Chapter 1 **Why read papers at all?**

Does 'evidence-based medicine' simply mean 'reading papers in medical journals'?

Evidence-based medicine (EBM) is much more than just reading papers. According to the most widely quoted definition, it is 'the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients' [1]. I find this definition very useful but it misses out what for me is a very important aspect of the subject – and that is the use of mathematics. Even if you know almost nothing about EBM, you probably know it talks a lot about numbers and ratios! Anna Donald and I decided to be upfront about this in our own teaching, and proposed this alternative definition:

> *Evidence-based medicine is the use of mathematical estimates of the risk of benefit and harm, derived from high-quality research on population samples, to inform clinical decision-making in the diagnosis, investigation or management of individual patients.*

The defining feature of EBM, then, is the use of figures derived from research on *populations* to inform decisions about *individuals*. This, of course, begs the question 'What is research?' – for which a reasonably accurate answer might be 'Focused, systematic enquiry aimed at generating new knowledge'. In later chapters, I will explain how this definition can help you distinguish genuine research (which should inform your practice) from the poor-quality endeavours of well-meaning amateurs (which you should politely ignore).

If you follow an evidence-based approach to clinical decision-making, therefore, all sorts of issues relating to your patients (or, if you work in public

health medicine, issues relating to groups of people) will prompt you to ask questions about scientific evidence, seek answers to those questions in a systematic way and alter your practice accordingly.

You might ask questions, for example, about a patient's symptoms ('In a 34-year-old man with left-sided chest pain, what is the probability that there is a serious heart problem, and, if there is, will it show up on a resting ECG?'), about physical or diagnostic signs ('In an otherwise uncomplicated childbirth, does the presence of meconium [indicating fetal bowel movement] in the amniotic fluid indicate significant deterioration in the physiological state of the fetus?'), about the prognosis of an illness ('If a previously well two-year-old has a short fit associated with a high temperature, what is the chance that she will subsequently develop epilepsy?'), about therapy ('In patients with an acute coronary syndrome [heart attack], are the risks associated with thrombolytic drugs [clot busters] outweighed by the benefits, whatever the patient's age, sex and ethnic origin?'), about cost-effectiveness ('Is the cost of this new anti-cancer drug justified, compared with other ways of spending limited healthcare resources?'), about patients' preferences ('In an 87-year-old woman with intermittent atrial fibrillation and a recent transient ischaemic attack, does the inconvenience of warfarin therapy outweigh the risks of not taking it?'), and about a host of other aspects of health and health services.

Professor Sackett, in the opening editorial of the very first issue of the journal *Evidence-Based Medicine* summarised the essential steps in the emerging science of EBM [2]:

1. To convert our information needs into answerable questions (i.e. to formulate the problem);
2. To track down, with maximum efficiency, the best evidence with which to answer these questions – which may come from the clinical examination, the diagnostic laboratory, the published literature or other sources;
3. To appraise the evidence critically (i.e. weigh it up) to assess its validity (closeness to the truth) and usefulness (clinical applicability);
4. To implement the results of this appraisal in our clinical practice;
5. To evaluate our performance.

Hence, EBM requires you not only to read papers but to read the *right* papers at the right time, and then to alter your behaviour (and, what is often more difficult, influence the behaviour of other people) in the light of what you have found. I am concerned that how-to-do-it courses in EBM too often concentrate on the third of these five steps (critical appraisal) to the exclusion of all the others. Yet if you have asked the wrong question or sought answers from the wrong sources, you might as well not read any papers at all. Equally,

all your training in search techniques and critical appraisal will go to waste if you do not put at least as much effort into implementing valid evidence and measuring progress towards your goals as you do into reading the paper. A few years ago, I added three more stages to Sackett's five-stage model to incorporate the patient's perspective: the resulting eight stages, which I have called a *context-sensitive checklist for evidence-based practice*, are shown in Appendix 1 [3].

If I were to be pedantic about the title of this book, these broader aspects of EBM should not even get a mention here. But I hope you would have demanded your money back if I had omitted the final section of this chapter (Before you start: formulate the problem), Chapter 2 (Searching the literature), Chapter 15 (Implementing evidence-based practice) and Chapter 16 (Applying evidence with patients). Chapters 3–14 describe step three of the EBM process: critical appraisal – that is, what you should do when you actually have the paper in front of you. Chapter 16 deals with common criticisms of EBM.

Incidentally, if you are computer literate and want to explore the subject of EBM on the Internet, you could try the websites listed in Box 1.1. If you're not, don't worry at this stage, but do put learning/use web-based resources to on your to-do list. Don't worry either when you discover that there are over 1000 websites dedicated to EBM – they all offer very similar material and you certainly don't need to visit them all.

Box 1.1 Web-based resources for Evidence-based medicine

Oxford Centre for Evidence-Based Medicine: A well-kept website from Oxford, UK, containing a wealth of resources and links for EBM. http://cebm.net.

National Institute for Health and Care Excellence: This UK-based website, which is also popular outside the UK, links to evidence-based guidelines and topic reviews. http://www.nice.org.uk/.

National Health Service (NHS) Centre for Reviews and Dissemination: The site for downloading the high-quality evidence-based reviews is part of the UK National Institute for Health Research – a good starting point for looking for evidence on complex questions such as 'what should we do about obesity?' http://www.york.ac.uk/inst/crd/.

Clinical Evidence: An online handbook of best evidence for clinical decisions such as 'what's the best current treatment for atrial fibrillation?' Produced by BMJ Publishing Group. http://clinicalevidence.bmj.com.

Why do people sometimes groan when you mention evidence-based medicine?

Critics of EBM might define it as 'the tendency of a group of young, confident and highly numerate medical academics to belittle the performance of experienced clinicians using a combination of epidemiological jargon and statistical sleight-of-hand' or 'the argument, usually presented with near-evangelistic zeal, that no health-related action should ever be taken by a doctor, a nurse, a purchaser of health services, or a policymaker, unless and until the results of several large and expensive research trials have appeared in print and approved by a committee of experts'.

The resentment amongst some health professionals towards the EBM movement is mostly a reaction to the implication that doctors (and nurses, midwives, physiotherapists and other health professionals) were functionally illiterate until they were shown the light, and that the few who weren't illiterate wilfully ignored published medical evidence. Anyone who works face-to-face with patients knows how often it is necessary to seek new information before making a clinical decision. Doctors have spent time in libraries since libraries were invented. In general, we don't put a patient on a new drug without evidence that it is likely to work. Apart from anything else, such off-licence use of medication is, strictly speaking, illegal. Surely we have all been practising EBM for years, except when we were deliberately bluffing (using the 'placebo' effect for good medical reasons), or when we were ill, overstressed or consciously being lazy?

Well, no, we haven't. There have been a number of surveys on the behaviour of doctors, nurses and related professionals. It was estimated in the 1970s in the USA that only around 10–20% of all health technologies then available (i.e. drugs, procedures, operations, etc.) were evidence-based; that figure improved to 21% in 1990, according to official US statistics [4]. Studies of the interventions offered to consecutive series of patients suggested that 60–90% of clinical decisions, depending on the specialty, were 'evidence-based' [5]. But as I have argued elsewhere, such studies had methodological limitations [3]. Apart from anything else, they were undertaken in specialised units and looked at the practice of world experts in EBM; hence, the figures arrived at can hardly be generalised beyond their immediate setting (see section 'Whom is the study about?'). In all probability, we are still selling our patients short quite most of the time.

A recent large survey by an Australian team looked at 1000 patients treated for the 22 most commonly seen conditions in a primary care setting. The researchers found that whilst 90% of patients received evidence-based care for coronary heart disease, only 13% did so for alcohol dependence [6].

Furthermore, the extent to which any individual practitioner provided evidence-based care varied in the sample from 32% of the time to 86% of the time. These findings suggest room for improvement all round.

Let's take a look at the various approaches that health professionals use to reach their decisions in reality – all of which are examples of what EBM *isn't*.

Decision-making by anecdote

When I was a medical student, I occasionally joined the retinue of a distinguished professor as he made his daily ward rounds. On seeing a new patient, he would enquire about the patient's symptoms, turn to the massed ranks of juniors around the bed, and relate the story of a similar patient encountered a few years previously. 'Ah, yes. I remember we gave her such-and-such, and she was fine after that'. He was cynical, often rightly, about new drugs and technologies and his clinical acumen was second to none. Nevertheless, it had taken him 40 years to accumulate his expertise, and the largest medical textbook of all – the collection of cases that were outside his personal experience – was forever closed to him.

Anecdote (storytelling) has an important place in clinical practice [7]. Psychologists have shown that students acquire the skills of medicine, nursing and so on by memorising what was wrong with particular patients, and what happened to them, in the form of stories or 'illness scripts'. Stories about patients are the unit of analysis (i.e. the thing we study) in grand rounds and teaching sessions. Clinicians glean crucial information from patients' illness narratives – most crucially, perhaps, what being ill *means* to the patient. And experienced doctors and nurses rightly take account of the accumulated 'illness scripts' of all their previous patients when managing subsequent patients. But that doesn't mean simply doing the same for patient B as you did for patient A if your treatment worked, and doing precisely the opposite if it didn't!

The dangers of decision-making by anecdote are well illustrated by considering the risk–benefit ratio of drugs and medicines. In my first pregnancy, I developed severe vomiting and was given the anti-sickness drug prochlorperazine (Stemetil). Within minutes, I went into an uncontrollable and very distressing neurological spasm. Two days later, I had recovered fully from this idiosyncratic reaction, but I have never prescribed the drug since, even though the estimated prevalence of neurological reactions to prochlorperazine is only one in several thousand cases. Conversely, it is tempting to dismiss the possibility of rare but potentially serious adverse effects from familiar drugs – such as thrombosis on the contraceptive pill – when one has never encountered such problems in oneself or one's patients.

We clinicians would not be human if we ignored our personal clinical experiences, but we would be better to base our decisions on the collective experience of thousands of clinicians treating millions of patients, rather than on what we as individuals have seen and felt. Chapter 5 (Statistics for the non-statistician) describes some more objective methods, such as the number needed to treat (NNT), for deciding whether a particular drug (or other intervention) is likely to do a patient significant good or harm.

When the EBM movement was still in its infancy, Sackett emphasised that evidence-based practice was no threat to old-fashioned clinical experience or judgement [1]. The question of *how* clinicians can manage to be both 'evidence-based' (i.e. systematically informing their decisions by research evidence) and 'narrative-based' (i.e. embodying all the richness of their accumulated clinical anecdotes and treating each patient's problem as a unique illness story rather than as a 'case of X') is a difficult one to address philosophically, and beyond the scope of this book. The interested reader might like to look up two articles I've written on this topic [8, 9].

Decision-making by press cutting

For the first 10 years after I qualified, I kept an expanding file of papers that I had ripped out of my medical weeklies before binning the less interesting parts. If an article or editorial seemed to have something new to say, I consciously altered my clinical practice in line with its conclusions. All children with suspected urinary tract infections should be sent for scans of the kidneys to exclude congenital abnormalities, said one article, so I began referring anyone under the age of 16 with urinary symptoms for specialist investigations. The advice was in print, and it was recent, so it must surely replace what had been standard practice – in this case, referring only the small minority of such children who display 'atypical' features [10].

This approach to clinical decision-making is still very common. How many doctors do you know who justify their approach to a particular clinical problem by citing the results section of a single published study, even though they could not tell you anything at all about the methods used to obtain those results? Was the trial randomised and controlled (see section 'Cross-sectional surveys')? How many patients, of what age, sex and disease severity, were involved (see section 'Whom is the study about?')? How many withdrew from ('dropped out of') the study, and why (see section 'Were preliminary statistical questions addressed?')? By what criteria were patients judged cured (see section 'Surrogate endpoints')? If the findings of the study appeared to contradict those of other researchers, what attempt was made to validate (confirm) and replicate (repeat) them (see section 'Ten questions to ask about a paper that claims to validate a diagnostic or screening test')? Were the statistical tests that allegedly proved the authors'

point appropriately chosen and correctly performed (see Chapter 5)? Has the patient's perspective been systematically sought and incorporated via a shared decision-making tool (see Chapter 16)? Doctors (and nurses, midwifes, medical managers, psychologists, medical students and consumer activists) who like to cite the results of medical research studies have a responsibility to ensure that they first go through a checklist of questions like these (more of which are listed in Appendix 1).

Decision-making by GOBSAT (good old boys sat around a table)

When I wrote the first edition of this book in the mid-1990s, the commonest sort of guideline was what was known as a *consensus statement* – the fruits of a weekend's hard work by a dozen or so eminent experts who had been shut in a luxury hotel, usually at the expense of a drug company. Such 'GOBSAT (good old boys sat around a table) guidelines' often fell out of the medical freebies (free medical journals and other 'information sheets' sponsored directly or indirectly by the pharmaceutical industry) as pocket-sized booklets replete with potted recommendations and at-a-glance management guides. But who says the advice given in a set of guidelines, a punchy editorial or an amply referenced overview is correct?

Professor Mulrow [11], one of the founders of the science of systematic review (see Chapter 9) showed a few years ago that experts in a particular clinical field are *less* likely to provide an objective review of all the available evidence than a non-expert who approaches the literature with unbiased eyes. In extreme cases, an 'expert opinion' may consist simply of the lifelong bad habits and personal press cuttings of an ageing clinician, and a gaggle of such experts would simply multiply the misguided views of any one of them. Table 1.1 gives examples of practices that were at one time widely accepted as good clinical practice (and which would have made it into the GOBSAT guideline of the day), but which have subsequently been discredited by high-quality clinical trials.

Chapter 9 takes you through a checklist for assessing whether a 'systematic review of the evidence' produced to support recommendations for practice or policymaking really merits the description, and Chapter 10 discusses the harm that can be done by applying guidelines that are not evidence-based. It is a major achievement of the EBM movement that almost no guideline these days is produced by GOBSAT!

Decision-making by cost-minimisation

The popular press tends to be horrified when they learn that a treatment has been withheld from a patient for reasons of cost. Managers, politicians and, increasingly, doctors can count on being pilloried when a child with a rare

Table 1.1 Examples of harmful practices once strongly supported by 'expert opinion'

Approximate time period	Clinical practice accepted by experts of the day	Practice shown to be harmful in	Impact on clinical practice
From 500 BC	Bloodletting (for just about any acute illness)	1820[a]	Bloodletting ceased around 1910
1957	Thalidomide for 'morning sickness' in early pregnancy, which led to the birth of over 8000 severely malformed babies worldwide	1960	The teratogenic effects of this drug were so dramatic that thalidomide was rapidly withdrawn when the first case report appeared
From at least 1900	Bed rest for acute low back pain	1986	Many doctors still advise people with back pain to 'rest up'
1960s	Benzodiazepines (e.g. diazepam) for mild anxiety and insomnia, initially marketed as 'non-addictive' but subsequently shown to cause severe dependence and withdrawal symptoms	1975	Benzodiazepine prescribing for these indications fell in the 1990s
1970s	Intravenous lignocaine in acute myocardial infarction, with a view to preventing arrhythmias, subsequently shown to have no overall benefit and in some cases to *cause* fatal arrhythmias	1974	Lignocaine continued to be given routinely until the mid-1980s
Late 1990s	Cox-2 inhibitors (a new class of non-steroidal anti-inflammatory drug), introduced for the treatment of arthritis, were later shown to increase the risk of heart attack and stroke	2004	Cox-2 inhibitors for pain were quickly withdrawn following some high-profile legal cases in the USA, although new uses for cancer treatment (where risks may be outweighed by benefits) are now being explored

[a]Interestingly, bloodletting was probably the first practice for which a randomised controlled trial was suggested. The physician van Helmont issued this challenge to his colleagues as early as 1662: *'Let us take 200 or 500 poor people that have fevers. Let us cast lots, that one half of them may fall to my share, and the others to yours. I will cure them without blood-letting, but you do as you know – and we shall see how many funerals both of us shall have'* [12]. I am grateful to Matthias Egger for drawing my attention to this example.

cancer is not sent to a specialist unit in America or a frail old lady is denied a drug to stop her visual loss from macular degeneration. Yet in the real world, all healthcare is provided from a limited budget and it is increasingly recognised that clinical decisions must take into account the economic costs of a given intervention. As Chapter 11 argues, clinical decision-making *purely* on the grounds of cost ('cost-minimisation' – purchasing the cheapest option with no regard to how effective it is) is generally ethically unjustified, and we are right to object vocally when this occurs.

Expensive interventions should not, however, be justified simply because they are new, or because they ought to work in theory, or because the only alternative is to do nothing – but because they are very likely to save life or significantly improve its quality. How, though, can the benefits of a hip replacement in a 75-year-old be meaningfully compared with that of cholesterol-lowering drugs in a middle-aged man or infertility investigations for a couple in their twenties? Somewhat counter-intuitively, there is no self-evident set of ethical principles or analytical tools that we can use to match limited resources to unlimited demand. As you will see in Chapter 11, the much-derided quality-adjusted life year (QALY), and similar utility-based units are simply attempts to lend some objectivity to the illogical but unavoidable comparison of apples with oranges in the field of human suffering. In the United Kingdom, the National Institute for Health and Care Excellence (see www.nice.org.uk) seeks to develop both evidence-based guidelines and fair allocation of NHS resources.

There is one more reason why some people find the term *evidence-based medicine* unpalatable. This chapter has argued that EBM is about coping with change, not about knowing all the answers before you start. In other words, it is not so much about what you have read in the past but about how you go about identifying and meeting your ongoing learning needs and applying your knowledge appropriately and consistently in new clinical situations. Doctors who were brought up in the old school style of never admitting ignorance may find it hard to accept that a major element of scientific uncertainty exists in practically every clinical encounter, although in most cases, the clinician fails to identify the uncertainty or to articulate it in terms of an answerable question (see next section). If you are interested in the research evidence on doctors' [lack of] questioning behaviour, see an excellent review by Swinglehurst [13].

The fact that none of us – not even the cleverest or most experienced – can answer all the questions that arise in the average clinical encounter means that the 'expert' is more fallible than he or she was traditionally cracked up to be. An evidence-based approach to ward rounds may turn the traditional medical hierarchy on its head when the staff nurse or junior doctor produces new evidence that challenges what the consultant taught everyone last week.

For some senior clinicians, learning the skills of critical appraisal is the least of their problems in adjusting to an evidence-based teaching style!

Having defended EBM against all the standard arguments put forward by clinicians, I should confess to being sympathetic to many of the more sophisticated arguments put forward by philosophers and social scientists. Such arguments, summarised in Chapter 17 (new for this edition), address the nature of knowledge and the question of how much medicine really rests on decisions at all. But please don't turn to that chapter (which is, philosophically speaking, a 'hard read') until you have fully grasped the basic arguments in the first few chapters of this book – or you risk becoming confused!

Before you start: formulate the problem

When I ask my medical students to write me an essay about high blood pressure, they often produce long, scholarly and essentially correct statements on what high blood pressure is, what causes it and what the different treatment options are. On the day they hand their essays in, most of them know far more about high blood pressure than I do. They are certainly aware that high blood pressure is the single most common cause of stroke, and that detecting and treating everyone's high blood pressure would cut the incidence of stroke by almost half. Most of them are aware that stroke, although devastating when it happens, is a fairly rare event, and that blood pressure tablets have side effects such as tiredness, dizziness, impotence and getting 'caught short' when a long way from the lavatory.

But when I ask my students a practical question such as 'Mrs Jones has developed light-headedness on these blood pressure tablets and she wants to stop all medication; what would you advise her to do?', they are often foxed. They sympathise with Mrs Jones' predicament, but they cannot distil from their pages of close-written text the one thing that Mrs Jones needs to know. As Smith (paraphrasing TS Eliot) asked a few years ago in a BMJ editorial: 'Where is the wisdom we have lost in knowledge, and the knowledge we have lost in information?'[14].

Experienced clinicians might think they can answer Mrs Jones' question from their own personal experience. As I argued in the previous section, few of them would be right. And even if they were right on this occasion, they would still need an overall system for converting the rag-bag of information about a patient (an ill-defined set of symptoms, physical signs, test results and knowledge of what happened to this patient or a similar patient last time), the particular values and preferences (utilities) of the patient and other things that could be relevant (a hunch, a half-remembered article, the opinion of

a more experienced colleague or a paragraph discovered by chance while flicking through a textbook) into a succinct summary of what the problem is and what specific additional items of information we need to solve that problem.

Sackett and colleagues, in a book subsequently revised by Straus [15], have helped us by dissecting the parts of a good clinical question:

- First, define precisely *whom* the question is about (i.e. ask 'How would I describe a group of patients similar to this one?').
- Next, define *which* manoeuvre you are considering in this patient or population (e.g. a drug treatment), and, if necessary, a comparison manoeuvre (e.g. placebo or current standard therapy).
- Finally, define the desired (or undesired) *outcome* (e.g. reduced mortality, better quality of life, and overall cost savings to the health service).

The second step may not concern a drug treatment, surgical operation or other intervention. The manoeuvre could, for example, be the exposure to a putative carcinogen (something that might cause cancer) or the detection of a particular surrogate endpoint in a blood test or other investigation. (A surrogate endpoint, as section 'Surrogate endpoints' explains, is something that predicts, or is said to predict, the later development or progression of disease. In reality, there are very few tests that reliably act as crystal balls for patients' medical future. The statement 'The doctor looked at the test results and told me I had six months to live' usually reflects either poor memory or irresponsible doctoring!) In both these cases, the 'outcome' would be the development of cancer (or some other disease) several years later. In most clinical problems with individual patients, however, the 'manoeuvre' consists of a specific intervention initiated by a health professional.

Thus, in Mrs Jones's case, we might ask, 'In a 68-year-old white woman with essential (i.e. common or garden) hypertension (high blood pressure), no coexisting illness, and no significant past medical history, whose blood pressure is currently X/Y, do the benefits of continuing therapy with bendroflumethiazide (chiefly, reduced risk of stroke) outweigh the inconvenience?'. Note that in framing the specific question, we have already established that Mrs Jones has never had a heart attack, stroke or early warning signs such as transient paralysis or loss of vision. If she had, her risk of subsequent stroke would be much higher and we would, rightly, load the risk–benefit equation to reflect this.

In order to answer the question we have posed, we must determine not just the risk of stroke in untreated hypertension but also the likely reduction in that risk which we can expect with drug treatment. This is, in fact, a rephrasing of a more general question (do the benefits of treatment in this

case outweigh the risks?) which we should have asked before we prescribed bendroflumethiazide to Mrs Jones in the first place, and which all doctors should, of course, ask themselves every time they reach for their prescription pad.

Remember that Mrs Jones' alternative to staying on this particular drug is not necessarily to take no drugs at all; there may be other drugs with equivalent efficacy but less disabling side effects (as Chapter 6 argues, too many clinical trials of new drugs compare the product with placebo rather than with the best available alternative), or non-medical treatments such as exercise, salt restriction, homeopathy or yoga. Not all of these approaches would help Mrs Jones or be acceptable to her, but it would be quite appropriate to seek evidence as to *whether* they might help her – especially if she was asking to try one or more of these remedies.

We will probably find answers to some of these questions in the medical literature, and Chapter 2 describes how to search for relevant papers once you have formulated the problem. But before you start, give one last thought to your patient with high blood pressure. In order to determine her personal priorities (how does she value a 10% reduction in her risk of stroke in 5 years' time compared to the inability to go shopping unaccompanied today?), you will need to approach Mrs Jones, not a blood pressure specialist or the Medline database! Chapter 16 sets out some structured approaches for doing this.

Exercise 1

1. Go back to the fourth paragraph in this chapter, where examples of clinical questions are given. Decide whether each of these is a properly focused question in terms of
    (a) the patient or problem;
    (b) the manoeuvre (intervention, prognostic marker, exposure);
    (c) the comparison manoeuvre, if appropriate;
    (d) the clinical outcome.
2. Now try the following:
    (a) A 5-year-old child has been on high-dose topical steroids for severe eczema since the age of 20 months. The mother believes that the steroids are stunting the child's growth, and wishes to change to homeopathic treatment. What information does the dermatologist need to decide (i) whether she is right about the topical steroids and (ii) whether homeopathic treatment will help this child?
    (b) A woman who is 9 weeks pregnant calls out her general practitioner (GP) because of abdominal pain and bleeding. A previous ultrasound

scan showed that the pregnancy was not ectopic. The GP decides that she might be having a miscarriage and tells her she must go into hospital for a scan and, possibly, an operation to clear out the womb. The woman is reluctant. What information do they both need in order to establish whether hospital admission is medically necessary?

(c) A 48-year-old man presents to a private physician complaining of low back pain. The physician administers an injection of corticosteroid. Sadly, the man develops fungal meningitis and dies. What information is needed to determine both the benefits and the potential harms of steroid injections in low back pain, in order to advise patients on the risk – benefit balance?

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