

Speaking for Ourselves

You are doomed because there is no evidence!

A. C. ANAND

The penalty for laughing in a courtroom is six months in jail; if it were not for this penalty, the jury would never hear the evidence.

—H. L. Mencken

I respect Pops not only as a surgeon but also as one who can analyse situations with a clear head. In the initial days of our friendship, we called him 'PP' because these were his initials. Then a nephrologist with the same initials came along and 'PP' somehow seemed more appropriate for a nephrologist. So this friend of mine became 'Pops'. He was my first choice when it came to referring my cases for surgical consultation. This was partly because of his good communication skills, mature and considered decision-making, and consistently good surgical results. His flamboyant and humorous nature, as well as his love for evidence-based medicine (EBM), were additional plus points.

Three separate incidents when Pops made some innocent remarks led me to ponder on certain contemporary issues.

The first incident occurred on 16 April 2011, when we were together in the audience at a continuing medical education (CME) programme on 'enteral nutrition' and were catching up with gossip about our colleagues. A foreign speaker was talking about the ASPEN guidelines published recently.¹ Pops suddenly deviated from our gossip and pointed out to me, 'AC! Look carefully. Of the 16 statements made by this gentleman, only 3 are grade A.'

I enquired, 'What does grade A mean?'

'You missed that slide,' he answered. 'Grade A means a statement based on at least 2 large randomized controlled trials (RCTs) with clear-cut results and with low risk of false-positive (alpha) and/or false-negative (beta) error.'²

'So what?' It was still not clear to me as to why he had objections to guidelines.

'AC, why have guidelines when you have no reliable evidence to support over 80% of your statements or recommendations?' He seemed a bit agitated. 'That, too, when you say upfront that there is no evidence that these guidelines will improve survival of patients?'

'Relax, Pops! No one is forcing you to follow these guidelines. They are just giving you the current state of information. And such CMEs get good financial support because the firms that make nutritional products have to sell their wares.'

The second incident occurred 2 days later. We were now waiting in the conference hall of our hospital for a 'statistical meeting' to start. He thrust before me a copy of our medical journal,³ and said, 'Is this really true?'

'What is true?' I was surprised at his intensity.

'That Chronic Kidney Disease Guidelines were doctored to favour drug companies and had harmed several patients?'

'Unfortunately, yes!' I knew that because our nephrologist, PP, had confirmed it to me. 'It has been quoted as a proof that clinical practice guidelines issued by professional bodies can be doctored. It has long been suspected that up to 90% of practice guideline developers have a financial relationship with companies that make at least one product addressed by those guidelines'.⁴ In this case, the National Kidney Foundation formulated guidelines in 2006 for the management of anaemia in patients with chronic kidney disease. Most leading experts of the initiative were consultants to companies manufacturing erythropoietin. The guidelines recommended the use of erythropoietin at levels higher than that warranted by scientific evidence. It was found to significantly increase the risk of death, myocardial infarction, congestive heart failure and stroke among the patients so treated.^{5,6}

Pops was agitated again. 'You mean they harmed the patients to gain monetarily?'

My response was formulated to avoid extreme reactions. I said, 'That is a very strong statement implying immoral or wicked intentions. I doubt they did it consciously. It is also possible that robust evidence did not exist at that time and experts added their opinion in the guidelines! Remember what you told me about the enteral nutrition guidelines the other day?'

'So patients are doomed if there is no evidence?', he asked.

My response was more philosophical. 'It has been said that half of what we practise today will be proven wrong in a few years' time. The sad part is that we do not know which half.'

The third incident was the case that was presented in the statistical meeting soon thereafter.

It was a 42-year-old woman, a known case of systemic lupus erythematosus (SLE) with nephritis, who had now presented with pneumonia and a few other complications. She had earlier been treated with methyl prednisolone and cyclophosphamide. During the current hospitalization, the debate about disease activity or infection as a cause of pneumonia was resolved by treating her for both. For SLE, she was initially given IVIG (intravenous immunoglobulin), then rituximab and finally, renal replacement therapy and plasmapheresis before she died.

Her death was explained by the treating physician as being due to the presence of several bad prognostic signs.⁷ However, some doctors strongly objected to the use of IVIG and rituximab in SLE due to the lack of definitive evidence of their benefit.

Rheumatologists accepted that there had been no large RCTs examining the efficacy of IVIG in SLE, but reiterated that data did exist from small studies and case reports.⁸⁻¹⁰ Similarly, rheumatologists also accepted that the use of rituximab was *off-label* but there were some reports to show that it might be useful.¹¹ There was an animated discussion. Some argued that clinicians may resort to using innovative treatments when pushed to a corner, *even if adequate evidence of benefit does not exist.*

Pops vehemently opposed the use of extremely expensive and potentially harmful drugs for the treatment of serious diseases

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when there was no proven evidence of their benefit. 'If adequate evidence was lacking, it would have been much better to tell the patient that nothing more was possible and they should prepare for the final event.' Pops said with great emphasis, 'Don't we do it all the time with terminal cancer patients?'

After the statistical meet, there was tea to wash down the differences of opinion. At this time, I walked up to him and said, 'Very effective therapy is now available for terminal cancer patients too. Examples are sorafenib for disseminated hepatocellular carcinoma and sunitinib for disseminated renal cell carcinoma. And let me quote from the first chapter of a textbook of medicine: "One thing is certain; it is not for you to don the black cap and, assuming the judicial function, take hope away from any patient." This quote was attributed to William Osler.'¹²

He was not pleased with my argument as his face still showed contempt. 'If you look up UK's National Institute of Health and Clinical Excellence (NICE) website, you will realize that sorafenib is not being recommended by the NHS as it is too expensive for the benefit it gives.'¹³

I knew that, but I added, 'The NICE guidelines are based on UK prices and on the results of detailed outcomes research done in their situation. Such evidence does not exist for Indian prices and conditions. However, there is evidence that sorafenib significantly prolongs life in such patients.'¹⁴

He retorted, 'There is no health technology outcome research in India. What do you do when there is no evidence?'

I just shrugged and said, 'I guess the same as we have been doing so far. Use our best judgement.' And that is how the conversation ended that day.

But we met again the very next day. I was coming out of a ward when I found Pops walking down the corridor on the opposite side. He took out a folded paper from his pocket and handed it to me. 'You may like to read this about 7 alternatives to EBM,' and he walked on.

As soon as I reached my room, I unfolded the paper handed to me by Pops. It was a photocopy of a paper published in the *BMJ* which described 7 alternatives to evidence-based medicine.¹⁵ It was amusing to see someone making light of a very serious subject. A summary of these 7 alternatives is given below.

1. *Eminence-based medicine*: Senior doctors do not rely on something as mundane as evidence. They have a touching faith in clinical experience—defined as 'making the same mistakes with increasing confidence over an impressive number of years'.
2. *Vehemence-based medicine*: The substitution of volume for evidence is an effective technique for browbeating your more timorous colleagues and for convincing relatives of your ability.
3. *Eloquence-based medicine*: Sartorial elegance and verbal eloquence are powerful substitutes for evidence.
4. *Providence-based medicine*: If the caring practitioner has no idea of what to do next, the decision may be best left in the hands of the Almighty.
5. *Diffidence-based medicine*: A diffident doctor may do nothing from a sense of despair. This, of course, may be better than doing something merely because it hurts the doctor's pride to do nothing.
6. *Nervousness-based medicine*: Fear of litigation is a powerful stimulus to over-investigation and over-treatment.
7. *Confidence-based medicine*: This is restricted to surgeons who like to play God.

This was not the end. When I searched the net, I realized that there were many others who had contributed equally effective alternatives.¹⁶ The following are some examples.

1. *Narrative-based medicine*: Some rely on indigenous traditions. Such medicine may be a combination of eminence-, eloquence- and confidence-based medicine.
2. *Arrogance-based medicine*: The unit of measurement here is the phrase 'because I said so'. It is often seen in teaching hospitals where the fate of students is in the professor's hands and they have no alternative but to accept what the professor says.
3. *Propaganda-based medicine*: Every day, busy practitioners are falling prey to interested pharmaceutical representatives who possess the best strategies for changing the physician's behaviour.
4. *Annoyance-based medicine* or *avoidance-based medicine*: This occurs when a patient, family or practitioners (other than the physician concerned) become so annoying in their demands for a specific course of care that the physician gives in.
5. *Rheumatism-based medicine*: Rheumatologists have a constant crib about this one. A patient with pain around the joints always has 'rheumatism' or 'arthritis'. There is no reason to investigate further or to refer him to a rheumatologist. The next step is treatment with corticosteroids and non-steroidal anti-inflammatory drugs.
6. *Profit- or opulence-based medicine*: One alternative—which may be especially prevalent in private practice and remuneration systems based on fee-for-service—is profit-based medicine (also known as opulence-based medicine). This is the conscientious, explicit and judicious use of the most profitable and lucrative interventions when making decisions about the care of individual patients.
7. *Webidence-based medicine*: Webidence is based on scientific (type 1) and pseudo-scientific (type 2) medical advice and opinion posted on a website.
8. *Effervescence-based medicine*: This is practised by physicians who have taken too much bubbly at the hospital party, and is marked by slurred speech and ataxia. The evidence yielded by a breathalyser will result in the confiscation of their driving licences.

Interestingly, someone also went on to mock the current view on the type of evidence that one accepts in medicine.¹⁶

'Evidence was classified into 7 levels:

Class 0: things I believe

Class 0a: things I believe despite the available data

Class 1: randomized, controlled clinical trials (RCCTs) that agree with what I believe

Class 2: other prospectively collected data that support what I believe

Class 3: expert opinion similar to mine

Class 4: RCCTs that don't agree with what I believe

Class 5: what you believe that I don't

Evidence with lesser class number indicates better evidence and those with higher number indicate poorer evidence, hence less reliable.'

The same evening, after finishing the day's work, I walked up to his room and said, 'Pops, there are two more alternatives I can suggest. One is *brass (or rank)-based medicine* for the services, where the weight of the brass on the shoulder rather than clinical evidence decides what treatment is given to the patient, and

another is *anecdote-based medicine*, in which people base their treatment decisions on what happened in the last case they saw or heard about 2 decades back!

Pops was not smiling. 'AC, think carefully, is it not what you see being practised all around you?'

'I agree, we all may be guilty to some extent of being empirical at some time or other. But it is mostly due to lack of credible evidence. In a developing country like ours, where 80% of health resources are in the private sector, doctors are forced to practise *economics-based medicine*. The best treatment for a disease may be so expensive that a patient may not be able to afford it. Then you prescribe what is affordable, even if it is the fourth best or worst treatment option.'

He said, 'We in the services are lucky that we do not have to deny the best treatment to our clientele for lack of funds. But I do understand the predicament of doctors in private practice. I have always tried to follow evidence-based practice, but now I am confused.'

I, too, had several doubts about what I should do in certain circumstances. 'You see, the role of a doctor is rapidly changing. But do you think that EBM is the most relevant method for us today?'

His answer was more like thinking aloud. 'The term EBM was coined in 1988 and utilized research methods that were nearly impossible without the use of electronic databases. The core idea of EBM is very logical—that we should evaluate the benefits and harms of different interventions before implementing them.¹⁷ In the olden days, not everything was scientifically and statistically proven and such proof was not even considered desirable.'

I interrupted him, 'How come not desirable? I can't imagine a situation where scientific evidence will not be desirable.'

He looked at me and replied, 'Okay! Tell me, has there been any RCT to prove the efficacy of parachutes? RCTs are the backbone of EBM, but in this case they are neither desirable, nor possible! Liver transplantation has become a routine treatment without any RCTs!'

I suddenly remembered something. 'A recent Cochrane systematic review found no evidence to show that Alcoholics Anonymous (AA) or other 12-step programmes are effective.¹⁸ It has been said that AA is *faith-based medicine* and not evidence-based.¹⁹ It is still popular the world over. Does that make it scientific or not?'

'I guess it will depend on your view on the role of faith in medicine,' he remarked.

'You said EBM started in 1988. It was around the same time that the practice of medicine also changed drastically.' I changed track to keep our discussion on course.

'Changed—how?'

I replied, 'A book published way back in 1984²⁰ criticized the traditional autocratic decision-making by doctors and suggested that the patient should be a party to all medical decisions made about him/her. Due to repeated debates on this topic, the medical profession started respecting the autonomy of patients with respect to treatment decisions by the 1990s.'

'Yes, it makes our task doubly difficult. We not only need to comprehend the complex statistical evidence, but also need to convince our patients about it, who may have no medical or statistical knowledge to grasp the facts.' His remarks reflected his frustration and the difficulty he was facing in doing what was being recommended.

I echoed his thoughts: 'It also means that the doctor will have a tougher time explaining to his/her patient why some of the "sales pitches" given on the internet may be wrong.'

Pops agreed with me, but raised another point, 'In fact, perfect evidence is not available for most situations. So, what does one do when evidence is sketchy or incomplete?'

I had my own views on this. 'EBM de-emphasizes intuition, unsystematic clinical experience and pathophysiological basis as sufficient grounds for clinical decision-making and instead, stresses the examination of evidence directly from clinical research.'¹⁷

'That's what separates EBM from the alternatives described above.'

I startled him with a remark he was not expecting. 'EBM has also been severely criticized. People have even called it absurd and irrational.'²¹

'Most people who criticize EBM forget that its primary goal is to be aware of the evidence on which one's practice is based, the soundness of the evidence, and the strength of inference the evidence permits. But evidence alone is never sufficient to make a clinical decision.'²² Anyway, what is the criticism against it? He was unwilling to accept any criticism against it.

'For example,' I tried to remember the case²³ I had read about some time back, 'Mr T has coronary artery disease, congestive heart failure and chronic kidney disease. He was prescribed a statin, a beta-blocker and an angiotensin-converting enzyme (ACE) inhibitor to treat his heart failure and kidney disease. Mr T had severe side-effects from all of these. Statins made his muscles ache so much that he couldn't walk; his beta-blocker lowered his blood pressure so much that he couldn't stand; and his ACE inhibitor raised his potassium so much that he was in danger of a deadly heart arrhythmia. So he stopped those drugs.'

'That is natural.'

'From time to time, Mr T needed to be hospitalized for an exacerbation of his condition and every time, without fail, a consultant prescribed the same 3 medications again with the same deleterious results, despite diligent documentation of his prior reactions in his papers.'

'Why did they do that?'

'Because evidence-based treatment recommendations have become too deeply ingrained in their definition of good medical care. Hospital accreditations may also depend on such protocols. Consultants are now more concerned with meeting measurable standards of quality than with providing individualized care. That is why people call EBM "microfascist" medicine, or you may call it "tyranny-based medicine".'²³

'But EBM prescribes that our practice should be based on the best available research evidence, taken in the context of a patient's clinical state and circumstances interpreted in the light of patient preferences and values.^{24,25} It is a wrong interpretation by those consultants. Is there any other criticism?' He seemed to be making up his mind.

'There are more!' I said, 'The evidence is gathered from groups of people, not individuals. And not all patients have the same set of values. It is like determining the adult dose of a drug by studying adults from 18 to 45 years of age and then prescribing the same dose to 75-year-olds! People call it a streetlight effect.'²⁶

'Why streetlight effect?'

'It has its origins in old folklore—an old lady was searching for her needle under the streetlight, even when she had lost it inside her hut.'

'What has that story to do with EBM?'

'Researchers tend to look for answers where the looking is good, rather than where the answers are likely to be hiding. After all, the discovery of new medications, devices and techniques is funded primarily by "for-profit" companies.'²⁷

'I see.' He was still contemplating his response.

'Then, EBM underpins guideline development. However, too often, guidelines claim to have a basis in evidence when they actually reflect major biases of the committee members who made them.²⁸ As a result, we may have several conflicting guidelines on a subject that use the same data to reach different conclusions.'

'You mentioned something earlier on this issue, too.' He was trying to remember our earlier discussion.

'Exactly! Sometimes guideline developers ignore valuable and life-saving research work for years (as they did in the case of the papers from the University of Arizona) on the pretext that it was "low-level evidence".^{29,30} This parachute was finally accepted several years later.³¹

Pops was listening intently and commented, 'That too is bad.'

'Guidelines are useful, but in actual practice, vested interests often hijack or manipulate the EBM process. As I said earlier, pharmaceutical companies influence the writing of evidence-based guidelines to favour their products.³² Such guidelines are written by doctors who have been paid by pharmaceutical companies that stand to benefit from the guidelines' recommendations.'³³

'EBM gets a bad name because of the bad behaviour of doctors. Such doctors should be punished!' Pops was upset again.

'Pharmaceutical and biotechnology companies also manipulate the design, implementation and analysis of research studies to increase the likelihood that the results will be favourable to their products.³⁴ Doctors are surprisingly gullible and let commercial sponsors control clinical research studies.³⁵ Pharmaceutical companies have, in the past, suppressed research whose outcomes they find offensive to their interests.'^{36,37}

'You mean scientific publications are often manipulated to mislead doctors?' He looked surprised.

'There have been a number of examples of such behaviour. Pharmaceutical companies have refused to provide all study data to the study team, reporting only 6 months of data in a trial designed to have 12 months of data as the primary outcome; engaging in incomplete reporting of serious adverse events; and concealing clinical trial data showing harm to patients.'³⁸

'I think one should only read the best journals, which cannot be influenced,' he muttered.

'Interestingly, a study about authors of scientific papers published in 2 of the most prestigious journals—*The New England Journal of Medicine (NEJM)* and *The Journal of the American Medical Association (JAMA)*—showed that there was widespread conflict of interest among the authors of published manuscripts and that such authors were more likely to present positive findings.'³⁹

'But those could be honest findings!' he exclaimed innocently.

'I wish it were so. These "spin doctors" have a way of showing that a treatment works, when in fact, it doesn't.⁴⁰ To get approval from FDA, GlaxoSmithKline (GSK), the manufacturer of rosiglitazone, may have suppressed early information that the drug could cause congestive heart failure and myocardial infarction.⁴¹ Similar is the story of a cox-2 inhibitor, viox (Merck), and alosetron (again GSK).'^{42,43}

'If the basic evidence is crooked, how can you blame EBM?' He turned around and threw me a questioning glance, and said, 'But I am sure EBM is still helpful?'

I felt bad to burst his bubble of smugness. 'Unfortunately, there is no evidence that it works!'⁴⁴

'What? Has it never been shown to be useful?'

'No, it is not that bad. When we were students, we were told that ventricular premature beats (VPBs) were a harbinger of fatal

ventricular fibrillation. Thus prophylaxis by antiarrhythmic agents was indicated. A study later showed that mortality in patients given antiarrhythmic agents was higher than in those not given these drugs. This has led to the discontinuation of these antiarrhythmic drugs.⁴⁵ This showed the need to distinguish evidence from propaganda (advertisement); data from assertions; rational belief from superstition; and science from folklore.'⁴⁶

Pops' eyes suddenly twinkled, 'What you have described is very similar to the story of Archie Cochrane, who was EBM's initial promoter.⁴⁷ This British physician was captured by Germans during World War II and placed in charge of 20 000 prisoners of war. Almost all of them were suffering from various communicable diseases, such as dysentery, malaria and typhoid. He only had aspirin and some other primitive methods of management at his command. He, therefore, expected that a majority would die before the war ended.'

'And they didn't die?' I asked.

'He was astonished that only 4 among them died, and that too, due to gunshot wounds. Hence, he argued that they all survived either because of their inherent immunity to fight the diseases or aspirin, helped only by a "placebo effect". He shot down the practice of *a pill for every ill* prevalent in the NHS during those days. But I think today's evidence-based guidelines should be helpful?'

'There is very little evidence for that either.' I added, 'The American Medical Association and the American Association of Health Plans, along with the National Guideline Clearing House (www.guideline.gov), list over 1500 guidelines dealing with various areas of medicine. *These guidelines remain untested*. One recent paper suggested that the recommendations issued in the current ACC/AHA clinical practice guidelines are largely developed from lower levels of evidence or expert opinion. The proportion of recommendations for which there is no conclusive evidence is also growing. These findings highlight the need to improve the process of writing guidelines and to expand the evidence base from which clinical practice guidelines are derived.'⁴⁸

Pops was surprised: 'You mean all these guidelines have neither influenced practice, nor raised the standard of care?'

I knew my answer would disappoint him. 'There is no evidence to show any benefit, though there is some to show the opposite—the harm caused by biased guidelines.'⁴⁹

'Are such guidelines not useful when doctors are dragged to court on charges of negligence?'

'You have a point there,' I replied. 'Medical negligence comprises 3 essential points. A petitioner must show that (i) the defendant doctor owed the petitioner a duty of care, (ii) the doctor failed to provide the required standard of medical care, and (iii) this failure actually caused the petitioner avoidable harm.'

'Clinical guidelines can guide the courts to establish the second point.'⁵⁰ Pops was quick to infer.

'Fortunately, so far courts have maintained that applying guidelines to individual care is always likely to require treating physician's judgement, even when recommendations are properly linked to evidence,' I said.

Pops' last question was about his surgical practice. 'Don't you think there is a paucity of studies to show which surgical therapy is superior to the other? We are usually left to make empirical or common-sense decisions!'

I looked at him carefully to see if he was testing me. He appeared sincere. So I said, 'The problems are different while interpreting surgical results. Very few RCTs are done because the benefit of surgery may be obvious, or there may be difficulties in

defining outcome measures or even greater difficulties in standardizing surgical skill/preference of a surgeon. Moreover, surgical techniques are continuously evolving.'

'We often compare endoscopic treatments with surgical treatments. Isn't it?' he asked.

'You are right, but there are problems in planning RCTs for several surgical treatments. Take, for example, incision and drainage of an abscess. An EBM statement would be that "there is no RCT evidence of its benefit". This does not mean that the treatment does not work! It may mean that there are no RCTs because surgeons know what to do with an abscess. They have known it for thousands of years. The benefit of the treatment is obvious. After an abscess has been drained, there is no abscess.'⁵¹

'True enough,' he remarked.

I added, 'And then even if RCTs are conducted, the results may not be applicable to your patients. It is like the "across the water shot" in golfing.'

'What does that mean?'

'The best shot for a green lying across a water-hazard would be straight over the water-hazard, provided you have the equipment and skill to do it. An RCT will show it to be superior to all other shots.'

'What are you trying to imply?'

'Just that a top golfer may succeed in making it across the pond in a single shot. But if your equipment is less than the best, and your confidence is low, the safest method will be to take the dog-leg and go around the hazard—it will require at least 2 strokes, but should get you to the green safe and sound. An average surgeon trying to follow RCT results with his average equipment and skill is likely to sink his patient.'⁵¹

'That means surgeons should stick to operations they are confident of doing and not change their style every time a new paper appears.' Pops was thoughtful when he said this. 'AC! You have said so much against EBM today that I am losing faith in it. What is the final verdict, the bottom line?'

'You will find that the virtues of EBM are written about everywhere because they are widely accepted. You asked for my comments, so I expressed my concerns about it.' I added, 'Your EBM has given ++ marks to homeopathy, saying that it works.'

'What?'

'Homeopathy uses drugs in which less than one molecule of an active agent may be present. Benefit with dilution beyond the Avogadro number contradicts pharmacological theory. But a meta-analysis of 89 placebo-controlled trials revealed combined odds of 2.45 in favour of homeopathy.'⁵²

I added with a smile, 'EBM has given a thumbs-down to acupuncture. But researchers have been hesitant to reject it outright.'⁵³ They always end up saying that more research work is needed. So that someone else may deliver the bad news!'

I saw that Pops had by now made up his mind and had decided to throw a challenge at me. 'AC, let me see how you deal with this! Suppose you have two patients with the same diagnosis. Let us call them "A" and "B". Both have a similar malignancy at the same stage and performance status. RCTs have shown that palliative treatment with radiotherapy is superior to chemotherapy for this disease. Now "A" lives in Delhi and has a devoted wife who can drive him to hospital every day, but "B" does not have a living wife and has come with his young college-going son from Jharkhand. How would your treatment approach to these two patients differ?'

I knew that now he was testing me. I had seen a similar discussion elsewhere,⁵⁴ but this scenario was novel. 'I think, "A" would be prescribed radiotherapy, to be given at this hospital for

sure. And I would discuss both treatment options with "B" and would highlight the marginal difference in their efficacy. Finally, I would suggest that he should receive chemotherapy in the local hospital in his hometown, if he so chooses.'

Pops seemed to agree with me. 'So that he and his family do not suffer?'

'There are several intangibles that need to be considered in clinical decision-making.'⁵⁵ I looked and added, 'I would also need to convince his local doctor about this plan, otherwise he would be referred right back to me for radiotherapy if his local doctor was an EBM enthusiast!'

Pops laughed. 'I will call that *experience-based medicine!*'

'Pops, EBM is the surest and most objective way to determine and maintain medical care and safety standards of a high quality. It also has the potential to reduce healthcare costs significantly.'⁵⁶ *But we must realize that EBM is not a paradigm shift.*⁵⁷ It is only one step further in making medicine more scientific. I am sure there will be others. And the art of medicine still needs to be perfected and practised.'

'And pray,' Pops asked, 'What is that?'

'It is something you are already good at. Spend some time in sincerely listening to your patient to *get a real perception of his feelings and fears*. And in all your decision-making, factor that in. It may be called *empathy-based medicine*, a soul-mate of EBM.'

REFERENCES

- 1 August DA, Huhmann MB; American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors. A.S.P.E.N. clinical guidelines: Nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. *JPEN J Parenter Enteral Nutr* 2009;**33**:472–500.
- 2 Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, *et al.*; Surviving Sepsis Campaign Management Guidelines Committee. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. *Crit Care Med* 2004;**32**:858–73. Erratum in: *Crit Care Med* 2004;**32**:1448. Dosage error in article text. *Crit Care Med* 2004;**32**:2169–70.
- 3 Anand AC. Professional conferences, unprofessional conduct. *Med J Armed Forces India* 2011;**67**:2–6.
- 4 Choudhry NK, Stelfox HT, Detsky AS. Relationships between authors of clinical practice guidelines and the pharmaceutical industry. *JAMA* 2002;**287**:612–17.
- 5 Coyne DW. Influence of industry on renal guideline development. *Clin J Am Soc Nephrol* 2007;**2**:3–7.
- 6 Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, Wolfson M, *et al.* Correction of anemia with epoetin alfa in chronic kidney disease. *N Engl J Med* 2006;**355**:2085–98.
- 7 Abu-Shakra M, Urowitz MB, Gladman DD, Gough J. Mortality studies in systemic lupus erythematosus: Results from a single center—II: Predictor variables for mortality. *J Rheumatol* 1995;**22**:1265–70.
- 8 Sherer Y, Kuechler S, Jose Scali J, Rovensky J, Levy Y, Zandman-Goddard G, *et al.* Low dose intravenous immunoglobulin in systemic lupus erythematosus: analysis of 62 cases. *Isr Med Assoc J* 2008;**10**:55–7.
- 9 Lazurova I, Macejova Z, Benhatchi K, Oetterová M, Antolová E, Asherson RA, *et al.* Efficacy of intravenous immunoglobulin treatment in lupus erythematosus chorea. *Clin Rheumatol* 2007;**26**:2145–7.
- 10 Vaitla PM, McDermott EM. The role of high-dose intravenous immunoglobulin in rheumatology. *Rheumatology (Oxford)* 2010;**49**:1040–48. Available at <http://www.medscape.com/viewarticle/722176> (accessed on 17 Apr 2011).
- 11 Ramos-Casals M. Rituximab in systemic lupus erythematosus: A systematic review of off-label use in 188 cases. *Lupus* 2009;**18**:767–76. Available at http://www.reumatominas.com.br/downloads/artigos/resumo_06052010.pdf (accessed on 17 Apr 2011).
- 12 The practice of medicine (chapter I). In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, *et al.* (eds). *Harrison's principles of internal medicine, Vol. 1, 17th edition*. Philadelphia: McGraw-Hill Medical; 2008:1–6.
- 13 NICE Single Technology Appraisal Guidance No 189—Sorafenib for the treatment of advanced hepatocellular carcinoma. Appraisal 189. Available at <http://guidance.nice.org.uk/TA189> (accessed on 26 Apr 2011).
- 14 Llovet JM, Ricci S, Mazzaferro V, Hilgard P, Gane E, Blanc JF, *et al.* Sorafenib in advanced hepatocellular carcinoma. *N Engl J Med* 2008;**359**:378–90.
- 15 Isaacs D, Fitzgerald D. Seven alternatives to evidence based medicine. *BMJ* 1999;**319**:1618.
- 16 Rapid responses to Llovet JM, Ricci S, Mazzaferro V, Hilgard P, Gane E, Blanc JF, *et al.* Sorafenib in advanced hepatocellular carcinoma. *N Engl J Med* 2008;**359**:378–

90. Available at http://www.bmj.com/content/319/7225/1618.full/reply#bmj_el_65892 (accessed on 17 Apr 2011).
- 17 Evidence-Based Medicine Working Group. Evidence-based medicine: A new approach to teaching the practice of medicine. *JAMA* 1992;**268**: 2420–25.
- 18 Ferri M, Amato L, Davoli M. Alcoholics Anonymous and other 12-step programmes for alcohol dependence. *Cochrane Database Syst Rev* 2006;**3**:CD005032. Available at <http://onlinelibrary.wiley.com/doi/cochrane/clsyrev/articles/CD005032/frame.html> (accessed on 23 Apr 2011).
- 19 Hall H. AA is faith-based, not evidence-based. Available at <http://www.sciencebasedmedicine.org/?=490> (accessed on 23 Apr 2011).
- 20 Katz J. *The silent world of doctor and patient*. New York:Free Press, 1984.
- 21 Couto JS. Evidence-based medicine: A Kuhnian perspective of a transvestite non-theory. *J Eval Clin Pract* 1998;**4**:267–75.
- 22 Guyatt G, Rennie D (eds). *Users' guides to the medical literature: A manual for evidence-based clinical practice*. Chicago (IL):AMA Press, 2002.
- 23 Holmes D, Murray SJ, Perron A, Rail G. Deconstructing the evidence-based discourse in health sciences: Truth, power and fascism. *Int J Evid Based Healthc* 2006;**4**:180–6.
- 24 Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. *Evidence based medicine. How to practice and teach EBM*. (2nd edition). New York:Churchill Livingstone; 2000.
- 25 Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: What it is and what it isn't. *BMJ* 1996;**312**:71–2.
- 26 Freedman DH. Why scientific studies are so often wrong: The streetlight effect. *Discover Magazine* Jul–Aug 2010. Available at <http://discovermagazine.com/2010/jul-aug/29-why-scientific-studies-often-wrong-streetlight-effect> (accessed on 23 Apr 2011).
- 27 Moses H 3rd, Dorsey ER, Matheson DH, Thier SO. Financial anatomy of biomedical research. *JAMA* 2005;**294**:1333–42.
- 28 Healy B. Who Says What's Best? *US News and World Report*, 3 Sept 2006. Available at <http://health.usnews.com/usnews/health/articles/060903/11healy.htm> (accessed on 20 Apr 2011).
- 29 Berg RA, Sanders AB, Kern KB, Hilwig RW, Heidenreich JW, Porter ME, et al. Adverse hemodynamic effects of interrupting chest compressions for rescue breathing during cardiopulmonary resuscitation for ventricular fibrillation cardiac arrest. *Circulation* 2001;**104**:2465–70.
- 30 Valenzuela TD, Kern KB, Clark LL, Berg RA, Berg MD, Berg DD, et al. Interruptions of chest compressions during emergency medical systems resuscitation. *Circulation* 2005;**112**:1259–65.
- 31 Kellum MJ, Kennedy KW, Ewy GA. Cardiocerebral resuscitation improves survival of patients with out-of-hospital cardiac arrest. *Am J Med* 2006;**119**:335–40.
- 32 Eichacker PQ, Natanson C, Danner RL. Surviving sepsis—Practice guidelines, marketing campaigns, and Eli Lilly. *N Engl J Med* 2006;**355**:1640–2.
- 33 Taylor R, Giles J. Cash interests taint drug advice. *Nature* 2005;**437**:1070–1.
- 34 Brophy JM. Selling Safety—Lessons From Muraglitazar. *JAMA* 2005;**294**: 2633–35.
- 35 Mello MM, Clarridge BR, Studdert DM. Academic medical centers' standards for clinical-trial agreements with industry. *N Engl J Med* 2005;**352**:2202–10.
- 36 LaDou J. The rise and fall of occupational medicine in the United States. *Am J Prev Med* 2002;**22**:285–95.
- 37 Avorn J. Dangerous deception—hiding the evidence of adverse drug effects. *N Engl J Med* 2006;**355**:2169–71.
- 38 DeAngelis CD. The influence of money on medical science. *JAMA* 2006;**296**: 996–8.
- 39 Friedman LS, Richter ED. Relationship between conflicts of interest and research results. *J Gen Intern Med* 2004;**19**:51–6.
- 40 Curfman GD, Morrissey S, Drazen JM. Expression of concern: Bombardier et al., 'Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis.' *N Engl J Med* 2005;**353**:2813–14.
- 41 Bresalier RS, Sandler RS, Quan H, Bolognese JA, Oxenius B, Horgan K, et al. Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial. *N Engl J Med* 2005;**352**:1092–102.
- 42 Moynihan R. Alossetron: A case study in regulatory capture, or a victory for patients' rights? *BMJ* 2002;**325**:592–5.
- 43 Choudhry NK, Stelfox HT, Detsky AS. Relationships between authors of clinical practice guidelines and the pharmaceutical industry. *JAMA* 2002;**287**:612–17.
- 44 Straus SE, McAlister FA. Evidence-based medicine: A commentary on common criticisms. *CMAJ* 2000;**163**: 837–41.
- 45 The Cardiac Arrhythmia Suppression Trial (CAST) Investigators. Preliminary report: Effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. *N Engl J Med* 1989;**321**: 406–12.
- 46 Dawes M, Summerskill W, Glasziou P, Cartabellotta A, Martin J, Hopayian K, et al.; Second International Conference of Evidence-Based Health Care Teachers and Developers. Sicily statement on evidence-based practice. *BMC Med Educ* 2005;**5**:1.
- 47 Rajashekhar HB, Kodkany BS, Naik VA, Kotur PF, Goudar SS. Evidence based medicine and its impact on medical education. *Indian J Anaesth* 2002;**46**:96–103.
- 48 Tricoci P, Allen JM, Kramer JM, Califf RM, Smith SC Jr. Scientific evidence underlying the ACC/AHA clinical practice guidelines. *JAMA* 2009;**301**:831–41.
- 49 Amerling R, Winchester JF, Ronco C. Guidelines for guidelines. *Blood Purif* 2007;**25**:36–8.
- 50 Hurwitz B. Legal and political considerations of clinical practice guidelines. *BMJ* 1999;**318**:36–8.
- 51 Fairley JW. Limitations of evidence based medicine: Should Cochrane reviews of surgical interventions concluding 'no evidence of benefit' come with a health warning? Available at <http://www.entkent.com/ebm-cochranehealthwng.html> (accessed on 23 Apr 2011).
- 52 Tobin MJ. Counterpoint: Evidence-based medicine lacks a sound scientific base. *Chest* 2008;**133**:1071–4.
- 53 Novella S. Acupuncture doesn't work, believers ignore evidence. *Better Health Network*, 23 Mar 2009. Available at <http://getbetterhealth.com/acupuncture-doesnt-work-believers-ignore-evidence/2009.03.23> (accessed on 18 May 2011).
- 54 Goldman JJ, Shih TL. The limitations of evidence-based medicine—Applying population-based recommendations to individual patients. *Virtual Mentor* 2011;**13**:26–30. Available at <http://virtualmentor.ama-assn.org/2011/01/pdf/jdsc1-1101.pdf> (accessed on 18 May 2011).
- 55 Tonelli MR. The philosophical limits of evidence-based medicine. *Acad Med* 1998;**73**:1234–40.
- 56 Guyatt G, Cook D, Haynes B. Evidence based medicine has come a long way. *BMJ* 2004;**329**:990–1.
- 57 Sehon SR, Stanley DE. A philosophical analysis of the evidence-based medicine debate. *BMC Health Services Research* 2003;**3**:14. Available at <http://www.biomedcentral.com/1472-6963/3/14> (accessed on 23 April 2011).