Therapeutic priorities of Canadian internists

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We surveyed 175 members of the Canadian Society of Internal Medicine to determine how they would rank seven commonly used treatments as to their clinical usefulness. A total of 70% of the respondents judged that the treatment of severe hypertension was the most beneficial. Coronary artery bypass surgery and treatment with acetylsalicylic acid for transient ischemic attacks were ranked next most useful. Cholestyramine therapy for hypercholesterolemia, the treatment of mild hypertension, isoniazid therapy for inactive tuberculosis and carotid endarterectomy in patients with mild stroke formed the final cluster. Except for treatment of severe hypertension there was a wide variation in the physicians' enthusiasm for the various treatments. Possible explanations for this variation include physicians' lack of awareness of the results of clinical trials, the wide range of risk reductions found in various trials of the same therapy, an unwillingness by physicians to generalize from clinical trials to individual patients, individual physicians' placement of different values on the morbidity associated with various diseases, and the fact that physicians may rarely explicitly compare the usefulness of therapies. In general, the number of patients needed to be treated to save one life better reflected the physicians' judgements than did the relative risk reduction.

À l'occasion d'un sondage, nous avons demandé à 175 membres de la Société canadienne de médecine interne d'évaluer l'utilité clinique de sept traitements courants. Des répondants, 70% ont estimé que le traitement de l'hypertension aiguë est le plus probant de tous. Le pontage coronarien et les traitements par l'acide acétylsalicylique pour les accès ischémiques transitoires cérébraux ont obtenu la seconde place. La thérapie par la cholestyramine contre l'hypercholestérolémie, le traitement de l'hypertension légère, la thérapie par l'isoniazide contre la tuberculose inactive et l'endartérectomie carotidienne chez des victimes d'accidents cérébrovasculaires légers sont arrivés en queue de peloton. À l'exception du traitement contre l'hypertension aiguë, on a constaté d'importants écarts dans l'enthousiasme affiché par les médecins vis-à-vis des différents traitements. Plusieurs raisons peuvent expliquer cela: méconnaissance relative qu'ils ont des résultats d'essais cliniques; constat de l'existence, lors des différents essais d'une même thérapie, d'une gamme étendue de diminutions du risque; réticence des médecins à généraliser les essais cliniques sur leurs patients; placement par chaque médecin des valeurs différentes à la morbidité associée aux différentes maladies; fait que les médecins sont rarement en mesure de comparer de façon explicite l'utilité des thérapies qu'ils emploient. En règle générale, le nombre de patients qu'ils doivent traiter pour sauver une seule vie préoccupe beaucoup plus les médecins que la diminution du risque relatif.

Although the results of randomized controlled trials provide the most internally valid evidence for physicians who are making therapeutic decisions,[1] the extent to which physicians actually use such results in practice varies and is sometimes demonstrably low.[2] In an initial attempt to evaluate how physicians compare the efficacy of various interventions and to determine how well physicians agree with each other we asked a random sample of the membership of the Canadian Society

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of Internal Medicine to rank various therapies (all but one of which had been studied in at least one randomized controlled trial) as to their clinical usefulness. We then compared these rankings with the rankings generated by two different measures of efficacy calculated from randomized trials of the same therapies.

Methods

A systematic sample was obtained by choosing every third name on an alphabetic list of the Canadian Society of Internal Medicine, a voluntary organization of over 900 Canadian general internists. Between February and April 1986 those chosen received questionnaires in English and French by mail. They were asked to compare seven treatments and to rank them according to their clinical usefulness: (a) daily cholestyramine therapy in an asymptomatic patient with elevated serum levels of cholesterol (greater than 6.83 mmol/L) and low-density lipoprotein (greater than 4.89 mmol/L) despite a cholesterol-reducing diet (our survey was done before the publication of a trial showing the efficacy of gemfibrozil in preventing cardiovascular events[3]), (b) antihypertensive therapy in an asymptomatic patient with a persistent diastolic blood pressure of 95 mm Hg and no evidence of target organ damage, (c) antihypertensive therapy in an asymptomatic patient with a persistent diastolic blood pressure of 120 mm Hg and no evidence of secondary hypertension, (d) daily acetylsalicylic acid (ASA) therapy in a patient with transient ischemic attacks but no tight carotid stenosis, (e) carotid endarterectomy in a patient with good recovery from a mild stroke and 80% stenosis of the pertinent carotid artery, (f) coronary artery bypass surgery (CABS) in a patient with stable angina and greater than 50% stenosis of the left main coronary artery and (g) 1 year of daily isoniazid therapy in a previously untreated asymptomatic patient with a positive result of a Mantoux test and stable (for 1 year) apical scarring suggestive of tuberculosis. We had identified valid published randomized trials demonstrating statistically significant efficacy for each of these therapies except for carotid endarterectomy.[4-9] When more than one trial existed we selected the one with patients we judged most similar to those seen in Canada.

The respondents were asked to rank the seven treatments in two different ways. The first time they were asked to disregard the side effects, cost and inconvenience of therapy and to simply rank the therapies in terms of their benefit to the patient who followed all instructions and experienced no side effects. The second time the physicians were asked to rank the therapies considering side effects, cost and inconvenience. They also were asked to flag any treatments they judged to be either worthless or simply not worth the effort required to implement them.

In scoring the responses the therapy judged most efficacious received a rank of 1, the least efficacious a rank of 7. When therapies received an equal rank a mean of the ranks was assigned, and the rank of subsequent treatments was adjusted accordingly (e.g., if two therapies were ranked third, they would both receive a rank of 3.5 [(3 + 4)/2], and the therapy that was ranked fourth would receive a rank of 5).

Two measures of efficacy were calculated from the results of each trial: the relative risk reduction and the number of patients needed to be treated to save one life.[10] The relative risk reduction is (event rate in controls − event rate in treated)/event rate in controls. The number of patients needed to be treated is the reciprocal of the absolute risk reduction: 1/(event rate in controls − event rate in treated).

Results

After repeated mailings 175 physicians (58% of the target sample) were willing to complete and return the questionnaires. Of the 175, 57% had received their medical degree before 1970, 39% had received their degree between 1970 and 1980, and 4% did not indicate their year of graduation. A total of 23% of the respondents had full-time university appointments, 24% had part-time university appointments, and 53% were in private practice.

Table 1 shows the ranks assigned by the physicians to each therapy (along with the mean rank and modal rank [the rank that was most frequently chosen for a given therapy]). When side effects, cost and inconvenience were ignored there was high agreement about the most beneficial treatment but low agreement about the others: 70% of the respondents judged that the treatment of severe hypertension was the most beneficial therapy. CABS and ASA therapy for transient ischemic attacks formed the next cluster, with closely similar average ranks, and a third cluster contained the remaining treatments. Except for treatment of severe hypertension the proportion of responses for the modal rank ranged from only 18% to 25%. Although all the physicians would treat severe hypertension in the situation presented in the questionnaire, 17% would not use cholestyramine for elevated serum cholesterol levels or isoniazid for inactive tuberculosis, 13% would not recommend carotid endarterectomy, 7% would not treat mild hypertension, 5% would not recommend CABS and 2% would not treat transient ischemic attacks with ASA.

When the therapies were ranked with side effects, cost and inconvenience being taken into ac-

count there was only a slight change in the mean ranks, CABS and cholestyramine therapy being judged less beneficial and the treatment of transient ischemic attacks with ASA more beneficial than in the previous ranking.

The relative risk reduction and the number of patients needed to be treated for each therapy are shown in Table 2. In general, the number needed to be treated was high for therapies with a low relative risk reduction and low for therapies with a high relative risk reduction. The exception was the use of isoniazid for inactive tuberculosis, for which both the relative risk reduction and the number needed to be treated were high. Thus, among the seven therapies isoniazid treatment is a discriminator for determining whether the relative risk reduction or the number needed to be treated might more accurately reflect the physicians' clinical judgements.

When the physicians' rankings of relative benefit were compared with the measures of efficacy generated from the trials, the number needed to be treated for isoniazid therapy better reflected the physicians' judgements than did the relative risk reduction. Isoniazid therapy had the second highest relative risk reduction and the fifth highest number needed to be treated; the modal rank was 6.

Discussion

Our results suggest that Canadian internists feel that the treatment of severe hypertension is by far the most clinically useful of the seven therapies presented to them. Their enthusiasm for the other treatments varied considerably, with only 18% to 25% judging one of the other therapies as being most beneficial.

There are several possible explanations for the observed variation in the responses. First, many

Table 1: Ranking by internists of seven commonly used therapies

Therapy*	Rank; no. of respondents 1	2	3	4	5	6	7	Mean rank	Modal rank (and % of respondents)
Disregarding side effects, cost and inconvenience									
Treatment of severe hypertension	122	38	7	1	2	3	2	1.5	1 (70)
Coronary artery bypass surgery (CABS)	33	39	23	22	23	20	15	3.5	2 (22)
Acetylsalicylic acid (ASA) therapy for transient ischemic attacks	11	33	36	39	33	15	8	3.7	4 (22)
Cholestyramine therapy for hypercholesterolemia	4	11	22	24	43	41	30	4.9	5 (25)
Treatment of mild hypertension	4	26	28	28	32	32	25	4.5	5/6 (18)
Isoniazid therapy for inactive tuberculosis	4	21	23	29	28	36	34	4.7	6 (21)
Carotid endarterectomy for mild stroke	7	16	29	30	19	32	42	4.7	7 (24)
Taking into account side effects, cost and inconvenience									
Treatment of severe hypertension	130	29	5	3	3	5	0	1.5	1 (74)
CABS	22	33	25	29	23	28	15	3.8	2 (19)
ASA therapy for transient ischemic attacks	20	44	45	28	24	10	4	3.2	3 (26)
Cholestyramine therapy for hypercholesterolemia	2	3	18	30	43	42	37	5.2	5 (25)
Treatment of mild hypertension	1	35	28	27	36	35	13	4.3	5 (21)
Isoniazid therapy for inactive tuberculosis	3	16	27	31	25	41	32	4.8	6 (23)
Carotid endarterectomy for mild stroke	5	21	19	31	21	40	38	4.8	6 (23)

*See Methods section for full description.

physicians may simply have been unaware of the existence or the results of the trials.[2] Second, individual physicians may place different values on the morbidity associated with the disease described in each scenario. As well, the outcomes of interest for the various therapies were different (in the isoniazid scenario the primary outcome was the prevention of a case of tuberculosis, whereas all the other scenarios included death as an outcome). Third, physicians may prefer to think in "absolute" terms of whether a therapy is likely to be useful to an individual patient and may rarely explicitly compare the usefulness of therapies. However, this exercise becomes clinically relevant when a patient has two disorders but can be given only one therapy. For example, warfarin may be indicated for the prevention of cerebral embolism in a patient with an acute anterior myocardial infarction,[11] but ASA is indicated for the same patient's unstable angina.[12] Because of the risk of bleeding when the two treatments are given together, one therapy may have to be chosen over the other,[13] the choice being made by comparing the benefits and risks of the two treatments. Fourth, the results of different randomized trials of the same therapy may vary. For example, there is a wide range in the risk reductions found in the trials of ASA for transient ischemic attacks.[14] Thus, the enthusiasm with which physicians advocate a therapy may depend on the specific trial with which they are familiar. If this is so, the use of meta-analysis,[15] in which the results of all known randomized trials of a certain therapy are statistically combined to yield a single, overall result, may lead to greater consistency in clinical opinion. Fifth, clinicians may feel that the patients entered into the published trials are unlike their own patients and that the trial results are therefore not generalizable to them.[16-18] Finally, physician behavioural factors, such as misperceived experience and general acceptance of traditional treatments, may cause physicians to disregard results from scientifically valid clinical studies.[19]

The main impetus for our study came from bedside discussions about which measure of therapeutic efficacy is most useful for clinicians who are deciding whether to begin a particular therapy in a particular patient. Although the relative risk reduction is a statistically valid expression of the effect of therapy, it does not incorporate what we considered an important aspect of clinical decision-making: the risk to health without therapy.[10] We believe that the enthusiasm with which physicians advocate a therapy is affected by the magnitude of the baseline risk (although, to our knowledge, no rigorous studies of this issue exist). For example, timolol has been shown to cause a reduction of 36% in the relative risk of death 1.5 years after a myocardial infarction.[20] In the trial in which this was demonstrated, the case-fatality rate in the placebo group (baseline risk) was 16.2%, so that the number needed to be treated was 17. This result is considered to be clinically as well as statistically significant. However, in a low-risk group of patients who survive myocardial infarction, in whom the risk of death is only approximately 2%,[21] this same relative risk reduction of 36% would generate a number needed to be treated of 139 (139 patients would need to be treated with timolol for 1.5 years to save one life). Thus, in this group of patients, in whom the baseline risk is very low, the risks of therapy may be judged to outweigh the benefits.[22]

The physicians' responses to the isoniazid scenario in our survey are consistent with the hy-

Table 2: Benefits of six of the seven therapies, as established from randomized controlled trials

Therapy	Event	Length of follow-up, yr	Baseline risk	Relative risk reduction, %	No. of patients needed to be treated	
					Absolute*	Adjusted†
Treatment of severe hypertension[5]	Death, stroke, myocardial infarction	1.5	0.13	89	9	3
CABS[3]	Death	5	0.32	56	6	6
ASA therapy for transient ischemic attacks[8]	Death, stroke	2.2	0.23	31	14	6
Cholestyramine therapy for hypercholesterolemia[4]	Death, myocardial infarction	7.4	0.12	14	60	89
Treatment of mild hypertension[7]	Death, stroke, myocardial infarction	5.5	0.05	14	128	141
Isoniazid therapy for inactive tuberculosis[6]	Active tuberculosis	5	0.01	75	96	96

*Calculated for the actual length of follow-up in each trial.
†Adjusted to 5 years, assuming constant benefit over time, with the formula observed number needed to be treated × (duration of trial in years/5).

pothesis that the number needed to be treated reflects their priorities more closely than does the relative risk reduction. However, this observation must be replicated for other clinical situations and actual patients before it can be considered a general rule, especially since the correlation between what physicians say they will do when answering a questionnaire and their actual clinical behaviour is frequently poor.[23,24]

It must be remembered, of course, that clinicians may not use the results of randomized trials as the sole, or even predominant, method for making therapeutic decisions. It is thus interesting that carotid endarterectomy for mild stroke, a therapy that has never been studied in a rigorous randomized trial, was ranked as highly as two other therapies that have been validated in trials.

We documented a wide difference in opinion among Canadian internists as to the relative clinical usefulness of six of the seven therapies considered. The reasons for these differences are not clear and warrant further study. In the isoniazid scenario the number needed to be treated better reflected the physicians' priorities than did the relative risk reduction. It is not known whether this is a true observation or a chance finding. Understanding and assisting physicians' therapeutic decisions deserve attention from researchers and educators alike.

We are grateful to the Canadian Society of Internal Medicine for allowing us to canvas their members and in particular thank Dr. Peter Clarke and Ted Giles. We thank Barbara Montesanto for mailing the questionnaire and compiling the results and Janice Coffey for typing the manuscript.

Dr. Laupacis is a Career Scientist of the Ontario Ministry of Health. Part of this work was done while he was a fellow of the Medical Research Council of Canada.

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