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Restoring Guidelines: EBM-X to Bring Critical Thinking and Humility Back to Evidence-Based Medicine

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Introduction

When Gordon Guyatt at McMaster University introduced the term Evidence-Based Medicine (EBM) in 1992, building on the work of David Sackett and colleagues, the idea was revolutionary (Wyer, 2019). Rooted in problem-based learning (Wyer, 2019), EBM asked students and clinicians to move beyond tradition and authority, combining three key elements: the best available evidence, professional expertise, and the patient's values. The Users' Guides to the Medical Literature in JAMA (Users' Guide to the Medical Literature, JAMA Network, n.d.) provided this vision structure, showing clinicians how to ask sharper questions, appraise studies with rigor, and apply findings at the bedside. The approach spread rapidly through medical schools and residency programs, reshaping how a generation of physicians thought about care.

Nonetheless, its success brought a paradox. A movement that began as a call for critical engagement with research too often hardened into something else: protocolized obedience. Evidence was treated as if it were fixed truth rather than evolving knowledge (Boyd et al., 2005). Guidelines, meant to guide, risked becoming dogma. Uncertainty was pushed to the margins, and harms were sometimes overlooked. As Groopman warns in How Doctors Think, when doctors stop pausing to ask questions, they slip into autopilot—decisions guided by algorithms and shortcuts rather than genuine reasoning. It may feel efficient, but it blinds us to nuance, context, and the exceptions that define real patients (Groopman, 2007).

The COVID-19 pandemic exacerbated this tension. At its best, EBM delivered large, pragmatic trials within months, such as RECOVERY, which identified dexamethasone as a lifesaving therapy while ruling out ineffective ones (Pessoa-Amorim et al., 2021). At its worst, weak or preliminary studies—on hydroxychloroquine, ivermectin, convalescent plasma—were amplified as definitive truths, driven by media attention, political pressure, and a hunger for certainty (Barnett et al., 2022). Observational findings were treated as fact while more rigorous randomized evidence lagged (Schwartz et al., 2021). Even after better evidence emerged, practice often got stuck with first impressions. This swing between evidence neglected and evidence overstated sits at the heart of EBM's paradox.

The goal of this paper is not to reject EBM but to recover its critical core. Evidence should be valued, yes—but applied with judgment, humility, and awareness of context. When practiced as a reflective process—one that questions assumptions, carefully appraises methods, and communicates uncertainty openly—EBM can reach its full potential: not a rigid doctrine, but a living practice that learns and adapts alongside science and patients.

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The Power and Promise of EBM

EBM evolved from the recognition that care varied dramatically depending on where and by whom patients were treated. In 1990, the U.S. Institute of Medicine called for more standardized guidelines to ensure that recommendations were based on reproducible evidence. From this came frameworks like the GRADE system, now widely used to rate both the strength of evidence and the weight of recommendations (Committee to Advise the Public Health Service on Clinical Practice Guidelines & Institute of Medicine, 1990).

Systematic reviews and randomized controlled trials (RCTs) have become the foundation of this movement, while high-quality observational studies have provided crucial insights into safety, rare outcomes, underrepresented groups, and real-world practice. Over the past three decades, EBM has not only reshaped research and education but also transformed the daily culture of medicine. It gave clinicians a common language of rigor and transparency, replacing "eminence-based" authority with structured methods of appraisal (Djulbegovic & Guyatt, 2017). However, no framework can eliminate the human tendencies that shape reasoning. Biases and first impressions may still influence clinical decisions. The real promise of EBM lies not in its methods alone but in how we use them: as a compass, not a script.

The Fragility of Evidence Without Context

The tools of EBM are only as strong as the context in which they are applied. However, the hierarchy of evidence can be misleading. A poorly designed RCT may still outrank a carefully conducted observational study, and systematic reviews are only as solid as the studies they compile (Vatkar et al., 2025; Wallace et al., 2022). What appears to be the "highest level" of evidence can, in practice, rest on fragile foundations.

Evidence is never absolute. It can be distorted by small sample sizes, selective populations, publication bias, and commercial or political pressures, and still be considered "high-quality" simply based on the type of study. To confuse "Level 1 evidence" with reliability is to mistake hierarchy for quality (Every-Palmer & Howick, 2014; Greenhalgh et al., 2014).

Also, evidence should not exist in a vacuum—it should be filtered through the physician's thinking. Cognitive traps, such as the availability heuristic, where the most vivid or recent case overshadows the full differential diagnosis, can lead clinicians into a misguided decision. Anchoring and premature closure further compound the risk, turning decisions labeled as "evidence-based" into bias-driven judgments that only mimic science. Croskerry (2003) provides a systematic account of these cognitive dispositions to respond, cataloguing common biases and outlining strategies to counter them. Central among these is metacognition—a reflective stance that prompts clinicians to step back, examine their own reasoning, and thereby reduce diagnostic error. This practice not only strengthens decision-making but also holds considerable promise for improving patient safety.

The COVID-19 pandemic magnified this fragility. Early enthusiasm for small, low-quality studies drove waves of unproven therapies. Only later did well-powered studies, such as RECOVERY, provide clarity, often contradicting initial claims. Even then, research efforts continued to chase dead ends. The remdesivir saga is telling: conflicting trial results led to shifting recommendations and regulatory confusion (Janiaud et al., 2021). Meanwhile, an unprecedented flood of more than 2,800 RCTs was registered in the first year of the COVID-19 pandemic, with most proving to be underpowered, duplicative, and wasteful (Nasrallah et al., 2020). Rather than restoring trust in science, the noise ultimately deepened skepticism.

This problem is not unique to pandemics. Statins tell a similar story. Initially approved for secondary prevention, their use quickly expanded to low-risk populations after guideline thresholds were lowered. Many of those decisions were made by committees with industry ties (Demasi, 2018). Trial data remain inaccessible to independent review (Meade et al., 1999). Run-in periods excluded patients who could not tolerate the drugs, artificially minimizing reported harms. For primary prevention, the gains may amount to only a few days of added life expectancy (Meade et al., 1999). This is not shared decision-making—it is the medicalization of risk, built on selectively presented data.

Here, the same warning again applies: impeccable logic, applied to incomplete or distorted evidence, can produce confident but misguided recommendations.

False Security and Iatrogenic Risk

The rapid growth of medical science has deepened the EBM paradox. More evidence and more guidelines can fragment reasoning and distance practice from context. In this environment, it is tempting to believe that simply "following the guidelines" guarantees good care. Yet rules applied without reflection can be as harmful as ignoring them.

At the bedside, this uncritical reliance can lead to iatrogenesis—not because the evidence itself is weak, but because it is applied without nuance, detached from the patient's story. In academia, the same risks are evident in the way literature is consumed: ab-

stracts are skimmed, algorithmic summaries replace careful reading, and conclusions are accepted without scrutiny. The result is an appearance of knowledge without its substance.

Overtreatment often arises from this blind adherence. Among older adults, polypharmacy can trigger cascades of adverse events, with benefits that may be marginal when weighed against frailty and life expectancy (Boyd et al., 2005). Undertreatment, by contrast, occurs when populations excluded from major RCTs—frail elders, patients with multimorbidity, underrepresented minorities—are left without evidence to guide care (Boyd et al., 2005; Denson & Mahipal, 2014). Guidelines then fail to capture the realities of those most in need. What promises safety becomes an illusion (Ioannidis, 2016), echoing Greenhalgh et al.'s (2014) warning against the captivity of uncritical evidence use.

Medical training illustrates the same tension. The second-year student wrestles with complexity, building durable knowledge through effortful learning. By the final year, speed and convenience take over, and information can be mistaken for mastery. Quoting trial abstracts without engaging with full studies may give the appearance of expertise, but it risks overlooking bias, limits of applicability, and the nuance of bedside insight (Croskerry, 2003).

This erosion of critical engagement extends into practice. Abdulnour et al. (2025) describe the hazards of "never-skilling," "mis-skilling," and "deskilling"—doctors who avoid deep study, absorb oversimplified takeaways, or lose competence through overreliance on digital tools. The risks are twofold: patients are harmed by oversight, and the surrender of critical thought weakens the profession itself (Hayes et al., 2017).

EBM and the Problem of Overdiagnosis

Screening tests were meant to showcase EBM's strengths. Instead, they revealed one of its most troubling paradoxes: overdiagnosis. By identifying conditions that would never have caused symptoms or death, screening can turn healthy people into patients—exposing them to biopsies, surgeries, and treatments they never needed. The result is anxiety, harm, and medicalization without benefit (Welch & Black, 2010).

Prostate cancer screening with PSA is a striking example. In the 1990s, incidence soared, but many tumors were indolent. Trials later showed little to no mortality benefit, while countless men endured the complications of unnecessary biopsies, surgery, or hormonal therapy (Welch& Albertsen, 2020). Breast cancer tells a similar story: trials like the Malmö Mammographic Screening Trial revealed that 20–25% of screen-detected tumors represented overdiagnosis, their apparent survival gains a statistical mirage (Bleyer & Welch, 2012).

The pattern repeats across diseases. In thyroid cancer, imaging advances tripled incidence since the 1970s, yet mortality remained flat—most papillary cancers never required treatment (Ahn et al., 2014). In melanoma, public screening campaigns fueled a six-fold rise in thin lesions diagnosed since 1975, but deaths did not decline (Welch et al., 2019). These examples illustrate how an unexamined push for early detection can inflate survival statistics, drive overtreatment, and subtly erode patient trust.

The Efficacy–Safety Imbalance in EBM

Most trials are designed to prove benefit, not harm. Endpoints are chosen to demonstrate efficacy—reduced mortality, improved symptoms, or favorable surrogate markers—while safety is often treated as a secondary consideration. Sample sizes, statistical power, and analytic plans are built to maximize the chances of detecting benefit. Harms, especially rare or long-term ones, are left for later. (Ioannidis, 2016) This imbalance also reflects funding priorities. Sponsors want approval, and trials are designed to demonstrate that a drug is effective. Minor side effects are tolerated; major harms emerge later, once the drug is already in use. By then, millions may have been exposed. (Jacob, 2018; Unger et al., 2020; Waxman, 2005)

The story of Vioxx® (rofecoxib) is a stark reminder. Approved in 1999 for its impressive efficacy in pain and inflammation, it was soon prescribed to millions. But within a few years, the VIGOR trial revealed a markedly increased risk of cardiovascular events, including heart attacks and strokes (Bombardier et al., 2000; Jüni et al., 2004). Withdrawn in 2004, it left behind thousands of preventable deaths.

Smith et al. (2003) made this imbalance vivid with their satirical "systematic review" of parachute use, concluding that there was insufficient RCT evidence to prove parachutes prevent death. The joke underscored a serious point: EBM has often undervalued observational evidence, even when it clearly speaks to safety. In practice, long-term risks are rarely captured in RCTs but are revealed in real-world cohorts and case–control studies (Nazha et al., 2021). If efficacy continues to dominate trial design and appraisal, patients will remain vulnerable to unseen harms.

Critical Thinking as the Missing Element

Critical thinking begins with skepticism, but medicine has not always trained its students to doubt. For years, science was presented as objective truth,

only to have trainees later discover how often research is skewed by flawed design, selective reporting, or practices such as p-hacking and HARKing (Volpe et al., 2025; Wyer, 2019). To acknowledge this fallibility is not to weaken science, but to strengthen it: evidence is always provisional, always open to re-examination.

RCTs are powerful, but even they can mislead. Trials that stop early for apparent benefit often exaggerate effects. Others may be funded or designed with hidden assumptions that tilt results. Asking who funded this, why it ended, and under what assumptions it was built? It should be as natural to clinicians as checking a patient's vital signs.

Patients, too, are not average. Biology, background, and values vary, and evidence that applies to one group may not apply to another. The risks of ignoring this are already clear: health algorithms trained on biased data underestimate the needs of Black patients, perpetuating inequity. To avoid repeating such mistakes, clinicians must ask: Whose evidence is this? For which patient? Under what assumptions? Clinicians are prone to shortcuts, such as anchoring or availability bias—where the most vivid case overshadows the correct diagnosis (Norman & Eva, 2010). Critical thinking is the antidote. It prompts us to ask, What else could it be? What doesn't fit? Combined with humility and patient values, it restores balance to EBM, turning evidence from dogma into a compass (Groopman, 2007; Volpe et al., 2025).

Restoring Balance: Toward EBM-X (Evidence-Based Medicine for Complexity)

The future of EBM is not abandonment, but transformation. The hierarchy of evidence remains valuable, but it must be integrated into a framework that is balanced, context-sensitive, and humble. We propose EBM-X, where the "X" stands for examination, epistemic humility, and complexity. This model not only asks what we know, but also what we don't. It requires clinicians to question evidence, think about the mechanisms of disease, and remain mindful of the "unknown unknowns" that shape health.

In this model, guidelines are not blueprints but starting points. Evidence is weighed against biological plausibility and systems thinking, recognizing that most conditions—such as chronic pain, diabetes, and depression—emerge from complex interplays between biology, environment, behavior, and social context. Mechanistic reasoning helps bridge the gap between trial data and the realities of patients who rarely meet trial criteria.

One might argue that critical thinking is already part of the current vision of EBM—and in principle, it is. The challenge is that it is rarely emphasized or safeguarded, leaving clinicians vulnerable to practicing "evidence" without reflection. Other high-stakes fields show how this gap can be closed. In aviation, for example, pilots know that flaps must be extended before takeoff; failing to do so risks catastrophic crashes.

Checklists exist for this reason, but fourth-generation aviation systems now take it a step further, using alarms and automatic overrides to ensure that this critical step is not missed. The "X" in EBM-X serves as a similar reminder. It is not a reinvention of EBM, but a safeguard against its most dangerous omission—ensuring that questioning, reflection, and contextual reasoning are not optional extras, but essential procedures embedded into daily practice.

A defining feature of EBM-X is time with patients. Reflection, questioning, and context are only possible when clinicians listen carefully to the patient's story, understand their fears and priorities, and situate evidence within lived experience. Time at the bedside is not inefficiency—it is the raw material of clinical reasoning.

This rebalancing requires humility. No study, meta-analysis, or guideline should dictate care independently. Training must go beyond statistics to include epistemology, clinical reasoning, and decision-making under uncertainty (Janiaud et al., 2021). As Ginsburg has argued, valuing bedside teaching and reasoning alongside research productivity is vital to cultivating clinicians who think critically (Nasrallah et al., 2020).

Ultimately, EBM-X does not replace the old model; it completes it. It reframes EBM from a rigid hierarchy into an evidence ecosystem—where data, mechanisms, patient values, and uncertainty come together. In this way, EBM shifts from being a rulebook to being a compass: one that points not only to what is known, but to what we must still discover.

Conclusion

Evidence has always been central to medicine, but evidence alone cannot think. The stories of Vioxx, PSA screening, mammography, and COVID-19 therapies remind us how easily EBM can mislead when stripped from context or applied without reflection. There should be a clear warning: physicians who stop questioning risk being guided not by reasoning but by habit, shortcut, or algorithm (Groopman, 2007).

EBM-X offers a way forward. It asks us to combine evidence with humility, to weigh data alongside mechanisms, and to restore the centrality of the patient's story. It reminds us that time spent at the bedside is not wasted, but rather the foundation of wise care. Practiced this way, EBM becomes what

it was meant to be: not static doctrine, but a living process that adapts with science and with patients, reducing—not compounding—the risks of error.

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Conflicts of Interest

The authors declare no conflict of interest.

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