# MEDICAL POLICY

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| **POLICY TITLE** | **GENOTYPING FOR 9P21 SINGLE NUCLEOTIDE POLYMORPHISMS TO PREDICT RISK OF CARDIOVASCULAR DISEASE OR ANEURYSM** |
| **POLICY NUMBER** | **MP 2.311** |

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| **CLINICAL BENEFIT** | ☐ MINIMIZE SAFETY RISK OR CONCERN.<br>☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS.<br>☐ ASSURE APPROPRIATE LEVEL OF CARE.<br>☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS.<br>☐ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET.<br>☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE. |
| **Effective Date:** | **RETIRED 7/1/2026** |


POLICY | PRODUCT VARIATIONS | DESCRIPTION/BACKGROUND
RATIONALE | DEFINITIONS | DISCLAIMER
CODING INFORMATION | REFERENCES | POLICY HISTORY




## I. POLICY

The use of genotyping for *9p21* single nucleotide polymorphisms (SNPs) is considered **investigational** for all clinical uses, including but not limited to identification of patients who may be at increased risk of cardiovascular disease or its manifestations (e.g., Myocardial Infarction, ischemic stroke, peripheral arterial disease, coronary artery calcification) or identification of patients who may be at increased risk of aneurysmal disease (abdominal aortic aneurysm, intracranial aneurysm or polypoidal choroidal vasculopathy). There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

### Policy Guidelines

There is no specific CPT code for this test. If the specific analyte is listed in codes 81200-81355 or 81400- 81408, that CPT code would be reported along with the unlisted code 81479 for the analytes that are not listed. If none of the analytes are listed in the more specific CPT codes, unlisted code 81479 would be reported for the whole test.

The Quest website reports that their Cardio IQ® 9p21 Genotype test is reported with code 81479.

## II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

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**FEP PPO** - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies

## III. DESCRIPTION/BACKGROUND

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A number of highly correlated single nucleotide polymorphisms (SNPs) found at the 9p21 locus have been significantly associated with risk of myocardial infarction (MI), particularly early onset MI, and other manifestations of cardiovascular disease (CVD). Associations with 9p21 SNPs and risk of abdominal aortic aneurysm, intracranial aneurysm and other vascular disorders have also been reported. Genotyping for 9p21 SNPs has been investigated to identify patients at risk of cardiovascular disorders.

In 2007, multiple investigators nearly simultaneously reported the first common genetic variant affecting the risk of coronary heart disease (CHD; defined as inadequate circulation to cardiac muscle and surrounding tissue resulting in MI, unstable angina pectoris, coronary revascularization, or death) in whites through genome-wide association studies (GWAS) using SNP arrays. Additional studies identified other SNPs with similar estimates of CHD risk. These SNPs were confirmed in case control replication studies in a variety of study populations, showing that the identified SNPs were associated with CHD and even more specifically with MI. All of the SNPs were found within a locus spanning a 58-kilobase region at chromosome 9p21.3 (thus the locus is sometimes represented more specifically as 9p21.3; for simplicity, 9p21 will be used for the rest of this document), are highly correlated ($r2>0.8$) and thus are said to be in linkage disequilibrium (nonrandom association of alleles). The association of any identified SNP with CHD risk was shown to be independent of traditional risk factors.

Several studies have extended the 9p21 association to other vascular diseases including ischemic stroke; thus, 9p21 may be reported as being associated with cardiovascular disease (CVD; defined as CHD and cerebrovascular disease) outcomes. Associations have also been reported with abdominal aortic aneurysm and with intracranial arterial aneurysm and other vascular diseases.

Several genes are found at the 9p21 locus, including *ANRIL*, which encodes a large noncoding RNA that may have regulatory functions, and *CDKN2A* and *CDKN2B*, which encode cyclin-dependent kinase inhibitors. The mechanisms by which the SNPs lead to increased CHD risk have been largely unknown. Harismendy et al identified several potential enhancer regulatory DNA sequences in the 9p21 region. They reported that the SNP rs10747278, consistently associated with increased risk of CHD, occurs in one of these enhancer sequences and that the risk allele disrupts a transcription factor binding site involved in the inflammatory response (STAT1). The interaction of STAT1 with part of the inflammatory signaling pathway, interferon-gamma, is impaired in 9p21 risk carriers. Congrains et al genotyped 18 SNPs across the CVD-associated region and encompassing *ANRIL* and *CDKN2A/B* to determine the impact of 9p21

variants on gene expression. The authors reported that "…+several SNPs in 9p21 locus affect the expression of *ANRIL*, which is further in control of the regulation of *CDKN2A/B* and cell growth. Cell proliferation mediates the progression of atherosclerosis and is also directly or indirectly involved in the pathogenesis of diseases associated with this locus."

A 2014 systemic review and meta-analysis of 31 cohorts including 193,372 persons confirmed the association between 9p21 variants and the likelihood of a first CHD event (HR 1.19 per risk allele, 95% CI 1.17-1.22). However, 9p21 variants were not associated with an increased likelihood of subsequent CHD events among persons with known CHD (HR 1.01 per risk allele, 95% CI 0.97-1.06).

### Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). 9p21 genotyping tests are available under the auspices of CLIA. Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

## III. RATIONALE

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### Summary of Evidence

The association of single-nucleotide polymorphisms at the 9p21 locus with coronary artery/heart disease (CAD/CHD) outcomes (clinical validity) is well-established and consistent in multiple independent populations, with evidence of increasing severity of outcomes with increasing risk allele dosage. The clinical validity for the association of *9p21* polymorphisms with ischemic stroke, aneurysms, or other vascular disorders is less well-studied and less certain. Despite evidence that *9p21* polymorphisms are associated with CAD/CHD incidence and outcomes, the clinical utility of *9p21* genotyping has not been established. Studies have not conclusively demonstrated that *9p21* genotyping significantly improves risk reclassification after initial classification by traditional risk factors or that the addition of *9p21* genotyping to traditional risk factors improves risk assessment. No studies were identified that evaluate whether use of *9p21* genotyping is associated with changes in patient management, improvements in clinical outcomes, or both. The evidence is insufficient to determine the effects of the technology on health outcomes.

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## IV. DEFINITIONS

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N/A

## V. DISCLAIMER

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*Capital Blue Cross' medical policies are used to determine coverage for specific medical technologies, procedures, equipment, and services. These medical policies do not constitute medical advice and are subject to change as required by law or applicable clinical evidence from independent treatment guidelines. Treating providers are solely responsible for medical advice and treatment of members. These polices are not a guarantee of coverage or payment. Payment of claims is subject to a determination regarding the member's benefit program and eligibility on the date of service, and a determination that the services are medically necessary and appropriate. Final processing of a claim is based upon the terms of contract that applies to the members' benefit program, including benefit limitations and exclusions. If a provider or a member has a question concerning this medical policy, please contact Capital Blue Cross' Provider Services or Member Services.*

## VI. CODING INFORMATION

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**Note:** This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

**The following CPT code is investigational when used to report genotyping for 9p21 single nucleotide polymorphisms to predict risk of cardiovascular disease or aneurysm as outlined in the policy statement:**

| Procedure Codes | | | | | | | | |
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| 81479 | | | | | | | | |

## VII. REFERENCES

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1. *Wellcome Trust Case Control Consortium: Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. Nature. Jun 7 2007;447(7145):661-678. PMID 17554300*
2. *McPherson R, Pertsemlidis A, Kavaslar N, et al. A common allele on chromosome 9 associated with coronary heart disease. Science. Jun 8 2007;316(5830):1488-1491. PMID 17478681*

3. *Helgadottir A, Thorleifsson G, Manolescu A, et al. A common variant on chromosome 9p21 affects the risk of myocardial infarction. Science. Jun 8 2007;316(5830):1491-1493. PMID 17478679*
4. *Samani NJ, Erdmann J, Hall AS, et al. Genomewide association analysis of coronary artery disease. N Engl J Med. Aug 2 2007;357(5):443-453. PMID 17634449*
5. *Scheffold T, Kullmann S, Huge A, et al. Six sequence variants on chromosome 9p21.3 are associated with a positive family history of myocardial infarction: a multicenter registry. BMC Cardiovasc Disord. 2011;11:9. PMID 21385355*
6. *Johansen CT, Lanktree MB, Hegele RA. Translating genomic analyses into improved management of coronary artery disease. Future Cardiol. Jul 2010;6(4):507-521. PMID 20608823*
7. *Harismendy O, Notani D, Song X, et al. 9p21 DNA variants associated with coronary artery disease impair interferon-gamma signalling response. Nature. Feb 10 2011;470(7333):264-268. PMID 21307941*
8. *Congrains A, Kamide K, Oguro R, et al. Genetic variants at the 9p21 locus contribute to atherosclerosis through modulation of ANRIL and CDKN2A/B. Atherosclerosis. Feb 2012;220(2):449-455. PMID 22178423*
9. *Palomaki GE, Melillo S, Bradley LA. Association between 9p21 genomic markers and heart disease: a meta-analysis. JAMA. Feb 17 2010;303(7):648-656. PMID 20159873*
10. *Teutsch SM, Bradley LA, Palomaki GE, et al. The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Initiative: methods of the EGAPP Working Group. Genet Med. Jan 2009;11(1):3-14. PMID 18813139*
11. *Schunkert H, Konig IR, Kathiresan S, et al. Large-scale association analysis identifies 13 new susceptibility loci for coronary artery disease. Nat Genet. 2011;43(4):333-338. PMID 21378990*
12. *Preuss M, Konig IR, Thompson JR, et al. Design of the Coronary Artery Disease Genome-Wide Replication And Meta-Analysis (CARDIOGRAM) Study: A Genome-wide association meta-analysis involving more than 22 000 cases and 60 000 controls. Circ Cardiovasc Genet. Oct 1 2010;3(5):475-483. PMID 20923989*
13. *A genome-wide association study in Europeans and South Asians identifies five new loci for coronary artery disease. Nat Genet. 2011;43(4):339-344. PMID 21378988*
14. *Zhou LT, Qin L, Zheng DC, et al. Meta-analysis of genetic association of chromosome 9p21 with early-onset coronary artery disease. Gene. Dec 1 2012;510(2):185-188. PMID 22975211*
15. *Chan K, Patel RS, Newcombe P, et al. Association between the chromosome 9p21 locus and angiographic coronary artery disease burden: a collaborative meta-analysis. J Am Coll Cardiol. Mar 5 2013;61(9):957-970. PMID 23352782*
16. *Dong L, Wang H, Wang DW, et al. Association of chromosome 9p21 genetic variants with risk of coronary heart disease in the East Asian population: a meta-analysis. Ann Hum Genet. May 2013;77(3):183-190. PMID 23347249*

17. *Lian J, Ba Y, Dai D, et al. A replication study and a meta-analysis of the association between the CDKN2A rs1333049 polymorphism and coronary heart disease. J Atheroscler Thromb. 2014;21(11):1109-1120. PMID 24930384*
18. *Paynter NP, Chasman DI, Pare G, et al. Association between a literature-based genetic risk score and cardiovascular events in women. JAMA. Feb 17 2010;303(7):631-637. PMID 20159871*
19. *Ripatti S, Tikkanen E, Orho-Melander M, et al. A multilocus genetic risk score for coronary heart disease: case-control and prospective cohort analyses. Lancet. Oct 23 2010;376(9750):1393-1400. PMID 20971364*
20. *Dandona S, Stewart AF, Chen L, et al. Gene dosage of the common variant 9p21 predicts severity of coronary artery disease. J Am Coll Cardiol. Aug 3 2010;56(6):479-486. PMID 20670758*
21. *Patel RS, Su S, Neeland IJ, et al. The chromosome 9p21 risk locus is associated with angiographic severity and progression of coronary artery disease. Eur Heart J. Dec 2010;31(24):3017-3023. PMID 20729229*
22. *Davies RW, Dandona S, Stewart AF, et al. Improved prediction of cardiovascular disease based on a panel of single nucleotide polymorphisms identified through genome-wide association studies. Circ Cardiovasc Genet. Oct 1 2010;3(5):468-474. PMID 20729558*
23. *Beckie TM, Groer MW, Beckstead JW. The relationship between polymorphisms on chromosome 9p21 and age of onset of coronary heart disease in black and white women. Genet Test Mol Biomarkers. Jun 2011;15(6):435442. PMID 21375403*
24. *Beckie TM, Beckstead JW, Groer MW. The association between variants on chromosome 9p21 and inflammatory biomarkers in ethnically diverse women with coronary heart disease: a pilot study. Biol Res Nurs. Jul 2011;13(3):306-319. PMID 21705410*
25. *Dutta A, Henley W, Lang IA, et al. The coronary artery disease-associated 9p21 variant and later life 20-year survival to cohort extinction. Circ Cardiovasc Genet. Oct 2011;4(5):542-548. PMID 21852414*
26. *Shiffman D, O'Meara ES, Rowland CM, et al. The contribution of a 9p21.3 variant, a KIF6 variant, and C-reactive protein to predicting risk of myocardial infarction in a prospective study. BMC Cardiovasc Disord. 2011;11:10. PMID 21406102*
27. *Wang W, Peng WH, Lu L, et al. Polymorphism on chromosome 9p21.3 contributes to early-onset and severity of coronary artery disease in non-diabetic and type 2 diabetic patients. Chin Med J (Engl). Jan 2011;124(1):66-71. PMID 21362310*
28. *Ardissino D, Berzuini C, Merlini PA, et al. Influence of 9p21.3 genetic variants on clinical and angiographic outcomes in early-onset myocardial infarction. J Am Coll Cardiol. Jul 19 2011;58(4):426-434. PMID 21757122*
29. *Szpakowicz A, Kiliszek M, Pepinski W, et al. Polymorphism of 9p21.3 locus is associated with 5-year survival in high-risk patients with myocardial infarction. PLoS One. 2014;9(8):e104635. PMID 25105296*

30. *Anderson CD, Biffi A, Rost NS, et al. Chromosome 9p21 in ischemic stroke: population structure and meta-analysis. Stroke. Jun 2010;41(6):1123-1131. PMID 20395606*
31. *Traylor M, Farrall M, Holliday EG, et al. Genetic risk factors for ischaemic stroke and its subtypes (the METASTROKE collaboration): a meta-analysis of genome-wide association studies. Lancet Neurol. Nov 2012;11(11):951-962. PMID 23041239*
32. *Dichgans M, Malik R, Konig IR, et al. Shared genetic susceptibility to ischemic stroke and coronary artery disease: a genome-wide analysis of common variants. Stroke. Jan 2014;45(1):24-36. PMID 24262325*
33. *Ni X, Zhang J. Association between 9p21 genomic markers and ischemic stroke risk: evidence based on 21 studies. PLoS One. 2014;9(3):e90255. PMID 24625579*
34. *Chou SH, Shulman JM, Keenan BT, et al. Genetic susceptibility for ischemic infarction and arteriolosclerosis based on neuropathologic evaluations. Cerebrovasc Dis. 2013;36(3):181-188. PMID 24135527*
35. *Olsson S, Jood K, Blomstrand C, et al. Genetic variation on chromosome 9p21 shows association with the ischaemic stroke subtype large-vessel disease in a Swedish sample aged </= 70. Eur J Neurol. Feb 2011;18(2):365-367. PMID 20500804*
36. *Yue X, Tian L, Fan X, et al. Chromosome 9p21.3 Variants Are Associated with Cerebral Infarction in Chinese Population. J Mol Neurosci. Feb 11 2015. PMID 25665551*
37. *Alg VS, Sofat R, Houlden H, et al. Genetic risk factors for intracranial aneurysms: a meta-analysis in more than 116,000 individuals. Neurology. Jun 4 2013;80(23):2154-2165. PMID 23733552*
38. *Thompson AR, Golledge J, Cooper JA, et al. Sequence variant on 9p21 is associated with the presence of abdominal aortic aneurysm disease but does not have an impact on aneurysmal expansion. Eur J Hum Genet. Mar 2009;17(3):391-394. PMID 18854858*
39. *Helgadottir A, Thorleifsson G, Magnusson KP, et al. The same sequence variant on 9p21 associates with myocardial infarction, abdominal aortic aneurysm and intracranial aneurysm. Nat Genet. Feb 2008;40(2):217224. PMID 18176561*
40. *Bown MJ, Braund PS, Thompson J, et al. Association between the coronary artery disease risk locus on chromosome 9p21.3 and abdominal aortic aneurysm. Circ Cardiovasc Genet. Oct 2008;1(1):39-42. PMID 20031540*
41. *Biros E, Cooper M, Palmer LJ, et al. Association of an allele on chromosome 9 and abdominal aortic aneurysm. Atherosclerosis. Oct 2010;212(2):539-542. PMID 20605023*
42. *Wei Y, Xiong J, Zuo S, et al. Association of polymorphisms on chromosome 9p21.3 region with increased susceptibility of abdominal aortic aneurysm in a Chinese Han population. J Vasc Surg. Dec 20 2013. PMID 24365123*
43. *Lederle FA, Johnson GR, Wilson SE, et al. The aneurysm detection and management study screening program: validation cohort and final results. Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. Arch Intern Med. May 22 2000;160(10):1425-1430. PMID 10826454*

44. *Wei Y, Xiong J, Zuo S, et al. Association of polymorphisms on chromosome 9p21.3 region with increased susceptibility of abdominal aortic aneurysm in a Chinese Han population. J Vasc Surg. Apr 2014;59(4):879-885. PMID 24365123*
45. *Murabito JM, White CC, Kavousi M, et al. Association between chromosome 9p21 variants and the ankle-brachial index identified by a meta-analysis of 21 genome-wide association studies. Circ Cardiovasc Genet. Feb 1 2012;5(1):100-112. PMID 22199011*
46. *O'Donnell CJ, Kavousi M, Smith AV, et al. Genome-wide association study for coronary artery calcification with follow-up in myocardial infarction. Circulation. Dec 20 2011;124(25):2855-2864. PMID 22144573*
47. *van Setten J, Isgum I, Smolonska J, et al. Genome-wide association study of coronary and aortic calcification implicates risk loci for coronary artery disease and myocardial infarction. Atherosclerosis. Jun 2013;228(2):400405. PMID 23561647*
48. *Zhang X, Wen F, Zuo C, et al. Association of genetic variation on chromosome 9p21 with polypoidal choroidal vasculopathy and neovascular age-related macular degeneration. Invest Ophthalmol Vis Sci. Oct 2011;52(11):8063-8067. PMID 21896860*
49. *Cesana F, Nava S, Menni C, et al. Does the 9p region affect arterial stiffness? Results from a cohort of hypertensive individuals. Blood Press. Oct 2013;22(5):302-306. PMID 23445356*
50. *Sturiale CL, Fontanella MM, Gatto I, et al. Association between polymorphisms rs1333040 and rs7865618 of chromosome 9p21 and sporadic brain arteriovenous malformations. Cerebrovasc Dis. 2014;37(4):290-295. PMID 24820060*
51. *Bendjilali N, Nelson J, Weinsheimer S, et al. Common variants on 9p21.3 are associated with brain arteriovenous malformations with accompanying arterial aneurysms. J Neurol Neurosurg Psychiatry. Nov 2014;85(11):1280-1283. PMID 24777168*
52. *Folsom AR, Pankow JS, Li X, et al. No association of 9p21 with arterial elasticity and retinal microvascular findings. Atherosclerosis. Oct 2013;230(2):301-303. PMID 24075760*
53. *Paynter NP, Chasman DI, Buring JE, et al. Cardiovascular disease risk prediction with and without knowledge of genetic variation at chromosome 9p21.3. Ann Intern Med. Jan 20 2009;150(2):65-72. PMID 19153409*
54. *Talmud PJ, Cooper JA, Palmen J, et al. Chromosome 9p21.3 coronary heart disease locus genotype and prospective risk of CHD in healthy middle-aged men. Clin Chem. Mar 2008;54(3):467-474. PMID 18250146*
55. *Brautbar A, Ballantyne CM, Lawson K, et al. Impact of adding a single allele in the 9p21 locus to traditional risk factors on reclassification of coronary heart disease risk and implications for lipid-modifying therapy in the Atherosclerosis Risk in Communities study. Circ Cardiovasc Genet. Jun 2009;2(3):279-285. PMID 20031596*
56. *Sposito AC, Ramires JA, Jukema JW, et al. Physicians' attitudes and adherence to use of risk scores for primary prevention of cardiovascular disease: cross-sectional survey in three world regions. Curr Med Res Opin. May 2009;25(5):1171-1178. PMID 19323611*

57. *Sheridan SL, Crespo E. Does the routine use of global coronary heart disease risk scores translate into clinical benefits or harms? A systematic review of the literature. BMC Health Serv Res. 2008;8:60. PMID 18366711*
58. *Do R, Xie C, Zhang X, et al. The effect of chromosome 9p21 variants on cardiovascular disease may be modified by dietary intake: evidence from a case/control and a prospective study. PLoS Med. Oct 2011;8(10):e1001106. PMID 22022235*
59. *Gransbo K, Almgren P, Sjogren M, et al. Chromosome 9p21 genetic variation explains 13% of cardiovascular disease incidence but does not improve risk prediction. J Intern Med. Sep 2013;274(3):233-240. PMID 23480785*
60. *Downing KP, Nead KT, Kojima Y, et al. The combination of 9p21.3 genotype and biomarker profile improves a peripheral artery disease risk prediction model. Vasc Med. Feb 2014;19(1):3-8. PMID 24323119*
61. *Goff DC, Jr., Lloyd-Jones DM, Bennett G, 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. J Am Coll Cardiol. Jul 1 2014;63(25 Pt B):2935-2959. PMID 24239921*
62. *Recommendations from the EGAPP Working Group: genomic profiling to assess cardiovascular risk to improve cardiovascular health. Genet Med. Dec 2010;12(12):839-843. PMID 21042222*
63. *Samani NJ, Schunkert H. Chromosome 9p21 and cardiovascular disease: the story unfolds. Circ Cardiovasc Genet. 2008;1(2):81-84. doi:10.1161/CIRCGENETICS.108.832527*
64. *Patel RS, Asselbergs FW, Quyyumi AA, Palmer TM, Finan CI, Tragante V, Deanfield J, Hemingway H, Hingorani AD, Holmes MV. Genetic variants at chromosome 9p21 and risk of first versus subsequent coronary heart disease events: a systematic review and meta-analysis. J Am Coll Cardiol. 2014 Jun 3;63(21):2234-45. doi: 10.1016/j.jacc.2014.01.065. Epub 2014 Mar 7. PMID: 24607648; PMCID: PMC4035794.*
65. *Almontashiri NAM. The 9p21.3 risk locus for coronary artery disease: A 10-year search for its mechanism. J Taibah Univ Med Sci. 2017 Apr 25;12(3):199-204. PMID: 31435240*
66. *Wilson, P. Overview of possible risk factors for cardiovascular disease. In: UpToDate Online Journal [serial online]. Waltham, MA: UpToDate; updated November 21, 2024. Literature review current through November 2024.*

## IX. POLICY HISTORY

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| | **03/09/2020 Consensus Review.** No changes to policy statement. References updated. Variations updated. Coding verified. |
| | **02/11/2021 Consensus Review.** Policy statement unchanged. Referenced updated. Cross referenced policy removed as retired. FEP variation updated. |
| | **01/21/2022 Consensus Review.** FEP, background, and references updated. |

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| | **12/08/2023 Consensus Review.** No changes to coding. |
| | **12/11/2024 Consensus Review.** Created policy guidelines. Updated background, rationale, and references. No changes to coding. |
| | **08/13/2025 Consensus Review.** Policy statement unchanged. |
| | **03/09/2026 Retirement Review.** EviCore Delegation. |

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