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ISSUE 5

JUNE 2001

clinical evidence

The international source of the best available evidence for effective health care

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Editorial Office
BMJ Publishing Group, BMA House, Tavistock Square, London, WC1H 9JR, United Kingdom. Tel: +44 (0)20 7387 4499; Fax: +44 (0)20 7383 6242 www.bmjpg.com

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UnitedHealth Foundation

UnitedHealth Foundation
MN008-T500 P.O. Box 1459 Minneapolis, MN 55440-1459

July, 2001

Dear Colleague:

The UnitedHealth Foundation is pleased to provide you with a complimentary copy of *Clinical Evidence*, Issue 5.

We at UnitedHealth Foundation share in the belief that the practice of science and evidence-based medicine is an essential requirement for quality and safe health outcomes. We also share in the understanding that physicians, other health care professionals, and their patients should be free to make the best possible health care decisions and that those decisions should be supported by the best possible clinical information. Because the science of medicine is continuously enhanced, reviewed and updated, so too is *Clinical Evidence*. In February you received a copy of Issue 4 and now we are pleased that we can provide you with this fifth edition.

We have noticed that busy physicians are increasingly making use of the internet as a source for clinical information. As such we are particularly excited that UnitedHealth Foundation recipients of *Clinical Evidence* are eligible for free access to *Clinical Evidence* Online, which provides full text and fully searchable access to *Clinical Evidence*. To make use of this feature go to www.clinicalevidence.org. Once there, click on "CE-On-line" and follow the instructions to register.

Clinical Evidence is an international resource that provides easy access to the most up-to-date information on what is proven to work in medicine. Produced and published under the strict editorial leadership of the 160-year old British Medical Journal, it is the result of the best efforts of internationally recognized leaders in a variety of medical disciplines. *Clinical Evidence* has been proven to be an important aid to clinical decision making when used in conjunction with other credible medical information. The BMJ Publishing Group is solely responsible for the content of all issues of *Clinical Evidence* and is continually revising *Clinical Evidence* based on feedback from practicing physicians and clinical experts. I encourage you to provide them with comments via CEfeedback@bmjgroup.com.

If you would like to receive a copy of *Clinical Evidence*, Issue 6, upon its' release in January 2002, please visit our website at www.unitedhealthfoundation.org or complete the postcard included with this issue. Either will ensure you are on the mailing list for Issue 6. You may also write us at UnitedHealth Foundation, *Clinical Evidence*, MN008-T500, P.O. Box 1459, Minneapolis, Minnesota 55429.

All of us at the Foundation look forward to supporting you in your efforts to provide the best possible health and medical care to your patients. We are convinced that providing you with this edition of *Clinical Evidence* will go a long way to accomplishing our shared objectives.

Sincerely,

Bill McGuire

William W. McGuire, M.D.
Chairman
UnitedHealth Foundation

Team and advisors

Acknowledgements

We thank the following people and organisations for their advice and support: The Cochrane Collaboration, and especially Iain Chalmers, Mike Clarke, Phil Alderson, and Carol Lefebvre; the NHS Centre for Reviews and Dissemination, and especially Jos Kleijnen and Julie Glanville; the NHS Executive, and especially Andrew Burnett, Chris Henshall, and Tom Mann; the British National Formulary, and especially Dinesh Mehta; the Health Information Research Unit at McMaster University, and especially Brian Haynes and Ann McKibbon; the Sowerby Centre for Health Informatics at Newcastle, especially Nick Booth, Peter Johnson, and Neill Jones; and the clinicians, epidemiologists, and members of patient support groups who have acted as peer reviewers. We are grateful to the clinicians and patients who spare time to take part in focus groups, which are crucial to the development of *Clinical Evidence*. Finally, we would like to acknowledge the readers who have taken the time to send us their comments and suggestions.

Welcome to Issue 5

Welcome to Issue 5 of *Clinical Evidence*, the six monthly, updated compendium of evidence on the effects of clinical interventions. *Clinical Evidence* summarises the current state of knowledge and uncertainty about the prevention and treatment of clinical conditions, based on thorough searches and appraisal of the literature. It is not a textbook of medicine nor a book of guidelines. It describes the best available evidence, and if there is no good evidence, it says so.

RESPONSE TO ISSUE 4

The printed Issue 4 of *Clinical Evidence* was received by around 600 000 people around the world, including 500 000 physicians, nurses, and medical students in the USA, and 50 000 people in the UK (mainly general practitioners in England). Translations are now available in French[1] and in German,[2] and are received by another 11 000 health carers. Each day, a further 50 people register on the Internet. *Clinical Evidence* is also available in England via the NHS National Electronic Library for Health.[3]

We continue to be encouraged by the positive messages from people receiving *Clinical Evidence* for the first time. We also receive many specific requests for information. We are often asked how *Clinical Evidence* should be used, and whether it is designed to be read topic by topic, or whether it should be used for specific problems. The central concept is that *Clinical Evidence* is designed to save the time, effort, and frustration of trying to keep up to date with the literature.

Our hope is that *Clinical Evidence* will improve patient care.[4] A recent independent survey[5] indicates that doctors already rank *Clinical Evidence* in their top three favourite sources of information. A questionnaire of 389 GP principals and consultants in two English Health Authorities assessed how useful *Clinical Evidence* had been in their clinical practice, and how it compared with other sources of evidence. Of these, 95 respondents (24%) already identified *Clinical Evidence* as one of their three favourite sources of information. When asked about frequency of use, 1% said they used it daily, 28% weekly, and 43% monthly. *Clinical Evidence* was used in or after a consultation by 59%. The book, rather than the online version, was preferred by 61% of the doctors, but 64% were interested in using a combination of media.

Evidence from the new website gives a few clues about how *Clinical Evidence* is being used. Soon after registering, many users browse through most sections—seeing what is there and how far the links go. Later, the frequency of contacts varies, ranging from 1–112 contacts a month (mean 2.4 contacts/month/user). Most sessions are brief (4 minutes) and involve only a few content pages (5 pages). Each content page is examined for around a minute. The current "top 10" topics (chapters) are listed in the table (p xi); they are major cardiovascular and respiratory topics, and back pain. Popular options receive more hits, but the time spent per page is about the same. We think this is consistent with *Clinical Evidence* being used like a telephone directory—most users dropping in repeatedly for specific items, rather than reading large tracts in one go.

We have had many requests to provide PowerPoint™ slides of the content that can be adapted for presentations to do with education or research. These are now available for the "top 10" topics and, if they are useful, we will provide PowerPoint™ presentations for all topics.

Another common request has been for a CD-ROM version of *Clinical Evidence*. This is now available. You can find out more about it on the website.

WHAT'S NEW IN ISSUE 5?

There are 14 new topics (including Influenza, Acute atrial fibrillation, Colonic diverticular disease, *Helicobacter pylori* eradication, Meniere's disease, Trigeminal neuralgia, and Lyme disease). All the new topics are labelled on the contents page. Secondly, 20 topics have been expanded, including Asthma, Schizophrenia, Alzheimer's disease, Breast cancer (non-metastatic), and Unstable angina. The new interventions are labelled on the summary page for each topic. Thirdly, 96 of the 120 topics from Issue 4 have been updated and re-edited. This has involved performing a *Clinical Evidence* search from the date of the previous search, appraising any new studies that were identified, and incorporating the new evidence into the *Clinical Evidence* review (for example, that angiotensin II receptor blockers reduce mortality from heart failure, and that paracetamol is likely to be beneficial in reducing pain from acute otitis media).

UPDATING

Medical knowledge is fluid and rapidly changing. The biggest challenge facing *Clinical Evidence* is to produce high quality updates for a large number of topics at regular intervals. The delays in producing a quality paper publication are appreciable, and an inevitable trade-off exists between speed of updating and time for quality control. Issue 5 will be distributed in June 2001. It will have been printed during May. Authoring, peer review, clinical editing, and quality control checks ended in early April. Literature searches for the updated topics in this issue were performed between Summer 2000 and January 2001. The lag from search to publication is 5 to 9 months, and by the time the next issue is published, the unavoidable lag is 11 to 15 months. We are now stating the search date under the title of every topic.

We have redesigned the *Clinical Evidence* website so that, from the launch of Issue 5, all updated and corrected topics will be posted directly and regularly to the web. This will reduce the search to publication time by 2 to 8 months. We aim to ensure that topics on the website are within 12 months of their search dates.

ERRORS

New research is the main reason for updating the evidence, but changes also arise because of the need to correct errors. Error correction arises when previously published research is amended,[6] is withdrawn because of proven or suspected fraud,[7] or when simple errors have arisen during editing or preparation for press. These corrections need to be available quickly. Readers who want to ensure that the information they use is current should either check the website periodically for updates and corrections, or should register on the website to receive e-mail alerts about all important updates. The specific procedures we have devised for dealing with corrections are listed on page xviii. Errors from previous issues are detailed there.

THE FUTURE

We have firm plans for *Clinical Evidence* to include more topics, but to provide a thinner book that fits in a pocket. A concise paper version, which can be used in conjunction with a larger book, CD-ROM, or online version of *Clinical Evidence* will be piloted with issue 6 and, if successful, will be made available for issue 7 (June 2002). The concise version will contain "smart" summaries of the questions and key messages. Our aim is to use the available space to hold the most useful evidence we can identify. More detail will be presented for frequently accessed topics. Specialist versions will allow tailoring of the content to meet particular needs. We will include questions about diagnosis in Issue 7.

Your views are very important to us. Requests from readers are now one of the most important factors in identifying the questions that need answering in *Clinical Evidence*. You can influence the development of *Clinical Evidence* by letting us know your views on what we are doing and how we could do it better.

TABLE **The 10 most frequently visited topics on the website.**

	Mean viewing time per page (minutes)	Hits (relative to mean for all topics)
Heart failure	1.38	5.5
Primary prevention	1.51	5.3
Secondary prevention of ischaemic cardiac events	1.33	5.2
Acute myocardial infarction	1.32	5.2
DVT and pulmonary embolism	1.10	4.2
Stroke management	1.36	3.9
Unstable angina	1.10	3.6
Low back pain	1.59	3.5
Asthma	1.31	2.9
Gastro-oesophageal reflux	1.13	2.8

Figures for March 2001 showing the time spent viewing individual web pages by individual viewers during a single session, and the number of hits (relative to the mean for all topics).

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About Clinical Evidence

The inspiration for *Clinical Evidence* came in a phone call in 1995. Tom Mann and his colleagues at the NHS Executive asked the BMJ Publishing Group to explore the possibility of developing an evidence "formulary" along the lines of the *British National Formulary*. They recognised that clinicians were under increasing pressure to keep up to date and to base their practice more firmly on evidence, but that few had the necessary time or skills to do this. Their idea was to provide a pocket book containing concise and regularly updated summaries of the best available evidence on clinical interventions. However, they didn't think that the NHS could develop such a formulary itself. "It would be marvellous", said Tom Mann, "if somebody would just do it." A small team at the BMJ set to work to produce a pilot version of what was then called the *Clinical Effectiveness Directory*.

Since that pilot, a great deal has changed. In collaboration with the American College of Physicians–American Society of Internal Medicine, we convened an international advisory board, held focus groups of clinicians, talked to patient support groups, and adopted countless good ideas from early drafts by our contributors. Throughout we have kept in mind an equation set out by Slawson et al.[1] This states that the usefulness of any source of information is equal to its relevance, multiplied by its validity, divided by the work required to extract the information. In order to be as useful as possible, we aimed for high relevance, high validity, and low work in terms of the reader's time and effort. We also kept in mind principles of transparency and explicitness. Readers needed to understand where our information came from and how it was assembled.

A UNIQUE RESOURCE

Clinical Evidence joins a growing number of sources of evidence based information for clinicians. But it has several features that, we think, make it unique.

- Its contents are driven by questions rather than by the availability of research evidence. Rather than start with the evidence and summarise what is there, we have tried to identify important clinical questions, and then to search for and summarise the best available evidence to answer them.
- It identifies but does not try to fill important gaps in the evidence. In a phrase used by Jerry Osheroff, who has led much of the recent research on clinicians' information needs,[2] *Clinical Evidence* presents the dark as well as the light side of the moon. We feel that it will be helpful for clinicians to know when their uncertainty stems from gaps in the evidence rather than gaps in their own knowledge.
- It is updated every six months. This means that you can rely on it to keep you up to date in the areas that are covered.
- It specifically aims not to make recommendations. This is because we feel that simply summarising the evidence will make it more widely useful. The experience of the clinical practice guideline movement has shown that it is nearly impossible to make recommendations that are appropriate in every situation. Differences in individual patients' baseline risks and preferences, and in the local availability of interventions, will always mean that the evidence must be individually interpreted rather than applied across the board. *Clinical Evidence* provides the raw material for developing locally applicable clinical practice guidelines, and for clinicians and patients to make up their own minds on the best course of action. We supply the evidence, you make the decisions.

COMPLEMENTARY BUT DIFFERENT

We are often asked how *Clinical Evidence* differs from two other high quality sources of evidence based information: The Cochrane Library; and the evidence based journals *ACP Journal Club, Evidence Based Medicine, Evidence Based Mental Health,* and *Evidence Based Nursing*.

Clinical Evidence is complementary to but different from the work of the Cochrane Collaboration, which produces and publishes high quality systematic reviews of controlled trials.[3] *Clinical Evidence* has been called the friendly front end of the Cochrane Library, since it takes this, and other, high quality information, and pulls it together in one place in a concise format. Many of our advisors and contributors are active members of the Cochrane Collaboration, and we are exploring closer ties between *Clinical Evidence* and the Collaboration in the way the evidence is searched for, summarised, and accessed by users.

Clinical Evidence is also complementary to but different from the evidence based journals, which select and abstract the best and most clinically relevant articles as they appear in the world's medical literature. Together these journals form a growing archive of high quality abstracts of individual articles, many of which are now pooled on the *Best Evidence* CD. *Clinical Evidence* takes a different approach. It begins not with the journals but with clinical questions. It is able to answer some. For others it simply reports that no good evidence was found.

A WORK IN PROGRESS

Clinical Evidence is an evolving project. We knew before we started that we were undertaking an enormous task, but the more we worked the more we realised its enormity. We recognise that there is some mismatch between what we aim eventually to achieve and what we have achieved so far. While we have made every effort to ensure that the searches were thorough and that the appraisals of studies were objective (see p xvii), we will inevitably have missed some important studies. In order not to make unjustified claims about the accuracy of the information, we use phrases such as "we found no systematic review" rather than "there is no systematic review". In order to be as explicit as possible about the methods used for each contribution, we have asked each set of contributors to provide a brief methods section, describing the searches that were performed and how individual studies were selected.

UPDATING AND EXPANDING CLINICAL EVIDENCE

Our expectation is that *Clinical Evidence* will evolve rapidly in its early years. Indeed, it is already becoming a family of products, appearing in different formats and languages for different audiences: German and French editions have just been published, and Italian and Japanese language versions are already in development. In particular, *Clinical Evidence* will evolve in response to the needs of clinicians. We have tried hard to anticipate those needs (not least by involving clinicians at every stage), but it is only when people begin to use *Clinical Evidence* in daily practice that we can know how best to develop it. That's why your feedback is so important to us, and we are arranging for various ways to evaluate the product.

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2. Ely JW, Osheroff JA, Ebell MJ, et al. Analysis of questions asked by family doctors regarding patient care. *BMJ* 1999; 319:358–361.
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A guide to the text

SUMMARY PAGE

The summary page for each topic presents the questions addressed, some key messages, and a list of the interventions covered, categorised according to whether they have been found to be effective or not. We have developed the categories of effectiveness from one of the Cochrane Collaboration's first and most popular products, *A guide to effective care in pregnancy and childbirth*.[1] The categories we now use are explained in the table below.

Fitting interventions into these categories is not always straightforward. For one thing, the categories represent a mix of several hierarchies: the level of benefit (or harm), the level of evidence (RCT or observational data), and the level of certainty around the finding (represented by the confidence interval). Another problem is that much of the evidence that is most relevant to clinical decisions relates to comparisons between different interventions rather than to comparison with placebo or no intervention. Where necessary, we have indicated the comparisons in brackets. A third problem is that interventions may have been tested, or found to be effective, in only one group of people, such as those at high risk of an outcome. Again, we have indicated this where possible. But perhaps most difficult of all has been to trying to maintain consistency across different topics. We are working on refining the criteria for putting interventions under each category.

Interventions that cannot be tested in an RCT (perhaps because of ethical or practical reasons) are sometimes cited in the categorisation table, but they are always identified clearly with an asterix (for example, oxygen in severe acute asthma).

TABLE **Categorisation of treatment effects in *Clinical Evidence*.**

Beneficial	Interventions whose effectiveness has been demonstrated by clear evidence from randomised controlled trials, and expectation of harms that is small compared with the benefits.
Likely to be beneficial	Interventions for which effectiveness is less well established than for those listed under "beneficial".
Trade off between benefits and harms	Interventions for which clinicians and patients should weigh up the beneficial and harmful effects according to individual circumstances and priorities.
Unknown effectiveness	Interventions for which there are currently insufficient data or data of inadequate quality.
Unlikely to be beneficial	Interventions for which lack of effectiveness is less well established than for those listed under "likely to be ineffective or harmful".
Likely to be ineffective or harmful	Interventions whose ineffectiveness or harmfulness has been demonstrated by clear evidence.

NEGATIVE FINDINGS

A surprisingly hard aspect to get right has been the reporting of negative findings. As we have had to keep reminding ourselves, saying that there is no good evidence that a treatment works is not the same as saying that the treatment doesn't work. In trying to get this right, we may have erred too much on the side of caution; when in doubt we have changed summary phrases from, for example, "the review found no difference", to "the review found no evidence of a difference". We recognise that to get this right, we need a better handle on the power of individual systematic reviews and trials to demonstrate statistically significant differences between groups, and better information on what constitutes clinically important differences in the major outcomes for each intervention. In the meantime, we hope that the text makes a clear distinction between lack of benefit and lack of evidence of benefit.

OUTCOMES

Clinical Evidence focuses on outcomes that matter to patients, meaning those that patients themselves are aware of, such as symptom severity, quality of life, survival, disability, walking distance, and live birth rate. We are less interested in proxy outcomes such as blood lipid concentrations, blood pressure, or ovulation rates. Each topic includes a list of the main patient oriented outcomes, and where possible describes how these are measured. We have for the moment decided not to address the vexed question of what constitutes a clinically important change in an outcome, but we would welcome any suggestions.

EFFECTS, NOT EFFECTIVENESS

A key aim of *Clinical Evidence* is to emphasise the important trade offs between advantages and disadvantages of different treatment options. We therefore talk about the effects of interventions, both positive and negative, rather than the effectiveness, and for each question or intervention option we present data on benefits and harms under separate headings.

HARMS

"Harms" include adverse effects of treatment and inconvenience to the patient. Finding good evidence on harms of treatments is not easy. Ideally these would come from RCTs, but many trials are not sufficiently large or long term to capture rarer or more distant events, and many do not adequately report adverse effects. We have asked contributors to keep the negative effects of interventions in mind at all times. Where good evidence is available, we indicate the frequency of adverse effects. However, because RCTs are not reliable sources of evidence about harms, and because of the principle that a physician should strive to do no harm, we also include weaker forms of evidence about harms.

DRUG INFORMATION

We make no systematic attempt to provide information on drug dosages, formulations, indications, and contraindications. For this information, we refer readers to their national drug formularies. Drug dosages are included when a question explores the relative effects of different doses.

INFORMATION ON COST

We have decided not to include information on the cost or cost effectiveness of interventions. This is not because we believe cost to be unimportant, but because the question of what constitutes good evidence on cost is much disputed and because costs vary greatly both within and between countries. However, we believe that it will become increasingly untenable for clinicians to act without paying attention to resources. Future companion publications of *Clinical Evidence* may provide relevant information on costs.

NUMERICAL DATA

Whenever possible, data are presented in the same form as in the original studies. However, sometimes we have changed the units or type of information in an attempt to present the results in a systematic and easily interpretable form.

AN INTERNATIONAL APPROACH TO THE EVIDENCE

Clinical Evidence takes an international approach to the evidence. This means including drugs that are not licensed in some countries. It also means keeping in mind the practicalities of treating people in rich as well as poorer countries, by covering interventions even if they have been superceded (for example, single drug treatment for HIV infection as opposed to three drug treatment).

COMPETING INTERESTS

In line with the *BMJ*'s policy,[2] our aim is not to try to eliminate conflicts of interest but to make them explicit, so that readers can judge for themselves what influence if any these may have had on the contributors' interpretation of the evidence. We therefore ask all contributors to let us know about any potential competing interests, and we append any that are declared to the end of the contribution. Where the contributor gives no competing interests, we record "none declared".

CHANGES SINCE THE LAST ISSUE

The text has been edited and updated. Substantive changes since the last issue are listed at the end of each topic. These are defined as:

- Presentation of additional evidence that either confirms or alters the conclusions
- Re-evaluation of the evidence
- Correction of an important error

HOW TO USE THE INFORMATION IN CLINICAL EVIDENCE

The type of information contained in *Clinical Evidence* is necessary but not sufficient for the provision of effective, high quality health care. It is intended as an aid to clinical decision making, to be used in conjunction with other important sources of information. These other sources include estimates of people's baseline risk of a condition or outcome based on history, physical examination, and clinical investigations; individual preferences; economic arguments; availability of treatments; and local expertise.

Some guidance on how to apply research evidence in practice is available on our website (www.clinicalevidence.org) and in appendix 3 in this issue.

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How Clinical Evidence is put together

The summaries in *Clinical Evidence* result from a rigorous process aimed at ensuring that the information they contain is both reliable and relevant to clinical practice.

SELECTING TOPICS

Clinical Evidence aims to cover common or important clinical conditions seen in primary and hospital care. To decide which conditions to cover in the first few issues, we reviewed national data on consultation rates, morbidity, and mortality, and took advice from generalist clinicians and patient groups. See our website (www.clinicalevidence.org) for a list of conditions that we are planning to cover in future issues. Further suggestions are welcome.

SELECTING THE QUESTIONS

The questions in *Clinical Evidence* concern the benefits and harms of preventative and therapeutic interventions, with emphasis on outcomes that matter to patients. Questions are selected for their relevance to clinical practice by section advisors and contributors, in collaboration with primary care clinicians and patient groups. Each new issue of *Clinical Evidence* will include new questions as well as updates of existing questions. Readers can suggest new clinical questions using the feedback slips to be found at the back of the book and on the *Clinical Evidence* website (www.clinicalevidence.org), or by writing directly to *Clinical Evidence*.

SEARCHING AND APPRAISING THE LITERATURE

For each question, the literature is searched using the Cochrane Library, Medline, Embase and, occasionally, other electronic databases, looking first for good systematic reviews of RCTs; then for good RCTs published since the search date of the review. Where we find no good recent systematic reviews, we search for individual RCTs. The date of the search is recorded in the methods section for each topic. Of the studies that are identified in the search, we select and summarise only a small proportion. The selection is done by critically appraising the abstracts of the studies identified in the search, a task performed independently by two information scientists using validated criteria similar to those of Sackett, et al[1] and Jadad.[2,3] Where the search identifies more than one or two good reviews or trials, we select those we judge to be the most robust or relevant, using the full text of the article. Where we identify few or no good reviews or trials, we include other studies but highlight their limitations. Contributors, who are chosen for their expertise in the field and their skills in epidemiology, are asked to review our selection of studies, and to justify any additions or exclusions they wish to make.

Our search strategy and critical appraisal criteria are available on our website (www.clinicalevidence.org).

SUMMARISING THE EVIDENCE, PEER REVIEW, AND EDITING

The contributors summarise the evidence relating to each question. Each topic is then peer reviewed by the section advisors, and by at least three external expert clinicians. The revised text is then extensively edited by editors with clinical and epidemiological training, and data are checked against the original study reports.

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Feedback and Error Correction

Despite the extensive peer review and quality checks, we expect that the text will contain some errors and inconsistencies. Please let us know if you find any errors, either by using the comment card at the back of the book or by emailing us at CEfeedback@bmjgroup.com.

Errors are graded as minor, moderate, and major based on an assessment of their potential impact. All errors are corrected in the next printed issue of *Clinical Evidence*. Anything other than a minor error is immediately corrected in the text displayed on our website (http://www.clinicalevidence.org) and a list of errors corrected is available there. Any major errors are highlighted on the log in page of the website.

If you wish to be notified automatically by e-mail of any corrections and updates, then register for the *Clinical Evidence* alerting service on our website. If you are using the information in *Clinical Evidence* to guide your clinical practice then it is essential to register so that you can be remain as up to date as possible. Typographical errors in Issue 4 are listed below.

TABLE **Issue 4 typographical errors and corrections.**

Topic	Page	Error	Correction
Obesity	328	Dexfenfluramine, fenfluramine, and fenfluramine plus phentermine are incorrectly labelled as *Likely to be beneficial.*	The correct categorisation is *Likely to be ineffective or harmful*. The rest of the text to support the categorisation is correct.
Opportunistic infections and HIV	411	Clofazimine of high dose clarithromycin (for MAC in people with previous MAC), and Valaciclovir (CMV) are incorrectly labelled as *Likely to be beneficial*.	The correct categorisation is *Likely to be ineffective or harmful*. The rest of the text to support the categorisation is correct.

Clinical Evidence Glossary

Absolute risk (AR) This is the probability that an individual will experience the specified outcome during a specified period. It lies in the range 0 to 1, or is expressed as a percentage. In contrast to common usage, the word "risk" may refer to adverse events (such as myocardial infarction), or desirable events (such as cure).

Absolute risk reduction (ARR) The absolute difference in risk between the experimental and control groups in a trial. It is used when the risk in the control group exceeds the risk in the experimental group, and is calculated by subtracting the AR in the experimental group from the AR in the control group. This figure does not give any idea of the proportional reduction between the two groups; for this, relative risk reduction (RRR) is needed (see below).

Absolute risk increase (ARI) The absolute difference in risk between the experimental and control groups in a trial. It is used when the risk in the experimental group exceeds the risk in the control group, and is calculated by subtracting the AR in the control group from the AR in the experimental group. This figure does not give any idea of the proportional increase between the two groups; for this, relative risk increase (RRI) is needed (see below).

Bias Systematic deviation of study results from the true results, due to the way(s) in which the study is conducted.

Case control study A study design that examines a group of people who have experienced an event (usually an adverse event) and a group of people who have not experienced the same event, and looks at how exposure to suspect (usually noxious) agents differed between the two groups. This type of study design is most useful for trying to ascertain the cause of rare events, such as rare cancers.

Clinically significant A finding that is clinically important. Here, "significant" takes its everyday meaning of "important" (compared with statistically significant, see below). Where the word "significant" or "significance" is used without qualification in the text, it is being used in its statistical sense.

Cohort study A non-experimental study design that follows a group of people (a cohort), and then looks at how events differ among people within the group. A study that examines a cohort, who differ in respect to exposure to some suspected risk factor (e.g. smoking), is useful for trying to ascertain whether exposure is likely to cause specified events (e.g. lung cancer). Prospective cohort studies (which track participants forward in time) are more reliable than retrospective cohort studies.

Completer analysis Analysis of data from only those participants who remained at the end of the study. Compare with intention to treat analysis, which uses data from all participants who enrolled (see below).

Confidence interval (CI) The 95% confidence interval (or 95% confidence limits) would include 95% of results from studies of the same size and design in the same population. This is close but not identical to saying that the true size of the effect (never exactly known) has a 95% chance of falling within the confidence interval. If the 95% confidence interval for a relative risk or an odds ratio crosses 1, then this is taken as no evidence of an effect. The practical advantages of a confidence interval (rather than a P value) is that they present the range of likely effects.

Controls in a randomised controlled trial refer to the participants in its comparison group. They are allocated either to placebo, no treatment, or a standard treatment.

Crossover randomised trial A trial in which participants receive one treatment and have outcomes measured, and then receive an