Supplementary Material

Shared Decision Making Following Disclosure of Coronary Heart Disease Genetic Risk: Results from a Randomized Clinical Trial

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Supplementary Table 1. ***Genetic Loci Associated with Coronary Heart Disease Used in Genetic Risk Score Calculation***

Supplementary Figure 1. ***Generic Disease Management Interface in the Electronic Health Record***

A sample of how the generic disease management interface appears in the electronic health record for a hypothetical patient at intermediate risk for CAD. GDMS summarizes pertinent information such as the most recent vitals, laboratory studies, Framingham risk score, and preventive measures. It also provides alerts regarding recommended actions as well as links to resources and guidelines. The red box above highlights the 10-year Framingham risk score and associated link that takes the provider to the statin decision aid tool simultaneously transmitting the relevant risk factors and laboratory values.

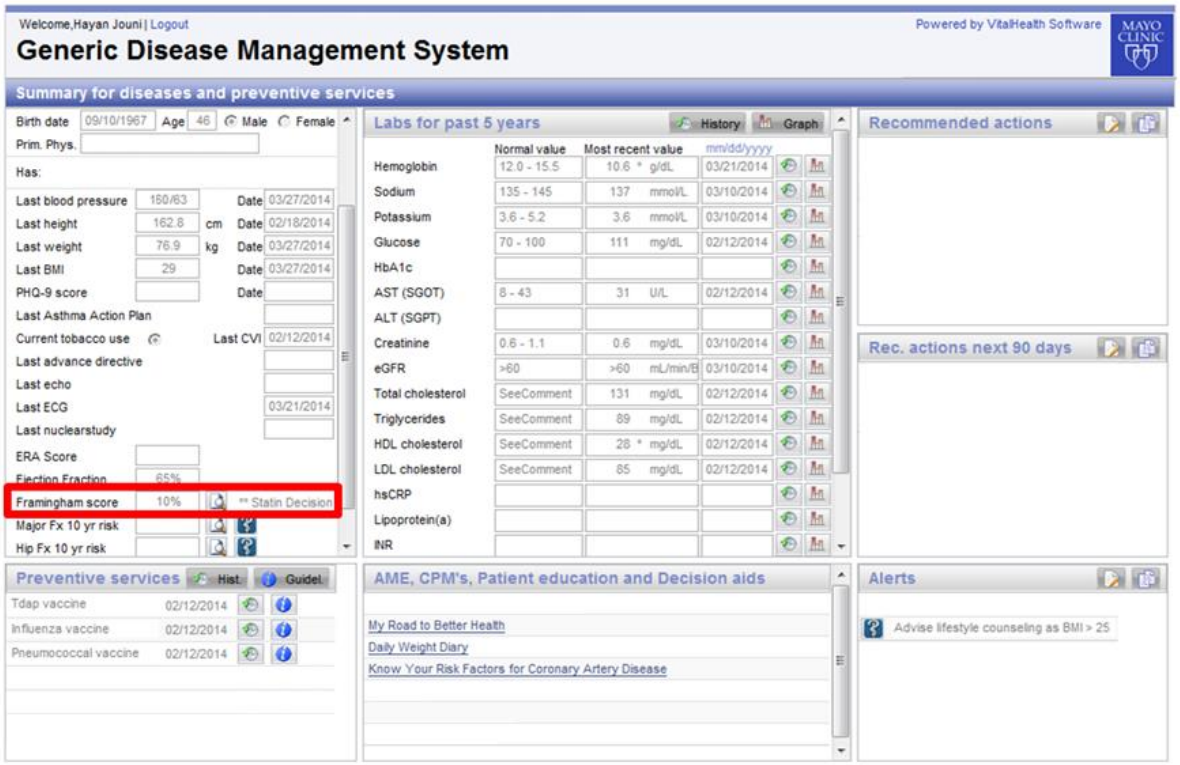
Supplementary Figure 2. ***Sample risk report as deposited in the electronic health record***

This figure displays a sample CHD risk report for a hypothetical study participant randomized to receive CRS*GRS. The first page lists the study participant's demographics, risk factors, family history of premature CHD, and conventional risk for CHD based on Framingham risk score. It also lists the genetic risk score (GRS) and the overall CHD risk taking into account the study participant's GRS. The second page of the risk report lists the alleles at each risk locus.

Supplementary Table 1. Genetic Loci Associated with CHD Risk

Gene	SNP	CHR	Risk Allele	Risk Allele OR
MIA3	rs17465637	1	C	1.14
PPAP2B	rs17114036	1	A	1.11
IL6R	rs4845625	1	T	1.04
WDR12	rs6725887	2	C	1.12
**ZEB2-AC074093.1*	rs2252641	2	G	1.04
**VAMP5-VAMP8-GGCX*	rs1561198	2	A	1.05
MRAS	rs9818870	3	T	1.07
EDNRA	rs1878406	4	T	1.06
**SLC22A4-SLC22A5*	rs273909	5	C	1.09
TCF21	rs12190287	6	C	1.07
PHACTR1	rs9369640	6	A	1.09
KCNK5	rs10947789	6	T	1.06
PLG	rs4252120	6	T	1.06
ANKS1A	rs17609940	6	G	1.07
7q22 *BCAP29*	rs10953541	7	C	1.08
**HDAC9*	rs2023938	7	G	1.07
CDKN2BAS1	rs1333049	9	C	1.23
**CXCL12*	rs2047009	10	C	1.05
KIAA1462	rs2505083	10	C	1.06
PDGFD	rs974819	11	A	1.07
COL4A1-COL4A2	rs4773144	13	G	1.07
COL4A1-COL4A2	†rs9515203	13	T	1.08
FLT1	rs9319428	13	A	1.05
HHIPL1	rs2895811	14	C	1.06
RAI1-PEMT-RASD1	rs12936587	17	G	1.06
SMG6	rs216172	17	C	1.07
UBE2Z	rs46522	17	T	1.06
Gene desert (*KCNE2*)	rs9982601	21	T	1.13

CHD: coronary artery disease; CHR: Chromosome; OR: odds ratio. * Reverse complement of these SNPs was used to match the reported risk alleles. † rs9515203 had an r2 of 0.01 with rs4773144.



Supplementary Figure 1.

MI-GENES
Myocardial Infarction Genes Study

Mayo Clinic

Coronary Heart Disease Genetic Risk Report

Clinic Number:	1-234-567	Birthdate:	10/01/1952
Name:	Jane Doe	Date:	01/01/2014
Age:	61	Provider:	Iftikhar J. Kullo, M.D.
Gender:	F	Service:	Cardiovascular Diseases

The patient was genotyped for **28 single nucleotide polymorphisms (SNPs)** associated with coronary heart disease (CHD).

Genetic Risk Score (GRS):	**1.47**
10-year probability of CHD (FRS):	**7%**
Overall 10-year probability of CHD (FRSxGRS):	**10.26%**
Family History of CHD:	☒ Yes ☐ No

** All parameters, including age, based upon initial study visit.
*Smoking: no; DM: no; SBP: 152; DBP:80; HDL: 83; TC: 205

Interpretation: Compared to the population average, this patient has a **47% higher** genetic risk for CHD. Note: Risk for CHD is probabilistic, not deterministic. Risk variants for CHD were selected from published genome-wide association studies (GWAS) excluding the variants associated with hypertension and lipid levels.[1-2] The genetic risk score was calculated as previously reported[3] assuming additive effects of the risk alleles. FRS = Framingham risk score.

Signed by Iftikhar J. Kullo, M.D.

Additional information related to the genetic risk score (GRS)

1. Odds ratios may over-estimate risk in the context of common diseases such as CHD.
2. Genetic risk scores may need to be periodically updated as new susceptibility variants are identified.
3. The SNPs used in this report were identified in adults of European ancestry; use of these SNPs may not apply uniformly to adults of other ethnic groups.
4. 10-year probability of CHD was calculated based on Wilson et al.[4]

References

1. Deloukas P et al. Large-scale association analysis identifies new risk loci for coronary artery disease. Nat Genet. 2013; 45(1):25-33.
2. C4D Group. A genome-wide association study in Europeans and south Asians identifies five new loci for coronary artery disease. Nat Genet. 2011; 43:339-344
3. Ding K et al. Genotype-informed estimation of risk of coronary heart disease based on genome-wide association data linked to the electronic medical record. BMC Cardiovasc Disord. 2011 Nov 3;11:66.
4. Wilson PW et al. Prediction of coronary heart disease using risk factor categories. Circulation. 1998; 12;97(18):1837-47.

MI-GENES
Myocardial Infarction Genes Study

Mayo Clinic

Genotypes at 28 loci associated with CHD

Gene	SNP	CHR	Risk Allele	Risk Allele OR	Genotype
MIA3	rs17465637	1	C	1.14	CC
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SNPs associated with CHD and also with hypertension and lipid levels are not included in this list.

Genotyping was performed at the Clinical Laboratory Improvement Amendments (CLIA)-certified Advanced Genomics Laboratory, Medical College of Wisconsin, Milwaukee WI (see appended report).

Supplementary Figure 2.