

# Introduction

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This is one of a series of evidence-based books from BMJ Books – others have included texts on cardiology, gastroenterology and hepatology, dermatology, ophthalmology, oncology, and pediatrics and child health.

Over the past three decades, the emergence of evidence-based health care (EBHC) has had a substantial impact on clinical practice. In the first half of the twentieth century, treatments, usually based on a strong scientific rationale and experimental work in animals, were routinely introduced into clinical care without adequate and appropriate scientific proof of efficacy in people. Fortunately, the need for a more critical approach to medical practice was recognized. In 1948 the first randomised controlled trial (RCT) in humans was performed under the direction of the British Medical Research Council.<sup>1</sup> Epidemiologists and statisticians, notably Sir Richard Doll and Sir Bradford Hill, provided scientific leadership to the medical community, which responded with improvements in the quality of clinical research. The use of randomised allocation to control confounding variables, and to minimise bias, was recognised as invaluable for the performance of valid studies of treatments. The initiation of these landmark experiments defined a new era in clinical research; the RCT soon became the benchmark for the evaluation of medical and surgical interventions.

Rheumatologists played an important part in these early days. In 1955, the Empire Rheumatism Council reported on perhaps the first randomised trial in the discipline of rheumatology.<sup>2</sup> They showed that cortisone was more effective than salicylates in the treatment of rheumatoid arthritis. As noted in Chapter 9 on rheumatoid arthritis, this treatment has stood the test of time.

Researchers currently understand the need for rigorous approaches to minimising the potential biases that may lead to erroneous conclusions. In addition, they are becoming increasingly aware that the “users” of research must share this understanding if they are to make evidence-based decisions on health and health care. The original “critical appraisal” movement was oriented to the clinician user.<sup>3</sup> This evolved into the evidence-based medicine movement that has been increasingly adopted by clinicians and incorporated into medical curricula. The “user” also includes others such as policymakers,<sup>4</sup> consumers,<sup>5,6</sup> and journalists.<sup>7</sup> We hope that evidence-based texts such as this BMJ series will speed up such change in practice.

## **What is evidence-based rheumatology?**

The term “evidence-based medicine” was coined at McMaster Medical School in the 1980s;<sup>8</sup> it refers to the process of systematically finding, appraising, and using contemporaneous research findings as the basis for clinical decisions. There are typically five steps: formulation of a clear clinical question from a patients’ problem; searching the literature for relevant clinical articles; evaluating using critical appraisal

criteria, the evidence for its validity and usefulness; implementing these findings in clinical practice; and continuous evaluation of the previous steps. Thus, evidence-based rheumatology is the application of the most valid scientific information to the care of patients with rheumatic diseases. Physicians who treat patients with musculoskeletal diseases must provide their patients with the most effective and safest therapy. To meet this high standard, individual clinicians must have access to, and be able to evaluate, scientific evidence. Although many practitioners argue that this has always been the standard of care in clinical medicine, a great deal of evidence exists to the contrary.

In rheumatology, the appreciation and application of the advances in psychometrics and clinimetrics has not been adopted quickly. In the 1970s, only “objective” outcomes, that is laboratory tests (such as the erythrocyte sedimentation rate (ESR)) or clinician findings (such as joint counts performed by physicians) were judged sufficiently credible for regulatory approval. Patient reported outcomes (PROs) have always had face validity but had to await the demonstration of adequate psychometric and clinimetric performances. This was a major stimulus for the involvement of the six OMERACT (Outcome Measures in Rheumatology) meetings to date.

OMERACT brings the key constituencies together to achieve consensus on establishing “core sets” of outcomes in the main rheumatologic conditions (ankylosing spondylitis, lupus, osteoarthritis, osteoporosis, rheumatoid arthritis, systemic sclerosis) that meet the methodological requirements of validity, responsiveness, and feasibility.<sup>9</sup> Patient reported outcomes, such as pain and disability, are now accepted as major endpoints in these conditions by clinicians and regulatory agencies.

Relevant outcomes are necessary but not sufficient. The choice of outcomes is but one of the elements of study design that is needed to arrive at the best estimates of benefits and harms for therapeutic interventions. There is now a general acceptance that randomised trials, when feasible, will provide the most rigorous estimates (and where these are available this text will restrict itself to them). Although randomized controlled trials (RCT) are the most valuable source of data for evaluating healthcare interventions, other kinds of evidence must sometimes be used. In some instances, most obviously in studies of toxicity when looking for rare or delayed effects, it is neither possible nor ethical to perform RCTs. Here, data from methodologically rigorous observational studies are extremely valuable. Examples include the increased risk of vertebral fractures with corticosteroids. Finally, case series can provide compelling evidence for the adoption of a new therapy in the absence of data from RCTs, if the natural history of disease is both well characterised and severe. An example is the use of hip replacement as a dramatically effective intervention for patients with disabling osteoarthritis of the joint.<sup>10</sup>

## The Cochrane Collaboration

The number of trials of therapy has grown too large for any individual to keep abreast of them. In response to this, the Cochrane Library was established to provide systematic, up-to-date reviews of all relevant RCTs of health care. This was named in honour of Archie Cochrane. In an influential book published in 1972,<sup>11</sup> Archie Cochrane, a British epidemiologist, drew attention to our great collective ignorance about the effects of health care. He recognised that people who want to make more informed decisions about health care do not have ready access to reliable reviews of the available evidence. In 1979, he wrote: “*It is surely a great criticism of our profession that we have not organised a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomised controlled trials.*”<sup>12</sup>

This suggestion inspired Iain Chalmers and others to establish the Cochrane Collaboration, an international initiative to facilitate the availability on a website (and CDs) of systematic reviews of trials of interventions across all areas of health care.<sup>11,13</sup>

The Cochrane Musculoskeletal Group (CMSG), established in 1993, consists of over 200 individuals representing healthcare professionals, researchers, and consumers. The coverage of musculoskeletal conditions includes: gout, lupus erythematosus, osteoarthritis, osteoporosis, pediatric rheumatology, rheumatoid arthritis, soft tissue conditions, spondylo-arthropathy, systemic sclerosis, and vasculitis. This forms the scope of *Evidence-based Rheumatology*.

Good decisions about health care rely on more than good reviews of the results of research. The Cochrane Collaboration will make the results of research assessing the effects of health care more easily available. However, as Cochrane made clear in “Effectiveness and Efficiency”,<sup>11</sup> reliable evidence about the effects of specific elements of health care, although essential for improving decisions about health care and research, is only part of what is needed for better decision making.

If better decisions are to lead to improved health, then effective mechanisms are needed for implementing them efficiently. Forms of care that have been shown to do more good than harm should be encouraged, while those that do more harm than good need to be discarded. Some forms of care will require weighing benefits and harms within patients' individual circumstances, given their classification as trade off or close call decisions. The many forms of care which have unknown effects should, as far as possible, be used in the context of a research program to find out whether they help or do harm.

In addition, if people are to receive care which is appropriate, then policy makers and decision makers – ranging from ministers of health to individual clinicians and patients – must consider people's needs, the availability of resources, and priorities.

In making decisions about the care of individual patients, the results of the reviews must be integrated with the clinician's expertise, which has been acquired through experience and practice. The results must also be integrated with the patient's expertise, which derives from their knowledge of their condition (particularly if it is a chronic or recurrent health problem), the treatments on offer, and the receptivity of both the clinician and patient to shared decision making.

If operating in synchrony, these complementary forms of expertise are reflected in more efficient diagnosis and in more thoughtful identification and compassionate use of the predicaments, rights, and preferences of individual patients in making decisions about their care.

Despite the opposition of some, the popularity of EBHC continues to grow. Many practitioners recognise that ethical patient care should be based on the best possible evidence. In addition, increasing numbers of patients are demanding the right to participate in health decisions and requesting the evidence for available options. For these and other reasons, the fundamental concept behind evidence-based medicine and the use of the scientific method in the practice of clinical medicine – has been widely endorsed by medical opinion leaders, patients, and governments.

## Rationale for this book

Generalist and specialist physicians and surgeons, nurses, occupational therapists, physiotherapists, and the other professionals caring for patients with musculoskeletal diseases are fortunate to have many excellent textbooks that provide a wealth of information regarding rheumatologic diseases. Such traditional textbooks concentrate on the pathophysiology of disease and are comprehensive in their scope. *Evidence-based Rheumatology* is not intended to replace these texts, since its focus is on clinical evidence.

Excellent electronic databases are available, and many traditional publications contain relevant research evidence and important summaries and reviews to support evidence-based practice. However, Cumbers and Donald<sup>14</sup> have found that physicians in clinical practice find the acquisition of data from these sources time-consuming. Their study revealed that even locating relevant articles required, on average, three days for practitioners with an onsite library and a week for those without such a facility. This book has been written for the purpose of saving valuable time for busy practitioners caring for patients with rheumatic disease.

The book cannot claim to be comprehensive; for example, the reader will not find chapters on some rare conditions. While we would have preferred to provide our readers with a more complete coverage of the topics, we had to establish a list of priority areas where we felt there was important evidence to be reviewed and summarised on one hand and available authors with the required expertise on the other. We hope that future editions will expand the number of topics that are included.

A limitation of any textbook is the timeliness of the information that it is possible to provide in print form. New evidence accumulates rapidly in clinical medicine and it is impossible to include the most up-to-date information in a textbook because of the time required for production. To meet the needs of our readers for the timeliest information it is planned to produce electronic updates of chapters at regular intervals. These updates, like those for the companion *Evidence-based* books, will appear on the book website <http://www.evidbasedrheum.com>

## Special features

This text aims to do more than just summarise the best evidence for therapy. There has been an additional focus on the dissemination and integration of quality evidence into health and healthcare decisions, sometimes referred to as “knowledge translation”. A feature of this text is the attempt to make the evidence more “usable” for both clinicians and consumers in five ways: web availability, simple quality grading, use of percentages, visual aids for Number Needed to Treat (NNT), and patient handouts.

Firstly, the clinician and consumer materials for each topic are available on the CD Rom (free with the book), and also on the free access book website <http://www.evidbasedrheum.com>. These sections will be organised for clinicians and consumers to easily print off for use as handouts for the clinic and the classroom. For instructions, please follow this Introduction.

Secondly, given the importance of an appreciation of the quality of the study, we have decided to use a scale that can be easily understood by all categories and levels of “users” – using the categories of Platinum, Gold, Silver, Bronze. Based on our previous experience and the challenges to numerative

scales posed by Juni *et al*,<sup>15</sup> we have decided to focus on requiring a few validated criteria to decide which studies warrant the highest levels of Gold and Platinum; namely adequate sample size, completeness of follow-up, blinding of outcome assessors and patients and concealment of allocation.

### Levels of evidence used in this book

Methods for grading the scientific evidence have evolved over the past decade as EBHC has become increasingly important in clinical practice. There are a number of different grading systems available and some are very complex since they incorporate both the type of study and the quality of evidence.

We decided to use a common system of grading throughout the book to rank the strength of scientific evidence for each therapeutic agent. We reviewed multiple grading systems, including that recommended by the US Preventive Services Task Force Guidelines 2001,<sup>16</sup> the summary of systems rating strength of evidence by the Agency for Healthcare Research and Quality (ARHQ),<sup>17</sup> and the Oxford Centre for EBM 2001.<sup>18</sup> These grading systems were reviewed and by consensus process we derived a simplified grading system that included an assessment of quality and could be used by clinicians and patients as previously alluded. We chose four categories to rank the evidence from research studies: Platinum, Gold, Silver, and Bronze. These same levels of evidence are used to present consumer summaries throughout the book.

## Grading for Evidence-based Rheumatology

### Platinum level

The Platinum ranking is given to evidence that meets the following criteria, as reported: is a published systematic review that has at least two individual randomised controlled trials each satisfying the following:

- Sample sizes of at least 50 per group. If they do not find a statistically significant difference, they are adequately powered for a 20% relative difference in the relevant outcome.
- Blinding of patients and assessors for outcomes.
- Handling of withdrawals >80% follow up (imputations based on methods such as Last Observation Carried Forward (LOCF) acceptable).
- Concealment of treatment allocation.<sup>19</sup>

### Gold level

The Gold ranking is given to evidence if at least one randomised controlled trial meets all of the following criteria for the major outcome(s), as reported:

- Sample sizes of at least 50 per group. If they do not find a statistically significant difference, they are adequately powered for a 20% relative difference in the relevant outcome.
- Blinding of patients and assessors for outcomes.
- Handling of withdrawals > 80% follow up (imputations based on methods such as Last Observation Carried Forward (LOCF) acceptable).
- Concealment of treatment allocation.<sup>19</sup>

### Silver level

The Silver ranking is given to evidence if a systematic review or randomised trial that does not meet the above criteria. Silver ranking would also include evidence from at least one study of non-randomised cohorts who did and did not receive the therapy or evidence from at least one case-control study. A randomised trial with a “head-to-head” comparison of agents is considered Silver level ranking unless a reference is provided to a comparison of one of the agents to placebo showing at least a 20% relative difference.

### Bronze level

The bronze ranking is given to evidence if at least one case series without controls (including simple before/after studies in which the patient acts as their own control) or is derived from expert opinion based on clinical experience without reference to any of the foregoing (for example, argument from physiology, bench research or first principles).

Evidence grades appear in shaded boxes.

The third item to aid “knowledge translation” is the provision of the information in tables in a clinically useful format. Where possible, the following data are provided: (a) if a scale, the range; (b) baseline rates; (c) relative effects; (d) NNT (number needed to treat), NNH (number needed to harm). The example table shown here is taken from Chapter 8 of the book (see end of Introduction for description).

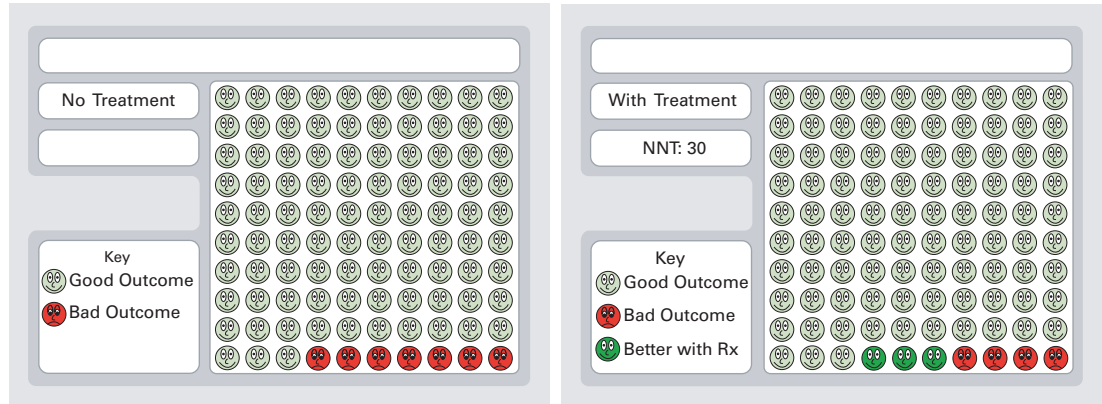
**Table 8.3 NNT for five year (high risk woman) and lifetime risk of fracture, with alendronate compared with no treatment (Cranney *et al*, 2002)<sup>31</sup>**

Outcome	5 year and lifetime risk of fracture in untreated population	5 year and lifetime risk in a treated population	Relative risk with treatment (95% CI)	NNT
Vertebral fracture	5 year: 7.1%	5 year: 4%	0.52	5 year: 29
	Lifetime: 9.6%	Lifetime: 5%	(0.43–0.65)	Lifetime: 22
Non-vertebral fracture	5 year: 19.8%	5 year: 10%	0.51	5 year: 10
	Lifetime: 42.1%	Lifetime: 21%	(0.38–0.69)	Lifetime: 5

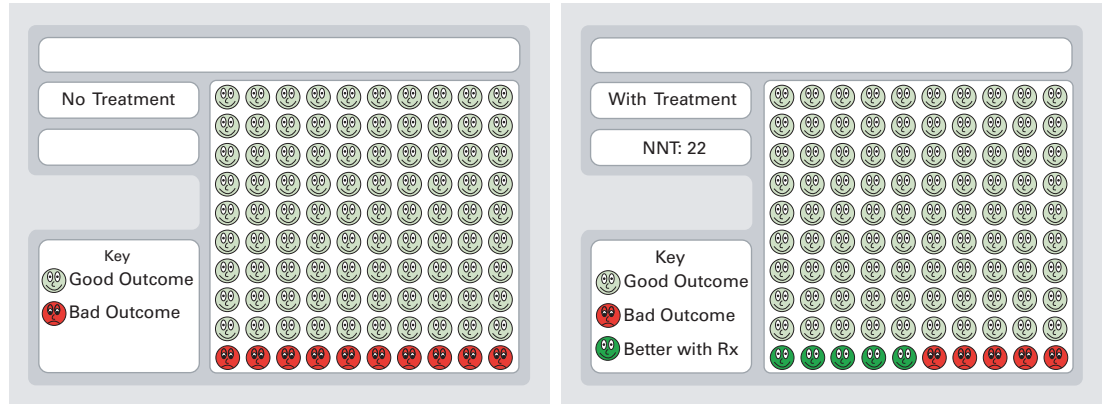
Fourthly, “face figures” are also included for a number of the outcomes. They use the transformation of the NNT (or NNH) data to “face tables”. Visual Rx, a software program that was developed by Peter and Chris Cates<sup>22</sup> was used to calculate and convert the data to the face tables. The tables for the five year and lifetime risk of vertebral fractures for 100 high risk women comparing no treatment versus treatment with alendronate are presented on p xix.

Each display represents a total of 100 faces that are divided into three categories. The pale green faces are those patients who have a good outcome on both the control treatment and the active treatment. The red faces are those who suffer a bad outcome, whichever treatment they receive. The dark green faces are those patients that change their category of outcome depending on whether they are given the active

## NNT for high risk women for 5 year prevention of vertebral fractures



## NNT for high risk women for lifetime prevention of vertebral fractures.



treatment or not. If the treatment is beneficial, as a consequence of being given the active treatment, the faces will appear as dark green. However, since it is not possible to tell who these patients are, all 100 have to be given active treatment for this group to benefit.

The above example of a face table displays the 5 year risk of vertebral fractures of 100 high risk women treated with or without alendronate. The first table, No Treatment, illustrates that 7 out of 100 women will have vertebral fractures if left untreated (red faces), while 93 out of 100 women left untreated will not have a vertebral fracture (pale green faces) with or without treatment. The second table, With Treatment, illustrates that if the 100 high risk women were treated with alendronate, then 4 out of 100 women will have vertebral fractures (red faces), while 3 out of 100 women will not have vertebral fractures due to alendronate – benefiting from treatment (dark green faces).

Fifthly, we have translated the evidence-based information about a number of treatments into a set of handouts for patients. These are reproduced in the book and are also available on the book website at <http://www.evidbasedrheum.com> to provide to patients and to use in consultation and for teaching and will also be made available on the Arthritis Society website at <http://www.arthritis.ca>.

The information about a treatment is presented as a consumer package in two parts: as a series of consumer summaries (1, 5, 15 minute handouts) and as a decision aid (45 minute handout). The series of consumer summaries consist of short consumer summaries and a long consumer summary that describe the disease and treatment at three different levels of detail. The different versions address the varying needs of the different patients who want varying quantities of detail about a treatment.

The “1 minute” consumer summary consists of a brief “bottom line” statement about the treatment. The “5 minute” summary includes some additional general information about the condition and treatment and a brief description of the results from studies regarding benefits and harms. The “15 minute” consumer summary provides more details about the evidence than the shorter summaries. It also provides more information about the condition and treatment, details about the types of studies analysed in the review of the literature, numerical data from the studies depicting the benefits and harms of the treatment and the “bottom line”. The numerical data is presented as the number of patients out of 100 who improved with placebo or as the number of patients out of 100 who benefited from a treatment.

The second part of the consumer package, the Decision Aid, is a tool that incorporates the information from the consumer summaries together with the values and preferences identified by the patient; it guides patients in the decision making process, and enhances physician–patient interaction. Patients might take 45 minutes to use the decision aid and can use it in consultation with their physician. (See Chapter 4 for more details about decision aids.)

## 1 MINUTE CONSUMER SUMMARY (bottom line)

**How well does alendronate (Fosamax) work to treat and prevent osteoporosis in women after menopause?**

**What is the bottom line?**

There is “Platinum” level evidence that women after menopause with osteoporosis, have fewer spine fractures when taking alendronate at 5 to 40 mg daily for 2 to 3 years. Women after menopause with osteoporosis have fewer hip and non-spinal fractures with 10 to 40 mg of alendronate for 2 to 3 years.

Alendronate for 2 to 3 years, increases bone mineral density.

Side effects such as heartburn or ulcers in the oesophagus or gullet may occur.

From Cranney A, Simon LS, Tugwell P, Adachi R, Ottawa Methods Group. Osteoporosis. In: *Evidence-based Rheumatology*. London: BMJ Books, 2003.

## 5 MINUTE CONSUMER SUMMARY

### How well does alendronate (Fosamax) work to treat and prevent osteoporosis in women after menopause?

To answer this question, scientists found and analysed 11 studies testing alendronate in over 12 500 women after menopause. Women received 5 to 40 mg of alendronate as a pill daily for 1 to 4 years. These studies provide the best evidence we have today.

#### What is osteoporosis and how can alendronate help?

Osteoporosis is a condition of weak brittle bones that break easily. Breaks or fractures of the spine and hip or wrist (non-spinal fractures) may occur and often without a fall. Alendronate is a bisphosphonate and "antiresorptive agent" used to decrease fractures by slowing bone loss. There is some debate about whether alendronate decreases fractures, in women with normal or near normal bone density.

#### How well did alendronate decrease fractures and increase bone density?

In women after menopause who have osteoporosis, alendronate decreased the number of **spine** fractures more than a placebo or sugar pill. 10 to 40 mg of alendronate daily decreased the number of **non-spinal fractures** (such as wrist and hip) more than a placebo or sugar pill in women with osteoporosis, but not in women who have normal to near normal bone density.

Bone mineral density increased in the spine, hip and somewhat in the forearm.

#### Were there any side effects?

Heartburn or ulcers in the oesophagus or gullet may occur. But the number of women who stopped taking alendronate due to side effects was no different than the number of women who stopped taking a placebo.

#### What is the bottom line?

There is "Platinum" level evidence that women after menopause with osteoporosis, have fewer spine fractures when taking alendronate at 5 to 40 mg daily for 2 to 3 years. Women after menopause with osteoporosis have fewer hip and non-spinal fractures with 10 to 40 mg of alendronate for 2 to 3 years.

Alendronate for 2 to 3 years, increases bone mineral density.

Side effects such as heartburn or ulcers in the oesophagus or gullet may occur.

From Cranney A, Simon LS, Tugwell P, Adachi R, Ottawa Methods Group. Osteoporosis. In: Evidence-based Rheumatology. London: BMJ Books, 2003.

1 minute summary



## 15 MINUTE CONSUMER SUMMARY

PAGE 1

### How well does alendronate (Fosamax) work to treat and prevent osteoporosis in women after menopause?

#### What is osteoporosis and how can alendronate help?

Osteoporosis is a condition of weak brittle bones that break easily. In osteoporosis, breaks or fractures of the spine and hip, wrist or forearm (non-spinal fractures) may occur and often without a fall. Osteoporosis is detected using a bone density test that measures the amount of bone loss. A result that is at least 2.5 "standard deviations" below normal confirms the diagnosis. This means people have lost at least 25 per cent of their bone mass or density. Drugs have been developed to slow the bone loss.

Alendronate is a bisphosphonate drug and an "antiresorptive agent" that was developed for women after menopause to decrease fractures. Alendronate works by slowing bone loss or "resorption" and does not interfere with bone building or mineralisation. There is some debate about whether alendronate increases bone density in women after menopause who have normal to near normal bone density or who already have bone loss (as in osteoporosis) and whether it decrease all types of fractures, such as spine and non-spinal fractures.

#### How did the scientists find the information and analyse it?

To find out just how well alendronate works, the scientists searched for studies testing alendronate. Unfortunately, not all studies found were of a high quality and so only those studies that met high standards were examined in this summary.

Studies had to be randomised controlled trials – where a group of women after menopause (post menopausal) received alendronate and was compared to postmenopausal women who received a placebo (or sugar pill) for at least one year.

Studies had to show how well alendronate works by measuring bone mineral density (BMD) and the number of fractures (or breaks).

#### Which high quality studies were examined in the summary?

Eleven high quality studies were examined. The studies included 12 855 women after menopause (postmenopausal women) receiving 5 to 40 mg of alendronate daily for 1 to 4 years. Two studies provided alendronate to women with normal to near normal bone density to prevent bone loss and fractures and 9 studies provided alendronate to women who already had bone losses (or low bone mineral density – BMD). Some studies included women who already had a spine fracture.

#### How well did alendronate decrease fractures and increase bone density?

**Spine fractures:** Over a lifetime, in women who have normal to near normal bone density or osteoporosis:

5 out of 100 women receiving 5 to 40 mg of alendronate daily will have a spine fracture  
10 out of 100 women receiving no treatment or a placebo (sugar pill) will have a spine fracture.

## 15 MINUTE CONSUMER SUMMARY

PAGE 2

- results from  
Cochrane Review  
and included trials

### Hip and non-spinal fractures (wrist, etc.):

Over a lifetime, in women who have **osteoporosis**:  
21 out of 100 women receiving 10 to 40 mg of alendronate daily will have a hip fracture or other non-spinal fracture  
42 out of 100 women receiving no treatment or a placebo (sugar pill) will have a hip fracture or other non-spinal fracture.

This means that 21 out of 100 more women benefited from taking alendronate than a placebo.

In women who have **normal to near normal** bone density:

the benefit of taking alendronate to prevent hip fracture or other non-spinal fractures is still in question since most of these women are at a lower risk of having a fracture.

The number of women taking 10 to 40 mg of alendronate daily over 2 to 3 years who will have a hip fracture is no different than the number of women taking a placebo (2 out of 100 compared to 4 out of 100 women). These numbers may also be due to chance and not to treatment with alendronate.

**Bone mineral density (BMD):** Bone mineral density increased in the lower spine and in the hip in **postmenopausal women** who had normal to near normal bone density and in women with osteoporosis who received 5 to 40 mg of alendronate. The increase in the bone density of the forearm was also increased but not as much as in the lower spine and hip.

Despite the fact that bone density increased after each year, the amount of the increase was less after each year.

### Were there any side effects?

Side effects such as heartburn or ulcers in the oesophagus (or gullet) may occur. But the number of women who stopped taking alendronate due to side effects was no different than the number of women who stopped taking a placebo.

In the biggest study, 7 out of 100 women taking 5 to 40 mg of alendronate and 6 out of 100 women taking a placebo stopped their medication.

It will be long before we can assess what the rare and late side effects of alendronate.

## 15 MINUTE CONSUMER SUMMARY

PAGE 3

Bottom line

### What is the bottom line?

There is "Platinum" level of evidence that women after menopause with normal to near normal bone density or osteoporosis, have fewer spine fractures when taking alendronate at 5 to 40 mg daily for 2 to 3 years.

Women after menopause with osteoporosis have fewer hip fractures and other non-spinal fractures with 10 to 40 mg of alendronate for 2 to 3 years. It is unclear whether women with normal or near normal bone density have fewer non-spinal fractures with alendronate.

Alendronate, at 10 to 40 mg daily for 2 to 3 years, increases bone mineral density in women after menopause with normal to near normal bone density or osteoporosis. This effect appeared to increase with larger doses of alendronate over longer periods of treatment.

Side effects such as heartburn or ulcers in the oesophagus (or gullet) may occur. However after 2 to 3 years of taking the pills, women after menopause do not appear to experience side effects that would cause them to stop taking alendronate. It is not certain yet what are the rare side effects of alendronate.

From Cranney A, Simon LS, Tugwell P, Adachi R, Ottawa Methods Group. Osteoporosis. In: Evidence-based Rheumatology. London: BMJ Books, 2003.

## 45 MINUTE DECISION AID

PAGE 1

**Information about osteoporosis and treatment****What is osteoporosis?**

Osteoporosis is a condition of weak, brittle bones that break easily. The most common breaks or fractures are in the spine, hip, wrist or forearm, and these may occur without a fall. Osteoporosis is detected using a bone density test that measures the amount of bone loss. A result that is at least 2.5 "standard deviations" below normal confirms the diagnosis. This means people have lost at least 25 per cent of their bone mass or density.

Hip fractures can cause severe disability or death.

Among 100 women with normal bone density, about **15** may break a hip in their lifetime.  
Among 100 women with low bone density, about **35 to 75** may break a hip in their lifetime.

This number depends on amount of bone loss, age, and other risk factors, such as:

*major bone-related risks:* previous broken bones since age 50 (not from trauma); family history of fracture (e.g. mother who broke a hip, wrist, spine)

*major fall-related risks:* poor health; unable to rise from a chair without help; use of sleeping pills.

Spine fractures are more common, disabling, and painful. They can cause stooped posture and loss of height of up to 6 inches.

To find out your personal risk of broken bones, ask your doctor.

**What can I do on my own to manage my disease?**

Calcium and vitamin D      Regular impact exercises (e.g. walking)

**What treatments are used for osteoporosis?**

Three kinds of treatment may be used alone or together. The common (generic) names of treatment are shown below.

- Bone-specific drugs*

Alendronate	Calcitonin	Etidronate	Risedronate
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- Hormones that affect bones and other organs*

Parathyroid hormone	Raloxifene	Hormone replacement therapy (oestrogen and progestin)
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- Other*

Hip protector pads

**What about other treatments I have heard about?**

There is not enough evidence about the effects of some treatments. Other treatments do not work. For example:

Calcitonin for non-spinal fractures

Etidronate for non-spinal fractures

Raloxifene for non-spinal fractures

**What are my choices? How can I decide?**

Treatment for your disease will depend on your condition. You need to know the good points (pros) and bad points (cons) about each treatment before you can decide.

## 45 MINUTE DECISION AID

PAGE 2

**Osteoporosis decision aid****Should I take alendronate?**

This guide can help you make decisions about the treatment your doctor is asking you to consider.

It will help you to:

- Clarify what you need to decide.
- Consider the pros and cons of different choices.
- Decide what role you want to have in choosing your treatment.
- Identify what you need to help you make the decision.
- Plan the next steps.
- Share your thinking with your doctor.

**Step 1: Clarify what you need to decide****What is the decision?**

Should I take alendronate to slow bone loss or prevent breaks?

Alendronate may be taken as a pill daily or once a week.

**When does this decision have to be made? Check **one****

within days     within weeks     within months

**How far along are you with this decision? Check **one****

- I have not thought about it yet
- I am considering the choices
- I am close to making a choice
- I have already made a choice

## 45 MINUTE DECISION AID

PAGE 3

### Step 2: Consider the pros and cons of different choices

#### What does the research show?

Alendronate is classified as **Beneficial**

There is "Platinum" level evidence from 11 studies of 12 855 women after menopause that tested alendronate and lasted up to 4 years. The women had osteoporosis (low bone density) or normal to near normal bone density. These studies found pros and cons that are listed in the chart below.

#### What do I think of the pros and cons of alendronate?

1. Review the common pros and cons that are shown below.
2. Add any other pros and cons that are important to you.
3. Show how important each pro and con is to you by circling from one (\*) star if it is a little important to you, to up to five (\*\*\*\*\*) stars if it is very important to you.

PROS AND CONS OF ALENDRONATE TREATMENT			
PROS (number of people affected)	How important is it to you?	CONS (number of people affected)	How important is it to you?
<b>Fewer broken bones in the spine</b> 5 less women out of 100 have breaks in their spine over a lifetime with alendronate.	*****	<b>Side effects: heartburn, stomach irritation</b>	*****
<b>Fewer broken bones in the hip or wrist</b> 23 less women out of 100 with osteoporosis have breaks in their hip or wrist over a lifetime.	*****	<b>Increase chance of developing ulcers in the oesophagus or gut</b>	*****
<b>Increase bone density</b>	*****	<b>Must be taken in morning 1 hour before eating and at or stand after taking the pill</b>	*****
<b>Flexible dosing</b> May be taken once a week	*****	<b>Personal cost of medicine</b>	*****
<b>Other pros</b>	*****	<b>Other cons</b>	*****

#### What do you think about taking alendronate? Check one

- Willing to consider this treatment  
 Pros are more important to me than the Cons
- Unsure
- Not willing to consider this treatment  
 Cons are more important to me than the Pros

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### Step 3: Choose the role you want to have in choosing your treatment

- Check  one
- I prefer to decide on my own after listening to the opinions of others  
 I prefer to share the decision with: \_\_\_\_\_  
 I prefer someone else to decide for me, namely: \_\_\_\_\_

### Step 4: Identify what you need to help you make the decision

<b>What I know</b>	Do you know enough about your condition to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know which options are available to you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know the good points (pros) of each option?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know the bad points (cons) of each option?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
<b>What's important</b>	Are you clear about which <b>pros</b> are most important to you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Are you clear about which <b>cons</b> are most important to you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
<b>How others help</b>	Do you have enough support from others to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Are you choosing without pressure from others?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you have enough advice to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
<b>How sure I feel</b>	Are you clear about the best choice for you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you feel sure about what to choose?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure

If you answered No or Unsure to many of these questions, you should talk to your doctor.

### Step 5: Plan the next steps

#### What do you need to do before you make this decision?

For example: talk to your doctor, read more about this treatment or other treatments for osteoporosis.

### Step 6: Share the information on this form with your doctor

It will help your doctor understand what you think about this treatment.

Decisional Conflict Scale © O'Connor 1993, Revised 1999.  
 Format based on the Ottawa Personal Decision Guide© 2000, A O'Connor, O Stacey, University of Ottawa, Ottawa Health Research Institute.

## Structure of the book

Chapters 1–4 are methodology chapters relevant to an evidence-based approach to rheumatology. Chapter 1 reviews the important area of literature searching. A pivotal feature of a systematic review is the use of an unbiased comprehensive search strategy. Healthcare professionals have access to many resources through the internet. However, the process of searching for information is not simply a matter of plugging in a few keywords to one's favourite search engine. This chapter describes searching for evidence-based literature in the field of rheumatology.

Chapter 2 reviews work in rheumatology on outcomes, combining the results of studies and comparing the effects of different interventions while requiring that the endpoint of the study be comparable. In 1989 a review showed that there were still many problems with the endpoints employed in rheumatoid arthritis (RA) clinical trials;<sup>21</sup> the endpoints were not comprehensive and yet showed considerable overlap, and were insensitive to change. The stalemate was impeding progress and hampering the development of new treatments. This led to the establishment of a series of consensus conferences to develop an agenda to establish minimum core sets of outcomes that meet the OMERACT Methods "Filter" of validity, responsiveness, and feasibility.

Chapter 3, for example, reviews the issues relevant to incorporating the economic perspective in making decisions around therapy in rheumatologic conditions, while Chapter 2 addresses the concepts and issues relevant to the effective communication of the evidence to enable the patient or consumer and clinician to make an informed choice.

Chapters 5–13 are related to the clinical content areas. Each one presents in a similar perspective the best available evidence for helping to make choices about healthcare decisions. The published methodology for conducting a systematic review was applied.<sup>19</sup> All languages were included in the literature searches and when necessary translations were conducted. Authors for the clinical chapters included reviewers from North America (Canada and USA), Europe (France, Romania and the Netherlands), Australia, and Thailand. A description of the statistical methodology used for the NNT and NNH is provided.

The clinical chapters each report the results of the systematic review, RCT or observational studies, which are then presented in a clinically relevant manner using a statistical approach. Clinical case presentations within each chapter demonstrate how the evidence would be applied in making healthcare choices in practice. As new studies are completed, new evidence will be added to the data.

## Number needed to treat (NNT)

When comparing a new treatment with a control (standard) treatment, the number needed to treat (NNT) is the number of patients who need to be treated with the new treatment rather than the control treatment in order for one additional patient to benefit. The NNT was calculated using one of several different methods depending on the clinical and research setting. More specifically, three methods were considered:

1. If a single study is available and the event rates in the treatment group ( $P_t$ ) and the control group ( $P_c$ ) are provided, then the NNT is the reciprocal of the risk difference (absolute risk reduction or ARR) given by  $1/(P_c - P_t)$  or, if the outcome is beneficial, by  $1/(P_t - P_c)$ . Note, when there is no treatment effect the confidence limit of the risk difference includes 0 and NNT is infinite. The methods used for confidence interval calculations are outlined in Chapter 11 of *Statistics with Confidence*, 2nd edition.<sup>22</sup> If the ARR was significant, the confidence interval for NNT was calculated based on the reciprocals of the confidence limits of the ARR. The CIA software was used for the actual calculation.<sup>22</sup>
2. If several studies are available and a meta-analysis has been conducted yielding an overall weighted average estimate of relative risk (RR), then the NNT estimates are obtained by substituting the RR, along with an estimate of the prevalence of the condition in the population of interest, into the NNT formulation based on RR:  $NNT [1/(\text{event rate} \times (1 - RR))]$ .<sup>22</sup> The Cates software,<sup>21</sup> Visual Rx 1.6, was used for the actual calculation. Visual Rx (available at <http://www.nntonline.net/ebm/visualrx/try.asp>) is designed to calculate numbers needed to treat (NNT) from the pooled results of a meta-analysis and produce a graphical display of the result.

The original concept of presenting NNT graphically using faces was published by Laupacis *et al.*<sup>23</sup> The idea was reinforced by empirical work that was presented at the Seventh Annual Cochrane Colloquium in Rome in October 1999. There are many different statistical methods which can be used in calculating a summary estimate from the results of individual clinical trials and the NNT can be derived in different ways from each of these. Since the results are not always identical, Visual Rx accommodates a variety of methods using relative risk, Peto odds ratio, odds ratio, and event rates. In order to make the concept of NNT understandable to clinicians and patients, Visual Rx produces a graphical display representing the likely outcomes for a theoretical group of 100 patients who are given a particular treatment.

Visual Rx is particularly useful in relation to the results of Cochrane Systematic Reviews, which are available electronically on the Cochrane Library at <http://www.update-software.com/Cochrane>. Visual Rx can only be used to display the results for dichotomous outcomes.

3. For continuous outcomes, the procedure by Altman was used to determine the estimate of NNT.<sup>22</sup> This procedure requires the identification of an effect size as a minimal important difference (MID) and the default value suggested was 0.5. The Wells software was used for the actual calculation.<sup>24</sup>

Number needed to harm (NNH) is similar to the NNT in the context of the mathematical calculation but differs in that the experimental treatment increases the probability of a harmful outcome compared to placebo<sup>24,25,26</sup>. This is to be considered when an adverse event is caused by the active treatment. The NNH is defined as the number of patients who receive the active therapy that will lead to one additional patient being harmed compared to those who receive placebo. The calculated NNH is usually accompanied by a 95% CI as that of the NNT. The NNH should be considered together with the NNT since an experimental treatment may help decrease the probability of one event, but may increase the probability of another adverse event, which might exceed the beneficial effect of the active therapy.

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