Cost-effectiveness of novel therapies in Cardio-Renal-Metabolic syndrome: a systematic review

I. Di Cesare [1] , A. Colicchio[2]
[1]Pharmacist, Local Health Authority No. 4 of Teramo, Territorial Pharmaceutical Service, CRFV Abruzzo, Italy
[2]Chief Pharmacist, Intercompany Pharmaceutical Department, Local Health Authority of Bologna, Italy

Introduction

Cardio-renal-metabolic syndrome (CRM) is a multifactorial disorder linking cardiac, renal, and metabolic dysfunction, with high clinical burden and economic impact from hospitalizations, end-stage renal disease, and cardiovascular complications.

Aim and objectives

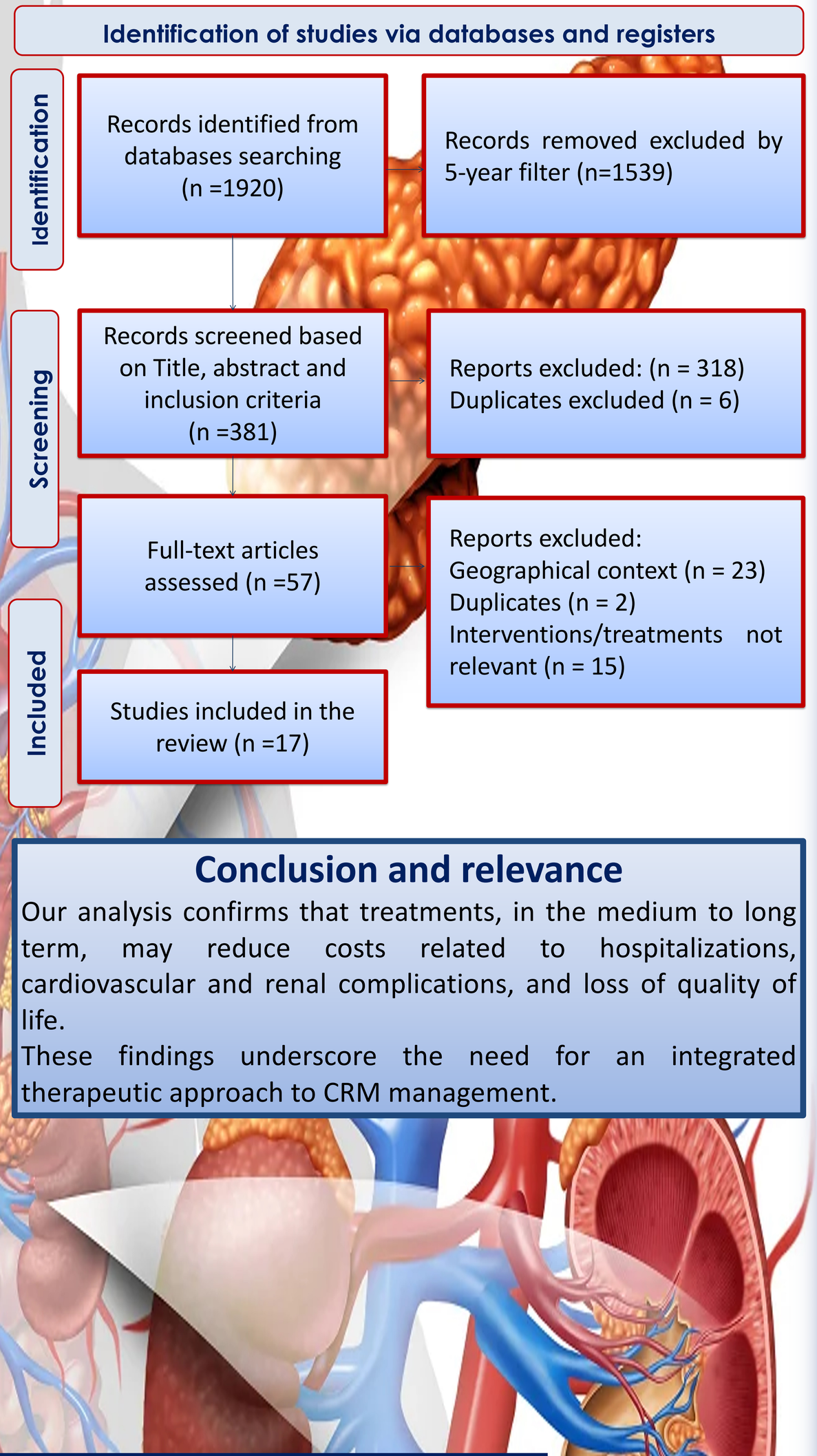
To assess the cost-effectiveness of CRM therapies, focusing on sodium-glucose cotransporter 2 inhibitors (SGLT2i), glucagon-like peptide-1 receptor agonists (GLP-1RA), and mineralocorticoid receptor antagonists (MRA).

Material and methods

A systematic review (SR) was performed in PubMed, according to the Prisma guidelines, for studies published between August 8, 2020, and August 8, 2025.
Two search strategies combined cost-effectiveness terms with diabetes, heart failure (HF), chronic kidney disease (CKD), and CRM. Eligible outcomes included healthcare economic indicators such as the incremental cost-effectiveness ratio (ICER), quality-adjusted life years (QALY), life-years gained, direct costs, and hospitalizations.

Results

SGLT2i (dapagliflozin, empagliflozin, canagliflozin) produced incremental gains of 0,06-1,22 QALY per patient, with ICERs generally below willingness-to-pay thresholds. Dapagliflozin was cost-saving in type 2 diabetes (T2D) in the United Kingdom (UK) and Spain, reducing HF hospitalizations and slowing renal decline; it was also cost-effective in CKD, with increased QALY and sub-threshold ICER in the UK, Germany, and Spain. In non-diabetic CKD in the United States(US), it yielded +2.0 life-years and +1.3 QALY with an ICER≈60.000$/QALY (threshold 100.000-150.000$/QALY), while reducing renal replacement therapy. Empagliflozin added to standard therapy in CKD was dominant in Europe (France, UK, Netherlands), delaying renal progression and reducing HF hospitalizations and dialysis. GLP-1RA were not cost-effective as first-line therapies for T2D at current US prices. However, semaglutide was cost-effective in selected high-risk contexts (cardiovascular disease, obesity), with an ICER≈136.271$/QALY. MRA, particularly finerenone, reduced cardio-renal events and was cost-effective in patients with CKD and T2D: it was found dominant in the Netherlands and with ICERs below thresholds elsewhere (e.g., 8.808£/QALY in England and Wales).



Conclusion and relevance

Our analysis confirms that treatments, in the medium to long term, may reduce costs related to hospitalizations, cardiovascular and renal complications, and loss of quality of life.
These findings underscore the need for an integrated therapeutic approach to CRM management.

Drug Class	Treatment	Main Result (ICER/Economic Status)	Key Clinical Benefits
SGLT2i	Dapagliflozin	Cost-saving in UK & Spain (T2D); Cost-effective in UK, Germany, Spain (CKD)	↓ HF hospitalizations; slowed renal decline
SGLT2i	Dapagliflozin	ICER ≈ $60,000/QALY in non-diabetic CKD (USA)	+2.0 life-years; +1.3 QALY; ↓ renal replacement therapy
SGLT2i	Empagliflozin	Dominant in France, UK, Netherlands for CKD	Delayed renal progression; ↓ HF hospitalizations and dialysis
GLP-1RA	Semaglutide	Cost-effective only in high-risk contexts (CVD, obesity)	ICER ≈ $136,271/QALY
MRA	Finerenone	Dominant in Netherlands Low ICER in England & Wales (£8,808/QALY	↓Cardio-renal events in CKD and T2D patients

Abstract Number: 6ER-007