

Precision Tools for Cardiovascular Prevention

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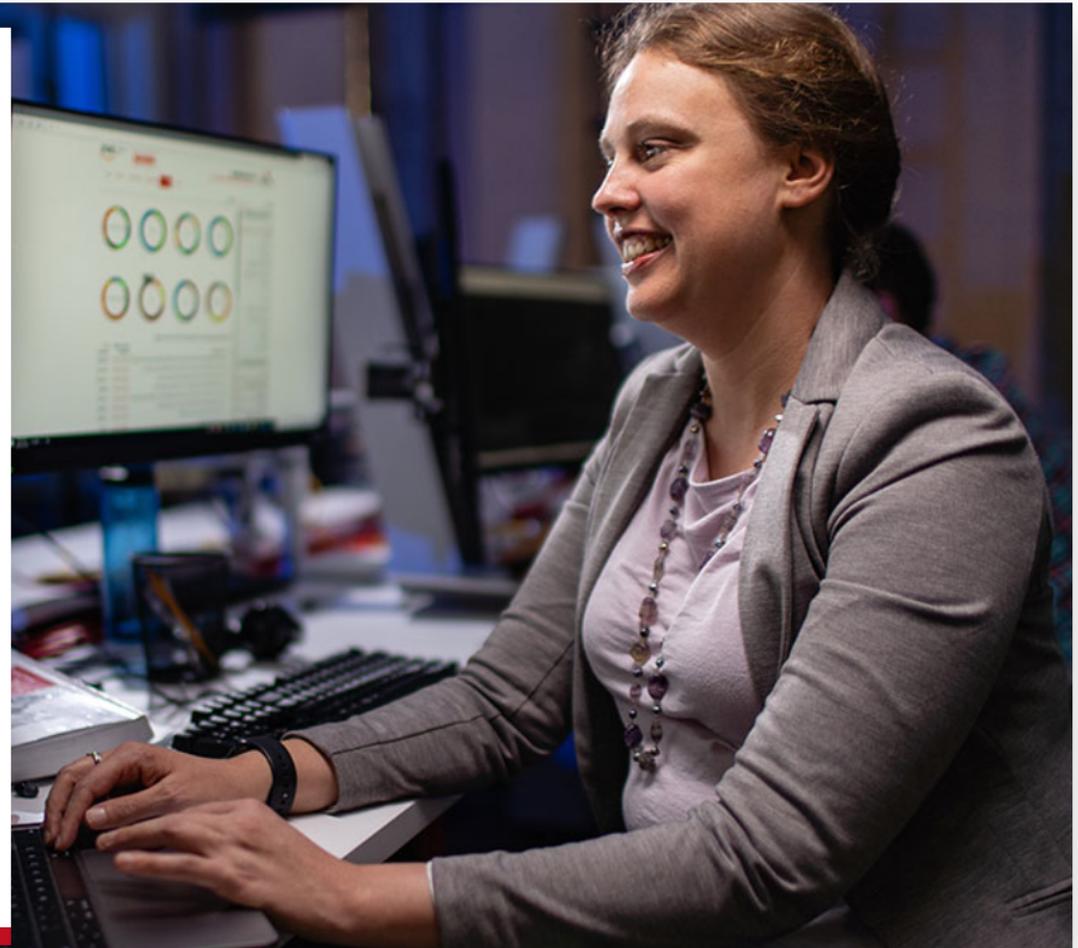


Precision Tools – Bridging the Gap between Science and Implementation

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Institute for Precision Cardiovascular Medicine

The AHA Institute for Precision Cardiovascular Medicine created a new model for bringing together science and technology to drive breakthroughs in cardiovascular and brain health and disease.



Precision Tools for Cardiovascular Prevention

- "In order to prevent heart attack or stroke, we really need to understand how atherosclerosis develops and how it evolves over time."
- "Looking beyond conventional factors is essential for accurate stroke and (heart attack)prevention, especially given that stroke (and heart attacks) are preventable, and its first sign may be fatal"

How Atherosclerosis Develops and How it Evolves?

- **Case 1:** 19 yo M presents to the Lipid Clinic at UCSF for evaluation after discharge for acute stroke.
- Conventional work up was unrevealing
- Lipoprotein (a) elevated to >600 nmol/L
- **Case 2:** 12 yo M presents to the Lipid Clinic at UCSF for evaluation after twin brother died of acute MI
- Cutaneous xanthomata extensor surfaces of his arms, knees, elbows, and Achilles tendon since age 1
- Total Chol > 1000



Precision in Early Detection and Prediction of Cardiovascular Risk

- **General neonatal Lp (a) screening** - detect families at risk of vascular accidents or prevent the early onset of thromboembolism? – Further studies are needed
- **What we do know:**
- Lipoprotein(a) (Lp(a)) is a highly atherogenic and heterogeneous lipoprotein that is inherited in an autosomal codominant trait.
- In the first months of life Lp(a) levels increase 2-fold compared with at birth, reaching full genetic expression in the first year of life
- Thereafter, Lp(a) levels show only very minor changes during life, i.e. levels in adulthood are similar to those in childhood
- Lp(a) levels in youth are fully expressed by the first or second year of life.
- Lp(a) is associated with an increased risk of arterial ischemic stroke in youth.

E. Kurvinen, K. Aasvee, R. Zordania, M. Jauhiainen & J. Sundvall (2005) Serum lipid and apolipoprotein profiles in newborns and six-year-old children: The Tallinn Young Family Study, Scandinavian Journal of Clinical and Laboratory Investigation, 65:7, 541-550, DOI: [10.1080/0365510500208324](https://doi.org/10.1080/0365510500208324)

Table 2. Comparison of Society Guidelines for Identification of Familial Hypercholesterolemia

NLA (2011) ⁷	AHA/ACC (2018) ^{11*†}	ESC (2019) ^{12†}
Universal screening for elevated serum cholesterol in all patients	Patients with primary elevation of LDL-C \geq 190mg/dL should be started on high-intensity statin therapy	Consider FH in patients with the following features:
Suspect FH in adults with LDL-C \geq 190mg/dL	Starting in childhood, FH should be detected and treated	CHD aged <55 (men) and <60 (women)
Suspect FH in children/young adults with LDL-C \geq 160mg/dL	<ul style="list-style-type: none">If early CVD or hypercholesterolemia by family history, it is reasonable to screen with a lipid profile at age 2 (Ia recommendation)	Relatives with premature fatal or non-fatal ASCVD
Suspect FH in patients with non-HDL cholesterol \geq 190mg/dL	<ul style="list-style-type: none">It is reasonable to screen patients aged 9-11 and again between 17-21 without history of early CVD with lipid profile or fasting non-HDL-C (IIb recommendation)	People with relatives who have tendon xanthomas
In all patients with LDL-C greater than these thresholds, a family history of age of onset of CHD should be taken		Adults with LDL-C \geq 190mg/dL
Screen children at age 2 with family history of premature CHD with lipid panel		Children with LDL-C \geq 150mg/dL
		First-degree relatives of FH patients

Atherogenic Lipoproteins in Early Development of Atherosclerotic Disease and Progression

- **Every 10 mg/dl (0.25 mmol/L) increment in non-HDL-Cholesterol is associated with an increase in atherosclerotic burden equivalent to 1 year of aging**
- **Elevated circulating markers of vascular inflammation and endothelial dysfunction are present in children with FH, reflecting early atherogenesis.**

Markers of atherosclerotic development in children with familial hypercholesterolemia: *Narverud I, Retterstøl K, Iversen et al Atherosclerosis. 2014 Aug; 235(2):299-309.*

Early Development of Atherosclerotic Disease and Progression

- **Higher carotid IMT** in phenotypic FH patients (from age 10 years) than normolipidemic controls; directly relates to LDL-C levels
- **Coronary calcification** is present in ~25% of 11–23 yo with phenotypic HeFH, and in the aorta in most adolescents with HoFH
- In contrast, CAC is barely detectable in atherosclerotic lesions in adolescents in the general population

Machine Learning and Statistical Approaches for Classification of Risk of Coronary Artery Disease using Plasma Cytokines.

- Use of ML algorithm is gaining momentum
 - Availability of high computational power and
 - Outstanding prediction accuracy
- Significant improvement of current qualitative assessment of images and crude quantitative measures of cardiac structure and function.
- ML algorithms can build a holistic framework using many informative features (images, biomarkers, genetics, etc) to obtain credible insights and early detection which will result in saving lives.

Machine Learning and Statistical Approaches for Classification of Risk of Coronary Artery Disease using Plasma Cytokines. Seema Singh Saharan, Pankaj Nagar, Kate Townsend Creasy, Eveline O. Stock, James Feng, Mary J. Malloy, John P. Kane. Biodata Mining 2021 (in press)

Machine Learning and Statistical Approaches for Classification of Risk of Coronary Artery Disease using Plasma Cytokines

- Classification 35 cytokines in plasma samples

Table 1: Clinical Demographic Profile. A collection of plasma samples from patients with diagnosed coronary artery disease (CAD) and healthy controls.

Gender	CAD (n=39)	Control (n=65)	Total (n=104)
Male	19	26	45(43.27%)
Female	20	39	59(56.73%)
Total	39(37.5%)	65(62.5%)	104

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Machine Learning and Statistical Approaches for Classification of Risk of Coronary Artery Disease using Plasma Cytokines.

- AUROC value of .95, representing the extent of separation of CAD vs Control was remarkable.
- Example of how Machine Learning techniques can be harnessed to predict patients at high risk for CAD

Algorithm	Classification Criterion	Predictor Feature Space	AUROC with 95% Confidence Interval	Prediction Accuracy	Sensitivity	Specificity
k-NN	Distance Measure: Euclidean with k=9	35 Cytokines	0.954 (.929, .979)	0.832	0.992	0.658

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