Evidence-based medicine: putting theory into practice

Mike Irani

Evidence-based medicine is an essential tool to ensure the effective and efficient management of patients. A practical and unbiased assessment of clinical evidence can be achieved by asking simple questions about the data. Undertaking this process can reveal a new perspective on traditional treatment approaches.

Although a relatively new concept — the phrase was first coined in Canada in the 1980s — the theory and ideas behind evidence-based medicine (EBM) are not new (Rosenberg and Donald, 1995). Clinicians throughout the ages have questioned their practice in a bid to establish the most effective and efficient means of managing their patients. This article aims to examine the role of EBM in today's NHS, provide a checklist for assessing the quality of data and use osteoporosis as an example of the new perspective that EBM can bring to everyday clinical practice.

BENEFITS OF EBM

EBM enables clinicians to select the most effective and efficient treatment for their patients. In clinical settings of incomplete pathophysiological background, EBM is an invaluable tool to aid decision making. This integration of medical education with clinical practice provides a sound base from which physicians can expand their knowledge and research skills through self-directed learning, and can help close the gulf between good clinical research and clinical practice (Rosenberg and Donald, 1995). Valid research findings should not be ignored, as serious consequences for patients may result if new data are neglected. Increased use of the internet by both journal publishers and doctors permits rapid access to relevant evidence, enabling the clinician to make best use of published research.

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THE ROLE OF THE HOSPITAL CONSULTANT IN EBM

Hospital consultants have an essential role to play in implementing EBM. With responsibility for the ongoing education of their team, including medical students, consultants are well placed to instil the importance of EBM at an early stage, so that it becomes routine practice. For example, at a weekly firm meeting, the consultant could select a critically appraised topic in order for a junior member of his/her firm to present a critical literature appraisal in a summarized form to the rest of the team (Rosenberg and Donald, 1995). During the subsequent ward round, the team could discuss the evidence and decide on the course of treatment, therefore providing a structure for effective teamwork and improving communication and understanding between colleagues.

Evidence is best learned through group discussions, where members can brainstorm ideas together to explore ways of incorporating the evidence into a patient's management. In terms of teaching skills, a willingness to admit uncertainty and encourage scepticism, and a flexible nature on the consultant's part may all encourage the team to regularly review their existing practice and accommodate new evidence which may contradict their previous assumption (Rosenberg and Donald, 1995).

EBM AND THE NHS

The need for EBM has never been greater than in today's NHS. As the NHS becomes increasingly cost-conscious and litigious, it is embracing EBM at all levels of patient care as a means of identifying the most cost-effective and efficient method of managing patients. EBM allows limited resources to be effectively utilized by enabling providers to evaluate the clinical effectiveness of treatments and services. EBM can also be used to formulate or change hospital guidelines and protocols. In some cases, it can revolutionize continuing medical education pro-

grammes or audit. In any situation where some doubt about an aspect of clinical diagnosis exists, EBM can be applied to improve the prognosis and management of the patient. It is essential that the NHS stay abreast of the latest developments, as gaps between research evidence and clinical practice can have serious consequences in terms of expensive, ineffective or even harmful decision making.

CONSIDERATIONS WHEN PRACTISING EBM

EBM is not without pitfalls. Insufficient time, limited search skills and restricted access to evidence can all form a barrier to the practice of EBM. The implementation of flawed guidelines could cause harm and it is therefore essential that clinicians have the necessary skills to sift through the ever-growing database of medical research in order to extract the most useful and relevant information for their practice.

ASSESSING THE QUALITY OF EVIDENCE

When assessing the quality of clinical evidence, there are a number of questions that can be asked in order to develop an unbiased and practical assessment of the data.

What is the quality of the evidence?
There are four defined levels of clinical evidence (*Table 1*). The first question demanded by EBM is the source and quality of the evidence under review.

Are the study endpoints relevant?
Study endpoints should be considered within the clinical context. For example, in osteoporosis treatment studies, were the endpoints bone turnover, bone density or the clinically relevant endpoint of fracture?

What is the design of the study?
The design of the study is directly related to the quality of the evidence (*Table 1*).

What is the power of the study?
Clinical studies should be assessed to identify whether they really can answer the question they aim to address. For example were there enough subjects, was the duration appropriate? This is particularly important in studies where the results do not show an improvement with the studied agent or technique, here at least 80% power is needed.

Are the study subjects relevant?
Ideally, the subjects in the study should match those in whom treatment is proposed in terms of factors such as age, sex, race, disease state.

How do we understand the results?
The statistical relevance of the results should be considered to assess the likelihood of the outcome happening by chance. Thought should also be given to the effect size, how it compares to the control group and what it will mean in practice.

REVIEWING THE EVIDENCE IN OSTEOPOROSIS

The prevention of osteoporotic fractures is a major challenge to the NHS. With over 200 000 fractures each year, osteoporosis costs the NHS a staggering £942 million annually, with hip fracture alone costing £250 million (Royal College of Physicians, 1999). Applying an evidence-based approach to preventing fractures is therefore essential. In response to this, the Royal College of Physicians has published a detailed evidence-based review of osteoporosis treatments, which provides clear guidance for clinician's involved in managing osteoporosis and

TABLE 1.
Levels of clinical evidence

Quality of evidence	Type of evidence	Comments
4 (poor)	Expert opinion	Often based on personal opinion/experiences. Not objective
3	Descriptive studies	Includes comparative and case control studies. Treatment groups may not be equivalent at baseline and may have behaved differently if they had received a different therapy. Bias tends to overestimate the treatment effect
2	Other experimental studies	Includes controlled studies without randomization and intervention without a control. Treatment groups may not be equivalent at baseline and may have behaved differently if they had received a different therapy
1 (good)	Controlled trials	Gold standard evidence. Avoids bias. Compares intervention against a known standard. Quality is maximized if studies are blinded and use intention to treat analysis. Meta-analysis of randomized controlled trials is the optimum

From Sackett et al (1996)

developing local protocols (Royal College of Physicians, 1999). These guidelines have recently been updated by the Bone and Tooth Society (Bone and Tooth Society and Royal College of Physicians, 2000).

The first-line treatments for preventing fractures in postmenopausal women with established osteoporosis are hormone replacement treatment (HRT) and the bisphosphonates. To identify high quality evidence for these treatments, taking account of factors such as study design, subjects and endpoints, specific inclusion and exclusion criteria can be considered (*Table 2*).

If these criteria are applied to studies of HRT and the bisphosphonates, core data are identified that can be used to review the comparative benefits of different treatments. These data are summarized in *Tables 3–6*.

What does the evidence tell us?

Undertaking an objective review can raise interesting questions about common management approaches. In the management of osteoporosis, HRT is generally considered the gold standard treatment for younger postmenopausal women. A number of HRT preparations are available, although many are only indicated for prevention of postmenopausal osteoporosis, rather than treatment of the condition. Despite being the standard treatment for managing osteoporosis to prevent fractures, there are few randomized controlled trials that show a significant effect on fracture reduction. These studies are also small.

Table 3 summarizes the effect of HRT on vertebral and hip fractures. There is no high quality evidence to support a reduction in hip fractures in patients on HRT. The main evidence for HRT actually derives from epidemiological studies which suggest that women who use HRT for at least 5 years, starting soon after the menopause, reduce their risk of subsequent vertebral, wrist and hip fracture by 50–60% while continuing therapy. Recently, the safety of HRT has been questioned by the findings of studies such as Heart and Estrogen/Progestin Replacement Study (HERS; Hulley et al, 1998).

There are three bisphosphonates available for the treatment of osteoporosis. An evidence-based review highlights significant differences between the different options in terms of fracture reduction.

Alendronate is the only osteoporosis treatment licensed for the prevention of all osteoporotic fractures, including those at the hip. There are a number of high quality clinical trials that demonstrate the effect of the treatment for the prevention of fractures, with reductions of about 50% at all clinically relevant sites (*Table 4*).

Etidronate is a widely prescribed bisphosphonate, which is licensed for the treatment of osteoporosis. However, there is limited randomized controlled trial evidence to support its use (*Table 5*). In the studies eligible for this review, etidronate did not achieve significant reduction of vertebral or hip fractures. A substudy reported within the data does, however, find a significant reduction in vertebral fracture in 68 patients at high risk of fracture receiving etidronate (Harris, 1993).

The third bisphosphonate, risedronate, is licensed for the treatment of established postmenopausal osteoporosis to reduce the risk of vertebral fracture. In line with this, a review of published data highlights that risedronate reduces vertebral fractures by 30–40%, although no effect on hip fracture has been proven to date (see *Table 6*).

TABLE 2.
Inclusion and exclusion criteria to identify high quality clinical studies in osteoporosis

Inclusion criteria	Randomized, double blind, placebo controlled prospective studies
	Subjects with reduced bone density with or without fractures
	Fracture endpoints
Exclusion criteria	Medicines not licensed for the treatment of osteoporosis
	Study protocols which were non-randomized, not double blind, uncontrolled or retrospective
	Studies including other bone diseases
	Combined therapies in the treatment group
	Epidemiological studies
	Studies in men

TABLE 3.
The effect of oestrogen on new vertebral and femoral neck fractures

			Control group		Treatment group			
	Study	Treatment	N with #	N	N with #	N	Risk reduction	Significance
Individual risk of ≥ 1 new vertebral fracture	Lufkin (1992)	0.1 mg/d E2 + 10 mg medroxyprogesterone for 1 year	12	34	7	34	–42%	Significant
	Recker (1999)	0.3mg/d EE + 2.5mg/d medroxyprogesterone for 1 year	4	51	3	50	–23%	NS
Individual risk of ≥ 1 new femoral neck fracture	Lufkin (1992)	0.1mg E2 for 1 year			No data			
	Recker (1999)	0.1mg/d E2 + 10mg medroxyprogesterone for 1 year			No data			

EE= equine oestrogen; E2 = oestradiol; NS = not significant; # = fracture

TABLE 4.
The effect of alendronate on new vertebral and femoral neck fractures

			Control group		Treatment group			
	Study	Treatment	N with #	N	N with #	N	Risk reduction	Significance
Individual risk of ≥ 1 new vertebral fracture	Liberman (1995)	5/10/20mg/d alendronate for 3 years	22	355	17	526	–48%	Significant
	Bone (1997)	5 mg/d alendronate for 2 years	6	91	4	93	–35%	NS
	Black (1996)	5/10 mg/d alendronate for 3 years	145	1005	78	1022	–47%	Significant
	Cummings (1998) (all patients)	5/10 mg/d alendronate for 4 years	78	2218	43	2214	–44%	Significant
	(BMD T<-2.5)	5/10 mg/d alendronate for 4 years	44	758	22	759	–50%	Significant
Individual risk of ≥ 1 new femoral neck fracture	Liberman (1995)	5/10/20mg/d alendronate for 3 years	3	355	1	526	–78%	NS
	Bone (1997)	5mg/d alendronate for 2 years		No data				
	Black (1996)	5/10 mg/d alendronate for 3 years	22	1005	11	1022	–51%	Significant
	Cummings (1998) (all patients)	5/10 mg/d alendronate for 4 years	24	2218	19	2214	–21%	NS
	(BMD T<-2.5)	5/10 mg/d alendronate for 4 years	18	758	8	759	–56%	Significant

BMD T = bone mineral density of sex-matched healthy individuals; NS = not significant; # = fracture

TABLE 5.
The effect of etidronate on new vertebral and femoral neck fractures

		Control group		Treatment group			
Study	Treatment	N with #	N	N with #	N	Risk reduction	Significance
Individual risk of ≥ 1 new vertebral fracture	Harris (1993)	400 mg/d cyclical etidronate for 3 years	32	184	28	96	–18%	NS
Individual risk of ≥ 1 new femoral neck fracture	Harris (1993)	400 mg/d cyclical etidronate for 3 years	2	184	1	196	–54%	NS

NS = not significant; # = fracture

TABLE 6.
The effect of risedronate on new vertebral and femoral neck fractures

			Control group		Treatment group			
	Study	Treatment	N with #	N	N with #	N	Risk reduction	Significance
Individual risk of ≥ 1 new vertebral fracture	Harris (1999)	5 mg/d risedronate for 3 years	93	815	61	813	–34%	Significant
	Reginster (2000)	5 mg/d risedronate for 3 years	89	407	53	407	–40%	Significant
	Fogelman (2000)	5 mg/d risedronate for 2 years	17	125	8	112	–48%	NS
Individual risk of ≥ 1 new femoral neck fracture	Harris (1999)	5 mg/d risedronate for 3 years	15*	815	12*	813	–20%	NS
	Reginster (2000)	5 mg/d risedronate for 3 years	11	407	9	407	–18%	NS
	Fogelman (2000)	5 mg/d risedronate for 2 years			No data			

NS = not significant; # = fracture

Other considerations

There are other factors that need to be considered in conjunction with clinical evidence which influence choice of treatment. Cost efficacy, patient preference and compliance are likely to figure in decision making. Ensuring patients commit to long-term use of therapy is essential to achieve optimum benefits. Compliance with HRT is a particular problem. In the future, a once-weekly dosage of alendronate will provide a new and more convenient option for osteoporosis patients, which may also help improve concordance.

Applying EBM to the management of osteoporosis

- Osteoporotic fractures have been estimated to cost the government £1.5 billion per year
- Published guidelines provide an evidence based review of osteoporosis treatments, offering clear guidance for clinicians
- Few randomized controlled trials on HRT show a significant effect on fracture reduction
- A number of high quality clinical trials demonstrate the effect of alendronate on the prevention of fractures, with reductions of about 50% at all clinically relevant sites, including the hip
- Limited randomized controlled trial evidence exists to support the use of etidronate
- A review of published data for risedronate highlights a reduction in vertebral fractures of 30–40%, although no effect on hip fracture has been proven to date.

KEY POINTS

- Evidence-based medicine (EBM) is an invaluable tool to aid decision making.
- EBM enables clinicians to select the most effective and efficient treatment for their patients.
- Hospital consultants have an essential role to play in implementing EBM.

CONCLUSION

Critically reviewing the evidence for disease management is essential if optimal care is to be provided to patients. Reviewing the evidence may cast a new perspective on traditional treatment approaches. HM

Conflict of interest: none.

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