

CKM, the Liver, and Reaven's Legacy: What a Recurring Naming Debate teaches us about Systemic Disease

Emmanuel Andrès, M.D Ph.D* and Noel Lorenzo-Villalba, M.D

Service de Médecine Interne, Hôpitaux Universitaires de Strasbourg, Strasbourg, France.

*Correspondence:

Emmanuel Andrès, M.D Ph.D, Service de Médecine Interne, Hôpitaux Universitaires de Strasbourg, Strasbourg, France.

Received: 12 Aug 2026; **Accepted:** 07 Sep 2026; **Published:** 18 Sep 2026

Citation: Emmanuel Andrès, Noel Lorenzo-Villalba. CKM, the Liver, and Reaven's Legacy: What a Recurring Naming Debate teaches us about Systemic Disease. *Endocrinol Metab Nutr.* 2026; 5(2): 1-3.

Keywords

Obesity and diabetes, insulin resistance, metabolic syndrome.

In 2023, the American Heart Association proposed the cardiovascular-kidney-metabolic (CKM) syndrome, organizing a growing body of evidence around three interconnected organ systems — heart, kidney, and the broader metabolic terrain of obesity and diabetes [1,2]. This was a considerable achievement: a four-stage clinical framework, a common vocabulary shared by cardiologists, nephrologists and endocrinologists, and a staging tool that has already found its way into risk calculators, guideline language and the design of outcome trials [3]. Any critical reading of this framework should begin by acknowledging that achievement in good faith. What follows is offered in that spirit — as a respectful question about scope, not a challenge to the underlying science, which remains sound and clinically useful.

The question worth asking, carefully, is whether three organs are the right number. The AHA's own advisory text is candid about this: it notes that “nearly every major organ system” is affected by the process it describes, mentioning kidney failure, premature cognitive decline, obstructive sleep apnea, increased cancer risk, and steatosis liver disease within its pages [1,4]. The acronym itself, understandably, could not accommodate every one of those observations. But metabolic dysfunction-associated steatosis liver disease (MASLD) occupies a somewhat different position than the others: it is not merely a downstream complication but, on the AHA's own mechanistic account, close to the origin of the process — excess and dysfunctional adipose tissue expresses itself in the liver early, and the resulting hepatic inflammation and insulin resistance appear to amplify the cardiovascular and renal injury the syndrome was built to describe [4,5]. If that reading of the physiology holds, the liver may deserve more prominence in the

framework's architecture than it currently receives — a point made with increasing frequency, and increasing data, by hepatology colleagues rather than as a criticism from outside the field.

The clinical data supporting this view are accumulating. A large multinational cohort of patients with biopsy- or elastography-confirmed MASLD found that liver-stiffness progression and liver-related clinical events — hepatic decompensation, hepatocellular carcinoma, transplantation — tracked with CKM stage in a graded, step-wise fashion [6]. This suggests a bidirectional relationship worth taking seriously: CKM staging appears informative for liver outcomes, and it seems reasonable to ask whether liver disease severity should, in turn, inform cardiovascular and renal risk stratification. At present, the framework primarily allows for the first direction of that relationship, which may simply reflect how young this evidence base still is rather than any deliberate omission.

Several groups of colleagues have already proposed, thoughtfully, that the liver be made explicit within the framework — variously suggesting cardiovascular-kidney-liver-metabolic (CKLM) or liver-cardiovascular-kidney-metabolic (CLKM), depending on whether the liver is placed alongside the kidney or given a more upstream position consistent with its role in the adipose-tissue cascade [4,6,7]. These proposals have not yet converged on a single validated staging system, which is understandable given how recent the supporting cohort data are; it may be premature to expect consensus this quickly, and the absence of agreement should be read as a sign of active, healthy scientific discussion rather than confusion.

A parallel effort, organized independently in Europe, chose a different path. Rather than adding a further letter to an organ-based

acronym, the European Atherosclerosis Society proposed “systemic metabolic disorder” (SMD), a three-stage framework built around shared pathophysiological mechanisms — dysfunctional adiposity, insulin resistance, atherogenic dyslipidemia — with heart, liver and kidney treated from the outset as co-equal targets of the same underlying process, and metabolic dysfunction-associated steatohepatitis (MASH) written into the diagnostic criteria for Stage 2 [8]. It is a considered, alternative answer to the same question the AHA framework raises, and both should be read as complementary attempts to solve a genuinely difficult problem rather than as competing claims to be right.

A debate the field has had before

It is worth remembering, with some humility, that this is not the first-time internal medicine has faced this exact question. In 1988, in his Banting Lecture, Gerald Reaven described what he called “syndrome X” — not a checklist of organs or measurable criteria, but a physiological argument that insulin resistance and compensatory hyperinsulinemia linked glucose intolerance, dyslipidemia, hypertension and cardiovascular risk through a single, shared mechanism [9]. Reaven deliberately declined to propose fixed diagnostic thresholds, arguing that the physiological concept mattered more than any particular checklist used to operationalize it. When professional societies later did convert the concept into a checklist — waist circumference, triglycerides, HDL cholesterol, blood pressure, fasting glucose, under the label “metabolic syndrome” — a joint statement from the American Diabetes Association and the European Association for the Study of

Diabetes offered a careful, and at the time controversial, appraisal questioning whether the syndrome, so defined, added diagnostic or therapeutic value beyond the sum of its individual components [10]. That appraisal did not settle the matter definitively, and metabolic syndrome remains in wide clinical use to this day, but it is a useful precedent: the tension we are describing here — between a mechanistic, process-based understanding of multi-organ disease and a checklist built for clinical convenience — is a recurring one in this field, not a new failing specific to CKM. Syndrome X, metabolic syndrome, CKM, and SMD can reasonably be read as four successive attempts, over nearly four decades, to describe the same underlying biological continuum with the tools available at the time.

What this recurring debate says about the internist’s vantage point

There is, we would suggest, a genuine and somewhat understated lesson here for internal medicine as a discipline. Internists are, by training and by tradition, the clinicians least attached to any single organ boundary and most accustomed to following a pathophysiological process wherever it leads — across the heart, the kidney, the liver, and beyond — without needing the process to first be renamed in their own specialty’s honor. This is not a claim of superiority over our cardiology, nephrology, hepatology or endocrinology colleagues, whose organ-specific expertise remains indispensable and whose advisories are the very foundation of this discussion; it is, rather, an observation about vantage point, illustrated schematically in the Figure. The recurring difficulty

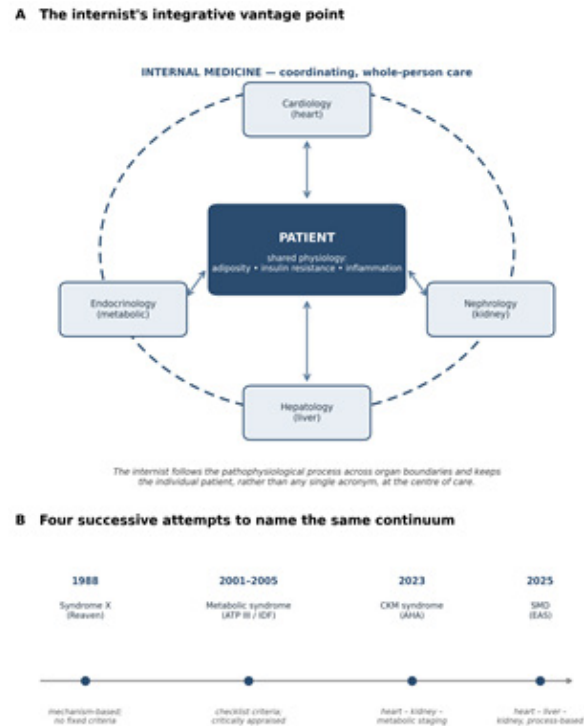


Figure Panel A: The internist’s position relative to organ-specific specialties within a shared, adiposity-driven pathophysiological continuum. **Panel B:** four successive frameworks proposed, over nearly four decades, to describe the same underlying continuum.

these successive frameworks have had in settling on a fixed set of organs may be less a shortcoming of any one committee and more an inherent property of systemic, adiposity-driven disease itself — a disease that does not, by its nature, respect the divisions between specialties.

The point of the schema is not that internists should displace cardiology, nephrology, hepatology or endocrinology in managing any one organ — they should not, and do not — but that someone in the care pathway needs to hold the whole person in view while the organ-specific evidence continues to evolve and while the nomenclature continues to be debated. That role, historically, has belonged to internal medicine: caring for the whole patient, coordinating between specialties, and treating the patient's physiology as one continuous system rather than a set of separately governed organs. This global, integrative posture is precisely what allows a clinician to hold frameworks such as CKM or SMD lightly — using each where it is validated and useful, remaining open to hepatology's growing evidence base on the liver's role, and resisting the temptation to treat any single acronym as a final or complete description of the patient in front of them. This is offered not as a criticism of any of the societies involved, all of whom have advanced the field considerably, but as a reminder of a value internal medicine has long tried to protect in the global management of the individual: that the patient, considered as a whole, comes before the label attached to any one of their organs.

A concluding, modest proposal

None of this argues for abandoning CKM, nor for uncritically adopting SMD, nor for reviving syndrome X under a new name. Emerging therapeutics reviews already evaluate SGLT2 inhibitors, GLP-1 receptor agonists and finerenone for their combined cardiac, renal and hepatic effects, which suggests that clinical pharmacology has, in practice, already moved toward treating these organs together, regardless of which acronym eventually prevails [11]. Perhaps the most useful step, in the meantime, is simply for each new framework to state plainly which organs it does and does not yet include, and why — so that clinicians outside the authoring specialties can situate their own patients, and their own organs of expertise, within the picture with appropriate nuance. The liver, on the evidence currently available, appears to merit a clearer place at that table [1-8].

Disclosures: The authors report no conflict of interest related to the content of this Perspective. Professor E. Andr s has received honorarium for multiple laboratories implicated in GLP-1 receptor agonists and SGLT2 inhibitors.

Contributors: EA and NLV drafted the manuscript. All authors approved the final version. Use of Artificial Intelligence Tools: During manuscript preparation, the authors used large language model-based tools for editorial assistance, including ChatGPT

(OpenAI) and Claude AI (Anthropic). These tools were used exclusively for language editing, structural refinement, and stylistic improvement of the text. All scientific content, data interpretation, and conclusions were generated and validated by the authors, who retain full responsibility for the integrity of the manuscript.

References

1. Ndumele CE, Rangaswami J, Chow SL, et al. American Heart Association. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. *Circulation*. 2023; 148: 1606-1635.
2. Ndumele CE, Neeland IJ, Tuttle KR, et al. American Heart Association. A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association. *Circulation*. 2023; 148: 1636-1664.
3. Ferdinand KC. An overview of cardiovascular-kidney-metabolic syndrome. *Am J Manag Care*. 2024; 30: 181-188.
4. Massy ZA, Druke TB. Combination of cardiovascular, kidney, and metabolic diseases in a syndrome named cardiovascular-kidney-metabolic, with new risk prediction equations. *Kidney Int Rep*. 2024; 9: 2608-2618.
5. Soliman GA. Cardiovascular-Kidney-Metabolic (CKM) syndrome staging and relevance to precision nutrition. *Nutrients*. 2026; 18: 1430.
6. Zhou XD, Chen QF, Fan QY, et al. Cardiovascular-kidney-metabolic syndrome and the risk of liver fibrosis progression and liver-related events in MASLD. *Hepatology*. 2026; 84: 529-541.
7. Zhou XD, Fan QY, Targher G, et al. MASLD as a systemic metabolic disease: expanding the scope of cardiovascular-kidney-metabolic (CKM) syndrome. *Sci China Life Sci*. 2026; 69: 1950-1965.
8. Romeo S, Vidal Puig A, Husain M, et al. European Atherosclerosis Society Consensus Panel. Clinical staging to guide management of metabolic disorders and their sequelae: a European Atherosclerosis Society consensus statement. *Eur Heart J*. 2025; 46: 3685-3713.
9. Reaven GM. Banting Lecture 1988. Role of insulin resistance in human disease. *Diabetes*. 1988; 37: 1595-1607.
10. Kahn R, Buse J, Ferrannini E, et al. American Diabetes Association; European Association for the Study of Diabetes. The metabolic syndrome: time for a critical appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2005; 28: 2289-2304.
11. Bharaj IS, Brar A, Kacheria A, et al. Contemporary and emerging therapeutics in cardiovascular-kidney-metabolic (CKM) syndrome: in memory of Professor Akira Endo. *Biomedicines*. 2025; 13: 2192.