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AN EVALUATION OF MINIMAL CLINICALLY IMPORTANT DIFFERENCES FOR THE INITIATION OF ANTIHYPERTENSIVE THERAPY FROM THE PERSPECTIVE OF CANADIAN PATIENTS AND PHYSICIANS

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ABSTRACT

Background: Traditional hypertension guidelines from different countries or organizations often specified different treatment thresholds. These discrepancies have enormous public health implications. The current movement toward evidence-based guidelines and risk-based guidelines, while intuitively appealing, does not solve the problem of choosing treatment thresholds. None of the current hypertension guidelines explicitly state how their treatment thresholds were chosen. As the choice of treatment threshold is a utility-sensitive decision, determination of the preferences of practicing physicians and hypertensive patients is important for future policy making.

Methods: A survey to determine the minimal clinically important differences (MCIDs) of patients and physicians for the initiation of antihypertensive therapy in the primary prevention of cardiovascular disease. Physicians were randomly selected from the population of all family physicians in the Ottawa-Carleton region and hypertensive patients without symptomatic cardiovascular disease were recruited from a convenience sample of five family physicians and four general internists. Both groups were presented with six hypothetical scenarios which described the same blood pressure (150/95 mm Hg) but different baseline cardiovascular risks (2%, 5%, and 10% in five years, and 15%, 30%, and 50% in twenty years). For each scenario, subjects were asked whether they would prescribe/accept treatment and, if they would, a probability trade-off technique was used to determine their MCID for antihypertensive therapy.

Results: 77% of eligible family physicians (72/94) and 38% (74/196) of eligible patients participated. Baseline demographics of participants closely

mirrored those of the target populations. Physicians were more likely to prescribe antihypertensive therapy than informed patients were to want it, particularly when the baseline risks were low: 64% vs. 49% (p=0.06), 92% vs. 68% (p<0.001), and 100% vs. 86% (p=0.001) for five year risks of 2%, 5%, and 10%, respectively. Moreover, when accepting treatment, patients expressed larger MCIDs (ie. wanted greater benefits) than physicians. Taking into account the 25% relative risk reduction expected from antihypertensive therapy, the mean implicit treatment thresholds of these physicians were an absolute CV risk of 10% in 5 years or 19% in twenty years; the patient thresholds were 10% and 29%. On multivariate analysis, no sociodemographic factors strongly predicted the treatment preferences of either group.

Conclusion: Patients were more conservative in their treatment preferences than physicians: a higher proportion did not want therapy and those that did want therapy specified higher treatment thresholds than physicians. Both groups chose lower annual treatment thresholds (that is, were more aggressive) when longer-term risks and benefits were considered. There was marked variation in the treatment preferences expressed by both patients and physicians.

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CHAPTER 1: INTRODUCTION

1.1 The shortcomings of traditional hypertension guidelines

In the past decade, a number of national and international bodies have produced evidence-based clinical practice guidelines for the management of hypertension.[1-7] All agree that treatment should be offered to the elderly with isolated systolic hypertension, patients of all ages with moderate or severe hypertension, and patients with hypertension in the presence of target organ damage or diabetes mellitus. However, these guidelines differ in their recommendations for the management of patients with mild hypertension- a significant discrepancy because the vast majority of hypertensive patients have blood pressures in this range. Although all of the guidelines note the importance of other cardiovascular risk factors or target organ damage, and advocate earlier treatment in the presence of these co-morbidities, the stated thresholds for patients with uncomplicated hypertension range from 90 to 100 mm Hg. This discrepancy has important implications for the proportion of the population who will require treatment, the total cost of treatment, the number needed to treat (NNT) to prevent one cardiovascular event, the health of the population, and the cost-effectiveness of hypertension care (Tables 1 and 2). A recent study[8] revealed that five current hypertension guidelines (from the United Kingdom, Canada, the United States, New Zealand, and the World Health Organization) agreed on the need for treatment in only 31% of hypertensive patients. As pointed out by Ramsey et al[9], "the reasons for these differences... have never been set out explicitly and debated".

Table 1: Implications of different treatment thresholds in essential hypertension

Diastolic Blood Pressure Threshold:	100 mm Hg	95 mm Hg	90 mm Hg
% Population eligible for treatment*	8	14	25
5 Year Risk:			
-of any CV event**	29	11	8
-of all-cause mortality***	7	5	3
NNT for 5 years to prevent:****			
-one CV event	14	36	50
-one death	143	200	333

Notes: Reproduced with permission from McAlister et al.[27] This data applies to patients without target organ damage or other cardiovascular risk factors.

* Derived from the screening data for the Hypertension Detection and Followup Program.[50]

** CV event=stroke/transient ischemic attack, myocardial infarction/ischemic heart disease, congestive heart failure, renal failure, aortic aneurysm, grade III or IV hypertensive retinopathy, or death. Derived from the followup data in the placebo group (n=1617) of the Australian Therapeutic Trial in Mild Hypertension[51], subdivided by long-term diastolic pressure measured in the trial, and adjusted to 5 years assuming constant hazard over time.

*** Derived from the Chicago Heart Association Detection Project in Industry[52] (n=21,047), subdivided by baseline diastolic pressure, and adjusted to 5 years assuming constant hazard over time.

**** Assuming relative risk reductions with treatment of 25% for any cardiovascular event and 10% for all-cause mortality.[25]

Table 2: Cost-effectiveness ratios (Cost per life year gained) for treatment of uncomplicated mild hypertension, by pretreatment diastolic blood pressure, age, and gender

	< 45 years		45-69 years		70 years +	
DBP (mm Hg)	Males	Females	Males	Females	Males	Females
100	116,400	254,000	180	10,800	550	+
95	142,700	346,600	6,200	24,300	2,600	1,300
90	173,300	458,600	12,400	39,300	4,600	3,800

Notes:

\+ Denotes cost saving (ie. it is cheaper to treat than not to treat)

Costs are expressed in 1992 Canadian dollars (converted from Swedish Krona) and effects were estimated using the Framingham risk prediction equations and assuming risk reductions for coronary artery disease and stroke of 16% and 38%, respectively, with a discount rate of 5% per annum. Adapted from Johannesson[53] and reproduced with permission from McAlister et al.[27]

Although the efficacy of antihypertensive therapy is well established and all five hypertension guidelines are evidence-based, the different recommendations for the initiation of treatment are not surprising when one considers the issues underlying the choice of a particular treatment threshold. For one, population epidemiologic studies have clearly established that the risk of

cardiovascular events (stroke or myocardial infarction) is directly related to blood pressure at all levels and there is no threshold value for blood pressure which accurately separates those who will and will not suffer a cardiovascular event.[10,11] In fact, over half of all strokes and myocardial infarctions occur in individuals with normal blood pressures.[10] Moreover, it is now evident that hypertension is only one of the many risk factors for cardiovascular disease[12,13] and, in individuals with mild hypertension, their risk of cardiovascular morbidity or mortality depends more on their constellation of risk factors than their actual blood pressure reading.[13-16] For example, a 40 year old male (patient A) with a blood pressure of 160/95 mm Hg who is otherwise healthy and does not smoke has a 10 year risk of cardiovascular events of less than 10%; on the other hand, a 40 year old male (patient B) with the same blood pressure (160/95) who smokes, is obese, and has hyperlipidemia has a 10 year risk of approximately 20-40%.[1] The current generation of hypertension guidelines, in specifying a particular blood pressure level as the threshold for therapy, fail to adequately consider the absolute risks and benefits of treatment in the individual patient. As pointed out by others, the risks and costs of antihypertensive drugs may outweigh the benefits in low-risk patients[17] and "antihypertensive drug therapy will be most efficient and effective if directed at those who, by virtue of their constellation of risk factors or evidence of preclinical vascular disease, are likely to have a heart attack or stroke."[10]

1.2 Risk-based hypertension guidelines

The New Zealand Hypertension Guidelines[1] were the first hypertension guidelines to advocate explicit consideration of an individual patient's risk of subsequent cardiovascular disease in the decision to initiate therapy. These "risk-based" guidelines have generated a great deal of debate and received widespread support.[9,10,17-22] Certainly, recent guidelines on the treatment of hypercholesterolemia follow this approach.[23] However, despite the current enthusiasm for the concept of basing treatment decisions on absolute risk profiles, this does not solve the problem of deciding on a treatment threshold as there is no consensus as to what degree of absolute risk would warrant therapeutic intervention. While the relative risk reduction (RRR) with antihypertensive therapy is the same regardless of the patient's initial blood pressure level (approximately 25% reduction in total cardiovascular events)[24,25], the absolute benefits of treatment vary widely depending on the patient's baseline risk. Using the hypothetical patients given above, the expected benefit (absolute risk reduction or ARR) from a five year course of antihypertensive therapy in patient A would be approximately 3% (10% absolute risk at baseline X RRR of 30%), while the expected benefit in patient B would be about 8% (25% baseline absolute risk X 30% RRR). From the perspective of the clinician, this implies that 33 patients like patient A would have to be treated to get the same overall benefit (ie. the prevention of one stroke or myocardial infarction over five years) as treating 12 patients like patient B.

1.3 Choosing the treatment threshold

Ideally, the use of risk-based guidelines should obviate the need for explicit treatment thresholds and instead could be used to "inform patients and to individualize decisions and values, in the context of the patient's other risks and values".[26] However, there is legitimate concern that this may lead to guidelines which are too complex and time-consuming to apply in routine practice.[27] Thus, thresholds must be chosen. Although this is a key issue (Tables 1 and 2), none of the current hypertension guidelines have explicitly stated how they chose their treatment thresholds. For example, both the New Zealand Hypertension Guidelines[1] and the JNC-VI[7] appear to have derived their thresholds from expert opinion alone. In fact, to this point in time, hypertension guidelines have tended to neglect the values of patients (and indeed physicians not involved in guideline generation) in setting treatment thresholds.

Naylor and Llewellyn-Thomas argued for a more patient-centred approach to the determination of clinically important effect sizes in randomized clinical trials[28]; as an extension of their argument, other authors[27,29-35] have called for the incorporation of patient and practicing physician preferences into guidelines. Kassirer[34] outlined seven situations in which decisions are "utility-sensitive" and patient preferences should be explicitly incorporated in treatment decisions: "(1) when there are major differences in the kinds of possible outcomes (for example, death versus disability); (2) when there are major differences between treatments in the likelihood and impact of complications; (3) when choices involve trade-offs between near-term and long-term outcomes; (4) when one of the choices can

result in a small chance of a grave outcome; (5) when the apparent difference between options is marginal; (6) when a patient is particularly averse to taking risks; and (7) when a patient attaches unusual importance to certain possible outcomes." The initiation of antihypertensive therapy fulfills many of these criteria and the time appears ripe to determine and incorporate the preferences of patients and practicing physicians in establishing explicit treatment thresholds for hypertension guidelines.

1.4 The Minimal Clinically Important Difference

As a first step in incorporating patient and physician preferences in guidelines, it is necessary to determine how much benefit (in terms of the prevention of cardiovascular events) they feel is needed to outweigh the side effects, cost, and inconvenience of long-term antihypertensive therapy. Jaeschke et al[36] introduced the concept of the minimal clinically important difference (MCID) associated with a treatment as "the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient's management". The MCID represents the preferred absolute risk reduction (ARR) and, as such, can be used to calculate the number needed to treat (NNT) that each subject feels appropriate in that situation. By determining the MCIDs of patients and physicians for the initiation of antihypertensive therapy at various blood pressure levels, we are able to determine their preferred treatment thresholds.

1.5 Determining the Minimal Clinically Important Difference

As outlined by Naylor and Llewellyn-Thomas[28], probability trade-off techniques (PTOT) originally developed for use in cancer patients[37] can be modified to elicit patients' MCIDs for other therapies. The first step in any PTOT is the presentation of background information about the disease/condition, potential outcomes, and treatment options.[38] As physicians[39-41] and patients[42,43] have inflated perceptions of baseline risk and the benefits of preventive therapies, it is important that this descriptive information be accompanied by explicit probabilistic information. Many different techniques have been used to present this background information, and the most appropriate method is unknown.[44] However, the use of flipcharts and/or patient booklets has been validated in several other disease states[42,45,46] and can be readily adapted to a study of antihypertensive therapy. The second step in the PTOT is the elicitation of patient preferences. Again, while many different techniques can be used, the most easily adapted to this study is that outlined by Man-Son-Hing and colleagues[42]:

> "patients are presented with 2 choices: a baseline risk of having an adverse outcome without the treatment of interest or, if undergoing the therapeutic intervention, a lesser chance of suffering that outcome but also incurring the inconvenience, side effects, and costs of that intervention. They are asked to choose one or the other. Then, the hypothetical efficacy of the intervention is systematically varied until the lowest risk reduction at which patients are willing to take therapy is found. This is the MCID."

As the framing of the projected benefits (for example, 10% chance of death versus 90% chance of survival) may influence decision-making,[47,48] it is important

that both the positive and negative frames are presented in the same PTOT (see Appendix A for example). Moreover, although it is easier for the interviewer if the hypothetical benefits from an intervention are systematically varied in one direction only (for example, increasing efficacy with each subsequent question), this may give results which are biased due to the shifting frame effect.[49] As systematically varying the probabilities from one extreme to another ("ping-ponging") has been shown to elicit less biased MCID determinations[42], this is the preferred technique for probability trade-off tasks. A number of other questions about MCID elicitation (such as whether MCIDs are sensitive to baseline risk or projected time frames) remain unanswered and require further investigation.

CHAPTER 2: OBJECTIVES

1. To develop a probability trade-off technique to determine the minimal clinically important differences (MCIDs) for antihypertensive treatment from the perspective of patients and physicians.

2. To describe the MCIDs for the initiation of antihypertensive therapy from the perspective of patients and physicians when presented with hypothetical cases with varying baseline cardiovascular risks.

3. To compare the MCIDs specified by patients and physicians.

4. To determine the correlates of MCIDs (sociodemographic factors, prior exposure to antihypertensive drugs, absolute cardiovascular risk at baseline in the scenario, gender of case in scenario, etc.) of physicians and patients.

CHAPTER 3: METHODS

3.1 Study Design:

The most appropriate design to assess the MCIDs of physicians and patients is a descriptive survey. A standardized questionnaire eliciting MCIDs for six hypothetical scenarios with different cardiovascular risk at baseline was designed. The six scenarios detailed cardiovascular risks (including fatal/nonfatal myocardial infarction, fatal/nonfatal stroke or transient ischemic attack, and coronary death) of 2%, 5%, and 10% at five years and 15%, 30%, and 50% at twenty years. These cardiovascular risks correspond to the five and twenty year risks for patients with sustained diastolic blood pressures of 90 mm Hg, 95 mm Hg, and 100 mm Hg and the average level of other cardiovascular risk factors in Canadian hypertensives (as documented in the Canadian Heart Health Surveys[12,54]). Risks were estimated using the Cardiovascular Disease Life Expectancy Model- a Markov Model developed using data from the Lipid Research Clinics Follow-up Cohort, the Canada Health Survey, and Canadian life tables.[55] The accuracy of this model in estimating absolute cardiovascular risk has been validated against data from numerous large trials of antihypertensives or lipid-lowering agents in the primary and secondary prevention of cardiovascular disease.[55] To determine if order of scenario presentation affected MCIDs, subjects were randomly assigned to one of six different forms of the questionnaire (each of which had a different scenario order) using a 6 X 6 latin square design. Physicians were randomized to two different gender versions of the questionnaire (one with all of the cases female and one

with all of the cases male, although the baseline risks presented in each scenario were identical in both questionnaires). Within each group, a 6 X 6 latin square design was employed to look for order effect.

While there is no data to determine which is the most appropriate data collection option for MCID projects, previous patient-based projects have used face-to-face interviews.[42,45,46] This seems necessary for patient-based projects as the outcome assumptions and MCID elicitation techniques would be easier to communicate visually to patients. On the other hand, since physicians are more accustomed to considering treatment issues, it is possible to elicit their MCIDs by telephone interview. The telephone interview format was used for physicians for several reasons: expediency of data collection, enhanced participation rate, minimization of data non-response, and less possibility of "social-desirability" bias in responses.

Each subject was interviewed once as previous MCID projects[42,49,56,57] have confirmed that an individual's MCIDs are relatively stable over time.

3.2 Study Population

3.2.1 Physician Sub-Study

Subjects: A random sample of family physicians from the Ottawa-Carleton region.

Exclusion Criteria: Those physicians who indicated on an initial screening question that they were retired, spent <25% of their work week in direct patient care, or did not see hypertensive patients in their practice were excluded from the study.

Sampling Strategy: The physicians were identified from a sampling frame constructed for another project.[58] This sampling frame consisted of all 665 family physicians in the Ottawa-Carleton region and was constructed by cross-referencing the Ottawa-Carleton Health Department Physician Database, the Canadian Medical Directory, the Ontario Medical Association physician list, and the Ottawa-Hull telephone directory. The completeness of the sampling frame has been validated.[58] Subjects were chosen from this sampling frame by random number generation (using the Statistical Analysis System RANNOR routine[59]).

3.2.2 *Patient Sub-Study*

Subjects: Adult patients (aged 18-60) with essential hypertension (ICD9 codes 401, 402, 403, 404, and 437.2) and no evidence of symptomatic cardiovascular disease were recruited from a convenience sample of family medicine and general medicine clinics in Ottawa and Edmonton, Canada.

Exclusion Criteria: Patients were excluded if they had: secondary hypertension (defined as renal failure [serum creatinine>200 umol/L], renovascular stenosis, hyperaldosteronism, pheochromocytoma, cortisol excess, untreated thyroid disease, coarctation of aorta, or medication-induced hypertension), pregnancy-associated hypertension, already suffered a cardiovascular event (stroke, transient ischemic attack, myocardial infarction, stable or unstable angina, peripheral vascular

disease, aortic dissection or aneurysm), or if they were not fluent in English or unable/unwilling to give consent.

Sampling Strategy: A convenience sample of patients were drawn from the practices of 5 family physicians and 2 general internists in the Ottawa-Carleton region and 2 general internists in Edmonton. Patients were identified from the recent (prior three months) medical records of participating physicians and a consecutive sample were invited to participate in the survey.

3.3 Measurement Tools

The patient (Appendix A) and physician (Appendix B) surveys were pretested with five healthy volunteers and five physicians to ensure completeness and comprehensibility. Copies of the script used for patient interviews, the forms used to record the MCIDs, and the forms used to record physician calls are included as Appendices C, D, and E. The survey questionnaire consisted of three parts as outlined below.

3.3.1 Part One-Demographics

For each patient, data collected included date of birth, gender, level of education, duration of hypertension diagnosis, current use of (and compliance with[60]) antihypertensive drugs, and personal knowledge of close friends/family members with stroke or myocardial infarction. For each physician, data collected included date of birth, gender, year of medical qualification, time in practice, academic or hospital affiliations, and practice profile.

3.3.2 Part Two- Background Information

The following information was presented: definition of hypertension, description of stroke and usual prognosis, description of myocardial infarction and usual prognosis, and description of possible side effects, inconvenience, and costs from antihypertensive medication. The outcome assumptions for stroke and myocardial infarction were derived from recently published prospective cohort studies[61-66] and developed in consultation with experts in the field; the frequency of antihypertensive side effects were derived from recent randomized clinical trials[67-69] and antihypertensive costs from a survey[70] of Canadian pharmacies. Patients were presented with this information during face-to-face interviews that lasted an average of 20 minutes. Probabilities were presented both numerically and graphically (using 100 stick figure icons to show percent frequencies- see Appendix A) to patients. Physicians were presented with the background information on usual prognoses after stroke or myocardial infarction and frequency of side effects with antihypertensive medications, in numeric format only. All probabilities were presented in both a negative and positive frame (for example, chance of event A occuring is 5% in five years; in other words, there is a 95% chance that event A will not occur).

3.3.3 Part Three- MCID Elicitation

After a brief test of comprehension regarding tradeoffs (asking whether the individual prefers treatment or no treatment when treatment causes harm), MCID elicitation using the standardized questionnaire was performed. Subjects were presented with the six hypothetical scenarios in which the probability of a cardiovascular event differed as described in section 3.1. For each scenario, the

benefits of treatment were presented as absolute risk reduction (ARR). The anticipated ARR from antihypertensive therapy was systematically varied until the MCID of each subject was apparent (ie. that ARR at which their decision changes from "take/prescribe treatment" to "do not take/prescribe treatment").

3.4 Sample Size

The sample size was based on the primary comparison (the mean MCID of patients vs. the mean MCID of physicians) for scenario 3 and was chosen by deciding how precisely the MCIDs needed to be estimated. A priori it was decided that seeking an MCID difference no smaller than 1 (out of 100) absolute cardiovascular disease risk reduction would be sufficiently precise. The outcome variable (MCID) is continuous and, as no studies had been published on the MCIDs of patients or physicians for hypertension treatment, we assumed the standard deviation would be similar to that found in a project investigating the MCIDs of patients for atrial fibrillation treatment.[42] Using the standard tables of Hulley and Cummings[71], a two-tailed significance level of α=0.05, and a power of 90%, the estimated sample sizes are outlined in Appendix F. Thus, we planned to recruit 60 patients and 60 physicians for this study. As per our original protocol, a preliminary analysis was carried out after enrolling 30 subjects to determine the actual standard deviation for scenario 3 (10% risk in 5 years). The observed standard deviation of responses was larger than anticipated (1.85 versus estimated SD of 1.60) and the sample size requirements were adjusted upwards to 72 in each group to take this into account.

3.5 Data Handling and Statistical Analysis

Responses from completed surveys were entered into an SPSS (Statistical Package for the Social Sciences) database. Checks for missing data and extreme values were done at the time of data entry. Demographic and practice details for non-respondent physicians were extracted from the 1997 Canadian Medical Directory. The data set was analyzed using SPSS for Windows version 8.0.[72]

Respondent demographics were examined and comparisons between patients and physicians (and between males and females within each of the groups, and between physician respondents and non-respondents) were carried out using the Chi-square test for nominal variables and Student's t-test for continuous variables.

The proportion of patients and physicians choosing treatment in each case were compared with the Chi-square test. Logistic regression analyses were used to adjust for any differences in baseline demographics between the two groups. The distribution of values for the MCIDs in each hypothetical scenario were examined graphically and the Kolmogorov-Smirnov test was used to examine for normality. As the MCIDs did not exhibit a Guassian distribution, median, 25th and 75th percentiles, and mode were calculated for each scenario. The MCIDs of patients and physicians were compared using the non-parametric Mann-Whitney test and, as both groups included more than 30 subjects (thereby satisfying the requirements for the Central Limit Theorem), the mean MCIDs and 95% confidence intervals for those that chose to prescribe/accept therapy were

compared using Student's t-test. Multivariate analyses were done to assess the influence of respondent (patient or physician) on the decision to treat/not treat and the size of the specified MCIDs, after adjusting for any differences in baseline demographics between the two groups.

The mean and median MCIDs for five years (using scenarios 2 and 3 only given the high proportion of respondents who would not prescribe/accept treatment for scenario 1) and twenty years (using scenarios 4, 5, and 6) were calculated and used to estimate treatment thresholds of physicians and patients using the formula:

$$\text{Treatment threshold} = \text{MCID} / \text{RRR}$$

The RRR in cardiovascular events with antihypertensive therapy is approximately 25% and is constant across the range of baseline risks assessed in this study.[24,25] For example, the treatment threshold for an MCID of 5% in twenty years would be calculated as 20% in twenty years (5% / 0.25).

Bivariate analyses were done to examine the relationship between treatment decisions (and specified MCIDs) in each scenario and baseline demographics of respondents, order of scenario presentation, and, for physicians, gender of scenarios. For the logistic regressions (ie. nominal dependent variable), the following bivariate tests were done: Students' t-test for continuous independent variables, Chi-square test for nominal independent variables, and Chi-square test for trend for ordinal independent variables. For the linear regressions (ie. continuous dependent variable), the following bivariate tests were done: Pearson's Correlation Coefficients for continuous independent

variables, Spearman's Correlation Coefficients for ordinal independent variables, and Student's t-tests for nominal independent variables.

Logistic regression analysis (entering any factors believed to be important *a priori* or found to be associated with a p value ≤ 0.20 on bivariate analysis) was done to determine which variables were associated with the decision to prescribe/accept treatment. A forward stepwise model was employed with p value-to-enter set at 0.15 and p value-to-remove at 0.20. Multiple linear regression (also entering any factors believed to be important *a priori* or found to be associated with a p value ≤ 0.20 on bivariate analysis) was used to determine which independent variables were associated with the size of the specified MCIDs. Similarly, a forward stepwise model was employed with F-to-enter set at 0.05 and F-to-remove at 0.10. First order interaction terms were tested for significance and confounding was examined by comparing the regression coefficients for included variables in models containing different numbers of factors. Regression assumptions were examined for violation with regression residual scatterplots.

An alpha level of 0.05 was used to indicate statistical significance.

3.6 Ethics

The study protocol was approved by the Research Ethics Committees of the Ottawa Civic Hospital and the University of Alberta Hospital, Edmonton. Copies of the physician and patient information sheets, and the patient consent forms, are included as Appendices G, H, and I.

CHAPTER 4: RESULTS

4.1 Response Rate

Of the 100 randomly-selected family physicians (FPs) contacted for this project, six were ineligible as they stated they spent <25% of their work week in direct patient care (2) or did not see hypertensive patients in their practice (4). Of the eligible FPs, 77% (72/94) participated (the most frequent reason given for not participating was lack of time). A convenience sample of 74 patients were recruited from the practices of four general internists and five family physicians (a total of 196 eligible patients had been identified from their medical records and were mailed a letter inviting their participation).

4.2 Demographic Characteristics

The physician cohort were significantly younger (mean age 45.0 versus 49.4, p=0.001) and had a higher proportion of males (69% versus 53%, p=0.09) than the patient cohort.

4.2.1 Physicians

The baseline demographics of physician participants closely mirrored that of the target population[58] and the national population of Canadian family physicians (1995 Royal College of Physicians and Surgeons of Canada Work Force Study, unpublished data). In addition, the reported practice features (group vs. solo, hospital affiliation, academic appointment) were consistent with those of respondents to a recent national survey[73] of Canadian physicians. Physician non-respondents were similar to respondents (mean age 45.4, 59% male, 18% with academic appointments), but had been in practice longer (22.8

years vs. 18.4 years, p=0.02), were more likely to be in solo practice (73% vs. 57%, p=0.19), and were less likely to be affiliated with a hospital (50% vs. 69%, p=0.09).

Table 3: ***Demographics of physician respondents***			
	Males n=44 (61%)	Females n=28 (39%)	p
Age (mean ± SD)	45.6 ± 8.1	44.2 ± 6.7	.47
Years in practice (mean ± SD)	19.5 ± 6.7	16.7 ± 6.5	.11
Solo practice	28 (64%)	13 (46%)	.15
Hospital affiliation	33 (75%)	17 (61%)	.20
Academic appointment	12 (27%)	4 (14%)	.20
Male version of questionnaire	20 (45%)	16 (57%)	.33
Number of hypertensive pts seen per month (median [range])	50 (10-200)	55 (7-200)	.29

4.2.2 Patients

The baseline demographics of patient participants are listed in Table 4 and are similar to those of newly diagnosed hypertensive patients in other studies.[74] Seventeen (23%) had been diagnosed with hypertension within 12 months of the study interview. Of those subjects who admitted to occasionally missing pills, 7 (15%) reported forgetting to take their antihypertensive more frequently than once a week.

Table 4: ***Demographics of patient respondents***			
	Males n=35 (%)	**Females n=39 (%)**	**P**
Age (mean ± SD)	50.1 ± 8.3	48.6 ± 7.7	0.42
Duration of hypertension in yrs (median [range])	5 (0.2-22)	4 (0.3-32)	0.99
Currently taking antihypertensives	23 (66%)	25 (64%)	0.89
Miss pills (ever/#prescribed pills)	13/23 (56%)	15/25 (60%)	0.81
Relative/close friend with stroke	32 (91%)	34 (87%)	0.56
Relative/close friend with MI	34 (97%)	36 (92%)	0.36
Years of Education < 6 6-12 >12	 2 (6%) 9 (26%) 24 (69%)	 - 12 (31%) 27 (69%)	0.27

4.3 Proportion Choosing Treatment in Each Scenario

Physicians were more likely to prescribe antihypertensive therapy than informed patients were to want it, particularly when the absolute risks were low- as in scenarios 1, 2, 3, and 4 (Table 5). These differences remained highly significant even after adjusting for the different age and sex distributions in the two samples, with physicians more likely to choose treatment in all four scenarios: the odds ratios (and p values) were 2.9 (0.007), 7.1 (0.0002), and 6.9 (0.017) for scenarios 1, 2, and 4 respectively. The odds ratio for scenario 3 approached infinity since 100% of physician respondents chose treatment in that case.

Table 5: Proportion of respondents who would prescribe/accept treatment

	Physician (n=72)	Patient (n=74)	Significance (p value)
Scenario 1 (2% in 5 yrs)	46 (64%)	36 (49%)	0.06
Scenario 2 (5% in 5 yrs)	66 (92%)	50 (68%)	< 0.001
Scenario 3 (10% in 5 yrs)	72 (100%)	64 (86%)	0.001
Scenario 4 (15% in 20 yrs)	70 (97%)	62 (84%)	0.006
Scenario 5 (30% in 20 yrs)	72 (100%)	72 (97%)	NS
Scenario 6 (50% in 20 yrs)	72 (100%)	74 (100%)	NS

As expected, greater proportions of patients and physicians declined to prescribe/accept antihypertensive therapy with lower levels of baseline risk- this provided another check on respondents' comprehension.

4.4 Description of Minimal Clinically Important Differences

The MCIDs of patients and physicians were not normally distributed (Figures 1-6); in fact, the Kolmogorov-Smirnov tests for normality revealed $p<0.001$ in all six scenarios for each group. Three groups of patients were evident: those who were willing to take drug therapy even when benefits were negligible, those who were unwilling to take therapy regardless of benefits, and

those who's decision was sensitive to the magnitude of hypothetical benefit. For example, when presented with a baseline risk of 10% over five years (the estimated risk of the average Canadian hypertensive with a diastolic blood pressure of 100 mm Hg) 22% of patients were willing to take drug therapy even when there was no apparent benefit, 14% were unwilling to take therapy regardless of benefit, and 64% expressed MCIDs somewhere in between these two extremes (Figure 3).

Figure 1: Distribution of Minimal Clinically Important Differences in Scenario 1 (baseline CV risk 2% in 5 years)

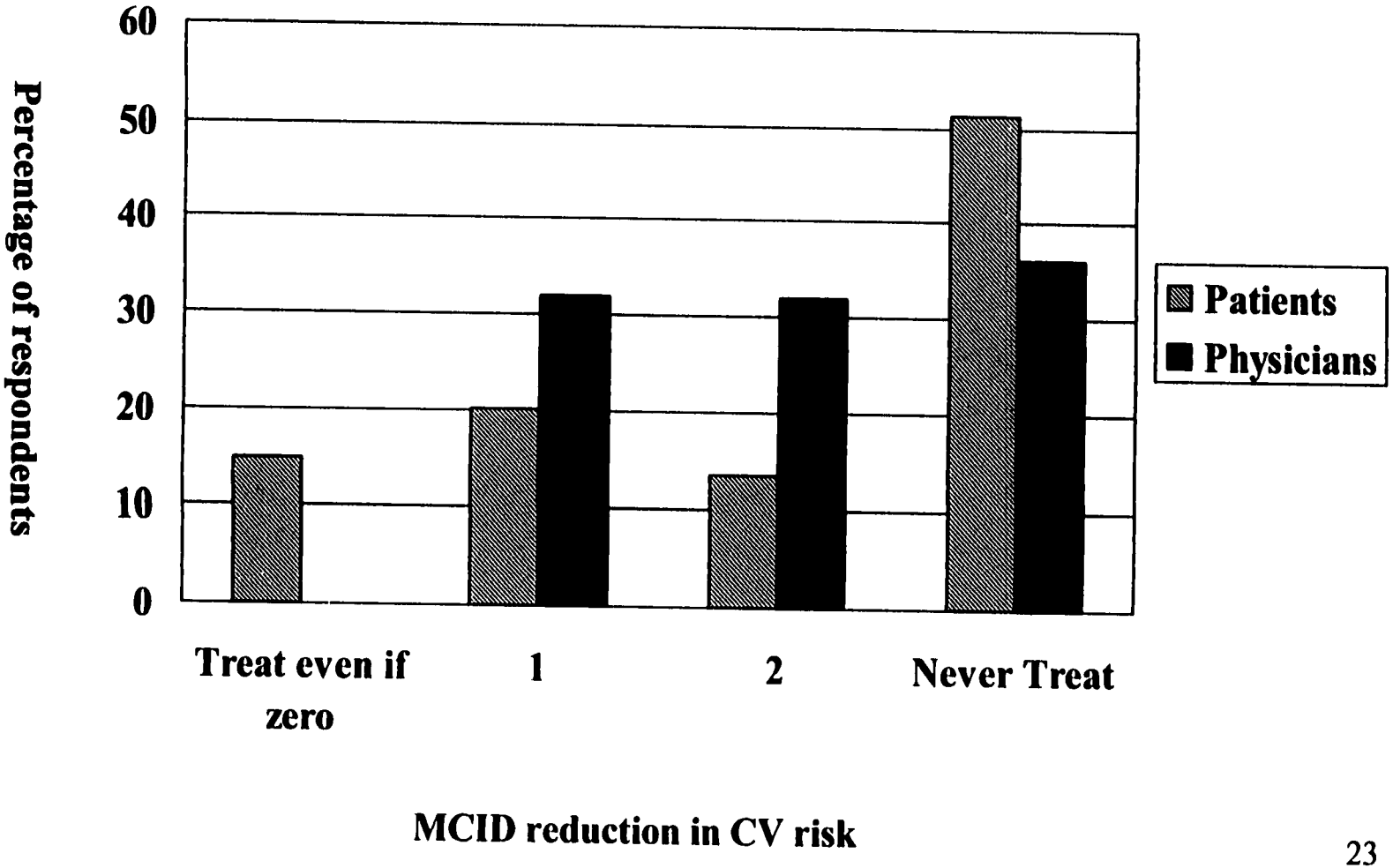


Figure 2: Distribution of Minimal Clinically Important Differences in Scenario 2 (baseline CV risk 5% in 5 years)

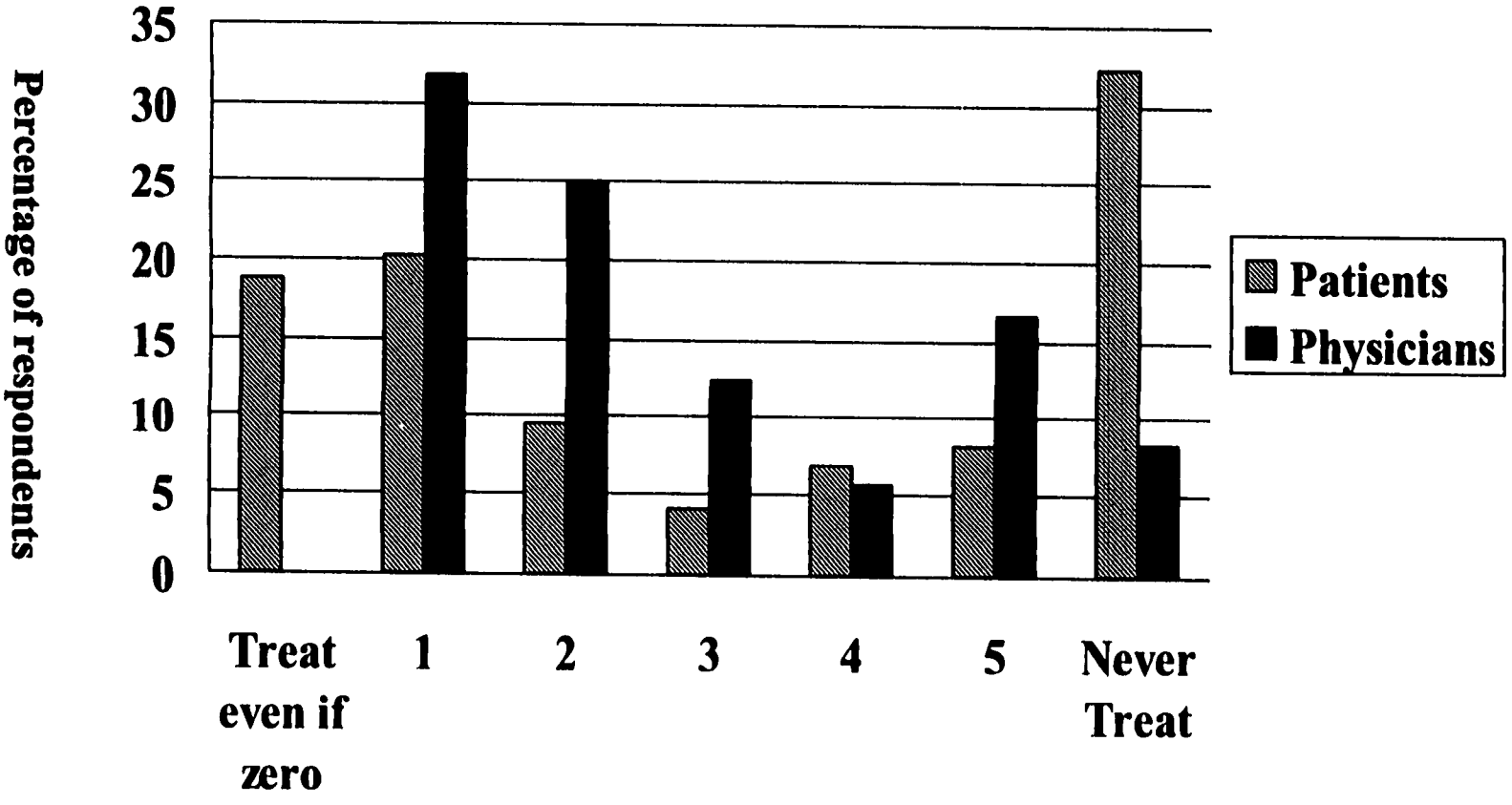


Figure 3: Distribution of Minimal Clinically Important Differences in Scenario 3 (baseline CV risk 10% in 5 years)

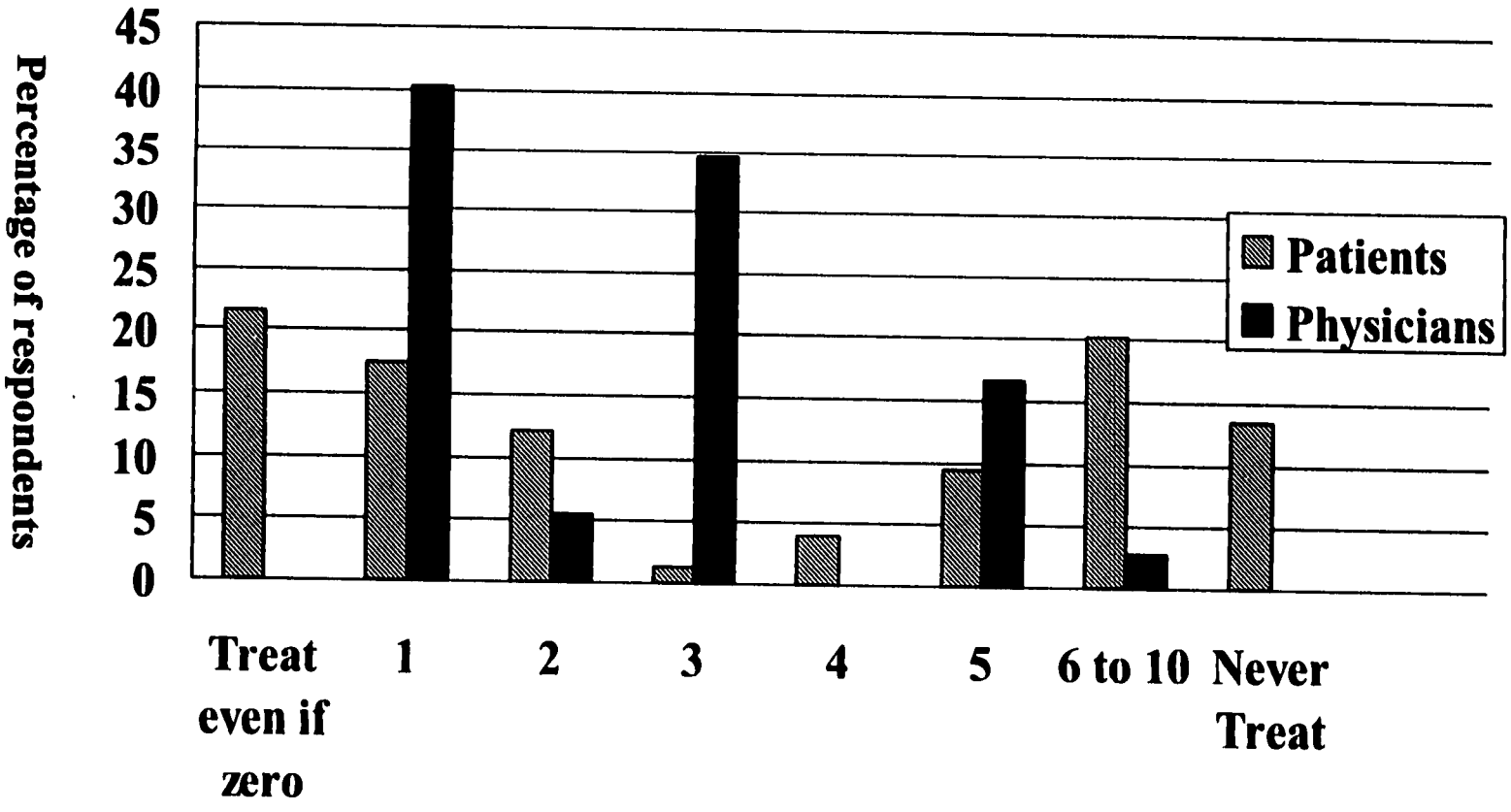


Figure 4: Distribution of Minimal Clinically Important Differences in Scenario 4 (baseline CV risk 15% in 20 years)

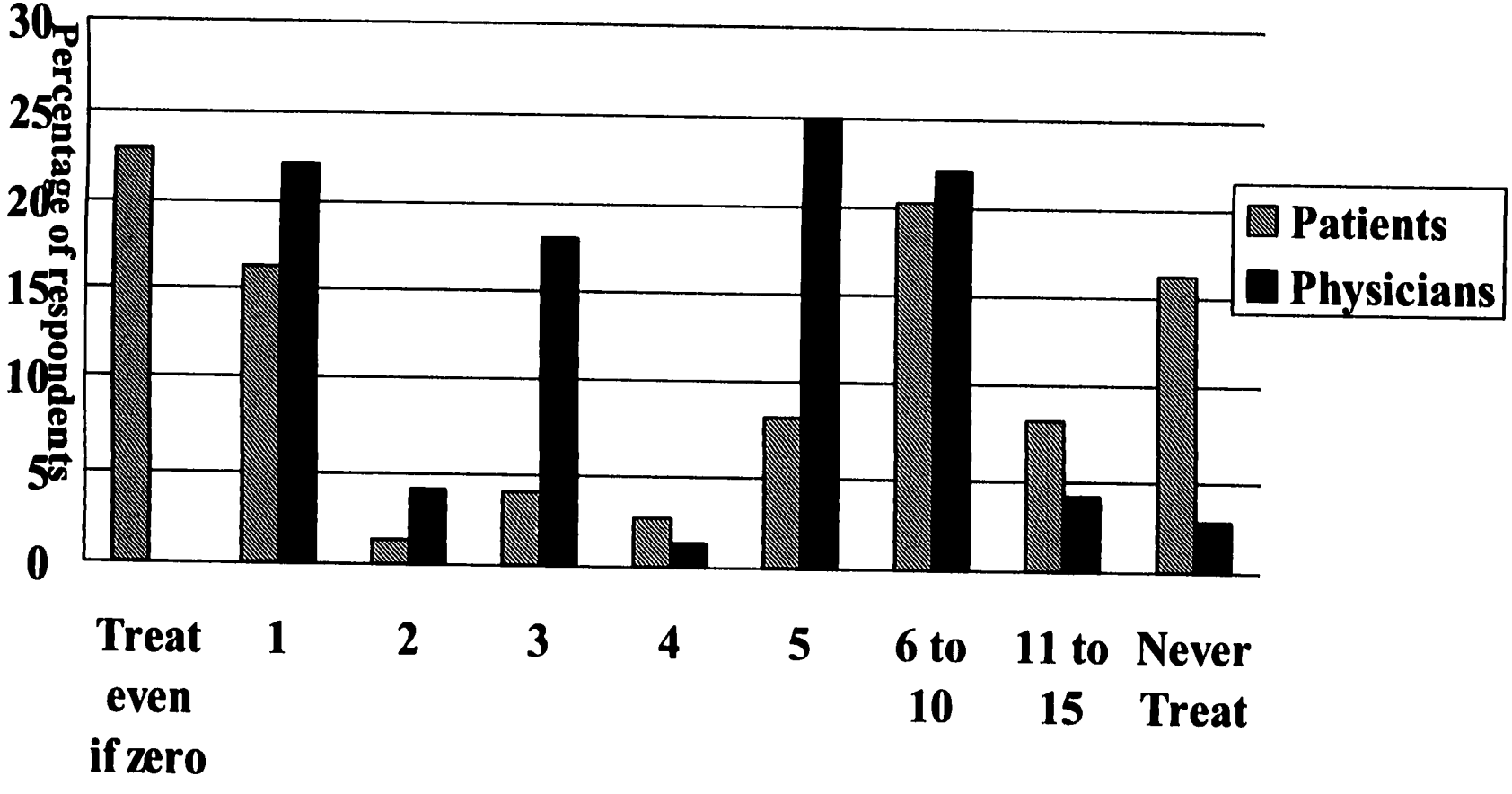


Figure 5: Distribution of Minimal Clinically Important Differences in Scenario 5 (baseline CV risk 30% in 20 years)

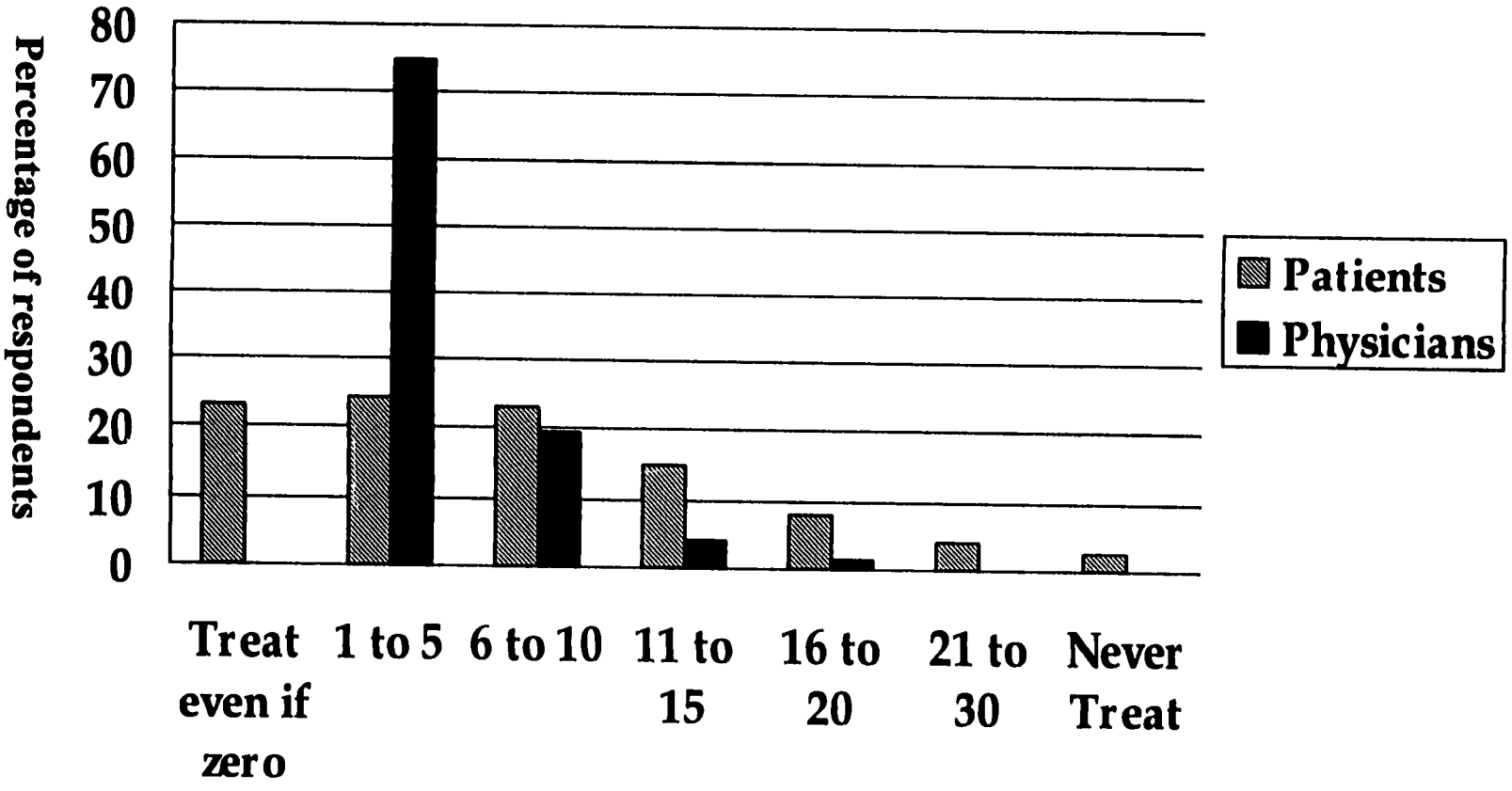
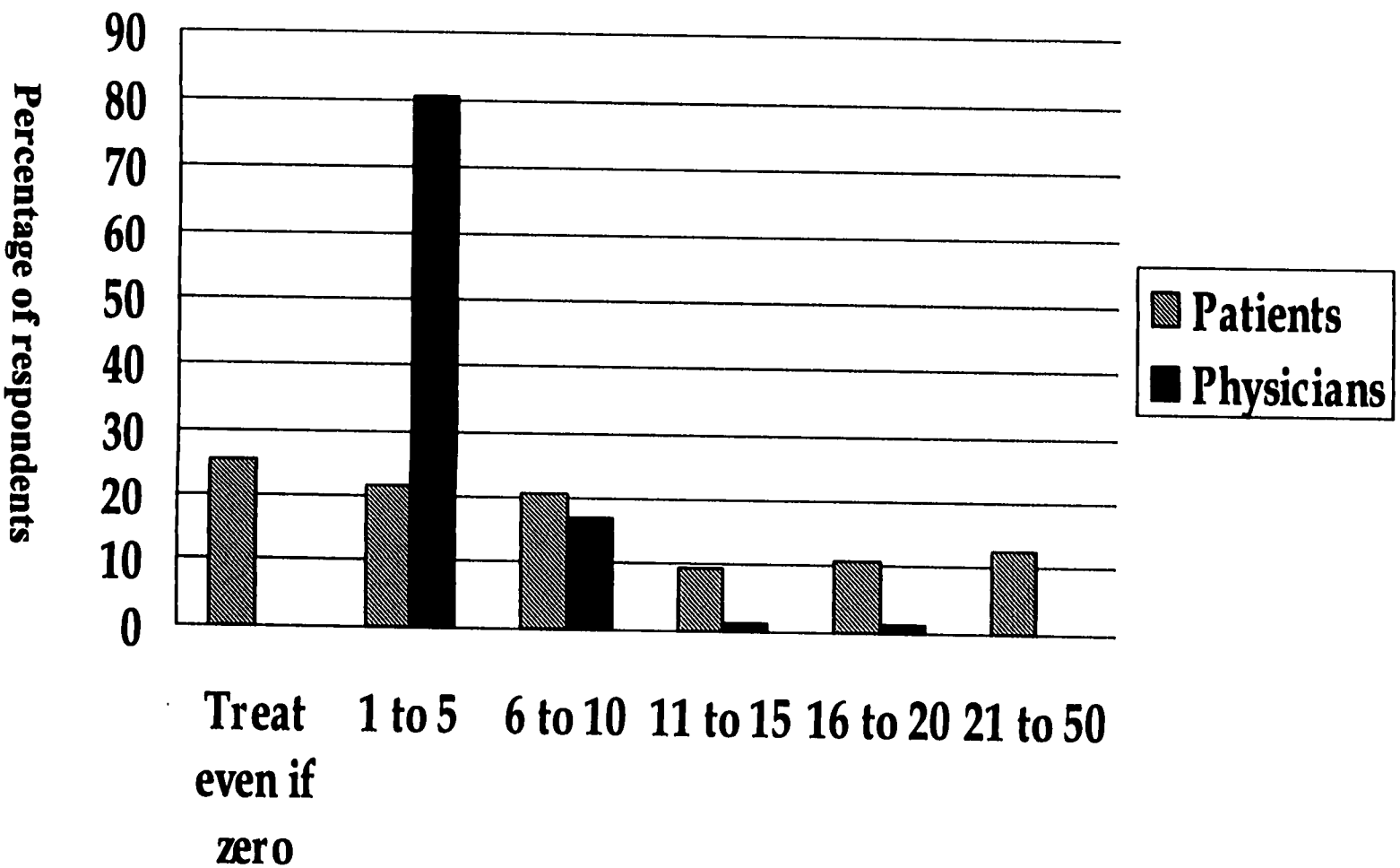


Figure 6: Distribution of Minimal Clinically Important Differences in Scenario 6 (baseline CV risk 50% in 20 years)



Non-parametric testing failed to detect any significant differences between the MCIDs of patients and physicians, although there was a trend towards higher MCIDs in patients (Table 6).

Table 6: Description of MCIDs

	Median	Percentiles (25^{th}, 75^{th})	Mode	Comparison*
Scenario 1 (2% in 5 yrs)				0.69
-physicians	2.0	1.0, Never Treat	Never Treat	
-patients	Never Treat	1.0, Never Treat	Never Treat	
Scenario 2 (5% in 5 yrs)				0.56
-physicians	2.0	1.0, 4.75	1.0	
-patients	3.0	1.0, Never Treat	Never Treat	
Scenario 3 (10% in 5 yrs)				0.32
-physicians	3.0	1.0, 3.0	1.0	
-patients	2.0	1.0, 7.0	Treat Regardless	
Scenario 4 (15% in 20 yrs)				0.93
-physicians	5.0	2.0, 6.75	5.0	
-patients	5.0	1.0, 10.25	Treat Regardless	
Scenario 5 (30% in 20 yrs)				0.36
-physicians	5.0	3.0, 5.75	5.0	
-patients	6.0	1.0, 12.75	Treat Regardless	
Scenario 6 (50% in 20 yrs)				0.19
-physicians	4.0	1.0, 5.0	5.0	
-patients	6.0	Treat Regardless, 15.0	Treat Regardless	

Notes:
* Results of the Mann-Whitney Test comparing the choices of physicians vs. patients for each scenario.
NeverTreat= those respondents who chose not to prescribe/accept therapy even when therapy was assumed to reduce absolute risk to zero
Treat Regardless= those respondents who chose to prescribe/accept therapy even when therapy was assumed not to reduce absolute risk

The MCIDs of patients from the two recruitment sites (Ottawa and Edmonton) were not significantly different on non-parametric testing: p values for scenarios 1 through 6 were 0.78, 0.90, 0.07, 0.60, 0.83, and 0.25 respectively.

4.5 Comparison of MCIDs in those who chose treatment

In addition to comparing physician and patient responses non-parametrically, it is possible to conduct parametric testing (since each group exceeds 30 subjects, fulfilling the requirements of the Central Limit Theorem). For parametric testing, those subjects choosing "never treat" were first excluded

from analysis (although those who chose treatment when there was no apparent benefit [MCID=0] were included). Of those respondents who chose to prescribe/accept therapy, patients expressed larger mean MCIDs than physicians in scenarios 3, 5 and 6 (Table 7). Comparison of the median MCIDs in these scenarios (Table 6) confirms that patients expressed higher MCIDs than physicians, although none of the comparisons reached statistical significance using the Mann-Whiney Test (not surprising since the conversion of continuous data to ordinal results in loss of power). The mean MCIDs for scenarios 1, 2, and 4 are misleading in this analysis as those subjects who stated they would not prescribe/accept therapy regardless of the degree of benefit attainable are not included.

Table 7: Minimal Clinically Important Differences in those prescribing/accepting treatment

	Physician	Patient	p
Scenario 1 (2% in 5 yrs)	1.50 (1.48-1.52)	0.97 (0.71-1.22)	< 0.001
Scenario 2 (5% in 5 yrs)	2.45 (2.10-2.80)	1.76 (1.29-2.23)	0.02
Scenario 3 (10% in 5 yrs)	2.64 (2.21-3.06)	3.09 (2.33-3.85)	0.31
Scenario 4 (15% in 20 yrs)	4.84 (4.02-5.66)	4.35 (3.21-5.49)	0.50
Scenario 5 (30% in 20 yrs)	4.89 (4.01-5.77)	7.21 (5.52-8.90)	0.02
Scenario 6 (50% in 20 yrs)	4.46 (3.62-5.30)	9.84 (7.12-12.55)	< 0.001

Repeating these analyses, but including all patients (by assigning the maximal possible MCID in each case to those who chose not to prescribe/accept therapy) confirms that patients expressed larger MCIDs than physicians, particularly in those scenarios where the vast majority of both groups chose treatment (Table 8). In other words, patients required more potential benefit to offset the cost, inconvenience, and risk of adverse effects associated with antihypertensive drugs than physicians. Multiple linear regression to correct for imbalances in age and gender distribution between patients and physicians

strengthened this conclusion since the differences were even more statistically significant: p values were 0.002 for scenario 3, 0.02 for scenario 5, and <0.001 for scenario 6.

Table 8: Minimal Clinically Important Differences in all respondents*			
	Physician	**Patient**	**P**
Scenario 1 (2% in 5 yrs)	1.68 (1.57-1.79)	1.50 (1.33-1.67)	0.08
Scenario 2 (5% in 5 yrs)	2.67 (2.29-3.04)	2.81 (2.33-3.29)	0.64
Scenario 3 (10% in 5 yrs)	2.64 (2.21-3.06)	4.03 (3.16-4.89)	0.005
Scenario 4 (15% in 20 yrs)	5.13 (4.22-6.03)	6.08 (4.75-7.42)	0.24
Scenario 5 (30% in 20 yrs)	4.89 (4.01-5.77)	7.82 (5.96-9.68)	0.006
Scenario 6 (50% in 20 yrs)	4.46 (3.62-5.30)	9.84 (7.12-12.55)	< 0.001
* calculated by assuming that those who didn't choose treatment had the maximum possible MCID in each scenario			

The observed differences appear to have been due to the reluctance of the previously-mentioned subgroup of patients to ever accept therapy, regardless of the degree of benefit. For example, excluding those respondents who were unwilling to prescribe/accept antihypertensive therapy in scenario 1 largely negates the differences in mean MCID between patients and physicians observed for scenarios 5 and 6 (patient mean MCIDs [and 95% CI] of 4.08 [1.96 to 6.20] for scenario 5 and 5.00 [1.96 to 8.04] for scenario 6 versus physician mean MCIDs of 3.59 [2.65 to 4.53] and 3.63 [2.63 to 4.63], p values 0.68 and 0.41 respectively).

4.6 Treatment Thresholds and Number Needed to Treat

As outlined in the Methods section, the respondents' implicit treatment thresholds can be extrapolated from their MCIDs. Both physicians and patients expressed similar thresholds when considering five year time horizons (10%), but patients were more conservative when considering treatment over a longer timeframe (29% risk threshold versus 19% for physicians).

Table 9: Treatment thresholds extrapolated from mean MCIDs		
	Physicians (n=72)	**Patients (n=74)**
Mean MCIDs (and 95% CI)*:		
-5 years	2.56 (2.28 to 2.84)	2.51 (2.01 to 3.00)
-20 years	4.73 (4.24 to 5.22)	7.29 (6.09 to 8.50)
Treatment Thresholds:**		
-5 years	10.2 (9.1 to 11.4)	10.0 (8.0 to 12.0)
-20 years	18.9 (17.0 to 20.9)	29.1 (24.4 to 34.0)
Number Needed to Treat:		
-5 years	39 (35 to 44)	40 (33 to 50)
-20 years	21 (19 to 24)	14 (12 to 16)
Notes: * As calculated from scenarios 2 and 3 for five years and scenarios 4, 5, and 6 for twenty years (only including those respondents who stated they would prescribe/accept treatment in that scenario) ** Mean treatment thresholds, assuming constant RRR of 25%, and calculated using the formula: Treatment threshold=MCID/RRR Number needed to treat is the inverse of the absolute risk reduction (approximated by the MCID) and is thus calculated using the formula: NNT=1/MCID		

Similar results are obtained if the median MCIDs are used. For physicians, the median MCIDs were 2.0 in the five year scenarios and 5.0 in the twenty year scenarios: these translate into treatment thresholds of 8% in five years and 20% in twenty years. For patients, the median MCIDs were 1.0 in five years and 5.0 in twenty years: the corresponding treatment thresholds were 4% and 20%. The expressed MCIDs correspond to NNTs of approximately 40 for five years (both groups) and 20 (physicians) or 14 (patients) for twenty years.

4.7 Determinants of MCIDs

As discussed in sections 4.3 and 4.5, type of respondent (patient or physician) significantly influenced the decision to treat and the size of the MCID. Analyses to determine what factors within each of these groups influenced their decision making are outlined below.

4.7.1 Physicians

4.7.1.1 Decision to prescribe treatment

On bivariate analysis, only "order of scenarios" and "hospital affiliation" were significantly associated with the decision to prescribe therapy in scenario 1 and only "number of hypertensive patients seen per month" was significant in scenario 2 (Table 10). As the variable "order" included 6 different levels, it was recoded into the nominal variable "dichotomized order" for all of the analyses described below: the 3 scenario orders in which the 20-year scenarios were described first were chosen as the referent group and coded as "0", the 3 orders in which the 5-year scenarios were presented first were coded as "1".

Table 10: Results of bivariate analysis for decision to (not) treat (scenarios 1 and 2, physicians)

Characteristic	Test Used	Scenario 1 (2% in 5 yrs)	Scenario 2 (5% in 5 yrs)
		Significance (p values)	Significance (p values)
Physician age	Students' t-test	0.58	0.77
Physician gender	Chi-square test	0.96	0.77
Physician experience	Students' t-test	0.83	0.55
Length of physician's training	Students' t-test	0.56	0.24
Physician practice type	Chi-square test	0.69	0.62
Physician status -hospital affiliation -academic appointment	 Chi-square test Chi-square test	 0.04 0.47	 0.44 0.49
Number of hypertensive patients seen per month	Students' t-test	0.61	0.04
Gender in scenarios	Chi-square test	0.33	0.39
Order of scenarios	Chi-square test for trend	0.03	0.26
Dichotomized order of scenarios	Chi-square test	0.001	0.39

For scenario 1, multivariate logistic regression revealed that both "hospital affiliation" and "dichotomized order of scenarios" (p=0.002) were significantly associated with the decision to prescribe. Specifically, those physicians presented with five year scenarios first were more likely to recommend therapy than those who received the twenty year scenarios initially (30/36 [83%] vs.

16/36 [44%], Odds Ratio [OR] 6.6) and those physicians with hospital affiliations were less likely to prescribe antihypertensive therapy (OR 0.26). However, these variables only explained 21% (Cox-Snell R^2=0.209) of the variability in the dependent variable. Further, the Hosmer-Lemeshow Goodness of Fit test revealed that this model was a poor fit (p=0.20).

A full description of the procedures followed and the regression model is included in Appendix J. The same procedures were followed for all of the logistic regression models in this thesis and thus only this one was included as an Appendix (the others are available from the author on request).

On multivariate logistic regression for scenario 2, only number of patients was significantly associated with the choice to treat (p=0.04), with those physicians who saw more patients being more likely to recommend therapy in this case. However, this variable only explained 10% of the variability in the dependent variable (Cox-Snell R^2=0.102).

Thus, substantial variation in MCIDs remained for each scenario after accounting for demographic and practice characteristics.

Bivariate and multivariate logistic regressions for the decision to (not) treat were not done for scenario 4 as all but two physicians recommended treatment in that case.

4.7.1.2 Size of MCID if decide to prescribe treatment

Bivariate analyses revealed that the only variables which were significantly associated with the size of specified MCIDs were: "hospital affiliation" in scenario 3; "hospital affiliation" and "order of scenarios" in scenario 4; "hospital affiliation",

"order of scenarios", and "gender version of scenarios" in scenario 5; "length of postgraduate training" and "gender version of scenarios" in scenario 6 (Table 11). As described in section 4.7.1.1, the ordinal variable "order" was recoded into the nominal variable "dichotomized order" for all of these analyses.

Table 11: Results of bivariate analysis for size of MCID if decide to treat (scenarios 3, 4, 5, and 6, physicians)

	Test Used	Scenario 3 (P values)	Scenario 4 (P values)*	Scenario 5 (P Values)	Scenario 6 (P Values)
Physician age	Pearson's Correlation	0.63	0.67	0.81	0.69
Physician gender	Students' t-test	0.88	0.97	0.49	0.09
Physician experience	Pearson's Correlation	0.55	0.81	0.86	0.45
Length of physician's training	Pearson's Correlation	0.37	0.16	0.11	0.03
Physician practice type	Students' t-test	0.92	0.59	0.64	0.78
Physician status -hospital affiliation -academic appointment	 Students' t-test Students' t-test	 0.006 0.07	 0.04 0.24	 0.01 0.11	 0.32 0.16
Number of hypertensive patients seen/ month	Pearson's Correlation	0.44	0.06	0.11	0.24
Gender in scenarios	Students' t-test	1.00	0.13	0.03	0.04
Order of scenarios	Spearman's Correlation	0.30	0.02	0.03	0.24
Dichotomized order of scenarios	Students' t-test	0.07	0.03	0.15	0.77

* The two physicians who chose not to treat for this scenario are excluded from this analysis.

On multivariate linear regression for scenario 3, only "hospital affiliation" remained significant (p=0.006); those physicians who had hospital affiliations expressed larger MCIDs than those without hospital affiliations (mean MCID 3.02 versus 1.77). However, this factor accounted for only 10% of the observed variation in specified MCIDs (R^2 for model 0.102).

On multivariate linear regression for scenario 4, only "hospital affiliation" (p=0.04) and "dichotomized order of scenarios" (p=0.04) remained significant; the interaction term was not significant. However, this multivariate model only explained 12% of the observed variation in the specified MCIDs (R^2 for model 0.123).

For scenario 5, only academic appointment (p=0.04) and gender of scenarios (P=0.04) were significant on multivariate analysis. The interaction term was not significant (p=0.55) and thus was not included. This multivariate model only accounted for 12% of the observed variation in the specified MCIDs (R^2 for model 0.121). A full description of the procedures followed and the regression model is included in Appendix K. The same procedures were followed for all of the linear regression models in this thesis and thus only this one was included as an Appendix (the others are available from the author on request).

Multivariate linear regression in case 6 revealed that length of postgraduate training (p=0.01) and academic appointment (p=0.02) were significantly associated with chosen MCID (but only accounted for 14% of the observed variability in MCIDs for case 6).

Thus, substantial variation in MCIDs remained for each scenario after accounting for demographic and practice characteristics.

Overall, the gender of the hypothetical patients presented in these scenarios did not appear to significantly influence physician decision making.

4.7.2 Patients

4.7.2.1 Decision to accept treatment

On bivariate analysis, only "taking antihypertensives" was significantly associated with the decision to accept therapy in all of the cases (Table 12). Patient age was also highly correlated with the decision to accept or reject therapy in some scenarios. Although duration of hypertension was not significantly associated with the decision to accept or reject therapy when

considered as a continuous variable, those patients diagnosed with hypertension within the past year were less likely to want therapy than those who were diagnosed more than a year ago: OR (and p values) were 0.49 (0.21), 0.61 (0.38), 0.23 (0.03), and 0.34 (0.09) for scenarios 1, 2, 3, and 4 respectively. As the variable "order" included 6 different levels, it was recoded into the nominal variable "dichotomized order" for all of the analyses described below: the 3 scenarios in which the 20-year scenarios were described first were chosen as the referent group and coded as "0", the 3 orders in which the 5-year scenarios were presented first were coded as "1".

Table 12: Results of bivariate analysis for decision to (not) accept therapy (scenarios 1, 2, 3, and 4, patients)

Characteristic	Test Used	Scenario 1 (2% in 5 yrs)	Scenario 2 (5% in 5 yrs)	Scenario 3 (10% in 5 yrs)	Scenario 4 (15% in 20 yrs)
Age	Students' t-test	0.01	0.06	0.09	0.63
Gender	Chi-square test	0.35	0.86	0.24	0.67
Duration of hypertension	Students' t-test	0.28	0.40	0.20	0.20
Taking antihypertensives	Chi-square test	0.001	0.004	0.001	<0.001
Miss pills*	Chi-square test	0.13	0.12	0.17	0.17
Frequency of missing pills**	Chi-square test for trend	0.62	0.91	0.17	0.12
Relative/close friend with stroke	Chi-square test	0.47	0.63	0.24	0.19
Relative/close friend with MI	Chi-square test	0.35	0.74	0.42	0.37
Years of education	Chi-square test for trend	0.62	0.42	0.69	0.40
Order of scenario	Chi-square test for trend	0.49	0.98	0.10	0.63
Dichotomized order of scenario	Chi-square test	0.81	0.87	0.44	0.60

Notes: The values in this table represent p values for the specified analyses.
* In the subgroup of 48 who were taking antihypertensive therapy.
** In the subgroup of 28 who were taking antihypertensive therapy and admitted to missing some pills.
*** Insufficient data for each cell of analysis

Multivariate logistic regression revealed that only "taking antihypertensives" was significantly associated with the decision to accept/reject therapy in each scenario. Those patients who were currently taking

antihypertensive drugs were more likely (than those not currently taking these medications) to favour treatment in each of the scenarios, odds ratios (and p values) were: 5.6 (0.002) for scenario 1, 4.4 (0.005) for scenario 2, 10.2 (0.006) for scenario 3, and 14.4 (0.001) for scenario 4. However, this variable only explained a minor amount of the variability in decision making: 11% to 18% in the 4 scenarios. "Duration of hypertension" was no longer significant in any of the scenarios after adjustment for other demographic features. In fact, substantial variation in MCIDs remained for each scenario after accounting for demographic characteristics.

4.7.2.2 Size of MCID if decide to accept treatment

Bivariate analyses also suggested that only "taking antihypertensives" was associated with the size of specified MCIDs- although this was not significant on bivariate comparison (Table 13).

Table 13: Results of bivariate analysis for size of MCID (scenarios 5 and 6, patients)

Characteristic	Test Used	Scenario 5 (30% in 20 yrs)	Scenario 6 (50% in 20 yrs)
Age	Pearson's Correlation	0.02	0.13
Gender	Students' t-test	0.96	0.43
Duration of hypertension	Pearson's Correlation	0.34	0.89
Taking antihypertensives	Students' t-test	0.14	0.18
Miss pills*	Students' t-test	0.19	0.14
Frequency of missing pills**	Spearman's Correlation	0.10	0.11
Relative/close friend with stroke	Students' t-test	0.66	0.19
Relative/close friend with MI	Students' t-test	0.79	0.46
Years of education	Spearman's Correlation	0.72	0.43
Order of scenarios	Spearman's Correlation	0.57	0.97
Dichotomized order of scenarios	Students' t-test	0.17	0.97

Notes:
* In the subgroup of 48 who were taking antihypertensive therapy.
** In the subgroup of 28 who were taking antihypertensive therapy and admitted to missing some pills.

However, on multivariate linear regression, "taking antihypertensives" was significantly associated with the size of the specified MCIDs; those patients who were currently taking antihypertensives expressed significantly smaller MCIDs than those not taking these medications (mean MCID 5.9 versus 9.9, p=0.03). However, this factor accounted for only 6% of the observed variation in specified MCIDs (R^2 for model 0.056) and substantial variation in MCIDs remained after accounting for demographic characteristics.

CHAPTER 5: DISCUSSION

5.1 Summary of Results

In this study, we have developed and tested a probability trade-off tool for determining the MCID for the efficacy of antihypertensive therapy from the perspective of patients and practising family physicians. Key findings were that patients were generally more conservative in their treatment choices than physicians (less were willing to accept drug therapy in scenarios 1-4 and mean MCIDs were significantly larger in scenarios 5 and 6), no sociodemographic factors consistently predicted the treatment preferences of either patients or physicians, and there was wide variability in patient preferences.

Given the mean MCIDs for scenarios 2 through 6, and assuming a constant 25% relative risk reduction with antihypertensive therapy across all baseline risks[24,25], practicing family physicians chose treatment thresholds of approximately 10% in five years and 20% in twenty years. Under the same assumptions, the patient MCIDs translated into treatment thresholds of approximately 10% in five years and 30% in twenty years.

5.2 Comparison with the Literature

While there has been little research comparing the MCIDs of patients and physicians, Man-Son-Hing and colleagues[42] found that elderly patients with atrial fibrillation expressed considerably smaller MCIDs for warfarin therapy than those usually identified by clinicians. However, all of the patients in the Man-Son-Hing study had been on, or were currently taking, warfarin, and this may have biased the results towards smaller MCIDs (patients in our study who were taking

antihypertensive drugs expressed smaller MCIDs than their untreated counterparts). Moreover, the Man-Son-Hing study only looked at MCIDs for two years of therapy and it seems reasonable to assume that therapies with long treatment courses and delayed benefits, but immediate costs, inconvenience, and potential adverse effects (such as antihypertensive drugs) are likely to be viewed with less enthusiasm by patients. Certainly, the patient preference literature suggests that informed patients may be more conservative than their physicians.[75] For example, of the six randomized trials of decision aid technology, two (both reported in one manuscript)[76] have demonstrated significant, and three[77-79] non-significant, trends towards more conservative decision making in informed patients. Thus, informed patients were less likely to want warfarin for atrial fibrillation (relative risk [RR] 0.63 in low risk patients)[77], surgery for ischemic heart disease (RR 0.60-0.78)[78], surgery for benign prostatic hypertrophy (RR 0.59)[79], or prostate specific antigen screening for the early detection of carcinoma (RR 0.53 in one study and 0.82 in the other)[76]. The only randomized trial to fail to demonstrate this relationship was small (28 subjects in each group) and tested a weak intervention that didn't appear to impact knowledge.[80]

Our finding that patient or physician sociodemographics don't accurately predict their MCID is also consistent with the literature. For example, two recent studies[57,81] have documented that patient utilities for various health states are not related to age, gender, race, or educational status. Taken together with our finding that patients expressed a wide range of preferences about

antihypertensive therapy, these results emphasize the importance of full communication with patients about the potential benefits, risks, and costs of therapy and the tailoring of treatment decisions to the individual.

The fact that a substantial minority of patients (20 to 33%, depending on the scenario) were willing to take antihypertensive therapy even when asked to imagine that it had no impact on the risk of cardiovascular events appears irrational. However, this has been documented in previous MCID elicitation projects[42,82-84] and raises the issue of whether patients have realistic expectations from therapy. For instance, in a study of 64 hypertensive adults, Llewellyn-Thomas and colleagues[84] found that one-third expressed MCIDs which were dramatically greater than those achievable even if their blood pressure was normalized with antihypertensive therapy. As these investigators pointed out, this "suggests a clear need for decision aids to help individuals comprehend their overall cardiovascular risk and then use that information in deciding to accept or refuse medication for the primary prevention of cardiovascular disease".[84]

The long-term treatment thresholds of patients and physicians are lower than those set out in the two guidelines which specify absolute risk thresholds- the New Zealand Hypertension Guidelines[1] and the JNC-VI[7]. For instance, the New Zealand Guidelines specified a risk threshold of 10% in five years, which can be extrapolated within the Canadian setting (using the Cardiovascular Disease Life Expectancy Model) to 50% in twenty years. While the JNC-VI is less explicit in defining treatment thresholds (for example, drug therapy is recommended for a patient with a blood pressure of 150/95 only if they have

target organ damage or diabetes mellitus, or if their blood pressure is persistently elevated despite six months of lifestyle modification and they have at least one other risk factor), they can be estimated using the Cardiovascular Disease Life Expectancy Model as approximately 5-10% in five years (and 30-50% in twenty years).

However, merely comparing the mean (or median) treatment thresholds of respondents with those published in guidelines ignores the important variations in patient preferences identified in this study and others.[84,85] In particular, one third of our patients decided against drug therapy when presented with risk profiles that would qualify for treatment under the Canadian Hypertension Society Guidelines[2] (scenario 3), while almost half wanted therapy when presented with a risk profile that was not felt to warrant treatment under these same guidelines (scenario 1). Thus, expert opinion appears to be a poor proxy for the preferences of actual patients. Moreover, the fact that the physicians in our study expressed larger MCIDs than British physicians[86] emphasizes the importance of assessing the preferences of local physicians or patients rather than extrapolating from data derived in other settings.

5.3 Limitations

This study has a number of limitations which must be acknowledged. For one, patient preferences should ideally be elicited from patients who are newly diagnosed with hypertension and actually considering medication for the first time. However, there are problems- both ethical (concerns over systematically affecting patients' actual decisions) and logistical (concerns over the difficulty in

identifying sufficient numbers of these patients)- with limiting the study to only these patients. As the duration of hypertension was not associated with expressed MCIDs on multivariate analysis and those patients who had been diagnosed within the past year reported similar preferences as those with long-standing hypertension, we believe our results are generalizable to similar patients with uncomplicated essential hypertension.

Secondly, as we only recruited hypertensive patients who were attending physicians (and the majority of hypertensive individuals are not under medical care[7,54]) there is a potential for selection bias. However, our finding that patients are more conservative in treatment decisions than physicians is, if anything, likely to be an underestimate of the true relationship since hypertensive individuals who pursue medical care are likely to be more favourably disposed to therapy than those who don't.

Thirdly, we did not include health care administrators, policy makers, or the general public in our study and, as they are likely to express different treatment preferences than physicians and hypertensive patients[87,88], it could be argued that the views of all of these groups should be sought. We would agree with this point of view and further studies are planned to elicit the preferences of these groups.

Fourth, while the method of presenting probabilities can affect patient and physician preferences[44], we employed a standard, well-validated method in this study that has been shown to optimize comprehension[89,90] and it is unlikely that any reasonable change in the presentation format would have significantly

impacted on the expressed MCIDs or the relationship between patient and physician responses. Moreover, while we only assessed the MCIDs of subjects at one point in time, previous projects have suggested that treatment preferences for chronic therapies are relatively stable over time.[42,49,56,57] Similarly, while it could be argued that reliable data on risks with hypertension only extend out to 5-10 years (the duration of most of the cohort studies), we used a risk prediction model which has been derived from North American data and validated in numerous other datasets (including most of the large primary or secondary prevention of cardiovascular disease trials done in the past two decades).

Fifth, while there is conflicting evidence[91] on how well responses to hypothetical scenarios predict actual behaviour, we[74,92] (and others[93]) have previously shown that physician responses to clinical vignettes on hypertension do serve as reasonable proxies for their actual practice behaviours.

Finally, it could be argued that the methodogy employed in this study is impractical for everyday use due to the need for labour-intensive face-to-face interviews with individual patients. As such, we are developing an audiobooklet decision aid[45] that can be used by patients prior to their physician appointment, with the goal of enhancing the efficiency of the patient-physician interaction (a recent randomized trial[77] of a decision aid versus usual care for communicating the results of a clinical trial demonstrated that the group assigned to the decision aid were better informed and required less time with the physician to make a treatment decision).

5.4 Implications for Guidelines and Future Research

We have found that patients express a wide range of preferences for hypertension treatment and that no sociodemographic factors can predict patient utilities. Moreover, practicing physicians and expert panels appear to be poor proxies for patient utilities. Thus, future guidelines should allow and encourage individualization of treatment, preferably with explicit assessment of patient preferences.

The probability trade-off tool developed in this project could be adapted and used for this purpose. Indeed, studies have suggested that active patient involvement in medical decision making improves compliance[94], quality of life[95], outcomes[96-102], and reduces use of health services[103] and expenditures[104]. The most commonly cited reasons against this patient-oriented approach are not supported by the preliminary evidence: fully informing patients of medication side effects does not increase the incidence of reported side effects[105], and incorporating individual patients' preferences into treatment decisions can be cost-effective.[106] Furthermore, patients increasingly desire detailed information about their prognosis and therapeutic options and want to be involved in decision making.[107-109] Given the wide distribution of patient preferences for antihypertensive therapy, a decision aid (presenting patients with their own risk of cardiovascular events and eliciting their treatment preferences) should be developed and tested against usual care in the management of hypertensive patients.[75] In the meantime, studies such as this one, in which MCIDs from the

perspective of different stakeholders are assessed, provide an empirical basis for future policy making.

CHAPTER 7: CONCLUSION

In summary, the decision to initiate antihypertensive therapy is utility-sensitive and expert panels appear to be poor proxies for the preferences of hypertensive patients. Moreover, physician preferences appear to poorly correlate with those of actual hypertensive patients. This calls into question the validity of rigidly adhering to treatment thresholds set by physician guideline panels (no matter how expert in that field). While the movement towards risk-based guidelines in hypertension management[1,7,27] should obviate the need for setting treatment thresholds, allowing physicians to "inform patients and individualize decisions and values, in the context of the patients' other risks and values",[26] this may lead to guidelines that are too complex and time consuming to apply in practice. Until such guidelines are tested in rigorous studies, it is likely that guideline developers will continue to set treatment thresholds. Recognizing this, it would seem appropriate that the preferences of patients, practicing physicians, and the general public should be assessed and incorporated in future attempts to establish explicit treatment thresholds.

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APPENDIX A- PATIENT SURVEY

Thank you for participating in this research study. This survey is divided into three parts. In the first part, we will ask some questions about you which will allow us to analyze your answers with those of other people similar to yourself. All of your answers will be kept confidential.

In the second part, we will describe high blood pressure and how it leads to stroke or heart attack. We will describe what usually happens when someone has a stroke or heart attack, and discuss a medication which can help to prevent strokes or heart attacks in people with high blood pressure.

In the third part, we will describe six situations and ask you to imagine each situation applied to you. Then we will ask your opinion about whether or not you would want to take a blood pressure-lowering medication in each situation. From this information, we will be able to let doctors know what people think about blood pressure medication.

The first part of this questionnaire contains ten questions about you. All of your answers will be kept confidential.
Please fill in the blanks or place a checkmark (√) in the most appropriate box.

1. What is your age? ☐☐ years

2. What is your sex? ☐ Female ☐ Male

3. How long have you known that you had high blood pressure?

   ☐☐ years (if less than one year, ☐ months)

4. Are you on blood pressure pills at this time?

   ☐ yes (please specify name: _____)
   ☐ no **(go to question 7)**
   ☐ not sure **(go to question 7)**

5. People often have difficulty taking their pills for one reason or another. Have you ever missed any of your blood pressure pills?

   ☐ Yes **(go to question 6)** ☐ No **(go to question 8)**

6. How often do you miss your pills?
   ☐ Once a day
   ☐ Once a week
   ☐ Once a month
   ☐ Once a year
   ☐ Less than once a year

7. Have you ever taken blood pressure pills? ☐ Yes ☐ No

8. Has anyone you know ever had a stroke? ☐ Yes ☐ No

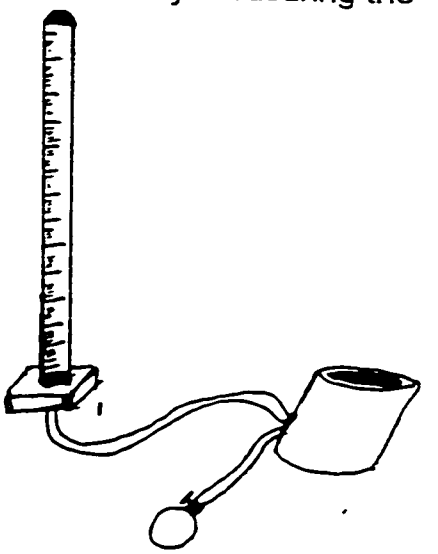
9. Has anyone you know ever had a heart attack? ☐ Yes ☐ No

10. How much formal education have you completed?
    ☐ Some grade (elementary) school
    ☐ Some high school
    ☐ High school diploma
    ☐ Some post-secondary education
    ☐ College diploma or certificate
    ☐ University degree

BACKGROUND INFORMATION

High Blood Pressure

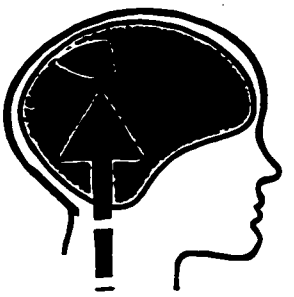
High blood pressure (also known as "hypertension") is a condition in which a person's blood pressure is higher than normal for someone their age and sex. Generally, high blood pressure doesn't cause any symptoms and people do not even know they have it. The only way it can be detected is by measuring the blood pressure with a blood pressure cuff.



High blood pressure is a very important condition as it can cause strokes or heart attacks. Turn the page to learn more about strokes and heart attacks.

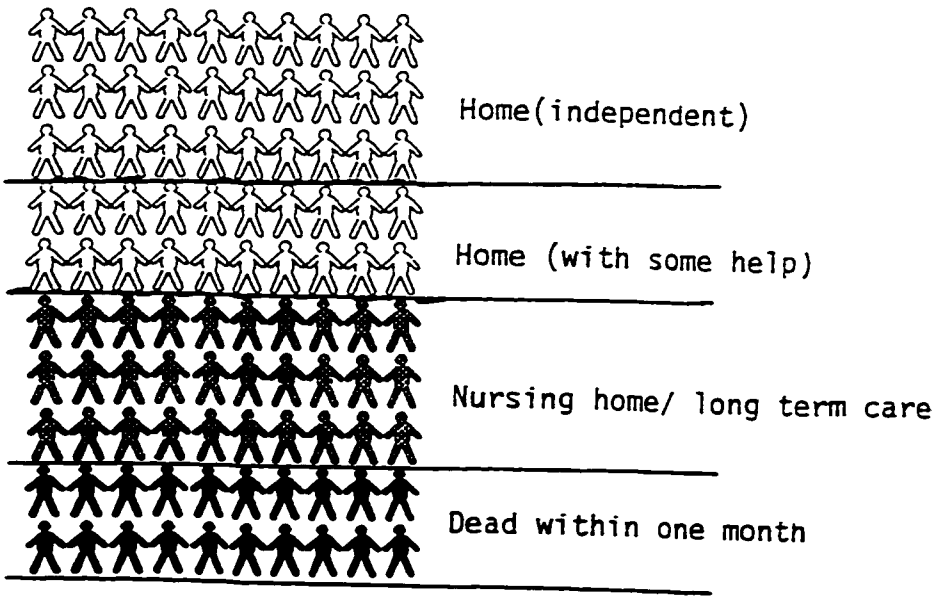
STROKE

A stroke is caused by a blockage in the blood supply to part of the brain.



The effects of a stroke range from being completely normal within a few minutes to being dependent on others for eating, toileting, and movement for the rest of your life. In between these extremes, most people have either minor symptoms or major symptoms.

The stick figures below represent 100 people who have had a stroke. They will be used to show the chances of different things happening. About 1 in 5 people who have a stroke die within the first month. Of the survivors, about one third recover completely and are able to return home, one third are able to return home but need some help with walking or talking, and one third need to go to a nursing home as they need help with feeding, toiletting, and walking.



On the next page, I will describe what a stroke is like.

STROKE

Initial Physical Symptoms:

-Suddenly unable to move or feel your arm and/or leg on one side
-No physical pain
-May not be able to swallow

Initial Mental Symptoms:

-May not be able to fully understand what is being said to you
-May not be able to say what you want to say
-Speech may be slurred and difficult for others to understand

Initial Recovery:

-Will be admitted to hospital
-Weakness, numbness, and speech may improve
-Stay in hospital for 1-2 weeks

Initial Chance of Dying:

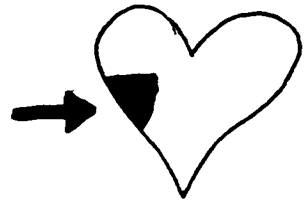
-About 1 in 5 people who have a stroke die within one month

Long-term Recovery:

-This varies from person to person (see previous page)
-About 1 in 2 people who suffer a stroke will recover and be able to return home again
-About 1 in 3 people who survive a stroke will have trouble with slurred speech
-About 1 in 10 people who survive a stroke will be unable to control their bowel or bladder

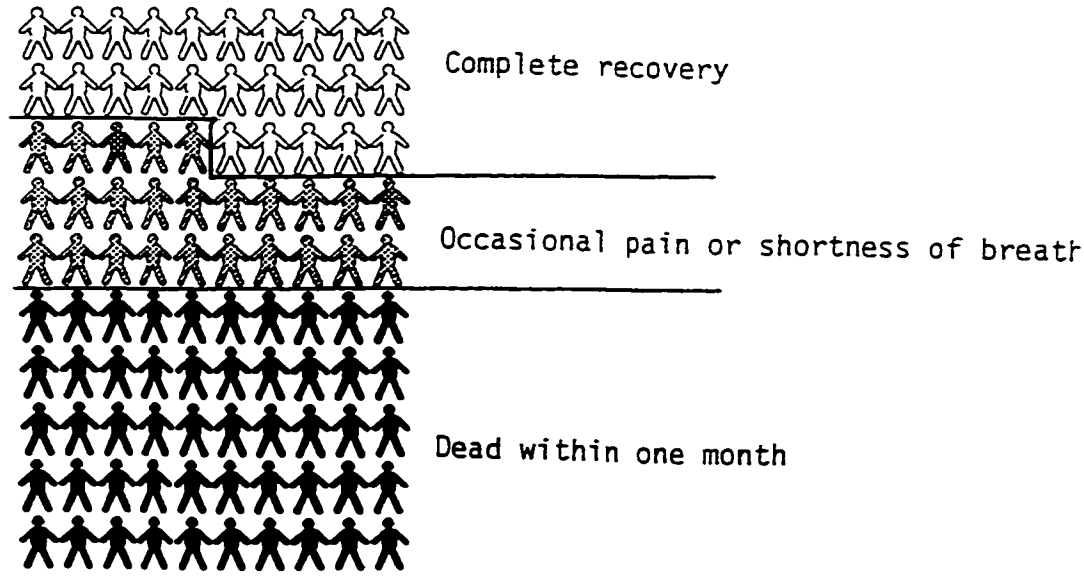
HEART ATTACK

A heart attack is caused by a lack of blood flow to a region of the heart muscle.



The stick figures below represent 100 people who have had a heart attack. They will be used to show the chances of different things happening.

About half of all people who have a heart attack die within one month. Of the people who survive one month, half will recover and be able to resume a normal life and the other half will recover but will have occasional chest pain (angina) or shortness of breath.



On the next page, I will describe what a heart attack is like.

HEART ATTACK

Initial Physical Symptoms:

-Suddenly get a heavy feeling or pain in the chest
-May feel dizzy, nauseated, or short of breath

Initial Mental Symptoms:

-May not be able to fully understand what is being said to you

Initial Recovery:

-Will be admitted to hospital
-Chest pain and other symptoms will improve with treatment
-Stay in hospital for about a week
-Won't be able to return to work for at least six weeks

Initial Chance of Dying:

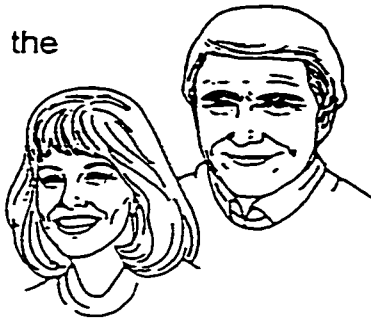
-About one in every two people who have a heart attack die within one month

Long-term Recovery:

-Will feel fatigued and low in energy for several weeks or months after
-About one in two people who recover from a heart attack are able to resume their normal activities after a few weeks
-About one in two people who recover from a heart attack are limited by further attacks of chest pain or shortness of breath while doing their usual activities

Treatment with a blood pressure-lowering medication

The goal of treatment with a blood pressure-lowering medication is to prevent a stroke or heart attack in people with high blood pressure. However, the pills are only partially effective and do not prevent strokes or heart attacks in everyone who takes them. This means that some people will benefit from taking the treatment while others will take the treatment without any benefit.

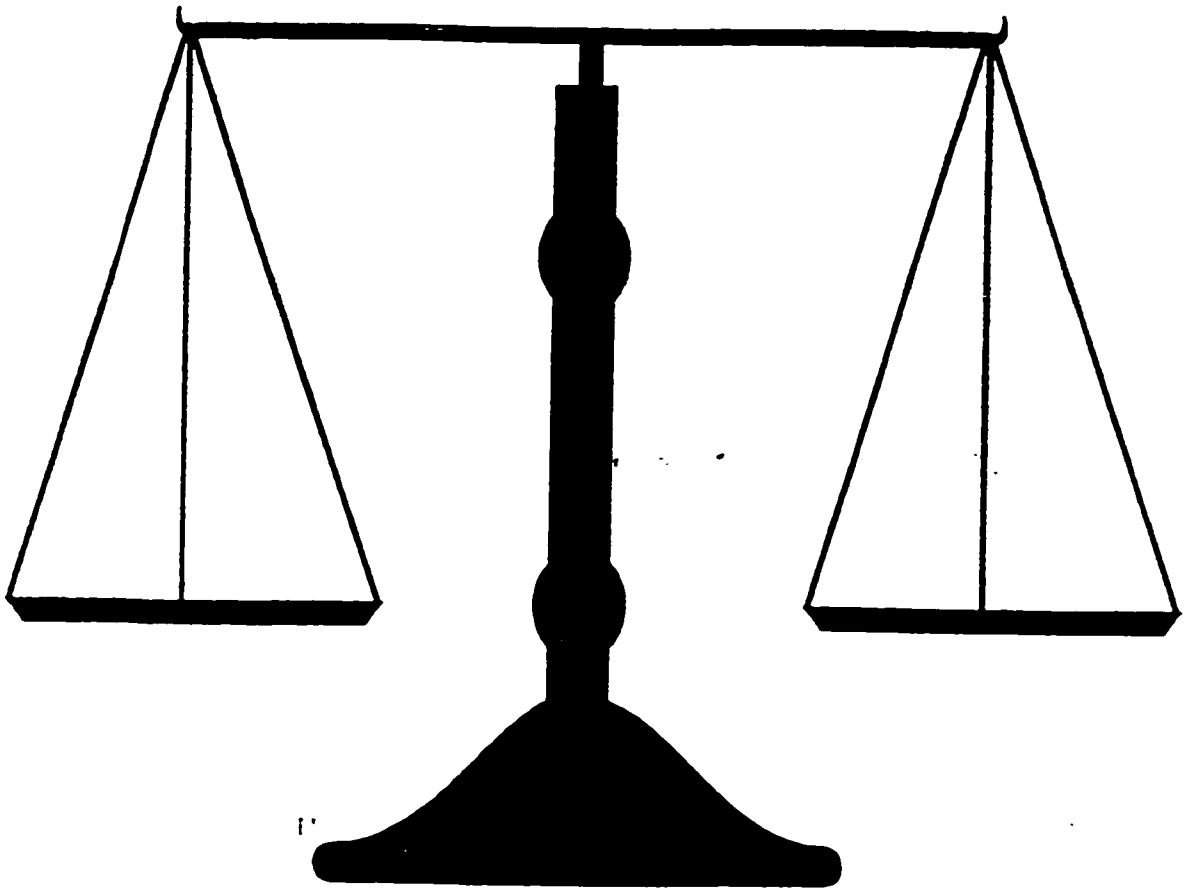


Because high blood pressure is a lifelong condition, most people will have to continue taking these pills for the rest of their life. These pills are usually taken once or twice a day.

Careful studies in thousands of patients have shown that most people don't feel any different when taking the pills and can still do their normal activities. Of every 100 people who take these pills, 7 have to stop because of side-effects (such as fatigue, difficulty sleeping, impotence, leg cramps, or minor abnormalities in the blood sodium or potassium). The other 93 people do not have any side effects from the pills. These side-effects usually disappear within two weeks after stopping the pills. Blood pressure-lowering pills cost about $30 per month, but are covered by most drug plans.

SUMMARY

Taking blood pressure-lowering medication has:



ADVANTAGES

-reduced chance of stroke or heart attack

DISADVANTAGES

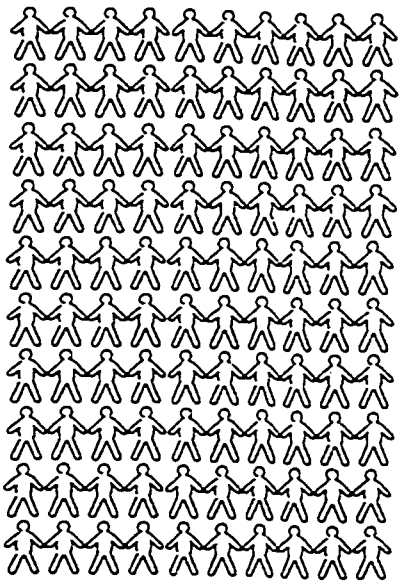
-inconvenience (take every day)
-side effects
-cost

Now its time to consider how much benefit you think you would want before taking the medication every day.

In this section, we will present a series of IMAGINARY situations and ask you to make a choice about whether you would want to take a blood pressure-lowering medication based on its advantages and disadvantages. These situations are imaginary and the same scenarios are being given to all of the people involved in this study.

Remember, this is not a test and there are no right or wrong answers. We are interested in your opinion. You can look at the Information charts from Part 2 and ask the interviewer questions to clarify any points.

We will use 100 stick figures to show the chances of different things happening.

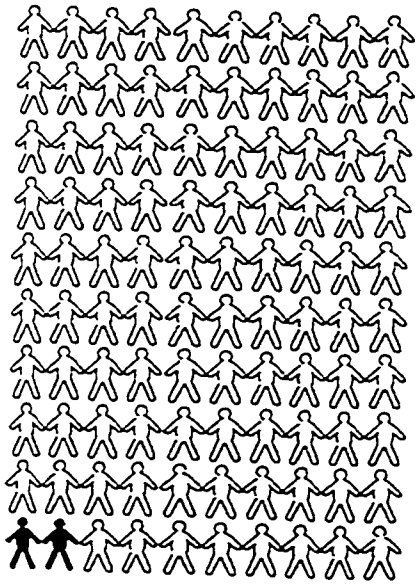
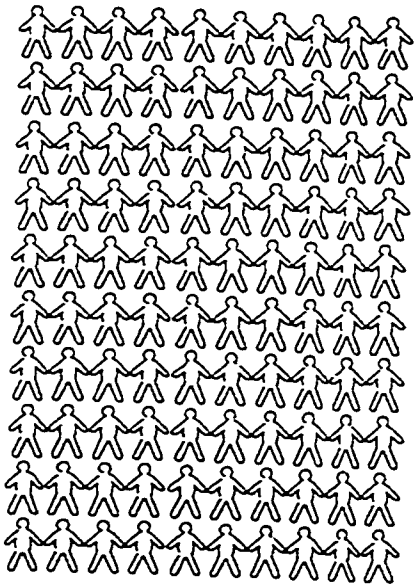


Scenario 1

Now, imagine that your risk of having a heart attack or stroke **in the next five years is 2%.** If you take a blood pressure-lowering medication every day for five years, you can reduce your chance of having a heart attack or stroke. You have two choices:

NO MEDICATION	MEDICATION
No inconvenience No side effects No cost	Take daily for five years May have side effects Costs about $30 per month

OUTCOMES IN NEXT FIVE YEARS

NO MEDICATION	MEDICATION
You have an **2%** risk of having a heart attack or stroke	You have a __% risk of having a heart attack or stroke
	
This means there is a 98% chance that you will not have a heart attack or stroke	This means there is a --% chance that you will not have a heart attack or stroke

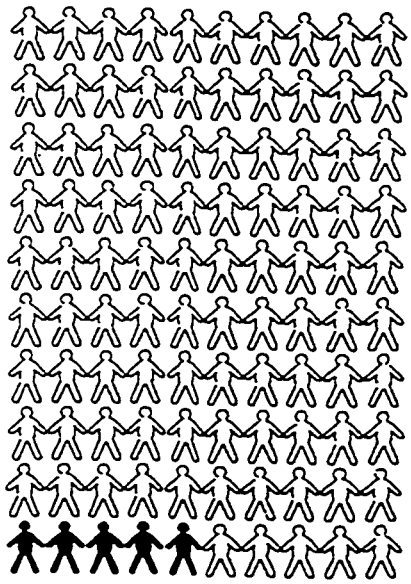
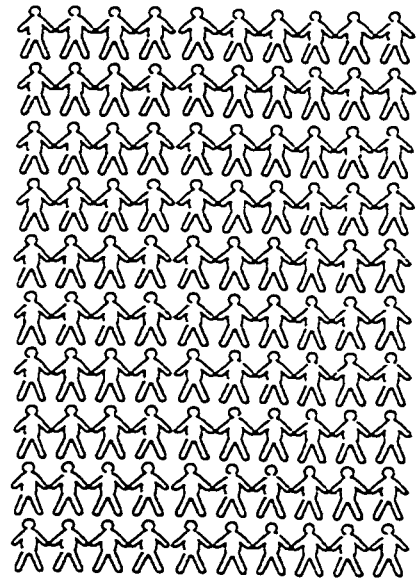
WOULD YOU TAKE THE MEDICATION?

Scenario 2

Now, imagine that your risk of having a heart attack or stroke **in the next five years is 5%.** If you take a blood pressure-lowering medication every day for five years, you can reduce your chance of having a heart attack or stroke. You have two choices:

NO MEDICATION	MEDICATION
No inconvenience No side effects No cost	Take daily for five years May have side effects Costs about $30 per month

OUTCOMES IN NEXT FIVE YEARS

NO MEDICATION	MEDICATION
You have a **5%** risk of having a heart attack or stroke	You have a ___% risk of having a heart attack or stroke
	
This means there is an 95% chance that you will not have a heart attack or stroke	This means there is a –% chance that you will not have a heart attack or stroke

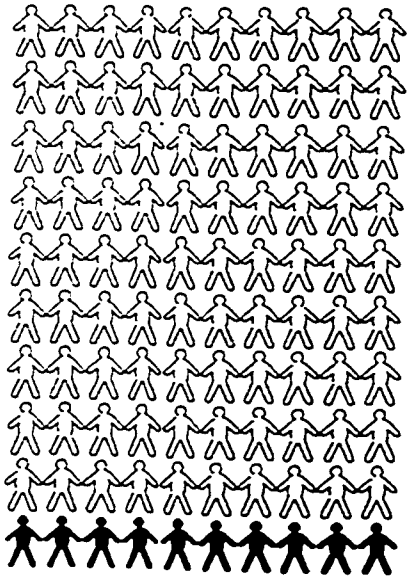
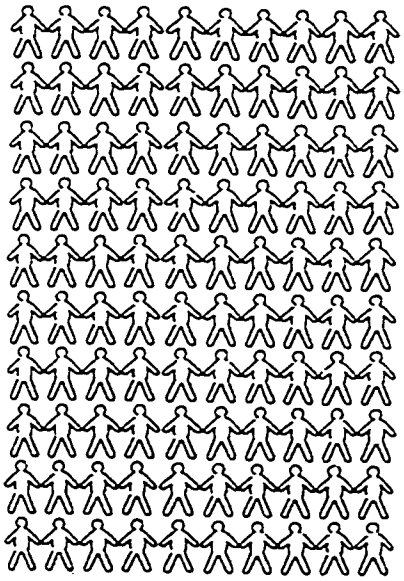
WOULD YOU TAKE THE MEDICATION?

Scenario 3

Now, imagine that your risk of having a heart attack or stroke **in the next five years is 10%.** If you take a blood pressure-lowering medication every day for five years, you can reduce your chance of having a heart attack or stroke. You have two choices:

NO MEDICATION	MEDICATION
No inconvenience No side effects No cost	Take daily for five years May have side effects Costs about $30 per month

OUTCOMES IN NEXT FIVE YEARS

NO MEDICATION	MEDICATION
You have an **10%** risk of having a heart attack or stroke	You have a __% risk of having a heart attack or stroke
	
This means there is a 90% chance that you will not have a heart attack or stroke	This means there is a --% chance that you will not have a heart attack or stroke

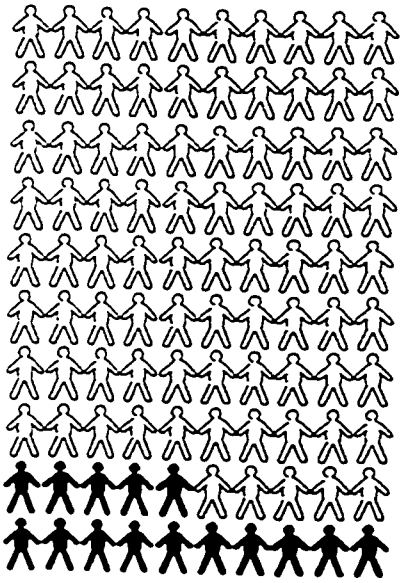
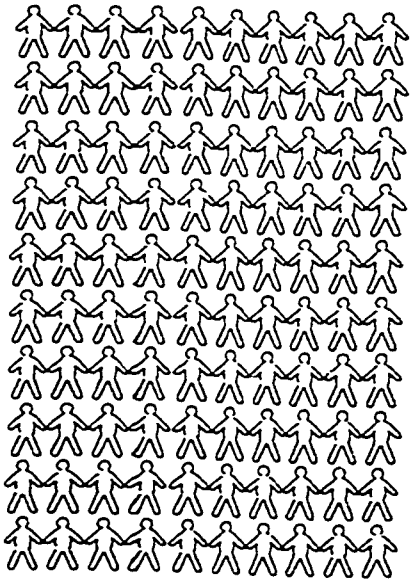
WOULD YOU TAKE THE MEDICATION?

Scenario 4

Now, imagine that your risk of having a heart attack or stroke **in the next twenty years is 15%.** If you take a blood pressure-lowering medication every day for twenty years, you can reduce your chance of having a heart attack or stroke. You have two choices:

NO MEDICATION	MEDICATION
No inconvenience No side effects No cost	Take daily for twenty years May have side effects Costs about $30 per month

OUTCOMES IN NEXT TWENTY YEARS

NO MEDICATION	MEDICATION
You have a **15%** risk of having a heart attack or stroke	You have a __% risk of having a heart attack or stroke
	
This means there is a 85% chance that you will not have a heart attack or stroke	This means there is a –% chance that you will not have a heart attack or stroke

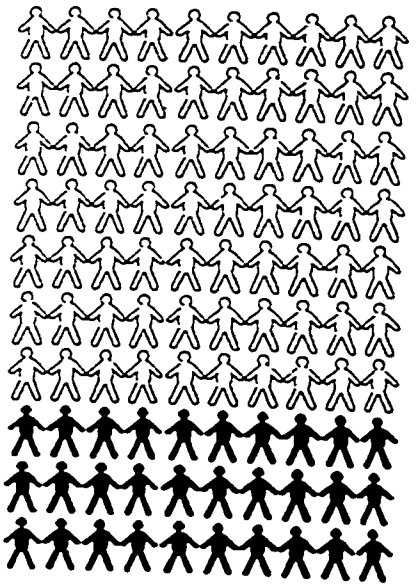
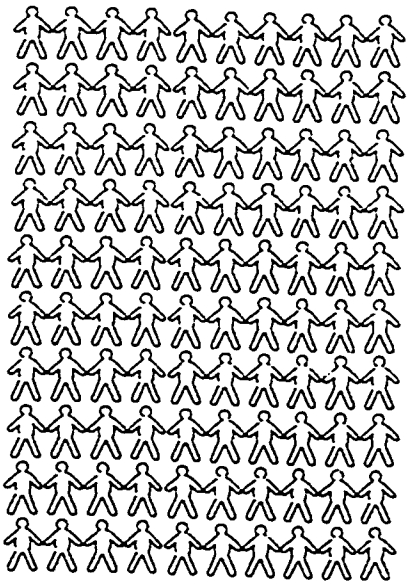
WOULD YOU TAKE THE MEDICATION?

Scenario 5

Now, imagine that your risk of having a heart attack or stroke **in the next twenty years is 30%.** If you take a blood pressure-lowering medication every day for twenty years, you can reduce your chance of having a heart attack or stroke. You have two choices:

NO MEDICATION	MEDICATION
No inconvenience No side effects No cost	Take daily for twenty years May have side effects Costs about $30 per month

OUTCOMES IN NEXT TWENTY YEARS

NO MEDICATION	MEDICATION
You have a **30%** risk of having a heart attack or stroke in the next twenty years.	You have a __% risk of having a heart attack or stroke in the next twenty years.
	
This means there is a 70% chance that you will not have a heart attack or stroke	This means there is a –% chance that you will not have a heart attack or stroke

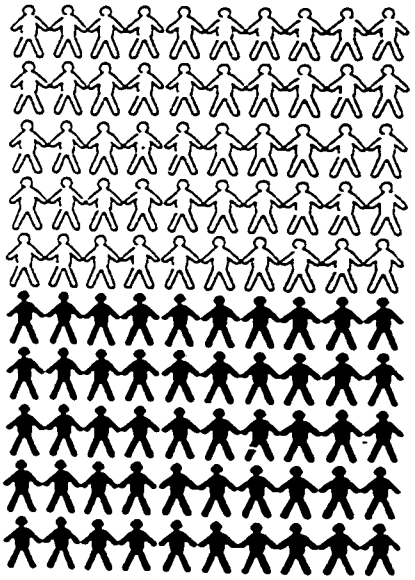
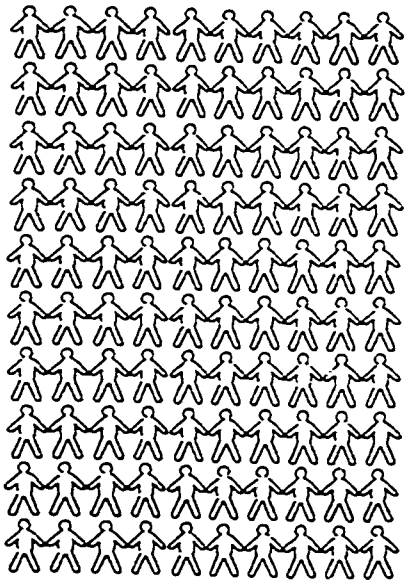
WOULD YOU TAKE THE MEDICATION?

Scenario 6

Now, imagine that your risk of having a heart attack or stroke **in the next twenty years is 50%.** If you take a blood pressure-lowering medication every day for twenty years, you can reduce your chance of having a heart attack or stroke. You have two choices:

NO MEDICATION	MEDICATION
No inconvenience No side effects No cost	Take daily for twenty years May have side effects Costs about $30 per month

OUTCOMES IN NEXT TWENTY YEARS

NO MEDICATION	MEDICATION
You have a **50%** risk of having a heart attack or stroke in the next twenty years.	You have a __% risk of having a heart attack or stroke in the next twenty years.
	
This means there is a 50% chance that you will not have a heart attack or stroke	This means there is a –% chance that you will not have a heart attack or stroke

WOULD YOU TAKE THE MEDICATION?

APPENDIX B- PHYSICIAN SURVEY

Note that although this is the female version of the questionnaire, physician participants were randomized to one of two different forms of the survey- one in which all scenarios were male and one in which all scenarios were female (although the absolute risks described were the same in both versions).

Thank you for agreeing to participate in this research study. This questionnaire is divided into three parts. In the first section, I will ask a number of questions about you which will allow us to analyze your answers with those of your peer group. All of your answers will be kept strictly confidential.

In the second part of the questionnaire, I will describe the implications of a myocardial infarction or stroke in hypertensive patients.

In the third part of the questionnaire, I will present six hypothetical scenarios and ask your opinion about whether or not you would prescribe an antihypertensive medication in each situation. From this information, we will be able to incorporate your opinions more effectively into subsequent clinical practice guidelines.

PART 1

1. What is the year of your birth? 19___

2. Are you ☐ female or ☐ male?

3. When did you graduate from medical school? 19___

4. How many years of post-graduate training did you complete?____ years

5. How would you describe your clinical practice?

   ☐ General/Family physician, solo practice
   ☐ General/Family physician, group practice
   ☐ General Internist, solo practice
   ☐ General Internist, group practice
   ☐ Other (please specify:_____)

6. Are you affiliated with a hospital? ☐ No ☐ Yes

7. Do you have an academic appointment at a university? ☐ No ☐ Yes

8. On average, do you spend at least 25% of your work week in direct patient care?
   ☐ No
   ☐ Yes

9. Do you care for patients with hypertension?

   ☐ Yes **(Please proceed to question 10 and the remainder of the questionnaire)**
   ☐ No **(Please stop here and terminate the interview. Thank-you for your participation)**

10. On average, how many patients with hypertension do you see per month?

    ____ patients

PART 2: BACKGROUND INFORMATION

1) Stroke

Review of the literature reveals the following prognosis for a patient suffering a stroke:

20% die within the first month
30% are unable to attend to their basic ADLs and require placement in a long-term care facility
20% need some help with basic ADLs but will be able to return home
30% recover and will be able to live at home independently

2) Myocardial Infarction

Review of the literature reveals the following prognosis for a patient suffering a myocardial infarction:

50% die within the first month
25% recover completely to lead a normal life
25% will be left with dyspnea or angina with varying degrees of exertion

3) Antihypertensive Medications:

Randomized clinical trials have revealed that patient quality of life is generally not adversely affected by antihypertensive therapy. For the scenarios following, we would request that you consider that the incidence of side effects is identical no matter which antihypertensive agent you were to prescribe. For the purposes of this study, please assume that **7%** of patients on antihypertensive therapy have minor side effects which resolve when the medication is discontinued (such as fatigue, insomnia, impotence, leg cramps, or hyponatremia/hypokalemia) and < 1% suffer serious adverse effects (such as hypersensitivity reactions, renal failure, or idiosyncratic drug reactions). In other words, 93% of patients taking antihypertensive therapy suffer no side effects.

PART 3: HYPOTHETICAL SCENARIOS

This questionnaire contains six hypothetical scenarios and asks you to make choices about whether you would, or would not, prescribe an antihypertensive drug to each patient based on that patient's risk of cardiovascular disease.

This is not a test. There are no right or wrong answers. We are only interested in eliciting your opinion.

For each scenario, please assume that non-pharmacologic therapy had no impact and that you had to decide whether to start an antihypertensive medication. Knowing that antihypertensives vary in their degree of efficacy, we are interested in determining the amount of benefit from treatment that you think warrants prescribing antihypertensive treatment.

Each scenario presents a woman of identical age, social history, and blood pressure. The only differences between the scenarios are the combination of atherosclerotic risk factors in each patient, and therefore her predicted risk of heart attack or stroke.

Scenario 1

ID: 46 year old female
Social History: accountant with two children
BP: average 150/95 mm Hg on four visits over six months

If her predicted risk of cardiovascular disease (stroke or heart attack) is **2%** in the next **FIVE YEARS** without treatment, in which of these situations would you prescribe medication?

Situation	Five Year Risk of Cardiovascular Disease		Prescribe Medication?	
	Without Antihypertensive Medication	With Antihypertensive Medication	Yes	No
a	2 %	2 %	☐	☐
b	2 %	1 %	☐	☐
c	2 %	0 %	☐	☐

Scenario 2

ID: 46 year old female
Social History: accountant with two children
BP: average 150/95 mm Hg on four visits over six months

If her predicted risk of cardiovascular disease (stroke or heart attack) is **5%** in the next **FIVE YEARS** without treatment, in which of these situations would you prescribe medication?

Situation	Five Year Risk of Cardiovascular Disease		Prescribe Medication?	
	Without Antihypertensive Medication	With Antihypertensive Medication	Yes	No
a	5 %	5 %	☐	☐
b	5 %	4 %	☐	☐
c	5 %	3 %	☐	☐
d	5 %	2 %	☐	☐
e	5 %	1 %	☐	☐
f	5 %	0 %	☐	☐

Scenario 3

ID: 46 year old female
Social History: accountant with two children
BP: average 150/95 mm Hg on four visits over six months

If her predicted risk of cardiovascular disease (stroke or heart attack) is **10%** in the next **FIVE YEARS** without treatment, in which of these situations would you prescribe medication?

Situation	Five Year Risk of Cardiovascular Disease		Prescribe Medication?	
	Without Antihypertensive Medication	With Antihypertensive Medication	Yes	No
a	10 %	9 %	☐	☐
b	10 %	8 %	☐	☐
c	10 %	7 %	☐	☐
d	10 %	6 %	☐	☐
e	10 %	5 %	☐	☐
f	10 %	4 %	☐	☐
g	10 %	3 %	☐	☐
h	10 %	2 %	☐	☐
i	10 %	1 %	☐	☐
j	10 %	0 %	☐	☐

SCENARIO 4

ID: 46 year old female
Social History: accountant with two children
BP: average 150/95 mm Hg on four visits over six months

If her predicted risk of cardiovascular disease (stroke or heart attack) is **15 %** in the next **TWENTY YEARS** without treatment, in which of these situations would you prescribe medication?

Situation	Twenty Year Risk of Cardiovascular Disease		Prescribe Medication?	
	Without Antihypertensive Medication	With Antihypertensive Medication	Yes	No
a	15 %	14 %	☐	☐
b	15 %	13 %	☐	☐
c	15 %	12 %	☐	☐
d	15 %	11 %	☐	☐
e	15 %	10 %	☐	☐
f	15 %	9 %	☐	☐
g	15 %	8 %	☐	☐
h	15 %	7 %	☐	☐
i	15 %	6 %	☐	☐
j	15 %	5 %	☐	☐
k	15 %	4 %	☐	☐
l	15 %	3 %	☐	☐
m	15 %	2 %	☐	☐
n	15 %	1 %	☐	☐
o	15 %	0 %	☐	☐

SCENARIO 5

ID: 46 year old female
Social History: accountant with two children
BP: average 150/95 mm Hg on four visits over six months

If her predicted risk of cardiovascular disease (stroke or heart attack) is **30%** in the next **TWENTY YEARS** without treatment, in which of these situations would you prescribe medication?

Situation	Twenty Year Risk of Cardiovascular Disease		Prescribe Medication?	
	Without Antihypertensive Medication	With Antihypertensive Medication	Yes	No
a	30 %	29 %	☐	☐
b	30 %	28 %	☐	☐
c	30 %	27 %	☐	☐
d	30 %	26 %	☐	☐
e	30 %	25 %	☐	☐
f	30 %	24 %	☐	☐
g	30 %	23 %	☐	☐
h	30 %	22 %	☐	☐
i	30 %	21 %	☐	☐
j	30 %	20 %	☐	☐
k	30 %	19 %	☐	☐
l	30 %	18 %	☐	☐
m	30 %	17 %	☐	☐
n	30 %	16 %	☐	☐
p	30 %	15 %	☐	☐
q	30 %	14 %	☐	☐
r	30 %	13 %	☐	☐
s	30 %	12 %	☐	☐
t	30 %	11 %	☐	☐
u	30 %	10 %	☐	☐
v	30 %	9 %	☐	☐
w	30 %	8 %	☐	☐
x	30 %	7 %	☐	☐
y	30 %	6 %	☐	☐
z	30 %	5 %	☐	☐
aa	30 %	4 %	☐	☐
ab	30 %	3 %	☐	☐
ac	30 %	2 %	☐	☐
ad	30 %	1 %	☐	☐
ae	30 %	0 %	☐	☐

SCENARIO 6

ID: 46 year old female
Social History: accountant with two children
BP: average 150/95 mm Hg on four visits over six months

If her predicted risk of cardiovascular disease (stroke or heart attack) is **50%** in the next **TWENTY YEARS** without treatment, in which of these situations would you prescribe medication?

Situation	Twenty Year Risk of Cardiovascular Disease		Prescribe Medication?	
	Without Antihypertensive Medication	With Antihypertensive Medication	Yes	No
a	50%	49%	☐	☐
b	50%	48%	☐	☐
c	50%	47%	☐	☐
d	50%	46%	☐	☐
e	50%	45%	☐	☐
f	50%	44%	☐	☐
g	50%	43%	☐	☐
h	50%	42%	☐	☐
i	50%	41%	☐	☐
j	50%	40%	☐	☐
k	50%	39%	☐	☐
l	50%	38%	☐	☐
m	50%	37%	☐	☐
n	50%	36%	☐	☐
p	50%	35%	☐	☐
q	50%	34%	☐	☐
r	50%	33%	☐	☐
s	50%	32%	☐	☐
t	50%	31 %	☐	☐
u	50%	30 %	☐	☐
v	50%	29 %	☐	☐
w	50%	28 %	☐	☐
x	50%	27 %	☐	☐
y	50%	26 %	☐	☐
z	50%	25 %	☐	☐
aa	50%	24 %	☐	☐
ab	50%	23 %	☐	☐
ac	50%	22 %	☐	☐
ad	50%	21 %	☐	☐
ae	50%	20 %	☐	☐
af	50%	19 %	☐	☐
ag	50%	18 %	☐	☐
ah	50%	17 %	☐	☐
ai	50%	16 %	☐	☐
aj	50%	15 %	☐	☐
ak	50%	14 %	☐	☐
al	50%	13 %	☐	☐
am	50%	12 %	☐	☐
an	50%	11 %	☐	☐
ao	50%	10 %	☐	☐
ap	50%	9 %	☐	☐
aq	50%	8 %	☐	☐
ar	50%	7 %	☐	☐
as	50%	6 %	☐	☐
at	50%	5 %	☐	☐
au	50%	4 %	☐	☐
av	50%	3 %	☐	☐
aw	50%	2 %	☐	☐
ax	50%	1 %	☐	☐
ay	50%	0 %	☐	☐

APPENDIX C- PATIENT INTERVIEW SCRIPT

1. **Get study subject to sign consent form.**
2. **Get the study subject to read the yellow information pages and fill out the second page of the yellow sheets- the personal information.**
3. **Proceed to the six hypothetical scenarios, in the order appropriate to subject's randomization number, using the following text:**

Now, imagine that researchers are able to develop a blood test which would be able to accurately predict your risk of a heart attack or stroke. (we don't have such a test yet)

Scenario 1:

If this blood test showed that you had a 2% risk of having a heart attack or stroke in the next five years, I want you to consider these options.

1) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 2% (so a 98% chance you would be okay).

   If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be zero.

   Would you take blood pressure lowering medication in this situation?
   (if says no, stop this scenario here and record 999 on the data collection sheet for this scenario)
   (if says yes, continue to #2)

2) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 2% (so a 98% chance you would be okay).

   If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 1%.

   Would you take blood pressure lowering medication in this situation?
   (if says no, stop this scenario here and record 2 on the data collection sheet for this scenario)
   (if says yes, continue to #3)

3) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 2% (so a 98% chance you would be okay).

   If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 2%.

Would you take blood pressure lowering medication in this situation?
(if says no, stop this scenario here and record 1 on the data collection sheet for this scenario)
(if says yes, record 0 on the data collection sheet for this scenario)

REMEMBER THAT THE NUMBER YOU RECORD ON THE DATA COLLECTION SHEET IS THE MCID (THE SMALLEST AMOUNT OF BENEFIT THAT THE SUBJECT FEELS WOULD JUSTIFY TAKING THE MEDICATION). THUS, IT IS CALCULATED BY SUBTRACTING "THE SMALLEST AMOUNT OF BENEFIT THEY SAY YES TO" FROM THE BASELINE RISK.

-eg: if they say yes they would take treatment if it lowered risk from 2 to 0, but no if it reduced risk from 2 to 1, the MCID is 2.

-eg: if they say yes they would take treatment if it lowered risk from 5 to 1, but not if it reduced risk from 5 to 2, the MCID is 4.

Scenario 2:

Now, if this blood test showed that you had a 5% risk of having a heart attack or stroke in the next five years, I want you to consider these options.

1) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 5% (so a 95% chance you would be okay).

   If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be zero.

   Would you take blood pressure lowering medication in this situation?
   (if says no, stop this scenario here and record 999 on the data collection sheet for this scenario)
   (if says yes, continue to #2)

2) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 5% (so a 95% chance you would be okay).

   If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 1%.

   Would you take blood pressure lowering medication in this situation?
   (if says no, stop this scenario here and record 5 on the data collection sheet for this scenario)
   (if says yes, continue to #3)

3) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 5% (so a 95% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 2%.

Would you take blood pressure lowering medication in this situation?
(if says no, stop this scenario here and record 4 on the data collection sheet for this scenario)
(if says yes, continue to #4)

4) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 5% (so a 95% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 3%.

Would you take blood pressure lowering medication in this situation?
(if says no, stop this scenario here and record 3 on the data collection sheet for this scenario)
(if says yes, continue to #5)

5) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 5% (so a 95% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 4%.

Would you take blood pressure lowering medication in this situation?
(if says no, stop this scenario here and record 2 on the data collection sheet for this scenario)
(if says yes, continue to #6)

6) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 5% (so a 95% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 5%.

Would you take blood pressure lowering medication in this situation?
(if says no, stop this scenario here and record 1 on the data collection sheet for this scenario)
(if says yes, stop this scenario here and record 0 on the data collection sheet for this scenario)

(same technique is used for scenarios 3 to 6. In those scenarios, because you are dealing with much larger numbers, it is easier to jump by 5 at a time and then narrow it down after they switch

from yes to no. One way that scenario 6 could go is outlined below as an example).

Scenario 6 (example only- exact sequence will depend on subject's responses):

Now, if this blood test showed that you had a 50% risk of having a heart attack or stroke in the next twenty years, I want you to consider these options.

1) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 50% (so a 50% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be zero.

Would you take blood pressure lowering medication in this situation?
(if says no, stop this scenario here and record 999 on the data collection sheet for this scenario)
(if says yes, continue to #2)

2) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 50% (so a 50% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 5%.

Would you take blood pressure lowering medication in this situation?
(if says no, continue to 2a)
(if says yes, continue to #3)

2a) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 50% (so a 50% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 1%.

Would you take blood pressure lowering medication in this situation?
(if says no, stop this scenario here and record 50 on the data collection sheet for this scenario)
(if says yes, continue to #2b)

2b) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 50% (so a 50% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 2%.

Would you take blood pressure lowering medication in this situation?
(if says no, stop this scenario here and record 49 on the data collection sheet for this scenario)

(if says yes, continue to #2c)

2c) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 50% (so a 50% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 3%.

Would you take blood pressure lowering medication in this situation?
(if says no, stop this scenario here and record 48 on the data collection sheet for this scenario)
(if says yes, continue to #2d)

2d) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 50% (so a 50% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 4%.

Would you take blood pressure lowering medication in this situation?
(if says no, stop this scenario here and record 47 on the data collection sheet for this scenario)
(if says yes, continue to #2e)

2e) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 50% (so a 50% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 5%.

Would you take blood pressure lowering medication in this situation?
(if says no, stop this scenario here and record 46 on the data collection sheet for this scenario)
(can't say yes as already said no to this option in #2 of this scenario)

3) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 50% (so a 50% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 10%.

Would you take blood pressure lowering medication in this situation?
(if says no, continue to 3a)
(if says yes, continue to #4)

3a-3e) Exactly the same as 2a-2e, only the numbers with treatment would change (ex. 50% vs. 6% rather than 50% vs. 1%, 50% vs. 7% rather than 50% vs. 2%, etc.)

4) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 50% (so a 50% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 15%.

Would you take blood pressure lowering medication in this situation?
(if says no, continue to 4a)
(if says yes, continue to #5)

4a-4e) Exactly the same as 2a-2e, only the numbers with treatment would change (ex. 50% vs. 11% rather than 50% vs. 1%, 50% vs. 12% rather than 50% vs. 2%, etc.)

5) If you didn't take a blood pressure lowering medication, your risk of a heart attack or stroke would be 50% (so a 50% chance you would be okay).

If you did take a blood pressure lowering medication, (which you would have to take every day, which would have a chance of side effects as outlined in the yellow pages, and which would cost about $30 per month) your risk of a heart attack or stroke would be 20%.

Would you take blood pressure lowering medication in this situation?
(if says no, continue to 5a)
(if says yes, continue to #6)

5a-5e) Exactly the same as 2a-2e, only the numbers with treatment would change (ex. 50% vs. 16% rather than 50% vs. 1%, 50% vs. 17% rather than 50% vs. 2%, etc.)

AND SO ON FOR THE REST OF THE SCENARIO

APPENDIX D- MCID DATA COLLECTION FORM

ID # ____

SCENARIO	MCID
1 (2% in 5 yrs)	
2 (5% in 5 yrs)	
3 (10% in 5 yrs)	
4 (15% in 20 yrs)	
5 (30% in 20 yrs)	
6 (50% in 20 yrs)	

APPENDIX E- PHYSICIAN CALLING RECORD FORM

ID # _____ Telephone # _____

Hello, my name is Dr. McAlister. I'm calling from the Ottawa Civic Hospital. May I please speak to Dr. xxxxxxx?

If the receptionist asks for more information:

(if faxed back consent form):
The Clinical Epidemiology Unit at the Ottawa Civic Hospital is conducting a survey to identify the opinions of family physicians about the treatment of hypertension. Dr. xxxxxx agreed to participate and asked that I call at this time to do the interview. The whole interview takes about 15 minutes. Is now a good time or would Dr. xxxxxx like to reschedule the appointment?

OR *(if didn't fax back a consent form):*
The Clinical Epidemiology Unit at the Ottawa Civic Hospital is conducting a survey to identify the opinions of family physicians about the treatment of hypertension. Dr. xxxxxx should have received a letter outlining the purpose of this survey within the past few weeks. The whole interview takes about 15 minutes. Is now a good time or would Dr. xxxxxx like to make an appointment for an interview?

When speaking to the physician:

(if faxed back consent form):
Hello Dr. xxxxxx, my name is Dr. McAlister. I'm calling from the Clinical Epidemiology Unit at the Ottawa Civic Hospital. I would like to ask you a few questions about the treatment of hypertension. Do you remember receiving a letter a couple of weeks ago about this study?

OR *(if didn't fax back a consent form):*
Hello Dr. xxxxxx, my name is Dr. McAlister. I'm calling from the Clinical Epidemiology Unit at the Ottawa Civic Hospital. I would like to ask you a few questions about the treatment of hypertension. Did you receive a letter about our survey?

If yes, proceed with the following:

The interview takes about 15 minutes to complete. Is now a good time or would you like me to call back at a more convenient time?

If no, proceed with the following:

The Clinical Epidemiology Unit at the Ottawa Civic Hospital is conducting a telephone survey to determine the opinions of practising physicians about the use of antihypertensive therapy. In particular, we are interested in eliciting the treatment thresholds you think are reasonable in six hypothetical scenarios.

The survey takes about 15 minutes to do and your participation is entirely voluntary. Aside from the interview itself, your identity will be kept completely confidential. Would you be able to talk for about 15 minutes now or would another time be more convenient?

EITHER PROCEED WITH INTERVIEW OR FILL IN CHART BELOW.

RECORD OF CALLS CHART

ID# ____ Telephone #_____

Attempt #	Time, date of call	Notes
1		
2		
3		
4		
5		

☐ Unable to contact after 5 tries

☐ Refusal (Reason:_____)

APPENDIX F- SAMPLE SIZE TABLES

Sample size (per group), for a two-tailed α of 0.05

Standardized Effect Size*	β = 0.05	β = 0.10	β = 0.20
0.5	104	84	63
0.6	**72**	**58**	**44**
0.7	**53**	**43**	**32**
0.8	41	33	25
0.9	32	26	19

* Standardized Effect Size= Expected Effect Size / Standard Deviation

Note that smallest expected effect size, by design, will be 1 (and standard deviation is estimated as 1.60).

APPENDIX G- PHYSICIAN INFORMATION SHEET AND CONSENT FORM

COVER LETTER TO PHYSICIANS

January 1998

Dr. xx
(Address)

Dear Dr. xx,

As you know, hypertension is one of the most common conditions dealt with by family physicians. Multiple organizations have produced clinical practice guidelines for the management of hypertension; unfortunately, many of these guidelines disagree on exactly who should be treated. To this point in time, treatment thresholds have been chosen by "expert consensus" involving only a handful of academic physicians. We believe that hypertension guidelines should attempt to incorporate the views of a much larger number of people, including community-based general physicians, patients, and the public at large.

As a first step, the Clinical Epidemiology Unit at the Loeb Research Institute is conducting a telephone survey to determine the opinions of practising physicians about the use of antihypertensive therapy. In particular, we are interested in eliciting the treatment thresholds you think are reasonable in six hypothetical scenarios. The telephone survey takes about 15 minutes to complete and will be conducted between January, 1998 and March, 1998.

We are writing to ask for your help with this survey. Your name was picked through a computer generated random sample of all family physicians in Ottawa-Carleton. This study is entirely voluntary and you are under no obligation to participate. Your identity will only be known at the time of the interview but otherwise is strictly confidential and will not appear in any reports or documents. Since we are interested in your opinions, you do not need to consult any reference material before the interview. If you would like to make an appointment, please complete the attached consent form and return it to 761-5351 (fax) or Dr. F. McAlister, Clinical Epidemiology Unit, Ottawa Civic Hospital, 1053 Carling Avenue, Ottawa, K1Y 4E9. If you are unable to participate or have any questions, please contact Dr. Finlay McAlister at 798-5555, extension 8763.

Your assistance is greatly appreciated and will hopefully help shape future hypertension guidelines. We look forward to speaking with you soon.

Yours sincerely,

Finlay McAlister, MD FRCPC

CONSENT FORM- PHYSICIANS

"An evaluation of minimal clinically important differences for the initiation of antihypertensive therapy from the perspective of Canadian patients and physicians"

The minimal clinically important difference (MCID) represents the smallest difference in benefit of a therapy that would result in a change in a patient's management. In other words, the point at which the benefits of a therapy outweigh the risks. We think it is crucial to determine the MCID of Canadian physicians for the initiation of antihypertensive therapy so that this information can be used in the next set of hypertension guidelines to set treatment thresholds.

The Clinical Epidemiology Unit at the Ottawa Civic Hospital is conducting a research study to determine the MCID of practising physicians for the initiation of antihypertensive therapy. The study involves a brief telephone survey to determine family physicians' opinions about when antihypertensive therapy should be prescribed in six hypothetical scenarios. Interviews will be conducted between January 1998 and March 1998 and will take approximately 15 minutes to complete.

We are asking you to participate as your name was picked through a computer generated random sample of all family physicians in Ottawa-Carleton. This study is entirely voluntary and you are under no obligation to participate. Your identity will only be known at the time of the interview but otherwise is strictly confidential and will not appear in any reports or documents.

We will provide a copy of the results of this study to you if you desire. All information collected will be held in the strictest confidence and any discussion of the results will be about the aggregate results from all participants and will not single out any one individual.

If you have any questions, please contact Dr. Finlay McAlister at 798-5555 (ext. 8763). If you agree to participate in this study, please sign below and indicate what times of the week would be best for you to be called by Dr. McAlister. Thank you for your consideration of this study.

Signature: _____

Name: _____

Date: _____

Best time to call me is: **Day:** _____ **Time:** _____

APPENDIX H- PATIENT INFORMATION SHEET

"An evaluation of minimal clinically important differences for the initiation of antihypertensive therapy from the perspective of Canadian patients and physicians"

This research study is being done in an effort to determine the opinion of people with high blood pressure about when treatment (blood pressure lowering medication) should be started. The information from this study will be very important for helping doctors develop guidelines about treating high blood pressure which take into account the opinions of patients.

We are asking you to participate because you have high blood pressure. You are under no obligation to participate, and you may withdraw from the study at any time and for any reason. Choosing to participate or not to participate will in no way affect the care you receive from your physicians.

If you choose to participate, this study involves a 30-45 minute interview with a member of the study team. We will ask you for your opinion about blood pressure lowering medications and present six imaginary situations and ask whether you would want to take blood pressure lowering medication in each case. We will provide a copy of the results of your interview to you if you desire. All information collected will be held in the strictest confidence and will not be released to your physicians. Any discussion of the results will be about the total results from all volunteers and will not single out any one individual.

If you are interested in volunteering for this study, please fill out the information below, sign this form, and return it to your physician. They will forward the form to Dr. Finlay McAlister and he will contact you within a few days to discuss the study in more depth.

Name (please print): _____

Telephone Number: _____

Signature: _____

Witness: _____
Date: _____

(Valid until October 10, 1998)

APPENDIX I- PATIENT CONSENT FORM

"An evaluation of minimal clinically important differences for the initiation of antihypertensive therapy from the perspective of Canadian patients and physicians"

This research study is being done in an effort to determine the opinion of people with high blood pressure about when treatment (blood pressure lowering medication) should be started. The information from this study will be very important for helping doctors develop guidelines about treating high blood pressure which take into account the opinions of patients.

We are asking you to participate because you have high blood pressure. You are under no obligation to participate, and you may withdraw from the study at any time and for any reason. Choosing to participate or not to participate will in no way affect the care you receive from your physicians.

If you choose to participate, this study involves a 30-45 minute interview with a member of the study team. We will provide a copy of the results of your interview to you if you desire. All information collected will be held in the strictest confidence and will not be released to your physicians. Any discussion of the results will be about the total results from all volunteers and will not single out any one individual.

If you have any questions, please contact Dr. Finlay McAlister at 798-5555 (ext. 8763). If you agree to participate in this study, please sign below.

Signature: _____

Witness: _____

Date: _____

(Valid until October 10, 1998)

APPENDIX J: SAMPLE LOGISTIC REGRESSION PROCEDURE (PHYSICIAN SCENARIO 1)

Step 1- Choice of variables

Results of bivariate analyses testing the significance of each variable separately against the dependent variable (decision to prescribe antihypertensive therapy) are listed in Table 10.

In addition to those variables which had p values <0.20 on bivariate analysis ("hospital affiliation" and "order of scenarios"), two variables which were believed to be important a priori ("physician age" and "physician gender") were selected for the model. As the variable "order" included 6 different levels, it was dichotomized into "dichotomized order": the 3 orders in which the 5-year scenarios were described first were coded as "1" and the 3 orders in which the 20-year scenarios were presented first were coded as "0". The variable "dichotomized order" was significant on bivariate analysis (Chi-square for trend, p < 0.001).

Step 2- Selection of variables

The forward stewise model was employed with p value-to-enter set at 0.15 and p value-to-remove set at 0.20. The results of the final iteration of this model are displayed below:

Number of cases included in the analysis: 72
Dependent Variable... RXORNO1
Estimation terminated at iteration number 4 because
Log Likelihood decreased by less than .01 percent.

-2 Log Likelihood	77.293
Goodness of Fit	81.220
Cox & Snell - R^2	.209
Nagelkerke - R^2	.287

Classification Table for RXORNO1: Overall 77.78%

Comparing to model containing only the constant term, the Chi-square statistic (G) was:

	Chi-Square	df	Significance
Model	16.891	2	.0002

Variables in the Equation

Variable	B	S.E.	Wald	df	Sig	R	Exp(B)
AFFILIAT	-1.3554	.6706	2.0212	1	.0433	-.1488	.2579
DICHORD	1.8870	.5800	3.2534	1	.0011	.3019	6.5994
Constant	.7533	.6034	1.2484	1	.2119		

---------- Model if Term Removed ----------

Term Removed	Log Likelihood	-2 Log LR	df	Significance of Log LR
AFFILIAT	-40.951	4.609	1	.0318
DICHORD	-44.728	12.163	1	.0005

(Thus, both variables were statistically significant and were included in the model)

---------- Variables not in the Equation ----------

Residual Chi Square 1.279 with 2 df; Sig =.5277

Variable	Score	df	Sig	R
AGE	.8792	1	.3484	.0000
SEX	.2930	1	.5883	.0000

No more variables can be deleted or added.
(Testing of models with "physician age" or "physician gender" entered with "hospital affiliation" and "dichotomized order of scenarios" revealed non-significant likelihood ratio chi square tests: p values were 0.3502 and 0.5870 respectively. Thus, these variables added little to the model).

Thus, the penultimate model is:
g(x)= 0.7533 + 1.8870 ("dichotomized order of scenarios") –1.3554 ("hospital affiliation")

Step 3- Importance of variables in model verified

This was assessed by comparing the final model with a model including only the constant term using the Likelihood Ratio Chi-Square Test.

-2 Log likelihood for model including only the constant term= 94.184
-2 Log likelihood for model including "dichotomized order of scenarios" and "hospital affiliation"= 77.293
G= 16.891
P value= 0.0002

The importance of each variable ("dichotomized order of scenarios" and "hospital affiliation") was also assessed by comparing the estimated coefficient in the penultimate model with that in the univariate model containing only that variable. These were similar (1.8324 vs. 1.8870 for "dichotomized order of scenarios" and –1.2628 vs. –1.3554 for "hospital affiliation").

Step 4- Testing for interaction terms or confounders

To determine whether the excluded variables "physician age" and "physician gender" were important confounders that should be included in the final model,

the estimated coefficients in the penultimate model were compared to those in a full model including all four chosen variables. These were similar (2.0039 vs. 1.8870 for "dichotomized order of scenarios" and –1.3567 vs. –1.3554 for "hospital affiliation"), suggesting that the excluded variables were not important confounders. Thus, they were left out of the final model.

The interaction term "dichotomized order of scenarios" X "hospital affiliation" was created and its significance was tested by comparing the model including the interaction term with the penultimate model outlined above (using the Likelihood Ratio Chi-Square Test). Thus:

Variable(s) entered on Block Number 1:
AFFILIAT
DICHORD
-2 Log Likelihood 77.293

Variable(s) entered on Block Number 2
AFFILIAT
DICHORD
INTERACT
-2 Log Likelihod 74.545

Thus, comparing the two models reveals G=2.748 (p value 0.097).

---------- Variables in the Equation ----------

Variable	B	S.E.	Wald	df	Sig	R	Exp(B)
DICHORD	.2230	1.1068	.2015	1	.8403	.0000	1.2498
AFFILIAT	-2.1972	.8975	2.4481	1	.0144	-.2273	.1111
INTERACT	2.1972	1.3059	1.6825	1	.0925	.1037	8.9998
Constant	1.3863	.7906	1.7535	1	.0795		

The interaction term was not statistically significant and was not biologically meaningful, therefore it was excluded from the final model. Thus, the final logistic regression model for the decision to treat or not for physician scenario 1 is:
g(x)= 0.7533 + 1.8870 ("dichotomized order of scenarios") –1.3554 ("hospital affiliation")

The Hosmer-Lemeshow Goodness of Fit Test gave a Chi-square statistic of 3.19 (p=0.20), suggesting that this model fit the data poorly.

APPENDIX K: SAMPLE MULTIPLE LINEAR REGRESSION PROCEDURE (PHYSICIAN SCENARIO 5)

Step 1- Choice of variables

Results of bivariate analyses testing the significance of each variable separately against the dependent variable (magnitude of specified MCID) are listed in Table 10. In addition to those variables which had p values < 0.20 on bivariate analysis ("hospital affiliation", "academic appointment", "number of hypertensive patients per month", "gender in scenarios", "length of postgraduate training", and "order of scenarios"), two variables which were believed to be important *a priori* ("physician age" and "physician gender") were also selected for the model. As per all the analyses in section 4.7, the variable "dichotomized order" was used in lieu of "order of scenarios".

Step 2- Stepwise selection of variables

The forward stepwise model was employed with F-to-enter set at 0.05 and F-to-remove set at 0.10. The results of the final iteration of this model are displayed below:

Variables Entered:
ACADEMIC
VERSION

Model Summary:

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.256	.066	.052	3.68
2	.348	.121	.095	3.60

1) Predictors: (Constant), ACADEMIC
2) Predictors: (Constant), ACADEMIC, VERSION

ANOVA:

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	66.549	1	66.549	4.911	.030
	Residual	948.562	70	13.551		
	Total	1015.111	71			
2	Regression	122.582	2	61.291	4.738	.012
	Residual	892.529	69	12.935		
	Residual	892.529	69	12.935		
	Total	1015.111	71			
	Total	1015.111	71			

1) Predictors: (Constant), ACADEMIC
2) Predictors: (Constant), ACADEMIC, VERSION

Coefficients:

		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
Model		B	Std. Error	Beta		
1	(Constant)	4.375	.492		8.894	.000
	ACADEMIC	2.313	1.044	.256	2.216	.030
2	(Constant)	3.522	.631		5.578	.000
	ACADEMIC	2.170	1.022	.240	2.124	.037
	VERSION	1.768	.850	.235	2.081	.041

Excluded Variables:

		Beta In	t	Sig.	Partial Correlation	Collinearity Statistics
Model						Tolerance
1	AGE	.059	.506	.615	.061	.987
	SEX	-.045	-.380	.705	-.046	.977
	AFFILIAT	.186	1.519	.133	.180	.874
	NOPTS	.185	1.617	.110	.191	.999
	VERSION	.235	2.081	.041	.243	.996
	POSTGR	-.232	-2.030	.046	-.237	.978
	DICHORD	-.154	-1.335	.186	-.159	.996
2	AGE	.073	.642	.523	.078	.984
	SEX	-.020	-.172	.864	-.021	.966
	AFFILIAT	.176	1.472	.146	.176	.873
	NOPTS	.184	1.651	.103	.196	.999
	POSTGR	-.206	-1.819	.073	-.215	.963
	POSTGR	-.206	-1.819	.073	-.215	.963
	DICHORD	-.155	-1.377	.173	-.165	.996

1) Predictors in the Model: (Constant), ACADEMIC
2) Predictors in the Model: (Constant), ACADEMIC, VERSION

Step 3- Importance of variables in model verified

This was assessed by considering the t-test for each of the included variables. As can be seen above, both included variables were statistically significant (p values 0.037 for "academic appointment" and 0.041 for "gender version of questionnaire"). Partial F tests (comparing models with and without the included variables) provided identical results.

Step 4- Testing for interaction terms or confounders

To test for the significance of the interaction term, a partial F test was performed comparing the reduced model (that model without the interaction term) with the

full model (the model including the interaction term) outlined below. Details of the reduced model are given in Step 2; details of the full model follow:

Variables Entered: ACADEMIC, VERSION, ACXVER

Model Summary:

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.354	.126	.087	3.61

1) Predictors: (Constant), ACADEMIC, VERSION, ACXVER

ANOVA:

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	127.406	3	42.469	3.253	.027
	Residual	887.705	68	13.504		
	Total	1015.111	71			

1) Predictors: (Constant), ACADEMIC, VERSION, ACXVER

Coefficients:

		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
Model		B	Std. Error	Beta		
1	(Constant)	3.655	.671		5.448	.000
	ACADEMIC	1.488	1.522	.165	.978	.332
	VERSION	1.493	.966	.199	1.545	.127
	ACXVER	1.253	2.061	.110	.608	.545

The partial F-test results are:

$$F = \frac{\text{regression SS (full model)} - \text{regression SS (reduced model)}}{\text{MS residual (full model)}}$$

$$F = \frac{127.406 - 122.582}{13.504} = 0.3572$$

Given the F distribution with 1 and 68 degrees of freedom, the p value is >0.50. Thus, the interaction term is not significant and can be left out of the final model. An identical result is obtained by using the t-test to assess the significance of the coefficient for the interaction term.

To determine whether the excluded variables "physician age", "physician gender", "hospital affiliation", "number of hypertensive patients per month", "length of postgraduate training", and "dichotomized order of scenarios" were important confounders that should be included in the final model, the estimated coefficients in the penultimate model (Step 2) were compared to those in a full

model including all 8 variables. These were similar (0.199 vs. 0.235 for "gender version of questionnaire" and 0.210 vs. 0.240 for "academic appointment") suggesting that the excluded variables were not important confounders. Thus, they were left out of the final model.

Thus, the final multiple linear regression model for physician scenario 5 is:

MCID= 3.522 + 2.170 (ACADEMIC APPOINTMENT) + 1.768 (GENDER VERSION OF QUESTIONNAIRE) + E

Step 5- Diagnostics

Violation of assumptions for linear regression were tested by examining scatterplots of regression residuals. Specifically, the regression standardized predictive values were plotted against the studentized residuals. The random distribution of the residuals indicated that the assumption of linearity was intact. As the spread of the residuals did not greatly increase or decrease with the absolute magnitude of the predicted values, the homoscedasticity assumption appeared valid. Finally, residual analysis revealed that the assumption of normality had not been violated.