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Prevalence and Overlap of Cardiac, Renal, and Metabolic Conditions: Highlights of an Analysis of NHANES Data

This AJMC® Clinical Brief provides key information regarding a study by Ostrominski et al, which was published in *JAMA Cardiology* (doi:10.1001/jamacardio.2023.3241).¹ Please consult the full publication for complete study information and author affiliations.

INTRODUCTION

The heart, kidney, and metabolic systems are interconnected; diseases affecting these systems share a common pathophysiology and have overlapping risk factors including hypertension, obesity, and abnormal blood glucose and blood lipid levels.^{2,3} With the evolution of treatment options, certain medications, including sodium-glucose cotransporter 2 inhibitors (SGLT2 inhibitors), have been beneficial in treating multiple cardiac, renal, and metabolic (CRM) conditions.⁴ Because some medications have been shown to reduce more than 1 CRM disease in patients with multiple inter-related CRM conditions,^{4,5} clinical practice guidelines for managing patients with CRM conditions call for collaboration among members of the care team.^{2,6-8} Notably, the Diabetes, Cardiorenal & Metabolic Diseases Task Force has issued multidisciplinary guidance specific to the management of patients with multiple CRM conditions.⁵

Although the prevalence of cardiovascular disease (CVD), chronic kidney disease (CKD), and diabetes have been estimated in US adult populations,⁹⁻¹¹ the degree to which these conditions overlap has not been systematically evaluated. To address this knowledge gap, Ostrominski and colleagues analyzed data from the National Health and Nutrition Examination Survey (NHANES) to determine the prevalence of CRM conditions and the degree of overlap of these conditions among US adults.¹ This article provides an overview of the study and its results.

METHODS

NHANES data are collected by the National Center for Health Statistics; these data provide an overview of the health and nutritional status of the civilian, noninstitutionalized population in the United States.^{1,12} Data are collected through both interviews and measurements of medical, dental, and physiological factors by trained personnel.¹² The data may be used to inform public health policies and services as well as to uncover factors that may increase the risk of various diseases.¹² It is important to note that the reliability of certain NHANES data, such as the self-reported caloric energy intake, has been reported to be low.¹³

In this study, Ostrominski and colleagues used cross-sectional, nationally representative data from NHANES to evaluate the proportion of participants with CRM conditions. The analysis included data from nonpregnant adults aged at least 20 years. Data from survey cycles performed from 1999 to 2000 and 2017 to March 2020 (prepandemic continuous NHANES survey cycles) were analyzed. Data from 2015 to 2016 and 2017 to March 2020 were used to improve the reliability and precision of the results.¹

CVD was defined as atherosclerotic CVD (ASCVD), heart failure, or both (CVD group). Renal impairment was defined as moderate- or high-risk CKD, with participants identified according to

their estimated glomerular filtration rates and albuminuria (CKD group). Metabolic disease was defined as the presence of type 2 diabetes (T2D) (T2D group); participants with type 1 diabetes (T1D) were excluded (T1D was identified based on the use and timing of the initiation of medication). Participants who had a hemoglobin A_{1c} level of at least 6.5% and who were not diagnosed before the age of 20 years were considered to have T2D. Furthermore, the authors evaluated the proportion of participants with additional conditions that are considered to be CRM risk factors and are associated with metabolic syndrome, including prediabetes, obesity, hypertension, and hypercholesterolemia. Finally, trends in the prevalence of CRM conditions over time were evaluated by comparing data from survey cycles spanning from 1999 to March 2020.¹

Sampling weights from the National Center for Health Statistics were used to estimate the prevalence of CRM conditions based on the study population.¹ Population counts were determined by multiplying the weighted CRM prevalence estimates by the estimated number of US adults 20 years or older (N = 244,657,212)¹ according to 5-year population estimates obtained in the 2020 American Community Survey.¹⁴ Overall estimates were determined, as well as those for participants 65 years or younger.¹ The prevalence of CVD, CKD, and T2D, as well as each combination of conditions, was estimated (which yielded 8 CRM categories ranging from none to CVD+CKD+T2D). Temporal trends in the prevalence and overlap of CRM conditions were explored using data from 1999 through 2002, 2003 through 2008, 2009 through 2014, and 2015 through March 2020.¹

RESULTS

Sample Characteristics and Disease Burden

The unweighted sample included 11,607 participants who met the inclusion criteria. In the overall population, CKD showed the highest prevalence among the diseases evaluated (13.9%), followed by T2D (13.3%) and CVD (8.6%). Stratification of participants by age showed that the burden of CRM conditions increased with age (Table).¹

Overall Trends in CRM Prevalence

From 2015 to March 2020, 26.3% of adults (approximately 65 million adults) had at least 1 CRM condition, including 18.2% (44.9 million) with 1 CRM condition, 6.5% (16.3 million) with 2 CRM conditions, and 1.5% (3.8 million) with 3 CRM conditions. Time-based analysis showed a significant increase in the proportion of adults with at least 1 CRM condition, from 21.2% in 1999 through 2002 to 26.3% in 2015 through 2020 (P < .001). Over time, the proportion of US adults with at least 2 CRM conditions increased from 5.3% to 8.0%, showing a significant difference between these 2 periods (P < .001). In particular, significant increases in the numbers of participants with T2D (from 7.5% to 13.3%; P < .001) and CVD (from 6.8% to 8.6%; P = .02) were observed between the 2 study periods (Figure). The most common combination in participants with 2 CRM conditions was CKD+T2D (3.2%), followed by CVD+T2D (1.7%) and CVD+CKD (1.6%). Furthermore, participants who had multiple CRM conditions were also more likely to have high-risk stages of CKD than were participants with CKD alone.¹

CRM Conditions by Age

Older participants tended to have more CRM conditions. Participants 65 years or older accounted for 69.0% of all participants with 3 CRM conditions; only 12.4% of participants in this age group did not have a CRM condition. The most common condition among older participants was CKD (33.1%); the prevalences of CVD (23.8%) and T2D (26.0%) were also high. The proportion of high-risk CKD was greater for all CRM statuses among older participants than among younger participants. However, T2D was more often undiagnosed in younger participants versus older participants.¹

CRM Conditions by Sex, Race, and Race/Ethnicity

Women showed a greater prevalence of any CVD, CKD, or T2D condition when compared with men (26.9% vs 25.6%, respectively). However, men were more likely than women to have multiple CRM conditions (9.1% vs 7.0%, respectively).¹

Women carried a slightly greater burden of any CVD, CKD, or T2D compared with men (26.9% vs 25.6%). However, men were more prone

Table. Prevalence of Any CRM Condition in US Adults, Overall and Stratified by Age, 2015 Through March 2020¹

Population	CVD (Any ASCVD or HF)		CKD (Any non-low CKD risk)		Any T2D	
	Prevalence ^a	Population (millions)	Prevalence ^a	Population (millions)	Prevalence ^a	Population (millions)
Overall	8.6% (7.6%-9.7%)	21.5	13.9% (12.9%-14.9%)	34.4	13.3% (12.4%-14.1%)	32.8
20-64 years	4.7% (3.9%-5.5%)	9.0	8.9% (8.1%-9.6%)	17.1	10.0% (9.3%-10.7%)	19.2
≥ 65 years	23.8% (21.3%-26.2%)	12.5	33.1% (30.6%-35.6%)	33.1	26.0% (23.5%-28.4%)	13.6

ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CRM, cardiac, renal, and metabolic; CVD, cardiovascular disease; HF, heart failure; T2D, type 2 diabetes.

^aPrevalence is shown as a weighted percentage (95% CI).

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than women to have multiple CRM conditions (9.1% vs 7.0%). The percentage of non-Hispanic Black individuals with a CRM condition generally increased as the burden of CRM comorbidities increased, mainly because of a higher prevalence of T2D and its associated overlap. Conversely, the proportion of participants identifying as Hispanic decreased as the CRM comorbidity burden increased. Hispanic participants showed the second-highest overall prevalence of T2D but the lowest prevalence of any CVD, any CKD, and multiple CRM conditions.¹

Prescription Medication Use

Evaluation of prescription medication use showed that statin use was reported by 47% of participants with T2D alone, 45% for those with CKD+T2D, 76% for individuals with CVD+T2D, and 70% for participants with CVD+CKD+T2D. Among the participants with 3 CRM conditions, only 4.8% used glucagon-like peptide-1 receptor agonists (GLP1-RAs) and 3.0% used SGLT2 inhibitors.¹

Presence of Ancillary Conditions in Participants With CRM Conditions

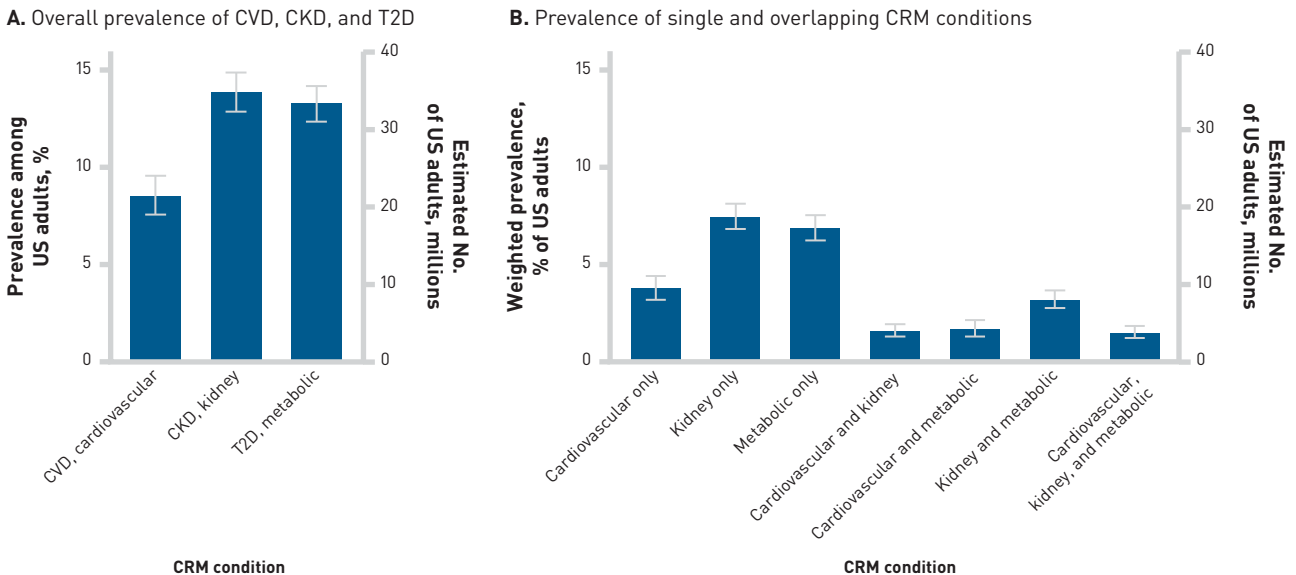
Among all participants, 26% had prediabetes, 29% had hypercholesterolemia, 38% had hypertension, and 41% had obesity.¹ The prevalence of ancillary conditions increased commensurate with the number of CRM multimorbidities.¹

DISCUSSION

The results reported by Ostrominski and colleagues provide insight into the scale and temporal patterns of CRM multimorbidity, which is common among US adults. According to study estimates, more than 25% of adults in the United States had a CRM condition, and 10% had multiple CRM conditions. These values were particularly high in older adults, with more than 50% and 25% showing at least 1 and at least 2 CRM conditions, respectively. Treatment gaps were also observed; for example, SGLT2 inhibitor or GLP1-RA therapy was not widely administered, even to participants with CVD+CKD+T2D multimorbidity. These results support the need to apply improved strategies when treating patients with multiple CRM conditions. In the US population evaluated in the current study, there was a disparity in the prevalence of CRM conditions between non-Hispanic Black, Hispanic, and other participants. The high rates of CRM comorbidity in these patient groups indicate ongoing difficulties related to patient health equity, social determinants of health, and pharmacotherapies.¹

Notably, according to the results of the current study, the prevalence of CRM conditions is expected to further increase over time. Concerningly, the prevalence of obesity, a strong risk factor for multimorbidity, was greater than one-third in people with no CRM condition.¹

Figure. Prevalence and Overlap of CRM Conditions in US Adults, 2015 Through March 2020^{1,a-c}



CKD, chronic kidney disease; CRM, cardiac, renal, and metabolic; CVD, cardiovascular disease; T2D, type 2 diabetes.

^aPercentage and weighted prevalence (in millions of persons) of noninstitutionalized US adults with CVD, CKD, and T2D overall (A), as well as single and overlapping CRM conditions (B).

^bError bars indicate 95% CIs.

^cUnweighted Ns by CRM status: 486 participants with CVD only, 1000 with CKD only, 1099 with T2D only, 272 with CVD plus CKD, 213 with CVD plus T2D, 546 with CKD plus T2D, and 267 with CVD plus CKD plus T2D.

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Limitations

There were some limitations to this study. NHANES reports serial survey data from noninstitutionalized civilian adults in the United States; therefore, the results may not be applicable to other time periods and other populations and settings. Furthermore, the algorithm used to differentiate T1D from T2D is only applicable to participants with a diagnosis of diabetes, as the decision between T1D and T2D was made based on a review of medications taken and the temporal relationship with the diagnosis.¹

CONCLUSION

CRM multimorbidity is common, particularly in older, non-Hispanic Black individuals as well as in those with adverse socioeconomic characteristics. Collaborative, comprehensive management strategies are required to address the needs and treatment gaps of patients with, or at risk of developing, CRM conditions. •

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Ask the Investigator: Q&A With John W. Ostrominski, MD

An editor from *The American Journal of Managed Care*® (AJMC®) spoke with **John W. Ostrominski, MD**, lead author of "Prevalence and overlap of cardiac, renal, and metabolic conditions in US adults, 2015-2019," which was published online by *JAMA Cardiology* in September 2023.¹ Ostrominski is a fellow in cardiovascular medicine and obesity medicine in the divisions of cardiovascular medicine and endocrinology, diabetes, and hypertension at Brigham and Women's Hospital and Harvard Medical School in Boston, Massachusetts.

AJMC: Why was this study conducted? What knowledge gap does it address?

Ostrominski: Historically, clinical practice and research efforts have focused on cardiovascular disease, chronic kidney disease, and type 2 diabetes as isolated medical conditions. In clinical practice, though, coexistence of these conditions is increasingly the rule rather than the exception. Some part of this is because of population aging and shared risk factors. For instance, chronic kidney disease and stroke are unified by the common risk factor of hypertension. However, these

conditions may also lie along sequential or even bidirectional pathways of onset and progression. For example, we know that chronic kidney disease confers a higher risk of heart failure, but that heart failure also confers a higher risk of chronic kidney disease and worsening kidney function. The same is true with diabetes. Owing to shared pathophysiology, these conditions increasingly have shared therapeutic opportunities. Recent pharmacotherapeutic innovations—such as sodium-glucose cotransporter 2 [SGLT2] inhibitors, incretin-based therapies, and nonsteroidal mineralocorticoid antagonists

[MRAs]—have emerged and explicitly target cardiovascular, renal, and metabolic—or CRM—intersections.² As such, contemporary clinical practice guidelines increasingly call for collaborative and comprehensive management of high-risk patients with CRM conditions.² Despite this, though, the frequency with which these conditions coexist had not been comprehensively characterized. Hence, we were motivated to do this study to further characterize the prevalence and treatment of CRM overlap, as well as its evolution over time. Another goal was to inform clinicians and policy makers about novel research efforts focused on these intersections and [encourage] the design of new health care approaches capable of delivering high-quality, high-value, and collaborative care to individuals impacted by CRM multimorbidity.

AJMC: What were the main results?

Ostrominski: Overall, we found that more than 1 in 4 US adults has at least 1 CRM condition and that CRM multimorbidity has become increasingly prevalent among US adults within the last 2 decades alone. And [we discovered] that even at the highest risk CRM intersections—those having all 3 conditions simultaneously—the utilization of key pharmacotherapies was quite low.¹

AJMC: Can you describe CRM a little more? What conditions does it include? What are the risk factors? Is it a new term?

Ostrominski: While cardiorenal and cardiometabolic are 2 terms that are widely used and perhaps more easily recognized, cardiac, renal, and metabolic (or cardiac-kidney-metabolic) is a term that has emerged within the past probably 5 to 6 years, and I feel that it more completely captures the interconnected nature of these organ systems as well as their increasingly shared therapeutic opportunities. Although there may be a few different conceptual approaches, I typically think of atherosclerotic cardiovascular disease (ASCVD), heart failure, type 2 diabetes, and chronic kidney disease as really the core CRM conditions. Obesity, which is commonly proximate to each of these conditions, as well as nonalcoholic fatty liver disease, should also be thought of as being along this spectrum.

The key risk factors for CRM conditions are things that most people would readily recognize—conditions like hypertension, dyslipidemia or hypercholesterolemia, and obesity. In the interest of also thinking holistically, social determinants of health—such as adverse experiences, economic conditions, and environmental drivers—are also key contributors. Recent evidence has also stressed the importance of considering reproductive risk factors, such as gestational diabetes, as part of holistic risk stratification approaches in women.³

AJMC: What are some of the key takeaways regarding the utilization patterns of various drug classes (such as angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and SGLT2 inhibitors) used to treat patients with CRM conditions?

Ostrominski: This is one of the key takeaways from our paper. Even among [patients] at the highest risk CRM intersection—so, again, patients with 2 or all 3 conditions—key pharmacotherapies important to risk factor control and reducing adverse outcomes were substantially underutilized. For instance, among participants with 3 CRM conditions, only 4.8% reported GLP1 [glucagon-like peptide 1] receptor agonist use, and only 3.0% reported SGLT2 inhibitor use. Further, even in the presence of multiple indications, statins were found to be underutilized. Among those with all 3 CRM conditions, nearly 30% were not taking a statin.¹

The other key takeaway related to this theme is that even among those who had single CRM conditions, the utilization of these key therapies was relatively low. For example, statin use was reported by less than half of participants with type 2 diabetes.¹ In practice, it must be recognized that, in addition to disease-specific morbidity and mortality, individual CRM conditions are often the initial expression of a wider CRM syndrome. As such, in addition to optimizing treatment of individual CRM conditions, holistic approaches that improve utilization of key therapies may be central to the prevention of subsequent CRM comorbidity cascades.

AJMC: Do you have further plans to investigate these medication utilization trends?

Ostrominski: The landscape of available pharmacotherapies has evolved substantially over the course of the past 2 decades. Evaluating the temporality of differences in uptake of these medications, [and evaluating] whether they are improving or decreasing or stabilizing [in] certain groups, will support additional comprehensive efforts to improve quality of care in these high-risk patient groups. Another key aspect is evaluating how control of important CRM risk factors differs by baseline CRM comorbidity status.

AJMC: What is the relevance of these results for managed care professionals? How could this information be useful? How can managed care help address the needs of patients with multiple CRM conditions?

Ostrominski: Through their longitudinal focus on integration and quality, I think managed care organizations may be at a unique advantage in creating the multidisciplinary interventions, such as dedicated multidisciplinary teams, or even clinical spaces, such as care homes, that cater specifically to

patients with CRM conditions and multimorbidity. Whatever their form, integrative approaches and approaches that are not siloed are critically needed. There have been preliminary efforts focusing on care home-based approaches or on cardiac, renal, and metabolic or cardiometabolic centers of excellence that have demonstrated important benefits on improving alignment between evidence and practice. I think one additional element is that shared networks create the ability [for managed care organizations] to forge the long-term relationships that are likely critical for securing the best possible outcomes and for ensuring that patients remain on track across the lifespan.

Another important component is that managed care entities may be in a great position to conduct rigorous effectiveness research and thereby discover the approaches to care delivery that are conducive to not only optimizing outcomes but also maximizing value. However, these programs must be sufficiently flexible to account for provider shortages to ensure timely and equitable access to care for all patient populations.

AJMC: Are quality indicators in place to evaluate the care of patients with CRM conditions? If not, what quality indicators could be added?

Ostrominski: Similar to the traditional perspective of clinical guidance documents or guidelines, quality indicators have historically focused on screening or therapeutic interventions for specific diseases, such as screening for HbA_{1c} [hemoglobin A_{1c} level] among individuals who are at risk for diabetes. But specific intersections have become the basis for more recent quality metrics, and we're now seeing evolving quality metrics focusing specifically on patients with diabetes and hypertension, diabetes and chronic kidney disease, and even ASCVD and type 2 diabetes.

There are a few important metrics, though, that are currently missing. SGLT2 inhibitors for heart failure, irrespective of baseline ejection fraction, I think would be great to see in an American guideline. We've seen this emerge in the European Society of Cardiology guidelines.⁴ In addition, it would also be excellent to see a multidisciplinary quality improvement metric for the use of nonsteroidal MRAs among individuals with diabetes-related kidney disease. Also, in light of evolving trials of incretin-based therapies, such as semaglutide and tirzepatide in individuals with ASCVD and heart failure, we may also begin to see quality metrics for the use of these agents for secondary prevention among individuals with these target conditions and overweight or obesity, which is where they primarily have been studied.

One of the underlying themes here is that quality metrics have inconsistently evolved with the pace of therapeutic innovation. To incentivize clinicians and health care systems

to expedite delivery of the best available care, and thereby avert preventable death and disability, it would be great to ultimately see quality metrics evolve at the same pace as the field. Ideally, quality indicators would be as transparent as possible to promote patient trust and ultimately [to achieve] alignment with providers on health-related goals.

AJMC: Which physician specialties should be responsible for the care of patients with multiple CRM conditions? For example, what roles should primary care providers, nephrologists, endocrinologists, and cardiologists play?

Ostrominski: I think this really gets to one of the key messages of the manuscript. Perhaps the clearest path to success lies in engaging the diverse spectrum of clinicians who care for high-risk individuals with overlapping CRM conditions. Although some may assert that primary care clinicians should lead holistic care approaches in this population, primary care practices have historically been underfunded and are increasingly overstretched. In a recent analysis, it was suggested that primary care physicians require 27 hours in a day to actually adhere to all suggested guidelines.^{5,6} It's also been shown that, at least in the United States, linkage to primary care among adults has declined over time.⁷ In the same way that cardiac-renal-metabolic conditions interact bi- and multidirectionally, so, too, should the subspecialty clinicians with expertise along this axis. This means that to maximize opportunities to improve patient outcomes, cardiologists must also embrace the unique challenges and opportunities of practicing a bit of nephrology and endocrinology, and the same goes for nephrologists and endocrinologists. Of course, novel and integrated training pathways may be needed to realize this vision.

AJMC: In your clinical experience, how do socioeconomic factors impact access to care and clinical outcomes among your patients with CRM conditions? What can be done to improve access to care and clinical outcomes?

Ostrominski: This is another critically important question. I'll start by saying that it's well established that adverse socioeconomic characteristics, as well as other important social determinants of health—such as adverse neighborhood conditions, isolation from health care systems, and various forms of structural racism—are key drivers of health outcomes and the incidence of CRM conditions.⁸ As stressed in recent guidelines, systematic identification of these factors can improve the quality of care by enhancing risk stratification efforts and identifying important and modifiable barriers to care.⁹

Also, the patient-level cost of care must become more manageable. As suggested in recent financial toxicity analyses,

the cost of health care can be devastating and can contribute independently to adverse health outcomes.¹⁰⁻¹² Fortunately, as we've seen in the past several months alone, I think the landscape is changing. Multiple pivotal CRM pharmacotherapies are approaching patent expiration, and newer therapies are entering the market at a lower cost.¹³ Furthermore, 7 of the 10 pharmacotherapies that have entered into Medicare drug price negotiations are relevant to cardiometabolic medicine.¹⁴

Finally, the strong reciprocal interactions between CRM conditions and social determinants of health amplify the need for collaborative multisectoral interventions that target public policy, social networks, urban planning, food insecurity, health care access, and insurance coverage. Novel care delivery approaches, such as digital care or even community-based care delivery strategies, may improve access, improve equity, and ultimately reduce health care disparities if they are judiciously designed and implemented.¹⁵

AJMC: Based on the results of this study, what are the next steps? What additional research will be done?

Ostrominski: This analysis evokes many additional questions and research opportunities. In addition to evaluating temporal trends in pharmacotherapy utilization that I [previously] alluded to, I think one other key piece is evaluating how the control of the key CRM risk factors—such as hypertension, LDL [low-density lipoprotein] cholesterol, non-HDL [non-high-density lipoprotein] cholesterol, HbA_{1c}—differs by baseline CRM comorbidity status. We know that the health effects of a given risk factor are related to the duration of exposure and level of control over time. Thus, showing how well risk factors are controlled in these high-risk groups, in addition to how risk factor control has changed over time, will also be extremely important for identifying opportunities to improve how care is delivered in this population.

Obesity is also another exceedingly important disease and a root cause for not only CRM conditions and multimorbidity but also for several other disease states capable of eroding the quality and quantity of life. Because of this, it's unsurprising that the prevalence of obesity increased with increasing CRM comorbidity burden in this analysis.¹ An additional research goal is to determine how obesity influences the incidence and overlap of CRM conditions over time.

Another follow-up study is underway to determine the time to development of subsequent CRM conditions among individuals with a single cardiac, renal, or metabolic disease. These data will further reveal the sequential and interconnected nature of CRM conditions. •

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