

## Evidence-balanced Medicine: “Real” Evidence-based Medicine in the Elderly

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### Case History

Case 1: An 85-year-old male with past history of hypertension is otherwise healthy and enjoys his daily walks and good food. During a health screening, he was found to be hyperlipidaemic (LDL 3.4 mmol/L; HDL 1.0 mmol/L). He was started on simvastatin 20 mg nocte by his physician. He developed muscle pain and weakness that interfered greatly with his ability to exercise and quality of life.

Case 2: An 85-year-old female with advanced Alzheimer’s dementia who is bedbound and on nasogastric tube feeding has been newly diagnosed with chronic kidney disease stage 3. Her blood pressure is 125/80 mmHg. Her physician is wondering whether she will benefit from angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs) in preventing progression to end-stage renal disease (ESRD).

Developed countries around the world (including Singapore) are aging at an unprecedented rate. Against this backdrop, the above case scenarios have now become increasingly commonplace in daily “real” clinical practice. Often, the clinician is confronted with an elderly patient who does not fit the classical bill of the typical “surreal” patient recruited in randomised controlled trials (RCTs), either in terms of age, comorbidities, functional status or vulnerability to adverse drug reactions.<sup>1-4</sup>

Our first case developed significant side effects after a seemingly “standard” dose of statin, while in the second case, there is hesitancy as to whether the preventive benefits seen in more robust younger patients can be extrapolated to frail older adults with multiple comorbidities and limited life expectancy. Given the medical complexity, heterogeneity and diverse sociocultural background of the elderly, how does one realistically apply evidence-based medicine (EBM) so that care is customised to their unique needs?<sup>1,5</sup> Or is the pursuit of good EBM practice an elusive dream in the “real” world of frail elderly patients?

### Premise and Promise of EBM (Advent from Eminence-based Medicine)

To understand EBM thoroughly, it is important to review its history and the environment in which EBM arose (Fig. 1).<sup>6</sup> Up to the early 1970s, it was thought that medical decisions made by physicians were by far appropriate. Through medical education, continuing education, journals, individual clinical experience and interaction with other colleagues, it was assumed that physicians “always thought the right thoughts and did the right things”.<sup>6</sup> However, over the following 2 decades, wide practice variations were documented<sup>7</sup> and surprisingly, large proportions of procedures performed by physicians were judged by experts to be inappropriate.<sup>8</sup> In addition, the well known assertion that only 15% of medical practices were based on clinical trials was made.<sup>6,9</sup>

EBM was born into this environment in 1991 when Guyatt first coined the term “evidence-based medicine”.<sup>10</sup> The following year, he used this term again in another paper in the Journal of the American Medical Association (JAMA)

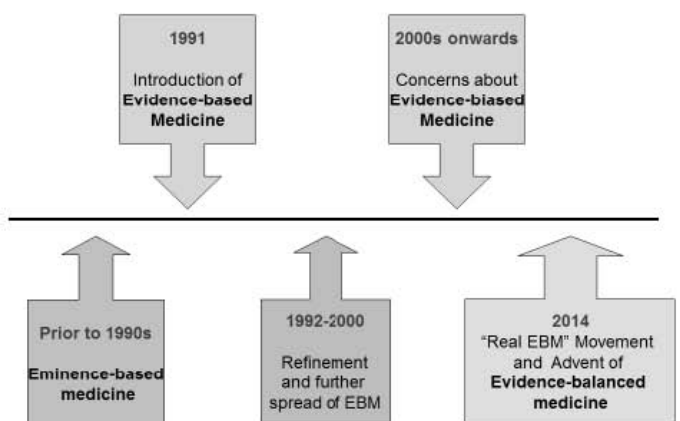


Fig. 1. Key milestones in evidence-based medicine.

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entitled “Evidence-based Medicine: A New Approach to Teaching the Practice of Medicine”.<sup>11</sup> The tradition, anecdote, and theoretical reasoning of “eminence-based medicine” would be replaced by the use of available research evidence to guide clinical decisions rather than relying on the opinion of clinical experts.<sup>11</sup> The initial introduction of EBM did not see much mention of patient values. Over the ensuing 5 years, patient values and preferences were incorporated into the concept of EBM. The most widely cited definition of EBM that emphasised “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients” was put forth by Sackett, who is widely regarded as the “father of EBM”.<sup>12</sup> Sackett further developed this definition to explicitly include patient values by stating that “EBM is the integration of best research evidence with clinical expertise and patient values”.<sup>13</sup> From there, the rest is history. Use of hierarchies of evidence, adoption of clinical practice guidelines based on research evidence, and widespread teaching of EBM were among some of its impressive results. To say that EBM has revolutionised the way many physicians including ourselves practise medicine would be a gross understatement.

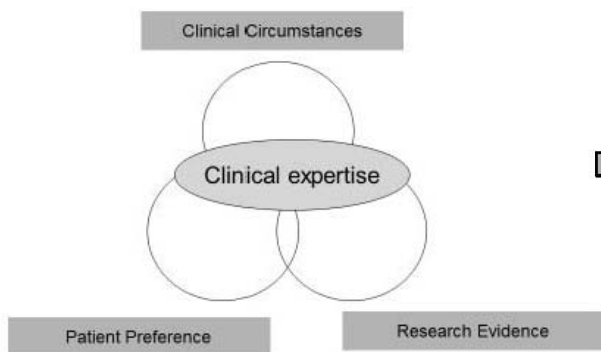
### Caveats of EBM

Yet, as with all good things, there is often a downside that is often only discovered later on. While it is clear that EBM has gone a long way in improving rational clinical practice, it has its pitfalls that we need to be cognisant about. Overly rigid application of evidence and clinical guidelines in routine patient care results in the practice of “cookbook” medicine and over-standardisation of clinical practice.<sup>5</sup> This could lead to inappropriate and suboptimal care where some patients may be harmed in the process. Furthermore, discouragement and eventual downgrading of good clinical

reasoning and judgment on the part of physicians may sadly result.<sup>1-3</sup> As mentioned, most randomised clinical trials (RCT) and consequently, clinical practice guidelines based on them reflect the best available evidence albeit for the “average” patient. More pointedly, since older and sicker patients have been excluded from reference clinical trials, many older people encountered in real life clinical practice simply do not fit the description of the “average” patient.<sup>1,4</sup> The unthinking application of clinical guidelines and rules in older people can adversely influence the clinical benefit-risk ratio of the intended intervention. For older, sicker, and more complex patients, the simplistic way of using EBM could result in “evidence-biased medicine” (Fig. 2).<sup>3</sup> The latter has been likened to “using evidence in the manner of the fabled drunkard who searched under the streetlamp for his doorkey because that is where the light was, even though he had dropped the key somewhere else”. In other words, it’s applying the inappropriate evidence to older frail people just because that’s the only evidence available.

So clearly, uncritical application of EBM in older persons can result in failure to individualise the care of heterogeneous patients seen on a daily basis.<sup>2,3</sup> Specific pitfalls relate to the failure to take into account their unique medical, functional and social aspects. Among medical aspects, multimorbidity and multiple medications may increase potential risks while remaining life expectancy may influence the anticipated benefits of the treatment in question. Physical and cognitive function may influence the selection of treatment options. Social aspects such as the home environment and availability of caregivers could also differentially weight the appropriateness of different treatment options. Over and above these points, the stated aspiration of EBM has been to take into account patient values and preferences in decision making.<sup>2,5</sup> We are of the opinion that this is often forgotten in the single-minded

### Evidence-based Medicine (EBM)



### Evidence-biased Medicine (EBiM)

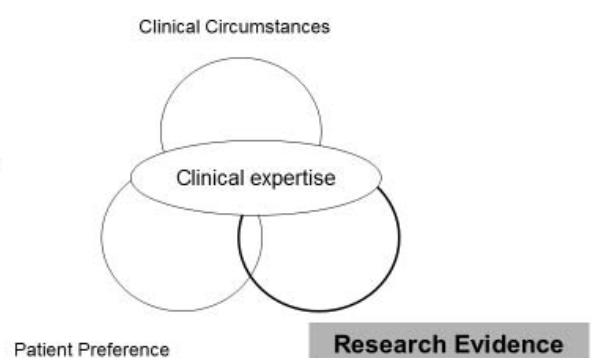


Fig. 2. Comparison of evidence-based medicine (EBM) vs evidence-biased medicine (EBiM). In EBM, clinical judgment is exercised in integrating the research evidence with clinical context and patient values and preferences. In contrast, EBiM emphasises the supremacy of evidence over other considerations, resulting in dogmatic rigid adherence to guidelines and cookbook medicine.

application of EBM-directed clinical guidelines in busy clinical practice. Eliciting values and preferences require a conversation with older patients and their caregivers that goes beyond technical care aspects and may involve some form of shared decision making.<sup>2,5</sup> Nevertheless, we are struck by the possibility that many of these pitfalls may be avoided when the true spirit of EBM envisioned by its founders is adhered to, particularly the emphasis on the individual patient and the need to account for patient values and preferences. There should also be a greater willingness to recognise that in many clinical situations involving care of frail older patients, no applicable research evidence really exists because they are so far removed from the “average” patient in RCTs.<sup>1-4</sup> In these instances, physicians must sail in uncharted territory.

### Renaissance of EBM (Advent of Evidence-balanced Medicine)

There are exciting developments in recent years in response to the repeated calls for EBM to emphasise person-centredness and retain relevance in the “new normal” of frail older adults who now form the “core business” of health services.<sup>2,3</sup> These include the “Choosing Wisely” campaign to promote discussions about the safety and appropriateness of medical tests, medications and procedures;<sup>14</sup> updated Beers Criteria for potentially inappropriate medication use in older adults;<sup>15</sup> development of elderly-friendly guidelines for specific diseases;<sup>16,17</sup> dedicated forums to discuss the application of EBM in the elderly;<sup>18</sup> and the recently launched “Campaign for Real EBM.” This campaign aims to address concerns with ersatz EBM by

refocusing on providing useable evidence that can be combined with context and professional expertise so that individual patients get optimal treatment.<sup>2</sup> This advent of evidence-balanced medicine (EBLM) is congruent with developments elsewhere,<sup>19</sup> and heralds a return to the original spirit of EBM.

We would therefore like to propose the “PCR triangle” of EBLM to advance its application and practice in geriatrics care (Fig. 3), comprising the three-pronged approach of patient at the apex, and supported at the base by clinician and research. The hallmark of EBLM is ethical person-centric care that embraces the complexity and diversity of frail older adults through an individualized approach.<sup>2,3</sup> Thoughtful application of preventative intervention such as cancer screening or primary prevention of cardiovascular diseases should incorporate an estimation of the older person’s life expectancy as well as the preventative intervention’s lag time to benefit to avoid overdiagnosis and overtreatment.<sup>1,5</sup> An individual’s health preference is another factor that should influence decisions about preventative interventions.<sup>1-3</sup> When deliberating about intensive or invasive treatments for serious illnesses, older persons are often less concerned with the chances of dying (mortality outcomes) compared with the prospect of surviving with disability (functional, cognitive and quality of life outcomes).<sup>3</sup> As illustrated by our first case example, their willingness to take medications for primary prevention of cardiovascular disease is often less related to potential benefits than to potential adverse effects.<sup>20</sup> Our task is to present the evidence in a format that older persons can understand so as to enable them to make informed decisions about what treatment they want.<sup>2</sup>

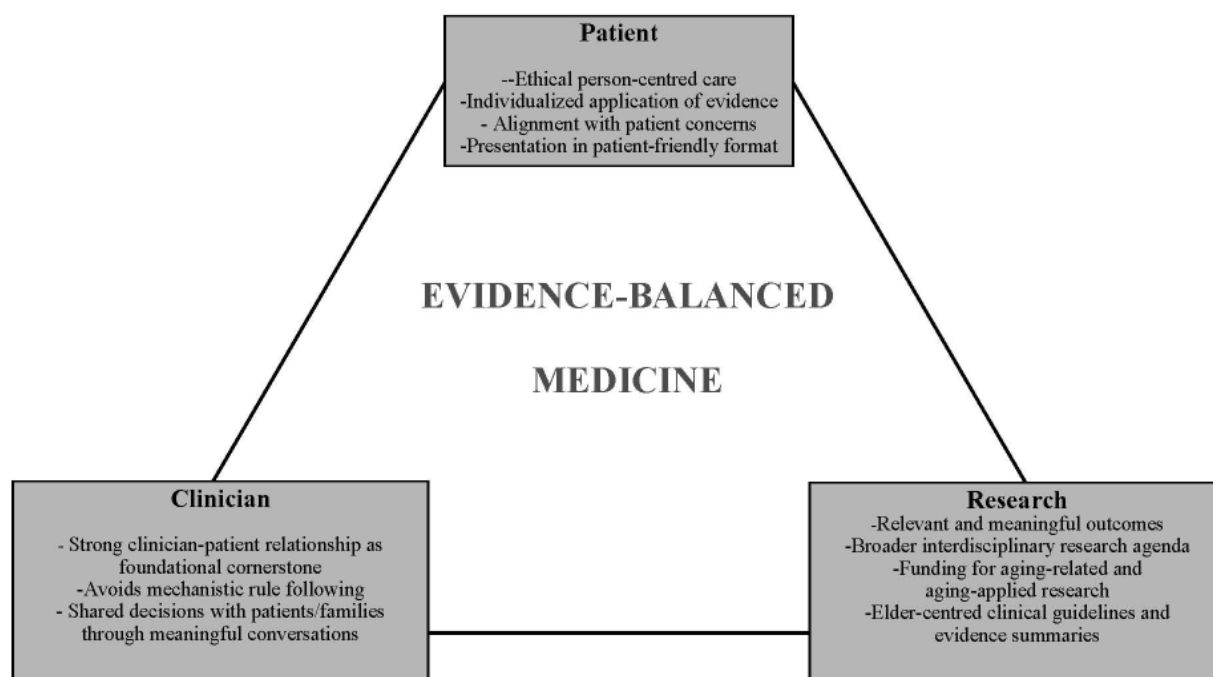


Fig. 3. The PCR triangle of evidence-balanced medicine (Adapted from Greenhalgh T, Howick J, Maskrey N, Evidence Based Medicine Renaissance Group. Evidence based medicine: a movement in crisis? *BMJ* 2014;348:g3725)

Clinicians therefore need to build upon a strong clinician-patient relationship as the foundational cornerstone to practice EBM.<sup>2</sup> Evidence should be individualised rather than applied mechanistically as inflexible rules or technology-driven prompts, as appropriate care decisions may not necessarily match what “best (average) evidence” seems to suggest.<sup>2</sup> The utility of EBM is ultimately dependent on expert judgment that combines context and patient preference in drawing valid analogy.<sup>2,3</sup> To this end, we propose the “ESCAPE” communication model to guide meaningful conversations with patients and their families in shared decisions about investigations and treatments (Table 1). By considering the benefits (number needed to treat, NNT), adverse effects (number needed to harm), actual costs of treatment, contextual factors, and patient concerns and preferences, clinicians can establish consensus about care decisions that are in the patient’s best interest. In our second case illustration, evidence suggests that the magnitude of benefit of ACEIs and ARBs in preventing ESRD seen in RCTs of younger participants is less well extrapolated to elderly patients (NNT: 9 to 25 to prevent 1 case of ESRD over 3 years versus greater than 1000 in many elderly subgroups).<sup>21</sup> Weighing the limited benefit against the potential harms of treatment (renal impairment, hyperkalaemia, and hypotension), the clinician may opt not to start ACEI or ARB in this patient with limited life expectancy.

To address this gap between clinical trials and the real world, it is imperative that we build up the evidence base to guide decision-making in elderly care.<sup>22-24</sup> Research in older adults should incorporate clinically relevant and meaningful outcomes such as quality of life, cognition, physical function and psychosocial consequences.<sup>1-3</sup> Given the importance of lag time to benefit in determining whether a preventative treatment is appropriate for an older adult, it is recommended that future research on preventative interventions should report the lag time to benefit (“When will it help?”) along with the magnitude of benefit (“How much will it help?”).<sup>4</sup> There should be a shift in emphasis beyond reductionist positivist study designs such as RCTs

Table 1. ESCAPE Communication Model to Promote Shared Decisions with Patients/Families

1.	Efficacy
2.	Side effects
3.	Cost of treatment
4.	Apply to context
5.	Patient preference and concerns
6.	Establish consensus

Steps 1 to 5 are iterative and need not be applied in a particular order. They provide the basis for the ultimate step of establishing consensus on care decisions with patient/family.

and meta-analyses to embrace a broader research agenda that is interdisciplinary and encompasses plurality of methods (including the rich diversity of qualitative methods) to answer use-inspired Pasteur’s quadrant research questions that matter.<sup>2,25</sup> This raises the need to create independent sources of funding for aging-related research (e.g. frailty, sarcopenia, delirium, geriatric rehabilitation, and end-of-life care)<sup>26,27</sup> and aging-applied research (e.g. models of care, lifestyle interventions, technology in healthcare, and interprofessional education).<sup>28,29</sup> For implementation studies, funding policy should look beyond chronological age as a crude criterion of aging research by delinking it from functional and cognitive age, and frailty status. We should also encourage the development of elder-centred clinical guidelines and evidence summaries.<sup>30,31</sup>

## Conclusion

EBM has come a long way since it was introduced more than 20 years ago as a “new paradigm” to counterbalance the then prevailing practice of eminence-based medicine. The ongoing discourse about the need to guard against evidence-biased medicine is timely and especially salient in the context of elderly care. While not amounting to a paradigm shift in the strictest sense, the return to real EBM in the elderly upholds the original ethos of providing best quality care that is undergirded in evidence, clinical judgment, context and patient preference.<sup>2</sup> As aptly put by Evans when describing EBM, “the name is crass but the idea is worthy.”<sup>3</sup> Evidence-balanced medicine in the elderly provides a way forward if EBM is to truly live up to its name.<sup>32</sup>

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