Tips for teachers of evidence-based medicine: 1. Relative risk reduction, absolute risk reduction and number needed to treat

Alexandra Barratt, Peter C. Wyer, Rose Hatala, Thomas McGinn, Antonio L. Dans, Sheri Keitz, Virginia Moyer, Gordon Guyatt, for the Evidence-Based Medicine Teaching Tips Working Group

Physicians, patients and policy-makers are affected not only by the results of studies but also by how authors present the results.[1-4] An adequate understanding of how to use quantitative estimates of effect is important for clinicians who seek to apply the results of clinical trials and systematic reviews to patient care. However, many physicians find the concepts, language and formulas of relative risk reduction, risk difference (absolute risk reduction) and number needed to treat daunting. Furthermore, depending on which measures of effect are presented in a given study, the impact of an intervention may appear very large or quite small, even though the underlying data are the same. In this article we present scripts that teachers of evidence-based medicine can use to help clinical learners understand these principles.

For these "teaching scripts" to be useful, the teacher must have a basic understanding of the relevant concepts. We have framed this article primarily for clinical teachers who already have a grasp of critical appraisal and some experience in teaching this type of material to clinical learners. Clinical teachers may use the approaches we offer with a broad range of clinical learners, including medical students, residents and practising physicians. However, it is not our primary goal to instruct novices in evidence-based medicine in the teaching of critical appraisal to any level of learner. The "tips" in this article are adapted from approaches developed by educators with experience in teaching evidence-based medicine skills to clinicians.[5,6] A related article, intended for people who are learning these concepts, has been published in *CMAJ*.[7]

For each of the 3 tips covered in this article, we have provided guidance on when to use the tip, the teaching script for the tip, a "bottom line" section and a summary card. Tip 1 presents a method of introducing learners to the importance of specific measures of effect, including relative risk reduction, absolute risk reduction (also called the "risk difference") and the number needed to treat. In tip 2, the teacher helps learners to use these "measures of association" to quantify the magnitude of benefit and harm for patients at various risks of a poor outcome. In tip 3, the teacher helps learners to derive estimates of clinically important benefit with respect to standard therapeutic interventions. For each tip, we identify the target learner (on the basis of level of experience) and provide estimates of the time required for the exercise.

Teaching tip 1: Understanding risk and risk reduction

When to use this tip

This tip is suitable for beginners and intermediate-level learners, and the exercise takes about 10 minutes. The general objective is to introduce learners to the concepts of risk and risk reduction, with the following specific objectives:

- Learn how to determine control and treatment event rates from published studies
- Learn how to determine relative and absolute risk reductions from published studies
- Understand how relative and absolute risk reductions usually apply to different populations

Stumbling blocks often arise in teaching risk and risk reduction. Arithmetic formulas can confuse new learners, particularly those who are not comfortable with numbers. As a result, we have deliberately avoided presenting formulas in this tip, instead presenting a framework for learners to develop ways of calculating the relative risk reduction and risk difference for themselves. We have also avoided defining rel-

Other available resources

- A companion version of this article directed to learners of evidence-based medicine has been published in *CMAJ*[7] and is available online through e*CMAJ* (www.cmaj.ca/cgi/content/full/171/4/353).
- An interactive version of this article as well as other tools and resources are available at www.ebmtips.net/risk001.asp.

ative risk as a prior step for calculating relative risk reduction; the formulas for both appear in Appendix 1. Finally, many learners have difficulty understanding that risk difference depends on the baseline risk and that relative risk reduction tends to be constant across populations.[8] The graphic approach we use makes this distinction intuitively evident.

The script

Figure 1 is the centrepiece of this tip, which focuses on the concept of 2 randomized trials of a therapy, performed on 2 populations with different baseline risks of the outcome. First, using a chalkboard, easel or overhead projector, draw the axes of the graph, labelling the vertical axis "Event rate." To explain what you are doing, you can say, "In a group of 100 patients, the number who experience an adverse event such as death is the event rate." Next, draw the first bar, telling learners that this is the event rate in a population with severe disease (that is, a group at high risk of an adverse event). The event rate is 40 out of 100, or 40%. Next, draw the second bar, telling learners that this is the event rate in severely diseased patients who receive a treatment. Ask participants to describe the effect of the treatment. Someone will probably say it reduces the event rate by one-quarter or by 25%. Now, ask them if there is any other way they could express the difference between the 2 bars. With luck, someone will suggest subtracting the event rate in the second (treated) group from the event rate in the first (control) group, which gives a value of 10%.

The learners have now intuitively calculated the relative risk reduction and the risk difference. Add these labels to your graph and explain that the risk difference is so called because it represents the difference between event rates, i.e., the subtraction of one rate from another. Relative risk reduction is so called because it involves presenting the change in risk as a proportion of (or relative to) the initial rate. At this point, you may want to tell them that absolute risk reduction is an alternative term for risk difference. For the remainder of this article we will use "risk difference" because we think the term is more self-explanatory and because it applies to both increases and decreases in risk.

Have learners record the relative risk reduction and the risk difference. Next, suggest that a second trial has been performed in a less severely affected patient population. Draw the third bar (showing an event rate of 10%), telling them that it represents the event rate in this lower-risk group. Ask them, "If these people are also given the treatment and it is as effective as it was in the more severely diseased patients (i.e., the relative risk reduction is constant), what will the event rate be in the treated group?" Someone will offer 7.5% as the answer, and you can draw, or ask the learner to draw, this bar on the graph. Finally, ask the learners to calculate the risk difference for the second pair of bars (only 2.5%). Have them compare the relative risk reduction and the risk difference in the high-risk population (25% and 10% respectively) with the same values for the low risk population (25% and 2.5% respectively).

The bottom line

- An event rate is the number of people experiencing an event as a proportion of the number of people in the population.
- The risk difference (absolute risk reduction) is the arithmetic difference between 2 event rates.
- The relative risk reduction is the difference in event rates expressed in a proportional or relative manner, in relation to the control event rate.
- Relative risk reduction is often more impressive than the risk difference. Furthermore, the lower the event rate in the control group, the larger the difference between relative risk reduction and risk difference.

See Appendix 2 for the summary card for this tip.

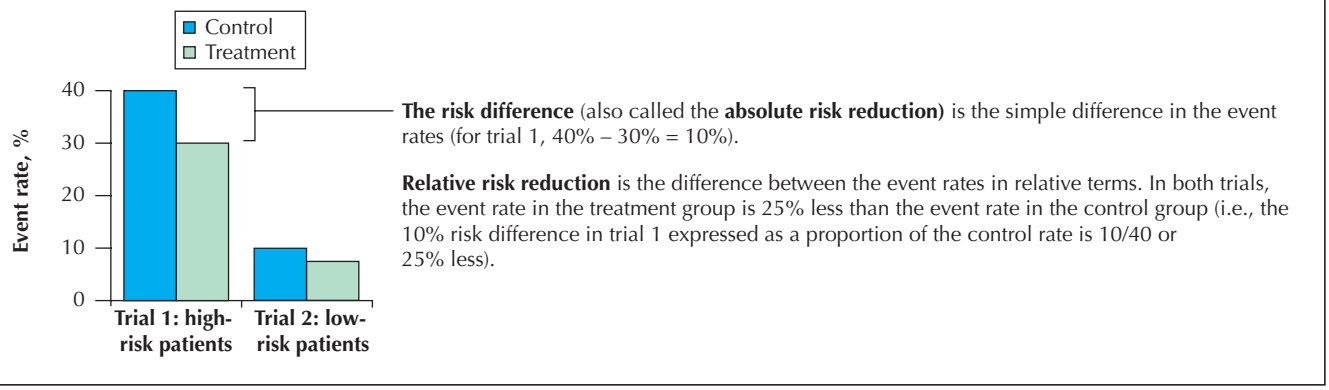

Fig. 1: Results of 2 hypothetical randomized controlled trials of a new therapy. The blue bar in each trial represents the rate of a specified adverse event in untreated patients, and the green bar represents the rate in patients treated with the new therapy. The 2 trials are performed in patients with different baseline risks for the adverse outcome: a high baseline risk for patients in trial 1 and a low baseline risk for those in trial 2.

Teaching tip 2: Balancing benefits and adverse effects in individual patients

When to use this tip

This tip is suitable for intermediate to advanced learners, and the exercise requires 10–15 minutes. The general objective is to help learners apply evidence about intervention benefits and risks to individual patients, with the following specific objectives:

- Learn how to use a known relative risk reduction to estimate the risk of an event for a patient undergoing treatment, given an estimate of that individual's risk of the event without treatment.
- Learn how to use risk differences (absolute risk reductions) to assess whether the benefits of therapy outweigh its harms.

The script

Walk the learners through the following hypothetical scenario. Each learner should imagine himself or herself as a family physician who is seeing Pat, a 69-year-old woman whose blood pressure during a routine examination is 170/100 mm Hg. When Pat is seen again in a few weeks, her blood pressure is unchanged. She is otherwise well and has no history of cardiovascular or cerebrovascular disease. Tell the learners that they assess Pat's risk of stroke at about 1% (or 1 in 100) per year.[9]

Tell the learners that a recent randomized trial of a newly released antihypertensive drug, drug X, reported a relative risk reduction for stroke of 33% over 3 years. Ask them to calculate Pat's risk of stroke over 3 years with and without treatment with drug X. (Her risk over 3 years is 3% without treatment and 2% with treatment, a risk difference of 1%.)

Next, tell the learners about Dorothy, who is also 69 years old and whose blood pressure is the same as Pat's, 170/100 mm Hg. However, because Dorothy had a stroke recently, the hypothetical physician assesses her risk of subsequent stroke as substantially greater than Pat's, perhaps 10% per year.[10] Now, ask the learners to calculate the risk difference for Dorothy over 3 years, with and without drug X, using the same relative risk reduction (33%). You can use a blank version of Table 1 to help learners determine the potential benefit of the drug. Insert the estimated 3-year event rates for Dorothy and then apply the relative risk reduction (33%) expected if she takes drug X. It should be evident that Dorothy's risk over 3 years falls from 30% to 20%, a risk difference of 10%.

Finally, remind the learners that they need to factor any potential harms (adverse effects associated with using the drug) into their clinical decisions. You can tell them that in the clinical trials of drug X, the risk of severe gastric bleeding increased 3-fold over 3 years in patients who received the drug (a relative risk of 3). You can also tell them that a population-based study has reported the risk of severe gastric bleeding for women in your patients' age group at about 0.1% per year (regardless of their risk of stroke). Have them work out the risk of severe gastric bleeding for both Pat and Dorothy over 3 years with and without treatment with drug X. They should find that the risk is 0.3% without treatment and 0.9% with treatment, an absolute difference of 0.6%.

By now, your learners should have filled in the table to look like Table 1.

Ask them whether, given the results of this exercise, they would give drug X to Pat, to Dorothy or to both. You can anticipate that the discussion will ensue along the following lines. Pat will experience a small benefit (risk difference over 3 years of about 1% for stroke), but this will be considerably offset by the increased risk of gastric bleeding (risk difference over 3 years of 0.6%). The potential benefit for Dorothy (risk difference over 3 years of about 10%) is much greater than the increased risk of harm (risk difference over 3 years of 0.6%). Therefore, the net benefit of treatment is likely to be greater for Dorothy (who is at higher risk of stroke) than for Pat (who is at lower risk). Learners may also notice that assessment of the balance between benefits and harms de-

Table 1: Benefit and harm table, as completed by learners (tip 2)

	3-yr event rate for stroke, %			3-yr event rate for severe gastric bleeding, %		
Patient group	No treatment	With treatment (drug X)	Absolute risk reduction (no treatment – treatment)	No treatment	With treatment (drug X)	Absolute risk increase (treatment – no treatment)
At lower risk (e.g., Pat)	3	2	1	0.3	0.9	0.6
At higher risk (e.g., Dorothy)	30	20	10	0.3	0.9	0.6

*Based on data from randomized controlled trials of drug X reporting a 33% relative risk reduction for the outcome (stroke) over 3 years and a 3-fold increase for the adverse effect (severe gastric bleeding) over the same period.

pends on the value that patients place on reducing their risk of stroke in relation to the increased risk of gastric bleeding.

Extension for more advanced learners

Explain to the learners that these assessments are only valid if the relative risk reduction associated with the treatment and the risk of harm are constant at different levels of risk for the relevant outcome. This is generally true,[8] and the assumption is helpful in calculating risk differences for individuals.[11] However, there are documented examples of relative risk varying with baseline risk.[12] Encourage the learners to discuss whether they think that the assumptions of constant relative risks pertaining to benefit of therapy are likely to hold in this example. In the case of harm, risk differences are likely to be stable and unrelated to the risks of adverse outcomes from the underlying disease.

The bottom line

- Clinicians can tailor trial data to an individual patient by calculating risk differences if they know or can estimate the individual's risk of the relevant outcomes (with and without treatment).
- Presenting data as risk differences makes the benefits and harms of therapy easier to compare.

See Appendix 2 for the summary card for this tip.

Teaching tip 3: Calculating and using number needed to treat

When to use this tip

This tip is suitable for intermediate-level learners, and the exercise takes 15–20 minutes. The general objective is to introduce learners to the calculation and use of number needed to treat (NNT), with the following specific objectives:

- Develop an understanding of the concept of NNT and how it is calculated from the risk difference.
- Gain familiarity with the concept of NNT by comparing the NNTs that correspond to common interventions.

Number needed to treat: definitions

Number needed to treat: the number of patients who would have to receive the treatment for one of them to benefit; calculated as 100 divided by the absolute risk reduction expressed as a percentage (or 1 divided by the absolute risk reduction expressed as a proportion; see Appendix 1)

Number needed to harm: the number of patients who would have to receive the treatment for one of them to experience an adverse effect; calculated as 100 divided by the absolute risk increase expressed as a percentage (or 1 divided by the absolute risk increase expressed as a proportion)

- Learn how to interpret the NNT and develop an understanding of how the "threshold NNT" varies depending on the patient's values and preferences, the severity of possible outcomes and the adverse effects (harms) of therapy.

Before they begin work on NNT, learners must already be familiar with event rates and risk difference. We have noticed that learners regularly stumble over the calculation of NNT. In particular, they experience confusion over whether to divide into 100 or into 1. However, once they have grasped the concept, many learners find NNT an intuitively helpful way of presenting estimates of effect. As a bonus, this tip offers learners some common values of NNTs that can act as reference points for the interpretation of other values.

The script

The key to this tip is a table that is built up from learner contributions and which is then compared with "the truth," as reported in published clinical trials. Three populations, interventions and outcomes form the basis of the tip (Table 2).

Start by asking the learners to imagine that a trial has been performed in connection with each of these 3 situations in which patients conforming to the population as described have been randomly assigned to receive either the specified intervention or a placebo. Ask them to *guess*,

Table 2: Table of patients, interventions and outcomes, presented to learners at outset of tip 3

Population	Intervention	Outcome of interest
60-year-old patients with mild hypertension (blood pressure 150/95 mm Hg)	Diuretics	Stroke over 5 years
60-year-old patients presenting 1 month after myocardial infarction, with no heart failure	β-Blockers	Death over 2 years
60-year-old patients presenting with acute myocardial infarction	Streptokinase	Death over 5 weeks

from their own experience or expectations, what the event rates would be in the control and treatment groups and also to guess the risk difference for each treatment and how many patients would have to be treated to prevent one outcome. For example, in 60-year-olds with mild hypertension (e.g., blood pressure 150/95 mm Hg), what event rate would be expected in the control group and the treatment group and what risk difference and NNT would be expected if the treatment group received diuretics over 5 years to prevent stroke?

Remember that the learners have not yet been told how to calculate NNT, nor have they been given a formal definition of it. As a result, they will usually struggle and complain that they do not know how to calculate the numbers. This is to be expected, and they should be encouraged to *guess* or *estimate* (rather than calculate) each number.

After the learners have struggled with this exercise for a few minutes, construct Table 3 and, without filling in any of the values yourself, ask them to independently write down their own estimates and then ask some (or all) of them to write these estimates on the board. The learners' guesses may be very strange — the risk differences may be huge and there will be no mathematical relationship between the risk difference and the NNT because the learners will have guessed rather than calculated the numbers. Put no restrictions on these guesses – if they are wildly wrong then the impact of the exercise is only enhanced.

After the learners have written their various estimates on the board, you can add the event rates for control and intervention groups for each condition, taken from published trials[13-15] (Table 3). The final column, labelled "NNT" will still be blank.

Using these event rates, you can explain how to calculate NNT for those who do not already know. Learners not familiar with NNT will almost certainly stumble over the calculations. Confusion is often caused by the possibility of presenting risk difference as a proportion (e.g., 0.25) or as a percentage (e.g., 25%). You can help them with this potential pitfall by emphasizing that if they have expressed risk difference as a percentage, then they calculate NNT by dividing the risk difference into 100. Alternatively, if they have used a proportion to express the risk difference, then they calculate NNT by dividing the risk difference into 1. In Table 3, we have expressed all the rates and risk differences as percentages.

An alternative to simply providing the formula for NNT is to use the following approach, in which learners derive the formula for themselves. Ask the following question: "If a disease has a mortality rate of 100% without treatment, and therapy reduces that mortality rate to 50%, how many people would you need to treat to prevent 1 death?" (Answer: 2.) Continue with more examples, until the learners work out for themselves that NNT = 1/risk difference expressed as a proportion or 100/risk difference expressed as a percentage.

You will now have completed the final column of Table 3, and you will probably find that the learners are interested in the actual numbers for treatments they may be offering on a daily basis. Most physicians overestimate the effects of their interventions, particularly in the treatment of hypertension.

This exercise gives learners an opportunity to discuss how they would decide what is a reasonable NNT and introduces them to the concept of a threshold NNT, the maximum NNT that they and their patients would accept as justifying the risks and costs of treatment. Determinants of the threshold NNT include the patient's values and preferences, the severity of the outcome prevented, and the costs and side effects of the intervention. The learners will discover there is no simple answer to the question of when an NNT is sufficiently low to warrant treatment.

Extension for more advanced learners

For highly motivated learners, or if you have the luxury of running a workshop rather than just a 1-hour session, you can extend the discussion by looking at the marginal gain of using tissue plasminogen activator (t-PA) instead of streptokinase in the treatment of acute myocardial infarction. The NNT for the marginal benefit of t-PA over streptokinase is about 100 to prevent 1 death over 30 days.[16] Ask the learners if they think that number is clinically significant and what their own threshold NNT might

Table 3: Estimates derived from published trials, to be presented to learners for comparison with their independent estimates (tip 3)

Population, intervention and outcome of interest	Event rate, %		Risk difference, %	NNT
	Control group	Treatment group		
60-year-old patients with hypertension, diuretics, stroke over 5 years[13]	2.9	1.9	1.0	100
60-year-old patients 1 month after MI, β-blockers, death over 2 years[14]	9.8	7.3	2.5	40
60-year-old patients with acute MI, streptokinase, death over 5 weeks[15]	12.0	9.2	2.8	36

Note: MI = myocardial infarction, NNT = number needed to treat.

be. Point out that the NNT (as well as the risk difference) may vary significantly with the mortality risk of the individual patient, as has been demonstrated in the earlier tips in this article.

The bottom line

- NNT is a concise, clinically useful presentation of the effect of an intervention.
- NNT is easily calculated from the risk difference.
- Check whether the risk difference is presented as a percentage or a proportion and use a numerator of 100 or 1 accordingly.
- Care should be taken not to overestimate the effect of treatments (i.e., use a value of risk difference that is too high) and thereby underestimate the NNT.[17]

See Appendix 2 for the summary card for this tip.

Report on field-testing

One of the authors (S.K.), an experienced teacher of evidence-based medicine who was not involved in developing the scripts, field-tested the scripts in February 2000 with 16 US medical residents during a 1.5-hour teaching session. Of the 16 residents, 3 were naive learners with very little experience in evidence-based medicine, 10 had a working knowledge of evidence-based medicine, and 3 were already familiar and comfortable with evidence-based medicine concepts and skills.

Tips 1 and 2 worked well to help learners understand relative risk reduction and risk difference, and the impact of different baseline risks on risk difference. Initially, the event and control rates in tip 1 were chosen to give a relative risk of 0.5. This had the advantage of very simple calculations but the disadvantage that the relative risk and the relative risk reduction had the same numeric value, which led to confusion. We therefore changed the event rates to avoid this problem.

Tip 3 was the most popular with learners and sparked lively discussion. In the version used in the field testing, relative risk reduction was included in the tables. Learners became comfortable converting between relative risk reduction, risk difference and NNT. The ability to do these conversions was rated as the most important skill learners acquired by working through these exercises. S.K. found it helpful to distribute abstracts from *ACP Journal Club*, with the event rates left in but the relative risk reduction, risk difference and NNT blanked out. This exercise gave learners a further opportunity to practice, using real data.

When asked about the relevance of the content and the clarity of the presentations, the learners gave high scores to all scripts (between 8.5 and 9.5 out of 10, on average), which indicates that they found the material both highly relevant and clear. As noted above, learners thought the most important message was the difference between relative risk reduction and risk difference and felt that it was important to be able to calculate both.

Conclusions

The ability to understand and calculate relative risk reduction, risk difference and NNT from data presented in clinical trials and systematic reviews is an essential skill for clinicians seeking to apply clinical evidence to the care of individual patients. We have presented a series of tips previously developed and used by experienced teachers of evidence-based medicine for the purpose of overcoming common pitfalls that learners experience in acquiring these skills. The results of field-testing of these tips by an independent teacher, who was skilled in teaching evidence-based medicine to clinical learners but was previously unfamiliar with these approaches, suggests that other educators may find this material useful in their own teaching.

This article has been peer reviewed.

From the School of Public Health, University of Sydney, Sydney, Australia (Barratt); the Columbia University College of Physicians and Surgeons, New York, NY (Wyer); the Department of Medicine, University of British Columbia, Vancouver, BC (Hatala); Mount Sinai Medical Center, New York, NY (McGinn); the Department of Internal Medicine, University of the Philippines College of Medicine, Manila, The Philippines (Dans); Durham Veterans Affairs Medical Center and Duke University Medical Center, Durham, NC (Keitz); the Department of Pediatrics, University of Texas, Houston, Tex. (Moyer); and the Departments of Medicine and of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ont. (Guyatt)

Competing interests: None declared.

Contributors: Alexandra Barratt contributed tip 2, drafted the manuscript, coordinated input from coauthors and reviewers and from field-testing, and revised all drafts. Peter Wyer edited drafts and provided guidance in developing the final format. Rose Hatala contributed tip 1, coordinated the internal review process and provided comments throughout development of the manuscript. Thomas McGinn contributed tip 3 and provided comments throughout development of the manuscript. Antonio Dans reviewed all drafts and provided comments throughout development of the manuscript. Sheri Keitz conducted field-testing of the tips and contributed material from the field-testing to the manuscript. Virginia Moyer reviewed and contributed to the final version of the manuscript. Gordon Guyatt helped to write the manuscript (as an editor and coauthor).

References

1. Malenka DJ, Baron JA, Johansen S, Wahrenberger JW, Ross JM. The framing effect of relative and absolute risk. *J Gen Intern Med* 1993;8:543-8.
2. Forrow L, Taylor WC, Arnold RM. Absolutely relative: How research results are summarized can affect treatment decisions. *Am J Med* 1992;92:121-4.
3. Naylor CD, Chen E, Strauss B. Measured enthusiasm: Does the method of reporting trial results alter perceptions of therapeutic effectiveness? *Ann Intern Med* 1992;117:916-21.
4. Fahey T, Griffiths S, Peters TJ. Evidence based purchasing: understanding results of clinical trials and systematic reviews. *BMJ* 1995;311:1056-60.
5. Wyer PC, Keitz S, Hatala R, Hayward R, Barratt A, Montori V, et al. Tips for learning and teaching evidence-based medicine: introduction to the series [editorial]. *CMAJ* 2004;171(4):347-8.
6. Guyatt G, Rennie D, editors. *Users' guides to the medical literature: a manual for evidence-based clinical practice*. Chicago: AMA Publications; 2002.
7. Barratt A, Wyer PC, Hatala R, McGinn T, Dans AL, Keitz S, et al. Tips for learners of evidence-based medicine: 1. Relative risk reduction, absolute risk reduction and number needed to treat. *CMAJ* 2004;171(4):353-8.
8. Schmid CH, Lau J, McIntosh MW, Cappelleri JC. An empirical study of the effect of the control rate as a predictor of treatment efficacy in meta-analysis of clinical trials. *Stat Med* 1998;17:1923-42.

9. SHEP Cooperative Research Group. Prevention of stroke by anti-hypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). *JAMA* 1991;265:3255-64.
10. SALT Collaborative Group. Swedish Aspirin Low-dose Trial (SALT) of 75mg aspirin as secondary prophylaxis after cerebrovascular events. *Lancet* 1991;338:1345-9.
11. Glasziou P, Irwig L. An evidence based approach to individualising treatment. *BMJ* 1995;311:356-9.
12. Rothwell PM. Can overall results of clinical trials be applied to all patients? *Lancet* 1995;345:1616-9.
13. Psaty BM, Smith NL, Siscovick DS, Koepsell TD, Weiss NS, Heckbert SR. Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis. *JAMA* 1997;277:739-45.
14. β-Blocker Health Attack Trial Research Group. A randomized trial of propranolol in patients with acute myocardial infarction. I. Mortality results. *JAMA* 1982;247:1707-14.
15. ISIS-2 Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both or neither among 17 187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet* 1988;2:349-60.
16. The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *N Engl J Med* 1993;329:673-82.
17. Chatellier G, Zapletal E, Lemaitre D, Menard J, Degoulet P. The number needed to treat: a clinically useful nomogram in its proper context. *BMJ* 1996;312:426-9.

Correspondence to: *Dr. Peter C. Wyer, 446 Pelhamdale Ave., Pelham NY 10803; fax 212 305-6792; pwyer@worldnet.att.net*

Members of the Evidence-Based Medicine Teaching Tips Working Group: *Peter C. Wyer (project director), Columbia University College of Physicians and Surgeons, New York, NY; Deborah Cook, Gordon Guyatt (general editor), Ted Haines, Roman Jaeschke, McMaster University, Hamilton, Ont.; Rose Hatala (internal review coordinator), Department of Medicine, University of British Columbia, Vancouver, BC; Robert Hayward (editor, online version), Bruce Fisher, University of Alberta, Edmonton, Alta.; Sheri Keitz (field test coordinator), Durham Veterans Affairs Medical Center and Duke University, Durham, NC; Alexandra Barratt, University of Sydney, Sydney, Australia; Pamela Charney, Albert Einstein College of Medicine, Bronx, NY; Antonio L. Dans, University of the Philippines College of Medicine, Manila, The Philippines; Barnet Eskin, Morristown Memorial Hospital, Morristown, NJ; Jennifer Kleinbart, Emory University, Atlanta, Ga.; Hui Lee, formerly Group Health Centre, Sault Ste. Marie, Ont. (deceased); Rosanne Leipzig, Thomas McGinn, Mount Sinai Medical Center, New York, NY; Victor M. Montori, Department of Medicine, Mayo Clinic College of Medicine, Rochester, MN; Virginia Moyer, University of Texas, Houston, Tex.; Thomas B. Newman, University of California, San Francisco, Calif.; Jim Nishikawa, University of Ottawa, Ottawa, Ont.; W. Scott Richardson, Wright State University, Dayton, Ohio; Mark C. Wilson, University of Iowa, Iowa City, Iowa*

Appendix 1: Formulas for commonly used measures of therapeutic effect

Measure of effect	Formula
Relative risk	(Event rate in intervention group) ÷ (event rate in control group)
Relative risk reduction	1 – relative risk or (Risk difference) ÷ (event rate in control group)
Risk difference (absolute risk reduction)	(Event rate in intervention group) – (event rate in control group)
Number needed to treat	1 ÷ (risk difference)

For Appendix 2, please turn over to the next page.

Appendix 2: Summary cards for 3 teaching tips on relative risk reduction, risk difference and number needed to treat

This appendix has been designed so that it can be printed on a single sheet of 8 fi × 11 inch paper. The individual summary cards can then be cut out, if desired, for use during teaching sessions.

Teaching tip 1: Understanding risk and risk reduction

Scenario: Consider randomized trials of a therapy done on 2 populations, one with a high rate of a serious disease and the other with a lower rate. In each population, half the people are randomly assigned to receive a treatment for the disease.

1. Draw 2 bars side by side to represent the results in the high-risk population:
   bar 1 is the event rate in the control group (40%), bar 2 is the event rate in the treatment group (30%).
2. Ask the learners to describe the impact of treatment (risk difference 10%, relative risk reduction 25%).
3. Repeat the process with bars 3 and 4 representing the results of the trial in the low-risk population: bar 3 is the event rate in the control group (10%), bar 4 is the event rate in the treatment group (7.5%), risk difference is 2.5%, and relative risk reduction is 25%.
4. Learners discover the relation between the risk difference and the event rate in the control group.

Summary points

- Event rate is the percentage of people in a group experiencing an outcome event of interest.
- Risk difference is the arithmetic difference in event rates achieved by therapy.
- Relative risk reduction is the *proportional* decrease in event rates achieved by therapy.
- Relative risk reduction is impressively larger than the risk difference when event rates are low.

Teaching tip 2: Balancing benefits and adverse effects in individual patients

Scenario: Consider 2 hypertensive patients (mean blood pressure 170/100 mm Hg); one patient (Pat) is asymptomatic, and the other (Dorothy) has a history of stroke. Both are being considered for a new antihypertensive, drug X, with relative risk reduction for stroke of 33% over 3 years. Drug X also increases the risk of severe gastric bleeding 3-fold over 3 years.

1. a) Estimate Pat's baseline risk of stroke as 1% per year or 3% over 3 years.
   b) Learners calculate Pat's 3-year risk of stroke with drug X (2%).
   c) Learners calculate Pat's 3-year risk difference for stroke (1%).
2. a) Estimate Dorothy's baseline risk of stroke as 10% per year or 30% over 3 years.
   b) Learners calculate Dorothy's 3-year risk of stroke with drug X (20%).
   c) Learners calculate Dorothy's 3-year risk difference for stroke (10%).
3. a) Estimate Pat's and Dorothy's risk of severe gastric bleeding as 0.1% per year.
   b) Learners calculate the risk difference for severe gastric bleeding over 3 years for Pat and Dorothy (baseline risk = 0.3% over 3 years; with drug X = 0.9%; risk difference = 0.6%.)
4. a) Learners compare the risk differences for Pat and Dorothy for both stroke and severe gastric bleeding.
   b) Learners discuss whether they would treat either of these 2 patients with drug X.

Summary point

- Trial data can be individualized by calculating and comparing risk differences for benefits and harms if a patient's risk of the relevant outcomes with and without treatment are known or can be estimated.

Teaching tip 3: Calculating and using number needed to treat (NNT)

Scenario: Consider 3 patients: a 60-year-old person with mild hypertension who is being treated with a diuretic to prevent stroke over 5 years; a 60-year-old who had a myocardial infarction 1 month previously, has no congestive heart failure and is being treated with a β-blocker to prevent death over 2 years; and a 60-year-old with acute myocardial infarction treated with streptokinase to prevent death over 5 weeks.

1. Learners *guess* the risk differences and NNTs for each treatment.
2. Provide event rates in control and treatment groups, and calculate the risk differences (event rates for control group 2.9%, 9.8%, 12.0% respectively; event rates for treatment groups 1.9%, 7.3%, 9.2% respectively; risk differences 1.0%, 2.5%, 2.8% respectively).
3. Explain how to calculate NNT from the risk difference (RD): NNT = 100/RD (NNTs 100, 40, 36 respectively)
4. Compare learners' guesses with the real data.
5. Discuss threshold NNT.

Summary points

- NNT is a clinically useful measure of effectiveness.
- NNT is easily calculated from risk difference.
- Risk difference = control event rate - treatment event rate.
- If the risk difference is expressed as a proportion, divide into 1; if expressed as a percentage, divide into 100.
- Physicians often overestimate the effectiveness of treatments and underestimate the corresponding NNTs.