

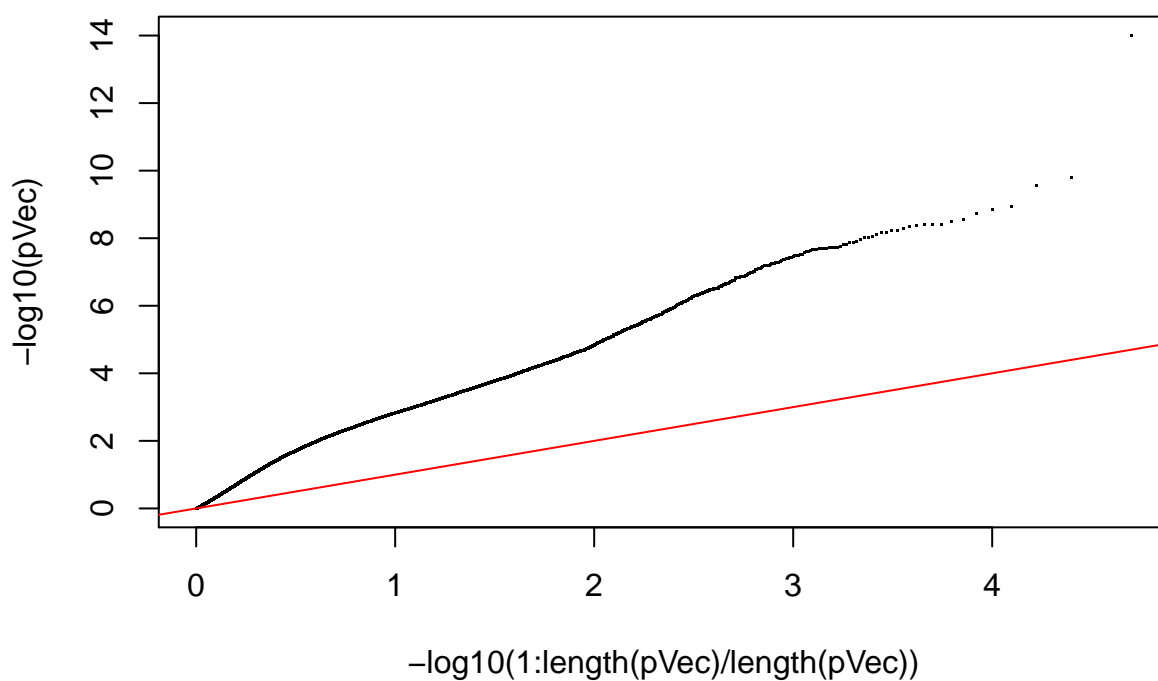
FHS Offspring CVD Incidence EWAS: model comparison

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These methylation data come from Framingham Offspring Study, Exam 8. Results are from Cox proportional hazards regression of incidence of cardiovascular events on baseline methylation levels.

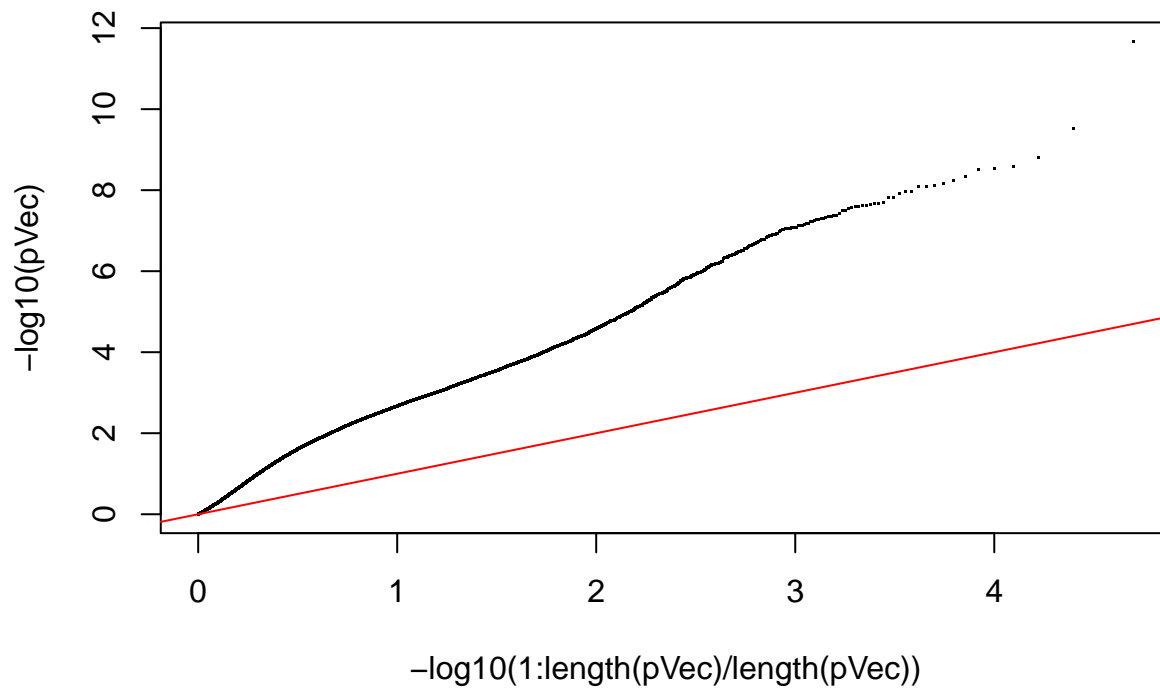
P-value analysis for model comparison

basic



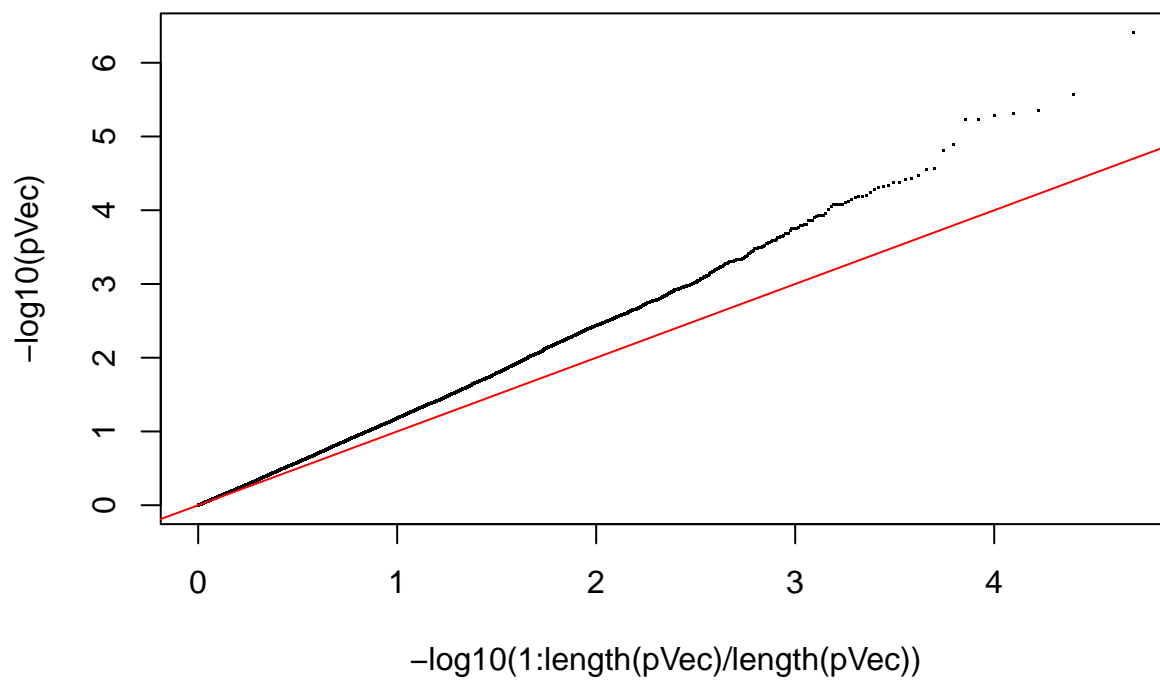
```
## [1] "lambda = 6.5406077060942"
```

basic_wbc



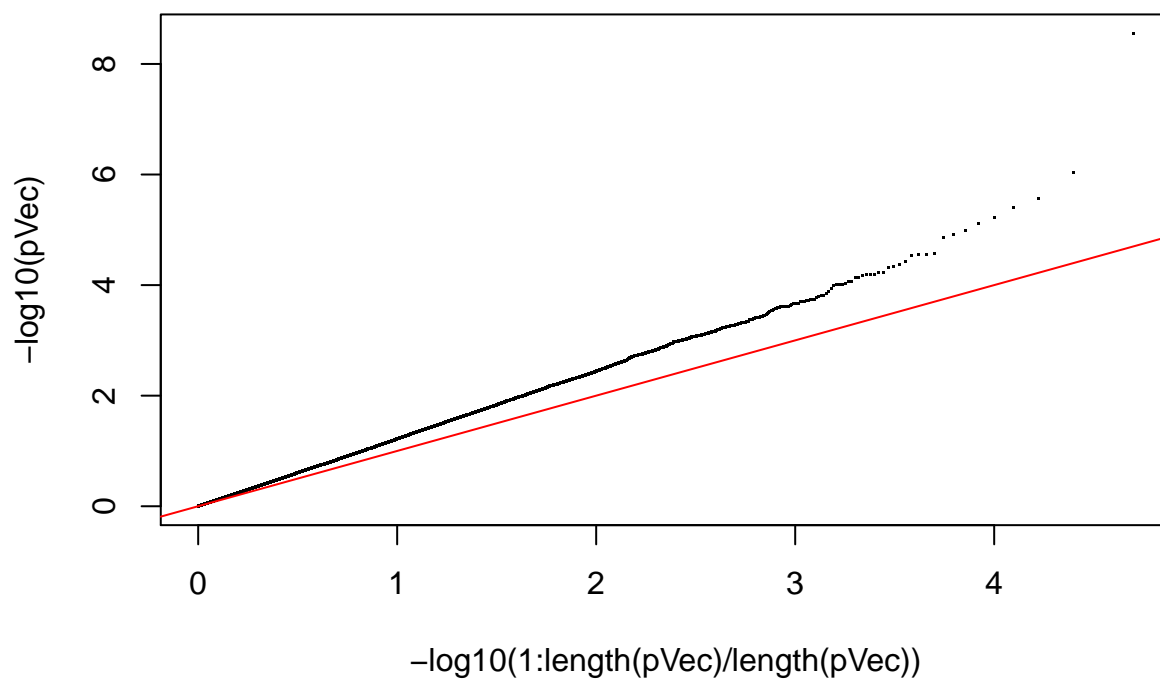
```
## [1] "lambda = 5.94065009568474"
```

basic_wbc_20PC



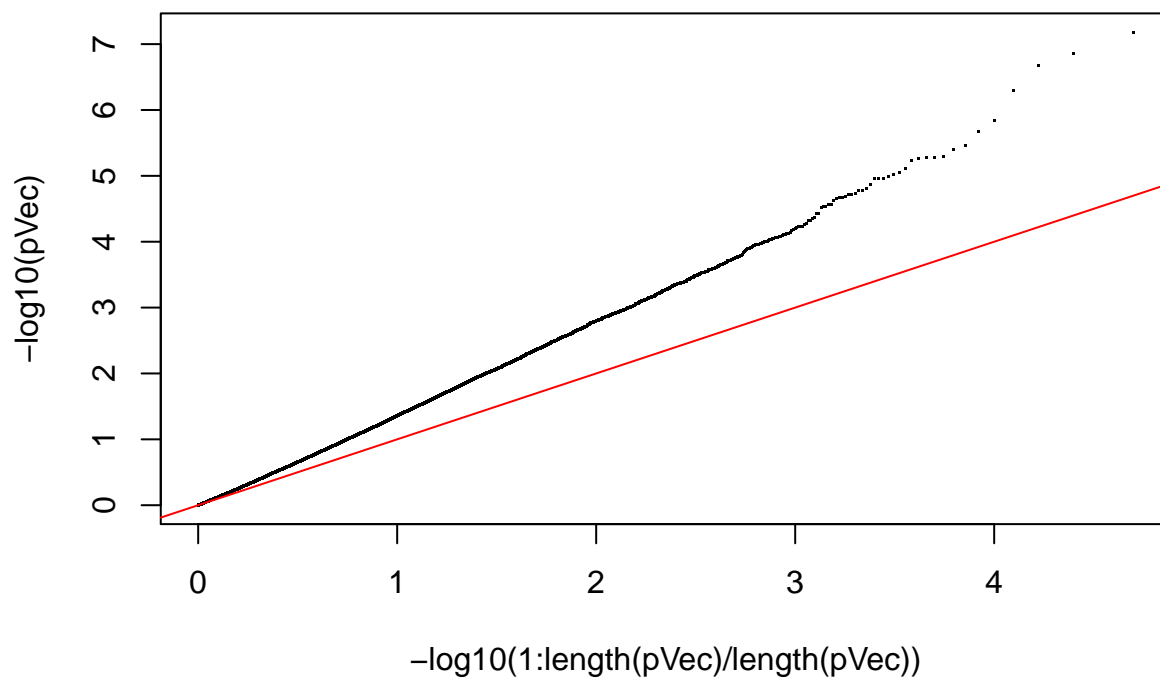
```
## [1] "lambda = 1.24861692737154"
```

basic_wbc_20CPA



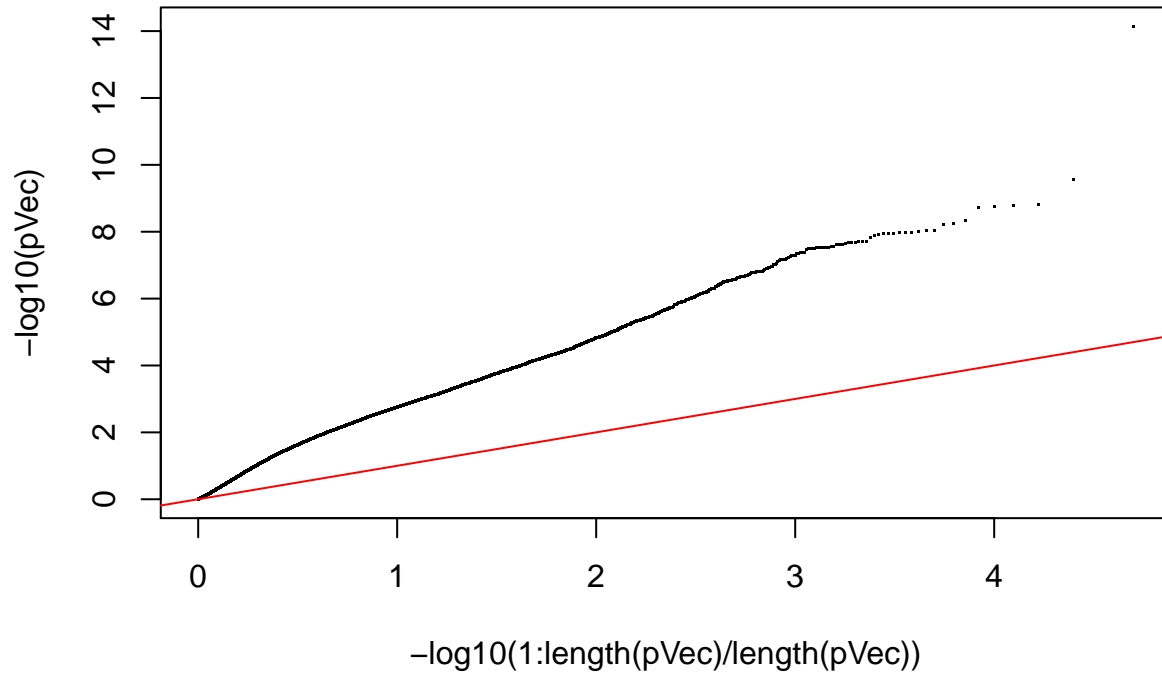
```
## [1] "lambda = 1.35266877219718"
```

basic_wbc_20PC_20CPA



```
## [1] "lambda = 1.48876018272763"
```

slideRowCol_RE



```
## [1] "lambda = 6.27728825728794"
```

```
## [1] "2 regressions failed."
```

Gene set enrichment analysis

Currently based only on single-CpG annotations rather than differentially methylated regions. Gene sets are taken from the Broad Institute's MSigDB v6 canonical pathways.

```
## [1] "4669 relevant genes found."
```

Category	p.value
KEGG_GLYCOLYSIS_GLUONEOGENESIS	NaN
KEGG_CITRATE_CYCLE_TCA_CYCLE	NaN
KEGG_PENTOSE_PHOSPHATE_PATHWAY	NaN
KEGG_PENTOSE_AND_GLUCURONATE_INTERCONVERSIONS	NaN
KEGG_FRUCTOSE_AND_MANNOSE_METABOLISM	NaN
KEGG_GALACTOSE_METABOLISM	NaN
KEGG_ASCORBATE_AND_ALDARATE_METABOLISM	NaN
KEGG_FATTY_ACID_METABOLISM	NaN
KEGG_STEROID_BIOSYNTHESIS	NaN
KEGG_PRIMARY_BILE_ACID_BIOSYNTHESIS	NaN
KEGG_STEROID_HORMONE_BIOSYNTHESIS	NaN
KEGG_OXIDATIVE_PHOSPHORYLATION	NaN
KEGG_PURINE_METABOLISM	NaN
KEGG_PYRIMIDINE_METABOLISM	NaN
KEGG_ALANINE_ASPARTATE_AND_GLUTAMATE_METABOLISM	NaN
KEGG_GLYCINE_SERINE_AND_THREONINE_METABOLISM	NaN
KEGG_CYSTEINE_AND_METHIONINE_METABOLISM	NaN

Category	p.value
KEGG_VALINE_LEUCINE_AND_ISOLEUCINE_DEGRADATION	NaN
KEGG_VALINE_LEUCINE_AND_ISOLEUCINE_BIOSYNTHESIS	NaN
KEGG_LYSINE_DEGRADATION	NaN
KEGG_ARGININE_AND_PROLINE_METABOLISM	NaN
KEGG_HISTIDINE_METABOLISM	NaN
KEGG_TYROSINE_METABOLISM	NaN
KEGG_PHENYLALANINE_METABOLISM	NaN
KEGG_TRYPTOPHAN_METABOLISM	NaN

Initial MRS calculation and evaluation

45 CpG sites were significant at $FDR < 0.01$. Multiple regression on methylation M-values at these sites gives coefficient beta values that were then used as weights to construct the MRS. Three regressions were then performed: Framingham risk score alone, methylation risk score alone, and the two together. Note: take these results with a huge grain of salt, since the evaluation is being done in the same dataset as was used to develop the MRS.

```
## [1] "Framingham risk score only (plus covariates)"
##           coef exp(coef)  se(coef)      z    Pr(>|z|)
## frs 0.3418095  1.407492 0.1240123  2.756253 0.005846767
## [1] "Methylation risk score only (plus covariates)"
##           coef exp(coef)  se(coef)      z    Pr(>|z|)
## mrs 0.8256974  2.283473 0.03806069 21.69423      0
## [1] "FRS and MRS together"
##           coef exp(coef)  se(coef)      z    Pr(>|z|)
## mrs 0.81891064  2.268028 0.03817415 21.4519662 0.0000000
## frs 0.07624225  1.079224 0.12639204  0.6032204 0.5463621
->
```