

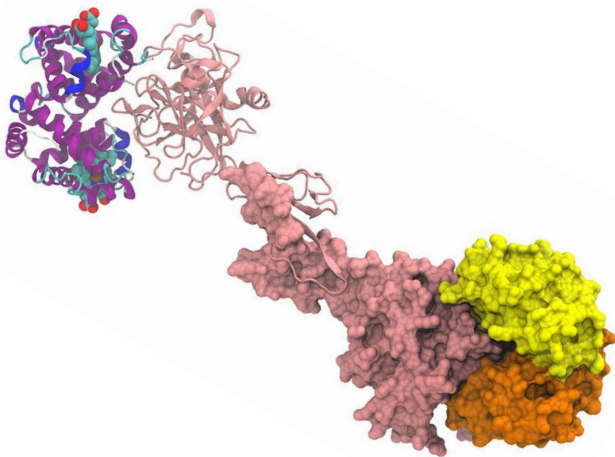
BOSTON HEART DIAGNOSTICS

HAPTOGLOBIN Hp1 AND Hp2 GENOTYPING

Boston Heart Diagnostics offers genotyping for the Haptoglobin Hp1 and Hp2 alleles. Haptoglobin is a protein produced by the liver that clears free hemoglobin from circulation.

HAPTOGLOBIN GENOTYPING IS ESPECIALLY IMPORTANT FOR INDIVIDUALS WITH DIABETES AND/OR KIDNEY DISEASE.

- In patients with diabetes and/or kidney disease who have the Hp 2/2 variant, clearance of hemoglobin-haptoglobin complexes is delayed thereby accelerating oxidative damage.¹⁻¹⁰
- In a meta-analysis of 13 studies in patients with diabetes, the risk of CVD events was approximately 44% higher in those with the Hp 2/2 variant compared to those with the Hp 1/1 or 1/2 variant.¹⁰
- In a meta-analysis of 3 randomized, placebo-controlled trials, patients with Hp 2/2 variant who received vitamin E had 34% lower risk of CVD events and 53% lower risk of CVD death compared to the placebo group.¹⁰



A Model of a Hemoglobin/Haptoglobin Complex

There are 2 alpha,beta-hemoglobin dimers depicted: one space filling model (yellow/orange), and one ribbon model (purple/blue). Each is bound by a haptoglobin molecule (both haptoglobin molecules are shown in pink, with one as a space filling model and one as a ribbon model).

**53% lower risk
of CVD death**

in diabetic patients with a
Hp2/2 genotype

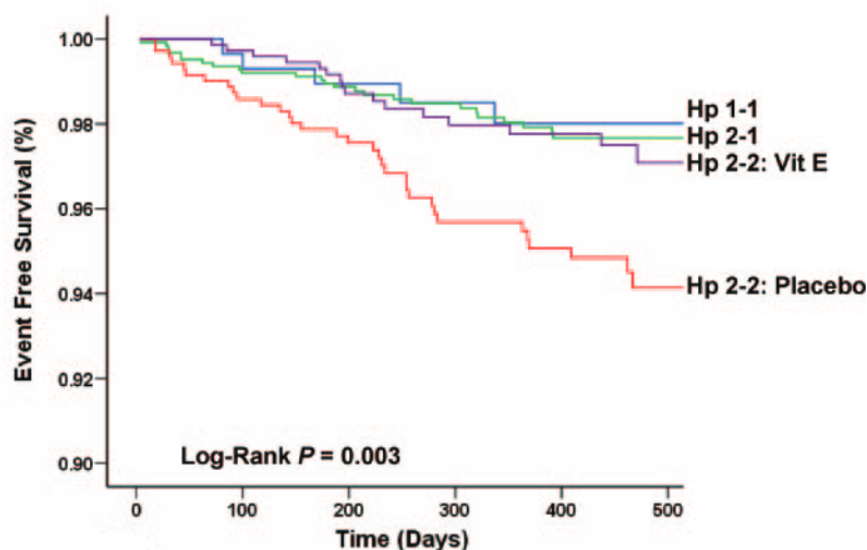
**when treated
with Vitamin E¹⁰**

ABOUT HAPTOGLOBIN

- **Haptoglobin is an acute-phase protein that binds or scavenges free hemoglobin.** Haptoglobin inhibits oxidative damage to end organs and prevents heme-iron loss via the kidneys by binding free hemoglobin.
- **The human Haptoglobin gene is polymorphic with two main alleles, Haptoglobin allele 1 (Hp1) and Haptoglobin allele 2 (Hp2).** There are three genotypes: Hp 1/1, Hp 1/2, and Hp 2/2. **35-40%** of patients have the Hp 2/2 genotype.
- **Individuals with diabetes and/or kidney disease are candidates for Haptoglobin genotyping.** Those with an Hp 2/2 genotype who have diabetes or kidney disease are at a significantly higher CVD risk which may be reduced by treatment with 400 IU (268 mg) of natural source vitamin E (d-alpha tocopherol) taken daily after a meal.⁷⁻¹⁰

Israel Cardiovascular Events Reduction with Vitamin E (ICARE) Study

In the ICARE study of 1434 participants with diabetes and Hp2/2 genotype, random assignment to vitamin E treatment offset the increased CVD risk seen in the placebo group.⁹



ORDERING, REPORTING, AND SAMPLE INFORMATION

Ordering Information

- The order code is: 887

Report Interpretations and Considerations

Reportable Result	Interpretation	Consideration
Hp 1/1 and Hp 1/2	No increased CVD risk other than from risk associated with underlying conditions	None
Hp 2/2	3-Fold increased CVD risk in patients with diabetes or kidney disease.	Risk may be significantly reduced with 400 units of vitamin E daily given after a meal.

Specimen Requirements

- 1.0 mL blood collected in a K2 EDTA whole blood tube (lavender top)

References

- Maeda N, Yang F, Barnett DR, Bowman BH, Smithies O. Duplication within the haptoglobin Hp2 gene. *Nature* 1984;309:131-5.
- Levy AP, Asleh R, Blum S, Levy NS, Miller-Lotan R, Kalet-Litman S, et al. Haptoglobin: basic and clinical aspects. *Antioxid Redox Signal* 2010;12:293-304.
- Renner W, Jahrbacher R, Marx-Neuhold E, Tischler S, Zulus B. A novel exonuclease (TaqMan) assay for rapid haptoglobin genotyping. *Clin Chem Lab Med* 2016;54: 781-783.
- Vardi M, Levy NS, Levy AP. Vitamin E in the prevention of cardiovascular disease: the importance of proper patient selection. *J. Lipid Res.* 2013. 54: 2307-2314.
- Cahill LE, Levy AP, Chiuve SE, et al. Haptoglobin genotype is a consistent marker of coronary heart disease risk among individuals with elevated glycosylated hemoglobin. *J Am Coll Cardiol* 2013; 61:728-37.
- Cahill LE, Jensen MK, Chiuve SE, Shalom H, Pai JK, Flint AJ, Mukamal KJ, Rexrode KM, Levy AP, Rimm EB. The risk of coronary heart disease associated with glycosylated hemoglobin of 6.5% or greater is pronounced in the Haptoglobin 2-2 Genotype. *J Am Coll. Cardiol* 2015; 66:1791-9. RACT
- Alshiek JA, Dayan L, Asleh R, Blum S, Levy AP, Jacon G. Anti-oxidative treatment with vitamin E improves peripheral vascular function in patients with diabetes mellitus and Haptoglobin 2-2 genotype: A double-blinded cross-over study. *Diabetes Research and Clinical Practice* 2017;131:200-207.
- Hochberg I, Berinstein EM, Milman U, Shapira C, Levy AP. Interaction Between the Haptoglobin Genotype and Vitamin E on Cardiovascular Disease in Diabetes. *Curr Diab Rep* 2017;1:17-42.
- Milman U, et al. Vitamin E supplementation reduces cardiovascular events in a subgroup of middle-aged individuals with both type 2 diabetes mellitus and the haptoglobin 2-2 genotype: a prospective double-blinded clinical trial. *Arterioscler Thromb Vasc Biol.* 2008 Feb;28(2):341-7
- Asleh R, et al. Meta-analysis of the association of the haptoglobin genotype with cardiovascular outcomes and the pharmacogenomic interactions with vitamin E supplementation. *Pharmacogenomics Pers Med.* 2018;11:71-82.

877.425.1252 bostonheartdiagnostics.com

