A genetic study on left atrium (LA) size in the Nothern Manhattan Study (NOMAS)

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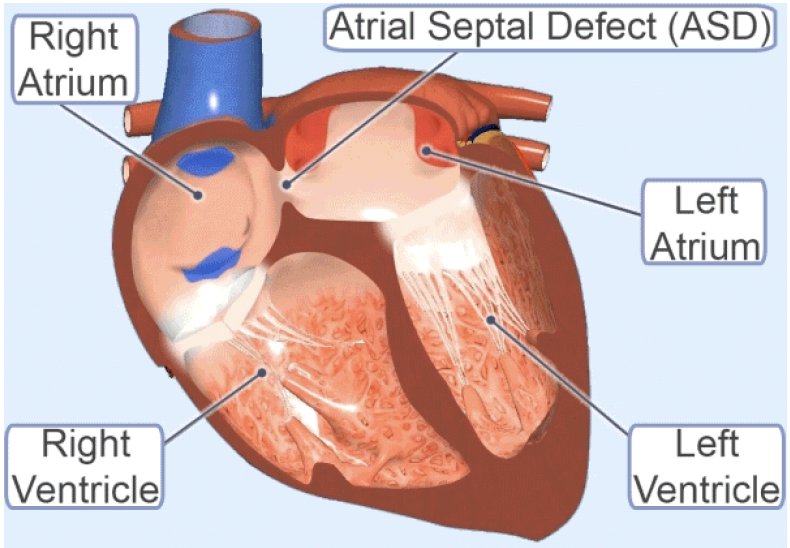
Introduction

- The association between increased risk of stroke and enlarged left atrial size has been well documented.
- Understanding the genetic influence and factors on left atrial size would help in identifying subjects at increased risk for developing an enlarged LA especially at an early stage.
- Several possible susceptibility genes identified: NTN1, MYH10, COX10 and MYOCD.



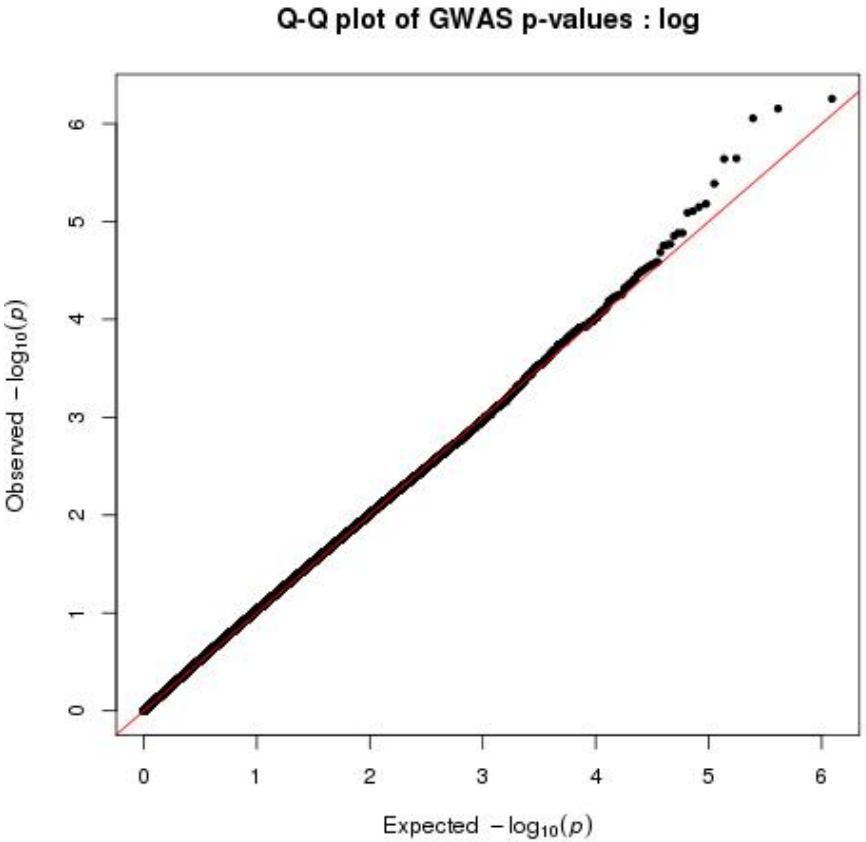
Methods

- **Research Question**: Is there any of the SNP loci genotyped in these data are associated with LA size?
- **NOMAS dataset**: 942 NOMAS individuals; LA size dichotomized with a threshold of $log(29) \approx 3.3672$.
- Genome-wide association study (GWAS):
  - Logistic Analysis:

$$\Pr(Y_i = 1|X_{ij}) = \frac{exp(\beta_0+\beta_1 X_{i1}+\beta_2 X_{i2}+...+\beta_j X_{ij}+\gamma_1 Z_{i1}+...+\gamma_k Z_{ik})}{1+exp(\beta_0+\beta_1 X_{i1}+\beta_2 X_{i2}+...+\beta_j X_{ij}+\gamma_1 Z_{i1}+...+\gamma_k Z_{ik})}$$

  - Association analysis with Bonferroni Correction: the significance level was defined at $0.05/631423 = 7.92 \times 10^{-8}$.

Results (1 of 4)



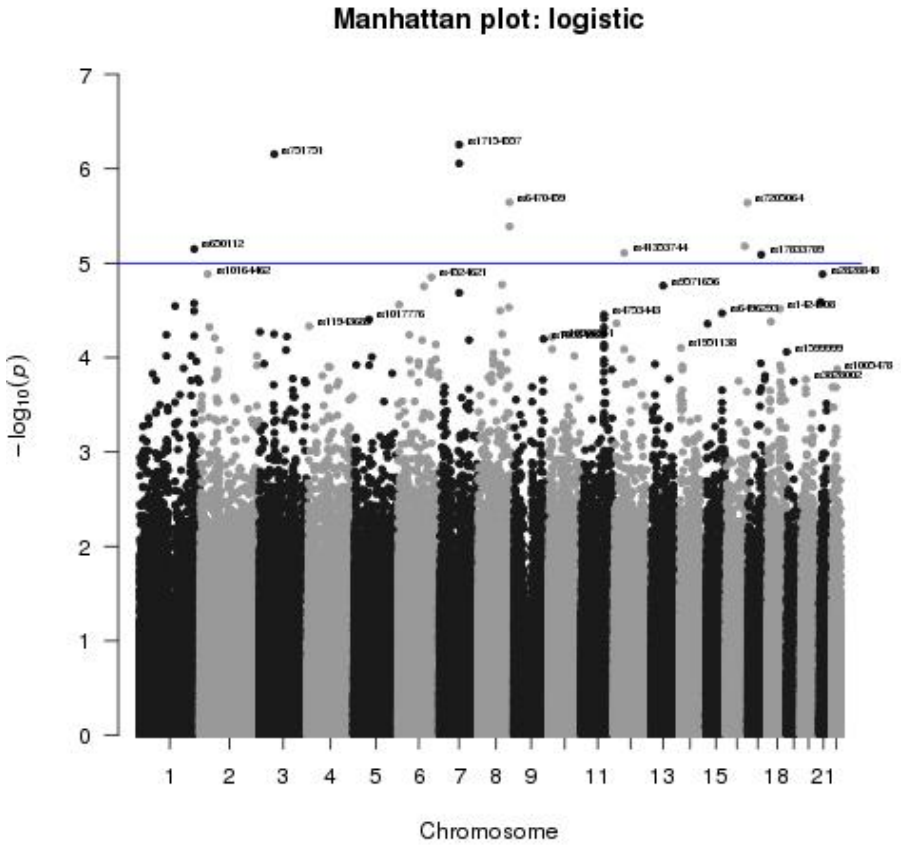
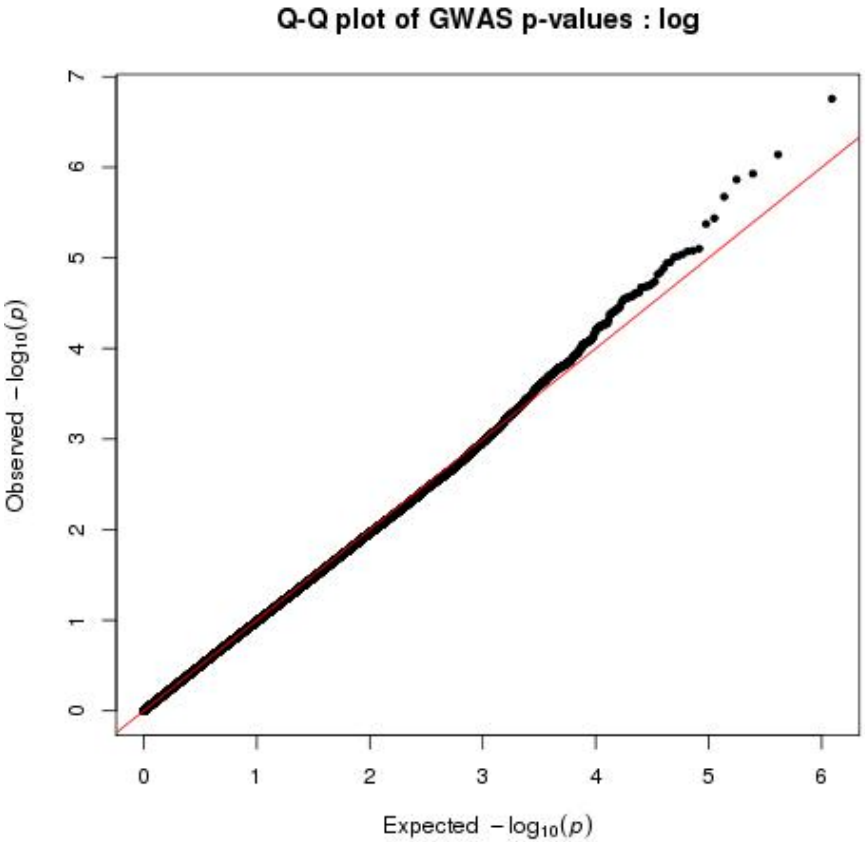


Figure: Results from logistic analysis.

Results (2 of 4)



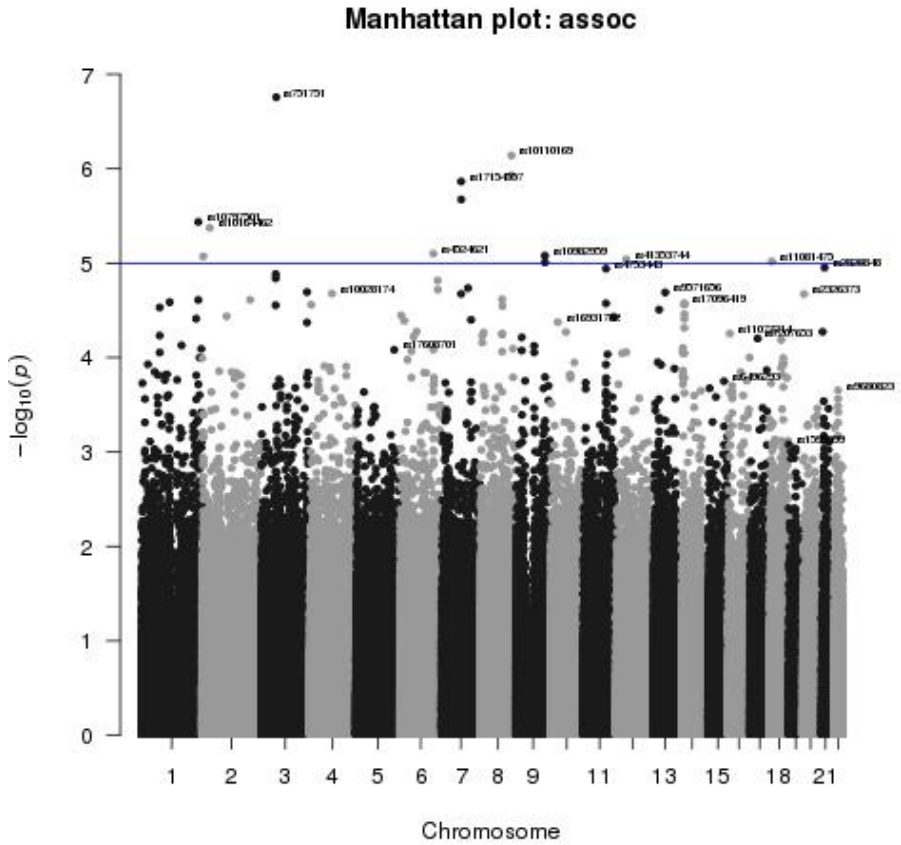


Figure: Results from association analysis with Bonferroni correction.

Results (3 of 4)

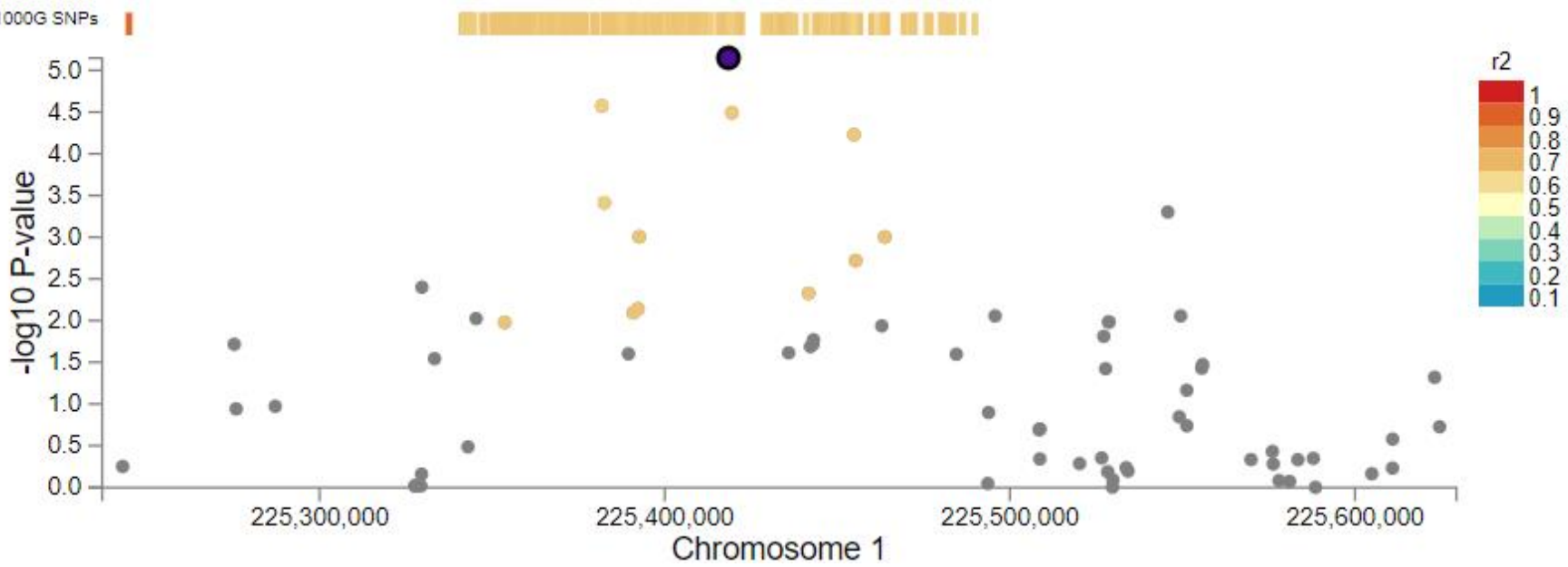


Figure: LD block of rs650112 on chromosome 1

Results (4 of 4)

No.	CHR	SNP	A1	Odds Ratio	P-value	Gene
1	1	rs650112	A	0.4045	7.078×10^{-6}	DNAH14
2	3	rs751751	G	0.3262	7.009×10^{-7}	PTPRG
3	7	rs17154557	A	0.3129	5.557×10^{-7}	SEMA3C
4	8	rs6470459	A	0.368	2.267×10^{-6}	PCAT1
5	12	rs41353744	A	0.3095	7.801×10^{-6}	na
6	16	rs17771505	G	0.3293	6.597×10^{-6}	na
7	16	rs7205064	A	0.1857	2.29×10^{-6}	CBFA2T3
8	17	rs17833789	A	0.3864	8.123×10^{-6}	na

Table: Identified SNPs in Logistic analysis and association analysis.

Reference

[1]Abhayaratna WP, Seward JB, Appleton CP, et al. Left atrial size: physiologic determinants and clinical applications. J Am Coll Cardiol 2006;47:2357–63

[2]Leung DY, Boyd A, Ng AA, et al. Echocardiographic evaluation of left atrial size and function: current understanding, pathophysiologic correlates, and prognostic implications. Am Heart J 2008;156:1056–64

[3]Douglas PS. The left atrium: a biomarker of chronic diastolic dysfunction and cardiovascular disease risk. J Am Coll Cardiol 2003;42:1206–7

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[5]Wang L, Di Tullio MR, Beecham A, et al. A comprehensive genetic study on left atrium size in Caribbean Hispanics identifies potential candidate genes in 17p10. Circ Cardiovasc Genet. 2010;3(4):386–392. doi:10.1161/CIRCGENETICS.110.938381