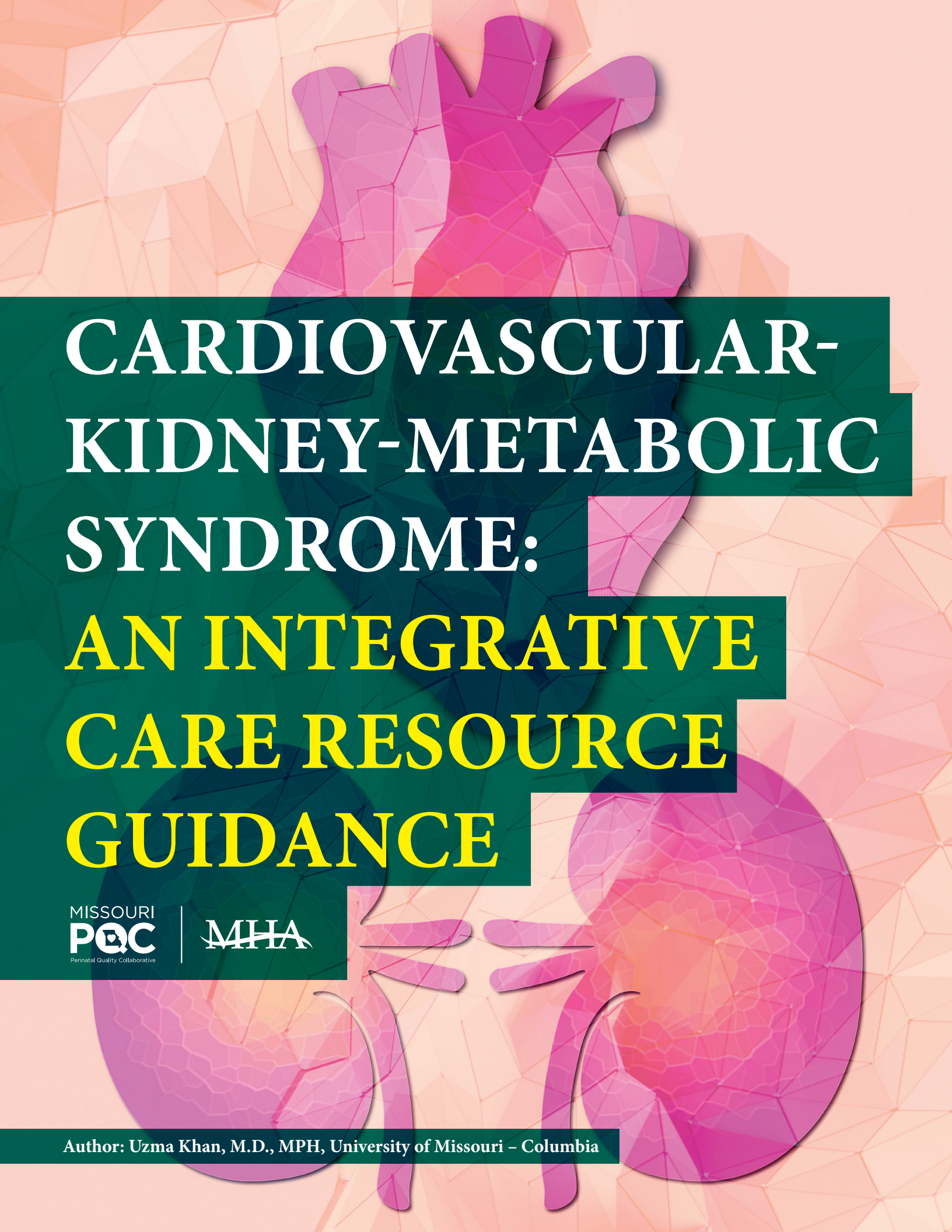

CARDIOVASCULAR-KIDNEY-METABOLIC SYNDROME: AN INTEGRATIVE CARE RESOURCE GUIDANCE

MISSOURI PQC Perinatal Quality Collaborative | MHA

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Chronic diseases contribute significantly to the burden of disease worldwide and in the United States. Many of these chronic diseases are highly preventable, including heart disease, chronic kidney disease, cancers and diabetes mellitus type 2. Together, these preventable diseases contribute significantly to morbidity, disability and mortality in the U.S. and around the world.

Background

The concept of a unifying syndrome has evolved over the last 50 years (Fig. 1). In the 1980s, it was called Syndrome X and was related to insulin resistance.[1] In 1999, the World Health Organization defined metabolic syndrome as having insulin resistance or high glucose and two additional findings, which could include low high-density lipoproteins, high triglycerides, high waist/hip ratio, high body mass index or high blood pressure.[2] In 2001, these additional findings were further refined as having the presence of three or more conditions, including high blood glucose, low HDL, high triglycerides, increased waist circumference or high blood pressure.[3] *Since 2000, it has become evident that rather than identifying specific conditions separately, it is important to identify the underlying pathophysiology.* This allows targeted prevention and development of clinical guidelines and tools to identify and treat these conditions.

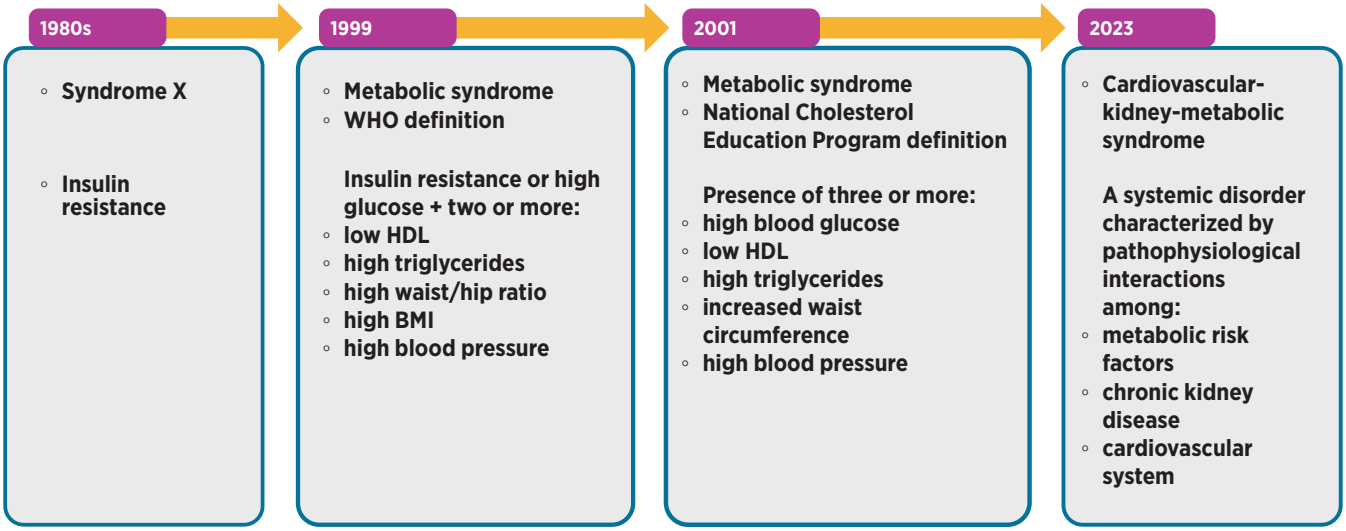

Figure 1: Evolvement of definition of cardiovascular-kidney-metabolic syndrome based on underlying pathophysiology.

In November 2023, the American Heart Association issued a presidential advisory defining a new condition to encompass the pathophysiological-related chronic diseases, including heart disease, kidney disease and diabetes mellitus.[4] In the U.S., from 2015 to 2020, one in four adults had at least one of these conditions, with overlapping conditions identified in one in 10 adults. This is even higher in adults above 65 years of age, where one in two had at least one condition, and nearly one in four had multiple conditions. Cardiovascular-kidney-metabolic syndrome allows these conditions to be identified as a focus area to improve health in community and clinical settings. In a cross-sectional cohort study, there was a significant increase in CKM syndrome from 5.3% in 1999 to 8% in 2020, indicating a need for a concerted effort on prevention, treatment and research in this area.[5]

Cardiovascular-Kidney-Metabolic Syndrome

The AHA defines CKM syndrome as a systemic disorder characterized by pathophysiological interactions among metabolic risk factors, chronic kidney disease and the cardiovascular system. These interactions lead to multi-organ dysfunction and a high rate of adverse cardiovascular outcomes. CKM syndrome is described in five stages (Table 1). Stage 0 includes people who have no risk factors allowing for early prevention and the opportunity to address population health determinants. Accumulation of fat in body organs underlies stages 1 to 4 of CKM syndrome. Stage 1 is defined as excessive body fat, especially in the abdominal area, and impaired glucose tolerance. The next three stages show a progressive increase in the number and severity of components of CKM syndrome, including diabetes mellitus, hypertension, heart disease and chronic kidney disease.

CKM Stage					
	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
Defining Components					
Excess adipose tissue Indicated by obesity, abdominal obesity or dysfunctional adipose tissue	No	Yes	Yes	Yes	Yes
Metabolic dysfunction Indicated by presence of hypertension, hypertriglyceridemia, metabolic syndrome or diabetes mellitus	No	Yes Presence of impaired fasting blood glucose or prediabetes	Yes Presence of hypertriglyceridemia, hypertension, metabolic syndrome or diabetes mellitus	Yes	Yes
Chronic kidney disease Indicated by presence of albuminuria or decreased kidney function	No	No	Yes	Yes	Yes 4a: No kidney failure 4b: Kidney failure present
Cardiovascular disease Indicated by atherosclerosis, heart failure, stroke, peripheral artery disease or atrial fibrillation	No	No	No	Yes Subclinical atherosclerosis or heart failure	Yes Clinical coronary heart disease, stroke, peripheral vascular disease, atrial fibrillation
Treatment					
Lifestyle Exercise	Yes	Yes	Yes	Yes	Yes
RAAS inhibitors	No	No	Yes	Yes	Yes
SGLT-2 inhibitors	No	No	Yes	Yes	Yes
GLP-1 RA	No	Yes	Yes	Yes	Yes
Nonsteroidal MRA	No	Yes	Yes	Yes	Yes
Resources					
Cardiovascular	The American Heart Association PREVENT™ online calculator https://professional.heart.org/en/guidelines-and-statements/prevent-calculator				
Kidney	National Kidney Foundation https://www.kidney.org/offices/nkf-serving-eastern-missouri-metro-east-and-arkansas				
Metabolic	Diabetes Prevention Program — Missouri Department of Health and Senior Services https://health.mo.gov/living/healthcondiseases/chronic/diabetes/index.php				
Pregnant Women	Missouri Perinatal Quality Collaborative https://mopqc.org/				

Table 1: Stages, components, treatment and resources for cardiovascular-kidney-metabolic syndrome.

Key:

- RAAS – Renin angiotensin aldosterone system
- SGLT-2 – sodium-glucose transport protein 2
- GLP-1 RA – Glucagon-like peptide-1 receptor agonists
- MRA – mineralocorticoid receptor antagonists

Table adapted from:

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The pathophysiology of CKM syndrome involves underlying inflammation and fibrosis in affected organs resulting in hemodynamic and metabolic imbalance. Incorporating this understanding allows for providers to use tools like the PREVENT™ online calculator, designed to calculate cardiovascular risk for each individual for purposes of education, prevention and treatment. Improved understanding of these processes led to the development of therapies targeting more than one pathogenic pathway resulting in complimentary actions and improved outcomes.

Evidence

CKM syndrome is more than a clinical diagnosis — it requires an understanding of the patient's underlying pathophysiology as well as an appreciation of their social and economic risk factors. Between 2011 and 2018, only 11.2% of all U.S. adults met criteria for stage 0 of CKM. Most of the adult population in the U.S. (47.4%) met criteria for stage 2 CKM, placing them at high risk of adverse cardiovascular events. Those in the highest risk stages (3 and 4 CKM) had associated poor social determinants of health including lower education, lower income and less employment. Those in the highest risk stage 4 CKM were mostly above age 60, males and non-Hispanic Black individuals.[6]

A group that is understudied regarding CKM syndrome is women. Compared to men, women have a lower prevalence of stage 3 CKM but show excess mortality risk across all CKM stages.[7] As compared to other developed countries, the U.S. lags behind in women's health outcomes as well as maternal mortality. Cardiovascular disease is the leading cause of death for women in the U.S. and is the leading cause of maternal mortality and morbidity, accounting for one-fourth of maternal deaths.[8] An estimated 10% to 25% of pregnant women develop gestational diabetes mellitus and 50% to 60% are overweight or obese, leading to worse maternal and fetal outcomes.[9] Cardiac conditions are major contributors to pregnancy-related deaths in Missouri. According to the most recent data from Missouri, an average of 70 women died while pregnant or within one year of pregnancy each year between the years of 2018 and 2022, with 80% of pregnancy-related deaths being preventable. The pregnancy-related mortality ratio was 2.5 times higher for Black women compared to white women. Women in micropolitan counties, those with mental health conditions and those insured by Medicaid had higher rates of pregnancy-related deaths.[10]

Advanced stages of CKM syndrome are more likely in adults over 65 years of age, men and Black adults. Early risk stratification and appropriate patient-centered care with a multidisciplinary team can improve outcomes. A healthy diet, regular exercise and weight control can prevent progression to higher stages and improve CKM health. Due to the complexity of CKM syndrome, involvement of multiple organ systems and increased risk of adverse outcomes, a multidisciplinary team is required for patient-centered care (Fig. 2).

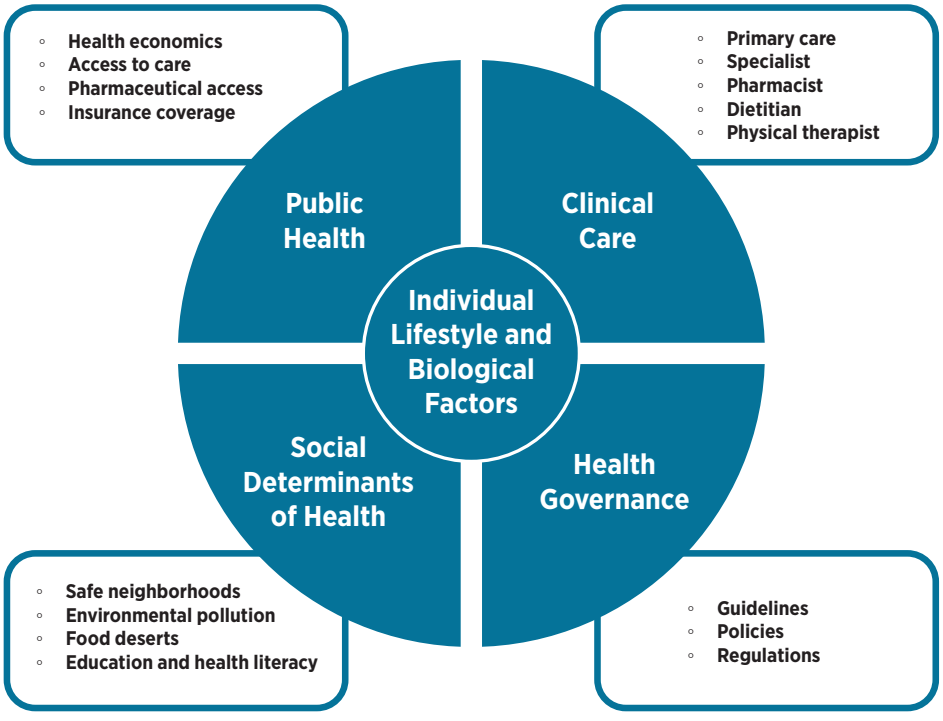

Figure 2: Multimodal approach to reduce cardiovascular risk in CKM syndrome

Call to Action

CKM syndrome provides a unifying concept of a complex, multisystem disorder, allowing patients and health care providers to focus on prevention and targeted interventions to improve cardiovascular and metabolic health of each person. Helpful resources are available for treating CKM syndrome, including specific evidence-based guidelines, which utilize newer medications that target more than one condition. Nationwide programs like the Diabetes Prevention Program, and statewide initiatives like the Missouri Perinatal Quality Collaborative's Cardiac Conditions in Obstetric Care are designed to decrease cardiac-related mortality in specific high-risk groups. The goals of these programs include risk assessment, screening standardization, training and education, and appropriate care through a multidisciplinary approach. A patient-centered focus through a team-based approach is necessary to implement preventive and treatment strategies for CKM syndrome.

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