Humanistic and Economic Burden of Patients with Cardiorenal Metabolic Conditions: A Systematic Review

Keith C. Ferdinand,[1] Keith C. Norris,[2] Helena W. Rodbard,[3] Jennifer M. Trujillo[4]

[1]Tulane Heart and Vascular Institute, Tulane University School of Medicine, New Orleans, LA, USA; [2]Department of Medicine, Division of General Internal Medicine and Health Services Research, University of California, Los Angeles, CA, USA; [3]Endocrine and Metabolic Consultants, Rockville, MD, USA; [4]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado, Aurora, CO, USA

BACKGROUND

- In 2021, the International Diabetes Federation estimated that 537 million (10%) adults aged 20–79 years worldwide had diabetes (240 million [44.7%] undiagnosed); this number is predicted to rise to 783 million people by 2045.[1] Type 2 diabetes mellitus (T2DM) accounts for 90–95% of diagnosed cases.[2]
- Research has shown that cardiorenal metabolic (CRM) conditions, which collectively refer to cardiovascular disease (CVD, including heart failure [HF]), kidney dysfunction, and metabolic disorders, are closely intertwined diseases that are complications of each other and also represent the major comorbidities of T2DM.[3-5]
- A 2018 study reported that an estimated 94% of people with T2DM had ≥1 other CRM condition and 51% had ≥3 other CRM conditions.[6] The Third National Health and Nutrition Examination Survey of over 15,000 participants in the US found that the 10-year incidence of cardiovascular death was 2–3 times higher in patients with either T2DM (6.7%) or chronic kidney disease (CKD; 9.9%) than in those without either condition (3.4%), and 5-fold higher in those with both conditions (19.6%).[7]
- CRM conditions are likely to represent a significant economic burden, with a greater number of comorbidities linked to increasing healthcare costs.

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OBJECTIVE

- To conduct a systematic literature review (SLR) to assess the humanistic and economic burden of CRM conditions in patients with CVD, CKD, and T2DM.

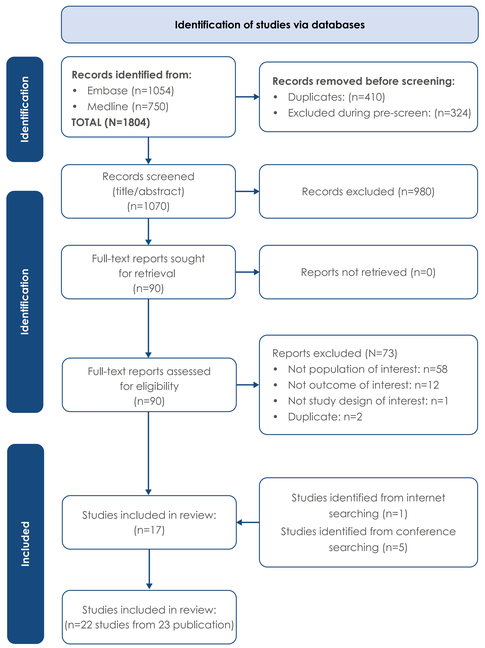
METHODS

- The search was run on Embase and Medline, and included English language publications from January 1, 2011 to January 10, 2022. Relevant abstracts were also identified from 4 conferences: American College of Cardiology (2021–2022), American Heart Association (2020–2021), American Society of Nephrology (2020–2021), and American Diabetes Association (2021–2022).
- Two independent reviewers performed a quality check and screening for eligible studies that met the inclusion criteria: observational studies, real-world evidence, and economic model studies examining humanistic and/or economic burden outcomes in individuals aged ≥18 years with CVD, CKD, and T2DM. Intervention and validation studies were excluded. The quality of included studies was assessed using the 9-point Newcastle-Ottawa Scale; a score of <5 points suggests poor-quality studies with a high risk of bias, and higher scores suggest a low risk of bias.
- Outcomes of interest included the humanistic burden (health-related quality of life [HRQoL], functional impairment, disability-adjusted life years, quality-adjusted life years, productivity, and caregiver burden) and economic burden (direct costs, indirect costs, and healthcare resource utilization [HCRU]).
- The SLR followed the Cochrane Methodology, Centre for Reviews and Dissemination and the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) 2020 statement. Pre-specified inclusion and exclusion criteria were formulated according to the PICOS (population, intervention, comparator, outcome, study type) framework.

RESULTS

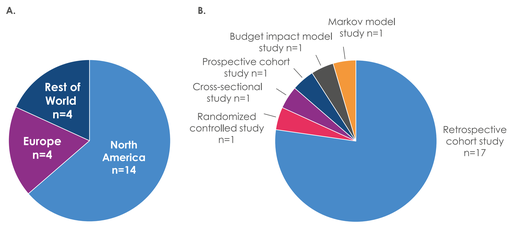
- Of 1804 records identified, a total of 22 studies were included in the analysis following screening (**Figure 1**). These studies involved 351,296,930 participants (1 modeled the US population).
- Low risk of bias was noted in 11/17 (65%) observational studies (8–9 points), whereas 6/17 (35%) observational studies and 1/1 cross-sectional study scored 6–7 indicating medium risk of bias.
- Most patients were ≥65 years, with US and European studies predominantly involving White patients.

Figure 1. Reporting for systematic reviews and meta-analyses (PRISMA) diagram



- The majority of studies were conducted in North America (n=14, 64%; **Figure 2A**) and most were retrospective cohort studies (n=17, 77%; **Figure 2B**).

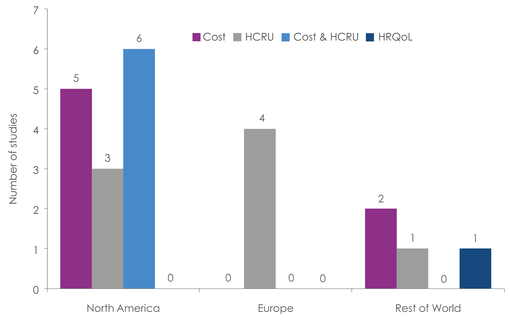
Figure 2. Overview of the 22 studies by A. region and B. type of study



Rest of World included studies in Malaysia, Hong Kong, China, and 1 multinational study.
Europe included studies in Sweden (2 studies), Spain, and the UK.

- Economic burden in the CRM population was reported in 21 studies (95%), while only 1 study reported data on the humanistic burden (**Figure 3**).

Figure 3. Studies by outcome and region

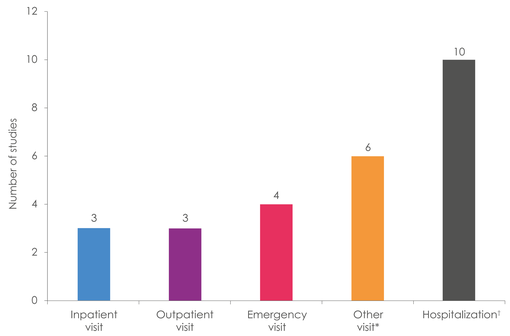


HCRU, healthcare resource utilization; HRQoL, health-related quality of life.
Rest of World included studies in Malaysia, Hong Kong, China, and 1 multinational study.
Europe included studies in Sweden (2 studies), Spain, and the UK.

Economic Burden: HCRU

- Hospitalizations were reported in 10 studies (71%) assessing HCRU outcomes, while only 3 studies (21%) reported inpatient visits, 3 (21%) reported outpatient visits, and 4 studies (29%) reported emergency visits (**Figure 4**).
- HF and CKD were associated with more hospitalizations and longer lengths of stay than other comorbidities; outpatient visits and emergency department visits also increased after HF and CKD diagnoses.
- Black patients were less likely to use healthcare services compared with other race/ethnicity groups, with utilization higher when they presented with more comorbidities.

Figure 4. Studies reporting HCRU outcomes (n=14)

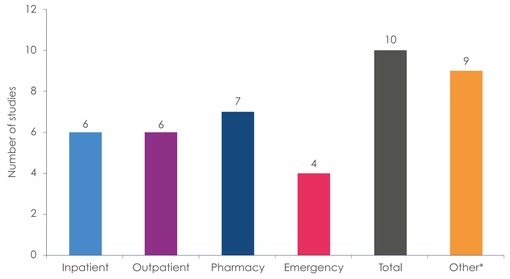


Studies that reported HCRU outcomes included 8 from the US, 2 from Sweden, 1 each from Canada, UK, and Spain, and 1 study involved multiple countries across Europe, Australia, and Asia.
*Other visit: duration of stay, average annualized number of visits, physician visits, number and percentage of HF events and IR for HF of patient subgroups, kidney transplant (events, rate), dialysis (events, rate), hyperkalemia (events, rate), kidney failure, kidney transplant, or dialysis codes (events, rate), dialysis clinic visits, physician visits, long-term care visits, mental health visits, same day surgeries visits, cancer clinic visits, use of any services, level of services use.
†Hospitalization: CVD, non-CVD, HF, other CVD.
CVD, cardiovascular disease; HCRU, healthcare resource utilization; HF, heart failure; IR, incidence rate.

Economic Burden: Cost Data

- The majority of studies with cost data reported total costs (n=10, 77%), but approximately half of the reported costs related to inpatient visits (n=6, 46%), outpatient visits (n=6, 46%), and pharmacy visits (n=7, 54%) (**Figure 5**).
- Inpatient hospital admissions were the highest source of increased costs in patients with CRM conditions, followed by outpatient visits, pharmacy costs, and visits to the emergency room.
- Increased healthcare costs and resource use were associated with a greater number of comorbidities, indicating a larger economic burden for patients with CRM conditions.
- Increasing age was associated with a higher number of comorbidities.
- Higher healthcare expenditure and service utilization were observed among urban insured patients than in the uninsured and racial/ethnic minority populations.

Figure 5. Studies reporting cost data (n=13)



Studies that reported cost data included 10 from the US, 1 each from Canada, Malaysia, and Hong Kong.
*Other: costs related to annual allied health professionals service costs, medical costs (any CVD/CKD diagnosis), prediagnosis, death costs, cancer clinic costs, rehabilitation services costs, mental health costs, same day surgeries costs, physician costs – general practitioner/family medicine, long-term care costs, dialysis clinic costs, budget impact treatment costs, budget impact costs of care.
CKD, chronic kidney disease; CVD, cardiovascular disease.

Humanistic Burden

- Only 1 study reported HRQoL data on patients with CRM; it assessed the depressive symptoms of CKD in 210 patients with T2DM. Significant risk factors were female sex, hypertension, and the severity of T2DM-related CKD.[8]

LIMITATIONS

- There was a sparsity of data from non-US geographies.
- Most studies were retrospective, and only 1 study reported HRQoL outcomes.
- The results were difficult to generalize and comparisons between groups based on social status, race/ethnic group, and geography were complicated.
- Healthcare costs were not adjusted for inflation or the national standard of living so could not be compared over time or between countries.

CONCLUSIONS

- Patients with all 3 CRM conditions had higher costs and HCRU compared with those with fewer comorbidities.
- Targeted interventions are needed in patients with CRM comorbidities to reduce healthcare costs and improve outcomes.
- Further research is warranted to determine the economic and humanistic impact of CRM conditions in lesser studied, high-risk groups, particularly in racial, ethnic minority, and uninsured populations, along with awareness programs and improved access to healthcare resources.

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Presenter: Helena Rodbard, Endocrine and Metabolic Consultants, Rockville, MD, USA; email: hrodbard@comcast.net.

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Disclosures
KC Ferdinand has served as a consultant for Amgen, Boehringer Ingelheim, Eli Lilly and Company, Janssen, and Medtronic. **KC Norris** has served as a consultant for Atlantis Health Care for quality improvement and is supported in part by NIH grants UL1TR000124, P30AG021684, and P50MD017366. **HW Rodbard** has served as a consultant for, and received research support from, Eli Lilly and Company, Medtronic, Merck, Novo Nordisk, Pacira, Regeneron, and Sanofi. **JM Trujillo** has served as a consultant for Novo Nordisk and Sanofi.

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