Poster Code: MSR49

Defining Atherosclerotic Cardiovascular Disease (ASCVD) in Real-World Research: An Analysis of Conceptual and Operational Definition Variability

Jared Kamauu BFA,[1] Michael Buck PhD,[1] Craig Parker MD MS,[1] Allise Kamauu MS,[1] Aimee Harrison MFA,[1] Scott L. DuVall PhD,[2] Aaron Kamauu MD MS MPH[1]

[1]Navidence Inc., USA; [2]PurpleLab Inc., USA

So What?

There is significant variation in definitions of ASCVD and therefore understanding the variance is important to consistent interpretation of results in RWR.

BACKGROUND

Context

In real-world research (RWR), complex clinical concepts, composed of multiple composite conditions, are often used to define cohort phenotypes. Meaningful results depend on consistent conceptual and computable operational definitions (CODefs).

The Gap / Problem

Variance in CODefs and code lists used in published studies may exist for some clinical concepts. Follow-on work (*see companion poster **PT7***) looks at the impact of these differences in definitions on cohorts in RWD.

PRIMARY OBJECTIVE

To describe variations in CODefs from reputable sources and RWR publications on patients with Atherosclerotic Cardiovascular Disease (ASCVD).

Computable Operational Definitions (CODefs™)

Study elements — exposures, outcomes, and covariates — were defined using Navidence CODefs™: rigorous, data source-agnostic algorithms that ensure precision and reproducibility across RWR.

REFERENCES

1. American Heart Association. Atherosclerotic Cardiovascular Disease (ASCVD). Available at: https://www.heart.org/en/professional/quality-improvement/ascvd.
2. National Heart, Lung, and Blood Institute. What Is Atherosclerosis? Available at: https://www.nhlbi.nih.gov/health/atherosclerosis.
3. Grundy SM, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019 Jun 18;139(25):e1082-e1143
4. National Research Council (US) Committee on Diet and Health. Diet and Health: Implications for Reducing Chronic Disease Risk. Washington (DC): National Academies Press (US); 1989. 19, Atherosclerotic Cardiovascular Diseases.
5. Institute for Clinical and Economic Review (ICER). A Look at Atherosclerotic Cardiovascular Disease (ASCVD). Available at: https://icer.org/wp-content/uploads/2020/10/ASCVD_RAAG_030221.pdf.
6. Mackinnon ES, et al. Increasing Prevalence and Incidence of Atherosclerotic Cardiovascular Disease in Adult Patients in Ontario, Canada From 2002 to 2018. CJC Open. 2021 Oct 20;4(2):206-213. doi: 10.1016/j.cjco.2021.10.003
7. Dai D, et al. Multimorbidity in Atherosclerotic Cardiovascular Disease and Its Associations With Adverse Cardiovascular Events and Healthcare Costs: A Real-World Evidence Study. J Health Econ Outcomes Res. 2024 Mar 22;11(1):75-85. doi: 10.36469/001c.94710.
8. Sajja A, et al. A simplified approach to identification of risk status in patients with atherosclerotic cardiovascular disease. Am J Prev Cardiol. 2021 Apr 27;7:100187. doi: 10.1016/j.ajpc.2021.100187.
9. Barrios V, et al. Treatment patterns and use of healthcare resources of patients with atherosclerotic cardiovascular disease and hypercholesterolemia and patients with familial hypercholesterolemia in Spain: Protocol of the Reality study. Front Cardiovasc Med. 2022 Aug 4;9:966049. doi: 10.3389/fcvm.2022.966049.
10. Mackinnon ES, et al. Real-World Risk of Recurrent Cardiovascular Events in Atherosclerotic Cardiovascular Disease Patients with LDL-C Above Guideline-Recommended Threshold: A Retrospective Observational Study. Cardiol Ther. 2024 Mar;13(1):205-220. doi: 10.1007/s40119-024-00349-6. Epub 2024 Jan 29.
11. Dunn TJ, et al. Comparing demographic/clinical characteristics, health care resource utilization, and costs among patients with type 2 diabetes and established atherosclerotic cardiovascular disease with and without the use of cardioprotective medications. J Manag Care Spec Pharm. 2025 Feb 1;31(2):117-126. doi: 10.18553/jmcp.2025.24251. Epub 2025 Jan 17.

METHODS

Study Design & Data Source

We reviewed literature and clinical references (e.g., American Heart Association) to identify clinical definitions of ASCVD. We extracted and analyzed multiple medical conditions used in ASCVD definitions, including peripheral artery disease (PAD) and myocardial infarction (MI). Our analysis included assessment of combinations of these conditions. When available, code lists were also compared.

Figure 1: Reference Selection

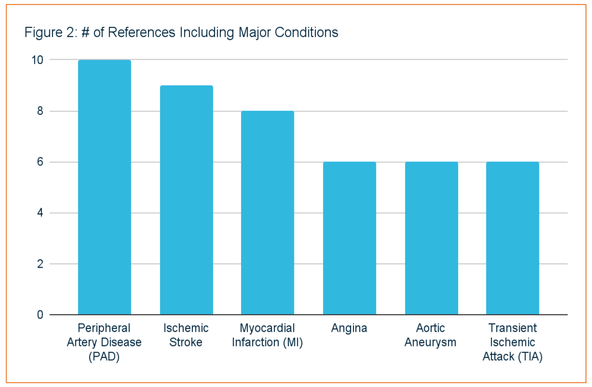
10 Total References Reviewed	**5 References Analyzed** with Published CODefs and Code Lists
20 Medical Conditions	13 Medical Conditions
9 Different ASCVD Definitions from these Conditions	10 Conditions with Moderate-Severe Variations

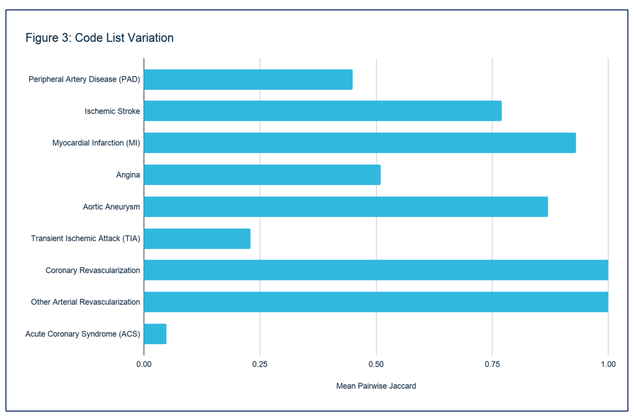
Study Population

11 references were analyzed including 6 of the references that published detailed CODefs with code lists.

RESULTS

- From the 10 references analyzed, there were 20 different medical conditions identified as part of an ASCVD definition, representing 10 different combinations.
- Figure 2 shows the 6 most common medical conditions identified and the number of references they were found in.
  - PAD was the most common medical conditions being included in 10/10 references.
  - Renal Artery Stenosis, Vertebral Artery Disease, Mesenteric Artery Ischemia, Chronic Kidney disease (CKD) were the least common medical conditions being included in 1/10 references.





- The 5 references that published detailed CODefs had code lists for 13 conditions.
  - 5 conditions showed significant code list variation (min. pairwise Jaccard < 0.4).
  - 3 showed minimal variation (min. pairwise Jaccard > 0.8).
  - The remainder showed moderate variation.
- Figure 3 shows the variation in mean pairwise Jaccard value for 9 of the conditions across the references.
- The conditions not shown in Figure 3 only had codes published from 1 reference.
- The variation shown in the published code lists shows a clear potential for cohort impact based on what ASCVD definition is used.

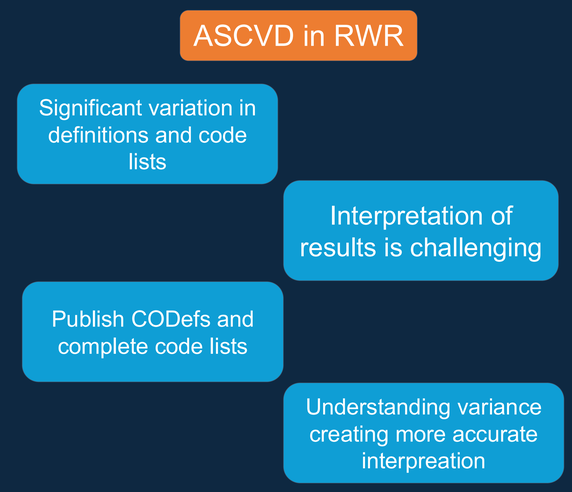
CONCLUSIONS

Key Findings

- ASCVD is a common concept studied in RWR. However, the variance in conceptual and operational definitions introduces challenges for consistent interpretation and extrapolation of results.
- Understanding the variance is essential in RWR as “small difference in the choice of operational definition … may have a large impact on study results.” [FDA 2023]

Clinical & Policy Implications

Going forward it is recommended that researchers publish specific and complete CODefs and code lists for definitions of ASCVD so that clinical interpretation can be more accurate.



DISCLOSURES & ACKNOWLEDGMENTS

A Kamauu, J Kamauu, M Buck & C Parker: Employees of Navidence Inc. A Kamauu, C Parker: Co-Founders of Navidence Inc. G Galustjan & K Kallmes: Employees of Nested Knowledge. K Kallmes: Co-Founder of Nested Knowledge.
No conflicts of interest to disclose.