322.5	0.373939	0.456554	22_1	46	318.07	0.397156	0.659834
22_2	14	391	0.11263	0.461654	22_2	22	369.507	0.183871	0.525947

**Table S10. Results for BHR in EUR families, for weighted and unweighted GSMA, using 30 cM bins.**

Pos: position, with 1 assigned to bin with highest summed rank and most significant  $p_{SR}$

SR: summed rank

$p_{SR}$ : summed rank p-value. The nominal probability that a bin would achieve or exceed the observed summed rank under the null hypothesis of no linkage in the bin.

$p_{OR}$ : ordered rank p-value. The probability that the  $k$ th highest summed rank achieves or exceeds an observed summed rank under the null hypothesis of no linkage in the bin.

HRB									
UNWEIGHTED ANALYSIS					WEIGHTED ANALYSIS				
BIN	Posn	SR	$p_{SR}$	$p_{OR}$	BIN	Posn	SR	$p_{SR}$	$p_{OR}$
1_1	104	243.5	0.913129	0.951205	1_1	100	253.488	0.874229	0.908009
1_2	83	316	0.685366	0.30327	1_2	80	316.32	0.670414	0.452155
1_3	70	338.5	0.585893	0.454355	1_3	70	324.892	0.63547	0.958104
1_4	73	336	0.597306	0.264274	1_4	46	382.285	0.389788	0.561144
1_5	100	267	0.85799	0.726727	1_5	68	329.165	0.617786	0.956304
1_6	76	328	0.633196	0.39986	1_6	81	310.511	0.693294	0.662834
1_7	65	345	0.555917	0.634237	1_7	85	290.409	0.7664	0.971803
1_8	96	273	0.840753	0.892711	1_8	106	227.231	0.927607	0.950205
1_9	95	279	0.822366	0.79702	1_9	87	288.071	0.774294	0.938606
1_10	41	387	0.362078	0.751525	1_10	27	440.703	0.178278	0.0307969
2_1	69	340.5	0.576803	0.446955	2_1	79	316.684	0.668913	0.551845
20_1	78	327	0.637688	0.237776	20_1	69	326.642	0.628224	0.963604
2_2	107	235.5	0.928003	0.89541	2_2	96	260.045	0.857681	0.975102
2_3	11	489	0.0574728	0.0470953	2_3	19	472.965	0.0989567	0.00519948
2_4	7	510	0.0327652	0.069793	2_4	5	537.664	0.0185568	0.0548945
2_5	22	448	0.140965	0.0443956	2_5	23	459.57	0.128356	0.00419958
2_6	79	325	0.646567	0.244676	2_6	64	338.633	0.577842	0.929707
2_7	87	303	0.737766	0.569543	2_7	101	252.181	0.877376	0.867213
2_8	101	266.5	0.859364	0.627037	2_8	112	208.044	0.955284	0.739026
2_9	97	269.5	0.851081	0.910609	2_9	109	218.698	0.941048	0.873313
3_1	112	203.5	0.969491	0.947705	3_1	110	212.489	0.949764	0.884012
3_2	82	316.5	0.683232	0.391361	3_2	71	324.079	0.6389	0.939006
3_3	15	472	0.0858152	0.0454955	3_3	20	469.581	0.105923	0.00549945
3_4	56	359.5	0.488152	0.737826	3_4	38	412.426	0.271181	0.0420958
3_5	47	378	0.402339	0.621138	3_5	37	416.089	0.258114	0.0271973
3_6	86	306.5	0.724143	0.491851	3_6	62	351.221	0.523653	0.537046
3_7	106	235.5	0.928003	0.951305	3_7	99	256.283	0.867254	0.917008
3_8	109	224.5	0.945249	0.919508	3_8	98	258.02	0.862886	0.935406
4_1	21	451	0.133001	0.0424958	4_1	11	502.707	0.0504322	0.0169983
4_2	50	373.5	0.422842	0.549645	4_2	28	437.987	0.186395	0.0316968
4_3	111	205.5	0.967671	0.975702	4_3	105	237.865	0.908302	0.853315
4_4	108	234	0.930603	0.840716	4_4	103	247.8	0.88739	0.794021
4_5	116	182	0.98475	0.734827	4_5	113	195.398	0.968733	0.851315
4_6	92	287.5	0.794169	0.764924	4_6	95	264.971	0.844672	0.961104
4_7	29	422	0.222202	0.225077	4_7	35	419.156	0.247345	0.0419958
5_1	30	420.5	0.227469	0.193381	5_1	32	421.647	0.23893	0.142186
5_2	94	282.5	0.811056	0.764424	5_2	89	284.359	0.786571	0.917408
5_3	114	189	0.980704	0.934907	5_3	116	186.292	0.976297	0.452855
5_4	68	340.5	0.576803	0.573243	5_4	44	386.097	0.374079	0.580742

5_5	59	356.5	0.502213	0.591041	5_5	31	423.314	0.233335	0.167583
5_6	6	513	0.0300805	0.120988	5_6	2	550.668	0.0119025	0.418558
5_7	39	395.5	0.325356	0.486951	5_7	25	448.821	0.155575	0.0162984
6_1	43	383.5	0.377651	0.738626	6_1	76	317.559	0.665432	0.832017
6_2	12	483.5	0.065722	0.0533947	6_2	9	515.333	0.0363423	0.0142986
6_3	2	544.5	0.0107763	0.366863	6_3	1	570.736	0.00553474	0.489451
6_4	35	407	0.278304	0.29957	6_4	34	419.516	0.246103	0.0746925
6_5	13	483	0.0665245	0.0231977	6_5	12	494.665	0.0614152	0.030497
6_6	44	382	0.384354	0.717628	6_6	40	404.462	0.300907	0.10279
7_1	14	479.5	0.0722999	0.0219978	7_1	13	493.031	0.0637762	0.0159984
7_2	4	518	0.0259508	0.369863	7_2	3	545.446	0.0142966	0.233077
7_3	8	503.5	0.0392788	0.0656934	7_3	17	473.833	0.0972067	0.0280972
7_4	27	430	0.19488	0.121188	7_4	29	437.839	0.186837	0.0153985
7_5	66	344.5	0.558269	0.544946	7_5	53	356.721	0.499814	0.980302
7_6	34	414.5	0.249445	0.10029	7_6	47	381.285	0.394001	0.50325
8_1	67	342	0.569969	0.59904	8_1	78	317.454	0.665857	0.632137
8_2	52	369	0.443633	0.60074	8_2	77	317.487	0.665716	0.743326
8_3	32	416.5	0.242006	0.174183	8_3	61	351.984	0.520393	0.616138
8_4	17	458.5	0.114485	0.134287	8_4	22	463.51	0.119176	0.00419958
8_5	24	441	0.160805	0.0612939	8_5	30	424.81	0.228246	0.20128
8_6	49	376.5	0.409241	0.475852	8_6	50	367.527	0.453011	0.89501
9_1	89	290.5	0.783735	0.89641	9_1	108	223.871	0.93307	0.867313
9_2	38	396.5	0.321091	0.547845	9_2	65	335.261	0.592193	0.955104
9_3	58	358.5	0.492838	0.577642	9_3	72	321.004	0.651522	0.954605
9_4	90	288.5	0.790752	0.887611	9_4	104	247.097	0.888926	0.70033
9_5	84	315.5	0.687449	0.224478	9_5	93	270.099	0.830302	0.969303
9_6	85	308.5	0.716076	0.49645	9_6	97	259.652	0.858733	0.952505
10_1	98	267.5	0.856631	0.890311	10_1	92	275.138	0.815526	0.943506
10_2	117	139	0.997381	0.962804	10_2	117	175.4	0.983588	0.40316
10_3	113	194	0.977241	0.958604	10_3	102	247.947	0.887062	0.879312
10_4	75	332	0.61557	0.276872	10_4	51	363.881	0.468841	0.937306
10_5	53	368.5	0.446065	0.516048	10_5	60	352.878	0.516511	0.678032
10_6	33	416	0.243865	0.120788	10_6	42	387.686	0.367499	0.719928
11_1	77	327	0.637688	0.344766	11_1	86	289.105	0.77076	0.959204
11_2	57	359	0.490521	0.661534	11_2	73	320.077	0.655318	0.936406
11_3	26	432	0.188417	0.137086	11_3	36	417.943	0.251606	0.029597
11_4	25	435.5	0.177353	0.113589	11_4	26	444.098	0.168732	0.0282972
11_5	9	491	0.0546457	0.166383	11_5	8	517.629	0.0340754	0.0292971
12_1	63	350.5	0.530303	0.508349	12_1	55	355.642	0.50444	0.941406
12_2	64	347.5	0.544401	0.591241	12_2	66	333.973	0.597644	0.943506
12_3	36	399.5	0.308631	0.609039	12_3	33	420.507	0.242765	0.108189
12_4	3	541.5	0.0119932	0.159384	12_4	4	543.339	0.0153254	0.0965903
12_5	19	455.5	0.121697	0.0661934	12_5	18	473.026	0.0988304	0.0147985
12_6	60	355	0.509311	0.572243	12_6	43	386.243	0.37346	0.691531
13_1	28	426	0.208396	0.163684	13_1	14	484.442	0.0776415	0.0379962
13_2	42	385.5	0.368749	0.733927	13_2	52	359.256	0.488822	0.975302
13_3	55	360.5	0.483554	0.784222	13_3	63	341.88	0.564067	0.89891
13_4	37	399.5	0.308631	0.483652	13_4	41	401.606	0.311692	0.122988
14_1	118	124	0.998825	0.869713	14_1	118	109.589	0.999367	0.928207
14_2	105	237.5	0.924517	0.970203	14_2	107	224.998	0.931302	0.925507
14_3	72	336	0.597306	0.372163	14_3	83	299.909	0.732878	0.89891
14_4	103	254.5	0.889501	0.819818	14_4	111	211.37	0.9512	0.80142
14_5	110	208.5	0.964771	0.988001	14_5	114	191.719	0.972092	0.778222
15_1	5	514.5	0.0288034	0.242476	15_1	7	524.6	0.0279144	0.0305969

15_2	23	447	0.14373	0.0272973	15_2	15	479.359	0.0866304	0.0463954
15_3	48	377.5	0.404662	0.536546	15_3	57	354.428	0.509661	0.874813
15_4	46	380	0.393343	0.612239	15_4	49	368.088	0.450631	0.929307
16_1	93	284.5	0.804446	0.781722	16_1	90	281.873	0.794587	0.917708
16_2	81	321.5	0.661787	0.223478	16_2	58	354.04	0.511315	0.817018
16_3	71	337	0.592745	0.433557	16_3	56	354.959	0.507402	0.915008
16_4	16	464.5	0.100912	0.0889911	16_4	24	453.25	0.143969	0.0115988
17_1	102	264.5	0.864705	0.576942	17_1	94	269.713	0.831376	0.939006
17_2	61	352.5	0.520936	0.614839	17_2	74	319.313	0.658439	0.908009
17_3	88	301	0.745405	0.561344	17_3	84	290.735	0.765275	0.984502
17_4	115	182.5	0.984487	0.90111	17_4	115	190.25	0.973242	0.612339
18_1	40	394	0.331702	0.453155	18_1	54	356.026	0.502776	0.966803
18_2	31	417.5	0.238309	0.220778	18_2	39	405.291	0.297772	0.142786
18_3	80	323	0.655282	0.246875	18_3	75	318.668	0.661077	0.868113
18_4	20	453.5	0.126708	0.0488951	18_4	16	476.105	0.0927542	0.039896
19_1	62	351	0.527966	0.59634	19_1	59	353.525	0.513622	0.751025
19_2	54	360.5	0.483554	0.861914	19_2	48	374.75	0.421621	0.761124
19_3	18	457	0.11806	0.0962904	19_3	21	469.283	0.106568	0.0019998
19_4	99	267.5	0.856631	0.817018	19_4	91	280.183	0.799848	0.89881
20_2	10	490	0.0560669	0.0934907	20_2	10	509.512	0.0423254	0.0137986
20_3	1	553.5	0.00781694	0.618938	20_3	6	535.087	0.0201695	0.0223978
21_1	45	381.5	0.386625	0.636536	21_1	45	382.78	0.387634	0.654435
21_2	91	287.5	0.794169	0.848815	21_2	88	286.081	0.780976	0.929407
22_1	51	373.5	0.422842	0.427857	22_1	82	304.793	0.714829	0.818718
22_2	74	335	0.601883	0.215378	22_2	67	332.373	0.604302	0.935006