Check Unit: evidence based medicine

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EVIDENCE BASED MEDICINE

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The five domains of general practice
1. Communication skills and the patient-doctor relationship
2. Applied professional knowledge and skills
3. Population health and the context of general practice
4. Professional and ethical role
5. Organisational and legal dimensions
This is an updated version of an original check unit on evidence based medicine (EBM) written by Chris Del Mar, Paul Glasziou and Chris Silagy in 1999. We are grateful to our authors, Chris Del Mar, MD, MA, MB, BChir, FRACGP, FAFPHM, and Jenny Doust, BMBS, PhD, FRACGP, for updating this unit for us.

Chris is Dean, Faculty Health Sciences and Medicine, Bond University, Gold Coast, Queensland, and Jenny is Professor of Public Health, Bond University and a general practitioner.

Our aim for this unit is to present a practical strategy in learning to use EBM in our everyday practice. To practise EBM means to make clinical decisions based on the best evidence currently available. It sounds simple, however, the ‘devil’ is in the detail! Exactly how do we go about it?

The first step is to ask a question that will specifically address what we need to find out to manage a patient at this time. It needs to be framed in a way that research evidence can provide a useful answer, i.e. for treatment questions, rather than asking, ‘Does treatment A work?’, we can ask, ‘Is treatment A better than no treatment (or treatment B) in reducing symptoms (or duration of illness)?’

Once we have our question, we need to identify relevant information sources that may help answer it, critically appraise that information, and apply the evidence to the patient.

We hope the cases in this unit specifically demonstrate each of these steps. The best way to use this unit is to go through the cases in front of a computer with internet access and follow the steps … learn by doing!

You will notice that the format of this unit is different to previous units. At the beginning we discuss what EBM is … and what it is not. In the case studies, the authors have not provided all the references of the evidence from which they have quoted. Their hope is that you will be interested in finding the evidence yourself from the source. The resource section provides guidelines and websites used in this unit, as well as other useful resources to assist you in following through these cases and finding the best available evidence to answer your clinical questions.

On completion of this unit we hope that participants will:

• appreciate the role that EBM can play in improving the quality of patient care and in involving patients in the decision making process
• display increased confidence in the steps involved in EBM: formulating questions, finding evidence, critically appraising evidence and applying evidence with the patient
• understand which information sources are most appropriate for different types of questions, e.g. therapeutic or diagnostic questions, and
• understand the basic principles to apply when appraising evidence, and confidently use the Cochrane and Pubmed databases to undertake basic searches.

We hope that you will find using EBM increases your enjoyment of, and enthusiasm for, your day-to-day practice.

Best wishes

Jenni Parsons
Medical Editor
What exactly is EBM?
Evidenced based medicine is simply a way of ensuring that clinical decisions are based on the best available research information. The best evidence is hard to define in one sentence, but it is characterised by an emphasis on empirical research (research based on the result of different approaches to clinical management) rather than assumed effects based on understanding the pathology, physiology or microbiology. The emphasis is less on understanding why as asking whether. Too often in the past we relied on knowing what should work by attempting to understand the mechanism of illness.

How can I practise EBM if there are no randomised controlled trials (RCTs) to answer my question?
Some clinicians think ‘EBM = RCTs’, ie. EBM is about relying on RCTs, and that unless there are RCTs for a particular question, EBM falls down. This is incorrect on several counts. First, although RCTs are the best design for answering questions of treatment (‘interventions’), there are many other types of questions (Table 1).

Table 1. Question types (with typical examples)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>“What is the better of these two treatments?”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>“What is the chance of disease if this test/sign is positive/negative?”</td>
</tr>
<tr>
<td>Prognosis</td>
<td>“If a patient has a disease at this stage and age, what is likely to happen?”</td>
</tr>
<tr>
<td>Aetiology</td>
<td>“How does this risk factor influence the chance of getting/course of the disease?”</td>
</tr>
<tr>
<td>Frequency</td>
<td>“How common is this disease among patients like those in my practice?”</td>
</tr>
</tbody>
</table>

Second, whatever the question, even if the best quality evidence is not available, then whatever is best is …the best! Even if this is only the clinician’s own experience, (see below), it is good to know the quality of information we are using to base decisions on.

What is wrong with experience?
The main problem is, although experience is often right, it is also often wrong. There are so many processes (eg. biases and selective memory) that we cannot rely on experience. Doctors (including Sir William Osler) were convinced for about 200 years that blood letting was essential in the treatment of pneumonia. This error of experience was not just wrong, but undoubtedly harmful. In our own professional lifetimes, we have done a 180 degree change in direction on rest for osteoarthritis (trials have found exercise is much better) or beta blockers for heart failure (previously thought to be harmful; trials now show evidence of benefit). What else do we take for granted from our experience that will change when new research is published? However, sometimes there is no better evidence than experience and we must rely on that – it is better to know when we are ‘skating on thin ice’.

What types of evidence are best?
This depends on the information required. For choice of management, the best available evidence comes from RCTs. For diagnostic tests, other types of information will be necessary, eg. from a consecutive series of patients given the test and ‘gold standard’. The best evidence comes from systematic reviews, in which all studies ever undertaken to answer a particular clinical question are combined together objectively. If the data collected are similar (there are some fine points of statistics), they can be combined into a meta-analysis (meta means ‘end’). In addition to being published in journals, meta-analyses are available in one convenient place. The largest and most useful is held in the Cochrane Library (named after Archie Cochrane). In Australia and New Zealand access is free (see Resources).

Better than review articles, meta-analyses make it easier to establish not only if a particular management option is better, but how much better. That is a quantification of benefit (and harm, sometimes!). Examples are shown in the case studies in this check unit.

Does evidence exist for what we do in general practice?
Medical literature is burgeoning with evidence. Every week research articles on the types of conditions managed in general practice are published in medical journals. The problem for clinicians is finding evidence efficiently and keeping up-to-date with the latest evidence.

Estimates suggest that well over half the therapeutic choices we make have evidence for them already in the literature.

Are review articles EBM?
In theory, review articles (summaries of the literature on a certain topic) should help guide us through the literature. The problem is that they are often incorrect because they are not up-to-date, or their authors are unsystematic and therefore biased. There are countless examples of unsystematic review articles giving incorrect advice simply because the information selected by the author was selected to fit in with his/her view. Recent information may not be included or may be misinterpreted.

What have guidelines to do with EBM?
Many clinicians think ‘EBM = guidelines’. Sometimes this is true – but only if the guidelines are evidence...
based. Plenty of clinicians practise EBM without referring to guidelines. They find their own original primary source research papers and make their judgments. Guidelines should be treated as another type of resource for research data to inform our decisions. When guidelines fulfil their best definition: systematised summaries of the research to inform clinical decisions, they are good. That is almost the same definition as a systematic review. However, guidelines are sometimes no more than opinion about best practice, ie. experience. The essential difference between guidelines and systematic reviews (and meta-analyses) is the intention: guidelines provide guidance whatever the state of the evidence. Guidelines can be as good as the best systematic reviews when evidence based, and as poor as the worst opinion based review article when not.

**How can I practise EBM in my clinical work?**

Follow these steps in applying evidence based general practice:

- What is the clinical question?
- What type of evidence would answer the question?
- Where can I find that evidence?
- Is the evidence of good enough quality?
- How do I put the answer into practice?

Evidence based medicine is an interesting way of practising. It requires thought to gain access to the evidence. It should be possible to discover the amount of benefit of different management options, one over the other. Quantifying the benefit (and harm) seems to be the direction in which general practice (and all medicine) is moving.

Enormous clinical judgment and skill is required to convert the evidence into a form that allows the clinician to come together with the patient to decide on the best way of managing the problem.

Remember to check your findings with an expert (EBM expert or specialist in the field in question) if the conclusions you reach appear to be outlandish. Sometimes you can be misled by a range of problems; from not finding the right evidence or selecting on the basis of best quality evidence, or misinterpreting the evidence. Like everything else, it takes practice.

Evidence based medicine is difficult to master. Participating in an EBM workshop is one way to increase confidence. Another way is to join a like minded EBM journal club and learn by doing.

The following case studies show examples that you could use if you have a day of basing as much of your practice on evidence as you could.

We have refrained from giving all the references of the evidence from which we have quoted. Our hope is that you will be interested in finding the evidence yourself and building your confidence and skills in this area.
Harry, aged 67 years, comes to see you for a repeat prescription for his chronic asthma. ‘You are still smoking, aren’t you?’ you ask. ‘Yep, doc, can’t give up now. It’s too late. Tried before and I just can’t stand it. My ‘fags’ is one of my last pleasures and I know it isn’t good for me. Just have to hope you will do the best for me if a cancer crops up’, he chuckles. This macabre display of mirth starts you thinking. Would a chest X-ray pick up carcinoma of the bronchus early enough to improve Harry’s chances if he developed one?

**Question 1**
What is the clinical question?

**Question 2**
What type of evidence would answer the question?

**Question 3**
Where would you find this evidence?

**Question 4**
How would you put the answer into practice?
Case 1

Answer 1
The question is: ‘Does using a chest X-ray in smokers without symptoms for early detection of lung cancer result in a better outcome than doing nothing?’

Note the question is not ‘Do chest X-rays pick up cancer earlier?’ This would be a necessary accompaniment of the correct question, but it is not enough. You need to know the result of this in terms of patient survival and quality of life.

We want to know which of the following ‘states of evidence’ exist:

- Is there any evidence about early detection of lung cancer leading to improved survival?
- If yes, is the evidence good?
- If yes, how much benefit or harm is there?

Answer 2
For this particular question, finding the right evidence is not straightforward. Whether screening for serious disease is useful is a difficult question to answer. To understand the reasons for this, and to ensure that the correct type of evidence is searched, it is important to understand ‘lead time bias’. This refers to the ‘extra’ time a person has if a diagnosis of their disease is identified early. Figure 1 helps explain the problem.

The problem is how to distinguish between people who have the diagnosis longer because they were diagnosed earlier, rather than because they live longer as well. The best way to ensure that the lead time does not introduce a bias is to employ a randomised control trial design.

Answer 3
You will find the evidence using the Cochrane Library, accessible at www.TheCochraneLibrary.com.

The search is easy: Enter ‘screen lung cancer’ into the SEARCH box. If you click the GO button you will get far too many ‘hits’. Re-enter it and click the drop down menu to select ‘Record Title’. This will limit the search to only systemic reviews and trials that include these items in their title.

This yields one Cochrane review, three other systematic reviews and 48 trials. (Figure 2).

Figure 2. Screen shot from the Cochrane Library

It is reasonable to go for the highest level of evidence (Cochrane review) for a quick search. (For a formal academic systematic review, your search needs to be more exhaustive.)

The summary of this review is that early detection in asymptomatic men does not result in improved survival.

In summary:

1. There is evidence about screening for lung cancer and improved survival.
2. It is quite good evidence.
3. The evidence is that early detection in asymptomatic men does not result in improved survival.

An alternative to searching the Cochrane database would be to look for a set of guidelines. Screening is a complicated and important activity, and several guidelines have been developed.

The RACGP Guidelines for preventive activities in general practice (‘red book’) does not mention screening for lung cancer. This implies there is no good evidence for its effectiveness.1 The NHMRC Preventive guidelines for cancer and cardiovascular disease devotes a chapter to this question.2 This guideline has the advantage over the RACGP red book summary in that it provides the basis for the recommendations.

Answer 4
Putting this into practice: don’t screen asymptomatic patients for lung cancer.

Case feedback

This is a good example of using guidelines. Good guidelines are available for preventive activities (see Resources). They are all evidence based which means that they have been based on empirical evidence (rather than on what may work based on understanding the principles or pathophysiology).
Kim is a 21 year old university student. She complains of a sore throat. She tells you that it started yesterday and it’s ‘so sore’ when she swallows. Her problem is that she has three assignments to hand in over the next 5 days and ‘wasn’t counting on this’.
She has no significant previous history. On examination there is a little inflammatory exudate. She has painful lymph nodes in the neck. Her ear drums appear normal. Her temperature is 37.7°C. Would you prescribe antibiotics for Kim?

Question 1
What is the clinical question?

Question 2
Where would you find the evidence to answer your question?

Question 3
How would you put the answer into practice?
Answer 1

Traditional teaching is to identify the organism and treat accordingly. This is a pathophysiological approach. In an evidence based approach, several questions could be asked such as:

- **Can we estimate what the organism is clinically?**
- **Can throat swabs be used to reliably identify the causative organism?**
- **Are there other useful tests?**

If we make no attempt to identify the organism, we could ask: ‘Is it helpful to treat a patient with antibiotics who has an inflamed throat such as Kim?’

Let us focus on the last question. First, we need to decide what is meant by the term ‘helpful’. What are the effects of sore throat?

Symptoms include the soreness of the throat and feeling systemically unwell. Complications include suppurative (e.g. acute otitis media, sinusitis, quinsy) and nonsuppurative (e.g. acute rheumatic fever, glomerulonephritis).

So a final question could be:

‘Will treating a patient such as Kim with antibiotics result in a reduction in length of symptoms or decreased complication rate?’

Answer 2

Specialists could provide the answer, but most ear, nose and throat surgeons rarely see patients such as Kim (patients are only referred with chronic or serious complications of sore throat).

What do guidelines say? Therapeutic guidelines: Antibiotic states that antibiotics have little to offer, yet gives detailed advice about which antibiotic to use. Instead, go to the Cochrane Library. Searching ‘sore throat’ in the ‘Record Title’ selected search box (use the drop down menu to select ‘Record Title’ from the other options) we find four Cochrane systematic reviews and three look relevant! (We also find two other non-Cochrane reviews in abstract only and 133 trials.)

One of the Cochrane reviews addresses the question of antibiotics for sore throat. On opening it, you can look at the data that address each of the clinical questions. You do this by selecting the ‘Figures (full size)’ option on the left hand side and scrolling down the (long) list of different questions looked at.

*Figure 3* looks at how many patients still have throat soreness after 3 days of antibiotics or placebo.

Note: We also selected the ‘Relative Risk’ from the ‘Show Statistical Analysis’ option rather than ‘Peto Odds Ratio’ option because this is slightly easier to apply clinically, but this is not mandatory as it is the same information.

We can summarise the findings as follows.

Fifteen studies looked at over 3500 patients. Those randomised to receive antibiotics were less likely (their relative risk being 0.72, i.e. 72% of those not receiving antibiotics) to suffer the symptom of throat soreness by day 3 of diagnosis.

Other outcomes, such as the risk of contracting acute rheumatic fever or supplicative complications, can be found in this Cochrane review.

At first sight this seems to encourage the use of antibiotics, but let us look behind the numbers.

Another analysis in the review shows that 90% of patients were better by day 7 whether they used antibiotics or not. (This is a self limiting disease.) The chance of acute rheumatic fever and quinsy is so low in Australia (except among Aboriginal communities) that it takes about 20 GP lifetimes to see a single case of acute rheumatic fever in the western world, even in the Netherlands where antibiotic usage is low.

As far as symptoms are concerned, the overall shortening of the illness that antibiotics confer is about 12 hours (and 14 hours at the time of maximal difference, at 3 days). Is it worth prescribing antibiotics and risking the chance of thrush, diarrhoea and abdominal pain associated with antibiotics?

(As the risk of acute rheumatic fever is high in Indigenous Australian communities, it would be best treated empirically with penicillin if any streptococcal infection is suspected.)
Answer 3

As the differences between using and not using antibiotics are marginal and involve patient values, it is reasonable to involve the patient in the decision. The difficulty is in expressing the information to allow them to do this. The way we express this will depend on our own styles, eg. ‘Kim, the chance is that antibiotics will only reduce the length of the illness by about half a day. It would reduce the chance of some complications, but these are very unlikely, eg. you would need to take antibiotics for about 140 episodes of sore throat to avoid a single case of middle ear infection. Bear in mind antibiotics commonly cause thrush and diarrhoea. You may be better off concentrating on drugs such as aspirin or paracetamol. What do you think?’

Whether Kim decides to take the antibiotics or not, either decision is fine.

Case feedback

Once again notice how the range of acceptable options is wider when the evidence suggests that one form of management has little benefit over another. This is the area of discretionary choice. This is an example where there is no mandatory management. What if Kim elected to have the treatment? Fine. She would have decided that the (small) benefits outweighed the costs (both financial and in terms of side effects). The evidence can only assist the patient and doctor come to agreement about the best treatment for that particular episode for that particular person. Previous research has shown how GPs take the patient’s psychosocial factors as seriously as their clinical ones.

Finding the evidence enables some estimate of the size of the benefit – not just whether the balance is for or against.
George, aged 47 years, has come to see you for a medical certificate to allow him to operate a crane. He has no previous relevant medical history. His urine has been routinely tested by the practice nurse. She has written ‘urine dipstick test: blood – moderate’ in the notes. The rest of his examination was normal.

You order a urine microscopy and culture. The culture was negative, but morphologically normal red cells in a concentration of 30 per high power field were present. George’s examination was normal. In particular, he had normal blood pressure and abdominal examination.

What do you do now?

Question 1 📚🔍
What is the clinical question?

Question 2 📚🔍
What type of evidence would answer the question?
Where would you find the answer?

Question 3 📚🔍🔍
How would you put the answer into practice?
Answer 1

The first question to ask is: ‘What are the common causes of microscopic haematuria?’

The causes can be divided into a number of logical ways, eg:

- general causes such as anticoagulation and bleeding diatheses
- glomerular causes such as IgA glomerulonephritis, and
- lesions of the transitional cell epithelium (including transitional cell carcinoma).

Some of these causes are life threatening.

So the question you would ask of the evidence is ‘In a patient with asymptomatic haematuria, what is the likelihood of bladder cancer or urinary calculi?’

Answer 2

After checking on another occasion and also doing a midstream urine to confirm the finding, you could check the Cochrane Library. This is not a logical place to look because this type of question is a diagnostic question. The Cochrane Library currently focuses on treatment questions.

It makes better sense to look in the ‘easiest-to-use’ and most accessible big database of medical research, ‘Medline’, in its PubMed web portal at www.pubmed.gov. One of the options on the left hand side is ‘Clinical Queries’ – a useful search engine for doctors. Clicking on it, we can enter the search and click on the ‘diagnosis’ button (leaving the default ‘narrow, specific search’) (Figure 4). Note that if we enter the search term ‘microscopic haematuria’, PubMed will automatically map to, and search for, the term ‘hematuria’. You can see exactly which terms the PubMed database has used by clicking on the ‘Details’ tab.

This results in four pages of hits (78 hits). You could either refine the search or simply eyeball what we found. One hit on the first page looks highly suitable – a systematic review (Figure 5).

In the abstract we find these sentences:

‘Six studies using haematuria as a test for the presence of a disease indicated that the detection of microhaematuria cannot alone be considered a useful test either to rule in or rule out the presence of a significant underlying pathology (urinary calculi or bladder cancer)’ and

‘Strategies that use routine microscopy may be associated with high numbers of false results, but evidence was lacking regarding the accuracy of routine microscopy…’

Answer 3

This leaves us in a quandary. Reading the entire report suggests that the number of false positive results (ie. haematuria but no bladder cancer or renal calculus) is as high as 20:1. This may be reassuring for the doctor and patient. Together you may elect to postpone further investigations and adopt a wait-and-see management style, in particular, asking George to return should he develop any symptoms. Alternatively you may adopt the more traditional series of investigations including cystoscopy, ultrasound and intravenous pyelogram.
Steve is a 29 year old bricklayer. He had previously been fit and healthy until 2 weeks ago when his wife noticed a dark pigmented lesion on his upper back.

The lesion is about 1 cm in diameter, slightly raised and with an irregular border. Physical examination was otherwise unremarkable. In particular, there was no evidence of any lymph node enlargement or other suspicious lesions.

You remove the lesion to exclude melanoma, in your surgery under local anaesthetic the following day, and advise Steve to return in 1 week for removal of his stitches and to discuss any further follow up.

Two days after removing the lesion you receive the pathology report:

‘… a malignant melanoma measuring 0.9 cm in diameter and 0.78 cm in thickness (according to the method of Breslow). Excision is complete with a 1 cm margin at the closest border. Histology is consistent with a superficial spreading melanoma with no evidence of invasion or microsatellites.’

You are concerned and unsure about whether a wider re-excision is required in view of the pathology.

Steve asks, ‘What’s the chance of it coming back, doctor?’

**Question 1**
What is the clinical question?

**Question 2**
What type of evidence would answer the question? Where would you find the answer?

**Question 3**
How would you put the answer into practice?
**Answer 1**

The evidence-based questions are: 'Is there evidence that patients with a level 1 melanoma require an excision margin >1 cm?' and 'What is the probability that the lesion will recur if you do not undertake a wider excision?'

The second step is to identify relevant information sources that may help answer your question. Once you have done so, you need to undertake the third step of critically appraising the information you have obtained, and finally, apply the evidence with the specific patient.

**Answer 2**

The type of evidence that would answer the questions could be found by calling your local dermatologist or surgeon to discuss the case. However, today why not alternatively search for the information yourself? Guidelines are often a good starting point. A useful website is the USA National Guidelines Clearinghouse at www.guideline.gov. Another site more locally relevant is the Cancer Council Australia at www.cancer.org.au.

The Australian Cancer Networks Working Party on the Management of Melanoma's draft Clinical practice guidelines for the management of melanoma recommends:

‘The minimum radial excision margins, measured clinically from the edge of the melanoma be: Melanoma in situ: margin 5 mm – grade C’ (see Feedback).

It also states:

‘Caution should be exercised for melanomas thicker than 4 mm because evidence concerning optimal excision margins is unclear. Where possible it may be desirable to take a wider margin (2 cm) for thicker tumours depending on tumour site and surgeon/patient preference.’

**Feedback**

What is meant by the term ‘Grade C recommendation’ evidence? Table 2 summarises the description of the gradings from the draft Clinical practice guidelines for the management of melanoma.

It is hard to find the evidence in this long set of guidelines. Another approach is to search for the evidence yourself. Going to the Cochrane Library and entering ‘melanoma AND excision’ in the ‘Record Titles’ option yields 17 hits.

One is a Cochrane protocol (meaning a review has been started but has not reported yet). There are two other systematic reviews and 14 trials listed.

In one of these trials (Veronesi 1988) the recurrence rate for melanomas of this type is 2.5% for distant metastases; 5.5% for lymph node recurrence; and 1% for local recurrence over a mean 7.5 years.

The width of the excision margin only affected the local recurrence rate. There were three local recurrences in 305 patients treated with a narrow (≤1 cm) margin and none in 307 patients with a wide margin. This is confirmed by two other studies.

**Answer 3**

Based on the evidence, does Steve require a wider excision? What is the difference in chance of the melanoma recurring from a smaller and larger excision?

The guidelines are reassuring. But the data suggest the chance of a local recurrence is so small for thin melanomas that any benefits of a wider excision are minuscule.

Steve should have the level of evidence upon which the recommendation regarding the need for wider excision has been made explained to him. Ideally, management follows a negotiated decision between the doctor and patient. Increasingly there are consumer versions of guidelines to accompany the version targeting health care professionals, which are useful for patient decision making. Offer Steve an opportunity to read the guidelines and ask if he has a view.

It would be reasonable for Steve to opt for no further excision after this, or if he expressed a preference for a wider excision, that would also be acceptable. The lower the level of evidence supporting a recommendation, the greater the likely variation in treatment practices.

What if Steve delegates the decision to you? eg, ‘I don’t know doctor. What do you think?’

Perhaps our duty is to best guess the patient’s views, values and preferences, and decide accordingly. In Steve’s case, we need to weigh up the benefits and harms of the additional surgery for a wider excision against the possible benefits of a decreased local recurrence rate. Often we tend to do this without realising it. General practitioners are usually in a good position to do this because often they know their patients well.

<table>
<thead>
<tr>
<th>Table 2. Gradings of evidence for recommendations in melanoma management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grade of recommendation</strong></td>
</tr>
<tr>
<td>A</td>
</tr>
<tr>
<td>B</td>
</tr>
<tr>
<td>C</td>
</tr>
<tr>
<td>D</td>
</tr>
</tbody>
</table>
Ken, aged 49 years, has smoked 20 cigarettes per day since he was 16. He has tried to quit on several occasions, but has not managed to sustain being a nonsmoker for more than 3 months. He has seen recent television advertisements advocating the use of nicotine replacement therapy (NRT). He has never used any form of NRT with his previous quit attempts.

Ken asks, ‘Is it worth a go, doctor? I heard it is expensive.’

A drug company representative recently told you that there is evidence from several recent systematic reviews that NRT is effective.

**Question 1**
What is the clinical question?

**Question 2**
What type of evidence would answer the question? Where would you find the answer?

**Question 3**
Summary data from the systematic review of randomised trials you find is included in Table 3. What do ‘odds ratio’ and ‘95% confidence intervals’ mean?

**Table 3. Summary data from systematic review of NRT trials**

<table>
<thead>
<tr>
<th></th>
<th>Number of trials</th>
<th>Odds ratio (and the 95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine gum</td>
<td>52</td>
<td>1.66 (1.52 – 1.81)</td>
</tr>
<tr>
<td>Nicotine patch</td>
<td>38</td>
<td>1.81 (1.63 – 2.02)</td>
</tr>
<tr>
<td>Nicotine inhaler</td>
<td>4</td>
<td>2.14 (1.44 – 3.18)</td>
</tr>
</tbody>
</table>

**Question 4**
Given the figures in Table 3, how would you answer Ken about whether NRT works?

**Question 5**
What is meant by the term ‘number needed to treat’ (NNT)?

**Question 6**
You would put the answer to your clinical question into practice by asking: ‘What additional factors (if any) do I need to take into account in making a treatment decision for Ken?’
Answer 1
Before Ken pays out hard earned money, the questions to ask are:

- ‘Does nicotine replacement therapy work (in comparison with no treatment) for successful smoking cessation (at 6 or 12 months)?’
- ‘If so, by how much?’

Answer 2
You realise this is a treatment question, and therefore best answered by RCTs. The Cochrane Library is the best place to search.

Being lazy, you only enter ‘nicotine’ into the search box with the ‘Record Title’ option selected in the drop menu. Surprisingly there are six Cochrane reviews (and 10 other systematic reviews and 1264 trials), but only one fits the bill – *Nicotine replacement therapy for smoking cessation*.

Answer 3
The odds ratio is the ratio of the intervention (NRT using) divided by the control (placebo using) odds.

The odds is the number of nonsmokers at the end of the trial divided by the number of smokers. The odds ratio compares the odds of being a nonsmoker 6–12 months following the use of NRT versus to placebo.

*Table 3* shows that there are about twice as many nonsmokers among those using NRT than among those using the placebo at the end of the trial. So using NRT approximately doubled the chances of successfully giving up smoking.

Confidence intervals are a useful way of accounting for the size of the sample (smaller samples result in less confidence of the result, and hence wider confidence intervals), and the variability of the results – (‘noisy’, ie. more variable samples, similarly result in less confidence of the result, and hence wider confidence intervals).

The figures in brackets in *Table 3* are the 95% confidence intervals. This is a statistical measure of the certainty that the figures are correct, eg. in the case of nicotine gum, we are 95% sure that the odds ratio lies 1.52–1.81; that there is only a 5:100 or 1:20 probability that the figure would lie outside this range by chance alone.

Answer 4
The evidence from the systematic review of RCTs clearly indicates that if Ken uses NRT he will nearly double (around 1.66–2.14, depending how the nicotine is delivered) his chance of quitting for 6–12 months.

A widely quoted figure for the success of giving up with nothing more than simple advice from a GP is about 4–6%. This means Ken’s absolute chance of giving up on this occasion is multiplying this by 2, or about 8–12%.

Answer 5
Another way to express the same benefit is to ask the following question: ‘How many patients would you need to treat with each of the three forms of NRT in order to result in one extra patient being a nonsmoker at 6–12 months compared with using placebo?’

This uses the difference between rates for intervention and control. If the rate of smoking cessation with advice alone is 6% and the rate with nicotine gum is 12%, the difference is 6%. This means that offering nicotine gum to 100 people trying to give up smoking will result in six succeeding because of the gum. 6/100 is the same as 1 out of 17. Out of every 17 people offered NRT, one will succeed. This measure of the absolute risk is called the number needed to treat (NNT). Clinicians find this a useful measure of the size of effect.

Note: the NNT = 1/event rate difference.

Answer 6
Recommending a particular form of treatment to a patient needs to take into account factors in addition to the evidence of effectiveness. These include:

- needs and preferences of the patient
- costs associated with treatment
- likely compliance with therapy, and
- potential side effect profile.

Smokers who have manual jobs and perspire may prefer to use nicotine gum because of the practical problems associated with adherence of the patches to the skin. Smokers who are concerned about stigmatisation associated with using an oral medication may prefer to use the patch. In each case, these decisions should be negotiated with the patient after considering the evidence of effectiveness for each of the therapeutic options, as well as the other factors that influence the likely use of the products.

Case feedback
Notice how far the evidence has taken us. We have been able to provide Ken with information that will help him feel well informed that NRT is effective and by how much.
You have been treating Angela, aged 53 years, for hypertension. Her blood pressure has been difficult to control with escalating doses of hypertensives. You have discussed Angela’s problem with your colleagues and decided to exclude renal artery stenosis. There are two choices for doing this test where you work: radio-isotope renal scan, and duplex ultrasound. The ultrasound is about 20% of the cost of the former, but is it as good?

**Question 1**
What is the performance measure of a test?

---

**Question 2**
What is the clinical question?

---

**Question 3**
What type of evidence would answer the clinical question? Where would you find the answer?

---

**Question 4**
How would you put the answer into practice?

---
Answer 1

The test performance can be described in two ways:

- How well can the test pick up patients with the disease? This is called the ‘sensitivity’.
- How well can it exclude patients who do not have it? This is the ‘specificity’.

Researchers can determine these characteristics by testing groups of people who have the illness and those who do not.

The sensitivity and specificity of the test can be set as in Table 4.

Table 4. Sensitivity and specificity test

<table>
<thead>
<tr>
<th></th>
<th>People with renal artery stenosis</th>
<th>People without renal artery stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test +ve</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Test -ve</td>
<td>C</td>
<td>D</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>a/(a+c)</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>d/(b+d)</td>
<td></td>
</tr>
</tbody>
</table>

Answer 2

The question is: ‘What is the performance of ultrasound in comparison with intra-arterial angiography?’

Answer 3

A good first place to look is the Clinical Queries section of PubMed. A simple search (using the term ‘renal artery’ AND ‘ultrasound’) would find the listing of a study4 in which the abstract indicated that the sensitivity of the test is 85% and specificity is also 92%.

Before you could answer the question, you would need to have an idea of the likelihood of Angela having renal artery stenosis. From Gorrel, May and Mulley (see Further reading at the end of the unit) the incidence of renal artery stenosis is about 1% of adults with hypertension. However, it is much higher in those with difficult to control hypertension. Therefore let us guess that the incidence in this case is inflated to about 10%.

Put this estimate into Table 5 below by imagining a population of 1000 people of whom 10% have renal artery stenosis.

Answer 4

We can now determine what chance duplex renal ultrasound would have of picking up a renal artery stenosis in Angela. Out of all those who had a positive test (in that row), 85 out of 85 + 72 would have renal artery stenosis; or 85/(85+72); or 54%. (This proportion is called the ‘positive predictive value’ or sometimes ‘post-test positive’). It means that if Angela had a positive test she would have 54% of having renal artery stenosis, in which case we could either order the more expensive alternative or refer to a specialist for further investigation, accepting that we would have done so unnecessarily only 46% of the time.

What if the test was negative? The equivalent calculation is 828/(828+15) = 98%. In other words, a negative ultrasound would be extremely good at ruling out renal artery stenosis.

Is this good enough? The answer is almost certainly yes. We are more interested in excluding the illness accurately.

Table 5. Determining predictive value

<table>
<thead>
<tr>
<th></th>
<th>People with renal artery stenosis</th>
<th>People without renal artery stenosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test +ve</td>
<td>A</td>
<td>B</td>
<td>85+72</td>
</tr>
<tr>
<td>Test -ve</td>
<td>C</td>
<td>D</td>
<td>15+828</td>
</tr>
<tr>
<td></td>
<td>100 &lt;— 900 &lt;— 1000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Now we apply the sensitivity and specificity in the columns:

<table>
<thead>
<tr>
<th></th>
<th>People with renal artery stenosis</th>
<th>People without renal artery stenosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test +ve</td>
<td>85</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Test -ve</td>
<td>15</td>
<td>828</td>
<td></td>
</tr>
<tr>
<td></td>
<td>100 &lt;— 900 &lt;— 1000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
References and resources


Guidelines and specific resources cited in this check unit
Please also refer to the references section above.

RACGP resources

RACGP John Murtagh Library www.racgp.org.au/library
Eligible users can request resources, information, journal articles and literature searches via the website, email, fax or telephone. Users can also directly access the library’s electronic resources (including full text articles from hundreds of journal titles) via the website including links to publicly available databases of Cochrane and Pubmed. Members also have access to Proquest and Meditext databases. All eligible users also now have access to DynaMed – an evidence based clinical reference tool for use primarily at the ‘point-of-care’. DynaMed provides clinically organised summaries for nearly 2000 topics.

MyGeneralPractice desktop
The desktop portal available to RACGP members. In the eLibrary section, links to a variety of online journals, guidelines and evidence based medicine resources are provided.

Internet resources

Cochrane Library www.thecochranelibrary.com
This is the National Library of Medicine’s free MEDLINE search site with the database prefiltered for the best evidence for different types of clinical questions: diagnosis, treatment, aetiology or frequency.

Centre for Evidence-Based Medicine www.cebm.net/
The Centre for Evidence-Based Medicine, in Oxford, aims to promote evidence based health care and provide support and resources to anyone who wants to make use of their.
The centre’s website contains an EBM toolbox at www.cebm.net/?o=1023. This has numerous aids to the practice and teaching of EBM, including pre-test probabilities, likelihood ratios, numbers needed to treat and other measures of effectiveness for diagnostic tests, therapy and prognosis, tips on asking clinical questions, searching and clinical appraisal and a glossary of EBM terms.

Bandolier www.jr2.ox.ac.uk/bandolier/
Bandolier is a website about the use of evidence in health, healthcare, and medicine by a team based in the John Radcliffe Hospital in Oxford. It contains information about EBM and how to use it [Learning Zone section], a glossary of EBM terms, a NNT calculator worksheet, free articles from the Bandolier journal, summaries of good quality evidence under a variety of different headings (knowledge library section) and evidenced based information for consumers on various health topics (healthy living section).

NHS Public Health Resource Unit
Appraised tools developed by the Critical Appraisal Skills Program (CASP) are available at www.phru.nhs.uk/Pages/PHD/resources.htm.

Critical appraisal and ‘how to’ texts


EBM journals and summary resources

BMJ Clinical Evidence. BMJ publishing group. Provides systematic reviews offering evidence interventions and answering clinical questions available in a range of formats including BMJ Clinical evidence handbook print version published twice yearly, database on PDA or online version. Available at clinicalevidence.bmj.com.

Further reading

Erratum
In the January/February 2008 unit on hypertension (Unit 430–431), page 18, Case, 7, Table 7, column 1, the underlying disease process is hyperaldosteronism and not hypaldosteronism.
The check program apologizes for any confusion this error may have caused and thanks readers who alerted us to this typographical error.
**Active learning module**

In order to qualify for 40 Category 1 QA&CPD points for this ALM:

**Step 1. Undertake this predisposing activity**
- Look at the clinical records of the last 20 patients you have seen. Write down the clinical decisions you have made in these consultations, eg. What tests have you ordered? What treatment have you initiated?
- What questions arise for you from these consultations? What is the evidence on which you have you based your clinical decisions in these consultations?
- Develop a list of at least three personal learning goals for this ALM. In doing this, it may be helpful to consider the following questions: Why did I choose this topic at this time? What would I like to do differently as a result of undertaking this ALM? What skills or knowledge would I like to gain?

**Step 2. Read and complete this unit of check**
You do not need to send in the completed check unit. Please retain your check unit and answers for your future reference.

Expected time commitment is approximately 2 hours.

**Step 3. Undertake the following practice based activity**
You can undertake this step on your own but it may be more interesting and educationally valuable to undertake it with 1–2 GP colleagues so that you can share knowledge and resources, and compare notes.

Expected time commitment is a minimum of 4 hours.

- Keep a notepad with you during your consultation sessions.
- Write down the clinical questions that arise from these consultations until you have a list of 20 questions. Frame these questions in a way that will help you search the literature for evidence.
- Choose six of these questions. Ideally choose questions of different types: intervention, diagnosis, prognosis, aetiology, frequency.
- Identify what type of evidence you need to answer each of these six questions: Cochrane database, Pubmed search, relevant guidelines or other evidence based source.
- Search relevant sources to find appropriate evidence.
- Critically evaluate this evidence. How well does the evidence answer your question? How good is this evidence? What are the biases in the evidence? What are the numbers needed to treat (or harm)?
- Consider how you would apply this evidence to your patient. What factors would you need to take in to consideration?

**Step 4. Fill in the reinforcing activity and evaluation summary**
Report on the activities you have undertaken and send to the coordinator who will coordinate the approval and point allocation process.

We encourage you to electronically fill in the evaluation summary and email to anne.valenta@racgp.org.au. A check Program ALM evaluation summary form can be downloaded from the RACGP website at www.racgp.org.au/check. Alternatively, you can photocopy and fill in the evaluation summary included in this unit and post it. Please allow up to 6 weeks upon receipt of your evaluation summary to receive your certificate of participation.

**Other activities to consider for the QA&CPD Program**

**Evidence based medicine journal club (40 Category 1 points)**
Is this topic one you would like to learn more about with your peers? This triennium you could use this unit of check and the resources listed to assist you in a new QA&CPD activity for an EBM journal club. Details of requirements are available on the QA&CPD section of the college website at www.racgp.org.au/qacpd/20082010triennium/gpforms#ebmj c or you can refer to the in the 2008–2010 QA&CPD Program handbook.

Ask other GPs in your practice or contact your division of general practice to find others interested in the same topic.

Facilitator training is run regularly by RACGP faculties and will equip you to run a small group process or journal club effectively.
Reinforcing activity and evaluation summary for the active learning module on EBM (unit 433)

Eligible for 40 Category 1 points in the RACGP QA&CPD Program. A minimum of 6 hours is required to complete an ALM excluding the time taken for predisposing and reinforcing activities. Applies to the 2008–2010 triennium. Photocopy and return the completed form to the Program Coordinator, The RACGP, 1 Palmerston Crescent, South Melbourne, Victoria 3205. Please retain a copy for your records.

QA no. __________________________ Name ________________________________ Contact telephone no. __________________________
Address ______________________________________________________________________________________________________

Have you completed this unit of check? Yes / No

1 Report on activities

Refer to your initial list of 20 patients. Review the clinical decisions you have made in these consultations: How would you now approach these consultations? What differences would there be now in the way you frame your questions? Where would you look for evidence for answers to those questions?

Write a brief description and attach evidence of the activity undertaken, ie. your list of 20 questions and a report on the six questions you have sought evidence to answer.

What did you learn from this activity?

What will you do differently in your practice as a result of this activity?

Time taken to complete your practice based activity ______________
2 Learning objectives
Please indicate to what extent after completing this activity you are able to meet the stated learning objectives.

<table>
<thead>
<tr>
<th>Learning objective</th>
<th>Not met</th>
<th>Partially met</th>
<th>Entirely met</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appreciate the role that EBM can play in improving the quality of patient care and in involvement of the patient in the decision making process.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Display increased confidence in the steps involved in EBM: formulating questions, finding evidence, critically appraising evidence and applying evidence with the patient.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Understand which information sources are most appropriate for different types of questions, eg. therapeutic questions or diagnostic questions.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Understand the basic principles to apply when appraising evidence.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confidently use the Cochrane database and PubMed databases to undertake basic searches.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3 Learning needs and relevance to practice

<table>
<thead>
<tr>
<th>Rate the degree to which your own learning needs were met.</th>
<th>Not met</th>
<th>Partially met</th>
<th>Entirely met</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Rate the degree to which this activity was relevant to your own practice.</th>
<th>Not relevant</th>
<th>Partially relevant</th>
<th>Entirely relevant</th>
</tr>
</thead>
</table>

4 Other information
Please rate the extent to which you agree with the following statements.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>There was sufficient information and resources for me to complete this activity well.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The writing and case histories were of a high standard.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>This activity increased my knowledge/understanding of this topic.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I am likely to change my clinical practice as a result of this activity.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>This activity was of benefit to other members of my practice.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5 What other topics would you like to see covered in check?

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

6 Do you have any additional comments?

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

Signed by participant ____________________________________________________ Date ________________

Office use only
Approved by Dr Jenni Parsons □ Signed ___________________________________________ Date ________________

Attendance forwarded to the National QA&CPD Unit Date ________________