

**THE EFFICACY OF WARFARIN FOR THE
PREVENTION OF STROKE IN NONVALVULAR
ATRIAL FIBRILLATION: MEASURING ITS MINIMAL
CLINICALLY IMPORTANT DIFFERENCE FROM THE
PATIENTS' PERSPECTIVE**

by

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Thesis submitted to
School of Graduate Studies and Research
in partial fulfilment of the requirements for the
MSc degree in Epidemiology

University of Ottawa

DATE: January 1996



Malcom Man-Son-Hing, Ottawa, Canada, 1996



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ISBN 0-612-15741-5

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ABSTRACT

Objectives: 1) to develop a probability trade-off technique (PTOT) for determining the minimal clinically important difference (MCID) of warfarin therapy from the patients' perspective; 2) to estimate the MCID for the efficacy of warfarin to prevent stroke in the treatment of nonvalvular atrial fibrillation (NVAf) from the perspective of patients with this disease and who have experienced a course of warfarin therapy; 3) to assess two different methods of eliciting the patients' MCID.

Design: a two-period, 4 sequence crossover trial. In each of the periods, patients were randomized to receive one of two elicitation methods.

Setting: the practices of 2 university-affiliated family medicine centres (8 physicians each), 14 community-based family physicians and 2 cardiologists.

Patients: 126 patients with NVAf who had been initiated on warfarin therapy at least three months prior to the first interview. Sixty-four patients completed the study.

Intervention: the PTOT was performed in two parts: 1) with use of a pictorial flipchart, during 30 minute face-to-face interviews, patients were presented with the following information: descriptions of atrial fibrillation, a minor stroke and a major stroke; the chance of stroke if not taking warfarin; a description of a major bleeding episode; the chance of a major bleeding episode if taking warfarin; and examples of the costs, inconvenience and minor side effects of warfarin therapy; and 2) using one of two elicitation methods, the patients' MCID (the smallest reduction in stroke risk at which they would take warfarin) was determined. The two elicitation methods were: 1) ping-ponging (PP), in which the hypothetical efficacy of warfarin to prevent

stroke was varied from one extreme to the other until the patients' MCID was determined; and 2) starting at known efficacy (SKE), in which the hypothetical efficacy was started at a midpoint value and then incrementally increased or decreased until the patients' MCID was determined. Patients' knowledge of their stroke risk, acceptability of the PTOT, and factors determining their preferences were also assessed. Patients were interviewed twice; the second time, two weeks after the first.

Main results: given a baseline risk of 10 out of 100 chance of having a stroke in the next two years if not taking warfarin, the mean MCID on the first interview was 2.01 out of 100 (95% confidence interval, 1.60 to 2.42). Prior to the PTOT, patients showed poor knowledge of their stroke risk, which improved after its administration. The PTOT was well accepted by the patients and they generally recommended that the methodology be adapted to other therapies and conditions. After the PTOT, patients reported increased knowledge of their disease and its treatment.

The method of elicitation resulted in a statistically significant difference in patients' MCIDs. The mean MCID was 1.015 out of 100 smaller using the PP elicitation method compared with the SKE method.

Conclusions: the MCID for this group of patients was much smaller than the known efficacy of warfarin to prevent stroke in patients with NVAf. The PTOT, using the flipchart approach, was well accepted and appeared to improve their knowledge of their disease, and its consequences and treatment.

The methodology used to develop the PTOT for this study could be useful in

three ways: 1) more clinically relevant sample sizes for prospective therapeutic trials are likely if the patients' perspective is considered; 2) it could clarify the patients' perspective in the interpretation of the results of completed clinical trials; and 3) from a clinical decision making perspective, it could allow patients to participate more interactively with their physicians, thus adding another dimension to informed decision making.

The method of elicitation used to determine the patients' MCIDs can have a clinically important effect on their responses. Theoretically, the ping-ponging elicitation method minimizes the 'shifting frame effect'. Thus, it may be the preferred method of elicitation compared with SKE and its variants.

ABBREVIATIONS

CAFA	- Canadian Atrial Fibrillation Anticoagulation Study
DNR	- Do not resuscitate
HAQ	- Health Assessment Questionnaire
MCID	- Minimal clinically important difference
MMSE	- Mini-mental State Examination
NVAF	- Nonvalvular atrial fibrillation
ODCS	- O'Connor Decisional Conflict Scale
PP	- Ping-ponging
PTOT	- Probability trade-off technique
SKE	- Starting at the known efficacy
SOB	- Shortness of breath
SPAF	- Stroke Prevention in Atrial Fibrillation Study
SPINAF	- Stroke Prevention in Nonvalvular Atrial Fibrillation Study

ACKNOWLEDGEMENTS

This study was supported by a grant from DuPont Pharma.

The design and execution of this study were part of Dr M. Man-Son-Hing's Masters thesis in epidemiology at the University of Ottawa.

I thank the supervisors of this thesis project; Drs. A. Laupacis (main supervisor), A. O'Connor, G. Wells and P. Tugwell for their time, effort and patience.

I thank the following physicians for allowing recruitment of their patients: Drs. R. Bernstein, B. Bruce, C. Bruce, G.H. Burke, N. Busing, C. Czarnowski, D. Davidson, M. Dermer, T. Elmslie, D.H. Ferguson, J.M. Forster, M. Fraser, S. Higham, W. Hogg, G. Hollingworth, C. Kuntz, C.J. Labelle, J. Lemelin, D. Levine, L. Moore, J. Niznick, D. Patten, B. Powell, B. Quinn, C. Rivet, L. Rosenkranz, J.K. Shearman, P.D. Stewart, R. Thomas, G. Viner, M.N. White and W. Wood.

I thank Dr. Neda Seki for conducting study interviews and Janet Brennan for manuscript preparation.

I thank the members of the Division of Geriatric Medicine at the University of Ottawa for their commitment of time and resources to allow me to pursue this degree.

Finally, I thank my wife, Julie Doyon, for her support through the years it took to complete this MSc.

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OBJECTIVES

The objectives of this study were to:

- 1) develop a probability trade-off technique for determining the minimal clinically important difference (MCID) for the efficacy of warfarin therapy from the patients' perspective.
- 2) estimate the MCID for the efficacy of warfarin in the treatment of nonvalvular atrial fibrillation from the perspective of patients with this disease and who have experienced a course of therapy.
- 3) assess two different methods of eliciting patients' MCIDs.

INTRODUCTION

The concept of the minimal clinically important difference

The minimal clinically important difference (MCID) associated with a therapy has been defined by Jaeschke and colleagues 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".¹ The inconvenience of the therapy is another potentially negative factor that could be incorporated into this definition.

Thus, the clinical importance of any therapy can be conceptualized as: **Clinical Importance = Therapeutic Efficacy -(Costs¹ + Inconvenience + Side Effects)**. Therefore, a therapy is without clinical importance if its efficacy is less than the sum of its costs, inconvenience and side effects. Alternatively, a therapy is clinically important if its efficacy outweighs its negative attributes. Thus, the MCID of a therapy can be conceptualized as the minimum efficacy necessary to more than offset its negative attributes.

The concept of a MCID is crucial in the design process of clinical trials. Before a clinical trial begins, determination of the appropriate sample size is a necessary part of the planning procedure. Sample size calculation is based upon four important parameters: the chance of concluding the treatments are different when they truly are not (alpha error), the chance of concluding that treatments are the same when they truly are not (beta error), the estimated probability of the outcome event in the control group and the MCID. General agreement about appropriate tolerance levels for both alpha and beta error have evolved amongst trialists over time.²

¹ Costs, in this case, refer to those directly paid by the patient or family.

However, the process of determining the MCID for prospective clinical trials has traditionally been the subject of less rigorous consideration. As written by Feinstein in 1977, "[j]udgements about the proper size of the [MCID] have received almost no concentrated attention via symposia, workshops, or other enclaves of experts assembled to adjudicate matters of clinical importance".³ He adds, "in the absence of established standards, the clinical investigator on being badgered by the statistician to choose a [MCID] so that the sample size can be calculated, picks what seems like a reasonable value. This value is tossed into the formula. If the sample size that emerges is unfeasible, the [MCID] gets adjusted accordingly ... until the n comes out right." This situation has changed little since then.

As outlined by Naylor and Llewellyn-Thomas,⁴ previous approaches used to attempt to determine the MCID for a therapy include:

- a) subjective judgement by clinicians⁵
- b) biological plausibility; the best estimate of its efficacy as derived from the basic science literature
- c) prior clinical data; the best estimate from pilot studies and/or previous trials
- d) methodologic convention;⁶ a standard absolute or relative risk reduction
- e) feasibility issues³ (e.g. number of patients available for recruitment).

Newer approaches include:

- f) economic;⁷ evaluation of cost-benefit issues
- g) public health;⁸ sample size based on detecting moderate treatment effects in common diseases.

However, no consensus yet exists on the most appropriate method or methods of determining the MCID.

Using another approach, Sackett and colleagues have stated that a trial result "becomes clinically significant when its publication leads to changes in clinical behaviour".⁹ In other words, the trial result is judged on its clinical significance after the trial has been performed. From their perspective, the impact of trial results upon clinical practice is a function of what different groups and individuals (both clinicians and patients alike) perceive to be the MCID. Also incorporated into the determination of clinical significance are the economic and social climates of that time. However, differences of opinion with respect to the MCID of a therapy can lead to controversy about the clinical significance of the trial result. For example, cholesterol lowering agents can reduce the incidence of coronary heart disease in certain populations. Whether this reduction is clinically important is an area of intense debate in the medical literature.^{10,11,12} Those that argue that the effect size is clinically important are likely to perceive a lower value for the MCID than those who do not. Interestingly, the perspective of patients has not been thoroughly addressed in this debate.

Recently, Naylor and Llewellyn-Thomas⁴ noted that the perspective of patients was missing from all approaches to determine the MCID for sample size determinations of randomized treatment trials. They argued for a more patient-centred approach. They suggested adding another step to the clinical trial design process; "patients or other members of the public [should] be given an active role in determining the magnitude of the clinically important treatment effect for trial planning." Their approach included systematically eliciting the MCID of the therapy

in question from the patients' perspective, and then using this value in the sample size calculation of the prospective clinical trial. While having the disadvantage of adding another step to the clinical trial design process, such a process would likely lead to more clinically relevant determinations of trial sample sizes, and may lead to different sample sizes than those determined by clinicians.

In summary, accurate determination of the MCID is of great methodological (sample size determination) and clinical (interpretation of trial results) importance. The question remains from whose perspective the MCID should be determined. In this era of increased patient demands for participation in their own treatment decisions,¹³ previous approaches based solely on the perspective of clinicians and researchers are methodologically, clinically and politically inadequate. Clearly, the patients' perspective about the MCID of any therapy needs to be incorporated into clinical and research practice. For prospective trials, their perspective of the MCID can be utilized in sample size calculations. For completed trials in which there is uncertainty about the clinical importance of the results, this could be judged by the patients themselves.

Determining patient preferences in health care decision making

Patient preferences for health care decision making were initially studied by asking patients to judge the desirability (or undesirability) of different health states (referred to as utility assessment).^{14,15} Patient preferences have also been determined for different cancer treatment protocols¹⁶ and the relative importance of different time periods (e.g. willingness to wait for coronary bypass surgery)¹⁷.

The first step in determining patient preferences is to describe the particular health state(s) and/or treatment options. Many different methods for presenting this

information to patients have been developed. Levine and colleagues used a velcro decision board to clarify preferences for treatment in patients with breast cancer.¹⁸ O'Connor and colleagues have used both flipchart¹⁹ presentations given by an trained interviewer and audiobooklets²⁰ (an audiotape accompanying a pictorial booklet) that the patients can use at their own convenience. Wennberg has developed an interactive videodisc to help patients with benign prostatic hypertrophy decide whether they prefer surgical or medical treatment.²¹ Different presentation methods have been shown to yield different preference scores.²² Therefore, it is unclear which of the above presentation methods best conveys the appropriate information to patients.

Patient preferences can also be profoundly influenced by the way health states and probabilities are described. Patient preferences have been shown to be sensitive to qualitative or quantitative descriptions of side effects²³ and the use of relative versus absolute risk reductions to describe possible benefits.²⁴ Previous studies have also shown that the way in which a problem is framed can influence patient preferences.^{25,26} For example, descriptions of treatment outcomes can be framed positively (e.g. chance of survival) or negatively (e.g. chance of dying). However, Siminoff and Fetting have shown that in actual clinical encounters, framing may not be as influential on patient preferences as previously thought.²⁷ Thus, further work is necessary to determine the full influence of these factors on patient decision making in real clinical encounters.

The second part of the process is actually eliciting the patient preference. Three methods are presently commonly utilized. The standard gamble²⁸ technique asks patients to choose between continuing in a less than optimal chronic health state

or to take a gamble. The gamble has two possible outcomes; attainment of perfect health or death. By systematically varying the probability of death (and thus also the probability of perfect health) the patients' utility for the chronic health state can be determined. For example, patients with osteoarthritic hips could be asked whether they would prefer to continue living with their chronic illness or take a gamble and undergo a procedure which has two possible outcomes; immediate perfect health or death. In the gamble portion, the probability of a successful outcome is systematically varied until the patient is indifferent to each option. The greater the risk of death that the patient is willing to accept, the lower the utility of the chronic health state; in this case, living with osteoarthritis of the hip. In the time trade-off²⁹ technique, patients are asked to choose between living a fixed number of years in a less than perfect health state and living a lesser number of years in perfect health. The length of life in perfect health is systematically varied until the patient is indifferent to the two options. The number of years of life that patients are willing to give up to gain perfect health is a measure of the patients' value for the chronic health state. A third approach is the use of rating scales.³⁰ A 10 centimetre line is anchored by death and perfect health at each end. Patients are asked to judge the relative desirability of different health states by marking a line on the scale.

There is evidence that each of these three elicitation techniques can produce different patient responses.³¹ This is not surprising considering that the standard gamble measures 'utilities', patient preferences under conditions of risk; and time trade-off and rating scales measure 'values', patient preferences in riskless situations.

Within the standard gamble and time trade-off elicitation techniques there is considerable variability in the actual elicitation **method** of determining the patient

preference. For instance, one approach is to start at one or the other probability extreme and then systematically move from a positive to negative frame or vice versa.³² A variation of this method is to start at the known efficacy of the treatment and then vary the hypothetical efficacy up or down, depending on the patient's initial response. We have coined this elicitation method "starting at the known efficacy" (SKE). Another approach is to systematically vary the probabilities from one extreme to the other. This elicitation method has been coined "ping-ponging" (PP).²⁸ It is unclear whether systematic differences in patient responses occur due to elicitation method. Determining the most valid and reliable elicitation method would be a valuable addition to the methodology used to determine patient preferences.

Using patient perceptions to determine the MCID of health states

Patient perceptions have been previously used to help determine the MCID of clinically derived rating scales.¹ These rating scales were developed to quantify difficult-to-measure outcomes such as quality of life. The clinical importance of changes in scores on these scales is often difficult to judge. For example, is a one point change on a ten-point scale that measures patients' subjective feeling of anxiety, a clinically important or only a trivial change? Redelmeier has suggested that, "a difference in functional status scores is clinically important if it is associated with a difference that a typical patient can notice."³³ In association with Wells and colleagues, he attempted to determine the MCID of the Health Assessment Questionnaire (HAQ), a rheumatoid arthritis scale that uses patients' symptoms and physical examination findings to measure their disease severity.³⁴ In this study, patients' disease severity was assessed using the HAQ. Then, a structured interview was arranged between two of the assessed patients. After the interview, using a 7-

point Likert scale, patients rated their own disease severity in relation to their interview partner. The difference in score on the HAQ that corresponded to a difference that the patients were just able to notice on interview, was deemed the MCID of the HAQ.

A slightly different approach to this problem has been to examine the relationship between changes on a scale measuring global well-being and changes in the score of the outcome measure of interest. For example, to determine the MCID of a scale derived to measure the severity of shortness of breath (SOB) in patients with congestive heart failure, patients were serially asked to rate both their global level of disability and the severity of their SOB.³⁵ The amount of change in the severity of the patients' shortness of breath that they noticed in a global sense was deemed the MCID of the SOB scale.

Such approaches are clearly not directly applicable to determining the MCID of a therapy as Jaeschke has defined it, because they measure patient perceptions of health states rather than patient preferences for treatment. An approach that adapts methodology for determining patient preferences (as opposed to patient perceptions) for health states and treatment choices can be used to determine the MCID of a therapy from a patient perspective.

The efficacy of warfarin for stroke prevention in nonvalvular atrial fibrillation: measuring its MCID from the patients' perspective

In this study, patients who have nonvalvular atrial fibrillation (NVAf), are at risk of an unfavourable outcome (stroke) and have experienced a course of preventive therapy (warfarin anticoagulation) have been selected to determine their MCID for the efficacy of warfarin therapy. The attributes of this group listed above

are of great importance if a valid determination of this MCID is to be made. First, it is very important that the group have the disease that is being studied. It is clear from the oncology literature that patients with cancer give different preferences for treatment and health states than persons without cancer.³⁶ For example, patients with rectal cancer give different utilities for living with a colostomy compared with healthy volunteers.³⁷ Second, the group being studied also must have experienced a course of therapy to properly judge its costs, inconvenience and side effects. Patients who have experienced a course of the therapy can give different preferences compared with those who have not. For example, preferences for pain relief differed amongst women undergoing childbirth according to previous experience with different modes of analgesia.³⁸ Thus, in light of their actual experience both with the disease and its therapy, the group chosen should be able to make an accurate and valid determination of the MCID for the efficacy of warfarin therapy.

NVAF is a heart rhythm abnormality associated with many diseases such as ischemic heart disease, congestive heart failure and hyperthyroidism. Patients with chronic NVAF have an increased risk of stroke. Long term anticoagulation is the most efficacious method of reducing this risk. Recent studies ^{39,40,41,42,43,44} have shown:

- 1) the risk of stroke in untreated patients with NVAF is approximately 5% per year and this risk is constant over subsequent years (i.e. 10% over two years).
- 2) treatment with warfarin anticoagulation reduces the risk of stroke in these patients by approximately 65% per year (i.e. to 1.75% per year or 3.5% over two years).
- 3) the increased risk of major bleeding associated with warfarin anticoagulation

is approximately 1.5% per year and this risk is also constant over subsequent years (i.e. 3% over two years).

There are other disadvantages associated with chronic warfarin therapy other than major bleeding. Patients must be willing to undergo the inconvenience and costs of having regular blood testing to monitor their anticoagulation status. Lifestyle modifications such as abstinence from alcohol and avoidance of activities with a high risk of physical injury are also necessary. Patients may also develop minor side-effects such as easy bruising and epistaxis. For patients to continue taking warfarin on a chronic basis, they must feel that the advantages of the therapy (stroke risk reduction) outweigh the disadvantages (costs, inconvenience and side effects).

Most experts consider the efficacy of warfarin to be clinically relevant and recommend patients with NVAf be anticoagulated if no contraindications exist.^{45,46} However, the results of the five high quality trials and treatment recommendations in favour of anticoagulation have not been enough to change the clinical practice of all physicians. Many physicians remain reluctant to prescribe warfarin to their eligible patients.^{47,48,49} From a physician perspective, reasons for not prescribing warfarin include the risk of bleeding,⁵⁰ the inconvenience,⁵¹ and costs⁵² of anticoagulation. However, one study found that long term warfarin therapy had little significant impact on patients' quality of life unless they suffered an complication such as a bleeding episode.⁵³ Thus, an extremely relevant question to this issue is whether patients who have experienced this therapy believe warfarin provides them with a clinically important reduction in stroke risk, given the disadvantages of the therapy.

To summarize the above, this study achieved three objectives. First, it

developed a PTOT to determine the MCID of warfarin therapy from the patient perspective. Second, it determined the patients' MCID for the efficacy of warfarin in the treatment of NVAf. Third, it determined whether the method of elicitation ("PP" or "SKE") systematically influenced the size of the patients' MCID.

METHODS

The study protocol was approved by the Research Ethics Committees of the Ottawa Civic Hospital and Elisabeth Bruyere Health Centre.

Physician Involvement

General agreement for participation in this study was obtained from the physicians associated with the Departments of Family Medicine located at the Ottawa Civic Hospital (8 physicians) and Elisabeth Bruyere Health Centre (8 physicians), 14 independent family physicians and 2 private practice cardiologists. An information sheet (Appendix A) was circulated to physicians describing the pertinent details of the study.

Eligible Patients

From each individual medical practice, all patients who were initiated on warfarin therapy for NVAf at least 3 months prior to the first study interview were identified. Participating physicians and nurses searched their data bases, anticoagulation log books and patient medical records to identify all patients with atrial fibrillation. These patients were then assessed to determine whether they had ever been initiated on warfarin therapy for NVAf. Patients were deemed eligible regardless of whether they were taking warfarin at the time of identification.

Exclusion Criteria

Patients were excluded if they:

- 1) were deemed by their physician to have a medical condition making participation impossible (e.g. significant dementia).
- 2) had suffered a stroke or complication of anticoagulation therapy that rendered them unable to comprehend the study interview.

- 3) were not fluent in English.
- 4) were unable/unwilling to give consent.
- 5) failed the cognitive testing or comprehension screening portion of the interview (see Comprehension Screening and Subjective Assessment of Patients' Comprehension sections below).

Consent

At each of the Departments of Family Medicine at the Ottawa Civic Hospital and Elisabeth Bruyere, an anticoagulation log book is kept to track the patients who require blood monitoring. A nurse at each centre is assigned to update the log book and contact patients as necessary for further blood testing and/or change in medication doses. Therefore, the nurses have developed a prior personal relationship with these patients. After identification of eligible patients through the data bases and log books, the nurses contacted patients in person or via telephone.

The objectives of the study, the identity of study personnel, and the support of their personal physicians for the study was explained by the nurses to eligible patients. It was emphasized that participation was entirely voluntary. If eligible patients wanted additional explanation, they were referred to their physicians. All potential participants were given as much time as necessary to make their decision. For example, if they wanted to discuss involvement with family members, it was suggested that the nurse would call them afterwards.

If patients were interested in participating, they were asked to allow a member of the study team to contact them. A list of those willing to be contacted was tabulated and given to the principal investigator. The number of potential participants who did not wish to be contacted was recorded in an anonymous

manner. Those willing to participate were contacted by study personnel and a mutually convenient time to meet was arranged. At that meeting, written consent for participation was requested (Appendix B).

The same method was used to obtain consent from potential participants at the 14 individual family physician sites except two physicians chose to personally contact their own patients. At the 2 cardiology practices, each physician mailed a personal letter to potentially eligible patients informing them about the basic details of the study. The letter also notified them that a telephone call would be made by a study team member at a later date. This method was used because each cardiologist had only limited contact with potential participants, having only seen them on a consultative basis. During the follow-up telephone call, patients were asked to give consent to participate in the first interview, at which time written consent was obtained.

Confidentiality

Confidentiality was maintained by assigning numbers to all patients. Reference to patients was made by study number only. Patient names were recorded only for the purpose of recontacting them for the second interview. Only study team members had access to the records. If patients wished to have a copy of their personal results, this was provided.

Study Design

The study design was a two period crossover with four sequences. The independent variable was the elicitation method. The time period between interviews was at least two weeks. Patients were randomized to one of four different groups (each group representing one sequence): Group 1: PP/PP (PP followed by PP);

Group 2: PP/SKE; Group 3: SKE/PP; Group 4: SKE/SKE.

Appendix C is a flow chart of the study design. Appendix D is the study time line.

Randomization

Randomization was performed through the Clinical Epidemiology Unit at the Ottawa Civic Hospital. The randomization list was computer generated from the Statistical Analysis System (SAS) RANNOR routine.⁵⁴ Randomization was in blocks of eight (8) to balance study groups in the event of early termination of the study. No stratification by hospital or practice was performed.

Intervention

Study interviews were performed by two physicians. Individual interviews were performed by a single interviewer, and the same interviewer performed both interviews with each patient.

With the use of a pictorial flipchart and prewritten text (Appendices E and F), patients were presented the following information:

- a definition of atrial fibrillation
- a description of a minor and major stroke, and the relative frequency of each
- the risk of stroke in untreated patients over the course of two years (10% over two years)
- a description of a major bleeding episode
- the risk of a major complication due to anticoagulation (3% over two years)
- possible inconveniences (e.g. regular visits for blood monitoring, changes in lifestyle)
- possible costs (e.g. transportation, parking)

- possible minor side effects (e.g. bruising, epistaxis).

During the flip chart presentation, patients were **not** told the known efficacy of warfarin to prevent stroke in NVAf.

Method of administration

1) Comprehension screening

Patients' comprehension of the information presented with the flipchart was screened using visual scenario cards and a prewritten text (see Appendices G and H). Patients were asked whether they would want to take warfarin in a situation in which there was clearly no benefit to taking it (a stroke risk of 10% whether or not taking warfarin). If patients chose to take warfarin, the information provided had not been adequately comprehended and further explanation was provided. If after a few attempts at explanation, it became evident that it was not possible for the patient to adequately comprehend the presentation, the interview was terminated. These patients were not included in the final analysis.

2) Elicitation methods

After patients passed the comprehension test, they were randomized to one of the two elicitation methods:

a) Ping-ponging (PP)

This elicitation method determined the patients' MCID by systematically varying the hypothetical efficacy of warfarin to prevent stroke from one extreme to the other.

It was performed as follows. Using appropriate visual scenario cards and a prewritten text (Appendices I and J), patients were presented with two hypothetical choices:

- 1) **Not Take Warfarin** and have a 10 out of 100 chance of having a stroke over the next two years.
- 2) **Take Warfarin** and have a 0 out of 100 chance of having a stroke (i.e. 100% efficacy) plus a 3 out of 100 chance of a major bleeding episode over the next two years.

If patients chose to Not Take Warfarin, this was a plausible answer, but implied that they would not take warfarin even it completely prevented having a stroke. This was explained to the patients who were then given an opportunity to change the choice to Take Warfarin. If their choice remained unchanged, they were recorded as having no MCID (i.e. they would never take warfarin).

If patients chose to Take Warfarin, the same scenario was then presented except a 9 out of 100 chance of stroke was substituted on the "Take Warfarin" card. Again patients were asked to choose to Take Warfarin or to Not Take Warfarin. For patients who chose to Take Warfarin, they were asked whether they would take warfarin with a 9.5 out of 100 chance of stroke. If they chose to take warfarin at a hypothetical efficacy of warfarin of 9.5 out of 100 chance of a stroke, their MCIDs were recorded as 0.5 out of 100 reduction in stroke risk over two years. In other words, given a baseline risk of 10 out of 100 chance of having a stroke in the next two years, these patients would take warfarin if their chance of stroke was reduced by 0.5 out of 100 over the next two years. Finer gradations in stroke risk reduction (e.g. 9.75 out of 100) were not attempted. If they chose not to take warfarin at a hypothetical efficacy of 9.5 out of 100, their MCIDs were recorded as 1 out of 100.

If at an efficacy of warfarin of 9 out of 100, patients chose to Not Take

Warfarin, the scenario was repeated with a hypothetical efficacy of 1 out of 100 chance of stroke if taking warfarin. Thus, the hypothetical efficacy of warfarin was "ping-ponged" from large to small efficacy until the smallest efficacy at which patients would take warfarin was determined. These points were considered their MCIDs.

Appendix K shows the flow chart for the PP elicitation method.

b) Starting at the Known Efficacy (SKE)

With the use of identical visual scenario cards as the PP elicitation method, the known efficacy of warfarin (reduction to approximately 4 out of 100 chance of stroke in the next two years) was used as the starting point. Depending on the patients' first choice (**Not Take Warfarin** or **Take Warfarin**), the hypothetical efficacy was then varied up or down.

The SKE elicitation method was performed as follows; patients were presented with two hypothetical choices:

- 1) **Not Take Warfarin** and have a 10 out of 100 chance of stroke over the next two years.
- 2) **Take Warfarin** and have a 4 out of 100 chance of stroke plus a 3 out of 100 chance of a major bleed over the next two years.

If patients chose to Not Take Warfarin, the chance of stroke was systematically decreased by 1 out of 100 increments until they switched preferences. The points at which the switches were made were their MCIDs.

If patients chose instead to Take Warfarin, the chance of stroke was systematically increased by 1 out of 100 increments until they switched preferences. If patients chose to take warfarin at a chance of stroke of 9 out of 100, they were

then asked whether at a 9.5 out of 100 chance of stroke, they would want to take warfarin. Again, the smallest risk reductions at which patients would take warfarin were their MCIDs.

Appendices L and M show the text and flow chart for the SKE elicitation method respectively. Appendix N shows further examples of visual scenario cards for eliciting the patients' MCID.

Data Collection

A. Prior to elicitation of MCID (Appendix O):

a) Demographic information

For each patient the following was recorded; name, address, telephone number, gender, date of birth, level of education, name of personal physician, approximate date of starting warfarin, and current use of warfarin.

b) Patients' estimation of stroke risk

Prior to the flipchart presentation, patients were asked to estimate their own risk of stroke if taking, and if not taking warfarin. They were asked to write their estimates on a blank line.

c) Abstract thought

The study investigators felt that it may be necessary for patients to possess the ability to think abstractly to fully comprehend the interview information. Therefore, patients were asked, "How are an apple and an orange similar?" The responses of the patients were categorized as concrete (e.g. both are round, both have skins) if these were the only types of answers given. Their responses were recorded as abstract (e.g. both are fruit) if they gave at least one abstract answer. Patients were encouraged to give multiple responses.

B. After elicitation of the MCID:

- a) O'Connor Decisional Conflict Scale (Appendix P) and semi-structured questionnaire (Appendix Q).

Patients were asked to complete a modified O'Connor Decisional Conflict Scale (ODCS) and a semi-structured qualitative de-briefing interview. Also, using the identical wording as in the initial questions, patients were again asked to estimate their own chance of having a stroke, if taking or not taking warfarin.

Completion of these tasks allowed evaluation of patient comprehension of the presentation, uncertainty of their choices and the factors leading to this uncertainty. The validation of the ODCS has recently been reported.⁵⁵

Patients were asked to complete the modified ODCS and questionnaire after the first interview only.

- b) Subjective assessment of patients' comprehension

After each interview, the study interviewer subjectively rated patients' comprehension of the interview information on a scale of 0 to 10. If patients did not score 10/10 on this scale after the first interview, a Folstein MMSE examination⁵⁶ (MMSE) (Appendix R) was performed. The reliability and validity of the MMSE are well documented.^{57,58} Only patients who scored 24/30 or greater on the MMSE were included in the final analysis. A score of less than 24/30 on the MMSE has been found to be approximately 80% sensitive and 80% specific for clinically significant cognitive impairment.⁵⁹

- c) Interview termination

At the end of the second interview, patients were told the actual efficacy of warfarin. They were allowed to discuss what implications, if any, they felt the

interview had on their own personal feelings about taking warfarin. If necessary, counselling (e.g. recommendation for discussion with family physician) was then offered.

Sample Size Calculation

The sample size for this study was chosen by deciding how precisely the patients' mean MCID needed to be estimated. A priori we felt that a 95% confidence interval (95% CI) of ± 0.5 (out of 100) absolute stroke risk reduction around the mean would be sufficiently precise. This corresponded to a $\pm 5\%$ relative risk reduction given a baseline stroke risk of 10 out of 100 over a two year period if not anticoagulated. Calculation of the sample size to achieve this precision resulted in an estimate of 32 patients (Appendix S). Before the start of the study, we chose to attempt to recruit 50 patients to each elicitation method on the **initial** interview (for a total of 100 patients) as this sample size appeared feasible. Also, the larger sample size ensured sufficient precision if the actual standard deviation of responses was larger than anticipated. Therefore, this study intended to enrol 25 patients to each of the four groups described in the Study Design and Randomization section.

Data analysis

Data analysis was performed as follows:

1) Patient characteristics

Means, ranges and standard deviations were calculated for pertinent patient characteristics.

2) Determination of the MCID

- a) Means with 95% CIs were calculated for the MCID responses,

according to interview and elicitation method.

- b) Analysis of variance was used to test the effects of time and elicitation method on the MCID.
- c) A point estimate for the effect of time was calculated by averaging the difference in MCID means from first to second interview for groups 1 and 4. A point estimate for the effect of elicitation method was calculated by averaging the difference in means for groups 2 and 3, then factoring in any significant carry-over effect.
- d) Student's t-tests were used to test for differences in mean MCID responses for the variables of education level and subjective comprehension (both as categorized in Table 1), abstract thought and current use of warfarin.

3) Assessment of the Reliability of the Two Elicitation Methods

- a) Spearman rank correlation coefficients were calculated for group test-retest reliability.

Two-tailed testing and a p-value of less than 0.05 were used to indicate statistical significance for all analyses.

RESULTS

Figure 1 shows a flow chart of patient recruitment. From the various physician practices, 126 patients with NVAf who had been commenced on long-term warfarin therapy at least three months prior to the first study interview were identified. Physicians deemed 2 patients inappropriate for the study due to high anxiety state (1) and significant dementia (1). Ninety-four (94) of the 124 potentially eligible patients were successfully contacted. The 30 potential patients who were not successfully contacted were exclusively identified from the practices of the two cardiologists. The two cardiologists understandably did not have as close a relationship with the patients as did the family practitioners, having often only seen the patient on a consultative basis. Therefore, their lists of eligible patients included many from outlying regions and with out-of-date telephone numbers. Of those persons who were contacted, 9 refused participation. Of the 85 patients who agreed to be interviewed, 18 failed comprehension testing and 1 was unaware that she ever took warfarin. They were excluded from the study. Two patients were unavailable for the second interview (1 became seriously ill and 1 went to Florida for the winter), leaving a total of 64 patients who completed both interviews. Forty-two (42) of these patients were recruited from family practitioners and 22 from cardiologists.

1) Patient Characteristics

Table 1 shows the demographic information of the study patients who completed both interviews and those who failed comprehension testing. Six (6) patients who completed the study were not taking warfarin at the time of their interviews. For all of these patients, their physicians had made the decision to stop prescribing warfarin. Their reasons included preference to treat with aspirin (2),

difficulty controlling anticoagulation status (1), and difficulty obtaining blood (1). Two (2) patients were unsure why their physician decided to discontinue warfarin therapy.

Approximately 70 per cent of the patients were male. Patients who failed comprehension testing were of higher mean age, more likely to have a lower level of education and less likely to think abstractly than those who completed the study. Of the patients who scored less than perfectly on subjective assessment of comprehension, all scored 24/30 or better on the MMSE.

2) The Minimal Clinically Important Difference

Figure 2 shows the distribution of individual MCID responses arranged according to interview and elicitation method. In general, the scores were not normally distributed. On the first interview, 50% (32 of 64) of patients willing to take warfarin for an absolute risk reduction of 1 out of 100 or less; and only 5% (3 of 64) of patients required a 5 out of 100 or greater risk reduction to want to take warfarin.

Table 2 shows patient means and 95% CIs for the MCID categorized according to first or second interview and the two elicitation methods. The MCID is reported as the minimum absolute risk reduction needed to take warfarin, given a baseline risk of 10 out of 100 chance of stroke in two years if not taking warfarin. The results show that the mean overall MCID of all patients on the first interview was 2.01 out of 100 (95% CI; 1.60 to 2.42) over two years.

Table 3 shows the results of the analysis of variance used to test for period (first or second interview) and treatment (elicitation method) effects. In general, the MCID was smaller on the second interview compared with the first ($p=0.17$). Use

of the ping-ponging elicitation method resulted in a smaller MCID compared with the SKE method ($p=0.007$). There was no evidence of a 'direct treatment x carry-over' interaction effect or a 'carry-over' effect. The point estimate of the effect of time on MCID responses was 0.51 out of 100 chance of stroke in the next two years. The point estimate of the effect of the elicitation method was 1.015 out of 100 chance of stroke in the next two years.

Log transformation of the data and non-parametric testing using the Wilcoxon signed rank test were performed because the MCID responses were not normally distributed. Analysis of variance using log transformed data was repeated (Table 4) and its results supported the original analysis of variance, although the period effect approached conventional statistical significance ($p=0.06$). Wilcoxon signed rank testing also showed a statistically significant difference in patients' MCID responses due to elicitation method (Table 5).

Spearman rank correlations comparing the MCID responses from the first to the second interview for each group were also performed (Table 6). The Spearman rank correlation coefficients for the two groups using the same elicitation method at both interviews (Groups 1 and 4) were positive and statistically significant. The Spearman coefficients for the two groups in which different elicitation methods were used at the two interviews (Groups 2 and 3) were close to zero and not statistically significant.

3) Patients' Estimates of Their Stroke Risk

Table 7 shows the patients' estimates of own risk of stroke before and after the first interview.

a) Prior to the first interview

There were 4 (6.3%) patients who thought their chance of stroke was zero even if not taking warfarin. Conversely, 13 (20.3%) of patients thought their chance of stroke, if untreated, was greater than 50%. Approximately one-third of patients reported taking warfarin would reduced their chance of stroke to zero.

b) After first interview

There was an improvement in the ability of the patients to estimate their stroke risk after the study interview. Forty-four percent (44%) of the patients stated that their chance of stroke if not taking warfarin was 10% over the next two years. Post interview estimates tended to be revised towards smaller values but the overall means still remained higher than the true overall risk of having a stroke if taking or not taking warfarin. A higher percentage of patients were willing to give estimates of stroke risk after the interview compared with before.

4) Subjective Assessment of Patients' Comprehension

Table 8 shows the subjective assessment of comprehension scores and a comparison of the results obtained from those patients rated as having perfect comprehension (10/10) of the first interview and those that did not (<10/10). Those with a less than perfect comprehension rating did not show a statistically significant difference in test-retest reliability compared with those rated as having perfect comprehension.

5) Comparison of MCID Responses According to Abstract Thinking Ability and Education Level

Table 9 compares the MCID results of patients with abstract and concrete thinking. There was no statistically significant difference in mean responses between the two groups. However, only four patients were classified as concrete thinkers.

Table 10 compares the responses of those with different education levels. The mean responses of those with 6 to 12 years of education were not significantly different compared with those with a higher level of education.

6) Comparison of MCID Responses According to Current Use of Warfarin

Table 11 compares the responses of patients who were currently taking warfarin at the time of the first interview with those who were not. The mean MCID of those currently taking warfarin was smaller (1.91 versus 2.92) compared with those who were not. This difference was not statistically significant ($p = 0.168$). However, only 6 patients were not taking warfarin at the time of the first interview.

7) The Semi-structured Questionnaire and ODCS

Figure 3 and Table 12 show the results of the semi-structured questionnaire. Table 13 shows the results of the ODCS. The majority of patients reported that the interview process improved their knowledge and certainty about their disease and its treatment. Two patients reported the wording of the ODCS confusing. No patients reported any part of the presentation upset them. A large majority of patients felt that the approach used in this study should be generalized to other conditions and therapies. Patients (91%) overwhelmingly reported that the major factor that affected their decision making process was the fear of stroke. Fear of death (38%) and to a lesser extent, major bleeding episodes (13%) were also often reported as a factor. The costs (2%), inconvenience (5%) and minor side effects (9%) of warfarin therapy were less often reported as important factors in the decision making process.

DISCUSSION

This study has developed a PTOT to determine the MCID for the efficacy of warfarin therapy in the treatment of NVAf from the patients' perspective. With the use of a pictorial flipchart, pertinent information about the risks and benefits of this therapy was presented to patients by a study interviewer. Patients were then asked to judge whether they would take warfarin in a series of hypothetical situations in which the efficacy of warfarin to prevent stroke was systematically varied. The lowest risk reduction at which patients were willing to take warfarin was their MCID.

The MCID

The results of this study suggest that the known efficacy of warfarin is sufficient for the large majority of patients with NVAf to want to take warfarin despite its costs, inconvenience and side effects. This was true even for those patients who had discontinued warfarin prior to the first interview, although this group did have a larger (though not statistically significant) mean MCID compared with those who continued to take warfarin. Given the patients' mean MCID of approximately 1 out of 100 per year (2 out of 100 over two years) and assuming a constant 68% relative risk reduction for warfarin across all baseline risks, they would have chosen warfarin therapy compared with no therapy at baseline stroke risks of greater than 1.5% per year. In fact, at the average NVAf patients' stroke risk of approximately 5% per year, only 1 of the 64 patients would have chosen not to take warfarin.

The patients' MCID for warfarin therapy also was much smaller than the values used in sample size calculations for the five major randomized trials.³⁹⁻⁴³ For example, the Canadian Atrial Fibrillation Anticoagulation⁴² (CAFA) and the Stroke

Prevention in Nonvalvular Atrial Fibrillation⁴³ (SPINAF) trials estimated the MCID as 2.5 and 3.0 out of 100 per year (5.0-6.0 over two years) respectively.

The major factor affecting patients' decision making process was the desire to maximally reduce their chance of having a stroke. Their responses were consistent with a study which showed patients rated a minor stroke as a significantly worse health state than perfect health, and many forms of major stroke as worse than death.⁶⁰ For almost all patients, this fear of stroke clearly was much more important than the costs, inconvenience and side effects of long-term warfarin therapy. A decision analysis by Naglie and Detsky⁶¹ has shown that the decision to anticoagulate a patient with chronic NVAf is extremely sensitive to the patient's disutility for taking warfarin. Even small values of patient disutility can shift the balance in favour of not taking warfarin. This study, while not directly measuring patient utilities, clearly shows that the costs, inconvenience and minor side effects of taking warfarin are of much lesser importance than other factors in the patient decision making process. Given the above, it is likely that those experts and clinicians who argue that the known efficacy of warfarin to prevent stroke in most persons with NVAf is not clinically important are not in agreement with the majority of patients with NVAf.

The effect of elicitation method on the MCID

Analysis of variance showed that the elicitation method by which the patients' MCID was determined produced a statistically significant difference in responses. This result appeared to be quite robust as it was supported by log transformation of the data with repeat analysis of variance and also determination of Spearman rank correlation coefficients for each group. The PP elicitation method resulted in an

estimated 1.015 (out of 100 chance of stroke in the next two years) smaller MCID compared with SKE. This difference is probably clinically, as well as statistically significant. Greater than 50% of the patients reported MCIDs of 1 out of 100 or less. Therefore, the magnitude of the difference in responses due to the elicitation method would be considered clinically important by the majority of patients.

Since completion of this study, Percy and Llewellyn-Thomas have reported that nursing students have different preferences for do not resuscitate (DNR) orders depending in which direction the PTOT occurs.⁶² DNR preference scores were higher (indicating greater acceptability for DNR) if the probabilities were systematically adjusted in an increasingly negative (increasing chance of death if undergoing resuscitation) direction. This result is analogous to what is referred to as 'anchor bias'.⁶³ In most PTOT, individuals make estimates by starting at an initial value that is adjusted to yield a final value.⁶³ Adjustments are typically insufficient.⁶⁴ Thus, different starting points yield different estimates which are biased towards the initial value. However, anchor bias has mainly been described when people provide their own estimates, and in most probability trade-off tasks people react to a series of different paired choices. Therefore, when people react to paired choices as in this study, this phenomenon is instead referred to as the 'shifting frame effect'.⁶² In this study, for almost all patients undergoing the SKE elicitation method, the probability of stroke was adjusted in an increasingly negative direction (increasing chance of stroke), and thus they were exposed to the shifting frame effect. Those undergoing PP were not exposed to this effect because the probabilities were continually alternated from a high to low probability of stroke.

On the surface, the results of this study appear contrary to those found by

Percy and Llewellyn-Thomas.⁶² Those undergoing SKE had a systematically larger MCID for the efficacy of warfarin (indicating less acceptability for warfarin treatment) compared with those undergoing PP. This apparent discrepancy is likely due to DNR orders being a "withholding of treatment" and warfarin anticoagulation being a "treatment". Therefore, one would expect a "mirror image" of the shifting frame effect in this study compared with the study of Percy and Llewellyn-Thomas.⁶²

In conclusion, the results confirm that different elicitation methods can lead to clinically relevant differences in patient responses. As would be expected if the shifting frame effect was present, the mean MCID of patients who completed the SKE method was larger than those who underwent the PP method. Thus, conceptually the PP method could possibly lead to more valid MCID determinations than the SKE method.

The effect of time on the MCID

There was a trend for the MCID to become smaller from the first to the second interview, though this was not statistically significant and thus may not be a true effect. However if this difference is a true effect, it poses a difficult question. Which determination of the MCID is the more valid one? Having already been through the interview process once, it is likely that patients were better able to understand and assimilate the interview information and procedure during the second interview compared with the first. Thus, second interview responses are possibly more accurate reflections of the patients' MCIDs. Would further interviews result in even smaller values for the MCID? Further research into this period effect is needed. However, for this group of patients, this trend tends to confirm that the MCID for the efficacy of warfarin is truly much smaller than its known efficacy.

Evaluation of the PTOTs

The PTOT used in this study was well accepted by the patients. This occurred despite the explicit description of the bad outcome associated with a severe stroke. The patients made what they perceived to be informed choices and the PTOT likely strengthened most their commitment to continuing warfarin therapy. Their knowledge of stroke risk also improved with the interview process. Further critical evaluation of the effect of PTOTs and similar decisional support technology upon patient choices, knowledge, compliance and satisfaction is needed. To this end, we are developing and evaluating an audiobooklet that is intended to be used by patients on an independent basis. The audiobooklet will consist of a 10 to 20 minute audiotape that will guide patients through a pictorial booklet in an interactive manner. Rather than focusing on the MCID, the audiobooklet will be used as a decision aid to help patients decide whether or not they wish to take warfarin, aspirin or neither.

Potential biases

This study has numerous potential biases. Approximately 70% of the patients were male. This reflects the gender distribution of all patients that were identified as eligible for this study. A review of the computerized data base at Elisabeth Bruyere revealed that there are as many females as males diagnosed as having NVAF. This dichotomy may represent a bias towards more aggressively anticoagulating males patients with chronic NVAF as compared with females, although females with NVAF tend to be older than males with NVAF.⁶⁵

We chose to include only those patients who had been previously initiated on warfarin for NVAF. The advantages of selecting this group are twofold. Firstly,

having personally experienced a course of warfarin therapy, they understood its costs, inconvenience and side effects. Secondly, having the disease (NVAF) and being personally at increased risk of stroke, they were more likely to have understood the ramifications of having NVAF. No other group of patients could offer both of these advantages. For example, patients with newly diagnosed NVAF in whom their physician is contemplating long-term anticoagulation have the disease, but they have not experienced a course of therapy. They are less likely to have an accurate perception of the disadvantages of warfarin therapy than the group we studied. It is important to remember that a major objective of this study was to determine the MCID from a patient perspective. If the objective had been to determine patient preferences for treatment, the patients with newly diagnosed NVAF would have been the ideal group to study.

Another possible group of patients whose perspective could been studied are those who had experienced a course of warfarin therapy but did not have NVAF (e.g. patients with deep vein thrombosis). However, there is uncertainty whether persons with a disease respond differently to trade-off tasks pertinent to that disease compared with individuals without the disease.^{66,67} Future studies could elicit and compare MCIDs from these different populations.

It is also possible that not all patients with NVAF who had discontinued warfarin therapy were identified when physicians' practices were screened. If this study preferentially identified those patients who continued taking warfarin, an artificially small MCID was likely found. That is, persons continuing to take warfarin are likely to have less difficulty with the costs, inconvenience and side effects of warfarin therapy compared with those who stopped. Identifying the full cohort of

eligible patients from the 25 physician practices with computerized data bases was not difficult. For the 7 physicians who did not have computerized data bases, their recall was used to identify eligible patients. Therefore, it is possible that some patients who stopped warfarin were missed. Six (6) of 64 (9.4%) patients who completed the study were not taking warfarin at the time of the first interview. This is consistent with the 6.8% withdrawal rate from warfarin therapy that occurred in the Stroke Prevention in Atrial Fibrillation II (SPAF II) trial.⁶⁸

The method of presentation of probabilities can clearly affect patient responses. The use of facial icons to present the actual probabilities for clinical outcomes allowed patients to process this information in their own manner. For instance, they could consider the stroke risk reduction that warfarin provides in either absolute or relative terms. One could argue that the flipchart presentation was either too detailed or not detailed enough. The descriptions of various disease states could have been described in an infinite number of ways. To ensure use of reasonable and comprehensible scenarios, we used similar descriptions of stroke and bleeding episodes previously developed and pre-tested with twenty patients with atrial fibrillation.⁶⁹ Considering most patients' strong strength of preference and their identification of a high desire to avoid strokes, it is unlikely that any reasonable change in the flipchart presentation would have significantly affected the outcome of this study.

The study was terminated before recruitment of 100 patients was achieved. An interim analysis performed after 59 patients were enrolled showed the standard deviation of patient responses was much smaller than that used to calculate the initial sample size. Therefore, we were able to achieve the desired level of precision in the

mean MCID with fewer patients. To ensure an equal number of patients in each group, a total of 64 patients were enrolled. Even with this smaller number of patients, the study was able to show that different elicitation methods produced statistically significant differences in responses.

Limitations

A drawback to the practicality of the methodology used in this study is the need for labour intensive face-to-face interviews with individual patients. If the methods of this study are to be widely adapted to clinical situations, a more convenient approach will be needed. As discussed earlier, we are developing an audiobooklet that can be used by patients in their home. Using the information learned with this aid, patients can subsequently have a more informed discussion about possible treatment options with their physician.

Another limitation is that a significant portion of participants (18 of 82) failed the comprehension testing portion of the PTOT (they were willing to take warfarin even if it did not reduce the risk of stroke). This seemingly irrational decision making has been observed before. O'Connor and colleagues⁷⁰ found that 12% of the general public preferred a more toxic treatment for cancer compared with a less toxic treatment even though survival rates were the same for both. In another study,⁷¹ 23 of 62 (36%) early stage breast cancer patients were unwilling to forego radiation therapy even when told that such treatment would not be of any benefit. They believed that "some treatment" was better than none at all. The same phenomenon appeared to occur in this study. Failure to pass comprehension testing was also associated with a greater likelihood of concrete thought. Clearly, those that were not able to comprehend the interview information are not the best candidates

for completing probability trade-off tasks. They will probably need to be excluded from further studies similar to this one. They will also need to continue to rely on the advice of others for their treatment choices. In other words, they will continue to give informed consent for treatment as opposed to participate in informed decision making.

Ideally one would like to present patients with information over a time horizon longer than two years. Unfortunately, reliable data beyond a two year time frame are not presently available. However, a two year time frame is probably sufficiently long to represent "chronic" warfarin therapy.

Since the initiation of this study, further information regarding stroke prevention in NVAf has been reported. More accurate estimates of the efficacy of aspirin to prevent stroke in patients with NVAf have been published.⁶⁸ Also, a recent meta-analysis of the five trials investigating the efficacy of warfarin and aspirin to prevent stroke in NVAf, has identified certain risk factors that increase a patient's chance of having a stroke.⁴⁴ Future studies could attempt to elicit patient preferences for warfarin compared with aspirin. Additional studies could also present the patients with their own risk of stroke, and then elicit treatment preferences.

It could be argued that the determination of MCIDs from the perspective of patients represents one of many possibly equally valid points-of-view. For example, there are those who argue that in health care systems where the costs of the sick are paid by the general public, they should be the arbiters rather than those affected. Future studies could determine the MCID for warfarin therapy from the perspective of other groups such as the general public, hospital administrators and health policy makers.

Conclusions

In summary, the PTOT using a flipchart approach was welcomed by patients and appeared to improve their knowledge about their disease, and its possible consequences and treatment. It can be easily adapted to an audiobooklet format which would help patients determine their preferences for treatment. The true benefit of technologies to help patients make informed decisions including flipcharts, audiobooklets, decision boards and videodiscs need to be prospectively evaluated using a number of outcome measures including patients' decisional conflict, knowledge and compliance with treatment. We have also shown that the method of elicitation can have a clinically important effect on patient responses. Future patient preference studies will need to consider this effect.

The methodology developed by this study could be helpful in three ways. First, it could be used to help derive more clinically relevant sample sizes for prospective randomized treatment trials. Second, it could also clarify the patient perspective in the interpretation of previous clinical trial results. For example, the medical community generally believes the proven additional benefit of ticlopidine to secondarily prevent stroke is not sufficient to recommend it as first-line therapy when compared with the efficacy of aspirin.⁷² Experts cite the high cost, potential for significant side effects (e.g. neutropenia), and inconvenience (e.g. initial regular blood monitoring) of ticlopidine as reasons for this recommendation. Given the results of this study, this consensus may not reflect the patient perspective. Third, this methodology could add another dimension to the patient-physician interaction. It promotes patient knowledge and helps clarify their values, possibly allowing them to interact in a more informed manner with their physicians. Thus, patients are able

to participate more fully in their treatment decisions. The result is likely to be greater patient satisfaction and compliance with their treatments.

The average MCID associated with warfarin therapy from the perspective of patients with NVAf who have experienced a course of warfarin therapy is considerably smaller than its known efficacy. Thus, it is our impression that the MCID from the patient perspective can be considerably smaller than that identified by clinicians. If this is true, the potential impact on sample size calculations for prospective clinical trials and the interpretation of completed clinical trials is considerable.

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TABLE 1. Patient characteristics

	completed study (n = 64)	failed comprehension testing (n = 18)
1) mean age in years (SD)	68.9 (9.0)	75.1(10.8)
2) number female (%)	19 (29.7)	8 (44.4)
3) education level (%)		
< 6 years	0 (0.0)	4 (22.2)
6-12 years	19 (29.7)	12 (66.7)
> 12 years	45 (70.3)	2 (11.1)
4) Taking warfarin at time of first interview (%)		
Yes	58 (90.6)	17 (94.4)
No	6 (9.4)	1 (5.6)
5) Mean number of years taking warfarin (SD)	2.68 (1.96)	3.93 (3.86)
6) Response to similiarities (%)		
Abstract	57 (89.0)	9 (50.0)
Concrete	4 (6.3)	9 (50.0)
Missing	3 (4.7)	-
7) Subjective comprehension (%)		
10/10	37 (57.8)	-
7-9.5/10	27 (42.2)	-
<7/10	0 (0.0)	

TABLE 2. The Minimal Clinically Important Difference

PP - ping ponging

SKE - starting at known efficacy

Group	First Interview		Second Interview	
	Elicitation Method		Elicitation Method	
	PP mean (95% CI)	SKE mean (95% CI)	PP mean (95% CI)	SKE mean (95% CI)
1 (n = 16)	2.44 (1.59,3.29)		1.91 (1.20, 2.62)	
2 (n = 16)	1.16 (0.60,1.72)			1.97 (0.88,3.06)
3 (n = 16)		2.44 (1.42,3.46)	1.22 (0.72,1.72)	
4 (n = 16)		2.00 (1.18,2.82)		1.50 (0.83,2.17)
mean (n=32)	1.80 (1.29,2.31)	2.22 (1.57,2.87)	1.56 (1.12,2.00)	1.73 (1.09,2.37)
interview mean (n = 64)	2.01 (1.60,2.42)		1.65 (1.27, 2.03)	

Given a baseline stroke risk of 10 out of 100 in the next two years, mean responses and 95% confidence intervals (95% CI) for the minimum reduction in stroke risk needed over the next two years for patients to want to take warfarin

Table 3**Summary of the Analysis of Variance of the Two Period Cross-Over Design with Four Sequences**

Source of Variation	df	SS	MS	F	P-value
Between Subjects	63	190.9688	3.0313		
Within Subjects					
Periods	1	4.1328	4.1328	1.9475	0.1680
Direct Treatments	1	16.5039	16.5039	7.7770	0.0071
Carry-over	1	0.0039	0.0039	0.0018	0.9663
Direct Trt x Carry-over	1	0.7813	0.7813	0.3682	0.5463
Residual	60	127.3281	2.1221		
Total (corrected)	127	339.7188			

(1) P=0.1680

There is insufficient evidence to reject the null hypothesis that the parameter corresponding to the 'period' effect is zero (ie. there is no 'period' effect).

(2) P=0.9663

There is insufficient evidence to reject the null hypothesis that the parameter corresponding to the 'direct treatment x carry-over' interaction effect is zero (ie. there is no 'direct treatment x carry-over' effect).

(3) P=0.5463

There is insufficient evidence to reject the null hypothesis that the parameter corresponding to the 'carry-over' effect is zero (ie. there is no 'carry-over' effect).

(4) P=0.0071

There is sufficient evidence to reject the null hypothesis that the parameter corresponding to the 'direct treatment' effect is zero (ie. there is a 'direct treatment' effect).

Point estimate of the treatment effect (difference in the treatments) is 1.015

Table 4.**Summary of the Analysis of Variance of the Two Period Cross-Over Design with Four Sequences (Log Transformation)**

Source of Variation	df	SS	MS	F	P-value
Between Subjects	63	11.2605	0.1787		
Within Subjects					
Periods	1	0.3719	0.3719	3.7005	0.0591
Direct Treatments	1	0.4922	0.4922	4.8975	0.0307
Carry-over	1	0.0002	0.0002	0.0020	0.9645
Direct Trt x Carry-over	1	0.0060	0.0060	0.0597	0.8078
Residual	60	6.0318	0.1005		
Total (corrected)	127	18.1625			

- (1) P=0.0591 There is insufficient evidence to reject the null hypothesis that the parameter corresponding to the 'period' effect is zero (ie. there is no 'period' effect).
- (2) P=0.9645 There is insufficient evidence to reject the null hypothesis that the parameter corresponding to the 'direct treatment x carry-over' interaction effect is zero (ie. there is no 'direct treatment x carry-over' effect).
- (3) P=0.8078 There is insufficient evidence to reject the null hypothesis that the parameter corresponding to the 'carry-over' effect is zero (ie. there is no 'carry-over' effect).
- (4) P=0.0307 There is sufficient evidence to reject the null hypothesis that the parameter corresponding to the 'direct treatment' effect is zero (ie. there is a 'direct treatment' effect).

TABLE 5. Wilcoxon Signed Rank Testing

Group	n	Sequence	P - value
2	16	PP → SKE	> .10
3	16	SKE → PP	> .10
2 + 3 combined	32	-	0.03

TABLE 6. Spearman Rank Correlation Coefficients

Group	Sequence of Elicitation Methods	Spearman Rank Correlation Coefficient	p value
1	PP→PP	0.624	0.01
2	PP→SKE	-0.088	0.75
3	SKE→PP	0.064	0.81
4	SKE→SKE	0.509	0.04

PP - ping ponging

SKE - starting at known efficacy

TABLE 7. Patient estimates of stroke risk in next 2 years (n = 64)

Percentage chance of having a stroke in next 2 years:	%	Prior to first interview		After first interview	
		n	%	n	%
if <u>not</u> taking warfarin	0	4	6.2	2	3.1
	0.5 - 10	8	12.6	37	57.8
	11 - 25	4	6.2	5	7.8
	26 - 50	14	21.9	6	9.4
	> 50	13	20.3	9	14.1
	unable to estimate	21	32.8	5	7.8
if taking warfarin	0	21	32.8	13	20.3
	0.5 - 10	13	20.3	42	65.6
	11 - 25	9	14.0	1	1.6
	26 - 50	2	3.1	0	0.0
	> 50	0	0.0	2	3.1
	unable to estimate	19	29.7	6	9.4

TABLE 8. Comparison of minimal clinically important difference (MCID) of patients according to subjective comprehension of interview information

	Subjective Comprehension		p - value
	perfect (n = 37)	not perfect (n = 27)	
Mean MCID response on first interview (SD)	1.89 (1.60)	2.17 (1.82)	p = .53
Mean difference in MCID responses from first to second interview (SD)	-.22 (1.64)	-.56 (2.71)	p = .54

TABLE 9. Comparison of the patient minimal clinically important difference (MCID) responses according to type of thinking

	Type of Thinking		p - value
	abstract (n = 51)	concrete (n = 4)	
Mean response MCID on first interview (SD)	2.04 (1.71)	1.38 (0.75)	p = .44
Mean difference in MCID responses from first to second interview (SD)	-.32 (2.16)	-.25 (1.66)	p = .47

TABLE 10. Comparison of patient minimal clinically important difference (MCID) responses according to level of education

	Education Level (years)		p - value
	6 - 12 (n = 19)	> 12 (n = 45)	
Mean MCID response on first interview (SD)	2.00 (2.21)	2.02 (1.44)	p = .98
Mean difference in MCID responses from first to second interview (SD)	-.50 (2.69)	-.30 (1.90)	p = .74

TABLE 11. Comparison of the patient minimal clinically important difference (MCID) responses according to whether or not taking warfarin at time of first interview

	Taking warfarin at time of first interview		p - value
	Yes (n = 58)	No (n = 6)	
Mean response MCID on first interview (SD)	1.91 (1.60)	2.92 (2.37)	p = .168
Mean difference in MCID responses from first to second interview (SD)	-0.24 (2.10)	-1.50 (2.53)	p = .173

TABLE 12. Patient responses to semi-structured questionnaire

	NUMBER (%)
Knew someone with a stroke	59(92.2)
Knew someone taking warfarin	32(50.0)
Found any part of presentation confusing	2 (3.1)
Found any part of presentation upsetting	0 (0.0)
Made more confident about decisions	50(78.1)

TABLE 13. Responses to O'Connor Decisional Conflict Scale (n = 64)

Scale Item	% Agree/Strongly Agree
<u>Certainty Making Decision</u>	
decision is easy	81.2
sure about what to do	98.4
clear what choice is best	79.7
<u>Informed About Options/Benefits/Risks</u>	
aware of warfarin to reduce risk of stroke	100.0
know benefits of warfarin	100.0
know risks of warfarin	96.9
have enough information/advice	79.7
<u>Clear About Importance Benefits/Risks</u>	
know importance of benefits	100.0
know importance of risks	87.6
sure which are more important	84.4
<u>Social Support</u>	
no pressure from others	96.9
right amount of support	96.9
<u>Perceived Effective Decision Making</u>	
informed choice	96.9
shows what's important to me	100.0
expect to stick with decision	96.9
satisfied with decision	100.0

Figure 1. Flow chart of study recruitment

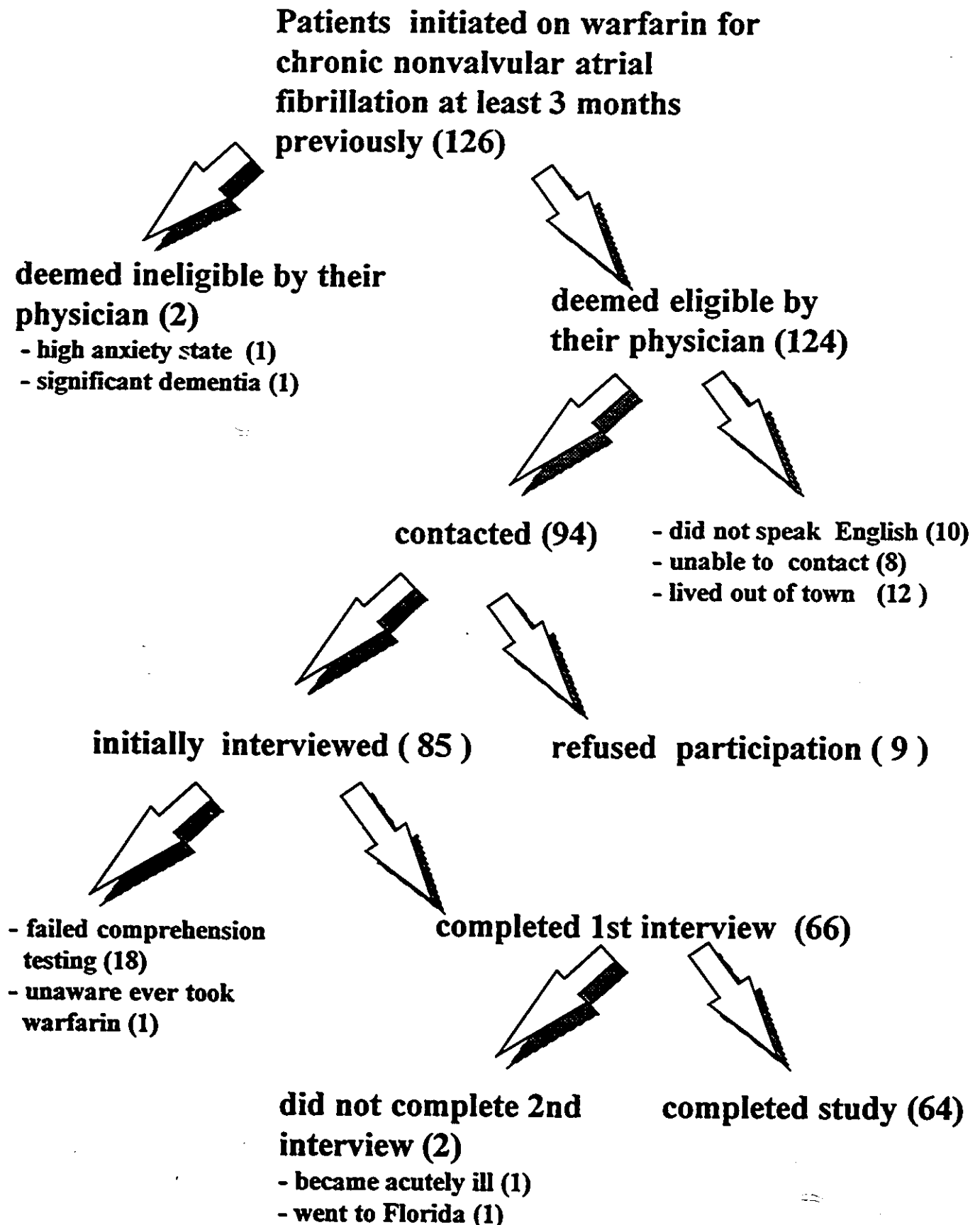
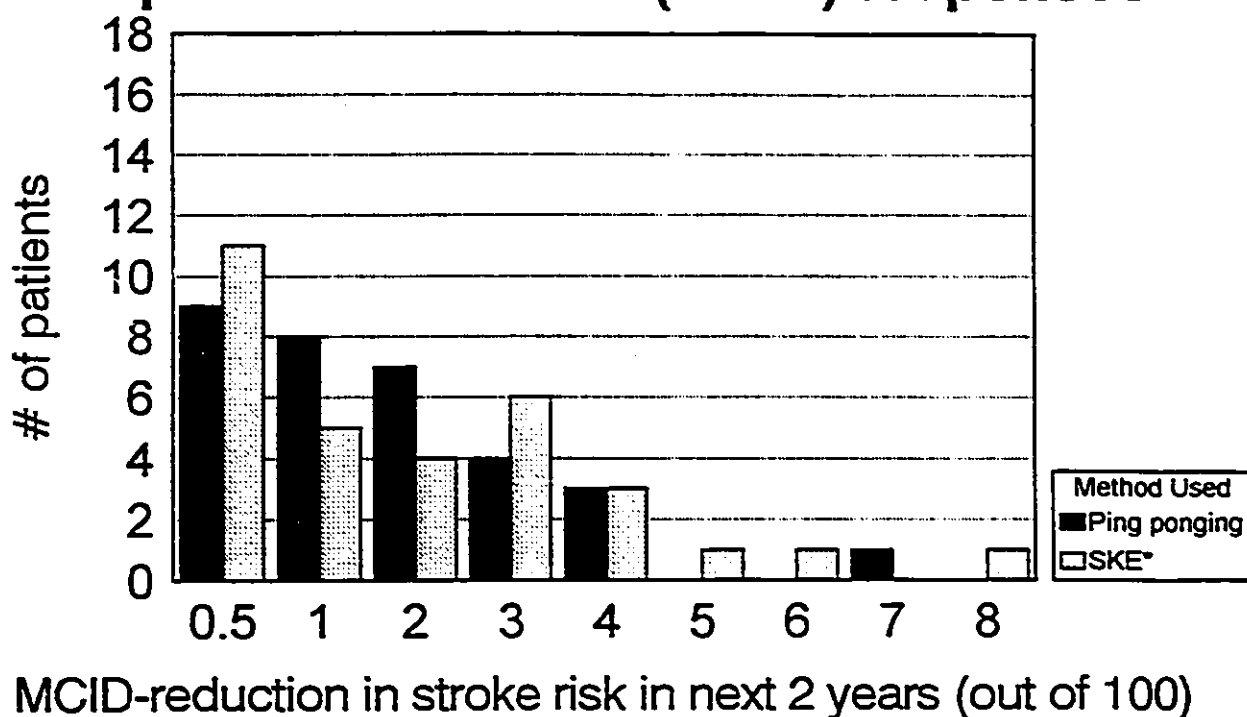
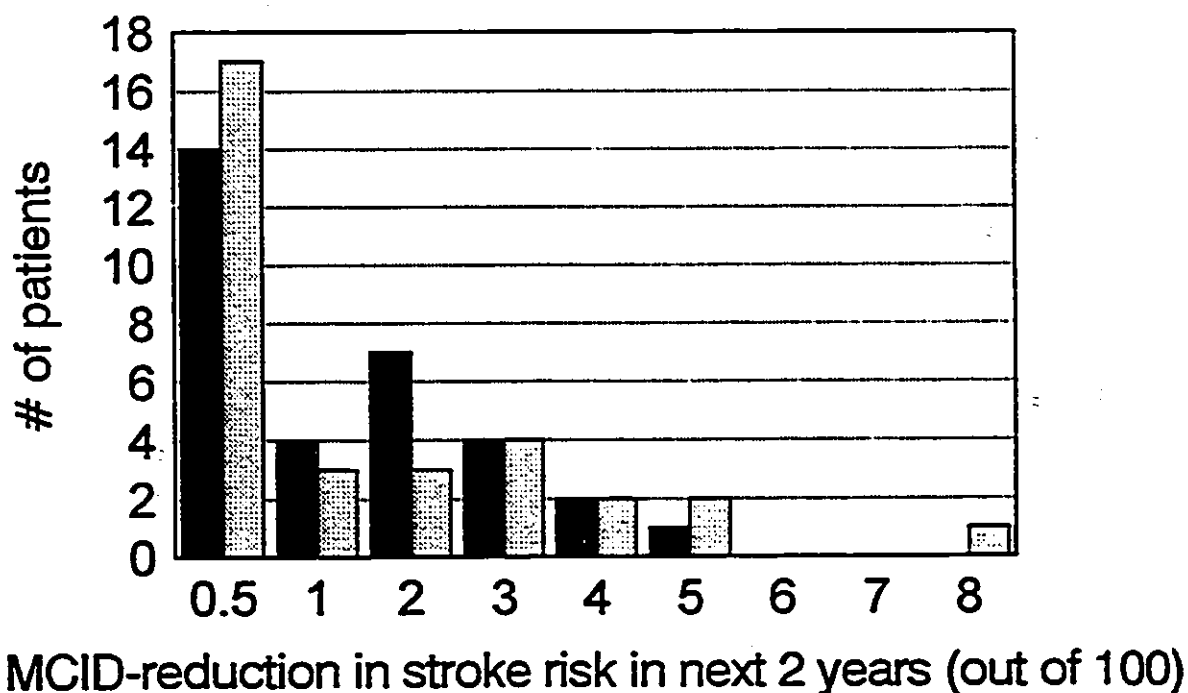


Figure 2. Distribution of patient minimal clinically important difference (MCID) responses

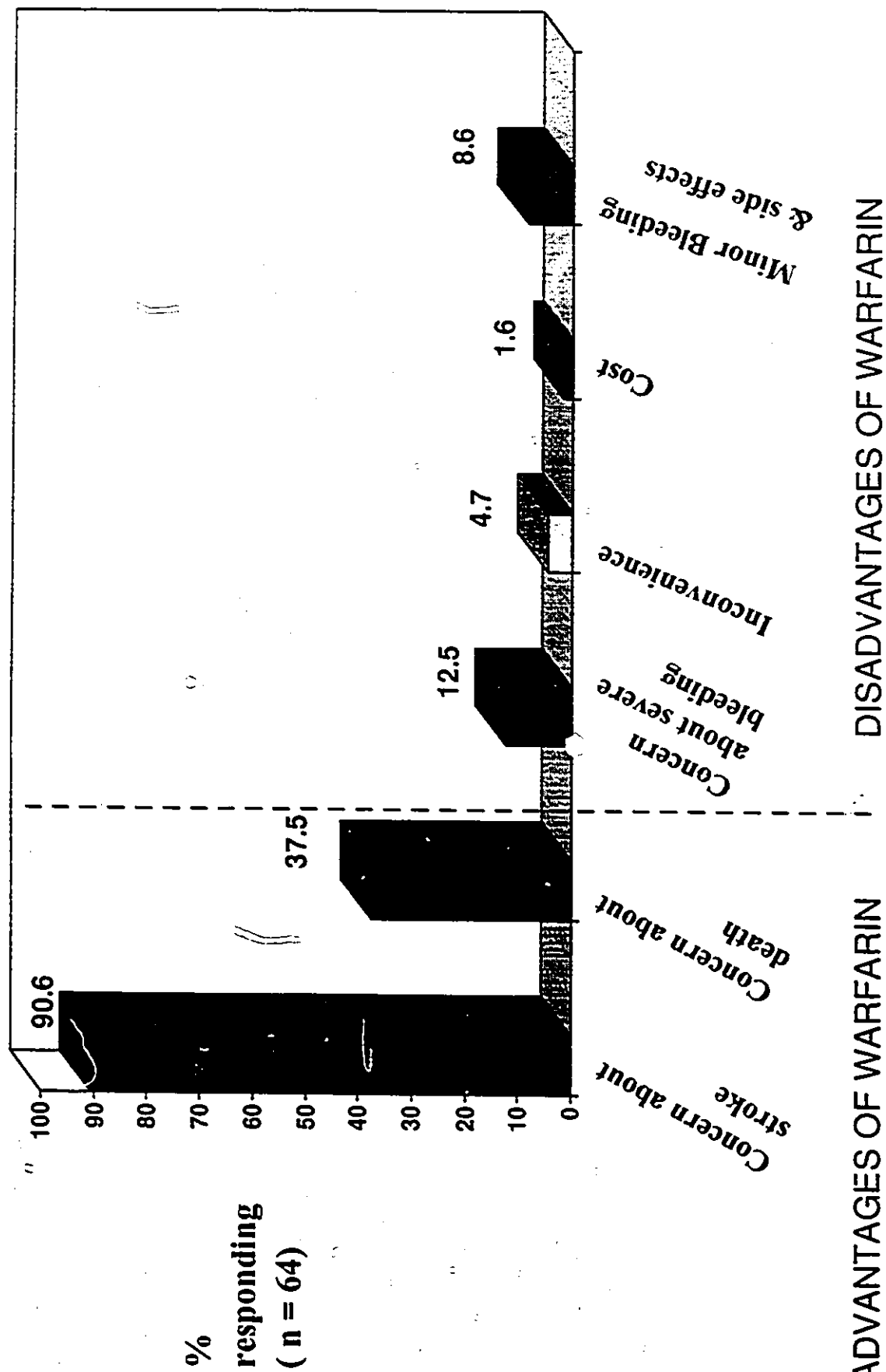


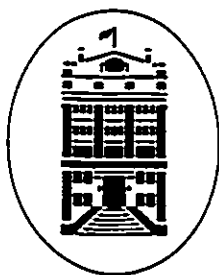
Second interview



*SKE: starting at known efficacy

Figure 3. Factors identified by patients as important in decision making (may answer more than one)





Appendix A

QUANTIFYING THE MINIMAL CLINICALLY IMPORTANT DIFFERENCE FROM A PATIENT PERSPECTIVE

**Ottawa
Civic Hospital**

1053 Carling Ave.,
Ottawa, Ontario
Canada K1Y 4E9
(613) 761-4000

Dear Doctor,

As you know, the Dept. of Family Medicine is involved in a research project which involves interviewing patients about their perceptions of taking warfarin for the prevention of stroke in atrial fibrillation. It is possible that one of your patients will be identified through the Department's data base or anticoagulation log book and be asked to participate. Your nurse will be telephoning each patient and informing them of the study, describing its pertinent details, answering any questions, and asking them if a study team member would be allowed to contact them. We will attempt to obtain their permission to have a study team member contact them without your involvement, however if the patient wishes to confer with you, this will be encouraged. If the patient agrees to have a study team member contact them, this person (likely, Dr. Neda Seki) will then attempt to arrange an interview with the patient at the patient's convenience. Prior to that interview, the patient will be asked for written formal consent.

To help you in your discussion with such patients, we would like to provide the following information about the study:

- each patient will be interviewed on two separate occasions two weeks apart by a study team member (Dr. Neda Seki) at the patient's convenience. The first interview will take approximately one hour and the second, approximately a half hour. The patient will be asked for no other involvement in this study.
- the subject matter of the interview will be their perceptions of the benefits and risks of taking warfarin to prevent stroke because they have atrial fibrillation. They will be asked to make hypothetical choices about warfarin therapy based on their assessment of the risks/benefits of warfarin treatment.
- the patient will be told during the interview:
 - a) their average risk of stroke over the next two years if not taking warfarin (10%)

b) their average risk of a severe bleed over the next two years if taking warfarin (3%).

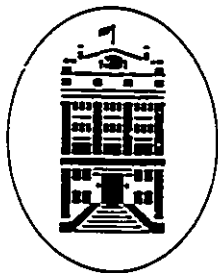
- there are no immediate benefits or risks to their participation.
- initial contact was made by the nurse in charge of the anti-coagulation log book
- if they agree to participate, then a study team member will contact them to arrange a meeting
- any subject may withdraw from the study at any time with no ramifications
- anonymity of each subject is guaranteed.

We hope the above information is useful in any discussion with your patient. If you have any further questions or comments, please contact us at 761-5110 or 761-4334.

Yours sincerely,

Malcolm Man-Son-Hing MD
Geriatric Assessment Unit
Ottawa Civic Hospital

Jacques Lemelin MD
Department of Family Medicine
Ottawa Civic Hospital



**Ottawa
Civic Hospital**

1053 Carling Ave.,
Ottawa, Ontario
Canada K1Y 4E9
(613) 761-4000

Appendix B

CONSENT FORM

DETERMINING THE MINIMAL CLINICALLY IMPORTANT DIFFERENCE FROM A PATIENT PERSPECTIVE

The minimal clinically important difference 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. Physicians have had great difficulty in precisely estimating this quantity.

The physicians conducting this research study are attempting to develop away of estimating the minimal clinically important difference from a patient perspective. This information would be helpful to patients and physicians in assessing whether any treatment is of overall benefit to the patient.

Because you have an irregular heart rhythm called atrial fibrillation and are taking a blood thinner named warfarin (coumadin), the study physicians would like to interview you about your experiences with this medication.

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, a member of the study team will conduct a 10-15 minute interview. You will be asked for no further involvement. 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.

If you agree to participate, please sign this consent.

NAME

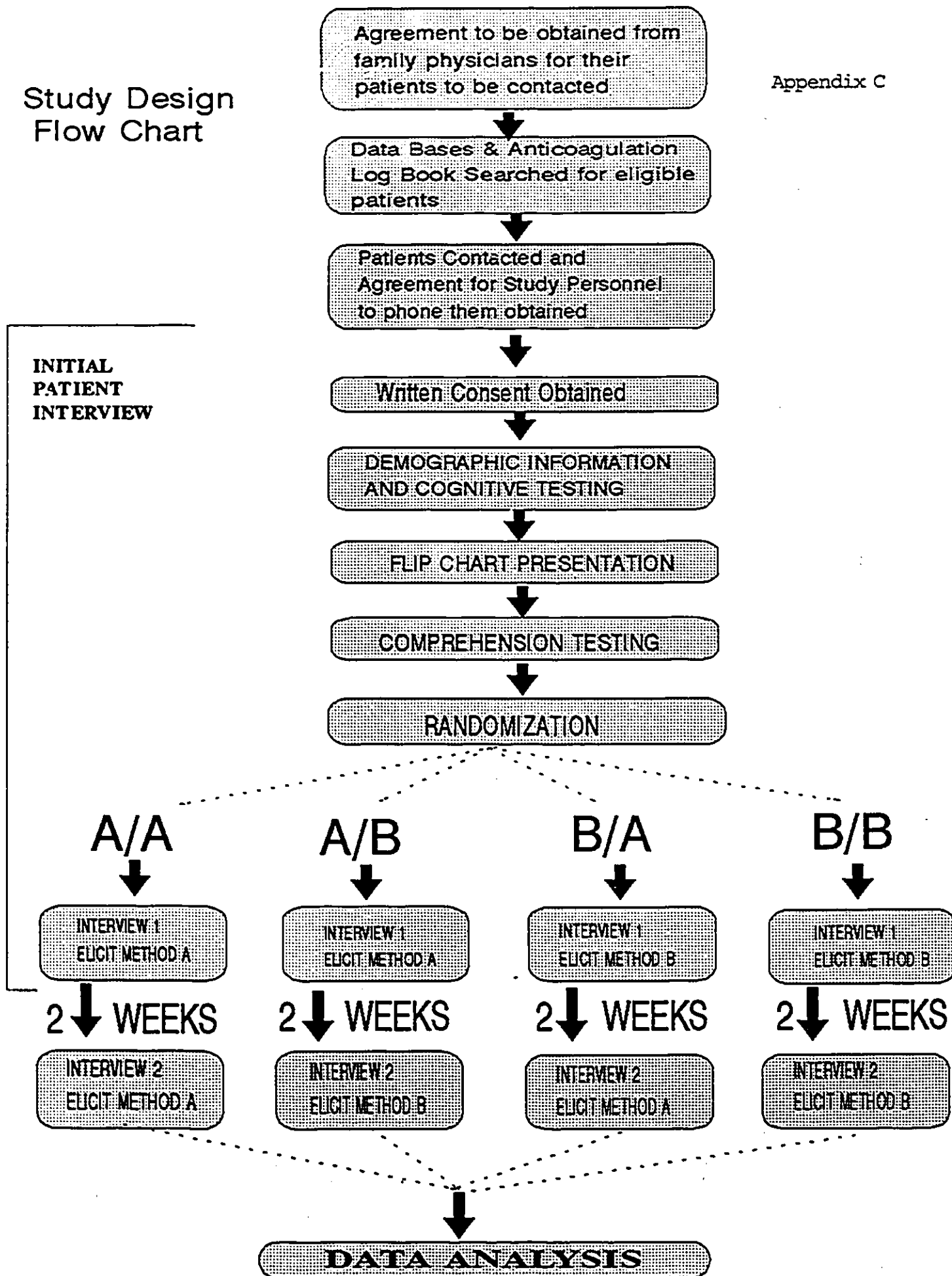
WITNESS

DATE

For further information, please contact Dr. M. Hing at
761-5110

Study Design Flow Chart

Appendix C



STUDY TIME CHART

	JAN	FEB	MAR	APR	MAY	JUNE	JULY	AUG	SEPT	OCT	NOV	DEC
Meeting with Family Physicians	X											
Mail Out of Physician Information Sheets		X										
Identification of Eligible Patients		X										
Patient Interviews			X	X	X	X	X	X	X	X	X	
Data Analysis												X

Appendix D

ATRIAL FIBRILLATION

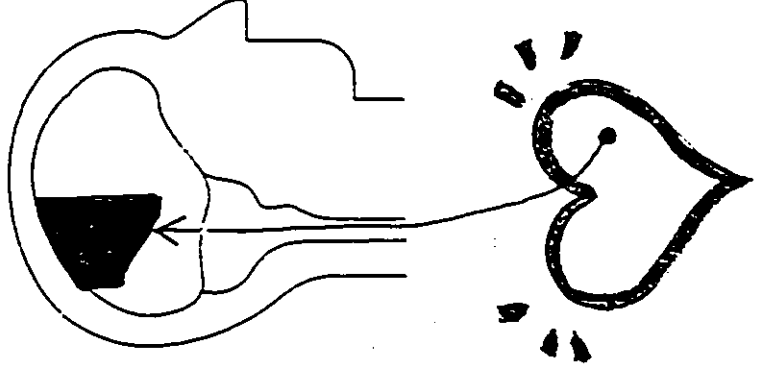


- disorder of the heart
- the heart beats irregularly
- a very common heart condition
- increases your risk of stroke ●

STROKE



- Occurs because a blood clot has formed in the heart, breaks off and travels to the brain



MINOR STROKE



PHYSICAL SYMPTOMS

- *You suddenly cannot move or feel one arm and one leg*

MENTAL SYMPTOMS

- *You are unable to fully understand what is being said to you*
- *You have difficulty expressing yourself*

PAIN

- *You feel no physical pain*

RECOVERY

- *You are admitted to hospital*
- *Your weakness, numbness and problem with understanding improve but you still feel slightly weak or numb in one arm and one leg*
- *You are able to do almost all of the activities you previously did before your stroke*
- *You can function independently*
- *You leave the hospital after one week*

FURTHER RISK

- *You have an increased risk of having more strokes*

MAJOR STROKE

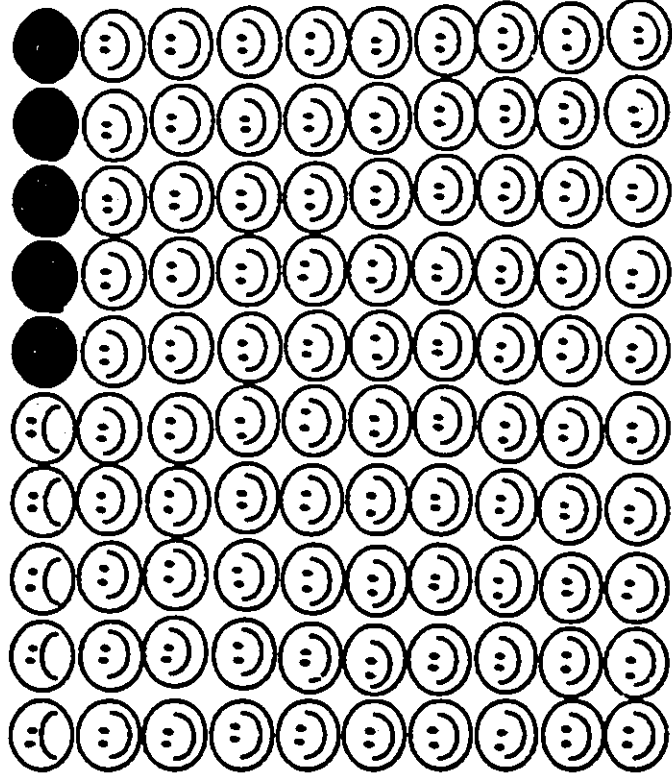
PHYSICAL SYMPTOMS	● <i>You suddenly are dizzy and black out</i> ● <i>You are unable to move one arm and one leg</i> ● <i>You cannot swallow or control your bladder and bowels</i>
MENTAL SYMPTOMS	● <i>You are unable to understand what is being said</i> ● <i>You are unable to talk</i>
PAIN	● <i>You feel no physical pain</i>
RECOVERY	● <i>You are admitted to hospital</i> ● <i>You cannot dress</i> ● <i>The nurses feed you</i> ● <i>You cannot walk</i> ● <i>After 1 month with physiotherapy, you are able to wiggle your toes and lift your arm off the bed</i>
FURTHER RISK	● <i>You remain this way for the rest of your life</i> ● <i>Another illness will likely cause your death</i>

STROKES CAN BE MINOR OR MAJOR IN SEVERITY

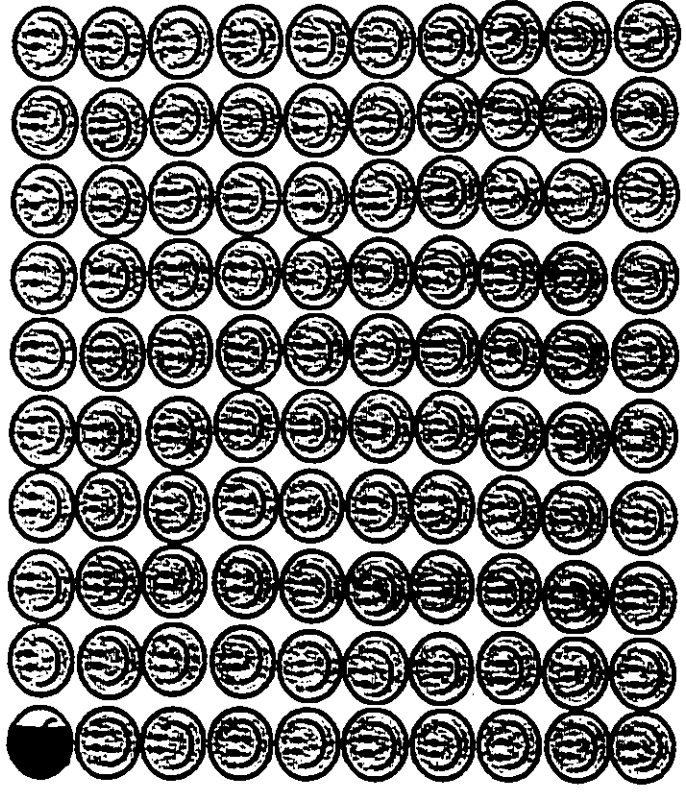
	MINOR STROKE 	MAJOR STROKE 
PHYSICAL SYMPTOMS	You suddenly cannot move or feel one arm and one leg	- You suddenly are dizzy and black out - You are unable to move one arm and one leg - You cannot swallow or control bladder and bowel
MENTAL SYMPTOMS	- You are unable to fully understand what is being said to you - You have difficulty expressing yourself	You are unable to understand what is being said
PAIN	You feel no physical pain	- You are unable to talk - You feel no physical pain
RECOVERY	- You are admitted to hospital - Your weakness, numbness and problem with understanding improve but you still feel slightly weak or numb in one arm and one leg - You are able to do almost all of the activities you previously did before the stroke - You can function independently - You leave the hospital after one week	- You are admitted to hospital - You cannot dress - The nurses feed you - You cannot walk - After 1 month with physiotherapy, you are able to wiggle your toes and lift your arm off the bed - You remain this way for the rest of your life
FURTHER RISK	You have an increased risk of having more strokes	Another illness will likely cause your death

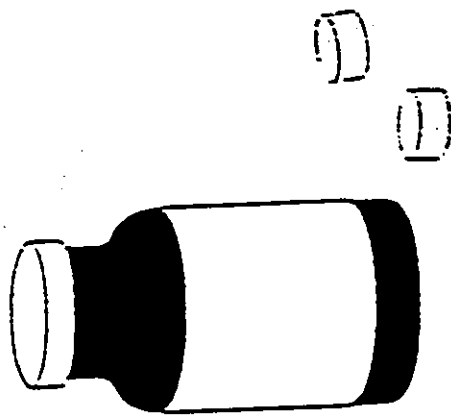
IF YOU HAVE A STROKE, YOUR CHANCE OF HAVING A MINOR OR MAJOR STROKE ARE EQUAL.

Because you have atrial fibrillation, you have a 10 out of 100 chance of having a stroke over the next two years.

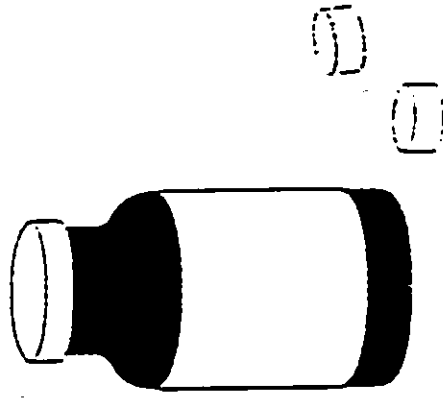


**People who do not have atrial fibrillation
have a less than 1 in a 100 chance of
having a stroke in the next two years**





Taking warfarin increases your chance of severe bleeding.



You are presently taking warfarin to help prevent a stroke.

SEVERE BLEEDING



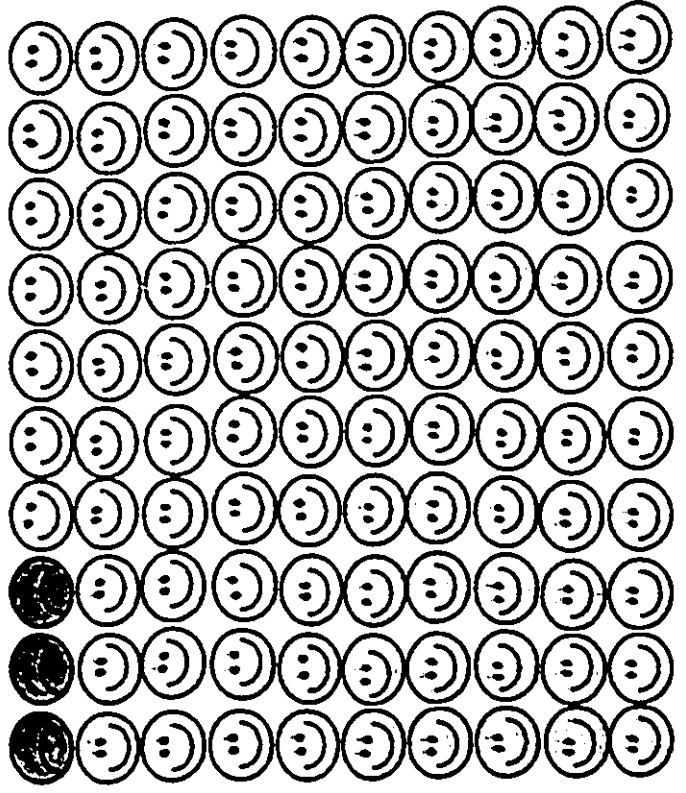
AN EXAMPLE OF THIS IS A STOMACH BLEED:

PHYSICAL	• you feel unwell for two days then suddenly you vomit blood
TREATMENT	• you are admitted to hospital • you stop taking warfarin • a doctor puts a tube down your throat to see where you are bleeding from • you receive sedation to ease the discomfort of the test • you do not need an operation • you receive blood transfusions to replace the blood you lost
RECOVERY	• you stay in hospital one week • you feel well at the end of your hospital stay • you need to take pills for the next six months to prevent further bleeding • you do not take warfarin anymore • after that you are back to normal

SEVERE BLEEDING



- can occur in 3 out of 100 people taking warfarin for two years.



 Taking warfarin can mean COSTS to yourself and family.

For example:

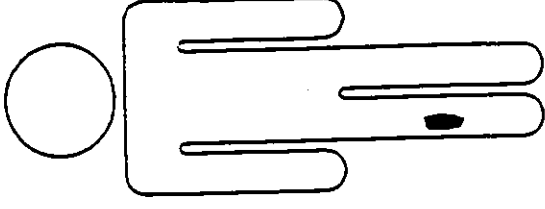
- parking 

- cost of warfarin

Taking warfarin can cause SIDE EFFECTS.

For example:

- **easy bruising**



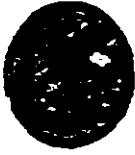
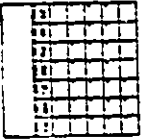
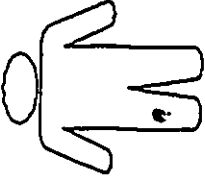
SUMMARY

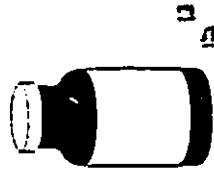
Taking warfarin  has:

Advantages

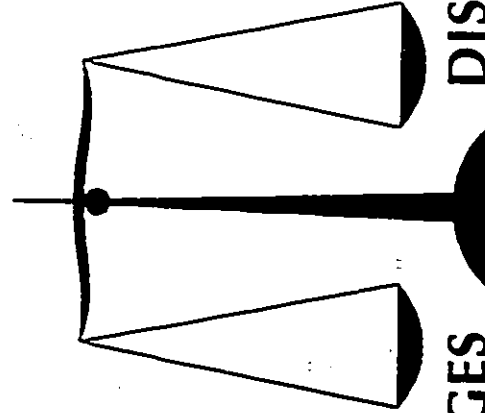
- reduced chance of stroke

Disadvantages

- increased chance of severe bleeding 
- inconveniences 
- costs 
- side effects 



WARFARIN



ADVANTAGES

DISADVANTAGES

TEXT FOR PATIENT INTERVIEW

Page 1

USING FLIP CHART

"Atrial fibrillation is a disorder of the heart in which the heart beats irregularly. It is a very common heart condition. Having atrial fibrillation increases your chance of having a stroke."

Page 2

"A stroke from atrial fibrillation occurs because a blood clot has formed in the heart, breaks off and travels to the brain. [PAUSE] Do you have any questions so far?"

REVIEW FIRST TWO PAGES IF NECESSARY

"Please interrupt me at any time if anything needs further explanation."

Page 3

"Strokes can be minor or major in severity. Let me describe what having a minor stroke would be like."

USING A CARD, GO DOWN THE LIST OF FEATURES DESCRIBING A MINOR STROKE

"That was a description of a minor stroke."

Page 4

"Now let me describe what having a major stroke would be like."

USING A CARD, GO DOWN THE LIST OF FEATURES FOR A DESCRIBING A MAJOR STROKE

Page 5

"Here is a summary of what a minor and major stroke would be like. Please remember that if you do have a stroke, your chance of having a minor or major stroke is about equal."

Page 6

"Because you have atrial fibrillation, you have a 10 out of 100 chance of having a stroke in the next two years if you do not take warfarin."

POINT TO ICON

"Another way of saying this is, here are 100 people with atrial fibrillation who are not taking warfarin. Five of these people will have a minor stroke. People with minor strokes are shown with light blue unhappy faces."

POINT TO LIGHT BLUE UNHAPPY FACES

"And five will have a major stroke. People with major strokes are shown with dark blue unhappy faces."

POINT TO DARK BLUE UNHAPPY FACES

"A total of 10 out of 100 people with atrial fibrillation who are not taking warfarin will have a stroke in the next two years. Or another way of saying the same thing is 90 out of 100 people with atrial fibrillation who are not taking warfarin will not have a stroke in the next two years."

POINT TO HAPPY FACES

Page 7

"In contrast, people who do not have atrial fibrillation have a less than 1 out of 100 chance of having a stroke."

POINT TO ICON

"Here are 100 people without atrial fibrillation. Less than 1 of them will have a stroke in the next two years. [PAUSE] So you can see that people with atrial fibrillation have a much greater chance of having a stroke than people who don't have atrial fibrillation."

Page 8a

"In people such as yourself who have atrial fibrillation, the best way of reducing the chance of having a stroke is to take warfarin on a regular basis. You are presently taking warfarin to help prevent a stroke."

Page 8b

"In people such as yourself who have atrial fibrillation, the best way of reducing the

chance of having a stroke is to take warfarin on a regular basis. You were taking warfarin in the past to help prevent a stroke."

Page 9

"The main risk of taking warfarin is that it increases your chance of severe bleeding."

Page 10

"There are several possible ways in which you may have a severe bleeding episode if taking warfarin. Let me describe to you an example of severe bleeding."

USING A CARD, GO DOWN THE LIST OF FEATURES DESCRIBING A STOMACH BLEED

Page 11

"Taking warfarin means that your chance of having a similar severe bleeding episode as I just described is 3 out of 100 in the next two years."

POINT TO ICON

"Here are 100 people with atrial fibrillation who are taking warfarin, 3 of them will have a severe bleed in the next two years... Do you have any questions so far?"

PAUSE TO ANSWER ANY QUESTIONS

Page 12

"Taking warfarin can be inconvenient. For example, you need to go to regular appointments to have your blood checked. You also have to be sure to avoid activities that may increase your chance of bleeding. I must stress that you certainly can do normal daily activities with no risk. It is only activities in which there is a large risk of injury that you need to avoid. An example of such an activity is contact sports. Are there any other things that you can think of that are inconvenient about taking warfarin?"

ENCOURAGE SUBJECT TO THINK OF PERSONAL EXAMPLES AND RECORD

Page 13

"Taking warfarin can also mean costs to you and your family. For example, you may need to pay for parking when having your blood checked."

"Can you think of any other costs that you or your family have because you take warfarin?"

ENCOURAGE SUBJECT TO THINK OF PERSONAL EXAMPLES AND RECORD

Page 14

"A side effect of warfarin is easy bruising. You might bump your knee against a piece of furniture and cause a skin bruise when normally nothing would happen. There is no possibility of anything serious happening to you because of this bruise. Have you noticed any side effects of taking warfarin?"

ENCOURAGE SUBJECT TO THINK OF PERSONAL EXAMPLES AND RECORD

Page 15

"To summarize what we have just talked about, because you have atrial fibrillation you have an increased chance of having a stroke. Taking warfarin has the advantage of reducing your chance of having a stroke, but at the same time, taking warfarin can also have disadvantages. One disadvantage is that you have an increased chance of severe bleeding. Taking warfarin can also be inconvenient, costly and cause minor side effects."

Page 16

"That finishes the presentation with the flip chart. Is there anything that I did not make clear?...It is important that you feel comfortable with the information we just reviewed. I would be happy to go over anything that I did not explain well enough."

REVIEW ANY ASPECTS OF PRESENTATION THAT THE SUBJECT WOULD LIKE

"I am going to leave the flip chart here. Please feel free to refer to it at anytime during the rest of the interview."

"During the rest of our interview, I am going to present a series of imaginary situations involving the use of warfarin. In each different imaginary situation, I will ask you to make a choice about whether you would want to take or not want to take warfarin based on its advantages and disadvantages. As the situations we do together are imaginary, there are no right or wrong answers, just judge for yourself what you would choose."

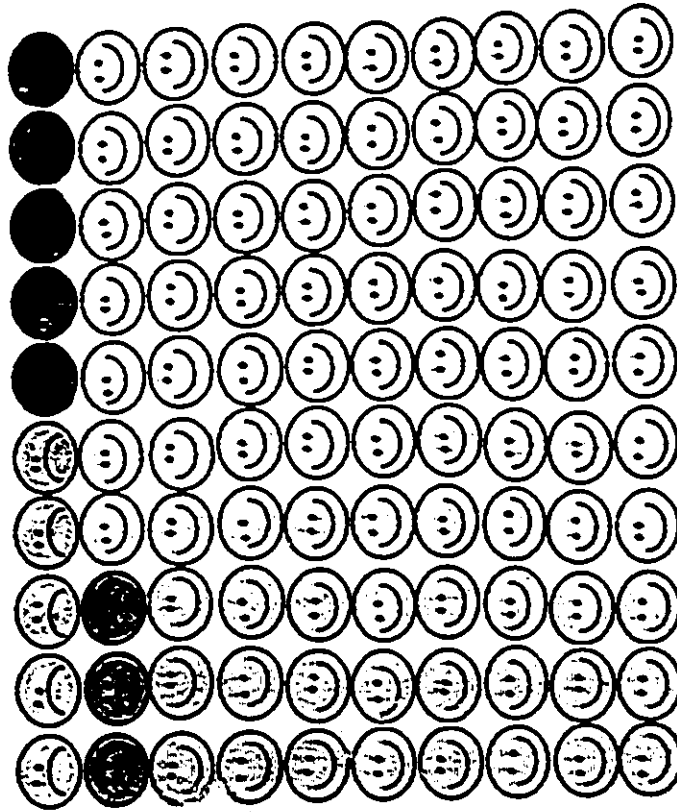
**PUT FLIP CHART IN FRONT OF SUBJECT AND LEAVE OPEN ON PAGE 15
(second last page)**

Chance of STROKE over next 2 years

● 10 out of 100

Chance of SEVERE BLEEDING over next 2 years

● 3 out of 100



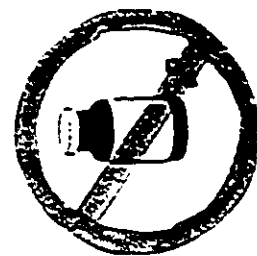
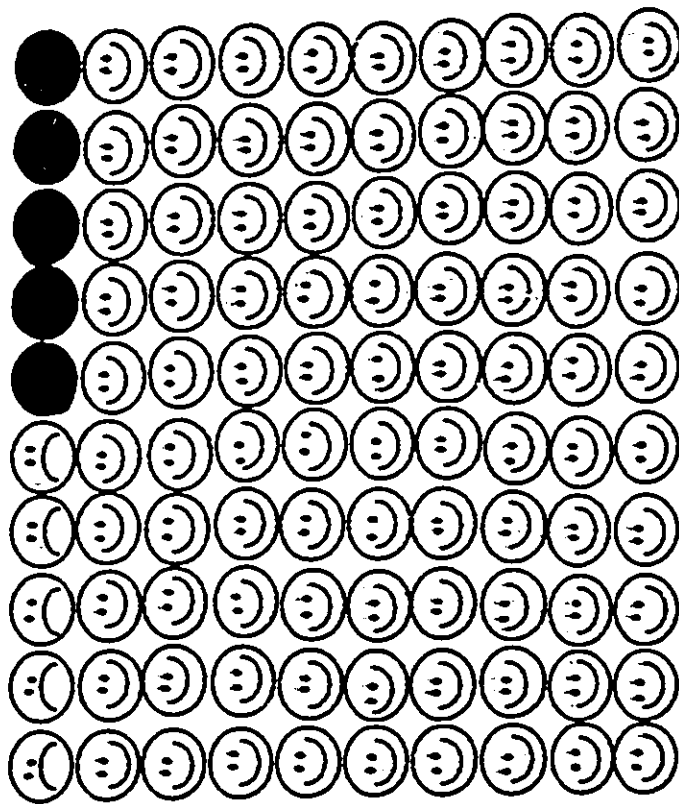
Appendix G



TAKING WARFARIN

Chance of STROKE over next 2 years

● 10 out of 100



NOT TAKING WARFARIN

COMPREHENSION TESTING

"Now for the first imaginary situation in which you will be asked to make a choice. Using the information about atrial fibrillation, minor and major strokes, and warfarin that we just discussed with the flip chart, I am interested in determining how important you feel taking warfarin for the prevention of stroke is. As we discussed with the flip chart, because you have atrial fibrillation your chance of having a stroke, if you do not take warfarin, is 10 out of 100 over the next two years. I will show this again here."

**PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK.
POINT TO ICON**

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING "TAKING WARFARIN" RISK

"Let us imagine, remember this is purely imaginary, that the newest information from medical science shows that taking warfarin has no effect on the chance of having a stroke in people who have atrial fibrillation. Again I emphasize that this situation is purely imaginary. In other words, in this imaginary situation, taking warfarin does not reduce the chance of having a stroke in people with atrial fibrillation. If these 100 people were taking warfarin instead of not taking warfarin, their chance of stroke remains the same at 10 out of 100 over the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Ten of them will have a stroke in the next two years. In this imaginary situation, warfarin has not reduced their chance of having a stroke. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or not to take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not to take warfarin?"

RECORD RESPONSE. SUBJECT SHOULD CHOOSE TO NOT TAKE WARFARIN. TO ANSWER OTHERWISE MEANS THAT THEY DO NOT UNDERSTAND THE SCENARIO. FURTHER EXPLANATION WITH THE FLIP CHART IS NECESSARY. ASK FOR CHOICE AGAIN.

CONTINUE AS PER PROTOCOL:

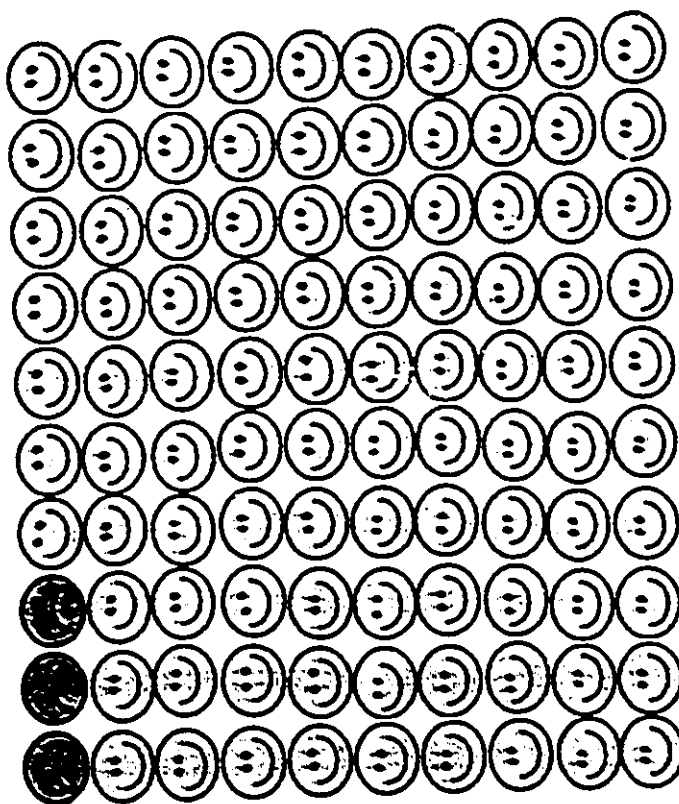
- a) Ping-ponging
 - go to ping-ponging text
- b) Starting at a Mid-point
 - go to starting at a mid-point text

Chance of STROKE over next 2 years

● 0 out of 100

Chance of SEVERE BLEEDING over next 2 years

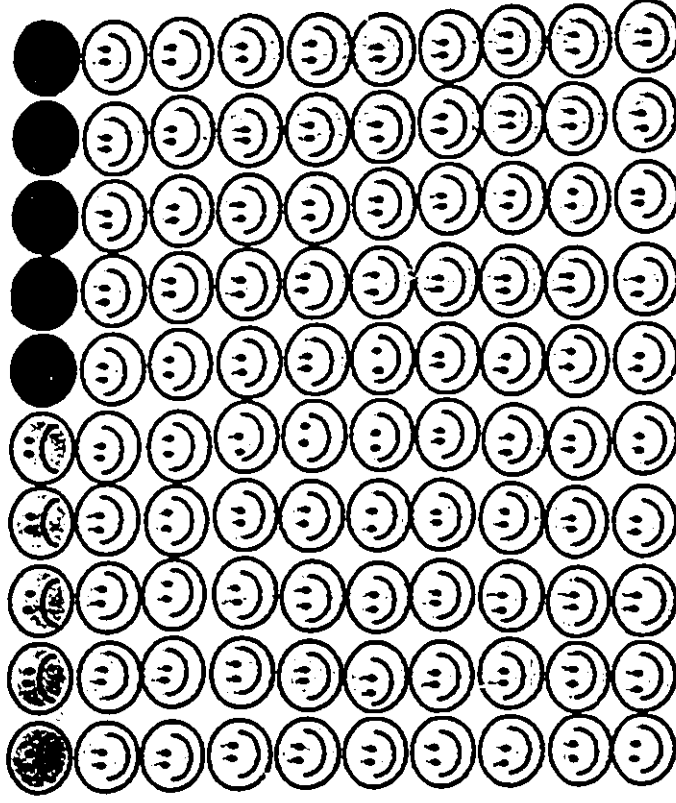
● 3 out of 100



TAKING WARFARIN 

Chance of STROKE over next 2 years

● 10 out of 100



NOT TAKING WARFARIN

TEXT FOR PING-PONGING ELICITATION METHOD

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 0 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 0 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. None of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or to not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

GO TO NEXT PAGE

☐ NOT TAKE WARFARIN

**FURTHER EXPLANATION,
MAY CHANGE ANSWER
(SEE BELOW *)**

- * **IF SUBJECT CHOOSES "NOT TAKE WARFARIN" THEN ASK FOR AN EXPLANATION. IF IT APPEARS THAT PATIENT DOES NOT UNDERSTAND THAT THERE IS NO CHANCE OF STROKE IN THIS SCENARIO, REPEAT PRESENTATION OF THIS SCENARIO. THE SUBJECT MAY CHANGE ANSWER IF HE/SHE CHOOSES TO. IF THE SUBJECT DOES NOT WANT TO CHANGE ANSWER THEN STOP.**

RECORD CHANGE OF ANSWER HERE ☐ GO TO NEXT PAGE

9 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 9 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 9 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Nine of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN TRY 9.5/100
 ☐ NOT TAKE WARFARIN GO TO 1/100

1 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 1 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 1 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. One of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

GO TO 8/100

☐ NOT TAKE WARFARIN

STOP

8 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 8 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 8 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Eight of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

STOP

☐ NOT TAKE WARFARIN

GO TO 2/100

2 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 2 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 2 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Two of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ **TAKE WARFARIN** **GO TO 7/100**
 ☐ **NOT TAKE WARFARIN** **STOP**

7 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 7 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 7 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Seven of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

STOP

☐ NOT TAKE WARFARIN

GO TO 3/100

3 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 3 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 3 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Three of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

GO TO 6/100

☐ NOT TAKE WARFARIN

STOP

6 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 6 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 6 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Six of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

STOP

☐ NOT TAKE WARFARIN

GO TO 4/100

4 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 4 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 4 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Four of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

GO TO 5/100

☐ NOT TAKE WARFARIN

STOP

5 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 5 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 5 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Five of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN STOP
 ☐ NOT TAKE WARFARIN STOP

PING-PONGING FLOW CHART

Patient # _____ Interview # _____ Date _____

Personal Examples of:

a) inconvenience _____

b) costs _____

c) side effects _____

Hypothetical Efficacy**Take warfarin****Not take warfarin**

0 OUT OF 100	☐ GO TO 9/100	☐ FURTHER EXPLANATION, MAY CHANGE ANSWER
9 OUT OF 100	☐ GO TO 9.5/100	☐ GO TO 1/100
1 OUT OF 100	☐ GO TO 8/100	☐ STOP
8 OUT OF 100	☐ STOP	☐ GO TO 2/100
2 OUT OF 100	☐ GO TO 7/100	☐ STOP
7 OUT OF 100	☐ STOP	☐ GO TO 3/100
3 OUT OF 100	☐ GO TO 6/100	☐ STOP
6 OUT OF 100	☐ STOP	☐ GO TO 4/100
4 OUT OF 100	☐ GO TO 5/100	☐ STOP
5 OUT OF 100	☐ STOP	☐ STOP
9.5 OUT OF 100	☐ STOP	☐ STOP

TEXT FOR STARTING AT KNOWN EFFICACY ELICITATION METHOD

4 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 4 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 4 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Four of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or to not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN GO TO 5/100

☐ NOT TAKE WARFARIN GO TO 3/100

5 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 5 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 5 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Five of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

GO TO 6/100

☐ NOT TAKE WARFARIN

STOP

6 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 6 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 6 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Six of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

GO TO 7/100

☐ NOT TAKE WARFARIN

STOP

7 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 7 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 7 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Seven of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

GO TO 8/100

☐ NOT TAKE WARFARIN

STOP

8 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 8 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 8 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Eight of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

GO TO 9/100

☐ NOT TAKE WARFARIN

STOP

9 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 9 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 9 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Nine of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

TRY 9.5/100

☐ NOT TAKE WARFARIN

STOP

3 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 3 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 3 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Three of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

STOP

☐ NOT TAKE WARFARIN

GO TO 2/100

2 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 2 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 2 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. Two of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

STOP

☐ NOT TAKE WARFARIN

GO TO 1/100

1 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 1 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 1 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. One of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN

STOP

☐ NOT TAKE WARFARIN

GO TO 0/100

0 OUT OF 100 CHANCE OF STROKE

"Now that you have made that choice, let us now try another imaginary situation. Again you will be asked to make a choice between taking or not taking warfarin. As we discussed before, your chance of having a stroke, if you do not take warfarin, is 10 out of 100 out of the next two years. I will show this again here."

PLACE SHEET ON TABLE SHOWING "NOT TAKING WARFARIN" RISK. POINT TO ICON.

"Here are 100 people with atrial fibrillation who are not taking warfarin, as you can see 10 of them will have a stroke in the next two years."

PLACE SHEET ON TABLE SHOWING 0 OUT OF 100 "TAKING WARFARIN" RISK

"Let us imagine that if these 100 people with atrial fibrillation were taking warfarin, instead of not taking warfarin, their chance of stroke fell to 0 out of 100 for the next two years."

POINT TO ICON

"Here are the 100 people with atrial fibrillation who are taking warfarin. None of them will have a stroke in the next two years. Of course, because they are taking warfarin, they also have a 3 out of 100 chance of a severe bleed."

"Which of these situations looks best to you, to take warfarin or to not take warfarin? Before you answer, please take into account the advantages and disadvantages we discussed with the flip chart."

REVIEW FLIP CHART IF NECESSARY

"In this imaginary situation, would you choose to take or not take warfarin."

SUBJECT CHOOSES TO: ☐ TAKE WARFARIN STOP

☐ NOT TAKE WARFARIN STOP

STARTING AT THE KNOWN EFFICACY FLOW CHART

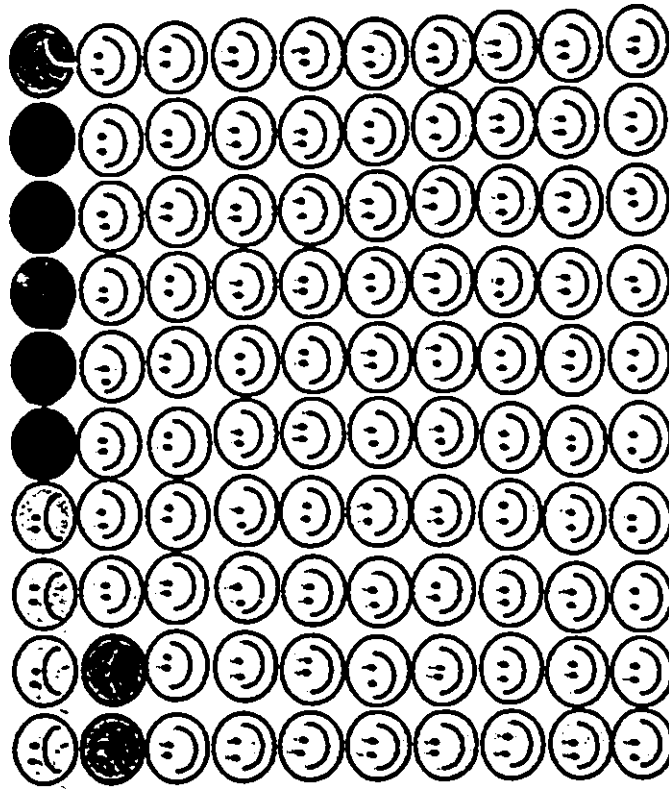
Patient # _____ Interview # _____ Date _____

Personal Examples of:

- a) inconvenience _____
- b) costs _____
- c) minor side effects _____

Hypothetical Efficacy**Take warfarin****Not take warfarin**

4 OUT OF 100	☐ GO TO 5/100	☐ GO TO 3/100
5 OUT OF 100	☐ GO TO 6/100	☐ STOP
6 OUT OF 100	☐ GO TO 7/100	☐ STOP
7 OUT OF 100	☐ GO TO 8/100	☐ STOP
8 OUT OF 100	☐ GO TO 9/100	☐ STOP
9 OUT OF 100	☐ GO TO 9.5/100	☐ STOP
9.5 OUT OF 100	☐ STOP	☐ STOP
3 OUT OF 100	☐ STOP	☐ GO TO 2/100
2 OUT OF 100	☐ STOP	☐ GO TO 1/100
1 OUT OF 100	☐ STOP	☐ GO TO 0/100
0 OUT OF 100	☐ STOP	☐ STOP



Chance of STROKE over next 2 years

● 9 out of 100

Chance of SEVERE BLEEDING over next 2 years

● 3 out of 100



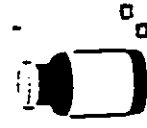
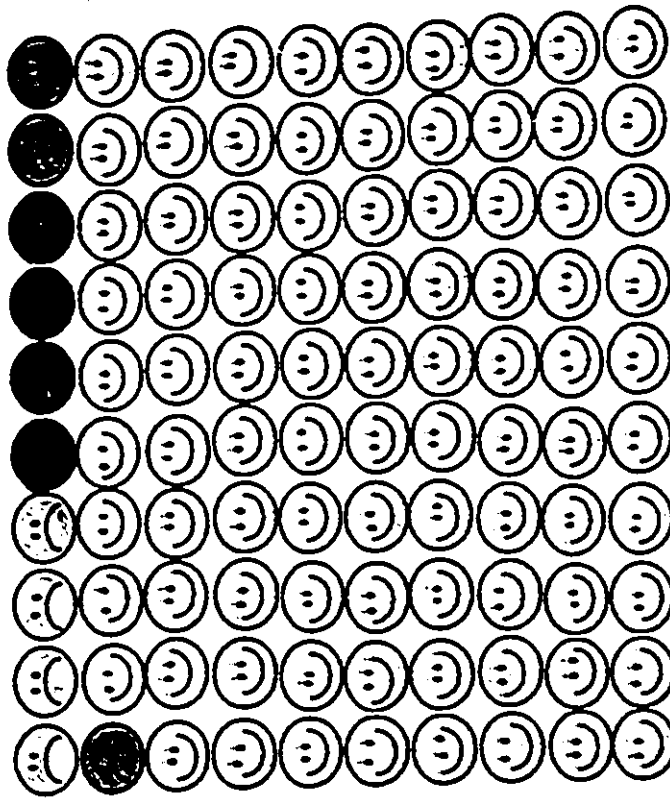
TAKING WARFARIN

Chance of STROKE over next 2 years

● 8 out of 100

Chance of SEVERE BLEEDING over next 2 years

● 3 out of 100



TAKING WARFARIN

Chance of STROKE over next 2 years

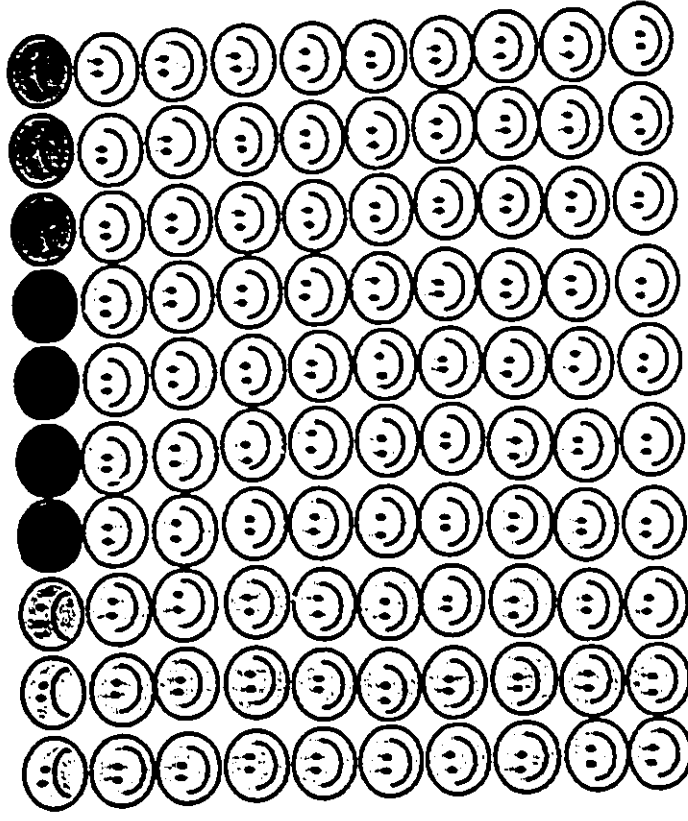


7 out of 100

Chance of SEVERE BLEEDING over next 2 years



3 out of 100



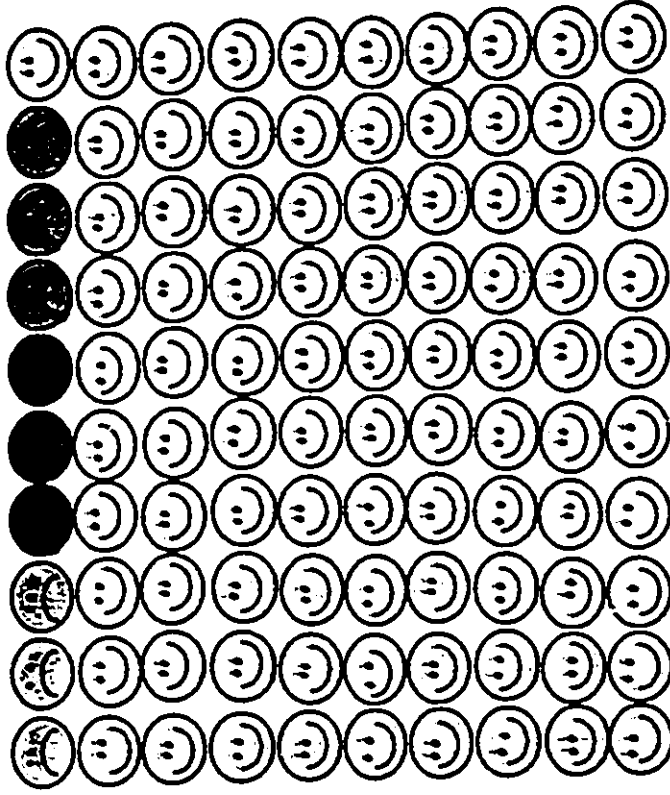
TAKING WARFARIN 

Chance of STROKE over next 2 years

● 6 out of 100

Chance of SEVERE BLEEDING over next 2 years

● 3 out of 100



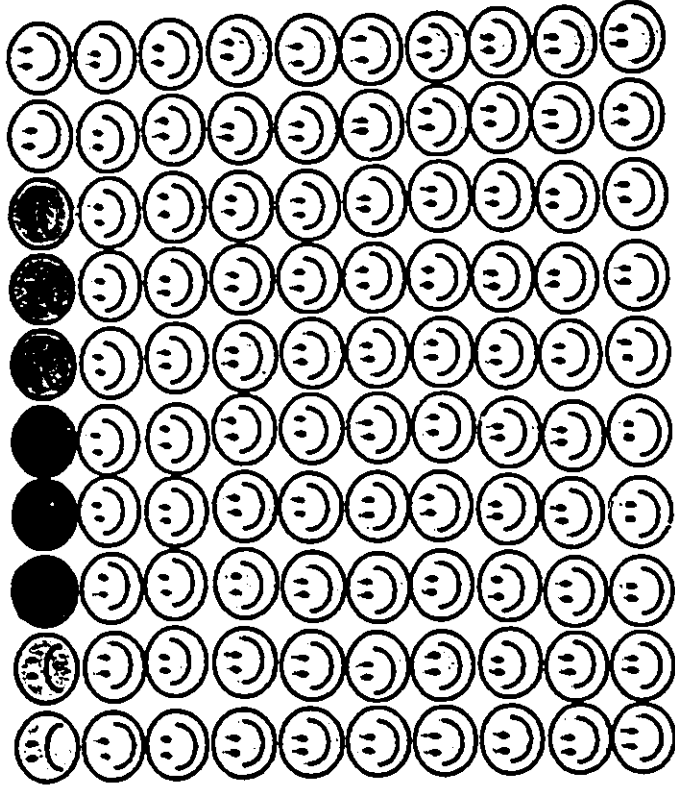
TAKING WARFARIN

Chance of STROKE over next 2 years

● 5 out of 100

Chance of SEVERE BLEEDING over next 2 years

● 3 out of 100



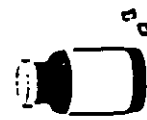
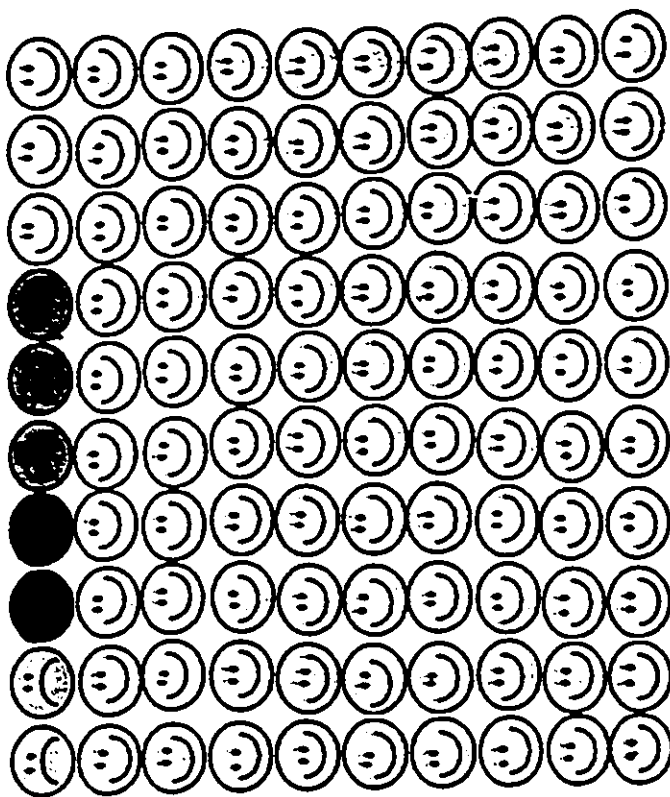
TAKING WARFARIN

Chance of STROKE over next 2 years

● 4 out of 100

Chance of SEVERE BLEEDING over next 2 years

● 3 out of 100



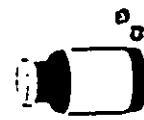
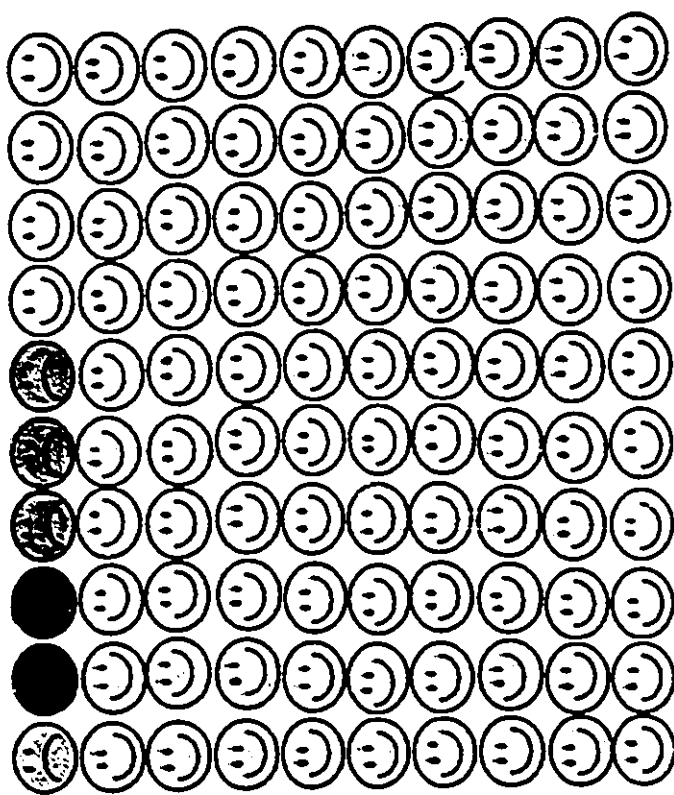
TAKING WARFARIN

Chance of STROKE over next 2 years

● 3 out of 100

Chance of SEVERE BLEEDING over next 2 years

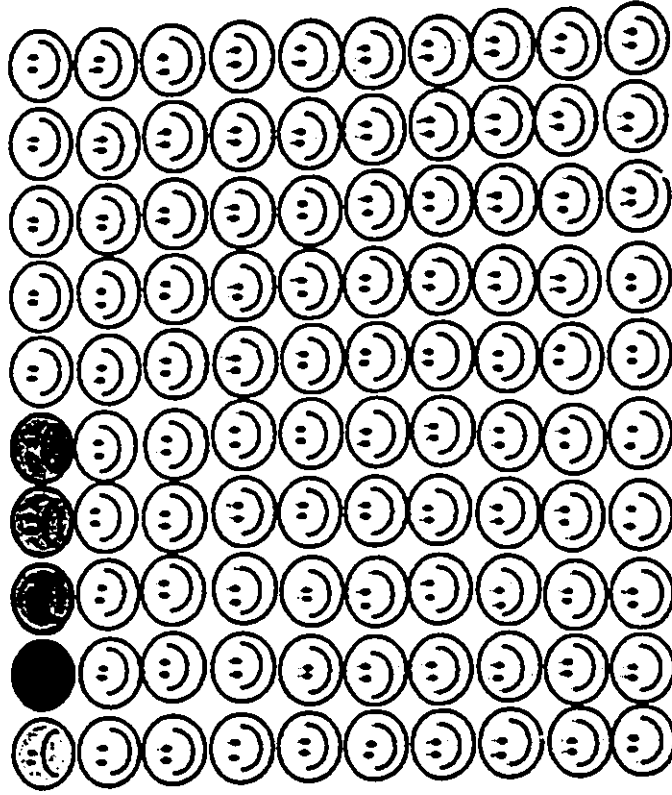
● 3 out of 100



TAKING WARFARIN

● 2 out of 100

3 out of 100

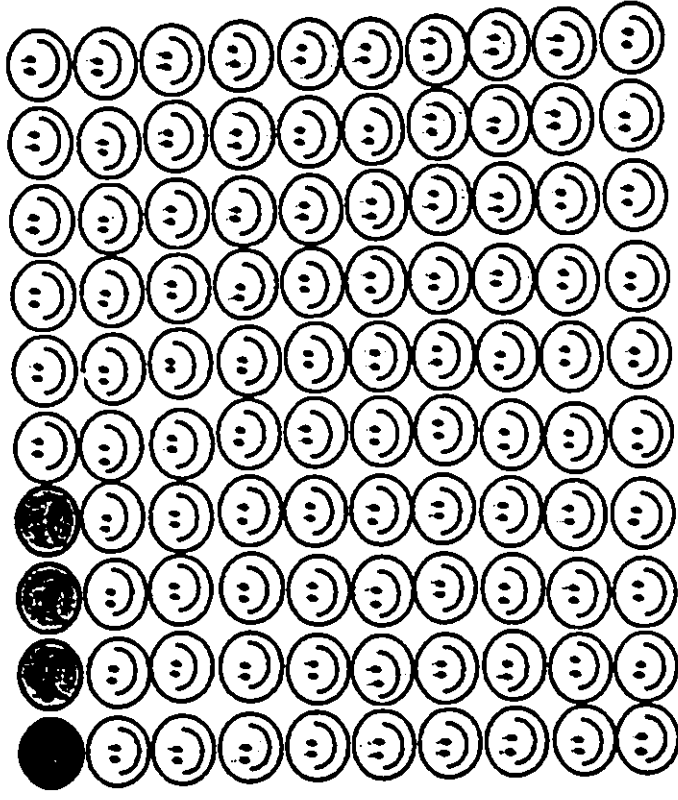


TAKING WARFARIN

Chance of STROKE over next 2 years



1 out of 100



Chance of SEVERE BLEEDING over next 2 years



3 out of 100



TAKING WARFARIN

QUANTIFYING THE MINIMAL CLINICALLY IMPORTANT DIFFERENCE FROM A PATIENT PERSPECTIVE

STUDY # ▶		DATE ▶	
SUBJECT NAME ▶			
ADDRESS ▶		CITY ▶	
PROV ▶	POSTAL CODE ▶	PHONE # ▶	
D.O.B. ▶ Y/M/D		GENDER ▶	F / M Please circle
EDUCATION LEVEL ▶ <6 YRS ☐ 6-12 YRS ☐ >12 YRS ☐			
FAMILY DOCTOR ▶			
DATE STARTED ON WARFARIN ▶			
DATE STOPPED (IF APPLICABLE) ▶			
CONSENT SIGNED ▶ YES ☐ NO ☐ IF NO, STOP			
FOLSTEIN SCORE ▶ __/30			
"HOW ARE AN APPLE AND AN ORANGE ALIKE?"			
ABSTRACT ☐ CONCRETE ☐			
WHAT DO YOU FEEL YOUR CHANCE OF HAVING A STROKE IN THE NEXT TWO YEARS IS, IF YOU DO NOT TAKE WARFARIN? __ OUT OF 100			
WHAT DO YOU FEEL YOUR CHANCE OF HAVING A STROKE IN THE NEXT TWO YEARS IS, IF YOU DO TAKE WARFARIN? __ OUT OF 100			

RANDOMIZATION

GROUP

1 (A/A)

☐

2 (A/B)

☐

3 (B/A)

☐

4 (B/B)

☐

FOLLOW-UP APPOINTMENT DATE: _____

DECISIONAL CONFLICT SCALE

"Now, thinking about the choices you have just made, please consider the following comments made by some people when making choices about treatment. Please show how strongly you agree or disagree with these statements by CIRCLING THE NUMBER from 1 (strongly agree) to 5 (strongly disagree) which best fits your views about the decision you just made."

HAVE SUBJECT COMPLETE DECISIONAL CONFLICT SCALE.

"Could you also complete this short questionnaire. Please don't hesitate to ask if you have any questions"

HAVE SUBJECT COMPLETE THE QUESTIONNAIRE.

AFTER COMPLETION OF THE DECISIONAL CONFLICT SCALE AND QUESTIONNAIRE, ARRANGE A FOLLOW UP APPOINTMENT IN TWO WEEKS IF THIS IS THE FIRST VISIT. THANK THE SUBJECT FOR PARTICIPATING.

O'CONNOR DECISIONAL CONFLICT SCALE (Applied to stroke prevention treatment problem)

Now, thinking about the choice you (are about to make/just made), please consider the following comments made by some people when making choices about treatment. Please show how strongly you agree or disagree with these statements by CIRCLING THE NUMBER THE NUMBER from 1 (strongly agree) to 5 (strongly disagree) which best fits your views about the decision you (are about to make/just made).

DECISION UNCERTAINTY

These decisions were hard for me to make	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
It was clear what choices were best for me	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
I was unsure what to do when making these decisions	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree

FACTORS CONTRIBUTING TO UNCERTAINTY

I'm aware that warfarin is available to protect me from stroke	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
I feel I know the benefits of taking warfarin	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
I feel I know the risks and side effects of taking warfarin	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
I needed more advice and information about the decisions I just made	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
I know how important the benefits of taking warfarin are to me	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
I know how important the inconveniences, costs and side effects of taking warfarin are to me	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
Its hard for me to decide if the benefits of taking warfarin are more important to me than the risks, or if the risks are more important than the benefits	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
I felt pressure from others in making these decisions	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
I had the right amount of support from others in making these choices	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree

PERCEIVED EFFECTIVE DM

I feel I have made informed decisions	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
My decisions show what is most important for me	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
I would expect to stick with my decisions	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree
I am satisfied with my decisions	1 Strongly Agree	2 Agree	3 Neither Agree Nor Disagree	4 Disagree	5 Strongly Disagree

Semi-structured Questionnaire

Appendix Q

The following questionnaire is intended to be fairly open in nature, in order to capture the respondents initial reaction when asked to rationalize their decision process. Structured questions have been included, however, to provide quantitative data on specific aspects presented by the flip chart.

You have made choices about when you take warfarin for the treatment of your atrial fibrillation.

The next few questions will further help us to understand how you made your choices.

1. What were the three (3) most important things that helped you to decide when you would take warfarin?

Were there any others?

2. Which of the following were important in your choice of when you would take warfarin:
(you may choose more than one)

- ☐ concern about stroke
- ☐ concern about death
- ☐ concern about stomach bleed
- ☐ inconvenience of taking warfarin
- ☐ costs of taking warfarin
- ☐ side effects of warfarin (e.g. easy bruising)

3. Do you know anyone else who has ever taken warfarin?

4. Do you know anyone who has had a stroke?

5. Thinking now of the flip chart and the information presented to you, what changes could you suggest to make the choices about warfarin therapy easier or more clear for patients like yourself?

6. Did any part of the presentation upset or confuse you? _____ Or did it make you more confident about your decision? _____

7. Do you think the flip chart approach is something doctors should use when discussing other treatment decisions?

_____ - IF YES:

Can you give us some examples of medical decisions you have had to make that would have been helped by a flip chart presentation.

8. What do you feel your chance of having a stroke in the next two years is, if you do not take warfarin?

_____ out of 100

9. What do you feel your chance of having a stroke in the next two years is, if you do take warfarin?

_____ out of 100

**FOLSTEIN "MINI-MENTAL STATE"
QUESTIONNAIRE**

**OTTAWA CIVIC HOSPITAL
GERIATRIC ASSESSMENT UNIT**

Appendix R

DATE _____

**MAXIMUM
SCORE**

SCORE

ORIENTATION

5 ()

What is the (year) (season) (date)
(day) (month)?

5 ()

Where are we? (province) (country) (town)
(hospital) (floor).

REGISTRATION

3 ()

Name 3 objects: 1 second to say each. Then
ask the patient all 3 after you have said
them. Give 1 point for each correct
answer. Then repeat them until he learns
all 3. Count trials and record.

ATTENTION AND CALCULATION

5 ()

Serial 7's point for each correct. Stop
after 5 answers. Alternatively spell
"world" backwards.

RECALL

3 ()

Ask for the 3 objects repeated above.
Give 1 point for each correct.

LANGUAGE

9 ()

Name a pencil, and watch (2 points)
Repeat the following "No ifs, ands or
buts," (1 point)

Follow a 3-stage command:

"Take a paper in your right hand, fold it
in half, and put it on the floor" (3
points)

Read and obey the following:

CLOSE YOUR EYES (1 point)

Write a sentence 1 point

Copy design (1 point)

TOTAL SCORE

ASSESS level of consciousness along a
continuum

alert drowsy stupor coma

TESTER'S SIGNATURE

SAMPLE SIZE CALCULATION

A hypothetical population was derived with the following responses:

RESPONSE (%reduction)	# of respondents
20	5
30	10
40	20
50	30
60	20
70	10
80	5

The mean = 50, variance = 210, SD = 14.5

To calculate a 95% CI for this mean, the following formula was used:

$$95\% \text{ CI} = \bar{x} \pm (1.96 \text{ SD}/\sqrt{N})$$

For a 95% CI around the mean of 5, N = 32.

For a 95% CI around the mean of 2.5, N = 130.