



Evidence in Practice

BMJ Clinical Evidence

May 2008

Updates in evidence-based medicine from *BMJ Clinical Evidence*

Making the GRADE

WELCOME to the May issue of Evidence in Practice, our newsletter designed to keep you abreast of the latest enhancements and updates to the *BMJ Clinical Evidence* website.

In 2007 *BMJ Clinical Evidence* launched a major initiative to introduce a method for assessing the quality of the research we review, and the strength of recommendations we provide. Our scoring system is based on the systematic and explicit approach developed by the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) working party. It aims to make the limitations of the research we review more transparent to healthcare professionals worldwide, and our reviews more clear with respect to which outcomes matter, and to whom the data relates.

The GRADE approach seeks to address many of the perceived shortcomings of existing models of evidence grading. Crucially, evidence is evaluated, not study by study, but across studies for specific clinical outcomes, taking into account:

- Methodological flaws within the component studies
- Consistency of results across different studies
- How generalisable the research results are to the wider patient base
- How beneficial or harmful the treatments have been shown to be

All treatment comparisons are given one of four GRADE scores reflecting the quality of the evidence — high-, moderate-, low-, or very low-quality evidence.

We have developed a pragmatic

approach for applying the principles of GRADE in a reproducible, simple, and efficient way. Please find full details of how we have decided to implement GRADE on our website at clinicalevidence.bmj.com. In January 2008, we published GRADE evaluations for over half our systematic reviews, and we will be adding and updating GRADE scores to all our reviews as they undergo their regular update cycle.



BMJ Clinical Evidence systematic reviews now include a table that identifies the basis on which judgements of evidence quality are made, and summary statements now include GRADE analyses. The evidence for each treatment option is now summarised for key clinical outcomes and for comparisons with placebo and other treatments, and is presented with links to the appropriate GRADE table.

In contrast to the GRADE scores, which reflect evidence quality, the *BMJ Clinical Evidence* categorisation continues to sum up treatment efficacy — whether we believe the treatment is likely to be beneficial, ineffective, or harmful, or indeed whether we don't know enough to assess its effects — but clinicians now have an additional transparent layer showing the quality of the evidence on which the categorisation has been based, and where further research really is needed.

Our aim is to provide clinicians with the best-quality appraised, summarised evidence to facilitate decision making. Although as editors we cannot directly protect patients against the effects of disease, we can and do use our experience to protect patients and doctors from

Reasons why *BMJ Clinical Evidence* is used worldwide

"I've been through all the current guidelines on colorectal cancer prevention and screening... and in my opinion, the BMJ Clinical Evidence analysis and discussion is the most evidence-based and patient-centered, best, and most valid resource." Doctor, USA

"I was doing things the same way over the years, until I had a look in BMJ Clinical Evidence and realized that the scope for checks had been reduced quite considerably. That has saved me a lot of time with a very common procedure." Primary Care Physician, UK

"Thank you for your excellent discussion on the two different types of studies on Vitamin D and CVD ... This type of analysis is one of the reasons I find BMJ Clinical Evidence so useful." Hospital Doctor, USA

the effects of confusion about medical evidence.

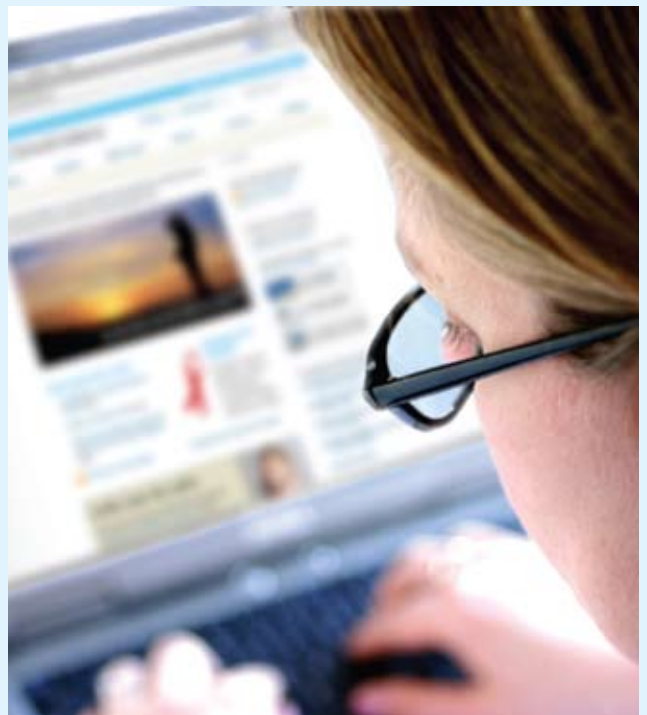
We hope you will find the newsletter interesting, and be tempted to subscribe to the *BMJ Clinical Evidence* website at clinicalevidence.bmj.com. We also welcome your feedback. Please use the convenient link on our website.

Charles Young
Editor, *BMJ Clinical Evidence*

Alison Martin
Deputy Editor, *BMJ Clinical Evidence*

Continuing enhancements

More than a million doctors and healthcare professionals internationally use *BMJ Clinical Evidence* to help them make the best possible management decisions. In order to make the website even more useful, we are constantly looking for ways to improve its content and layout.



BMJ Clinical Evidence website now features:

- **Foreign language navigation** with control tabs written in a variety of languages: Spanish, Chinese, Turkish, Japanese, and Thai
- **Patient Information Leaflets** based on *BMJ Clinical Evidence* systematic reviews: summarising important condition information in plain English

Rollout during 2008

- **GRADE scores:** Improved key messages for each intervention, structured around the most clinically important outcomes, incorporating GRADE scores for the quality of evidence, and links to a detailed GRADE table for each review
- **Improved search and browse functions:** many more synonyms and variant terms will be added to increase the ease and likelihood of finding the content you are looking for
- **Published inclusion-exclusion forms for new reviews:** further enhancing the transparency of our systematic review process
- **New PubMed abstracts for each systematic review:** allowing users to see at a glance a clear summary of each review

Number of studies (see legends)	Outcome	Comparison	Type of Evidence	Quality	Consistency	Directness	Effect size	Grade	Comment
15 (1646) [2]	Mortality	Postoperative platinum based chemotherapy v surgery alone	4	-1	-1	-1	0	Very low	Quality point deducted for poor adherence rates. Consistency point deducted for conflicting results. Directness point deducted for inclusion of a range of regimens.
12 (1016) [2]	Mortality	Postoperative tegafur (UFT) based chemotherapy v surgery alone	4	-1	0	-1	0	Low	Quality point deducted for poor adherence rates. Directness point deducted for inclusion of different regimens.
1 review, 2145 people [2]	Mortality	Postoperative alkylating agent based chemotherapy v surgery alone	4	-1	0	-1	0	Low	Quality point deducted for poor adherence rates. Directness point deducted for inclusion of different regimens.
4 RCTs [2]	Mortality	Chemotherapy plus radiotherapy plus surgery v surgery alone	4	-1	0	-1	0	Low	Quality point deducted for poor adherence rates. Directness point deducted for lack of direct comparisons.

What's new in *BMJ Clinical Evidence*?

Here are a few highlights from reviews we have added or updated since the last publication of the *BMJ Clinical Evidence handbook*. Please visit the *BMJ Clinical Evidence* Web site at clinicalevidence.bmj.com for in-depth summaries, background information, and reference lists.

1	HEART FAILURE	Positive inotropic agents (other than digoxin), calcium channel blockers, and antiarrhythmic drugs (other than amiodarone or beta blockers) may all increase mortality and should be used with caution, if at all, in people with heart failure (high-quality evidence*).
2	OBESITY IN ADULTS	There is moderate-quality evidence that biliopancreatic diversion may be more effective than gastric bypass in people with morbid obesity. <ul style="list-style-type: none"> • Rimonabant promotes weight loss in obese adults with lifestyle interventions in the same way as other commonly prescribed drugs, such as orlistat, phentermine, and sibutramine (high-quality evidence*). However, all these drugs can cause adverse effects.
3	RETINAL DETACHMENT (NEW REVIEW)	In people with retinal breaks or lattice degeneration, cryotherapy and photocoagulation are widely used for preventing progression to rhegmatogenous retinal detachment (RRD). <ul style="list-style-type: none"> • Although there is no direct evidence, there is consensus that they are effective, particularly in people with symptomatic flap tears and retinal dialysis.
4	PANCREATIC CANCER	Preventative treatment may prevent leakage from the residual pancreatic stump, a major complication and cause of death after pancreaticoduodenectomy. <ul style="list-style-type: none"> • Octreotide may prevent complications (pancreatic leak and intra-abdominal collections) of pancreatic surgery, but may not reduce mortality (very low-quality evidence*).
5	END-STAGE RENAL DISEASE (ESRD)	There is high-quality evidence that erythropoietin and darbepoetin are effective in maintaining hemoglobin levels in people with ESRD. <ul style="list-style-type: none"> • However, they are associated with increased mortality, and serious cardiovascular, arterial, and venous thromboembolic events.
6	FRACTURE PREVENTION IN POSTMENOPAUSAL WOMEN	New evidence about raloxifene suggests that clinicians and patients need to weigh up beneficial and harmful effects before use: <ul style="list-style-type: none"> • Raloxifene reduces vertebral fractures (moderate-quality evidence*), but it has not been shown to reduce non-vertebral fractures (high-quality evidence*). • However, raloxifene increases venous thromboembolic events and stroke compared with placebo.
7	CONSTIPATION, HAEMORRHOIDS, AND HEARTBURN IN PREGNANCY (NEW REVIEW)	Rutosides improve the symptoms of haemorrhoids compared with placebo (high-quality evidence*); however, further studies are needed to assess their potential adverse effects. <ul style="list-style-type: none"> • We found little evidence to support interventions for constipation and heartburn in pregnancy.
8	PARKINSON DISEASE	Further randomized trial evidence led to a change in the categorization of the most commonly used surgical interventions in later Parkinson disease, bilateral subthalamic nucleus deep-brain stimulation, and pallidal deep-brain stimulation from "Unknown effectiveness" to "Trade-off between benefits and harms".
9	DIABETIC RETINOPATHY	Laser photocoagulation reduces visual loss in people with clinically significant macular edema (high-quality evidence*). <ul style="list-style-type: none"> • However, it may be ineffective for reducing moderate visual loss in people with maculopathy but without clinically significant macular edema (moderate-quality evidence*).
10	CLUSTER HEADACHE (NEW REVIEW)	Cluster headache is rare, but its exact prevalence remains a matter of debate. <ul style="list-style-type: none"> • Sumatriptan and zolmitriptan may reduce the severity and duration of episodic or chronic cluster headache attacks once they have begun (low-quality evidence*). • Consensus holds that verapamil and lithium prevent cluster headache, but that verapamil is more effective than lithium, and causes fewer adverse effects.

* GRADE assessment of the quality of evidence:

High-quality evidence	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate-quality evidence	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low-quality evidence	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low-quality evidence	Any estimate of effect is very uncertain.

The art of information

Interview with Andrea Lane, Information Specialist Manager

ONE OF THE KEY elements to making secondary knowledge products a success is transparency, according to Andrea Lane, head of information at BMJ Knowledge, the team within the BMJ Group that brings you *BMJ Clinical Evidence*.

"Secondary knowledge resources save time, but it's important to choose one that is good quality and evidence-based," she says. "It needs to be based on good scientific research, but the input from experts is also important. What makes *BMJ Clinical Evidence* so strong is that it is very clear what we have and how we have found it. It is transparent."

Andrea leads a team of eight information specialists and one information administrator whose job it is to deliver a process that does just that. The team's rolling schedule of searches and appraisals of the medical literature are the lifeblood of *BMJ Clinical Evidence* and the consumer Web site *BMJ BestTreatments*. They feed these products with all the latest published research on the many thousands of treatments they cover, enabling other staff to meet the tight updating timetables the products demand.

But the information team's role in BMJ Knowledge runs much deeper than simply scanning the literature and driving through a rigorous updating process. Specialists are also actively involved in steering the direction of the products' coverage by helping to plan new topics and deciding whether new treatments need to be added to improve the breadth of particular conditions.

Unlike traditional librarians who respond to particular queries from their users, the role of the information specialists in BMJ Knowledge is more involved in "maintaining an information stream," says Andrea. The job is also more interactive than traditional librarianship, with specialists required to liaise with in-house editors and outside consultants and to deliver to tight deadlines.

Members of Andrea's team are required to have appropriate postgraduate training in library or information science with at least 2 years' experience in a biomedical library environment. They are also expected to appreciate the objectives of evidence-based medicine and the features that differentiate between research studies that meet the criteria demanded of an evidence-based product and those that don't.

Alongside their role of supporting over

50 clinical and scientific editors in their jobs, the information specialists take an active interest in their own professional development. This year the team has been more successful than ever at having abstracts and posters accepted at international conferences, says Andrea.

Members of the team will be representing BMJ Knowledge at the Medical Library Association meeting in Chicago in May, at the European Association of Health and Information Libraries in Finland in June, the Canadian Health Libraries' Association in June, the Health Libraries Group in Cardiff in July, and the Cochrane Colloquium in Germany in October.

The team's attendance at these events serves a number of purposes, says Andrea. As well as allowing specialists to see what's going on in their field, they also get the chance to showcase BMJ Knowledge products. In Chicago, for example, one of Andrea's team will present how patients were involved in developing *BMJ BestTreatments* and how this helps distinguish the site from other consumer health websites.

Zosia Kmietowicz,
freelance medical journalist

Supportive and palliative care

In their June editorial, Sam Ahmedzai and Paul Keeley explained the challenges of finding and collating evidence for supportive and palliative care.¹ Please read their online article in our Guest Editorial Archive.

In the same month, we launched the new *BMJ Clinical Evidence* supportive and palliative care section, which systematically reviews the evidence base behind these two distinct, but complementary medical specialties. In line with the inclusive remit of today's supportive care physicians, this new section will include reviews covering a broad range of clinical problems, initially constipation in people prescribed opioids, delirium at the end of life, nausea and vomiting in people with cancer and other chronic diseases, and opioids in people with cancer-related pain.

Based on these reviews and extensive additional literature searches, we are now happy to present the latest booklet in our Evidence in Practice series, a report on palliative and supportive care commissioned and distributed by the United Health Foundation. This large review explores a wide range of issues, including patient care needs and preferences, appropriate quality indicators, barriers to effective end of life care, as well as an evidence-based evaluation of the effectiveness of interventions aimed at improving communication, symptom management, and service provision. Professor Diane Meier provides a practical toolkit that will support primary care clinicians in managing patients with life-threatening chronic conditions.

Reference

1. Ahmedzai SH, Keeley PW. Guest editorial: Supportive and palliative care. *BMJ Clinical Evidence* June 18, 2007. Available at: <http://clinicalevidence.bmj.com/downloads/18-06-07.pdf>. Accessed April 17, 2008.

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