

Meta-analysis of 5 EUROSPAN GWAS: 322,498 SNPs
Genome-wide significance threshold: $0.05/322,498 = 1.55 \times 10^{-7}$

Discovery stage

Select SNPs promising for replication (*hypothesis generation process*):

- (i) p value < 10^{-5}
- (ii) 2 p values, one < 10^{-4} and one < 10^{-3} within 100 Kb
- (iii) 3+ p values < 10^{-3} within 100 Kb

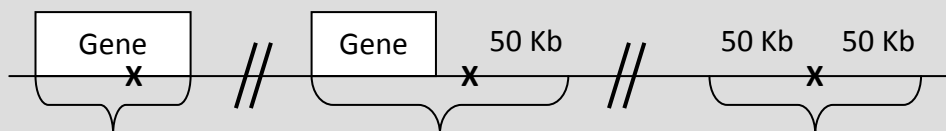
No. of SNPs identified = **91**

Using SNPs to identify genetic loci

1) SNP within a gene

2) SNP close to a gene

3) SNP in a gene desert



29 loci identified: 14 within a gene; 8 close to a gene; 7 in a gene desert

Replication stage

For each of the 29 loci

popgen

Test all K_1 SNPs
 k_1 will have a p value ≤ 0.05

Korcula

Test all K_2 SNPs
 k_2 will have a p value ≤ 0.05

Region-specific p value

$$p_1 = 1 - F_{K_1, 0.05}(k_1 - 1)$$
$$F(k_1) = \text{Binomial}(K_1, 0.05)$$

Region-specific p value

$$p_2 = 1 - F_{K_2, 0.05}(k_2 - 1)$$
$$F(k_2) = \text{Binomial}(K_2, 0.05)$$

Meta-analysis of region-specific p values:

$$-2(\log_e p_1 + \log_e p_2)$$

29 region-specific p-values from 29 independent tests
Significance threshold (Bonferroni) = $0.05/29 = 0.0017$
False Discovery Rate, $\alpha = 0.05$

No. of replicated regions = **3**
(p values = 1.0×10^{-6} , 1.7×10^{-4} , 3.6×10^{-3})