C-K-M Health: Patient Risk Assessment & Health Equity

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OHIO PHARMACISTS ASSOCIATION

1 VOICE VISION TEAM

Disclosure Statement

- Maria Coyle has no relevant financial relationship(s) with ineligible companies to disclose.

  and

- None of the planners for this activity have relevant financial relationships with ineligible companies to disclose.

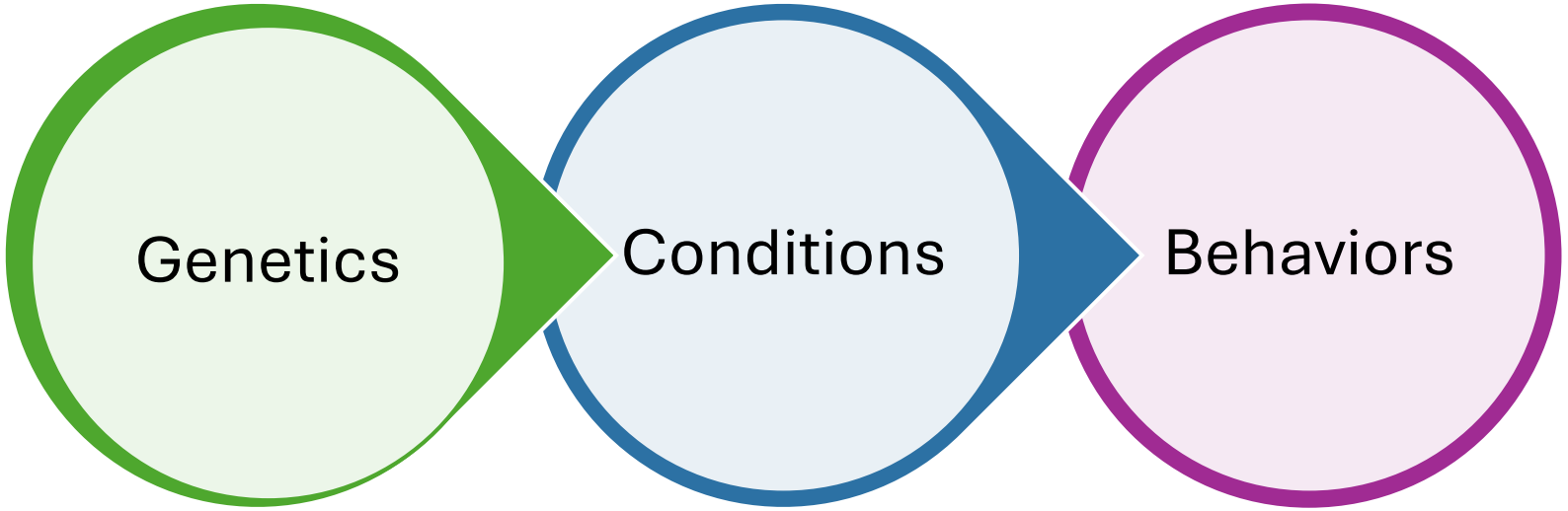
Learning Objectives

At the completion of this activity, the participant will be able to:

1. Define cardiovascular-kidney-metabolic (CKM) syndrome according to the 2023 American Heart Association (AHA) Scientific Statement, including key goals for the novel framework.
2. Summarize recent and developing updates for risk estimation equations commonly used in clinical practice, particularly sex-specific, race-free equations for estimating kidney function and the PREVENT™ equations for total cardiovascular disease (CVD) risk.
3. Describe nontraditional factors that may enhance predictive usefulness of CVD risk assessment tools in the future.
4. Demonstrate how the CKM model could include social determinants of health to improve health equity and benefit minority populations.
5. Discuss clinical implementation, risk communication, and education strategies that will facilitate future adoption of the CKM prevention model in various practice settings.

CVD in the United States

- Leading cause of death (since 1920)[1]
  - Men, women, and people of most racial and ethnic groups



1.National Center for Health Statistics. Multiple Cause of Death 2018–2021 on CDC WONDER Database. Accessed February 2, 2023.

CVD Burden – Projections

Prevalence of CVD [in millions of patients (%)]		
	2015	**2035**
All with CVD	102.7 (41.5%)	131.2 (45%)
High blood pressure	96.1	123.2
Coronary heart disease	16.8	24.0
Stroke	7.5	11.2
Congestive heart failure	5.8	8.8
Atrial fibrillation	5.2	7.2
Total Costs*	More than $550 billion	Estimated $1.1 trillion

*Includes medical costs (up ~135%) and indirect costs/lost productivity (up ~ 55%)

AHA 2017; website: heart.org. Accessed February 7, 2024. Available at: https://www.heart.org/-/media/Files/Get-Involved/Advocacy/Burden-Report-Consumer-Report.pd

CVD Mortality and Health Disparity

- Ganatra et al (2022)
- Age-adjusted mortality rate (AAMR) = 386.01 (95% CI: 385.73, 386.29)
  - AAMR reflective of incidence, treatments, and cardiometabolic outcomes
  - Varied by social vulnerability
    - Social Vulnerability Index (SVI) - dataset of CDC: Agency for Toxic Substances and Disease Registry)

Ganatra et al. JACC: CardioOncol. 2022 Sep 23;4:326-37.

Health Disparities in CVD

- Ganatra et al (2022)

Social Vulnerability Index (SVI)	
Themes	**Individual Factors**
Socioeconomic status	Below poverty level, unemployed, income level, no high school diploma
Household composition and disability	Age ≥ 65 years, age ≤ 17 years, individuals > 5 years with disability, single-parent households
Minority status and language	Minority, individual speaks English “less than well”
Housing type and transportation	Multi-unit structure, mobile home, crowding, group quarters, no vehicle
Scores sorted by percentile ranks: 0.00-1.00, with higher values equating to greater vulnerability • Rank of 0.00-0.25 is most favorable; rank of 0.75-1.00 is least favorable	

Ganatra et al. JACC: CardioOncol. 2022 Sep 23;4:326-37.

Age-Adjusted CVD Mortality

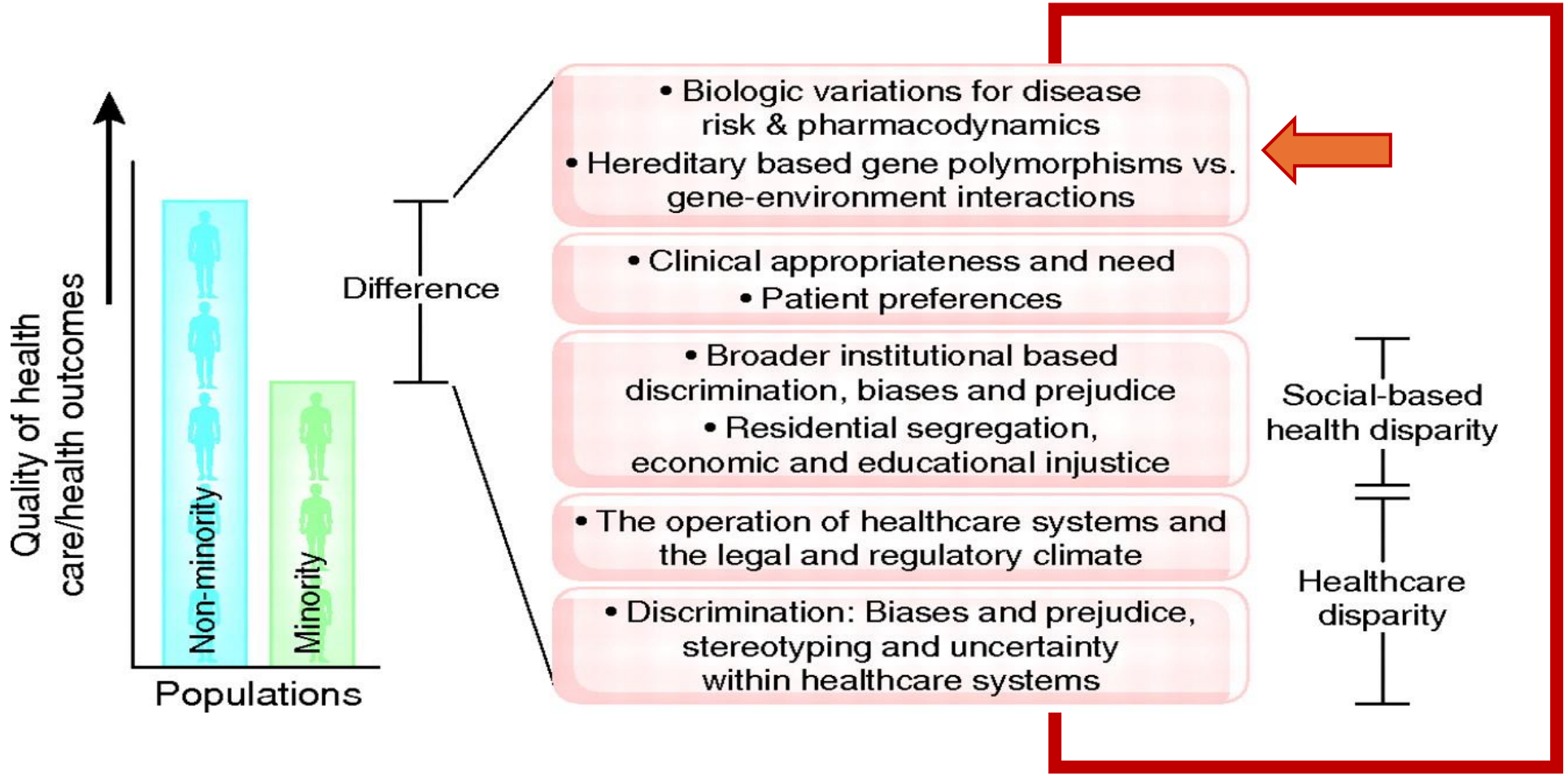
- Overall, CVD mortality was highest in adults > 45 years, men, Black individuals, and in rural counties

- CVD mortality was lowest in the 1st quartile, highest in the 4th quartile by Social Vulnerability Index (SVI)
  - 98.88 *excess* deaths per 100,000 person years
  - [344.25 (95% CI: 343.63-344.86) vs. 443.13 (95% CI: 442.49-443.77)

- Social vulnerability impact greatest in adults <45 years of age, men, Asian/ Pacific Islanders, American Indian or Alaska natives, Hispanics, and in rural counties

Ganatra et al. JACC: CardioOncol. 2022 Sep 23;4:326-37.

Differences & Disparities (Kidney Disease)



Norris and Nissenson. J Am Society Nephrol 2008;19:1261-70

Promoting Health Equity

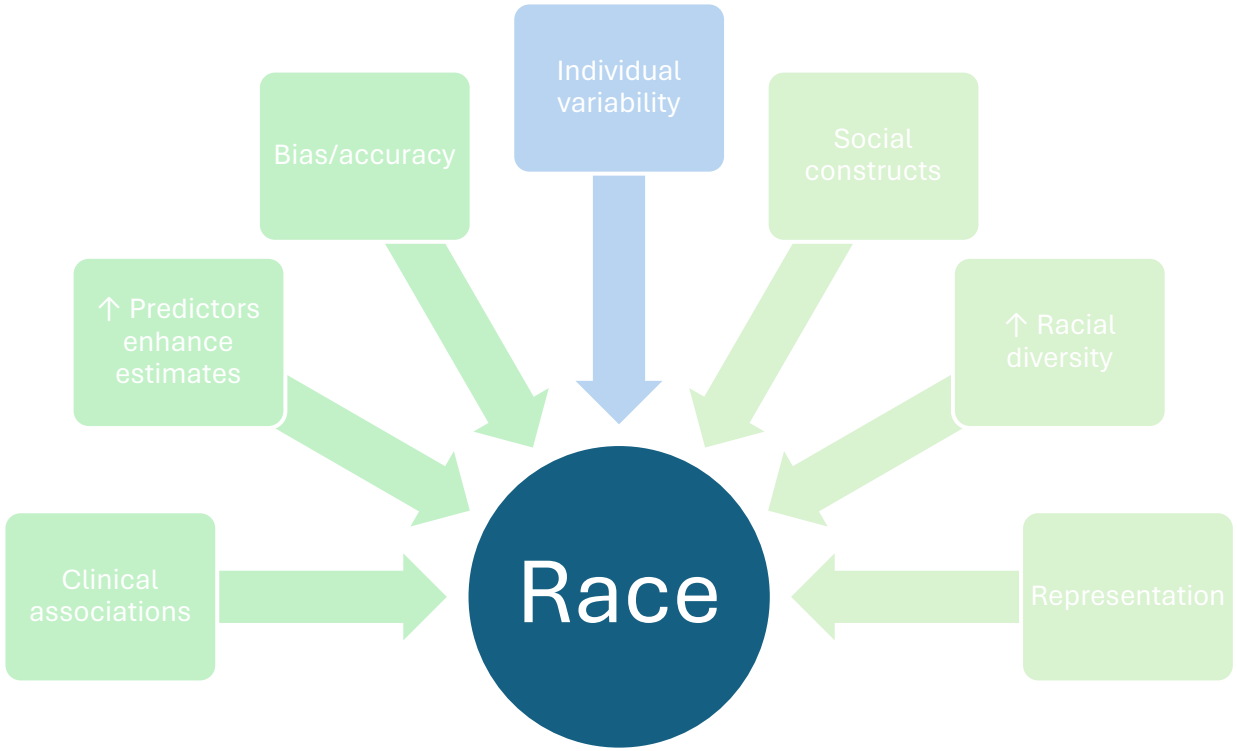
"It is much more important to know what sort of a patient has a disease, than what sort of disease a patient has."

William Osler (1849-1919)

Tan and Uyehara. Singapore Med J 2009;50(11):1048

Spotlight on Race

Considerations/Criticisms



Background (Sep 2020)

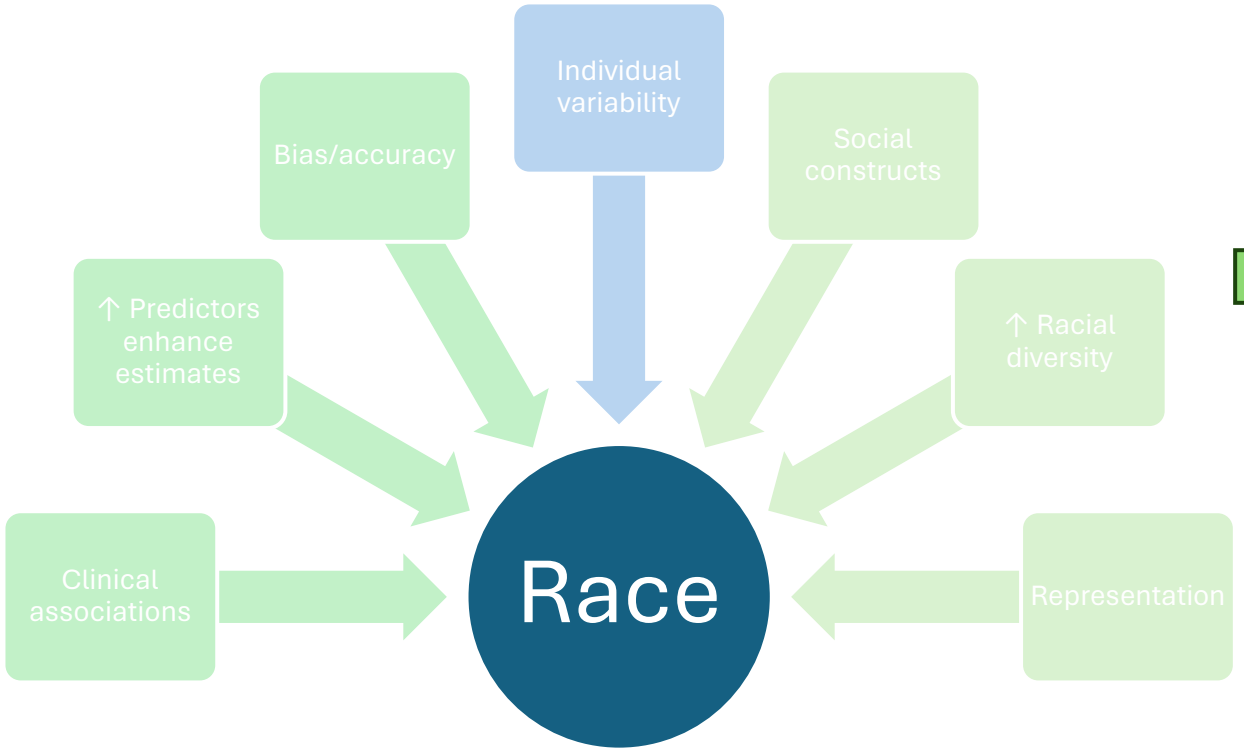
- National call to re-evaluate use of race in clinical algorithms
  - Letter of US Senators Warren, Wyden, Booker & Lee to AHQR
- Coincided with introduction of bill *Anti-Racism in Public Health Act* (Senator Warren, D-Mass)

↓

- ***Beliefs can influence clinical care***

Spotlight on Race

Considerations/Criticisms



Rx Applications:

- eGFR:MDRD Equation (1999; revised 2006)
  → **CKD-EPI 2021 Equation**
- ASCVD Risk: Pooled Cohort Equations (2013)
  → **PREVENT™ Equations?**

Removing Race from eGFR

Estimating GFR - Impact

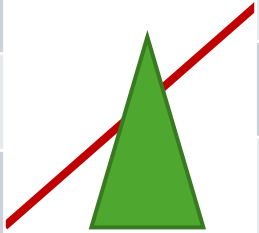
mGFR*	eGFR w/ CKD-EPI 2021		eGFR w/ MDRD	Potential Impact?
80	71		82	Eligible as kidney donor?
63	55		62	Dx for CKD Lower dose of carboplatin/cisplatin Lower dose methotrexate or ganciclovir
40	38		43	***Currently***
35	28		33	Exclusion from clinical trials Contraindication for metformin Lower dose for SGLT2 inhibitor
23	18		21	Eligible for kidney transplant

*mGFR=measured GFR; all GFRs expressed as mL/min/1.73m2

Adapted from: Levy et al. CJASN 2020;15(8)1203-12.

Estimating GFR: Impact

Reduced Eligibility for:
Examples
Living kidney donors
Ant-cancer therapies
Medications with renal dosing component



Expanded Eligibility for:
Examples
Referral to a nephrologist
Kidney transplant waitlist
Coverage for kidney disease education

"The kidney medical community will need to monitor the impact of the non-race-based eGFR to ensure continued patient safety and health equity."

Ng J. American Society of Nephrology Kidney News 2022;14(1):22

Removing race from ASCVD Risk Models

“Sentinel” Risk Factors*

Unhealthful nutrition	Physical inactivity	Dyslipidemia	Hyperglycemia
High blood pressure	Obesity (ABCD)	Smoking (thrombosis)	Kidney dysfunction

*Other relevant but non-modifiable risk factors include: older age, race/ethnicity, sex differences, genetics
ABCD = Adiposity-based chronic disease

Bays et al. Am J Prev Cardiol. 2021 Jan 23;5:100149.

2013 Risk Assessment Guideline

ACC/AHE Pooled Cohort Equations (PCE)

- Derived from #5 community-based cohorts, ages 40-79y
  - 11,240 White females and 9098 White males
  - 2641 Black females and 1647 Black males

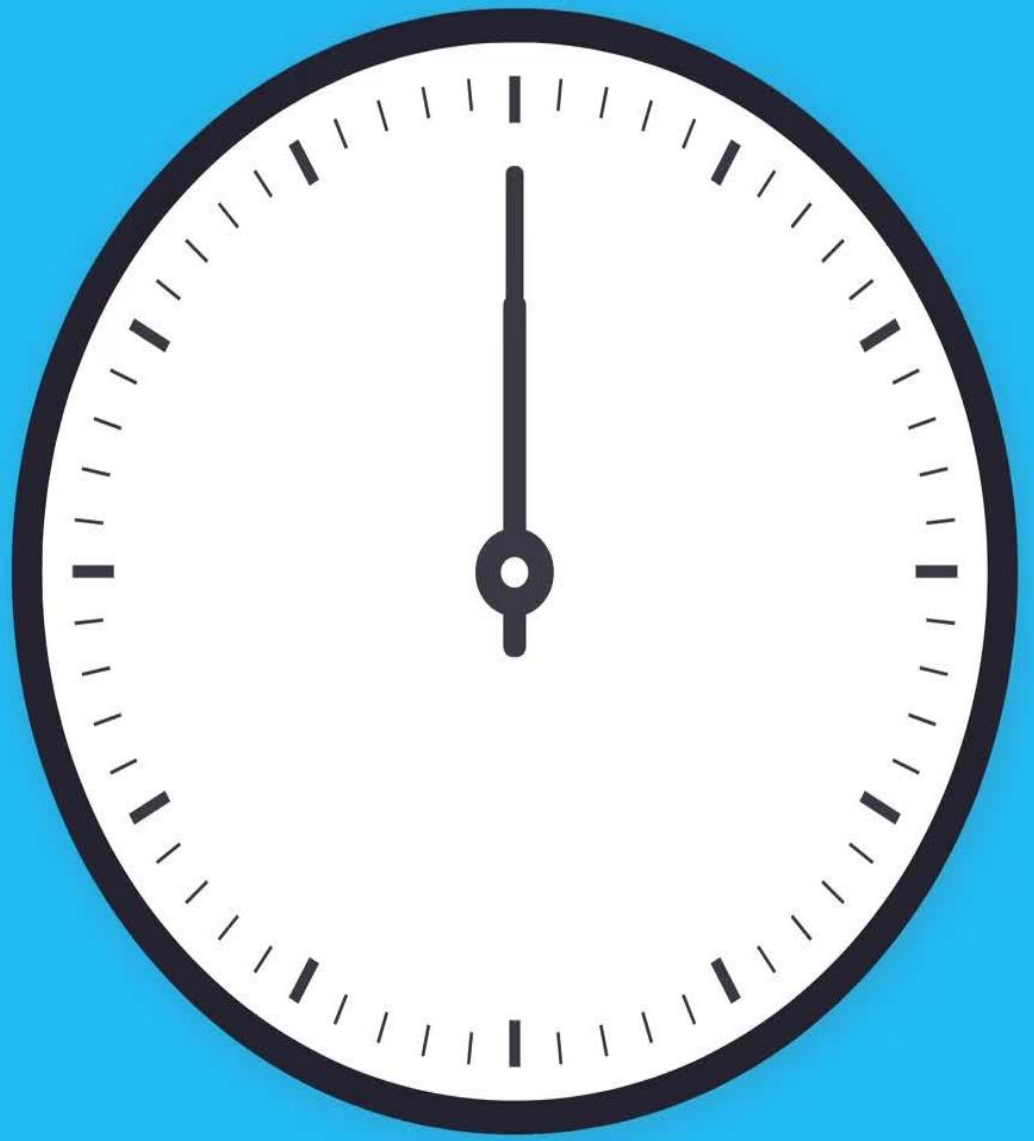
- Changed from Framingham approach (pre-2013)
  1. Outcomes of interest = ASCVD events (beyond CHD; also stroke, PAD)
  2. Inclusion of Black adults in sample → race variable in PCE
  3. Inclusion of diabetes as risk factor (previously "risk equivalent" only)

- PCE approach endorsed in updated guidelines for hypertension (2017), cholesterol (2018), primary prevention CVD (2019), & ADA (2024)

Goff et al. J Am Coll Cardiol 2014; 63:2935-59 .

Time for Change?

- Availability of EMR datasets
- Greater ability to consider risk factors as continuous data
- Importance of health behaviors
  - “Life course” perspective of disease
  - Cardiorespiratory fitness
- Statins/other preventive Rx effects
- Increased awareness of novel risk markers and metabolic/kidney diseases
- Opportunity to broaden CVD outcomes
  - **Address health disparities (race as variable)**
  - Inclusion of CVD subtypes (eg. heart failure)



Khan et al. Circulation 2023; 148:1982-2004

CV-Kidney-Metabolic Model (NEW!)

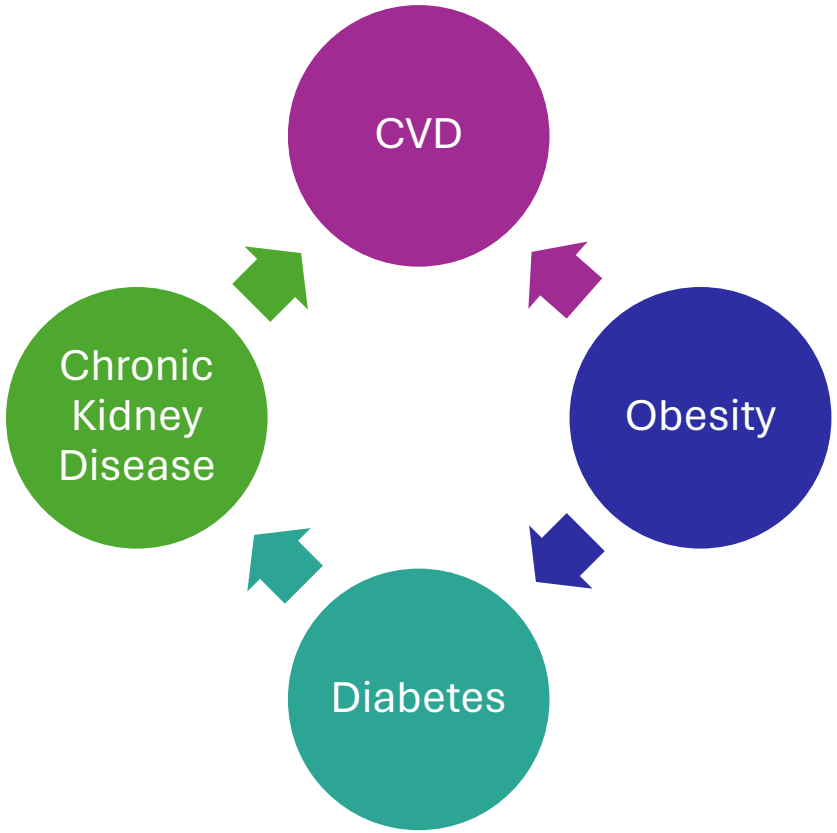
Definition

- CKM Syndrome: where a person has overlapping health problems of heart disease, kidney disease, and metabolic disease(s): obesity and/or diabetes

  - *American Heart Association*

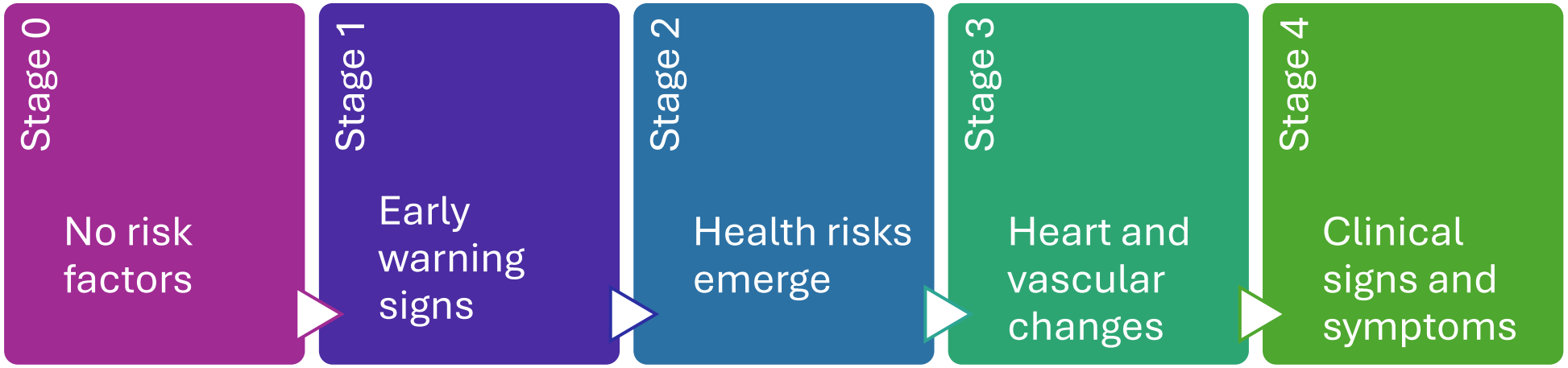
Purpose

- Moving beyond individual risk factors approach → more comprehensive framework



Khan et al. Circulation 2023; 148:1982-2004

CKM Conceptual Framework (2023)



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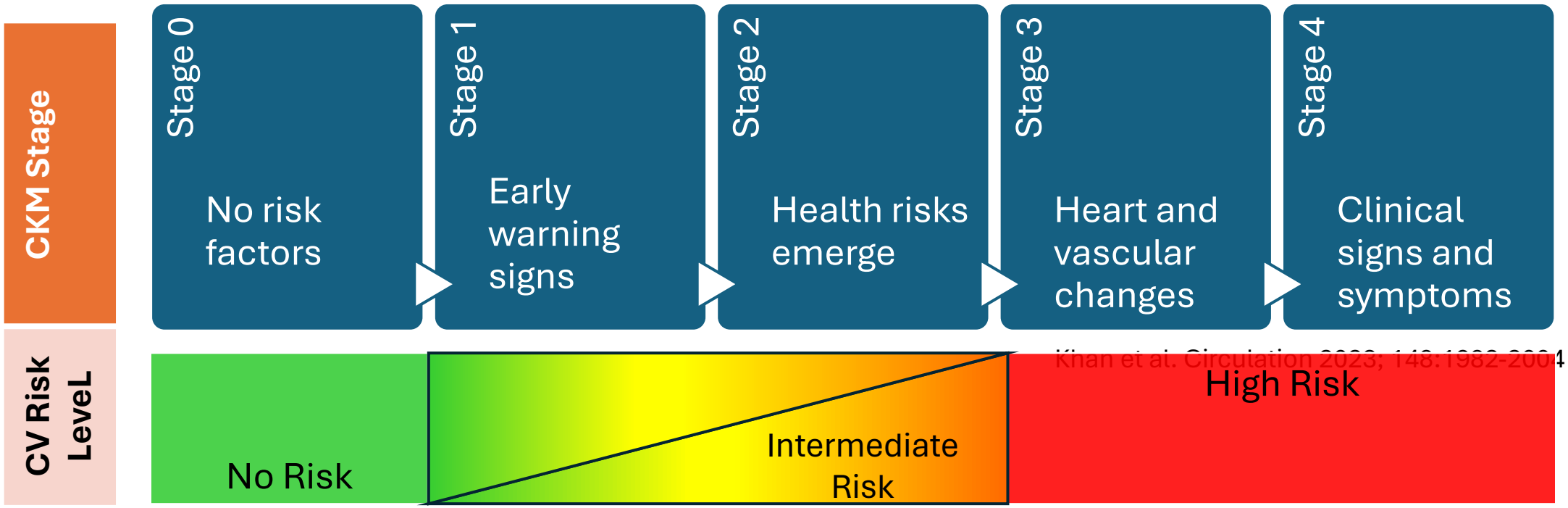
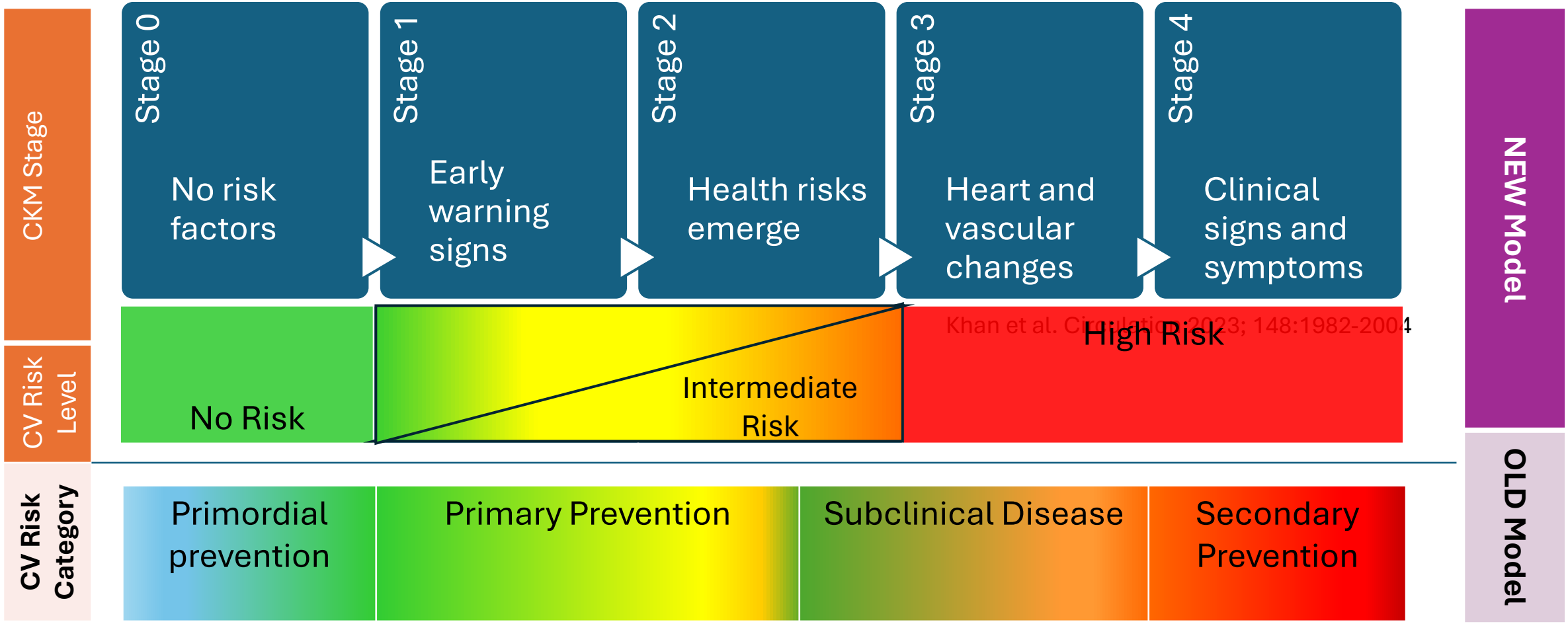


Khan et al. Circulation 2023; 148:1982-2004

Khan et al. Circulation 2023; 148:1982-2004

Compare and Contrast



CKM Risk Assessment Process

Screen - CKM Risk

- Life's Essential 8
- Consider A1c, UACR, etc

Assess - CVD Risk

- 10y/30y AR for CVD, ASCVD, HF → PREVENT
- Personalize and reclassify (as/if needed)

Stage CKM

- Stage 0 → Stage 4
- See previous slide

Reduce CKM Risk

- Promote health
- Prevent progression
- Prioritize regression

Khan et al. Circulation 2023; 148:1982-2004

Life's Essential 8 for CV Health (AHA)

Healthy diet	DASH-style eating pattern
Physical activity	Moderate-vigorous exercise, regularly each week
Avoiding nicotine	Avoid nicotine including nicotine delivery systems, secondhand smoke
Healthy sleep	Age-appropriate hours of sleep per night/per 24 hours
Healthy weight	**A**ppropriate BMI percentile for age and sex (starting in infancy)
Healthy cholesterol	Total and non-HDL (starting at least by 9-11y, and earlier if indicated)
Healthy blood glucose	Fasting BG <100 mg/dL or A1c < 5.7% (starting age 10y)
Healthy blood pressure	Optimal BP for age, using appropriate-size cuff (starting no later than 3y)

Lloyd-Jones et al. Circulation 2022; 146:e18-43

Assessing CVD Risk

PREVENT™ equations for CVD risk estimation (NEW!)

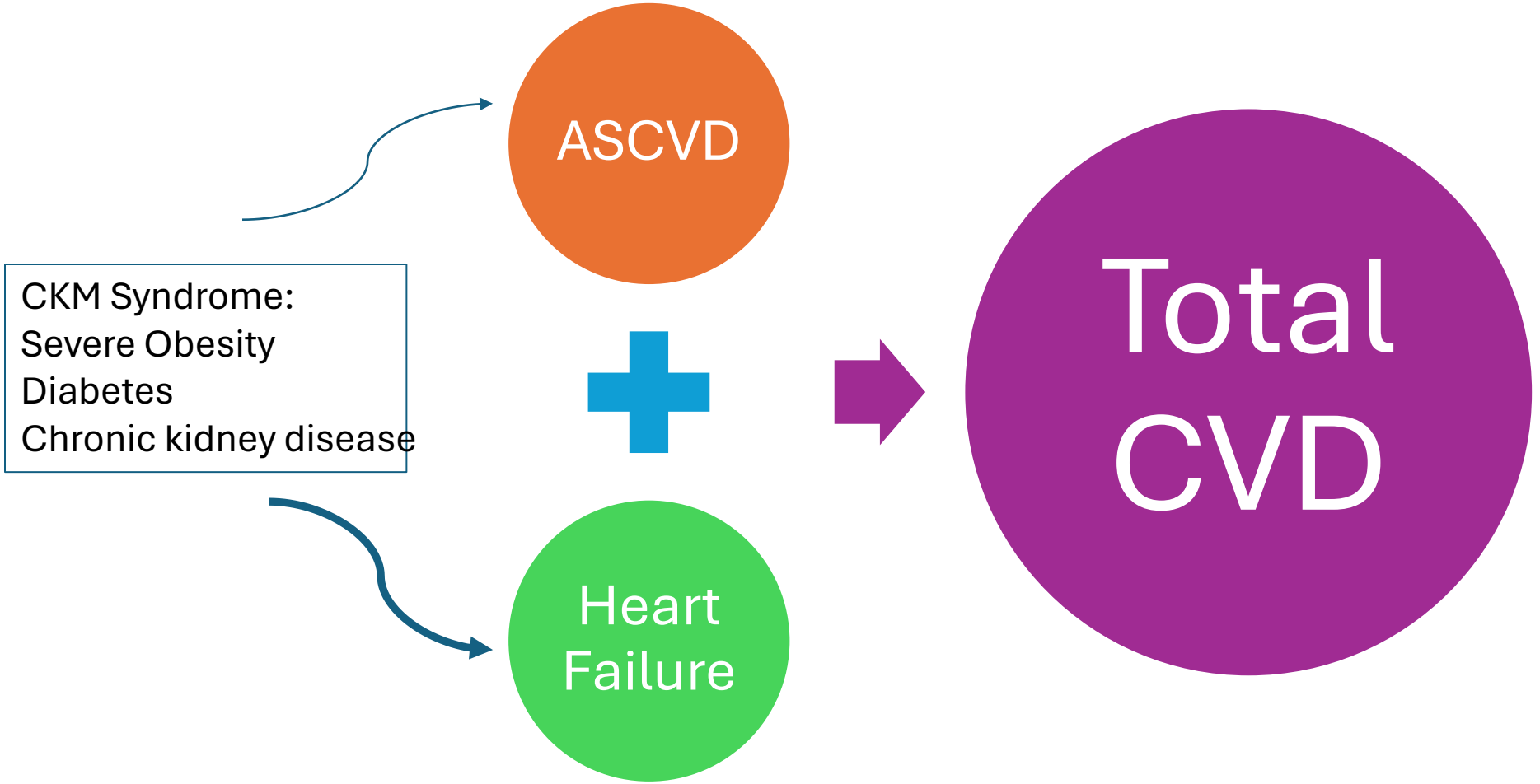
- About 6.6 million individuals (average age = 53 yrs)
- 46 data sets: population studies and health-system electronic records
- Asian, Black, Hispanic and White participants

Advantages:

- Universal (race-free) approach
- Early risk assessment: for ages 30 – 70 years
  - Emphasizes primordial prevention and lifestyle
- Broadens CVD outcomes = total CVD risk
  - Estimates ASCVD and heart failure (high concordance)
  - Includes poor CKM health (severe obesity, diabetes, CKD)
  - Enhances preventive opportunities (SGLT2 inhibitors, GLP1 agonists)

Larkin H. www. jamanetwork.com/journals/jama/fullarticle/2813510; Dec 27, 2023.

CVD and Subtypes



Khan et al. Circulation 2023; 148:1982-2004

PREVENT™ Equations

- Base Equation
  - Age, Sex
  - Systolic Blood Pressure (on Rx?)
  - Total and HDL Cholesterol **(on Rx?)**
  - Diabetes (Y/N)
  - Tobacco use (Y/N)
  - **Kidney function = eGFR**
- Full Equation (Optional)
  - **Kidney function = UACR***
  - **Diabetes control = HbA1c**
  - **Social deprivation index = zip code**
    [social determinants of health]

*UACR = urinary albumin-to-creatinine ratio

American Heart Association Predicting Risk of cardiovascular disease EVENTs (PREVENT)™

https://professional.heart.org/en/guidelines-and-statements/prevent-calculator; Jan 2024

PREVENT™ Online Calculator

CVD Risk Assessment	PCE[1]	PREVENT™-base[2]
55y female (White) - TC 240 mg/dL - HDL 45 mg/dL - SBP 110 (DBP 80) mmHg - BMI 28 kg/m^2 - eGFR 100 mL/min/1.73m^2 - DM=no - Current smoking=no - Rx for HTN/HLD=no	1.4% [10y] 39% [30y]	2.7% (10y] 17.6% [30y]

[1]https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/
[2]https://professional.heart.org/en/guidelines-and-statements/prevent-calculator

Patient Case – Impact

CVD Risk Assessment	PCE[1]	PREVENT™-base[2]	PREVENT™-full[2]
55y female (White) - TC 240 mg/dL - HDL 45 mg/dL - SBP 110 (DBP 80) mmHg - BMI 28 kg/m^2 - eGFR 100 mL/min/1.73m^2 - DM=no - Current smoking=no - Rx for HTN/HLD=no ---------- **- UACR=0 mg/g** **- HgA1c=5.6%** **- Zip Code 43220**	1.4% [10y] 39% [30y]	2.7% (10y] → 17.6% [30y] →	1.1% [10y] 10.1% [30y]

PREVENT™ – Other Case Example

CVD Risk	PCE[1]	PREVENT™-base[2]	PREVENT™-full[2]
55y female (Black) - Other variables remain same ---------- + Kidney disease: - eGFR 50 - UACR 100	1.8% [10y] 39% [30y] ---------- - N/A (risk enhancer)	2.7% (10y] 17.6% [30y] ---------- -- 4.5% [10y] 21.8% [30y]	1.1% [10y] 10.2% [30y] ---------- - 5.4% [10y] 22.5% [30y]

[1]https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/
[2]https://professional.heart.org/en/guidelines-and-statements/prevent-calculator

PREVENT™ – Other Case Example

CVD Risk	PCE[1]	PREVENT™-base[2]	PREVENT™-full[2]	Additional Scenarios		
55y female (Black) - Other variables remain same ---------- -- + Kidney disease: - eGFR 50 - UACR 100	1.8% [10y] 39% [30y] ---------- - N/A (risk enhancer)	2.7% (10y] 17.6% [30y] ---------- 4.5% [10y] 21.8% [30y]	1.1% [10y] 10.2% [30y] ---------- - 5.4% [10y] 22.5% [30y]	1.4% [10y] 12.0% [30y] (Zip 64147) ---------- -- 6.7% [10y] 25.9% [30y] (Zip 64147)	1.6% [10y] 12.5% [30y] (A1c 8.0%) ---------- -- 7.4% [10y] 36.8% [30y] (A1c 8.0%)	2.0% [10y] 14.6% [30y] (Both) ---------- -- 9.1% [10y] 30.6% [30y] (Both)

[1]https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/
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CVD Risk	PCE[1]	PREVENT™-base[2]	PREVENT™-full[2]	Additional Scenarios		
69y male (Black) - Other variables remain same ---------- + Kidney disease: - eGFR 50 - UACR 100	9.6% [10y] N/A [30y] ---------- - N/A (risk enhancer)	7.4% [10y] N/A [30y] ---------- -- 10.3% [10y]	3.1% [10y] N/A [30y] ---------- - 12.2% [10y]	3.9% [10y] (Zip 64147) ---------- -- 14.8% [10y] (Zip 64147)	4.3% [10y] (A1c 8.0%) ---------- -- 16.3% [10y] (A1c 8.0%)	5.4% [10y] (Both) ---------- -- 19.6% [10y] (Both)

Patient Case Condundrum?

- Might this change preventive Rx: eg. statin?

CVD Risk	PCE[1]	PREVENT™-base[2]	PREVENT™-full[2]	Additional Scenarios		
69y male (Black) - Other variables remain same	9.6% [10y] N/A [30y]	7.4% [10y] N/A [30y]	3.1% [10y] N/A [30y]	3.9% [10y] (Zip 64147)	4.3% [10y] (A1c 8.0%)	5.4% [10y] (Both)
+ Kidney disease: - eGFR 50 - UACR 100	N/A (risk enhancer)	10.3% [10y]	12.2% [10y]	14.8% [10y] (Zip 64147)	16.3% [10y] (A1c 8.0%)	19.6% [10y] (Both)

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[2]https://professional.heart.org/en/guidelines-and-statements/prevent-calculator

Current Recommendations

Social Deprivation Index (SDI)[1]

- Developed by Butler et al (2012)[2]
- Describes area-level deprivation data from *American Community Survey*
  - United States Census Bureau
  - Collected monthly, every year (differs from Decennial Census)
- Quantitative, composite measure
  - 7 demographic characteristics
  - Available by county, census tract, zip code, and Primary Care Service Areas
- [*Not* = Social Vulnerability Index]

SDI Components
% population < 100% of federal poverty level
% population 25 years or older, with < 12 years education
% non-employed, for populations 16-64 years
% households living in renter-occupied units
% households living in crowded housing units (no. occupants/room ≥ 1.01)
% single-parent families with dependents < 18 years
% households with no vehicle

[1]*Social deprivation index (SDI)* https://www.graham-center.org/rgc/maps-data-tools/sdi/social-deprivation-index.html; Nov 5, 2018

[2]Butler et al. BMC Health Serv Res 2013;48(2 Pt 1):539-59.

Implementation, Communication, Education

Implementation Considerations (Khan et al)

- Risk estimation → Clinical decision making
  - Currently rely on risk level/classification to determine action
    - Low, intermediate, high/very high risk (and primary/secondary prevention) is usual
  - Prefer transition to "net benefit" approach (ARR, absolute risk reduction)
    - Absolute risk (AR) of CVD x relative risk reduction from treatment (RRR)
- CVD risk assessment/prevention → move earlier in timing
  - Complete life course, from birth through young adulthood to older age
  - PREVENT™ equations: ages 30-70 years
    - Apply/evaluate in first trimester of pregnancy, if applicable
- More research to refine equations
  - Data from diverse populations, additional social factors, and on whether prediction of kidney disease progression can optimize CVD risk assessment

Khan et al. Circulation 2023; 148:1982-2004

Looking Ahead

- How might PREVENT™ equations be used in existing ACC/AHA framework?
  - Potential for change in future guidelines:

2024/2025
- ACC/AHA - Hypertension

2025
- ACC/AHA Blood Cholesterol

Proposed (timing?)
- ACC/AHA Primary Prevention

Larkin H. www. jamanetwork.com/journals/jama/fullarticle/2813510; Dec 27, 2023.

Communication and Education (Khan et al)

- Priorities for near-term – *what can you do right now?*:

  1. Historically, emphasis is on managing risk factors (negative construct)

  -- Create emphasis on CV health in early CKM stages

  - Eg. *Life's Essential 8*

  2. Historically, focus is on ASCVD risk assessment/management

  -- Focus also on conditions that co-occur/associate, and may have shared therapeutic strategies

  - Eg. heart failure, chronic kidney disease → GLP1, SGLT2i

Khan et al. Circulation 2023; 148:1982-2004

PREVENT™ Illustrations

Illustration of PREVENT™ base and additional equations

- Available at https://www.portailvasculaire.fr/sites/default/files/docs/2023_aha_khan_ss_prevent_circulation.pdf
- Page 1991

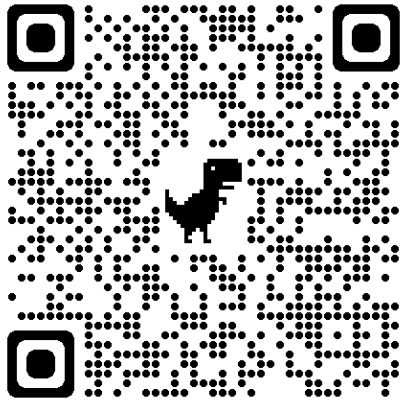
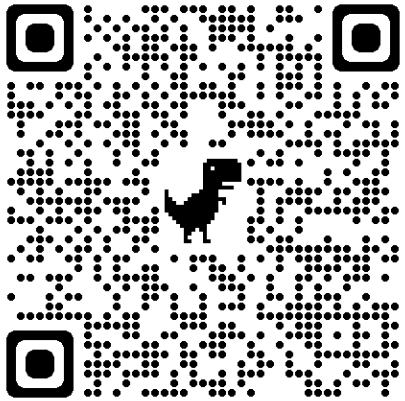


Illustration of life course approach to CV health, staging of CKM health, and total CVD risk assessment

- https://www.portailvasculaire.fr/sites/default/files/docs/2023_aha_khan_ss_prevent_circulation.pdf
- Page 1995



Summary

- CKM Syndrome is a novel framework recently defined by AHA
- Important, clinically-relevant estimation equations are being evolving toward race-free assessments
  - eGFR (kidney function)
  - CVD risk (ASCVD + heart failure risk)
- Social determinants of health are increasingly recognized as predictive variables for health outcomes, now and in future
  - Social Deprivation Index and others?
- Clinical implementation issues and changes in communication/ education regarding the novel framework will need addressed
  - May be included in upcoming, relevant CVD guidelines

Self-Assessment Questions

Question 1

CKD Syndrome is defined as:

A. A systemic disorder of overlapping health conditions: heart disease, kidney disease, obesity and/or diabetes
B. The same criteria used to define metabolic syndrome: blood glucose and blood pressure, HDL cholesterol, triglycerides, and waist circumference
C. The same criteria used to define chronic kidney disease: eGFR and urinary albumin to creatinine ratio (UACR)
D. An X-linked recessive disorder characterized by mild-severe cognitive impairment, seizures, and physiologic malformations

Question 2

Removing race from the calculation for kidney disease and CV disease assessment is appropriate because:

A. Race is a social rather than biological construct
B. A dichotomous race coefficient in mathematical formulae does not adequately represent racial diversity in the US, or inter-individual variations
C. Historically, adequate representation across studies has been a limitation in development of estimation models
D. All of the above

Question 3

In the AHA PREVENT™ Equations, the variable(s) not included in the base formula is/are:

A. eGFR
B. BMI
C. UACR
D. Both A and C are not included

Question 4

Social determinants of health are represented in the AHA PREVENT Equations as the:

A. Vulnerable Populations Index (by county)
B. Percentage of federal poverty level (by quartile)
C. Social Deprivation Index (by zip code)
D. Life’s Essential 8 (by count)

Question 5

True or False

- AHA has provided recommendations on how to utilize 10-year total CVD risk estimates within the framework of the 2019 Primary Prevention of CV Disease Guideline

References

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Need More Information?

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