# Proactive Health SINGLE-GENE RISK™ 84 GENES

## TEST CODE: PR22020

### Overview

MyOme Proactive Health Single-Gene risk report uses a Blended Genome-Exome (BGE) backbone built from whole exome sequencing and low coverage whole genome sequencing to identify a range of variant types. This allows MyOme to re-query a patient's data as healthcare needs change and new information about the genome is discovered.

### Clinical Use

Test is intended for a wellness screening of germline heritable conditions in individuals from an asymptomatic population. MyOme annotates and interprets variants according to American College of Medical Genetics (ACMG) guidelines[1], and reports pathogenic or likely pathogenic variants. Genetic testing may provide information about an individual's disease risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy in conjunction with standard clinical assessment.

### Method

PCR-free whole genome library is constructed and a sub-aliquot is taken through PCR amplification and exome selection. The blended genome and exome libraries are sequenced to generate 2x150 bp paired-end reads resulting in low-coverage whole genome and higher coverage exome data. In-house pipeline allows identification of single-nucleotide variants (SNVs) and small insertions and deletions (indels). Variant interpretation by qualified scientists based on guidelines by the ACMG.

### Sample Types

- Blood (2 EDTA tubes)
- Saliva (2 tubes)
- Buccal (3 swabs)

### Turn Around Time

- From initial sample received, approximately 6 to 8 weeks
- For previously processed sample, approximately 2 to 4 weeks

### Included

- Analysis of SNVs and small insertions and deletions
- Confirmation of Pathogenic/Likely Pathogenic variants by orthogonal method (e.g., Sanger sequencing)
- Cohesive report with actionable recommendations
- **84 Genes included:** *ACTA2, ACTC1, ACVRL1, APC, APOB, ATM, ATP7B, BAG3, BMPR1A, BRCA1, BRCA2, BTD, CACNA1S, CALM1, CALM2, CALM3, CASQ2, CHEK2, COL3A1, DES, DSC2, DSG2, DSP, ENG, FBN1, FLNC, GAA, GLA, HFE, HNF1A, KCNH2, KCNQ1, LDLR, LDLRAP1, LMNA, MAX, MEN1, MLH1, MSH2, MSH6, MUTYH, MYBPC3, MYH11, MYH7, MYL2, MYL3, NF2, OTC, PALB2, PCSK9, PKP2, PMS2, PRKAG2, PTEN, RB1, RBM20, RET, RPE65, RYR1, RYR2, SCN5A, SDHAF2, SDHB, SDHC, SDHD, SMAD3, SMAD4, STK11, TGFBR1, TGFBR2, TMEM127, TMEM43, TNNI3, TNNC1, TNNT2, TP53, TPM1,TRDN, TSC1, TSC2, TTN, TTR, VHL, WT1*

### Test Performance[2]

- ≥60x average exome-wide coverage
- ≥1x average genome-wide coverage
- ≥90% of exonic regions at ≥20x depth
- >99.5% sensitivity for SNVs
- >97.5% sensitivity for small insertions/deletions

1. American College of Medical Genetics and Genomics. SF v3.2 list for reporting of secondary findings in clinical exome and genome sequencing: A policy statement of the ACMG. *Genet Med.* June 22, 2023. doi: 10.1016/j.gim.2023.100866.
2. MyOme Inc, Data on File.

## CONDITION-GENE RELATIONSHIP

The genes listed below are analyzed in this report. MyOme selected them based on our Gene Inclusion Framework Guidelines. Genes are prioritized based on clinical validity, actionability, penetrance/prevalence, and feasibility.

| Cardiovascular | |
|---|---|
| **Condition** | **Gene(s)** |
| **Arrhythmogenic right ventricular cardiomyopathy** | *DES, DSC2, DSG2, DSP, PKP2, TMEM43* |
| **Brugada syndrome** | *SCN5A* |
| **Catecholaminergic polymorphic ventricular tachycardia** | *CALM1, CALM2, CALM3, CASQ2, RYR2, TRDN* |
| **Dilated cardiomyopathy** | *ACTC1, BAG3, DES, FLNC, LMNA, MYH7, SCN5A, TNNC1, TNNI3, TNNT2, TPM1, TTN, RBM20* |
| **Ehlers-Danlos syndrome, vascular type** | *COL3A1* |
| **Emery-Dreifuss muscular dystrophy** | *LMNA* |
| **Fabry disease** | *GLA* |
| **Familial hypercholesterolemia** | *APOB, LDLR, LDLRAP1, PCSK9* |
| **Familial thoracic aortic aneurysm and dissection** | *ACTA2, MYH11, SMAD3* |
| **Hereditary transthyretin-related amyloidosis** | *TTR* |
| **Hypertrophic cardiomyopathy** | *ACTC1, MYBPC3, MYH7, MYL2, MYL3, PRKAG2, TNNC1, TNNI3, TNNT2, TPM1* |
| **Loeys-Dietz syndrome** | *TGFBR1, TGFBR2, SMAD3* |
| **Long QT syndrome** | *CALM1, CALM2, CALM3, KCNH2, KCNQ1, SCN5A, TRDN* |
| **Marfan syndrome** | *FBN1* |
| **Myofibrillar myopathy** | *BAG3, DES, FLNC* |
| **Short QT syndrome** | *KCNH2, KCNQ1* |

| Other | |
|---|---|
| **Condition** | **Gene(s)** |
| **Biotinidase deficiency** | *BTD* |
| **Hereditary hemochromatosis** | *HFE* |
| **Hereditary hemorrhagic telangiectasia** | *ACVRL1, ENG, SMAD4* |
| **Malignant hyperthemia** | *CACNA1S, RYR1* |
| **Monogenic diabetes** | *HNF1A* |
| **Ornithine transcarbamylase deficiency** | *OTC* |
| **RPE65-related retinopathy** | *RPE65* |
| **Wilson disease** | *ATP7B* |

| Cancer | |
|---|---|
| **Condition** | **Gene(s)** |
| **Familial adenomatous polyposis** | *APC* |
| **Familial ovarian cancer** | *PALB2* |
| **Gastrointestinal stromal tumor** | *KIT* |
| **Hereditary breast cancer** | *ATM, CHEK2, PALB2* |
| **Hereditary breast and ovarian cancer** | *BRCA1, BRCA2* |
| **Hereditary nonpolyposis colon cancer** | *ATM* |
| **Hereditary paraganglioma-pheochromocytoma syndrome** | *MAX, SDHAF2, SDHB, SDHC, SDHD, TMEM127* |
| **Juvenile polyposis syndrome** | *BMPR1A* |
| **Juvenile polyposis with hereditary hemorrhagic telangiectasia** | *SMAD4* |
| **Li-Fraumeni syndrome** | *TP53* |
| **Lynch syndrome** | *MLH1, MSH2, MSH6, PMS2* |
| **Multiple endocrine neoplasia** | *MEN1, RET* |
| **MUTYH-associated polyposis** | *MUTYH* |
| **Neurofibromatosis type 2** | *NF2* |
| **Peutz-Jeghers syndrome** | *STK11* |
| **PTEN hamartoma tumor syndrome** | *PTEN* |
| **Retinoblastoma** | *RB1* |
| **Tuberous sclerosis complex** | *TSC1, TSC2* |
| **Von Hippel-Lindau syndrome** | *VHL* |
| **WT1-related Wilms tumor** | *WT1* |

# Proactive Health MEDICATION RESPONSE™

## TEST CODE: PR32005

### Overview

MyOme Proactive Health Medication Response report uses a Blended Genome-Exome (BGE) backbone to identify variants associated with medication response. This allows MyOme to re-query a patient's data as healthcare needs change and new information about the genome is discovered.

### Clinical Use

Test is intended to facilitate the use of pharmacogenomic guidance in a general care setting. MyOme reports variants and star alleles in 15 pharmacogenes that are known to impact an individual's response to medication. The results of this test should be interpreted by a trained healthcare provider based on the full context of a patient's medical situation.

### Method

Genomic DNA obtained from submitted samples is used to construct a PCR-free whole genome library and an exome library and sequenced using Illumina technology. Reads are aligned to the GRCh38 reference assembly. MyOme's Medication Response variant calling pipeline is used to call variants, star alleles, copy number variants, and assign pharmacogenomic diplotypes.

### Sample Types

- Blood (2 EDTA tubes)
- Saliva (2 tubes)
- Buccal (2 swabs)

### Turn Around Time

- From initial sample received, approximately 6-8 weeks

### Included

- Analysis of key genes with known pharmacogenomic implications for more than 70 drugs, including antidepressants, statins and opioids
- 96% Tier 1 variant alleles recommended by the Association for Molecular Pathology (AMP) PGx Working Group for *CYP2C19*[1], *CYP2C9*[2], *CYP2D6*[3] (excluding deletions/duplications), *TPMT* and *NUDT15*[4]
- All Tier 2 variant alleles recommended by the AMP PGx Working Group for *CYP2C19*[1], *CYP2C9*[2], *CYP2D6* (excluding hybridizations)[3]
- Independent healthcare provider review of analysis to make any potential drug recommendations based on gene-drug interactions outlined in the Clinical Pharmacogenetics Implementation Consortium (CPIC)[5] guidelines and FDA Table of Pharmacogenomic Associations[6]
- 15 genes analyzed: ***CYP2B6:*** **4; *6; *9; *18; *22* ***CYP2C9:*** **2; *3; *4; *5; *6; *8; *11; *12; *13; *15; *16; *26; *28; *29; *30; *31; *42; *55* ***CYP2C19:*** **2; *3; *4; *5; *6; *7; *8; *9; *10; *17; *35* ***CYP2D6:*** **2; *3; *4; *6; *7; *8; *9; *10; *11; *12; *14; *15; *17; *21; *31; *40; *41; *42; *49; *56; *59; *100; *114;* ***CYP3A4:*** **22* ***CYP3A5:*** **3; *6* ***CYP4F2:*** **3* ***DPYD:*** *rs3918290; rs55886062; rs59086055; rs67376798; rs75017182+rs56038477; rs112766203; rs115232898; rs146356975; rs183385770* ***F5:*** *rs6025* ***IFNL3:*** *rs12979860* ***NUDT15:*** **3; *4; *9,* ***SLCO1B1:*** **5; *9; *14; *20* ***TPMT:*** **2; *3A; *3B; *3C; *4; *11; *29* ***UGT1A1:*** **6; *27* ***VKORC1:*** *rs9923231*

### Test Performance[7]

- >98.5% accuracy for diplotypes
- 98% of core pharmacogenomic variants at ≥20x depth
- 60x average exome-wide coverage

1. Pratt VM et al. Recommendations for Clinical CYP2C19 Genotyping Allele Selection: A Report of the Association for Molecular Pathology. J Mol Diagn. 2018 May;20(3):269-276. doi: 10.1016/j.jmoldx.2018.01.011. 2. Pratt VM et al. Recommendations for Clinical CYP2C9 Genotyping Allele Selection. J Mol Diagn. 2019 Sep;21(5):746-755. doi: 10.1016/j.jmoldx.2019.04.003. 3. Pratt VM et al. Recommendations for Clinical CYP2D6 Genotyping Allele Selection. J Mol Diagn. 2021 Sep;23(9):1047-1064. doi: 10.1016/j.jmoldx.2021.05.013. 4. Pratt VM et al. TPMT and NUDT15 Genotyping Recommendations. J Mol Diagn. 2022 Oct;24(10):1051-1063. doi: 10.1016/j.jmoldx.2022.06.007. 5. CPIC. Genes-Drugs. Web. cpicpgx.org/genes-drugs. Accessed 2024 Dec. 6. US Food & Drug Administration. Table of Pharmacogenetic Associations. 2022 Oct. Web. Accessed 2024 Dec. 7.MyOme Inc, Data on File

## DRUG-GENE IMPACT

The list of drugs below can lead to a major or moderate drug-gene interaction based on guidelines described above.[5,6]

| Behavioral Health | |
|---|---|
| **Drug Name** | **Gene(s)** |
| amitriptyline | *CYP2D6, CYP2C19* |
| amoxapine | *CYP2D6* |
| amphetamine | *CYP2D6* |
| aripiprazole | *CYP2D6* |
| aripiprazole lauroxil | *CYP2D6* |
| atomoxetine | *CYP2D6* |
| brexpiprazole | *CYP2D6* |
| citalopram | *CYP2C19, CYP2D6* |
| clobazam | *CYP2C19* |
| clomipramine | *CYP2D6* |
| clozapine | *CYP2D6* |
| desipramine | *CYP2D6* |
| diazepam | *CYP2C19* |
| doxepin | *CYP2D6, CYP2C19* |
| duloxetine | *CYP2D6* |
| escitalopram | *CYP2C19* |
| fluoxetine | *CYP2D6* |
| fluvoxamine | *CYP2D6* |
| iloperidone | *CYP2D6* |
| imipramine | *CYP2D6* |
| lofexidine | *CYP2D6* |
| nortriptyline | *CYP2D6* |
| paroxetine | *CYP2D6* |
| perphenazine | *CYP2D6* |
| protriptyline | *CYP2D6* |
| sertraline | *CYP2C19* |
| thioridazine | *CYP2D6* |
| trimipramine | *CYP2D6, CYP2C19* |
| valbenazine | *CYP2D6* |
| venlafaxine | *CYP2D6* |
| vortioxetine | *CYP2D6* |

| Urology | |
|---|---|
| **Drug Name** | **Gene(s)** |
| darifenacin | *CYP2D6* |
| fesoterodine | *CYP2D6* |
| mirabegron | *CYP2D6* |
| tamsulosin | *CYP2D6* |
| tolterodine | *CYP2D6* |

| Reproductive and Sexual Health | |
|---|---|
| **Drug Name** | **Gene(s)** |
| flibanserin | *CYP2C19, CYP2C9, CYP2D6* |

| Gastroenterology | |
|---|---|
| **Drug Name** | **Gene(s)** |
| dexlansoprazole | *CYP2C19* |
| dronabinol | *CYP2C9* |
| esomeprazole | *CYP2C19* |
| lansoprazole | *CYP2C19* |
| metoclopramide | *CYP2D6* |
| nateglinide | *CYP2C9* |
| omeprazole | *CYP2C19* |
| ondansetron | *CYP2D6* |
| pantoprazole | *CYP2C19* |
| rabeprazole | *CYP2C19* |

| Infectious Disease | |
|---|---|
| **Drug Name** | **Gene(s)** |
| atazanavir | *UGT1A1* |
| dolutegravir | *UGT1A1* |
| efavirenz | *CYP2B6* |
| peginterferon alfa-2a | *IFNL3* |
| peginterferon alfa-2b | *IFNL3* |
| quinine | *CYP2D6* |
| voriconazole | *CYP2C19* |

| Cardiology | |
|---|---|
| **Drug Name** | **Gene(s)** |
| atorvastatin | *SLCO1B1* |
| carvedilol | *CYP2D6* |
| clopidogrel | *CYP2C19* |
| fluvastatin | *CYP2C9, SLCO1B1* |
| lovastatin | *SLCO1B1* |
| mavacamten | *CYP2C19* |
| pitavastatin | *SLCO1B1* |
| pravastatin | *SLCO1B1* |
| rosuvastatin | *SLCO1B1* |
| simvastatin | *SLCO1B1* |
| warfarin | *CYP2C9, CYP4F2, VKORC1* |

| Miscellaneous | |
|---|---|
| **Drug Name** | **Gene(s)** |
| abrocitinib | *CYP2C19* |
| cevimeline | *CYP2D6* |
| eliglustat | *CYP2D6* |
| lesinurad | *CYP2C9* |
| meclizine | *CYP2D6* |
| tropisetron | *CYP2D6* |

| Neurology | |
|---|---|
| **Drug Name** | **Gene(s)** |
| brivaracetam | *CYP2C19* |
| deutetrabenazine | *CYP2D6* |
| donepezil | *CYP2D6* |
| fosphenytoin | *CYP2C9* |
| modafinil | *CYP2D6* |
| phenytoin | *CYP2C9* |
| pimozide | *CYP2D6* |
| pitolisant | *CYP2D6* |
| siponimod | *CYP2C9* |
| tetrabenazine | *CYP2D6* |
| valbenazine | *CYP2D6* |

| Pain Management | |
|---|---|
| **Drug Name** | **Gene(s)** |
| carisoprodol | *CYP2C19* |
| celecoxib | *CYP2C9* |
| codeine | *CYP2D6* |
| elagolix | *SLCO1B1* |
| flurbiprofen | *CYP2C9* |
| ibuprofen | *CYP2C9* |
| lornoxicam | *CYP2C9* |
| meloxicam | *CYP2C9* |
| oliceridine | *CYP2D6* |
| piroxicam | *CYP2C9* |
| tenoxicam | *CYP2C9* |
| tramadol | *CYP2D6* |

| Hematology/Oncology | |
|---|---|
| **Drug Name** | **Gene(s)** |
| capecitabine | *DPYD* |
| erdafitinib | *CYP2C9* |
| eltrombopag | *F5* |
| fluorouracil | *DPYD* |
| gefitinib | *CYP2D6* |
| mercaptopurine | *TPMT, NUDT15* |
| tamoxifen | *CYP2D6* |
| thioguanine | *TPMT, NUDT15* |

| Transplant | |
|---|---|
| **Drug Name** | **Gene(s)** |
| azathioprine | *TPMT, NUDT15* |
| tacrolimus | *CYP3A5* |

5. CPIC. Genes-Drugs. Web. cpicpgx.org/genes-drugs. Accessed 2024 Dec. 6. US Food & Drug Administration. Table of Pharmacogenetic Associations. 2022 Oct. Web. Accessed 2024 Dec.

**Jane Doe**
Biological Sex: Female
Date of Birth: 11/13/2018
Sample ID: SM12805
Sample Type: BLOOD
Collection Date: 11/13/2018
Received Date: 11/14/2018

**Clinic: The City Clinic**
**Physician: Jane Smith, M.D.**
Phone: 555-555-5555
Fax: 555-555-5555
NPI: 0123456789

**Requisition ID:**
RQ12345
**Report Number:**
RP12345
**Report Date:**
11/01/2024

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https://myome.com/r/?id=RP12345

## Your lifetime risk of developing breast cancer is average (less than 20%) based on your integrated score.

**CLINICAL CONTEXT**: This test integrates known clinical risk factors and a polygenic risk score. It does NOT incorporate single gene findings in breast cancer predisposition genes.

### RISK DETAILS

| | LIFETIME RISK | 5-YEAR RISK |
|---|---|---|
| **Integrated Risk** | 14.2% | 0.5% |
| **Clinical Risk** | 12.2% | 0.4% |
| **General Population Risk** | 11.7% | 0.1% |

**Integrated Risk**: *The risk of developing breast cancer based on the combination of a polygenic risk score and the Tyrer-Cuzick clinical risk model.*
**Clinical Risk**: *The risk of developing breast cancer based on the Tyrer-Cuzick clinical risk model.*
**General Population Risk**: *The average risk of developing breast cancer for a biological female in the general population of the same age.*

### NEXT STEPS

- Next steps described in this section are based on lifetime risk as estimated by the integrated risk score.
- Individuals with an estimated lifetime breast cancer risk less than 20% can typically follow the general population recommendations from society guidelines, as outlined below. Please discuss the risk score as part of a comprehensive risk assessment with a healthcare provider, as some factors such as prior chest wall radiation, or mammographic breast density, may warrant additional breast cancer screening [1,4,5].
- Option to start annual mammograms at age 40 with recommendation to start by age 45.
- These results should be interpreted in the context of the individual's personal medical history or family history.

**MyOme, Inc.**
1455 Adams Drive, #1150
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

**Lab Director:**
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

## REFERENCES

1. Saslow et al. *American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography.* CA Cancer J Clin. 2007; 57(57):75-89. PMID: 17392385.
2. Tshiaba et al. *Integration of a Cross-Ancestry Polygenic Model With Clinical Risk Factors Improves Breast Cancer Risk Stratification.* JCO Precis Oncol. 2023; 7(7):e2200447. PMID: 36809055.
3. Tyrer et al. *A breast cancer prediction model incorporating familial and personal risk factors.* Stat Med. 2004; 23(23):1111-30. PMID: 15057881.
4. Oeffinger et al. *Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society.* JAMA. 2015; 314(314):1599-614. PMID: 26501536.
5. US et al. *Screening for Breast Cancer: US Preventive Services Task Force Recommendation Statement.* JAMA. 2024; 331(331):1918-1930. PMID: 38687503.
6. Monticciolo et al. *Breast Cancer Screening for Women at Higher-Than-Average Risk: Updated Recommendations From the ACR.* J Am Coll Radiol. 2023; 20(20):902-914. PMID: 37150275.

## TEST METHODS

- Patient data is provided by the ordering physician. Specimen receipt, accessioning, data analysis and interpretation is performed by MyOme, Inc., 1455 Adams Dr., Ste 1150, Menlo Park, CA 94025, CLIA#05D2203070. Whole Genome Sequencing, excluding data analysis and interpretation, is performed by Broad Clinical Labs LLC, 27 Blue Sky Dr, Burlington, MA 01803, CLIA#22D2055652.
- Genomic DNA obtained from submitted samples was sequenced using Illumina technology. Reads were aligned to the NCBI GRCh37.p13 reference assembly.
- A polygenic risk score (PRS) is calculated for each of 5 continental ancestries of which the patient is a part as the sum of the patient's risk alleles weighted by the allele-specific effect sizes. The raw scores are centered using four principal components and standardized with a population-specific standard deviation. Standardized PRSs weighted by fractional ancestry and ancestry-specific effect sizes are summed (caPRS) [2].
- The standardized PRS is integrated with the risk based on the Tyrer-Cuzick (TC) model to estimate a 5-year and remaining lifetime risk of developing breast cancer [3].
- **This tool cannot be used to detect rare pathogenic variants including those in hereditary cancer predisposition genes.**

**MyOme, Inc.**
1455 Adams Drive, #1150
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

**Lab Director:**
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

## TEST LIMITATIONS

- The results of this test may not be valid if the patient has a pathogenic variant in a breast cancer predisposition gene. The integrated risk score estimate does not account for pathogenic variants in genes with limited or disputed breast cancer association (e.g. BRIP1), as the available data is currently insufficient to accurately quantify the breast cancer risk associated with these genes.
- The clinical risk based on the Tyrer-Cuzick risk model was calculated based on the patient data provided by the ordering physician. Incorrect or missing information will impact this calculation and the integrated risk score.
- A risk calculation will not be performed for biological males. A risk calculation will also not be performed for biological females who are under the age of 18, over the age of 84, known to carry a pathogenic variant in a breast cancer predisposition gene or have a personal history of breast cancer.
- A risk calculation will not be performed when there is missing information necessary to perform the calculation, including but not limited to age and first degree family history of breast cancer.
- The breast cancer integrated risk is a risk assessment tool NOT a diagnostic. These results should be interpreted in the context of the individual's personal medical history and family history.
- Performance of this tool may be reduced in certain populations.
- Like most tests, this test carries a risk of false negative or false positive results, which may be caused by, without limitation, sample contamination from biological or non-biological sources, specimen marking issues, rare genetic variants interfering with analysis, and other technical issues and limitations.

## DISCLAIMERS

This test was developed, and its performance characteristics were determined, by MyOme, Inc., a clinical laboratory certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) to perform high complexity clinical laboratory testing. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA).

**MyOme, Inc.**
1455 Adams Drive, #1150
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

**Lab Director:**
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

**George Washington Carver**
Sex Assigned at Birth: Male
Date of Birth: 06/15/1967
Sample ID: SM-0000232
Sample Type: BLOOD
Collection Date: 02/01/2024
Received Date: 02/03/2024

**Clinic: Cardiovascular Health Center**
**Physician: Maria Chen, M.D., Ph.D.**
Phone: 510-555-0000
NPI: 1234567890

**Requisition ID:**
RQ0000059
**Report Number:**
RP12345
**Report Date:**
02/13/2025

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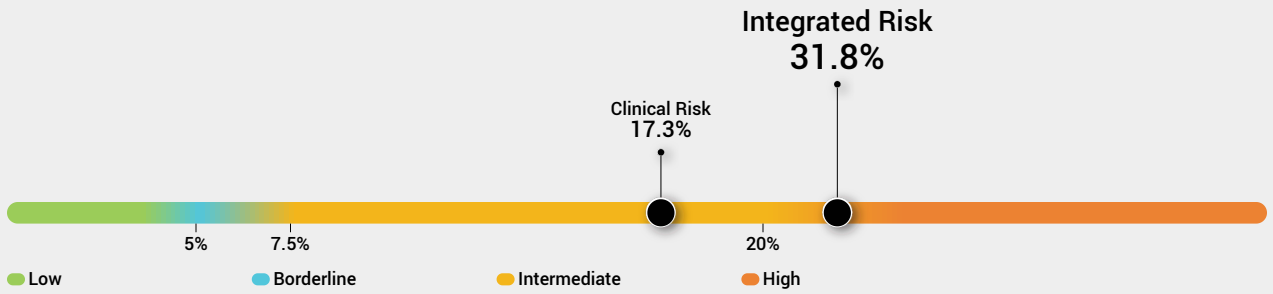
## High Risk

Based on the integrated risk score, this patient has a 31.8% chance of experiencing a coronary artery disease (CAD) event in the next 10 years.

### 10-YEAR ABSOLUTE RISK OF CAD




**Integrated Risk:** The probability of having a CAD-related event within the next 10 years based on the combination of a polygenic risk score (PRS) and clinical risk factors.

**Clinical Risk:** The probability of having a first atherosclerotic cardiovascular disease (ASCVD) event within the next 10 years based on clinical risk factors. Factors include age, race, total and HDL cholesterol, systolic blood pressure, smoking and diabetes status, and whether the patient is receiving treatment for blood pressure abnormalities.

**Based on the integrated risk score, this patient has a 31.8% chance of experiencing a coronary artery disease (CAD) event in the next 10 years.**

This test determined that the patient is at high risk for CAD, defined as an absolute 10-year integrated risk greater than 20%. Being at high risk for CAD does not mean that the patient will definitely develop the disease. There may be other genetic and non-genetic factors not considered here that influence the patient's risk.

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Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

**Lab Director:**
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

## NEXT STEPS

The AHA recommends all patients follow a heart-healthy lifestyle, including smoking cessation, regular physical activity, and a balanced diet [3].

For patients with a high 10-year ASCVD risk estimation, the AHA recommends starting a high-intensity statin and addressing comorbid conditions such as hypertension or diabetes [3].

## CLINICAL MEASUREMENTS

The clinical measurements used to estimate the patient's risk of developing CAD were provided by the ordering physician and are detailed below. Changes in these measurements will result in a change in the patient's risk estimation.

| | | | |
|---|---|---|---|
| **Age** | 57 | **Total Cholesterol** | 131 mg/dL |
| **Sex Assigned at Birth** | Male | **HDL Cholesterol** | 39 mg/dL |
| **Self-reported Race** | Black/African American | **History of Diabetes** | Yes |
| **Systolic Blood Pressure** | 118 mm Hg | **Smoking Status** | Current smoker |
| **Diastolic Blood Pressure** | 76 mm Hg | **Hypertension Treatment** | No |

## REFERENCES

1. Tshiaba, Placede et al. Genetics in Medicine Open, Volume 1, Issue 1, 100361
2. Goff et al. *2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.* Circulation. 2014; 129( 129):S49-73. PMID: 24222018.
3. Arnett et al. *2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.* Circulation. 2019; 140( 140):e563-e595. PMID: 30879339.

## TEST METHODS

- Patient data is provided by the ordering physician. Specimen receipt, accessioning, data analysis and interpretation is performed by MyOme, Inc., 1455 Adams Dr., Ste 1150, Menlo Park, CA 94025, CLIA#05D2203070. Whole Genome Sequencing, excluding data analysis and interpretation, is performed by Broad Clinical Labs LLC, 27 Blue Sky Dr, Burlington, MA 01803, CLIA#22D2055652.
- Genomic DNA obtained from submitted samples is sequenced using Illumina technology. Reads are aligned to the NCBI GRCh38 reference assembly.
- A polygenic risk score (PRS) is calculated for each of 5 continental ancestries of which the patient is a part as the sum of the patient's risk alleles weighted by the allele-specific effect sizes. The raw scores are centered using four principal components and standardized with a population-specific standard deviation. Standardized PRSs weighted by fractional ancestry and ancestry-specific effect sizes are summed (caPRS) [1].
- The standardized caPRS is integrated with the clinical risk based on the Atherosclerotic cardiovascular disease (ASCVD) Pooled Cohort Equations (PCE) model [2] to estimate the patient's 10-year risk of developing CAD.

**MyOme, Inc.**
1455 Adams Drive, #1150
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

**Lab Director:**
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

## TEST LIMITATIONS

- The clinical risk based on the ASCVD PCE risk model was calculated using the patient data provided by the ordering physician. Incorrect information will impact this calculation and the integrated risk score.
- A risk calculation will not be performed for individuals younger than 40 or older than 79 years old or for individuals missing clinical measurements or individuals with a personal history of CAD.
- This test is a risk assessment tool NOT a diagnostic. These results should be interpreted in the context of the individual's personal medical history and family history.
- Performance of this tool may be reduced in certain populations.
- A history of stem cell or bone marrow transplantation, or recent blood transfusion may impact the accuracy of the results.
- Testing is unavailable for samples damaged by human error or lost/destroyed due to weather, transit issues or other problems beyond the control of MyOme.
- Like most tests, this test carries a risk of false negative or false positive results, which may be caused by, without limitation, sample contamination from biological or non-biological sources, specimen marking issues, rare genetic variants interfering with analysis, and other technical issues and limitations.

## DISCLAIMERS

This test was developed, and its performance characteristics were determined, by MyOme, Inc., a clinical laboratory certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and College of American Pathologist (CAP) accredited to perform high complexity clinical laboratory testing. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). Test results should always be interpreted by a clinician in the context of clinical and familial data with the availability of genetic counseling when appropriate. MyOme is not responsible for the content of third-party websites referenced in this report.

## REVIEWED BY

MyOme

MyOme Example Lab Director

02/13/2025

Date

**MyOme, Inc.**
1455 Adams Drive, #1150
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

**Lab Director:**
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502