A randomised controlled trial of a gluten-free weight loss diet in HLA DQ2/DQ8 positive subjects

Marie Vranceanu, David de Lorenzo and Keith Grimaldi

Introduction and objectives

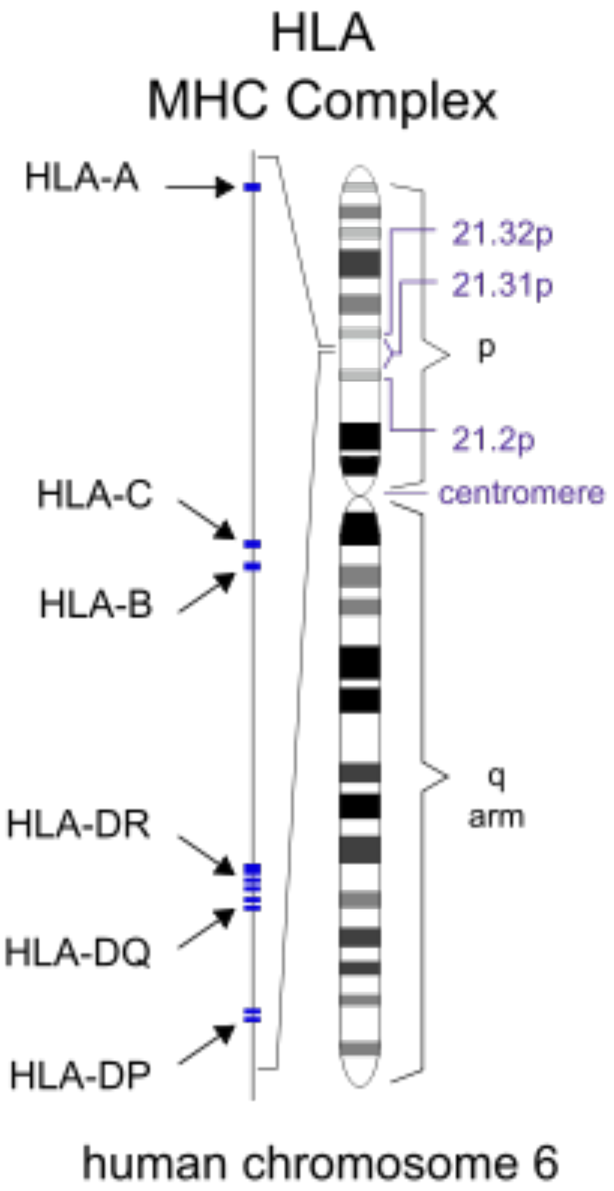
Gluten-free dieting has gained considerable popularity in the general population. Despite the health claims for gluten-free eating, there are no published reports showing that a gluten-free diet produces weight loss in persons without celiac disease.

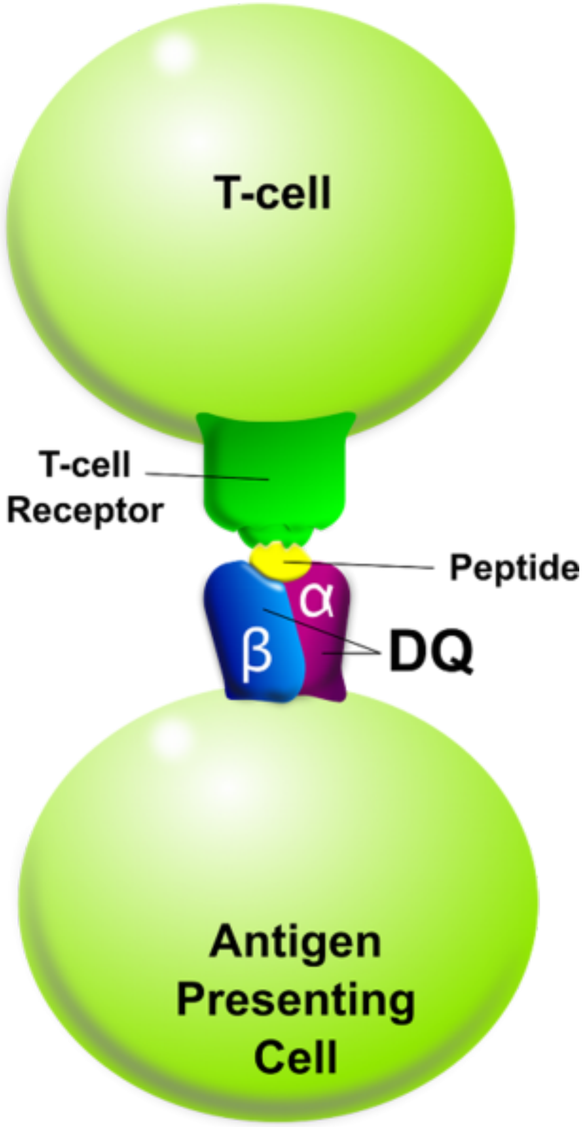
In fact, there are data to suggest that gluten itself may provide some health benefits, and that gluten avoidance may not be justified for otherwise healthy individuals.

Our primary purpose is to try to provide experimental evidence for the effect on weight loss of a gluten-free diet, and analyse the potential interactions between genetic factors affecting gluten sensitivity (located at the HLA-DQ gene) and gender.

HLA and Gluten

- The HLA-DQ is part of the leukocyte human antigen, and allows the immune system to distinguish between self and foreign cells.
- The two subunits of HLA-DQ protein are encoded by HLA-DQA1 and HLA-DQB1 genes, located on the short arm of chromosome six.
- The great majority of people with celiac disease have one of two types of HLA-DQ protein.



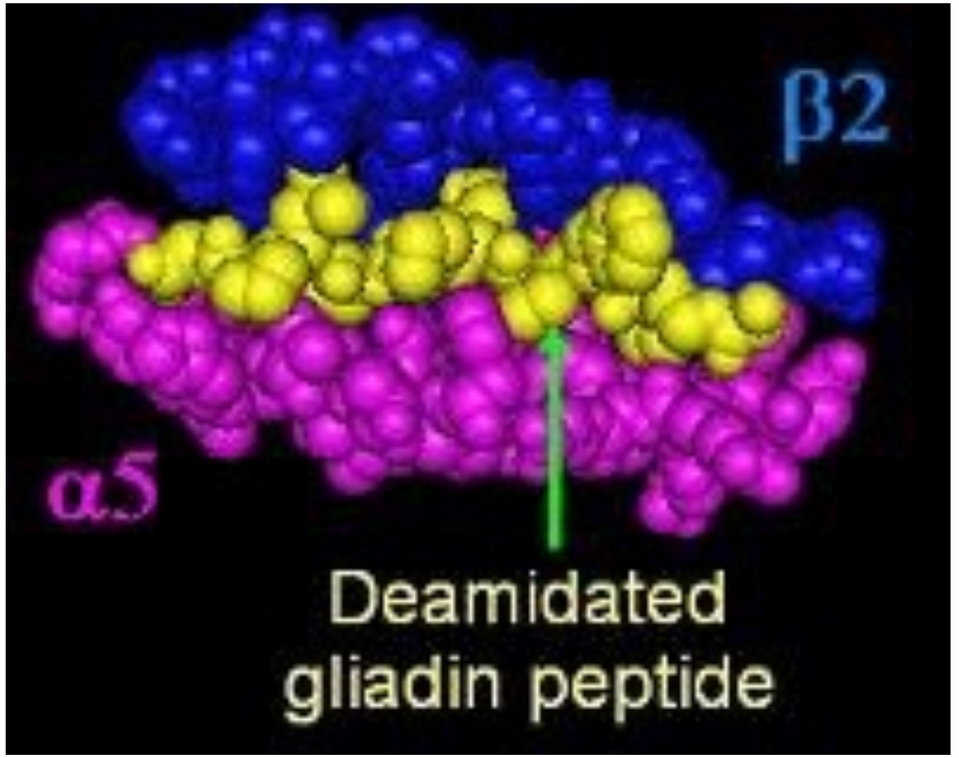


Dr. David de Lorenzo

CENTRO ESTUDIOS GENOMICA NUTRICION

HLA and Gluten

- There are seven HLA-DQ variants defined by serotyping (DQ2 and DQ4-DQ9).
- Approximately 99% of people with celiac disease have **DQ2** isoform (mainly subtype 2.5, a haplotype with two adjacent genes encoding the two subunits and β2 α5) or **DQ8** (subtype 8.1, a haplotype of two genes with variants α3-β8).
- The reason why these genes result in increased risk of celiac disease is that the receptors formed by them gliadin peptides (a component of gluten) stronger than other forms presenter bind antigen receptor.
- Thus, these forms of the receptor are more likely to activate T lymphocytes and initiate the immune process.



Antigen binding space of isoform DQ-β2 α5, showing a deamidated gliadin peptide (yellow)

Methodology

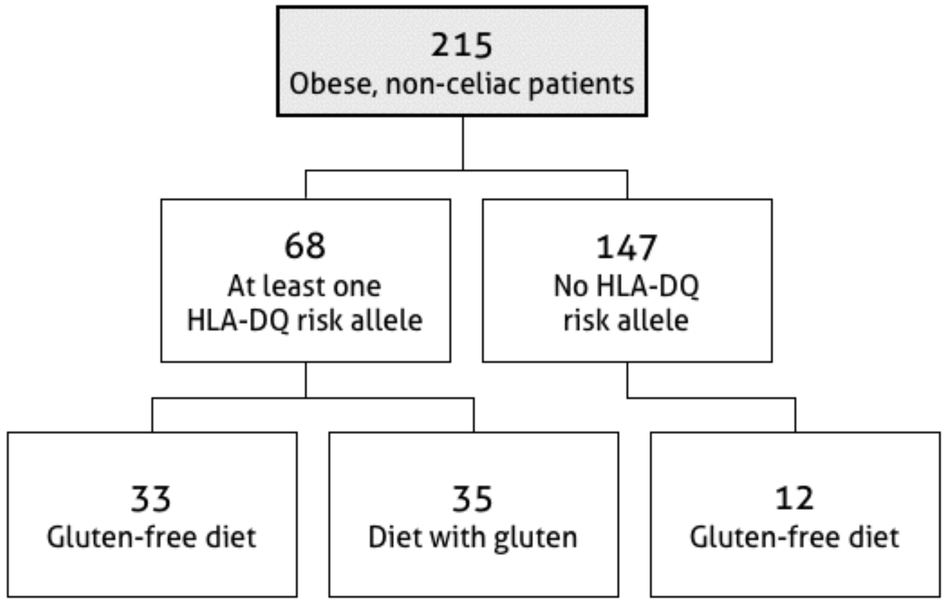
- DQ2.2, DQ2.5, DQ7 and DQ8 serotypes were estimated using the 7-SNP panel described by Monsuur et al (PLoS One 2008;3:e2270) with the Eurogenetica Nutrigene+ test.

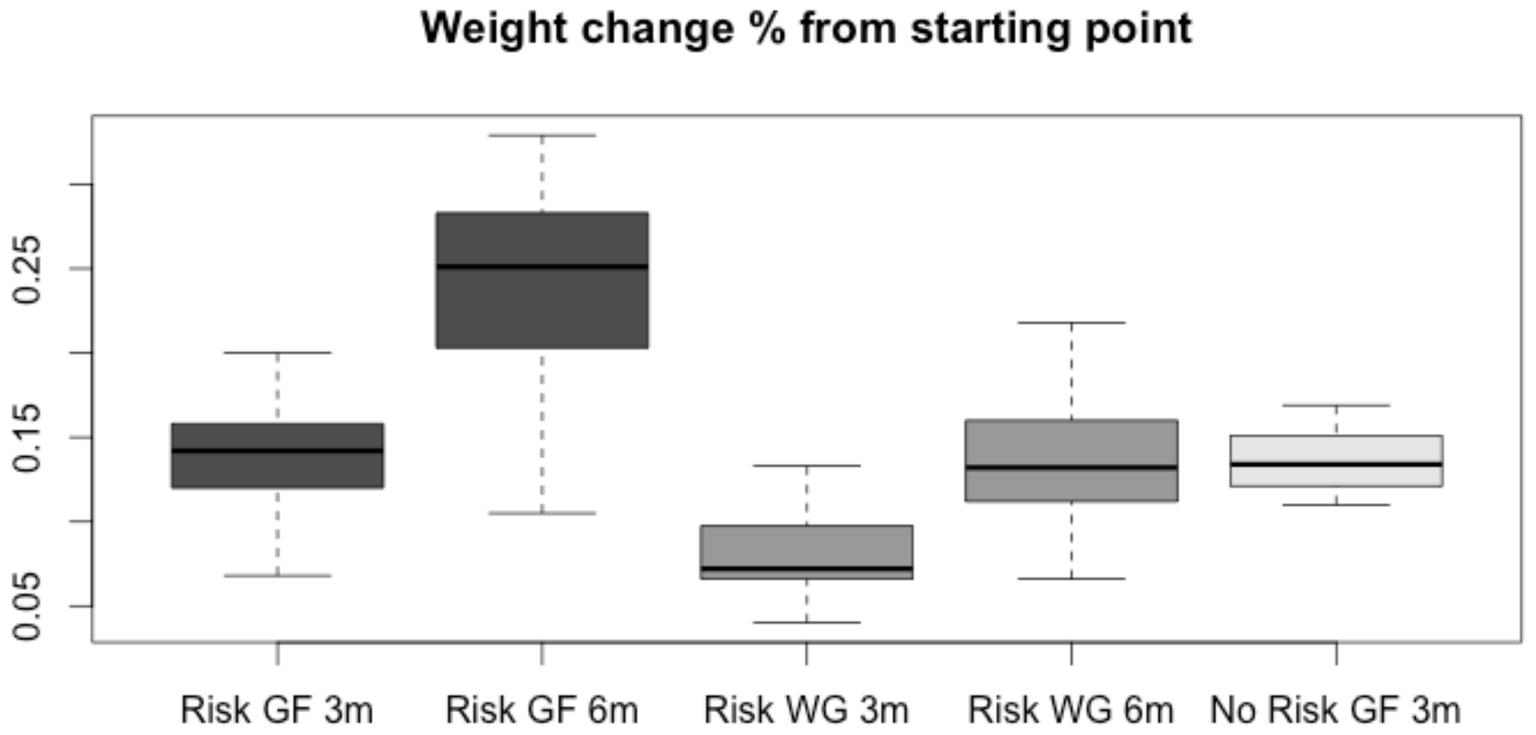
DQ type	DQA1	DQB1	DR	tag SNP	Positive predicting allele(s) (freqCEU)	tag SNP	Negative predicting allele
DQ2.2	0201	0202	7	rs2395182, rs7775228	T (0.71), G (0.10)	rs4713586	G (0.025)
DQ2.5	0501	0201	3	rs2187668	T (0.09)		
DQ7	0505	0301	5	rs4639334	A (0.09)		
DQ8	0301	0302	4	rs7454108	G (0.18)		

a) DQ molecules, the corresponding HLA-DQA1* and -DQB1* alleles, with the DR type and the tag SNPs. A person that has the T,G,A haplotype for rs2395182, rs7775228, rs4713586, is a DQ2.2.
A person that has the T,G,G haplotype for rs2395182, rs7775228, rs4713586, is not a DQ2.2 but a DQ4.
Freq(CEU) – frequency of annotated alleles in CEU HapMap population

Monsuur AJ et al. Effective detection of human leukocyte antigen risk alleles in celiac disease using tag single nucleotide polymorphisms. PLoS ONE. 2008;3:e2270

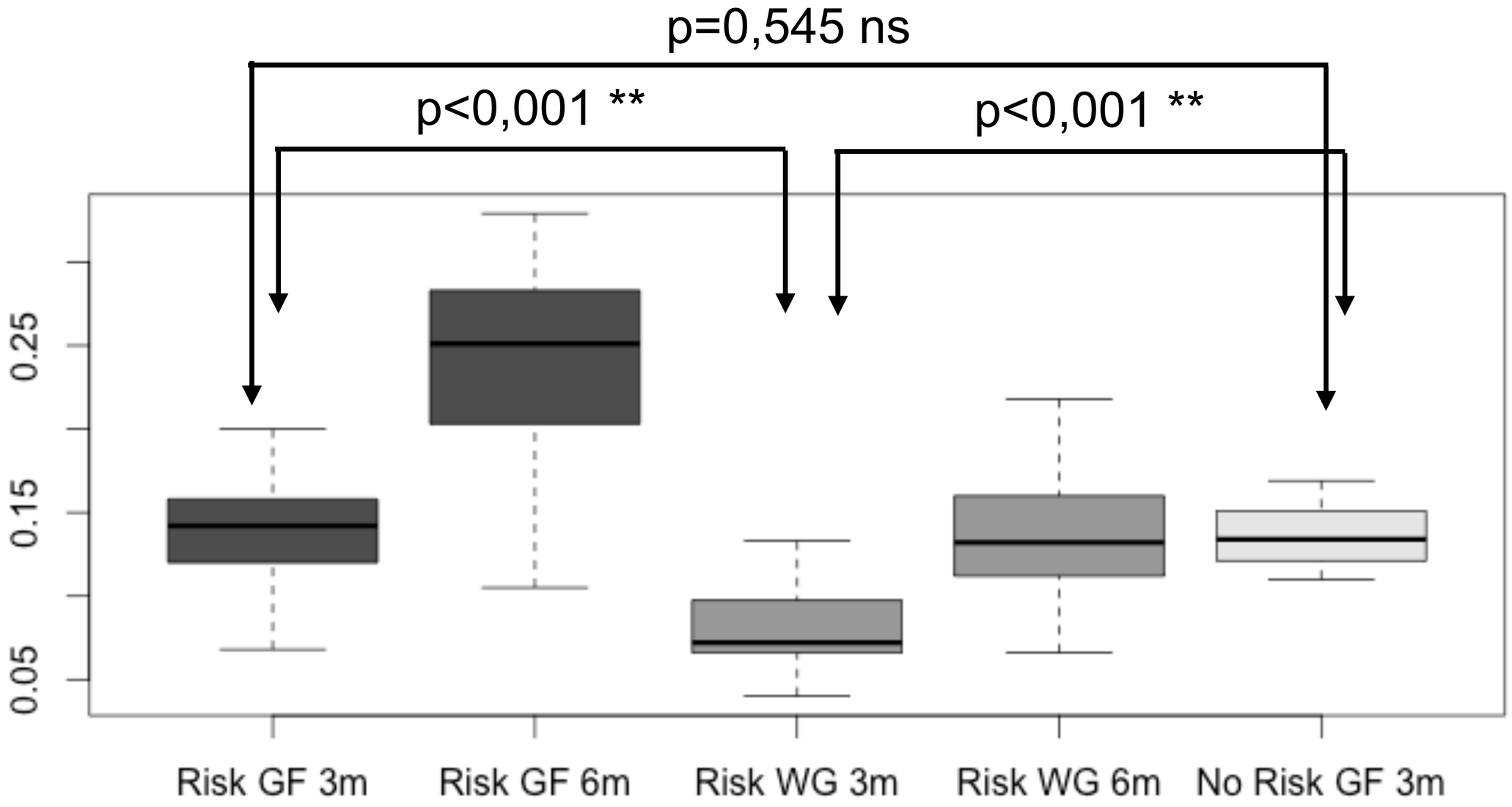
Results



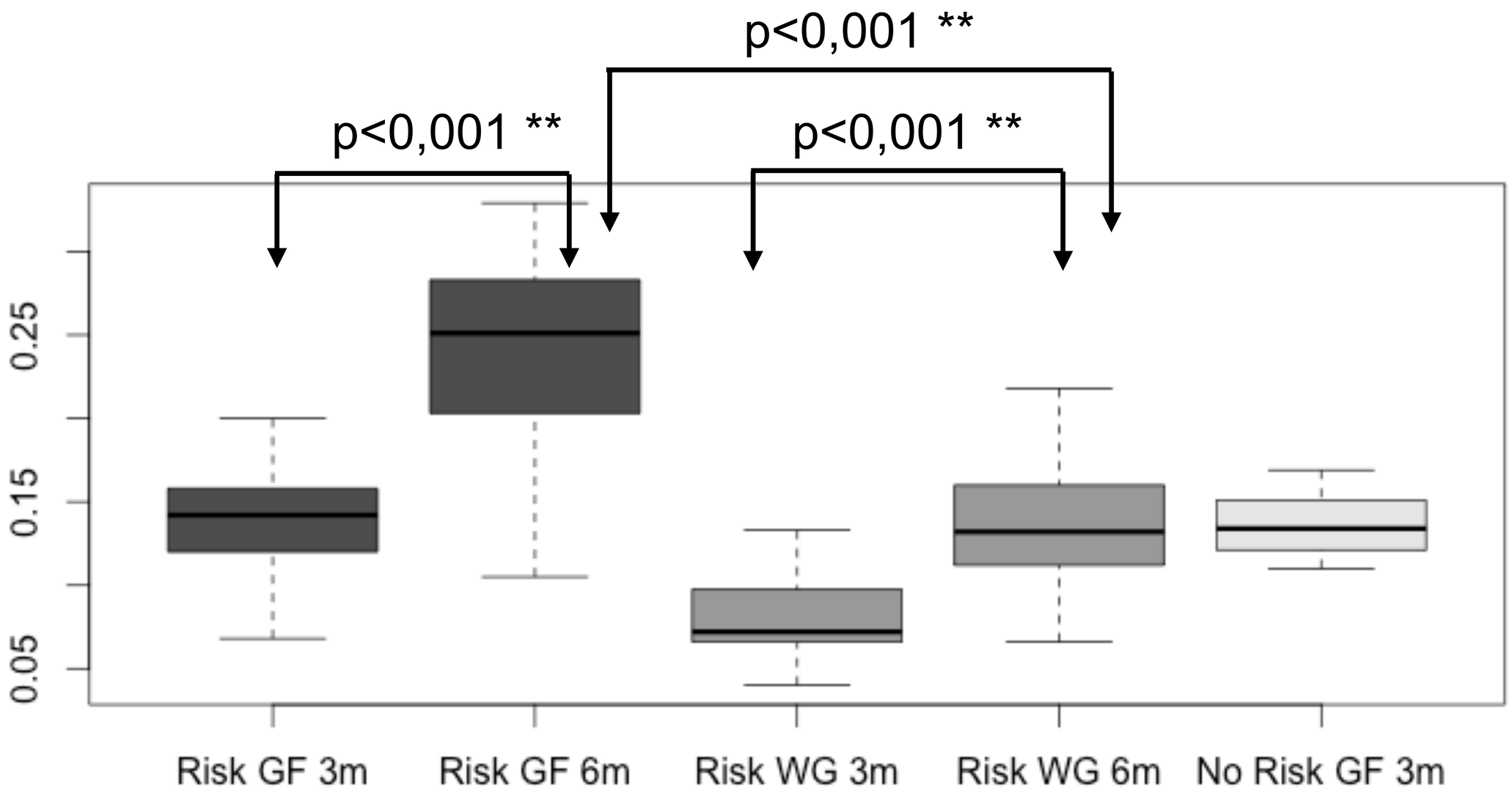


M/F Patients age range between 24-57 years
Measures of weight at 3 (and 6) months
Using % => Non-parametric testing

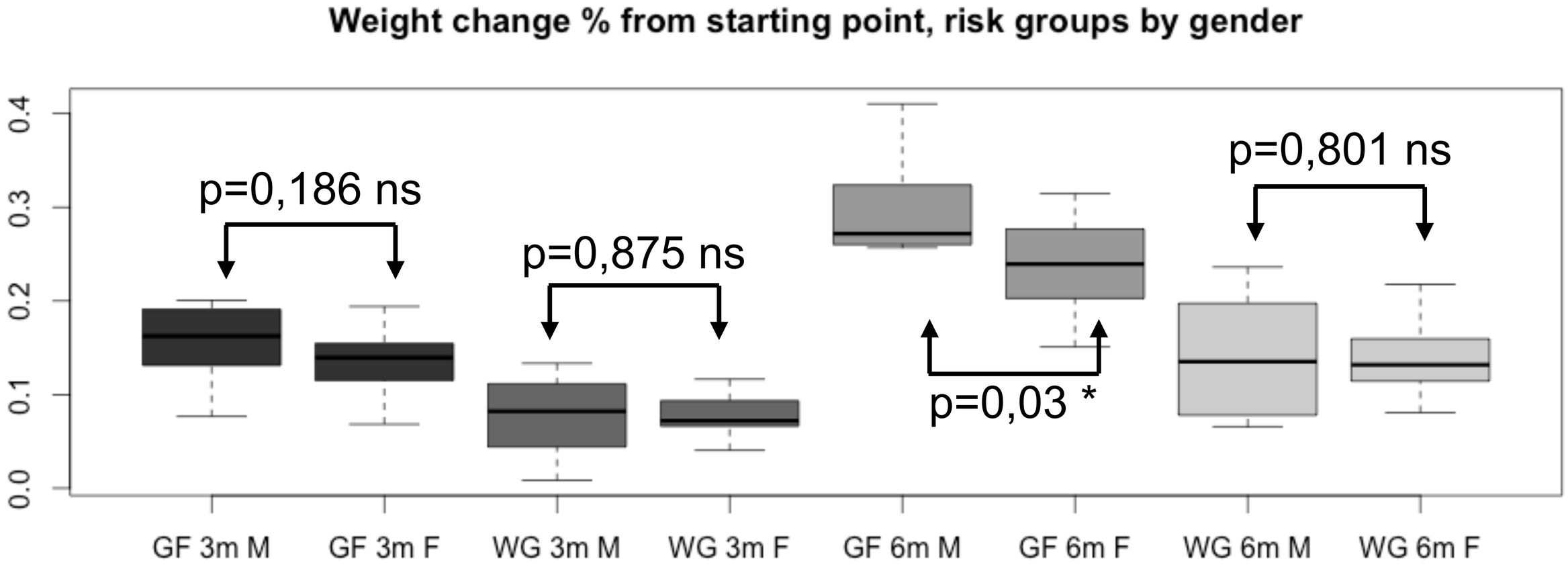
Results - Time related variation



Results - Time related variation



Results - Gender related variation



Conclussions

1. A gluten-free diet has been shown to be more effective in weight loss than a diet with gluten, independently of the genetic status for gluten intolerance risk (HLA-DQ).
2. The differences are already significant after 3 months of treatment, and increases in time in individuals carrying at least 1 risk allele for gluten intolerance (HLA-DQ).
3. The effect of time of a gluten-free diet in individuals with no risk alleles for gluten intolerance (HLA-DQ) needs still to be confirmed.
4. The effectiveness for weight loss of a gluten-free diet interacts with gender in individuals carrying at least 1 allele for gluten intolerance (HLA-DQ), being higher in males than in females already after 6 months of treatment.
5. The interaction between a gluten-free diet and gender in weight loss needs still to be confirmed in individuals with no risk alleles for gluten intolerance.

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