# Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Manrai AK, Funke BH, Rehm HL, et al. Genetic misdiagnoses and the potential for health disparities. N Engl J Med 2016;375:655-65. DOI: 10.1056/NEJMsa1507092

**Supplementary Appendix**

# The Potential for Health Disparities Due to Genomic Misdiagnosis

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## Table S1. Allele frequencies in global populations

| *Gene (Variant)* | AA | EA | ASW | YRI | LWK | CEU | IBS | GBR | TSI | FIN | JPT | dbSNP |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***TNNT2 (K247R)*** | 14.89% | 1.48% | 11.5% | 17.6% | 11.9% | 0.6% | 3.6% | 1.7% | 2.6% | 4.3% | 7.3% | rs3730238 |
| ***OBSCN (R4344Q)*** | 7.97% | 0.17% | 10.7% | 15.9% | 17.0% | 0% | 0% | 1.1% | 0% | 0% | 0% | rs79023478 |
| ***TNNI3 (P82S)*** | 2.03% | 0.01% | 3.3% | 1.7% | 0% | 0% | 0% | 0% | 0% | 0% | 0% | rs77615401 |
| ***MYBPC3 (G278E)*** | 1.57% | 0.01% | 0.8% | 1.1% | 2.1% | 0% | 0% | 0% | 0% | 0% | 0% | rs147315081 |
| ***JPH2 (G505S)*** | 1.46% | 0.40% | 3.3% | 3.4% | 3.6% | 0% | 0% | 0.6% | 3.1% | 2.2% | 0% | rs140740776 |

NHLBI Exome Sequence Project

1000 Genomes Project

Minor allele frequencies in populations around the world for the five HCM-associated high-frequency variants. African populations include ASW (Americans of African Ancestry in SW USA), YRI (Yoruba in Ibadan, Nigeria), and LWK (Luhya in Webuye, Kenya). European populations include CEU (Utah Residents (CEPH) with Northern and Western European ancestry), IBS (Iberian population in Spain), GBR (British in England and Scotland), TSI (Toscani in Italia), and FIN (Finnish in Finland). Also shown are minor allele frequencies for JPT (Japanese in Tokyo, Japan).

**Table S2. Number of segregating loci**

| | **CEU** | **ASW** | **YRI** |
|---|---|---|---|
| ***MYBPC3*** | 62 | 113 | 113 |
| ***TNNI3*** | 27 | 66 | 68 |

African Americans harbor significantly more segregating loci than European Americans in both *MYBPC3* and *TNNI3* (Mann-Whitney *U*-test $P < 0.05$).

**Figure S1. Computed penetrance of HCM-associated high-frequency variants in three different clinical contexts. (A)** General population (prevalence K = 1:500), **(B)** population enriched for HCM patients, e.g., mixed population of HCM patients and general population (K = 1:100), **(C)** first-degree relatives (K = 1:2). P(G|D) is the proportion of HCM patients with the variant.