

# Influence of the Methods of Reporting Clinical Trial Results on Pharmacists' Willingness to Recommend Drug Therapy

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## INTRODUCTION

Evidence-based medicine is a new paradigm being embraced by clinicians on an international basis.<sup>1</sup> This paradigm de-emphasizes intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision making and stresses the practice of integrating the best evidence from clinical research with clinical expertise and the individual characteristics of the patient into a decision-making process that leads to optimal therapy.<sup>1,3</sup>

The best available clinical evidence is often derived from randomized clinical trials (RCTs) which, because they yield less-biased evidence than other study designs, have become the gold standard by which the efficacy of drug treatment is assessed.<sup>1,4</sup> However, the results of an RCT can be presented in various ways including absolute risk reduction (ARR), the absolute difference in the risk of the outcome between the treatment arms; relative risk reduction (RRR), the extent to which we might expect the baseline risk to decrease when we administer the intervention; odds ratio (OR), the odds of an event occurring in the experimental group relative to the odds of the event occurring in the control group; and number needed to treat (NNT), the number of patients who must be treated to prevent a single event. The presentation of results in several ways can be a source of confusion for clinicians and makes comparisons between studies difficult.<sup>5</sup>

The benefits in clinical trials and pharmaceutical company advertisements are commonly presented in

terms of RRR. This number often has a large value and can be misleading to health-care professionals and patients. In fact, the authors of several studies have found that physicians, policy-makers, and patients are more likely to view drug therapy favourably when significant benefits are presented as RRR rather than ARR or NNT.<sup>6,9</sup>

Pharmacists, through their provision of pharmaceutical care, are often proactive in recommending drug therapy to prescribers. In addition, in many health-care environments pharmacists are being called upon to draft clinical practice guidelines related to pharmacotherapy. To our knowledge, no published study has evaluated the willingness of pharmacists to recommend drug therapy on the basis of the way in which clinical trial results are presented. Therefore, we investigated whether the phenomenon observed for other health-care professionals holds true for hospital pharmacists. We hypothesized that pharmacists' willingness to recommend drug therapy would be greater when clinical trial results were presented as RRR rather than in other formats.

## METHODS

### Subjects

Hospital pharmacists attending a continuing education event were eligible for inclusion in the study sample. The questionnaire was distributed to potential respondents immediately before a workshop about evidence-based medicine. Respondents were given 5 to

7 minutes to complete the questionnaire. The investigators invigilated, and the subjects were not permitted to talk or work together while they were filling out the questionnaire. At the end of the workshop, the results of the questionnaire were presented to the respondents and feedback was given.

## Intervention

All data presented in the questionnaire were drawn from a secondary analysis of the prevention of heart failure by antihypertensive drug treatment in older patients with isolated systolic hypertension (ISH) from the Systolic Hypertension in Elderly Patients (SHEP) trial.<sup>10</sup> This trial was a placebo-controlled, randomized, double-blind, multicentre clinical trial in which patients 60 years of age and older with ISH received stepped antihypertensive drug therapy (step 1, chlorthalidone 12.5 to 25 mg daily; step 2, atenolol 25 to 50 mg daily;  $n = 2365$ ) or placebo ( $n = 2371$ ). Benefit for the cardiovascular endpoints (fatal and nonfatal heart failure) was shown, but because the event rates were low, there was a clear discrepancy between absolute and relative measures of event rates. In the original paper, the trial results were presented as ARR, RRR, and NNT to prevent one event.

The questionnaire was organized under the following sections: *demographic information*: respondents were asked to indicate the number of years of pharmacy practice and the highest level of pharmacy training achieved; *case*: a hypothetical case was presented in which the respondents were asked by the medical team to evaluate the “evidence” from 4 “clinical drug trials” for the treatment of ISH in the elderly; *evidence evaluation*: respondents were asked to rate their willingness to recommend drug therapy for the patient outlined in the case on the basis of the evidence from the trials (which in reality were the same data presented as ARR, RRR, OR, or NNT); *therapy recommendation*: respondents were asked to select the drug that they were most likely to recommend to the medical team; and *comments*: respondents were asked to make comments about the questionnaire to the investigators.

To mask the fact that the data were all from the same trial, the questionnaire stated that the information was from “four trials that deal with drug therapy for ISH in the elderly. Each of these trials deals with a different drug and they each present their results in a different fashion.” Ratings were made on a 5-point scale from 0 to 100, where equally spaced whole numbers were shown at increments of 25. In the text of the case, “0” was defined as “would not recommend this therapy”

whereas “100” was defined as “would definitely recommend this therapy”.

## Outcome Measurement and Analysis

Responses were excluded if data were missing or if responses were marked in such a way that they were uninterpretable. The responses were entered into an inferential statistical and relational database software program (SPSS for Windows, Version 7.5, SPSS Inc., Cary, NC). The demographic information was summarized with descriptive statistics. Responses about willingness to recommend drug therapy were analyzed by one-way analysis of variance (significance level set at  $p < 0.05$ ) along with pairwise comparisons ( $t$ -tests) with post-hoc Bonferroni correction (significance level set at  $p < 0.01$ ). We could thus identify any significant differences between methods of data presentation in willingness to recommend drug therapy.

## RESULTS

### Respondents

Responses from 50 pharmacists were available for analysis. No responses were excluded because of lack of interpretability. A summary of the respondents' characteristics is shown in Table I. There was a similar proportion of recent pharmacy graduates (within 3 years of graduation) and those with 4 or more years of experience. The mean number of years of practice was 7.5. Most respondents had baccalaureate pharmacy degrees with or without a general clinical pharmacy residency. Four respondents had an advanced degree (MSc or PharmD).

**Table I. Characteristics of Respondents**

Category	No. of Respondents	(%)
<b>Years of pharmacy practice</b>		
0 to 3	22	(44)
4 to 7	9	(18)
8 to 11	9	(18)
>11	10	(20)
<b>Level of training</b>		
BSc(Pharm)	28	(56)
BSc(Pharm) + residency	18	(36)
MSc	2	(4)
PharmD	2	(4)

## Outcome Measures

One-way analysis of variance showed that the ratings of willingness to recommend therapy varied significantly among the different data presentation methods ( $p < 0.001$ ). In addition, pairwise comparisons between the mean scores of the data presentation methods revealed that there were significant differences in willingness to recommend therapy (Table II). Specifically, there were significant differences between the mean scores for the RRR and OR data presentations ( $p < 0.001$ ) and between the mean scores for the RRR and the NNT data presentations ( $p < 0.001$ ). There was a trend towards significance in the difference between the mean scores for the RRR and ARR data presentations ( $p = 0.028$ ). There were no other differences between presentation formats.

**Table II. Ratings of Willingness to Recommend Drug Therapy According to Data Presentation**

Method of Data Presentation	Mean Score <sup>a</sup>	(95% CI)
Relative risk reduction	64.4	(55.1 to 73.6)
Absolute risk reduction	45.2	(35.7 to 54.6)
Odds ratio	37.3	(27.3 to 47.3)
Number needed to treat	35.1	(25.7 to 44.5)

CI = confidence interval.

<sup>a</sup>Mean score based on respondents' ratings on a 5-point scale, where 0 represented "would not recommend this therapy" and 100 represented "would definitely recommend this therapy."

Respondents most often recommended the "drug therapy" that was presented as RRR (30%). The other recommendations, in order, were "no drug therapy" (26%), drug therapy presented as ARR (14%), drug therapy presented as OR (10%), and drug therapy presented as NNT (10%); there was no response for 10% of respondents. In the comments section of the questionnaire, 4 respondents noted that all of the results were the same, and 5 others assigned the same values to all of the data presentation formats, although they did not indicate that the data were the same for all formats.

## DISCUSSION

Several studies have attempted to determine whether the method of reporting clinical trial results influences decision making by physicians, health policy-makers, and patients.

Forrow and others<sup>11</sup> surveyed 235 hospital-based

physicians by means of a questionnaire that presented the same data as relative and absolute changes in outcome. When asked how each piece of information would influence their decisions about treatment, 46% of respondents scored the same data differently when it was presented in a different format. Presenting the data in terms of relative change was favoured by 90% of these respondents.

In a study published in 1992, Naylor and others<sup>9</sup> randomly assigned 1 of 2 surveys to a group of 100 physicians in a teaching hospital. One questionnaire presented the results of a clinical trial as ARR, while the other survey reported the same data as RRR. Physicians rated the therapies on a scale from "harmful" to "very effective." Physicians who received the absolute event data gave significantly lower effectiveness scores than those who received the RRR data. Nearly identical methodology was used by Bucher and others<sup>6</sup> in surveying 802 internists and general practitioners in Switzerland. This survey was related to the willingness of physicians to prescribe a cholesterol-lowering drug. When the results were presented as ARR and NNT the likelihood of prescribing the drug was significantly lower than when the results were presented as RRR.

A survey of 148 general practitioners in Italy who were given data from a clinical trial in 5 different formats (RRR, ARR, percent event-free, NNT, event reduction/mortality) yielded similar results.<sup>8</sup> Physicians were much more likely to recommend the therapy on the basis of the RRR data than any of the other 4 reporting methods (77%, 24%, 37%, 34%, and 23%, respectively;  $p < 0.001$ ).

Nonphysician groups have been studied as well. A British study of 182 health policy-makers responsible for purchasing health services gauged the willingness of respondents to fund a mammography program or a cardiac rehabilitation program.<sup>12</sup> Identical data were presented in different formats for both types of programs. The highest mean score for supporting both programs was produced by presenting the data as RRR. In addition, the NNT format produced significantly more support than the ARR format.

Finally, in an attempt to determine whether patients' willingness to accept lipid-lowering and antihypertensive therapy was influenced by the way the effectiveness data were presented to them, Hux and Naylor surveyed 100 outpatients.<sup>13</sup> When the data were presented in terms of RRR, 88% of the patients assented to therapy. All other formats of data presentation yielded a rate of assent of only 31% to 42%.

Previous studies of other populations have consistently demonstrated that the format of data

presentation influences decision making. Specifically, RRR appears to be the most influential way of presenting clinical trial data. One possible reason why RRR appears so compelling relative to other methods of data presentation is the apparent large effect size. To our knowledge, this is the first objective evaluation of this phenomenon among pharmacists. Not surprisingly, pharmacists appear to be as susceptible to being misled in this way as other health professionals. This observation is significant because pharmacists are increasingly being relied upon to make clinical decisions about drug therapy for individual patients, as well as policy decisions affecting larger health systems. Therefore, it appears that pharmacists require education about how to interpret trial data and how to convert between data formats to allow extraction of a more complete picture of the clinical relevance of trial results.

There is currently no standard format for data presentation for all journals. Since it would appear that pharmacists and other health-care providers are susceptible to being misled by the way data are presented, it may be prudent to consider such standardization, with emphasis on reporting clinically meaningful statistics such as ARR and NNT where applicable.

The present study included only hospital pharmacists, many of whom had postbaccalaureate residency training. Thus, the results are probably not generalizable to all pharmacists. We believe, however, that the population surveyed is representative of hospital pharmacists in British Columbia and probably elsewhere in Canada. However, since the sample consisted of pharmacists who were attending an educational session on EBM, it is possible that there was selection bias for individuals who were not familiar with the principles of EBM. Also, we recognize that clinical decision making is far more complex than was represented in our survey tool. The tool was intended only to measure the effect of presenting the same data in different ways and not to accurately simulate a patient case. Because the surveys were not randomly allocated to each subject, with the ARR, RRR, OR, and NNT results presented in different orders, we do not know if the order of presentation of the results affected the survey responses. Finally, the survey tool did not undergo rigorous validity and reliability testing beyond that of piloting with several hospital pharmacists.

Our methodology was similar to that employed by other studies of this type, all of which used a nonvalidated questionnaire presenting the same or similar clinical trial data in different ways.<sup>6,8,9,11-13</sup> One study used a randomly selected population.<sup>6</sup> All of the

studies solicited responses on a scale intended to determine how convincing the respondents believed the effect data to be or how likely they would be to choose a therapy on the basis of the data. Although more elaborate methodology such as randomizing the order of presentation of the questions or asking respondents to choose between only 2 options in each clinical scenario could be employed, we believe that the methods used in our and other studies yielded a relatively accurate reflection of the subjects' level of knowledge.

Several hypotheses are suggested by this study. Given that many of the subjects were recent graduates (44%), it is possible that Canadian pharmacy school and hospital residency curricula are not placing enough emphasis on the interpretation of evidence. In addition, experienced practitioners may need more continuing education dealing with the interpretation of evidence. It would also be interesting to determine if attendance at workshops, such as the one attended by the subjects, increases the ability to interpret evidence presented in the medical literature. The answer to this question should be explored in future studies.

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