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Health-Related Quality of Life Measures in Coronary Heart Disease Prevention and Treatment

By

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A thesis submitted to
the Faculty of Graduate Studies and Research
in partial fulfilment of the requirements of the degree of
Doctor in philosophy

Abrégé

Une étude transversale (n = 878) a été réalisée dans deux centres hospitaliers pour évaluer la qualité de vie de participants en santé et traités pour un désordre dyslipidémique et de patients souffrant de maladie ischémique coronarienne. Les échelles de mesure de la qualité de vie incluaient le SF-36, l'Échelle des états de santé (*Rating Scale* (RS)), la Durée de vie équivalente *(Time Trade-off* (TTO)) et le Pari-type (*Standard Gamble* (SG)).

La qualité de vie moyenne, ajustée en fonction de la comorbidité, de participants traités pour un désordre dyslipidémique était de 2.8 (p = 0.02) et 3.3 (p = 0.02) points inférieure à celle rapportée par un groupe similaire de participants sans traitement dyslipidémique, lorsque mesurée par le RS et l'Échelle de perception générale de la santé du SF-36, respectivement. Ces résultats n'étaient pas attribuables à des différences de comorbidité, d'âge, de genre ou d'indice de masse corporelle, entre les groupes comparés. Aucune différences significatives n'ont été détectées entre ces deux groupes avec le TTO et le SG.

Pour chacune des échelles de mesure, la qualité de vie moyenne, ajustée en fonction de la comorbidité, était comparable pour les patients avec un diagnostic d'angine, d'infarctus du myocarde, ou d'angine et d'infarctus du myocarde. De plus, les patients souffrant d'une défaillance cardiaque congestive semblaient être les plus éprouvés puisqu'ils ont rapporté les résultats les plus faibles sur toutes les échelles de mesure.

La fiabilité du test et du retest était acceptable pour toutes les échelles de mesure. Comparé au TTO et au SG, le RS était le plus fortement corrélé avec les différents aspects de la qualité de vie mesurés par le SF-36. Il pouvait plus efficacement différencier les patients cardiaques avec des abiletés physiques différentes, et les participants qui ont rapporté un nombre spécifique de problèmes de santé.

Ces mesures de la qualité de vie pourront être utilisées dans une analyse coût-efficacité du traitement des dyslipidémies dans la prévention primaire des maladies ischémiques coronariennes. L'impact de la détection et du traitement des dyslipidémies sur la qualité de vie pourra être important lors de l'évaluation des politiques de santé publique. Toutefois, d'autres recherches sont nécessaires pour confirmer ces résultats et élucider les causes et les conséquences de la détection et du traitement des dyslipidémies sur la qualité de vie.

Abstract

We performed a large (n = 878), multicenter, hospital-based, cross-sectional study to measure the health-related quality of life (HRQOL) of healthy participants treated for dyslipidemia and patients with coronary heart disease (CHD). The HRQOL measures included a nonpreference-based measure (SF-36 Health Survey) and three preference-based measures (Rating Scale (RS), Time Trade-off (TTO) and Standard Gamble (SG)).

The adjusted mean HRQOL, of healthy participants undergoing treatment for dyslipidemia was 2.8 ($p = 0.02$) and 3.3 ($p = 0.02$) points lower, when compared to a similar group of participants not being treated for dyslipidemia, on the RS and the SF-36 General Health Perception (GHP) subscale, respectively. These differences were unlikely to be due to confounding by comorbidity, age, gender and body mass index. No significant differences were detected on the TTO and SG scales.

For each preference-based scaling technique, the adjusted HRQOL mean scores obtained from patients diagnosed with angina, myocardial infarction, or angina and myocardial infarction were similar. Patients with congestive heart failure reported the worst HRQOL on all scales.

The test-retest reliability, over a 3 to 6 week period, was acceptable for all scaling techniques and the majority of participants reported consistent scores at the

test and the retest assessments. Correlation between the preference-based measures and each of the SF-36 subscales varied from poor to moderate. Compared to the TTO and the SG, the RS was the most highly correlated with the different aspects of the HRQOL measured by the SF-36 Health Survey and had the highest ability to discriminate CHD patients with various physical disabilities and participants reporting specific number of health problems.

This study provides a complete set of preference-based measures for use in cost-effectiveness analysis of CHD primary prevention. It suggests that the impact of detecting and treating dyslipidemia on the participant's HRQOL may be small but significant from a public policy point of view. Further research should be done confirming these results and elucidating the causes and the consequences of this negative effect on HRQOL of healthy individuals treated for dyslipidemia.

Remerciements

Cette étude a été rendue possible grâce à la collaboration de plusieurs personnes. J'aimerais tout d'abord remercier les 2 789 personnes qui ont bien voulu participer à ce projet en complétant les questionnaires de recherche.

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Preface

As stated in the Guidelines for Thesis Preparation,

> Candidates have the option of including, as part of the thesis, the text of one or more papers submitted or to be submitted for publication, or the clearly-duplicated text of one or more published papers. These texts must be bound as integral part of the thesis.
>
> If this option is chosen, connecting texts that provide logical bridges between the different papers are mandatory. The thesis must be written in such a way that it is more than a mere collection of manuscripts; in other words, results of a series of papers must be integrated.
>
> The thesis must still conform to all other requirements of the "Guidelines for Thesis Preparation". **The thesis must include:** A Table of Contents, an abstract in English and French, an introduction which clearly states the rational and objectives of the study, a review of the literature, a final conclusion and summary, and a thorough bibliography or reference list.
>
> Additional material must be provided where appropriate (e.g. in

appendices) and in sufficient detail to allow a clear and precise judgement to be made of the importance and originality of the research reported in the thesis.

In the case of manuscripts co-authored by the candidate and others, the candidate is required to make an explicit statement in the thesis as to who contributed to such work and to what extent. Supervisors must attest to the accuracy of such statements at the doctoral oral defense. Since the task of the examiners is made more difficult in these cases, it is the candidate's interest to make perfectly clear the responsibilities of all the authors of the co-authored papers.

This is a manuscript-based thesis. You will find in appendix I:

- An explicit statement of the responsibilities of all the authors of the co-authored papers and of the research assistants.
- A list of all authors of all three articles with appropriate signatures.
- Release forms from all co-authors.

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Section 3.3 Preference-based health-related quality of life measures in coronary heart disease prevention and treatment

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List of abbreviations

CHD:	Coronary Heart Disease
CHF:	Congestive Heart Failure
CI:	Confidence interval
GHP:	General Health Perception subscale of the SF-36 Health Survey
HDL-C:	High Density Lipoprotein-Cholesterol
HIV:	Human immunodeficiency virus
HRQOL:	Health-related quality of life
LDL-C:	Low Density Lipoprotein-Cholesterol
MI:	Myocardial infarction
METS:	Metabolic equivalent
QALY:	Quality-adjusted Life Year
QWB:	Quality of Well-Being
RS:	Rating Scale
SF-36 Health Survey:	Short Form-36 Health Survey
SF-36 GHP:	General Health Perception subscale of the Short Form-36 Health Survey
Total-C:	Total-Cholesterol
TTO:	Time Trade-Off
YOLS:	Years of Life Saved

1. *Introduction*

Coronary heart disease (CHD) is the primary cause of premature death in most industrialized countries and accounts for 40% of all deaths in Canada. The rate of CHD deaths has decreased by almost 40% over the past two decades. [1] However, based on the aging of the population, a significant increase in the prevalence, mortality and costs of CHD is expected in the next 30 years if there are no future changes in coronary risk factors.[2] In this context, accurate evaluation of CHD prevention strategies is important.

Several pharmacoeconomic studies have estimated that the cost-effectiveness (costs per year of life saved) of detecting and treating dyslipidemia might be acceptable in specific subgroups of the population. These analyses are incomplete for two reasons. It has been shown that treating dyslipidemia can prevent or delay the occurrence of CHD. By using an endpoint such as the number of years of life saved, these analyses do not consider the beneficial impact of treating dyslipidemia on the participants' morbidity. Additionally, these analyses are based on the assumption that the detection and treatment of dyslipidemia do not directly affect individuals' health-related quality of life (HRQOL). In fact, there is a substantial literature demonstrating that CHD risk factor modification in healthy individuals may have a substantial negative impact on the HRQOL. To fully assess the effectiveness of detecting and treating dyslipidemia, the use of the quality-adjusted life year (QALY) model has been recommended by The Panel on Cost-Effectiveness in Health

and Medicine. [3] In this model, the outcome measure is the number of QALYs gained. Simulations of QALY models, using hypothetical HRQOL values, have shown that the cost-effectiveness of detecting and treating dyslipidemia would be extremely sensitive to the impact of the preventive intervention on the participants' HRQOL. However, in practice, these models will only be useful if we can measure precisely and accurately the impact of preventive interventions on HRQOL. Preference-based HRQOL measures, such as the Standard Gamble, the Time Trade-off and the Rating Scale, are recommended as the HRQOL measures in QALY models. [3] There is no empirical data providing preference-based measures for dyslipidemia. Although preference-based measures are available for angina and myocardial infarction, it is difficult to combine the preference-based measures from various sources into a QALY model because these measures vary substantially according to the methodology used to assess them. This study was therefore undertaken to assess, using standardized methodology, the preference-based measures of all the health states involved in the evaluation of the cost-effectiveness of detecting and treating dyslipidemia in CHD primary prevention.

More specifically, the objectives of this research project were:

- To assess the preference-based HRQOL measures of healthy individuals undergoing treatment for dyslipidemia and CHD patients with angina, myocardial infarction and/or congestive heart failure.

- To evaluate and compare the reliability and validity of the preference-based measures and to identify the most appropriate scaling technique for future QALY analyses.

This project will allow a more complete evaluation of the effectiveness of detecting and treating dyslipidemia in CHD primary prevention.

2. *Literature review*

In this review, the current literature on the cost-effectiveness of treating dyslipidemia in CHD primary prevention is summarized. Because the cost-effectiveness of CHD preventive interventions is expected to be highly influenced by the HRQOL of individuals undergoing these interventions, there is an evaluation of the impact of modifying or attempting to modify CHD risk factors on the HRQOL of healthy individuals. This is done by reviewing the extensive literature documenting the HRQOL of hypertensives and also the limited empirical data on the HRQOL of dyslipidemic individuals. Finally, there is a summary of the current literature on the methodological aspects of the preference-based measures and their psychometric properties.

2.1 Effectiveness of dyslipidemia treatment

Data from the Framingham Heart Study and the Multiple Risk Factor Intervention Trial (MRFIT) have shown the existence of a positive, graded and progressive relationship between CHD and the total serum cholesterol level (TOTAL-C).[4-6] More specifically, an increase of the TOTAL-C and the low-density lipoprotein cholesterol (LDL-C) levels was shown to be associated with an increased risk of CHD, whereas an increased of the high-density lipoprotein cholesterol (HDL-

C) protected against CHD. [4,7-9] The risk of CHD was also influenced by other risk factors, including age, gender, elevated systolic blood pressure, the presence of left ventricular hypertrophy, glucose intolerance, smoking and family history of premature CHD. [4] In men and women, the risk of CHD increased linearly with advancing age but women had a lower risk than men, all other risk factors being equal.

The treatment of dyslipidemia includes pharmacotherapy and lifestyle changes, such as dietary intervention, weight reduction and exercise. Dietary interventions consist of reducing the intake of saturated fatty acids, increasing the intake of complex carbohydrates and either cis-monounsaturated or polyunsaturated fatty acids and restricting the number of calories for overweight people. [1] The National Cholesterol Education Program (NCEP) has proposed a step I and a step II diet to control dyslipidemia. [10] However, long-term effectiveness studies have shown that dietary changes were associated with relatively small decrements in the TOTAL-C and the LDL-C levels, varying from 5% to 13%. [11-16] Furthermore, drops in the HDL-C levels have also been reported. [11-13] As a low HDL-C level is associated with increased CHD risk, this may contribute to minimize the overall impact of dietary changes on the CHD risk.

Several classes of lipid-lowering drugs are available, namely the 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors called the statins (fluvastatin, lovastatin, pravastatin, simvastatin and atorvastatin), the bile acid sequestrant resins (cholestyramine and colestipol), nicotinic acid (niacin), and the fibric acid derivatives (gemfibrozil, clofibrate, bezafibrate). LDL-C levels decrease by about 20 to 40% with statins and by about 20% with bile sequestrant resins. Nicotinic acid decreases the LDL-C and the triglyceride levels and increases the HDL-C levels, as do fibric acid derivatives.[17]

Several intervention trials, such as the Lipid Research Clinics Coronary Primary Prevention Trial (LRCCPPT), the Helsinki Heart Study, and the West of Scotland Coronary Prevention Study, have shown that lowering the TOTAL-C and the LDL-C levels and increasing the levels of HDL-C in healthy individuals without symptoms of CHD were associated with a decreased risk of CHD events and deaths. [6-8,18-23] The impact of dyslipidemia management on the overall risk of death was slightly and non-significantly reduced in the LRCCPPT study because of a greater number of violent and accidental deaths in the cholestyramine group. [18] In the Helsinki study, the total death rate was similar in the treatment and the control groups. However, the total number of deaths was higher in the treatment group and was mainly due to accidents, violence and intracranial haemorrhage. [20] In the West of Scotland study, the total death rate was lower in the treatment group ($p = 0.051$) with no excess of deaths from noncardiovascular causes in the treatment arm. Among CHD patients, simvastatin was clearly associated with a decrease in the overall risk of death. [24]

Several pharmacoeconomic studies have estimated the cost and the effectiveness of detecting and treating dyslipidemia to prevent CHD. [25-36] It has been shown that the benefits of treating dyslipidemia vary across the population. For example, the average increase in life expectancy attributed to dyslipidemia treatment has been estimated to vary from 0.03 to 3.16 years depending on the pretreatment cholesterol level, age, gender, presence of other risk factors, and percent change in LDL-C, HDL-C and TOTAL-C levels. [35] For this reason, dyslipidemia treatment is estimated to be cost-effective only in selected subgroups of the population. In the Hamilton et al. study [25], lovastatin was relatively cost-effective for high-risk men of all ages ($20 882 to $50 079 per year of life saved (YOLS)), low-risk men aged 40 to 60 years ($46 571 to $48 214 per YOLS) and high-risk women aged 50 to 70 years ($36 627 to $43 127 per YOLS).

Although these analyses suggest that dyslipidemia treatment might be cost-effective in specific subgroups of the population, they had incompletely assessed the benefits of controlling dyslipidemia for two reasons. By using the number of YOLS as the measure of effectiveness, they only considered the impact of CHD prevention on the overall death rate. However, one of the major beneficial impacts of CHD prevention consists of avoiding or delaying the occurrence of CHD. It has been estimated that the average onset of symptomatic CHD could be delayed by about 0.06 to 4.98 years by treating dyslipidemia. [35] By using an endpoint such as the number of YOL saved, these analyses did not consider this beneficial impact of treating dyslipidemia on participants' morbidity. In addition, these analyses did not take into account the impact of the preventive intervention on the participants' HRQOL.

To fully appreciate the effectiveness of treating dyslipidemia and consider its impact in terms of changes in life expectancy and HRQOL, the use of the QALY model has been recommended. [37] In these models, the outcome measure is the number of QALYs generated by an intervention. It is calculated by assigning to each period of time a quality weight representing the HRQOL during that period. The total number of QALYs can be simply calculated by first multiplying the time spent in each health state by its quality weight and then by adding the number of adjusted years. Different weighting procedures are available to combine the time and the HRQOL weight [38,39] and the number of QALYs is generally discounted over time [37,40] Because every year of life in a given health state is weighted by a quality factor, the QALY model takes into account not only the impact of the intervention on mortality but also on HRQOL. [37]

In simulations of the QALY model, using hypothetical quality weights for dyslipidemia, the cost-effectiveness of treating dyslipidemia varied tremendously according to the estimate of the quality weight associated with the preventive intervention itself. [33,41,42] Incorporating the potential negative impact of treating

dyslipidemia decreased substantially the net effectiveness of the intervention. Although the impact of a primary preventive intervention on the HRQOL may be small, the number of QALYs lost during an intervention may be large if the intervention lasts for a very long period of time, is not very effective in terms of the number of years of life saved, and affects all participants even those who will never develop CHD. In addition, the discounting of future costs and benefits amplifies the short term negative impact of a preventive intervention on the HRQOL and attenuates the long term positive impact related to the prevention of CHD.

Because the cost-effectiveness of CHD primary prevention is expected to be extremely sensitive to the quality weight associated with the prventive intervention, precise and accurate evaluation of the impact of treating dyslipidemia on the HRQOL is important. To better understand how and to what extent modifying CHD risk factors can influence the HRQOL of healthy individuals, a review of the literature evaluating the impact of detecting and treating hypertension and dyslipidemia on the HRQOL has been performed.

2.2 The impact of modifying coronary heart disease risk factors on health-related quality of life

Hypertension and dyslipidemia share many characteristics: 1) they are both risk factors for CHD, 2) affected people are generally asymptomatic, and 3) they both require lifetime therapy which may include pharmacotherapy and lifestyle changes such as dietary change, weight loss and exercise.[43] Because of the similarity between these two conditions, the impact of the detection and treatment of dyslipidemia and hypertension on the health-related quality of life (HRQOL) may be similar. For this reason, we will review the literature evaluating the HRQOL associated with hypertension and dyslipidemia.

2.2.1 Hypertension

Epidemiologic studies have been conducted to evaluate the impact of the disease process, the labelling and the treatment effects of prescribed lifestyle changes and pharmacologic treatment on the HRQOL of hypertensives. A review of the behavioural (rate of absenteeism and income) and the psychological (sense of well-being) consequences of detecting and treating hypertension is presented below.

2.2.1.1 Disease process

Severe hypertension may cause various symptoms such as headache, dizziness and nocturia. However, most hypertensive individuals have mild to moderate hypertension and do not have symptoms.[44] Consequently, for the majority of hypertensive individuals, the disease process is not responsible for changes in HRQOL.[45]

As reported by Bulpitt and Fletcher [45], early studies tended to attribute many symptoms to uncomplicated hypertension. These findings were eventually found to be attributed to selection bias because older people, patients with comorbid conditions and people with a poorer sense of well-being were more likely to seek medical attention and to have their hypertension detected. Finally, cross-sectional studies of patients attending specialized hospital clinics may be subject to selection bias because those referred to hospital clinics may be more severe cases, more anxious and more difficult to treat compared to hypertensives treated in the community.

2.2.1.2 Labelling and treatment effect

Labelling is currently defined as *telling someone they have hypertension.*[46,47] Newly diagnosed hypertensives may consider themselves as ill and change the way they perceive their health status.[48] Because most hypertensives receive some kind of treatment it is often difficult to distinguish the *pure effect* of the labelling from the effect of treatment.

2.2.1.2.1 Behavioural consequences

Outcomes such as absenteeism (or disability days) and income have been used to assess the behavioural consequences of labelling and treating hypertensives. Table 2.2.1 summarizes the designs of the reviewed studies.

The **DOFASCO** study [49] provided the first report of an association between absenteeism and hypertension. In a large prospective study, absenteeism was compared before and after screening and referring workers at the Dominion Foundries and Steel Company for hypertension. Out of 5400 male employees, a total

Table 2.2.1 ● Studies on the effect of labelling and hypertension treatment on absenteeism (Part I)

	DOFASCO[a]	NYCW[b]	HDFU[c]	MMLI[d]	TWS[e]
➤**Design:**					
Prospective screening	✓	✓	✓	✓	
Cross-sectional					✓
Comparing management care	No	Yes	Yes	No	No
- Randomized			✓		
- Not randomized		✓			
➤**Study population:**					
- Men	✓				
- Men and women		✓	✓	✓	✓
Work place					
- one company	✓			✓	
- various companies					
same type					
various types		✓	✓		✓
➤**Sample size:**					
Participation rate (%):					
- Screening program	94	68	NR[1]	99	99
- Treatment program	90	75	92	95	
Number screened (n)	5400	8 467	158 906	2470	10000
Number of hypertensive (n)	208	1 413	10 049	259	50

Table 2.2.1 ● Studies on the effect of labelling and hypertension treatment on absenteeism (Part II)

	DOFASCO[a]	NYCW[b]	HDFU[c]	MMLI[d]	TWS[e]
➤**Treatment Management:**					
Referral	✓		✓	✓	✓
On-site treatment		✓			
Stepped care			✓		
➤**Outcome Assessment:**					
Type of absenteeism:		NR[¶]			
- days of illness	✓		✓	✓	✓
Data collection:					NR[¶]
-company or school records	✓	✓		✓	
-self-reported			✓		
Time frame (year):					NA[§]
- prior to screening	≥ 1	1	1	3	
- after screening	≥ 1	2	1	1	
Company policy:					
- lost pay for the first 3 days	✓				
- all sick days paid				✓	
- various policies		✓	✓		✓

a. Dofasco Study [49]; b. New York City Workers [50]; c. Hypertension Detection and Follow-up [51];
d. Massachusetts Mutual Life Insurance [52]; e. Toronto Workers Study [53].
¶. NR means *not reported*
§. NA means *not applicable*

of 208 hypertensives that have received no hypertensive therapy for at least six months, and not currently receiving other daily medications were identified. One hundred and thirty-eight (66%) were previously unaware of their hypertension. The following results were reported:

- During the year after labelling, hypertensive individuals previously unaware of their hypertension demonstrated a dramatic rise in illness absenteeism (mean of 5 days). It was unrelated to hypertension treatment, degree of blood pressure control or attempts to promote compliance and was increased substantially in noncompliers (< 80% compliance). Those previously aware of their hypertension showed only a small and not statistically significant rise of their absenteeism rate.

A five year follow-up revealed that this effect was persistent.[54] Furthermore, hypertensive employees were earning an average of $1093 (Can) less than normotensive employees despite similar incomes in the year before screening. In addition, 5.3% of the hypertensive participants felt that their health prevented them from being promoted compared to 0.6% in the normotensive group.[55]

In 1976, contradictory results emerged from another prospective screening study where 12 500 department store employees from **NEW YORK CITY** were offered to participate in a screening and on-site treatment of hypertension .[50] A total of 1413 hypertensives were identified: 85.6% were aware of their condition at the time of screening, 66.1% reported receiving hypertensive treatment and 75% elected an on-site therapy. They reported that:

- During the first year following the screening program, hypertensives included in the on-site therapy and in the conventional medical care

groups had fewer days of disability.

- During the second year, the number of disability days rose to prescreening level in the conventionally treated group and remained low in the on-site treated group.

Surprisingly, the observed change in disability days was based on a total of 320 hypertensive employees. It is not clear from this study why all the hypertensives (on-site treatment : n=1066, conventional treatment: n=347) were not included in this analysis. The statistical significance of the observed change in disability days was not reported and no stratification was done based on previous awareness of hypertension. In addition, as proposed by Sackett and colleagues [56], the low participation rate (68% accepted to be screened) may also explain these results. In the **DOFASCO** study [49] the sharpest rise in absenteeism was observed among the hypertensives with the lowest compliance. This group appeared to be the most labelled and the least cooperative. By extrapolation, it may be assumed that they would be the least likely to participate in a screening program. Consequently, when the participation rate is as low as in the **NEW YORK CITY** study, it is possible that those reluctant participants are not included. If this is the case, studies with low participation rates may show a decrease in the number of disability days while those with a high participation rate (> 90%) may show an increase in the absenteeism rate. Finally, if the increase in absenteeism is mostly observed among newly diagnosed hypertensives then no overall increase in absenteeism may be reported in studies where most participants were previously aware of their hypertension, like the **NEW YORK CITY** study.

The **Hypertension Detection Follow-up screening and treatment Program** (HDFP) compared the number of disability days in mild hypertensives referred to either "stepped care" (comprehensive clinics) or "referred care" (general community).[51] They reported that:

- For those unaware of their hypertension at screening, disability days increased between baseline and one year among referred care participants ($p=0.01$), while there was no change observed among stepped care participants.
- Neither referred care nor stepped care participants who were aware but untreated at baseline reported a change in disability days over the following year.
- For those aware and treated at baseline, there was no change in disability days in referred care, but a statistically significant decrease was reported in stepped care group.

These results suggest that under certain types of care, such as a comprehensive clinic, it is possible to prevent the increased rate of absenteeism among those who are labelled and treated.

A systematic program to improve blood pressure control was initiated in 1977 at the **Massachusetts Mutual Life Insurance Company** (MMLIC) [52,57] for its 2495 employees. Out of a total of 254 hypertensive participant employees, 48 (19%) were previously unaware of their hypertension. The following results were reported:

- Compared to the normotensives, the overall increase in absenteeism for hypertensives was not significantly higher.
- When hypertensives were stratified according to their prior awareness of hypertension, the rate of increase in absenteeism was 43% greater among newly diagnosed patients than among the previously aware hypertensives.
- An inverse relationship was observed between the annual absenteeism and the participant's compliance with the program.

The **Toronto Workers Study** (TWS) [53] used a cross-sectional design to evaluate the health perception and lifestyle of treated hypertensives. All study subjects were selected among individuals who participated in an industrial blood pressure screening program. Subjects reporting comorbid conditions were excluded. The number of days absent from work during the month preceding the interview was 0.3 for normotensives (n=50), 0.6 for previously diagnosed hypertensives (n=50) and 0.7 for hypertensives diagnosed within six months of the interview (n=50). The number of illness days was, respectively, equal to 0.4, 0.7 and 0.8 for each group. The observed differences were not statistically significant, however the data clearly suggested a graded response.

In summary, these studies on the behavioural consequences of labelling and treating individuals with hypertension demonstrate that:

- The detection and treatment of hypertension increase absenteeism especially among newly diagnosed patients.
- Certain types of care, such as comprehensive clinics, and high treatment compliance appear to prevent or reverse the increased rate of absenteeism.

As observed by Taylor, Haines and Sackett [54], it is not clear from these analyses that changes in absenteeism represent an "inappropriate over-reaction to hypertension label or a calm and rational decision to take better care of one's health". Increased absenteeism may be associated with either improvement or deterioration of the HRQOL.

2.2.1.2.2 Psychological consequences

Several studies have evaluated the psychological consequences of labelling and treating hypertensives. In Table 2.2.2, the indicators of psychological status used in the reviewed studies are reported.

In 1981, Bloom and Monterossa[48] compared the health perception and the number of depression symptoms in a group of individuals (n=71) mislabelled as having hypertension on the basis of a prevalence survey carried out in a low socioeconomic community. The mislabelled group was compared to an unmatched group consisting of the remaining normotensives and a normotensive group matched on gender, age, ethnicity, education and marital status. When compared to the matched and the unmatched control groups, the mislabelled group reported more depressive symptoms and lower health perception. The findings could not be attributed to a greater utilization of health care or comorbidity in the labelled group.

A similar study was reported by Wagner and Stogatz.[58] A total community survey was performed in two adjacent rural biracial North Carolina townships where 1849 untreated normotensive individuals were categorized in four groups: 1. history of hypertension (n=191); 2. a self-diagnosis of hypertension or a belief that they have hypertension (n=27); 3. history and self-diagnosis of hypertension (n=71); and 4. no label of hypertension (n=1560). After adjusting for age, race, gender and education, the labelled participants reported more depressive and medical symptoms. However, these results could be attributed to a selection bias because the labelled groups also reported more medical symptoms, more physician visits per year, and higher systolic and diastolic blood pressure.

Table 2.2.2 • Psychological consequences of labelling and treatment: Outcomes and assessment instruments

Study	Outcome	Assessment instrument
Mislabelling study[a]	Health perception	Two self-rating measures of health: 1. *How would you rate your health nowadays* - excellent, good, fair, or poor? 2. *Over the past five years, would you say that your health has been getting better, about the same, or getting worse*?
	Depression symptoms	The sum of positive responses to the following six items: trouble with nerves, sleep that was restless and disturbed, feeling depressed, poor appetite, feeling lonely, and always feeling tired.
Mislabelling study[b]	Self-perceived health	One self-rating measure of health: 1. *Compared to other people of your age, would you say your health is poor, fair, good or excellent?*
	Functional disability	On self-rating measure: 1. *Do you feel healthy enough to do the things you would like to do*? 1. Yes, often; 2. Yes, sometimes; 3. No
	Depression	Aggregate of positive responses to items 1,3 4, 5, 6, and negative response to 2. 1. *Have you ever talked to a doctor because you were depressed (sad and blue)*? 2. *Do you feel in good spirits*? 3. *Do you have trouble falling asleep*? 4. *Do you often feel sleepy during the day*? 5. *Do you use any medicines for your nerves or to calm yourself*? 6. *Do you often feel tired or without energy during the day*?
	Medical symptoms	Sum of positive responses to 12 symptoms including dryness of the mouth, muscle cramps, chest pain, diarrhoea, constipation, nausea, headaches, abdominal pain, joint pain, dizziness, blurred vision, and rhinorrhea.

Table 2.2.2 (contd.)● Psychological consequences of labelling and treatment: Outcomes and assessment instruments

Study	Outcome	Assessment instruments
HANES I[c]	Psychological	General Well-Being questionnaire, developed for this study, includes 18 items inquiring about energy level,status health concerns, depression and tension over the past month.
MHC[d]	Not reported	Five psychological questions:1) In the past year, have you often found that your worries make you feel sick a great deal of the time?; 2) In the past year, have you often found that you push or drive yourself most of the time?; 3)Do you consider yourself the worrying type?; 4) In the past year, have you often found that little things got on your nerves and wore you out?; 5) In the past year, have you often found that you were nervous most of the time?
MRC[e]	Psychiatric morbidity	A self-administered questionnaire (General Health Questionnaire)[59] and a Standard Psychiatric Interview[60]
Toronto Workers Study[f]	Health perception	1. Health status assessed on a 1 (poorest health) to 9 (best health) rating scale. A standardized health status index was obtained by dividing the patient health status rating by the Study subject's rating of an "average" individual of the same age and sex. 2. Sum of 16 symptoms assessed on a 1 (never present) to 7 (always present) scale . 3. Worry about health assessed by rating on a 9 nine point scale personal and expected worry about health.
	Lifestyle	1. Actual and previous year participation in physical and social activities was estimated by asking the number of hours spent in an average week attending community organizations, participating in sports and exercise, socializing with friends and relatives and working on hobbies. 2. Actual and expected ability to participate in all the activities they enjoyed and wanted to

Table 2.2.2 (contd.)● Psychological consequences of labelling and treatment: Outcomes and assessment instruments

Study	Outcome	Assessment instruments
		do on a 9 point scale. 3. Self-care behaviours in the previous two months related to weight, smoking and exercise were assessed as well as their concerns about these activities and their attempts to modify them.
Croog et al. [g]	Sense of well-being	General Well-Being Adjustment Scale
	Sexual function	The Sexual Symptoms Distress Index
	Work performance and satisfaction	A series of seven questions covering aspects such ability to keep pace with job
	Emotional status	The Positive Symptoms Index (5 items from the Brief Symptom Inventory [61])
	Cognitive function	The Wechsler Memory Scale (Form 1) [62,63] The Reitan Trail Making Test [64]
	Social participation	The Social Participation Index [65]
	Life satisfaction	The Life Satisfaction Index [3]
TAIM study [h]	Life Satisfaction	Life Satisfaction Scale [66]
	Side effects	Physical Complaints Inventory Scale (developed for this study)
	Symptoms and psychological functioning	Symptoms Check List [67]
TOMHS[i]	Health perception Emotional well-being Bodily well-being	35 items selected from the Rand Medical Outcomes Study [68]

Table 2.2.2 (contd.)● Psychological consequences of labelling and treatment: Outcomes and assessment instruments

Study	Outcome	Assessment instruments
	Functioning	
	Side effects	Side effect checklist and number of days spent in bed due to illness reported by the participants
Beaver Dam[j]	Quality of life value	Time Trade-off
		Quality of Well-being index [69]
	Eight aspects of quality of life	SF-36 Health Survey [70,71]

a. Bloom and Monterossa [48]
b. Wagner and Stogatz [58]
c. Health and Nutrition Examination Survey [72]
d. Multiphasic Health Checkup [73]
e. Medical Research Council [74]
f. Toronto Workers Study [53]
g. Croog et al. [75]
h. Trial of antihypertensive interventions and management [76]
I. Treatment of Mild Hypertension Study [77]
J. Beaver Dam Study [78]

Two cross-sectional surveys, the **Health and Nutrition Examination Survey** (HANES I)[72] and the **Multiphasic Health Checkup** (MHC) , evaluated the association between psychological status and hypertension. People being treated for hypertension or identified at some point as being hypertensive reported statistically significant lower feelings of well-being when compared to those who had never been told they had hypertension.

In a cross-sectional study, it is impossible to identify whether the hypertension labelling is responsible for the psychologic impairment or whether the psychologic impairment increases the likelihood of being diagnosed with hypertension. It has been suggested that people diagnosed with hypertension may suffer from the labelling effect and treatment, and consequently report more depression and lower health perception. However, as suggested by Wagner and Strogatz [58], alternative explanations are also possible. It is possible that people with a poorer sense of well-being have more frequent medical visits and a higher likelihood of being labelled with hypertension or may be more accepting of medical diagnoses. Prospective screening studies are required to identify the causal relationship between psychological well-being and hypertension.

The **Medical Research Council** (MRC) was a prospective, randomized, double-blind, placebo controlled, screening program.[74] The effect of blood pressure screening on psychological morbidity was studied in 235 consecutive participants matched for age, sex and psychiatric state to two control groups; one with a normal blood pressure at screening and one with hypertension at screening but untreated. Results from the General Health Questionnaire [59] administered at entry, and after one year of follow-up indicated that the prevalence of psychiatric morbidity fell among the trial entrants and was not statistically different from the two control groups. This was later on confirmed in a larger(n=18 000) uncontrolled trial.[79] As suggested by the authors, this improvement in psychiatric morbidity may be explained by the effect

of a supportive relationship between the entrants and the study nurses. In addition, in contrast to the HRQOL measures used in the other previously cited studies, the General Health Questionnaire was designed to detect the presence of overt psychiatric disturbance rather than the psychological well-being or distress [47] which may explain those contradictory results.

In the **Toronto Workers study** [53], newly and previously diagnosed hypertensives reported statistically significant lower health status and ability to participate in enjoyable activities and significantly higher symptom scores on their Index of Worry (described in Table 2.2.2) when compared to the normotensive group. There were no differences between the two hypertensive groups. The authors concluded that the impact of the labelling and the treatment of hypertension on health perception and lifestyle was significant and sustained over time in actively employed, relatively healthy, and medicated hypertensives for whom there were no medical indications to restrict their lifestyle.

One of the first reports on the adverse consequences of pharmacologic treatment was published in 1982 by Jachuck et al.[80] The impact of the hypotensive therapy (B-blocking drugs, alpha methyldopa or diuretic agent and other drugs) on the general well-being of patients was assessed by the treating physicians, the patients, and their immediate relatives or close companions. Although most physicians considered that the treatment was beneficial, the patient appraisal indicated that 48% felt better, 44% were unchanged and 8% believed that their general well-being was worsened by the therapy. Interestingly, the assessment from the patients' relatives indicated an even greater impact on the HRQOL of patients; 25% of patients were believed to have sustained negligible-to-mild adverse changes, 45% moderate adverse responses, and 35% severe adverse impairments. Adverse effect on well-being was described as undue preoccupation with sickness, decline in energy, general activity and sexual activity, and irritability.

Croog et al. [75] reported the results of a large, multicenter, randomized, double-blind trial conducted on 626 men with mild to moderate hypertension to determine the effect of captopril, methyldopa and propanolol on the HRQOL after a 24-week treatment period. The percentage of withdrawals due to adverse reactions was lower in the captopril group (8%) compared to 20% and 30% in the methyldopa and propanolol groups, respectively. The most common reason for withdrawal was fatigue and lethargy, followed by sexual dysfunction, sleep disorders and headaches. After 24 weeks, patients in the captopril group reported higher general well-being scores and less side effects compared to patients randomized to either propranolol or methyldopa. In addition, the captopril group had better scores on work performance, visual-motor functioning and measures of life satisfaction when compared to methyldopa. This prospective randomized trial, using validated HRQOL questionnaires, demonstrated that hypertensive treatment can affect the patient's HRQOL. Among those who withdrew from the study early, significant worsening on their HRQOL was observed on virtually all scales. The authors suggested that by giving appropriate weight to HRQOL measures, we may improve compliance with treatment.

The paper by Croog et al. [75] generated tremendous interest as seen by the number of similar reports published thereafter. A MEDLINE search, from 1986 to 1997, identified a total of 480 papers published on hypertension and HRQOL. A meta-analysis of nine published, blinded, randomized with baseline comparison or placebo controlled clinical trials identified no negative HRQOL effects associated with hypertension treatment.[81] However, the authors stated that studies showing negative effects or no significant differences between baseline and treatment were less likely to be published. In addition, their findings may also be attributed to the fact that clinical trial participants have expectations of better care and receive strong supportive patient-professional relationships which may explain the general HRQOL improvement during those trials. These trials did not directly address the HRQOL

within the primary care chronic treatment setting and consequently may not be generalizable to most hypertensives. In addition, the vast majority of the trials studied only the short term effect of antihypertensive drugs. Finally, these studies were not designed to capture the impact of labelling.

It has been shown that the pharmacologic treatment of hypertension causes adverse effects and is associated with low compliance. **The Hypertension Detection and Follow-up Program** [82], a large community-based trial, reported that among participants not receiving antihypertensive treatment at the beginning of the trial, 33% experienced at least one adverse reaction to medication leading to treatment discontinuation. Forty percent (40%) of these individuals reported more than one similar event. It is also reported that nearly half of newly treated, hypertensive patients discontinued therapy within one year because of adverse effects and only 50% of those who continued to comply and have their blood pressure adequately controlled.

Very few studies have been undertaken to evaluate the impact of non-pharmacologic interventions on the well-being of hypertensives. The **Trial of Antihypertensive Interventions and Management** (TAIM Study) [76] was a large (n=697), multicenter, randomized, placebo-controlled clinical trial. Using a 3 x 3 factorial design, overweight participants were assigned to one of three diets (usual, low-sodium and high-potassium, weight loss) and one of three low dose antihypertensive drugs (placebo, chlorthalidone, and atenolol). Drug therapy, including placebo, improved the participant's HRQOL over a six month period. Weight reduction was associated with a significant increase in the satisfaction with physical health, and improvement of sexual physical problems. However, low-sodium and high-potassium diet was associated with some worsening of sexual physical problems among men, and produced more adverse effects than usual diet on sleep disturbances and fatigue.

A similar study was performed by The **Treatment of Mild Hypertension Study** (TOMHS).[77] In a multicenter, randomized, placebo-controlled trial, 902 participants received a nutritional-hygienic intervention plus one of six treatments including placebo. The intensive nutritional-hygienic intervention aimed at weight loss with a fat-modified diet, lowering dietary sodium and alcohol intake, and increasing leisure-time physical activity. Results from the Rand Medical Outcomes Study questionnaire [68] indicated improvement in HRQOL for all groups. Weight loss was associated with an improved perception of the participants' general health, better functioning, more energy and less fatigue.

The **Beaver Dam Health Outcomes Study** [83], a population-based survey, measured the health status and health-related quality of life of a random sample of adults (45 to 89 years old) in the community of Beaver Dam, Wisconsin. A report from this study evaluated the health status of hypertensives.[78] A total of 1430 randomly selected adults were interviewed. Among those, 519 reported being affected by hypertension and 93% of those had a duration of hypertension of at least three years. Hypertensives reported statistically significant lower scores on the Time Trade-off and the SF-36 General Health Perception subscale [70,71] when compared to participants not reporting hypertension. The observed differences were equal to five points, which represented 5% of the scale. Similar differences were found in a subgroup of participants reporting no other health problems. A significant decline in health status was observed with increasing numbers of antihypertensive drugs, but there were no differences between the participants taking different classes of antihypertensive drugs. This study results suggest that in the community, hypertension has a negative impact on HRQOL. This impact is sustained over time and related to the number of antihypertensive drugs.

The results of the studies on the psychological consequences of labelling and treating individuals with hypertension can be summarized as followed:

- In four large cross-sectional observational studies [48,58,72,73], hypertensives or mislabelled normotensives reported lower well-being and more depressive and medical symptoms than unlabelled normotensives. These results may be caused by a labelling and treatment effect or by a selection bias.
- In one cross-sectional survey of participants involved in an industrial screening program [53], hypertensives reported lower health status, lower ability to participate in enjoyable activities and more worry about health. These results are not likely to be attributable to a selection bias because participants were selected from a screening program, and therefore support the hypothesis of causal relationship between detection and treatment of hypertension and HRQOL.
- Impairment in HRQOL of hypertensives may be influenced by the type of follow-up. Intense follow-up such as in the MRC program [74] and in clinical trials is generally associated with no impairment or improvement in HRQOL.
- A large community-based trial [82] indicated that hypertensive treatment was associated with high incidence of adverse effects and noncompliance, and therefore supports the hypothesis that the observed impairment of the HRQOL among hypertensives may be, at least partly, due to the treatment effect.
- Lifestyle changes were reported to influence HRQOL. In two studies [76,77], weight reduction diet was associated with improvement in the HRQOL. However, low-sodium and high-potassium diet [76] had a negative impact on participants.
- A recent community-based cross-sectional survey [83] reported that hypertension was associated with a five point (5%) decrement in the HRQOL. There were no differences observed across the different types of hypertensive drug classes. However, increased impairment

was observed with more numerous antihypertensive drugs.

There is evidence that hypertension detection and treatment can induce psychological and behavioural impairment. Identified psychologic consequences include lower general well-being [72], greater psychological distress[48,58,73] , poorer perceived health status [48,53,58,73], more physical symptoms and greater functional disability [53,58], decreased time spent in social activities [53] and increased illness-related absenteeism [49-52,55,57]. However, it is possible to attenuate these effects by providing adequate follow-up.

2.2.2 Dyslipidemia

As reported by Brett [84], several aspects of the diagnosis and treatment of dyslipidemia may cause adverse psychologic responses: 1) people may confuse risk factor with disease and consider themselves as unhealthy; 2) the inherent biologic variability of serum cholesterol levels may be a source of frustration and misunderstanding for patients; 3) dietary efforts to reduce the cholesterol level are not uniformly effective and may cause disappointment, confusion, and even a sense of failure; 4) confusing messages about the benefits and harms of certain foods may be an additional source of anxiety; 5) people may be faced with the dilemma between continuing their treatment or stopping their treatment and assuming a greater risk of CHD. The medical management of dyslipidemia may also affect the HRQOL due to the rigid dietary prescriptions, the side effects of medications, and the need for regular medical visits and repeated tests

Forrow et al. [85] reported (in abstract form) the results of a prospective study on 1052 voluntary participants in a cholesterol screening program. Based on their cholesterol level, participants were told that they were either at high, moderate or

low risk of CHD. They found that people at high risk had increased worry and concern about health 17 months after their diagnosis.

The **Massachusetts Model Systems for Blood Cholesterol Screening** Project [43] evaluated the effect of a screening program on psychological well-being and on reported impairment due to illness among individuals identified as having high blood cholesterol levels. Out of 3489 adults between the ages of 20 to 88 years old, a total of 1093 (31%) were identified as having high blood cholesterol ($\geq$ 6.21 mmol/L). All participants completed a questionnaire prior to screening, and those referred to a physician for high blood cholesterol completed the same questionnaire between 2 to 4 months after screening. This questionnaire included nine questions on labelling, adapted from the RAND Corporation's General Health Perceptions Questionnaire.[86] They found no evidence for negative labelling effects among the various age, sex, racial, income, and educational groups. Small, statistically significant, positive changes on the majority of the labelling questions were reported. The interpretation of these results was, however, limited by the lack of a control group. The authors concluded that the observed positive effects could be attributed to the positive, supportive approach to participant counselling.

In a prospective multistage screening study, conducted by Irvine and Logan [87], on male workers at a motor-car assembly and steel-making plant, the psychological profiles of 287 workers diagnosed as having hypercholesterolemia and of 236 randomly selected normal cholesterol controls were compared at baseline and one year later. Hypercholesterolemic individuals were randomized to one of three treatment groups: intensive dietary counselling at work site; referral to their family physician; or minimal dietary advice. Various psychological tests were used including the Rand Corporation's Mental Health Index [86], the Campbell's Life Satisfaction Index [88] and the House's Occupational Stress Questionnaire[89] . No adverse changes on the psychological measures were found irrespective of the type

of follow-up care. However, these conclusions are strongly limited by the fact that about half of the participants diagnosed as having hypercholesterolemia did not believe they had hypercholesterolemia at follow-up. The participation rate was relatively low and approximately equal to 76% at the first screening. As discussed previously, studies with low participation rates may be more likely to report positive effects with screening.

Dyslipidemia was a health condition evaluated in the **Beaver Dam Health Outcome Study**.[83] The health status of a total of 110 participants reporting hypercholesterolemia and 29 other participants who did not report hypercholesterolemia but who were on an antihyperlipidemic drug was reported.[90] After adjusting for age and number of comorbid conditions reported, the mean score for participants with hypercholesterolemia was significantly higher than the mean score of the other participants on the Time Trade-Off (TTO) [91] and the Quality of Well-Being scale (QWB)[69] (TTO: 90.3 versus 84.8, p=0.01; QWB: 0.746 versus 0.723, p=0.007) and no difference was observed on the SF-36 General Health Perception subscale [70,71] (77.0 versus 74.3, p=0.086). Using antihyperlipidemic drugs had no significant impact on the TTO and the QWB scale. However, the SF-36 General Health Perception subscale scores decreased by 3.5 points for each antihypercholesterolemic drug added.

Fifty-seven (57) patients with familial hypercholesterolemia participated in a follow-up examination 5.5 years after completion of a one year trial with lovastatin, cholestyramine, probucol, or ω-3 fatty acids.[92]Among this highly motivated group of patients, compliance with therapy was very high; only one patient did not take any medication at follow-up. HRQOL was assessed at follow-up only and scores were within the reference range of a general population. Interestingly, the patients' main concern, after more than 5 years of treatment, was to keep a diet low in saturated fat. The second most frequent main concern was taking medications.

Preliminary results from **The Air Force Coronary Atherosclerosis Prevention Study (AFCAPS)** [93], a randomized, double-blind, placebo-controlled primary prevention trial evaluating the efficacy of lovastatin to prevent CHD, were reported.[93] Emotional well-being and general health perceptions were evaluated using adapted questionnaires from the SF-36 Health Survey [70,71]. Preliminary analysis on 1100 patients indicated that the participants in the placebo and lovastatin groups report similar baseline scores and a similar change from baseline at one year.

In a randomized trial, the impact of diet (n=40), exercise (n=39), diet and exercise (n=39) and no active intervention (n=39), among healthy middle aged men with moderately raised cardiovascular risk factors, were compared. [94] HRQOL and well-being did not differ between the four groups and did not change significantly in any of the groups during the 6 month study. However, the small number of participants in each group may have reduced the ability to detect small differences.

The effects on HRQOL of lovastatin and pravastatin were compared in a multicenter, double-blind, randomized, parallel study of 426 male patients, between 20 to 65 years of age, with primary hypercholesterolemia.[95] Initially, patients were on a six week period of diet only, followed by another 6 week period of diet and placebo, and finally a 12 week period of diet and either lovastatin or pravastatin. Various HRQOL instruments including The Nottingham Health Profile [96], a 6-item sexual function questionnaire derived from the Medical Outcomes Study [97] and the Stress/Life Events Scale [98] were administered. There were no changes in HRQOL measures between the beginning and the end of the diet-only period. Eighty percent (80%) of participants reported no HRQOL change during the entire course of the study and 90% reported a $\leq$ 1.0 point change from baseline for all domains. Across all scales, there were no statistically significant differences between the two treatment groups.

In summary, with the exception of the Forrow et al. study [85], there is no data to support the hypothesis that detection and treatment of dyslipidemia affect the HRQOL. However, all reported studies have important limitations: no control groups [43,92], short follow-up [94,95], small sample size [83,94], and evaluation performed in the context of a clinical trial [92-95]. The design of the Irvine and Logan study [87] was excellent but, unfortunately, the majority of the participants did not believe they had dyslipidemia and the participation rate was relatively low.

2.2.3 Summary and conclusion

HRQOL of aware hypertensives is lower than normotensives. The decrement in their HRQOL can be attributed to the labelling effect and/or pharmacologic and nonpharmacologic treatments. The negative impact of hypertension may be reinforced by adding antihypertensive drugs and may be reversed or attenuated by intensive follow-up. Compared to hypertension, the number of studies evaluating the impact of the detection and treatment of dyslipidemia on the HRQOL is small. In the reviewed literature, there is no evidence that the diagnosis and treatment of dyslipidemia may affect the HRQOL, with the exception of one abstract. [85]

This review of the literature is useful in designing a study to evaluate the HRQOL of healthy participants on primary prevention treatment.

- In the absence of a universal screening program for the detection of dyslipidemia, individuals with dyslipidemia are mostly diagnosed through case finding procedures. For this reason, results from cross-sectional studies may be attributed to selection bias among patients seeking medical care. For this reason, it is important to control for comorbidity, age and utilization of health care. This selection bias

may be reinforced by selecting individuals from hospital specialized clinics.

- Prospective screening studies are not subject to this selection bias because participants with and without dyslipidemia are recruited through the same selection procedure. By comparing change before and after screening, where each participant is his/her own control, it is possible to identify the causal relationship between dyslipidemia and HRQOL. However, the results of these studies may vary according to the participation rate and type of follow-up.
- A randomized clinical trial is a poor design to evaluate the long term impact of detecting and treating dyslipidemia for several reasons. Most clinical trials are designed to compare the effects of different drugs on the HRQOL on previously diagnosed patients. There is no comparison with healthy participants without dyslipidemia. For these reasons, the labelling effect is not assessed in these studies. Only volunteers are included which may represent mostly compliant patients, patients unsatisfied with their current therapy, or interested in receiving hypocholesterolemic drugs at no costs. Consequently, clinical trial participants may not be representative of the general population. Additionally, HRQOL has been shown to be sensitive to the intensity of the follow-up. In the reviewed studies, HRQOL improved during those clinical trials even when taking placebo only and this may be attributed to the high intensity of follow-up in most clinical trials.

This review underlines the importance of conducting further studies to better evaluate the impact of detecting and treating dyslipidemia on the HRQOL of healthy individuals. In these studies, appropriate types of HRQOL instruments should be selected in order to be able to integrate these measures in a QALY model.

2.3 Preference-based health-related quality of life measures

To be used as a quality weight in a cost-effectiveness analysis, a HRQOL measure needs to fulfill some minimal requirements. [99] First, the HRQOL of each health state should be represented by a unique score. Second, in order to be able to compare the cost-effectiveness of different programs, the quality weight should be measured on a universal scale that can accommodate all possible health states. By convention, analysts use scales which range from zero to one, representing *death* and *perfect health*, respectively. Finally, the quality weights should be measured on at least an interval scale in order to be used in mathematical operations. An interval scale is characterized by an equal distance between the scale points and by an arbitrarily selected zero point.

HRQOL can be assessed by using either a nonpreference-based or a preference-based approach.[100] The nonpreference-based approach consists of describing various aspects of the HRQOL, for example, by asking questions about the presence, the severity and the frequency of symptoms or the ability to perform daily tasks. The SF-36 Health Survey is an example of a nonpreference-based HRQOL questionnaire. It consists of 36 items evaluating eight domains of the HRQOL: general health perception, physical functioning, role limitations due to physical health problems, role limitations due to emotional problems, social functioning, bodily pain, vitality, and general mental health. The general health perception subscale represents an overall evaluation of health. However, this subscale does not provide interval scale data [101] and is not preference weighted. For these reasons, its results cannot directly be used in cost-effectiveness analysis.

The preference-based approach consists of asking the respondents to make a judgement about the value of life with a given health state.[102] It measures the strength of the preference for health conditions. Preference-based measures are

currently used in cost-effectiveness analyses as quality weights because they provide a single HRQOL score for each health state measured on a universal and interval scale. In addition, they are particularly useful in allowing allocation of resources in accordance with a population's judgment about a range of health states. [99] We will review the methodological aspects and the psychometric properties of the preference-based measures to identify how these measures could be adapted to adequately measure the HRQOL of healthy individuals with and without dyslipidemia and CHD patients.

2.3.1 Methodological aspects

Prior to proceeding with the preference-based assessment, several aspects of the measurement need to be defined. These include the choice of the scaling technique, the measurement strategy, the relevant health dimensions, the source population, and how to control for context dependant variables. A review these methodologic aspects follows.

2.3.1.1 Scaling techniques

The most commonly used scaling techniques are the standard gamble (SG), the time trade-off (TTO) and the rating scale (RS). A description of these scaling techniques for the evaluation of chronic health states considered to be better than death follows.

2.3.1.1.1 Standard Gamble

Standard Gamble (SG) is used to estimate the utility of health states. The utility represents the individual's preference for a health state under conditions of uncertainty. It is often considered as the criterion by which the other preference-based scaling techniques are compared because it is based on a the axioms of the expected utility theory. [99.103-105]

In the SG assessment, the respondent is asked to choose between a sure outcome (**S**) and a lottery (Figure 2.3.1). The sure outcome represents the health state under evaluation. The lottery is composed of two alternatives; one with a probability ***p*** of a better outcome than the health state under evaluation (**G** = GAIN) and another with a probability (*1-**p***) of a worse outcome than the health state under evaluation (**L** = LOSS). During the interview three of these four elements (**S, G, L and *p***) are set constant and the fourth element is varied until the respondent becomes indifferent between the sure outcome and the lottery. At this indifference point, the utility of the sure outcome is equal to the expected utility of the lottery:

$$u(\mathbf{S}) = pu(\mathbf{G}) + (1-p)\,u(\mathbf{L})$$

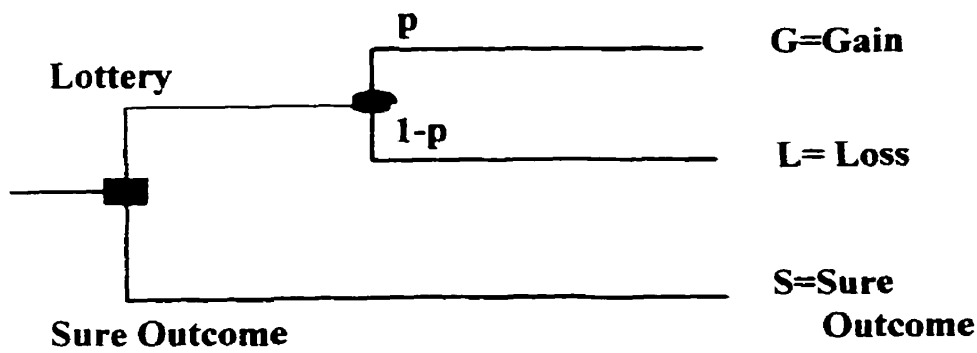
The expected utility of **S** can be derived by four different methods depending on which elements are set constant: [106]

Certainty equivalence: **G**, **L** and ***p*** are set constant and **S** is varied until the indifference point.

Probability equivalence: **G**, **L** and **S** are set constant and ***p*** is varied until the indifference point.

Gain equivalence: ***p***, **L** and **S** are set constant and **G** is varied until the indifference point.

Figure 2.3.1 Standard Gamble scaling technique



Loss equivalence: p, **G** and **S** are set constant and **L** is varied until the indifference point.

When evaluating the utility of health states, the probability equivalence is the current method of elicitation. Within this method, we can choose a lottery with either an extreme or adjacent gamble outcomes. When **G** and **L** represent, respectively, *perfect health* and *immediate death*, the outcomes of the lottery are considered as extreme. By convention the utility of *perfect health* is equal to one and the utility of *immediate death* is equal to zero. Consequently, at the indifference point, the utility of the sure outcome (u(**S**)) is equal to the probability p.

In the SG with adjacent gamble outcomes, the lottery outcomes (**G** and **L**) are "locally" better and worse than the sure outcome. When the sure outcome needs to be assessed on a continuum between zero (*immediate death*) and one (*perfect health*), it is necessary to assess the utility of each adjacent lottery outcome against a gamble with extreme lottery outcomes. This multistep approach is called the cascading approach [107] or the chained-approach [108]. This approach is currently recommended to assess the utility of health states very close to either *perfect health* or *immediate death* or to avoid constantly confronting the respondents with the risk of dying. [107] It is described in more detail in section 3.1.

During the SG assessment, the probability p is changed until the respondents become indifferent between the sure outcome and the lottery. The probability p can be varied using the titration or the ping-pong approach. In the titration approach, the probabilities are gradually increased or decreased until the indifference point is identified. For example, the first SG question may consist of asking respondents to choose between living with their *current health* for the rest of their life or choosing a lottery with 100% chance of living in *perfect health* and 0% chance of an *immediate death*. If the respondents choose the lottery outcome, then the probability

of *perfect health* is gradually decreased in each subsequent question until they become indifferent or refuse the lottery outcome. In the ping pong approach, ***p*** is varied across the lower (0%) and the upper (100%) level of probabilities until the respondents become indifferent between the two choices. For example, the probability of *perfect health* could be changed in the following order: 100%, 0%, 90%, 10%, 80%. If the respondents accept the lottery outcome with 90% chance of *perfect health* but refuse it when the probability is equal to 80%, then the indifference point is located in between and corresponds to 85%. The ping-pong approach is generally preferred to the titration approach because when the probabilities are constantly increased/decreased the respondents have a tendency to underestimate or overestimate the indifference point. [107]

SG is difficult for the respondents to understand and difficult for the interviewers to administer. For these reasons, the use of a visual aid, such as the chance board [107] or multimedia presentations [109] is recommended. These visual aids facilitate the understanding of probabilities by using probability wheels or diagrams. The probability wheel is a colour coded pie-chart where the probability of the worst outcome is represented by shading the appropriate proportion of the pie-chart. For example, if the probability of the worst lottery outcome is equal to 50%, then 50% of the pie-chart is shaded. [107] The diagram aid consists of one hundred faces where the probability of the worst outcome is represented by shading the corresponding number of faces. [110] For example, if the probability of the worst lottery outcome is equal to 50%, then 50 faces are shaded. In contrast to the probability wheel, the diagram may facilitate the discrimination of small probabilities. With the probability wheel, it would be difficult to visualise the difference between 1% and 2% risk of the worst outcome. With the diagram, these probabilities would correspond to shading one or two faces.

Visual aids are also helpful to the interviewer because they indicate whether

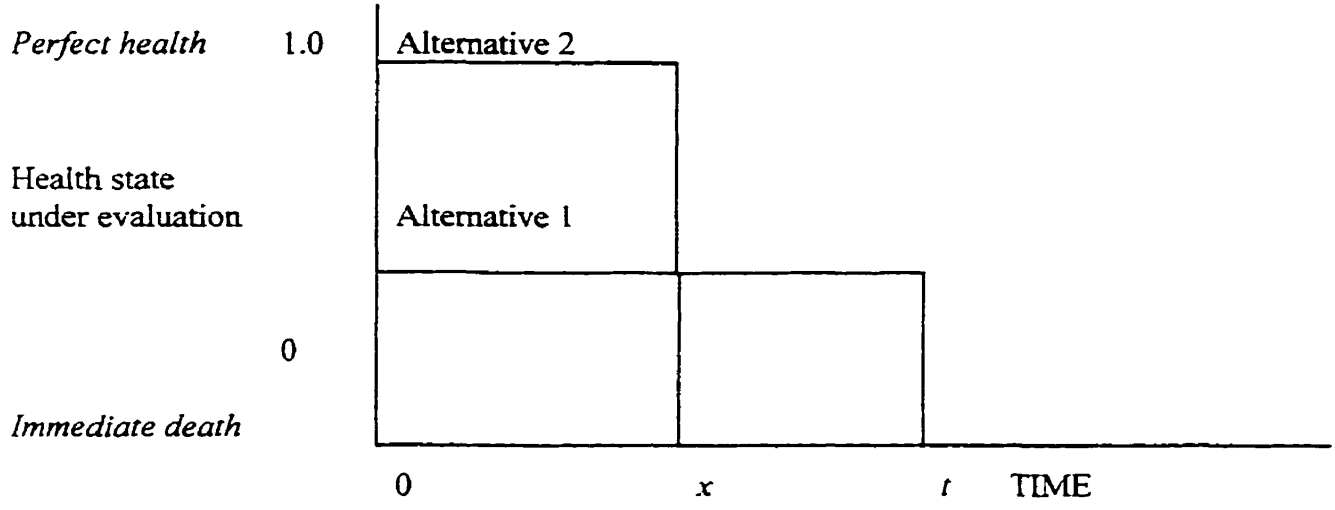
the probability ***p*** corresponds to the indifference point or which lottery outcomes should be presented next. For example, if a respondent accepts a lottery with 90% chance of *perfect health*, then the visual aid will indicate to the interviewer that the next lottery outcome is a lottery with a 10% chance of *perfect health*. If the respondent refuses this lottery, the next lottery outcome would consist of a lottery with 80% chance of *perfect health*. If the respondent refuses this lottery, then the visual aid will indicate to the interviewer that the assessment is completed and that the utility of the health state being evaluated is equal to 0.85.

2.3.1.1.2 Time Trade-off

Because some respondents find probabilities difficult to understand and work with, Torrance, Thomas and Sackett [111] developed a simpler approach, the time trade-off (TTO). In contrast to the SG, it is not based on the axioms of expected utility theory. Because the assessment is performed under conditions of certainty, the results are expressed in terms of value instead of utility.

During the TTO assessment, the respondents are asked to choose between two alternatives. The first alternative consists of living for time t with the health state under evaluation. The second alternative consists of living a shorter period of time x in a better health state (Figure 2.3.2). During the interview, time x is varied until the respondents become indifferent between the two alternatives. To be able to evaluate the health state on a continuum between zero and one, *perfect health* is used as the health state for the second alternative. When the respondents are indifferent between the two alternatives, the value of the health state under evaluation is equal to x/t. The use of a visual aid is recommended to facilitate the assessment. [107]

Figure 2.3.2 Time Trade-off scaling technique



2.3.1.1.3 Rating Scale

The rating scale (RS) instrument simply consists of a line on a page with clearly defined endpoints. The respondents are asked to place the health state under evaluation between these two endpoints. [105,112] To evaluate the health state on a continuum between zero and one, the best endpoint is *perfect health* and is placed at one extreme of the scale and the worst endpoint is *immediate death* and is placed at the other extreme of the scale. The value of the health state under evaluation is equal to the distance between the health state under evaluation and the *immediate death* endpoint divided by the distance between the two endpoints. The RS can be administered using a visual aid called the feeling thermometer. [107]

2.3.1.1.4 Selection of the scaling technique

Multiple studies have shown that for a given health state, these three preference-based measures produce different scores. [100,105,113-116] Because the cost-effectiveness ratio may vary according to the choice of the scaling technique, the choice of the scaling technique is an important methodological issue.

There is no consensus so far on which scaling technique is the most appropriate to use. [99] This probably reflects the fact that none of these scaling techniques is perfect. As reported previously, SG assessment is based on a solid theory. In addition, it measures the respondent's preference for health state under conditions of uncertainty. When medical decisions involve uncertainty, SG may assess preferences in a more realistic fashion than the non-risky preference-based measures. [107] However, the feasibility of administering such a complex instrument has been questioned by many. [99] Compared to the SG, TTO is easier to administer. In addition, TTO directly measures the number of healthy years that are equivalent

to a given time in a particular health state. In other words, it directly tests the willingness of the respondents to give up years of life in exchange for a better HRQOL, which is the foundation of the QALY model. The RS is the easiest technique to administer. However, it produces interval-level measures only when the respondents are instructed that the intervals between the location of the different health states reflect the difference they perceived between the health states. [99]

Recently, the US Panel on Cost-Effectiveness in Health and Medicine [3] recommended that preference-based techniques be used to assess quality weights. They suggested that when results are based upon measurement techniques such as the RS, they should be compared with results obtained using the TTO and the SG. However, a review of the cost-effectiveness analyses published between 1975 and 1995 (n=80) reported that only 5% and 18% used the SG and the TTO scores, respectively, as quality weights for QALY analyses.[117] This may reflect the difficulty of using complex instruments such as the TTO and the SG scaling techniques.

2.3.1.2 Measurement strategies

Two strategies are available to evaluate health states: the holistic and the decomposed approaches. In the holistic approach, a given health state is described and evaluated as a whole using a specific scaling technique such as the RS, TTO or SG. For example, the consequences of surviving a myocardial infarction could be described in terms of physical and social functioning, emotional well-being, pain and cognitive ability. A respondent inexperienced with this health state could be asked to consider all these attributes and assess the value or the utility of this health state. Another alternative would consist of asking myocardial infarction survivors to rate their current health.

In the decomposed approach, each attribute of a health state is evaluated

separately and the overall health state value or utility is expressed as a decomposed function of these attributes. Several instruments, using the decomposed approach, are available such as the MultiAttribute Utility (MAU) method [118] and its revised versions, the Mark I, II, III [119], the Quality of Well-being Scale [120], the Disability and Distress Index [119], and the EuroQol instrument[119] . Each of these instruments provides: 1) a classification system consisting of a set of attributes with multiple levels per attribute, 2) a quality weight for each level of each attribute and 3) a mathematical function to compute the overall value or utility of health states. The users need to map the health state under evaluation into the classification system and use the quality weights and the mathematical function to compute its overall value or utility. As seen in Table 2.3.1, these instruments use different classification systems. They also differ by the type of the scaling technique to measure the quality weights and the population of raters selected to assess the quality weights.

Compared to the holistic approach, the multiattribute instruments are very easy for the respondents and can be administered in a few minutes. They are particularly useful when a large number of health states needs to be evaluated.

2.3.1.3 Relevant health dimensions

Preference-based assessments provide one single score for each health state. To facilitate the interpretation of the preference-based scores, it is recommended to complement the assessment by using a nonpreference-based HRQOL instrument to identify which aspects of the HRQOL might be responsible for a high or low preference-based score. [121] It is necessary to select a nonpreference-based HRQOL instrument that assessed multiple aspects of the HRQOL relevant to patients with CHD as well as to healthy individuals with or without dyslipidemia. [122]

Table 2.3.1 • Multi-attribute preference scales

Instruments	Attribute	Number of levels/attribue
Health Utilities Index		
Mark I	Physical function	6
	Role function: self-care and role activity	5
	Social-emotional function	4
	Health problem	8
Mark II	Sensory	4
	Mobility	5
	Emotion	5
	Cognitive	4
	Self-care	4
	Pain	5
	Fertility	3
Mark III	Vision	6
	Hearing	5
	Speech	5
	Getting around (mobility)	7
	Hands and fingers (dexterity)	4
	Feelings (emotional function)	5
	Memory and thinking (cognitive function)	9
	Pain and discomfort	5

Table 2.3.1 • Multi-attribute preference scales (contd)

Instrument	Attribute	Number of levels/attribue
EuroQol	Mobility	3
	Self-care	3
	Usual activity	3
	Social relationships	3
	Pain	3
	Anxiety/depression	3
Quality of Well-being	Mobility	5
	Physical activity	.4
Rosser Index	General mobility	6
	Usual activity	4
	Self-care	4
	Social and personal relationship	4
	Distress	4

It has been shown that the detection and treatment of hypertension can influence several aspects of the HRQOL, namely the general well-being, health perception, psychological distress and social activities. These aspects may also be relevant when evaluating the HRQOL of healthy individuals with dyslipidemia and should be incorporated in the nonpreference-based HRQOL evaluation. These concepts are included in three major generic HRQOL questionnaires: the Nottingham Health Profile [96], the SF-36 Health Survey [70,71] and the Sickness Impact Profile [120] (Table 2.3.2).

HRQOL of patients with CHD may be affected by the nature and the severity of the disease, and the adverse effects of treatment. [123,124] Almost every aspect of the HRQOL can be affected by CHD. [125-127] For example, in the Medical Outcomes Study [128], patients with a previous myocardial infarction reported lower physical, role and social functioning, as well as lower scores on the mental health, health perception and bodily pain subscales when compared to individuals without chronic conditions. The SF-36 Health Survey has been validated in general [129] and in various patient populations [71,130-132], and used in CHD treatment [133] and prevention [78].

2.3.1.4 Source population

Quality weights can be obtained from different populations: health professionals, samples of the general public or from individuals experiencing the

Table 2.3.2 ● Major concepts of health-related quality of life evaluated in generic instruments‡

	Generic Quality of Life Instruments		
	Nottingham Health Profile	Short Form Health Survey (SF-36)	Sickness Impact Profile
Health Perceptions	✓	✓	✓
Functional Status			
Social	✓	✓	✓
Psychological	✓	✓	✓
Physical	✓	✓	✓
Impairment		✓	✓

‡ Adapted from Patrick and Erickson [134]

health state being evaluated (or their surrogates). Empirical data have demonstrated that for a given health state, the quality weights vary according to the type of raters. Generally, patients who experience the health state being evaluated report higher scores than individuals with no experience and members of the general public. [135,136] This may be explained by the fact that people with a particular disease or disability may learn to cope with it. [136,137] There is also some evidence that preference-based measures obtained from health professionals and patients differ. [138] Although health professionals are knowledgable with the health state evaluated, they may focus on functional status and fail to consider more subtle and subjective influences of an illness such as emotional problems, pain and discomfort.[139] Because quality weights vary according to the type of raters, the choice of the source population may influence the conclusions of the cost-effectiveness analyses.

In theory, quality weights obtained from a representative sample of fully informed, unbiased and competent members of the community would respect the societal perspective of a cost-effectiveness analysis. [3] However, from a practical point of view those quality weights may be difficult to obtain. Quality weights from unexperienced individuals may be biased by stereotypes and misunderstanding of the health states evaluated. [99]

2.3.1.5 Context dependent variables

Preference-based measures are influenced by several aspects of the health state description and the mode of presentation of the scaling techniques.

2.3.1.5.1 Health state description

Preference-based assessments are influenced by the format of the health state

description, the amount of information provided to the respondents [137,140-143], and by the duration and prognosis of the health state evaluated.

Preference for treatment may differ according to whether the outcome is characterized in terms of the probability of dying or the probability of surviving. For example, in the McNeill et al. study [140], 42% of the respondents preferred radiotherapy to surgery for lung cancer when mortality rates were used to describe the consequences of the surgery. In contrast, 25% preferred surgery when surgery was described using survival rates. Consequently, different SG scores may be obtained depending on whether the lottery outcome is described in terms of the probability of *perfect health* or in terms of the probability of an *immediate death*. To avoid this bias, it is suggested to present both, the probability of the best and the worst outcome during the assessment.

Preference-based assessments are also influenced by the format of the health state description (standard point-form versus narrative format) and the amount of detail provided in the description of the health state being evaluated. [141] For this reason, the same format and the same amount of information should be provided to the respondents when different health states are evaluated.

The value or the utility of a health state is influenced by its duration. To understand this concept, Torrance et al. [111] gives the following example:

1- Would you prefer to live one day of bed confinement or one day on a kidney-dialysis regimen?

2- Would you prefer to live five years in bed confinement or five years on a kidney-dialysis regimen?

Most people would prefer bed confinement in the first question and dialysis in the

second question. Although this example is extreme, it suggests that it is possible to change or even reverse a preference just by modifying its duration.

Empirical data have shown that risk attitude and preference vary according to the health state duration. In the Verhoef et al. study [144], when assessing the certainty equivalence of different time periods, they observed that respondents were risk-seeking in the short term and risk-averse in the long term. As mentioned by the authors, similar observations occur in real life when cancer patients choose risky treatments even when more conservative approaches with better short term prognosis are available. In other words, when people are faced with a bad prognosis they tend to prefer risky alternatives. In another study, patients with testicular or colorectal cancer rated their current health on three TTO assessments of different durations. [145] The TTO scores for the longer duration were smaller than those obtained for shorter durations. The results indicate that the duration of the health state influences the preference-based assessment. In the literature, the duration of the health state is either based on the respondent's age and gender-specific life expectancy [83,146] or fixed for all respondents [147].

The utility or value of the health state under evaluation should not be influenced by possible future health states.[111] To control for the prognosis effect, the same prognosis should be used for each alternative of the SG and for each scaling technique. In practice, this is done by specifying that the health state under evaluation will last for a specific period of time and will be followed by a painless death.

2.3.1.5.2 Mode of presentation

When multiple scaling techniques are used to evaluate a health state, the order of presentation of the scaling techniques may be important. In one study [141], the

category rating scores were substantially higher when SG was administered first.

Preference-based assessments are also reported to vary according to the choice of the anchors, i.e. the choice of the endpoints in the RS, the best health state in the TTO and the lottery outcomes in the SG. When preference-based measures are incorporated in cost-effectiveness analysis to eventually compare different programs or treatments, it is necessary to assess each health state on a zero to one scale representing *immediate death* and *perfect health*, respectively.

2.3.1.6 Summary

This review of preference-based assessment clearly indicates that different preference-based scores can be obtained for a given health state even when the same scaling technique and the same measurement strategy are used. Therefore, it is important to standardize the preference-based assessment for each of the health states included in a cost-effectiveness analysis. Standardization means using the same anchors (*perfect health and immediate* death), the same source population, the same format for the health state description and an appropriate duration and prognosis.

2.3.2 Psychometric properties

To be useful in economic evaluation, preference-based HRQOL measures should be reliable, valid and sensitive to clinically significant therapeutic or group differences. [148] The evaluation of the reliability and validity of each scaling technique is useful to determine to what extent these scaling techniques produce precise and valid estimates of the construct being measured. Psychometric properties may vary according to the population of raters and for this reason, should be assessed among

the individuals whose preferences will ultimately be used. [149]

Reliability is a measure of the extent to which the same results can be reproduced when repeated under the same conditions.[150] There are three types of reliability coefficients: intra-rater reliability, inter-rater reliability and test-retest reliability. Coefficients of reliability are estimated by repeating the measurements under the same conditions more than once during an interview (intra-rater reliability), or with different interviewers (inter-rater reliability). Test-retest reliability refers to the stability of scores over a period of time when the same respondents assess the same health state under the same conditions at different times.

In their review, Froberg and Kane [105] reported that the intra-rater reliability for the RS, TTO and SG varied from 0.70 to 0.94. The inter-rater reliability was reported only for the RS and varied from 0.75 to 0.77. The test-retest reliability decreased as time between the test and the retest increased. When the time period was less than 6 weeks, the reliability coefficients varied from 0.63 to 0.87 but were equal to approximately 0.5 when the retest was performed after one year. Nease et al. [151] reported the test-retest reliability of the RS, TTO and SG measures in angina patients over a two week period. All scores were stable over time with a mean change (95% confidence interval) equal to 0.0041 (-0.033 to 0.027), 0.003 (-0.033 to 0.041) and -0.010 (-0.049 to 0.029) for the RS, TTO and SG, respectively. The inter-rater reliability of the RS and TTO was evaluated in ten survivors of myocardial infarction when two interviewers administered the same questionnaire twice on the same day. [147] For each respondent almost identical scores were obtained on each scaling technique. These results suggest that the reliability of preference-based measures is acceptable in various populations of raters including CHD patients.

Validity is defined as the extent to which an instrument measures what it is intended to measure. [150] Traditionally, three aspects of validity are defined: content,

criterion and construct validity. In the field of preference-based assessment, content validity refers to the adequacy of the health state descriptions in terms of the selection of the health state attributes, its duration and prognosis. [105] Criterion-validity consists of comparing preference-based scores with "true" preference scores obtained at the same time (concurrent validity) or at some point in the future (predictive validity). Because there is no gold standard to measure preferences, this type of validity is not applicable. [105] Most validity studies were designed to test the construct being measured by each scaling technique. This has been done by evaluating the convergence between various preference-based measures and between preference-based and nonpreference-based measures. In addition, several studies have been performed to test the ability of each scaling technique to distinguish clinically different groups of patients.

Several studies have evaluated the convergence between the RS, TTO and SG measures. The correlation between these scaling techniques has been reported as being low to moderate and varied from 0.22 to 0.65.[100,105,113,152] These results suggest that these preference-based scaling techniques are not exactly measuring the same construct. In fact, as stated previously (section 2.3.1.1.4), for a given health state, these three scaling techniques produce different scores. [100,105,113-116] Generally, the highest scores are obtained with the SG and the lowest with the RS. Three factors can explain the observed differences: 1) the consequences associated with each scaling technique, 2) the respondent's risk attitude and, 3) time preference.

With the RS, respondents are asked to value a health state by simply indicating its location on an interval scale. In contrast, the TTO and the SG are associated with consequences. Respondents are asked to indicate how much time they would be willing to give up or how much risk of death they would be willing to take to avoid the health state under evaluation. A health state is considered as being less than perfect only if the respondents are willing to take an immediate risk of death

or are willing to give up some of their life expectancy to avoid it. For this reason, for many individuals, it is more difficult to assign a low score on the TTO and the SG scales than on the RS.

The risk attitude represents the attitude of an individual towards the act of gambling. In TTO and SG, the rater is asked to choose between two alternatives. However, in the TTO, the alternatives are two sure outcomes. In the SG, one of the outcomes is a gamble (lottery). When faced with uncertainty, people may be risk-averse, risk-prone or risk-neutral. Research on the psychology of choice under risk has demonstrated that risk attitude is context dependent. [106,142,153,154] Respondents may be averse or prone to take risk depending on the health state being evaluated. Generally, when the evaluated health condition is considered by the respondents as a gain relative to their aspiration level or expectation, risk aversion is the most prevalent attitude and, consequently, SG scores are expected to be higher than those obtained by non-risky preference-based measures such as the RS and TTO. In the Stiggelbout et al. study [116],when the TTO scores were adjusted for risk attitude, they were not statistically different from the SG scores. These results suggest that risk attitude is important in explaining the observed difference between TTO and SG scores.

Time preference may also partly explain the observed difference between the SG and the TTO scores. People are generally less concerned with losses or gains in the distant future than with losses or gains in the near future.[115,154] With the TTO, the number of years of life are sacrificed at the end of the rater's life whereas with the SG the risk of death is immediate. For this reason, it may be easier to sacrifice years of life in the TTO than to risk an immediate death in the SG. Again, this may explain why TTO scores tend to be lower than SG scores.

Convergence validity of preference-based measures has also been assessed

by evaluating the correlation between preference-based measures and nonpreference-based HRQOL measures. It is expected that the utility or the value of a given health state is influenced by its HRQOL. All reviewed studies reported poor to moderate correlations between nonpreference-based and preference-based measures. [100,155-157] In the Bosch et al. study [100], the correlation between the SF-36 Health Survey subscales and the RS, among patients with intermittent claudication, was moderate and varied between 0.37 to 0.67. Correlation between the SF-36 subscales and either the SG or TTO was generally poor and varied from 0.10 to 0.46. Several multivariate analyses were used to evaluate the proportion of the variation of the valuation scores explained by various nonpreference-based HRQOL aspects. In the Bosch et al. study [100], they reported that 61%, 28% and 14% of the total variance of the RS, TTO and SG, respectively, could be explained by the best combination of the SF-36 subscales. Other multiple linear [155,158] and non linear [159,160] regression models have also not been able to explain a large proportion of the SG or TTO scores based on nonpreference-based HRQOL measures. Bosch et al.[100] offered several explanations for the poor correlation between nonpreference-based HRQOL measures and either SG or TTO scores: 1) time preference and risk attitude may vary among respondents; 2) a large proportion of the TTO and SG scores were equal or very close to the maximum score and this ceiling effect may attenuate the correlations; 3) the importance of the various HRQOL dimensions may vary across respondents; 4) nonpreference-based HRQOL measures may not measure exactly what they are intended to measure; and 5) the cognitive complexity of the TTO and SG may add additional variability.

Other studies have tested the ability of the preference-based measures to distinguish clinically different groups of patients. In survivors of myocardial infarction, the RS scores were higher for patients with better New York Heart Association or Specific Activity Scale classes and those with better Karnofsky scores. There were no similar patterns observed with the TTO scores.[147] In the Nease et al.

study [151], the median RS scores from angina patients decreased with more physical disability as estimated by the Canadian Cardiovascular Society classification. RS scores from patients in Class I were statistically significantly higher than those in Class II and scores from patients in Class II were significantly higher than those in Class III/IV. On the TTO scale, there was no difference observed between patients in Class I and II. On the SG scale, there were no significant differences observed between patients in Class I, II and III/IV. For Nease et al., these results reflected the fact that patients may attribute different values to the same health state. [151] Cardiac patients with severe symptoms may assign a high or low value to their current health depending on how they feel about their symptoms.

The ability of the TTO to discriminate individuals involved in CHD prevention interventions from those who are not can be assessed using the results of the Beaver Dam Study. A significant 5% difference between respondents with and without hypertension was detected on the TTO scale and the SF-36 General Health Perception subscale. [78] The ability of the TTO to detect this difference was probably due to the large sample size (n= 1430). A similar type of analysis was performed comparing 110 respondents with dyslipidemia to participants not reporting dyslipidemia (n=1246). [90] No difference was observed between these two groups on the SF-36 General Health Perception subscale whereas a significant increase was detected on the TTO scale.

The discriminant ability of the preference-based measures was also assessed for respondents not involved in CHD prevention or treatment. Among HIV-infected patients, SG scores, in contrast to a nonpreference-based measure, did not discriminate asymptomatic patients, symptomatic patients and patients with acquired immune deficiency syndrome (AIDS) and were not correlated with clinical status. [161] Tsevat et al. [162] conducted a prospective study among HIV-infected patients at various stages of infection. At baseline, RS and Quality of Well-being Scales [120]

scores were inversely related to disease stage, but TTO scores were generally higher regardless of the disease stage. Nonpreference-based HRQOL measures, including the SF-36 Health Survey, indicated that the health status of patients with more advanced HIV-infection was worse. Over a six month period, nonpreference-based measures indicated deterioration of the HRQOL for patients with AIDS and patients manifesting progression of HIV-infection. In contrast, the preference-based measures, particularly TTO, remained stable. In one study [163], where end-stage renal patients evaluated their current health using the TTO scale, transplanted patients reported higher mean scores (0.82) than hospital haemodialysis patients (0.43). However, there were no differences observed between patients on hospital haemodialysis, home/self-care haemodialysis, or on continuous ambulatory peritoneal dialysis.

In summary, all scaling techniques have comparable and acceptable reliability. Low to moderate correlations were reported between nonpreference-based and preference-based measures. The ability of the TTO and SG to discriminate groups of clinically different patients is generally poor. Finally, to our knowledge, there are no empirical data documenting the reliability and validity of the preference-based measures among healthy populations.

3. *Methodology and results*

The literature review underlined the need for conducting further studies to better evaluate the health-related quality of life (HRQOL) of asymptomatic individuals with dyslipidemia and patients with coronary heart disease (CHD). It suggested that meaningful data could be obtained in a cross-sectional survey if a control group consisting of healthy individuals without dyslipidemia was included and if confounding factors, such as age and comorbidity, were adequately controlled.

We, therefore, conducted a cross-sectional survey. Healthy participants being treated or not for dyslipidemia and patients with CHD evaluated their current health using a nonpreference-based and three preference-based HRQOL instruments.

We defined the methodologic aspects of the preference-based HRQOL measurements according to the study population and the research objectives. These included the choice of the scaling techniques, the measurement strategy, the relevant health dimensions, the source population, and the control of context dependent variables.

There is no consensus on the most appropriate scaling technique to use to measure Preference-based HRQOL for cost-effectiveness analysis. [99] Because the Rating Scale (RS), the Time Trade-off (TTO) and the Standard Gamble (SG) are the most frequently used scaling techniques [99], we decided to use these three.

As described in section 2.3.1.2., the available multiattribute preference scales could be administered rapidly and easily in our study population. However, as reported in Table 2.3.1, most HRQOL aspects relevant to participants with dyslipidemia, namely the well-being, the health perception, the psychological distress and the social activities, are either missing or not described in sufficient detail. For this reason, they would probably not be sufficiently sensitive to evaluate precisely the impact of CHD primary prevention strategies. For this reason, we selected the holistic approach.

Three generic nonpreference-based HRQOL instruments measure the quality of life concepts relevant to the evaluation of healthy individuals with and without dyslipidemia treatment and cardiac patients: the Sickness Impact Profile [120], the Nottingham Health Profile [96] and the SF-36 Health Survey [70,71]. The Sickness Impact Profile is a long questionnaire composed of 136 statements grouped in 12 categories. This questionnaire was judged as inappropriate for the present study because it would be too long to administer (20 to 30 minutes by an interviewer). The SF-36 Health Survey was considered as preferable to the Nottingham Health Profile because its General Health Perception subscale, which represents an overall evaluation of health, has been shown to be sensitive to the detection of low levels of illness in otherwise healthy individuals. [129] Consequently, the SF-36 Health Survey may better discriminate healthy individuals with and without dyslipidemia than the Nottingham Health Profile. The SF-36 Health Survey has also been adapted and translated for use in Canada. [164] For theses reasons, we selected the SF-36 Health Survey for this research project.

All the HRQOL dimensions assessed by the SF-36 Health Survey should be considered by the respondents when they evaluate their *current health* on the preference-based scales. For this reason, the SF-36 Health Survey was administered prior to the preference-based assessment. In addition, during the Preference-based

assessment, the respondents were asked to read a narrative description describing or asking respondents to consider the aspects of quality of life described in the SF-36 Health Survey (see table 3.1.1 (English health state description) and section 7.4 (French health state description)). For their current health, participants were asked to consider how their health limited their physical activities, their ability to work and to do their regular daily activities (taking care of themselves, their family, their home...), as well as their social activities with their family, friends, neighbours or other groups.

Quality weights vary according to the source population. Patients who have had experience with the health state usually report higher Preference-based scores than people without experience. [135,136] As reported previously (section 2.3.1.4), some experts recommend the use a representative sample of the community as the source population to measure quality weights for cost-effectiveness analyses. [3] In our study, we decided to use individuals with experience with the health states because although it is plausible that the diagnosis and treatment of dyslipidemia may decrease the HRQOL of diagnosed individuals, there is little empirical data supporting this hypothesis. It was, therefore, important to test directly this hypothesis among dyslipidemia patients. However, as discussed in section 2.3.1.4, by using patients as the source population, we may have overestimated the quality weight for dyslipidemia and consequently the effectiveness of dyslipidemia treatment as a primary preventive intervention.

As reported in section 2.3.1.5, preference-based measures can be influenced by the format of the health state description, the amount of information provided to the respondents, and the duration and prognosis of the health state evaluated. For these reasons, the various health states descriptions were designed using the same format and amount of detail (Table 3.1.1 and section 7.4). Because CHD affects not only the HRQOL but also life expectancy, both aspects of the disease can be

incorporated in the preference-based assessment by using the appropriate health state duration. In doing so, we may have increased the likelyhood of reproducing the current participants' risk attitude and consequently our ability to value their HRQOL in a more realistic fashion. For this study, the health state duration was based on the participants' age and gender specific life expectancy for healthy respondents with and without dyslipidemia treatment. However, we used a shorter life expectancy for patients with CHD. The health state durations for the various study groups are reported in table 3.2.1.

We also controlled for the duration effect by using the same duration for the health state under evaluation and the lottery outcome in the SG. To control for the duration effect across the scaling techniques, we specified, for each participant, the duration of the health state under evaluation and used the same duration across the different scaling techniques. To control for the prognosis effect, we specified, that each health state would last for a specific duration of time after which they would die without pain.

As described in section 2.3.1.1, Preference-based scaling techniques may be difficult to understand for respondents and may also be difficult to administer for the interviewers. For these reasons, we adapted and pilot tested visual aids to administer the RS, the TTO and the SG. In Appendix III, a description of some of the available visual aids, the results of the pilot study, and a description of the visual aids used in this study can be found.

A review of psychometric properties (section 2.3.2) indicated that TTO and SG have poor discriminant ability. Besides the Beaver Dam Study [78], there was no indication that these techniques could differentiate healthy individuals involved in CHD primary prevention from those who are simply healthy. Consequently, we designed the TTO and the SG instruments to increase their potential to capture small

differences. For the SG measures, this was done by offering participants the choice between their *current health* and lotteries with small probabilities of *immediate death*. The smallest probability of *immediate death* was equal to 1%. In addition, we used a diagram with one hundred faces instead of a probability wheel to represent the probabilities. For the TTO assessment, respondents refusing to give up one year of their life to avoid their *current health* were asked if they would be willing to give up a shorter period of time. The shortest period of time was equal to 3 months.

Three manuscripts to be submitted for publication are presented herein. We report, in the first manuscript (section 3.1), the results of the pilot study comparing the discriminant ability of the chained SG to a nonpreference-based and three Preference-based scaling techniques. In the second manuscript (section 3.2), we compare the psychometric properties of the Preference-based scaling techniques to the SF-36 General Health Perception subscale. Finally, the preference-based and nonpreference-based scores obtained from healthy individuals with and without dyslipidemia and CHD patients are reported in the third manuscript (section 3.3). Appendix I includes an explicit statement of the responsibilities of all co-authors and collaborators.

3.1 Measuring the impact of primary preventive intervention on health-related quality of life: Can we improve the sensitivity of the Standard Gamble?

In this study, healthy participants with and without dyslipidemia may rate their current health as being very high on a conventional Standard Gamble (SG) scale using *perfect health* and *immediate death* as the lottery outcomes. Consequently, the use of the chained SG approach, as described in section 2.3.1.1.1, might be appropriate. However, to our knowledge, this approach has rarely been used [157,165] and is expected to be time-consuming to administer and difficult for the respondents to understand. For these reasons, we decided to conduct a pilot study to compare the discriminant ability of the chained SG to the conventional SG, the RS, the TTO and the SF-36 General Health Perception subscale. The first 104 study participants completed the entire study interview, which included the SF-36 Health Survey, the Rating Scale (RS), the Time Trade-off (TTO) and the conventional SG. In addition, they also completed the chained SG. The results of this pilot study are reported in this section.

Measuring the Impact of Primary Preventive Intervention on Health-Related Quality of Life: Can we Improve the Sensitivity of the Standard Gamble?

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Paper presented at the Medical Decision Making Conference, Houston (Texas) in October 1997.

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3.1.1 Abstract

We compared the ability of nonpreference-based and preference-based health-related quality of life (HRQOL) measures to discriminate healthy participants (n=39) from those on diets for dyslipidemia (n=35) and angina patients (n=30). On the Rating Scale (RS), the Time Trade-off (TTO) and the General Health Perception subscale of the SF-36 Health Survey, participants with dyslipidemia or angina reported lower mean scores than the healthy participants. No differences were detected between these groups on a conventional and a chained Standard Gamble (SG) scales. The distributions of the conventional and the chained SG scores were very skewed with the vast majority of scores being equal or very close to the maximum score. We conclude that the discriminant ability of the conventional and the chained SG is poor when compared to nonpreference-based and non-risky preference-based scaling techniques. This may be partially explained by a strong certainty effect and a misunderstanding of the chained approach by some participants.

KEY WORDS: Dyslipidemia, coronary heart disease prevention, angina, health-related quality of life, health status, SF-36 Health Survey, validity.

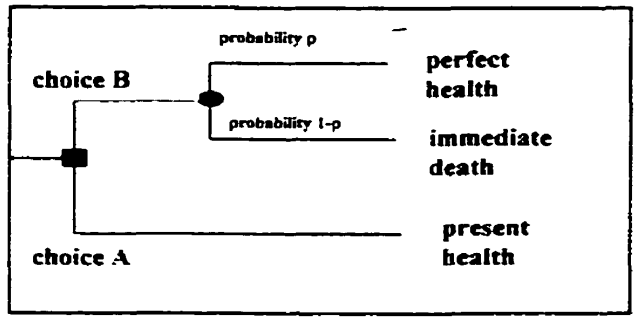
3.1.2 Introduction

The pharmacoeconomic evaluation of primary preventive interventions is highly dependent upon the interventions' immediate effects on the participants' health-related quality of life (HRQOL). [41,42] Although the negative impact of such interventions on HRQOL may be small, the number of quality-adjusted life years (QALYs) lost during those interventions may be large if the interventions last for a very long period of time, are not very effective and affect most participants including those who will never develop the preventable disease. Furthermore, the discounting process amplifies the short term negative impact of preventive interventions on the HRQOL and attenuates the long term positive impact related to the prevention of diseases. Accordingly, accurate evaluation of any negative impact of preventive interventions on the HRQOL of participants may be particularly important.

There is no consensus on the most appropriate preference-based scaling technique to estimate the HRQOL for cost-effectiveness analyses. [3] The Standard Gamble (SG) is often considered as the criterion by which the other preference-based scaling techniques are compared because it is based on solid theoretical foundations. [99,104,105] Measuring the utility associated with a primary prevention program with a conventional SG consists of asking individuals receiving the primary preventive treatment to choose between their *current health* and a risky alternative with specific probabilities of a better outcome (*perfect health*) and a worse outcome (*immediate death*) (Figure 3.1.1). In contrast to other scaling techniques, the SG measures not only the strength of preference for health conditions but also incorporates the respondent's attitude toward risk. Because most medical decisions are risky, the inclusion of the participant's risk attitude in the assessment of preferences is often seen as an advantage and is used to justify the selection of this scaling technique over the non-risky preference-based instruments in cost-effectiveness analyses. [107,166]

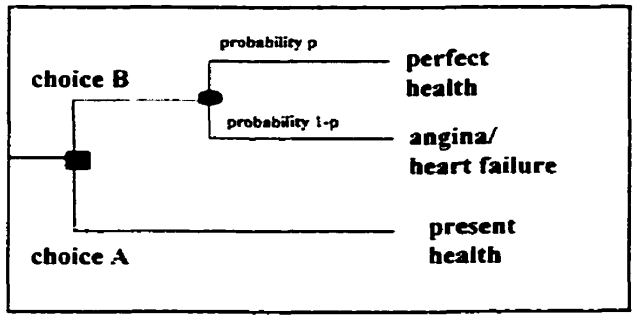
Figure 3.1.1 ● Conventional and chained Standard Gamble

Conventional Standard Gamble:

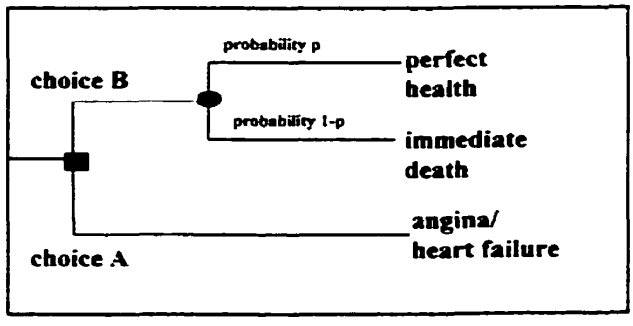


Chained Standard Gamble:

First Step:



Second Step:



Research on the psychology of choice under risk has demonstrated that risk attitude is context dependent. [106,142,153,154] Respondents may be averse or prone to take risk depending on the health state being evaluated. Generally, when the evaluated health condition is considered by the respondents as a gain relative to their aspiration level, risk aversion is the most prevalent attitude and consequently SG scores are expected to be higher than those obtained by non-risky preference-based measures such as the rating scale (RS) and the time trade-off (TTO). [105,113-115]

When the utility of the health state under evaluation is expected to be in the upper 10% of the SG scale, the respondent's risk aversion may be reinforced by a phenomenon called the distortion of probability. This is described as the tendency of respondents to overweight low probabilities and underweight intermediate and high probabilities relative to certainty. [142] This distortion of probabilities may be particularly pronounced when the worse outcome of the lottery is highly significant such as *immediate death*. For this reason, conventional SG is not recommended when the utility of the health state being evaluated is expected to be very high. [107]

We expect that participants involved in primary prevention program will rate the utility of their *current health* in the upper 10% of the SG scale, where the distortion of probability may be important. Consequently, when using a conventional SG, a large proportion of participants may be tempted to choose their *current health* over the lottery alternative even when the probability of *immediate death* is very small. In these circumstances, the measured utility for their *current health* may be very high and close to *perfect health*. This may create a strong ceiling effect and decrease the ability of a conventional SG to discriminate between respondents involved in primary preventive program and those who are not.

The chained SG approach has been proposed as a solution to improve the accuracy of SG for the measurement of health states with high utility. For

participants involved in primary prevention strategies, the chained approach consists of replacing the worse outcome of the lottery by a less severe condition to rescale the utility below the upper 10% of the scale and to attenuate the distortion of probability phenomenon. This is expected to reduce the participant's risk aversion and the ceiling effect. [107] In addition, by replacing the *immediate death* outcome by a less severe condition, this approach offers the possibility of designing a SG assessment which can better approximate the participants' risk attitude when faced with the decision to undertake preventive treatment.

In this study, we used a conventional and a chained SG to assess the *current health* of healthy participants with and without dyslipidemia treatment and patients with angina. We had made the hypothesis that the utility of the current health of healthy participants with and without dyslipidemia treatment measured with a conventional SG may be very high (in the upper 10% of the SG scale) and skewed. In contrast, scores obtained using a chained SG may be lower and less skewed. Consequently, the chained approach may have better discriminant ability than the conventional SG. The utility scores obtained from angina patients are expected to be in the central 80% of the SG scale, where the distortion of probability may not be important. For this reason, the conventional and the chained SG are expected to produce similar results and to have similar ability to discriminate angina and healthy participants. Although the chained SG is recommended to measure high utilities, to our knowledge, it has rarely been used or compared to other scaling techniques. [157,165,167]

The objective of this study was to measure and to compare the HRQOL of healthy participants with and without treatment for dyslipidemia and angina patients with a conventional and a chained SG, the time trade-off (TTO), the rating scale (RS) and the SF-36 General Health Perception (GHP) subscale. The ability of these scaling techniques to discriminate these groups of participants was compared.

3.1.3 Methodology

3.1.3.1 Study population

This study was part of a large cross-sectional, hospital-based survey designed to assess the preference-based HRQOL measures of patients involved in coronary heart disease (CHD) prevention or treatment. Participants were recruited among outpatients attending the cardiology and the internal medicine clinics. We also evaluated accompanying friends and family members of patients undergoing day surgery and hospital workers at one major university hospital in Montréal.

Study participants were recruited between April 1995 and October 1995. Men and women, between 30 to 74 years of age, were classified into one of three study groups: Healthy, Dyslipidemia and Angina. Participants were classified in the Angina group if a diagnosis of angina was reported on a hospital discharge summary or on a clinic note, and had been present for at least six months and if a prescription for nitroglycerin was documented. Participants without a heart problem were assigned to the Dyslipidemia group if they reported following, for at least one month, a prescribed diet to lower their serum cholesterol and if they were not taking lipid lowering agents. Participants without heart problems and dyslipidemia were included in the Healthy group.

Specific eligibility criteria were used to control for comorbidity. We excluded pregnant women, all subjects with a temporary illness such as a cold, and Healthy and Dyslipidemia subjects currently trying to quit smoking. In addition, subjects were asked to report any other health problem confirmed by a physician. Subjects in the Dyslipidemia or the Healthy group who reported symptoms from a comorbid condition in the past four weeks were not eligible for enrollment. We also asked angina patients which health problem had most affected their HRQOL in the

past four weeks. They were eligible for participation only if they answered *none* (meaning they had not been bothered by any health problem), *angina* or *a CHD risk factor* (hypertension or dyslipidemia).

3.1.3.2 Outcome measures

During the interviews, various questionnaires were administered. Participants first completed the SF-36 Health Survey. Thereafter, their medical history was reviewed in a face-to-face interview, and the preference-based HRQOL assessments were administered by one of four trained interviewers.

The SF-36 Health Survey is a generic HRQOL questionnaire describing eight different aspects of the HRQOL. [70,71,131] Among those, the SF-36 GHP subscale represents an overall evaluation of health, including current health, health outlook, and resistance to illness. [168] This subscale is the most closely related to the preference-based assessment and was used as a comparative scaling technique.

The preference-based HRQOL assessment included the RS, the TTO, the conventional and the chained SG. The RS was administered first and the order of presentation of the TTO and the SG was randomized. For each scaling technique, participants were first asked to rate a hypothetical health state, *blindness*, to familiarize themselves with the assessment.

Before the preference-based assessments, participants read a narrative description, written in the second person, of five health states: *perfect health*, *immediate death*, *blindness*, their *present health* and either *angina* for participants in the Healthy and the Dyslipidemia groups or *heart failure* for participants in the Angina group (Table 3.1.1). Participants were told that each health state would last

Table 3.1.1 • Health state descriptions for preference-based assessments

BLINDNESS

Last year you became blind after being exposed to a very rare virus. You will remain blind for the rest of your life. You are otherwise perfectly healthy. You do not need to take any medication or follow a diet. You have to see your physician once a year for a check-up.

You cannot do activities that require the ability to see such as skiing, playing hockey or gardening. At work, you are unable to do jobs that require the ability to see. You need help to do things like shopping for groceries. Your social activities with family, friends, neighbours or other groups are limited to those that do not require the ability to see.

YOUR PRESENT HEALTH

Your health will remain as you have felt for the **LAST 4 WEEKS**. Take into account any **medical problems, symptoms** or **discomfort** that you may have had. Consider also any **medications, diet, visits** to doctor, or other health professional, and **medical tests** you may have had.

Assess how your health has limited your physical activities, your ability to work and to do your regular daily activities (taking care of yourself, your family, your home...), as well as your social activities with your family, friends, neighbours or other groups.

PERFECT HEALTH

Your health is as good as you can imagine. You always feel well and full of energy. You never have any discomfort. You do not need to take any medication or follow a diet. You have to see your physician once a year for a check-up.

You can do any type of physical activity. At work, you are not limited in any way by your health. Your health does not limit your social activities with your family, friends, neighbours or other groups.

IMMEDIATE DEATH

You will die within the next week. Your death will occur suddenly and you will not suffer any pain.

Table 3.1.1 (contd) ● Health state descriptions for preference-based assessments

ANGINA

About once a month you suffer from chest pain, accompanied by palpitations and difficulty breathing. When you have these symptoms, you have to place a nitroglycerine tablet under your tongue and rest. After a few minutes your chest discomfort disappears. You take no other medication. You have to follow a special diet that is low in fat and cholesterol. You have to see your physician every 6 months for a check-up and tests.

You cannot do vigourous activities such as running or lifting heavy objects. At work, you are unable to do jobs that are physically demanding. Your social activities with family, friends, neighbours or other groups are not limited by your health.

HEART FAILURE

You feel weak most of the time. You are short of breath. You cough very often and feel congested. Your ankles are very swollen. You need to rest in bed for 2 hours every afternoon. You take 4 different kinks of medication every day and you have to follow a very strict, low-salt diet. You have to see youy physician at least once every 3 months for tests and a check-up. Once a year you may need to be hospitalized because you have difficulty breathing and your medication needs to be adjusted.

You can walk slowly but you cannot run or do any intense physical exercise. You are not able to work. It is very difficult for you to do things like shopping for groceries or gardening. Your social activities with family, friends, neighbours or other groups are limited by your lack of vitality.

for a specific duration of time after which they would die without pain. The duration of each health state was based on the Canadian age and gender specific life expectancy for the Healthy and the Dyslipidemia groups. [169] A shorter duration was used for Angina participants. Health state descriptions and duration were kept constant across all scaling techniques.

For the RS, we used a 30 cm feeling thermometer with 100 graduations.[107] *Perfect health* and *immediate death* were placed by the interviewer at the top (score=100) and bottom (score=0) of the scale, respectively. The participants were asked where they would place their *present health* on the thermometer. The RS score was the distance between the location of their *present health* and *immediate death.* Health states considered to be worse than death were given a score of zero.

For the TTO, participants were given the choice between living in *perfect health* for time t or living with their *present health* for time x, where $t < x$. Time t was varied in a three step ping-pong approach until the participant became indifferent between the two choices. In the first step, time t varied across the maximum ($t = x$) and the minimum (t = *immediate death*) duration to identify the indifference point area within a five year period. In the second step, time t was varied within the indifference point area with a precision of one year. Those refusing to give up one year of their life underwent a third step where they were asked if they would be willing to give up 3, 6 or 9 months of their life. The value of the participant's *present health* was equal to $[(t/x)100]$ at the indifference point. To facilitate the assessment, we used a visual aid similar to the one developed by the McMaster group.[107]

The SG assessment was administered using conventional and chained procedures (Figure 3.1.1). The conventional SG was always administered first and consisted of offering participants the choice between their *present health* (choice A)

and a lottery (choice B) with a probability *p* of *perfect health*, and a probability *(1-p)* of *immediate death*. The probability *p* was changed, using a two stage ping-pong approach, until the participant was indifferent to the two choices. At the indifference point, the utility of the participant's *present health* (*u(present health)*) was equal to:

$$u(\text{present health}) = [\ p\ u(\text{perfect health})\ ] + [\ (1-p)\ u(\text{immediate death})\ ]$$

We assumed the utility of *perfect health* and *immediate death* to be equal to 100 and 0, respectively, so that the utility of the participant's *present health* was equal to (100 *p*), where *p* was the probability of *perfect health* at the indifference point.

The chained SG consisted of a two step procedure (Figure 3.1.1). In the first step, participants were asked to choose between their *present health* (choice A) and a lottery (choice B) with a probability p_1 of *perfect health* and a probability $(1 - p_1)$ of either *angina* or *heart failure*. We used *angina* for the participants in the Healthy and the Dyslipidemia groups and *heart failure* for the participants in the Angina group. The probability p_1 was changed, using a two stage ping-pong approach, until the participants were indifferent to the two choices. For the participants in the Healthy and the Dyslipidemia groups, the utility of the participant's *present health* was equal to:

$$u(\text{present health}) = [\ p_1\ u(\text{perfect health})\ ] + [\ (1 - p_1)\ u\ (\text{angina})\ ]$$

and for the participants in the Angina group it was equal to:

$$u(\text{present health}) = [\ p_1\ u(\text{perfect health})\ ] + [\ (1 - p_1)\ u\ (\text{heart failure})\ ]$$

The second step of the chained SG consisted of assessing the utility of the hypothetical health state, *angina* or *heart failure*, using a lottery with extreme

outcomes: *perfect health* and *immediate death*. Again, we assumed the utility of *perfect health* and *immediate death* was equal to 100 and 0, respectively, and the utility of the health state under evaluation was defined to be equal to:

$$u(\textit{angina or heart failure}) = 100\ p_2$$

By combining the results of the first and the second steps, we estimated the utility of the participant's *present health*:

$$u(\textit{present health}) = 100\,p_1 + [(1 - p_1)\ 100\,p_2]$$

All SG assessments were administered by first varying the probability of the worse outcome of the lottery across the lower (0%) and the upper (100%) level of probability with a precision of 10% to identify the indifference point area. Then, the probability was varied within the specific indifference area with a precision of 1%. The lowest probability of the worse outcome was equal to 1%. A visual aid was used to facilitate the understanding of probability where each 1% risk of the worse outcome of the lottery was represented by shading one of one hundred faces.[110]

3.1.3.3 Statistical analysis

We computed the difference between the mean score of the Healthy group and either the Dyslipidemia or the Angina group and the 95% confidence interval (CI) around the mean difference. We obtained almost identical results when the 95% CIs were computed assuming equal and unequal variances. We reported the results assuming unequal variances.

3.1.4 Results

We performed a total of 104 interviews with eligible participants. We reported in Table 3.1.2 the sociodemograhic profile of the participants. Their mean age was 54 years, men and women were equally represented and they reported various levels of education, occupation, marital status, language and income. The face-to-face interviews lasted on average 42 minutes (± sd = 12 min). All participants completed the interview. We rejected eleven (11%) TTO assessments because errors were retrospectively detected in the sequence of the presentation of the choices. Two SF-36 GHP subscale scores were missing because of incomplete information. Scores from all other preference-based assessments were obtained from all participants.

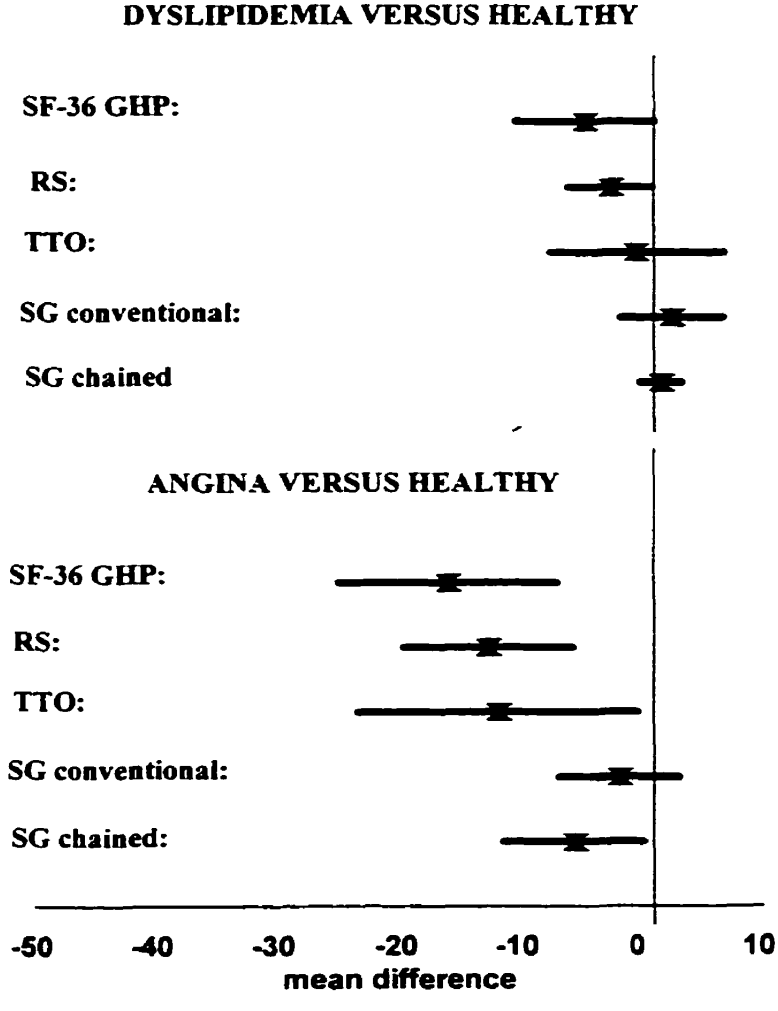
Participants in the Dyslipidemia group reported, on average, lower scores than those in the Healthy group on the RS, the TTO and the SF-36 GHP subscale (Figure 3.1.2). However, the 95% CI around the mean TTO difference was large and included zero. There were no differences between these two groups on the conventional and the chained SG. On all scaling techniques, participants in the Angina group reported lower mean scores than the participants in the Healthy group. However, the smallest difference was observed with the conventional SG and the 95% CI around the mean difference included zero. The use of the chained approach slightly increased the mean difference between the Healthy and the Angina groups. However, as reported in Table 3.1.3, the median chained SG scores of the Healthy and the Angina groups were almost identical (99.8 versus 99.0) suggesting that the observed mean difference between these two groups was mainly influenced by marginal observations. These results demonstrate that, in contrast to the SF-36 GHP subscale and the non-risky preference-based techniques, the conventional and the chained SG poorly discriminated Healthy participants from those in the Dyslipidemia and the Angina groups.

Table 3.1.2 ● Characteristics of participants

	n (%)*
Sample size	104 (100)
Healthy	39 (38)
Diet	35 (34)
Angina	30 (29)
Age (mean ± sd)	54 ± 12
Gender (male)	48 (46)
Education:	
Secondary school incomplete	19 (19)
Secondary school	23 (23)
C.E.G.E.P. or equivalent	33 (33)
University	26 (26)
Occupation:	
Employed	52 (52)
Unemployed	3 (3)
Retired	29 (29)
Keeping house or student	16 (16)
Current marital status:	
Single	12 (12)
Married	75 (73)
Divorced/ Separated	11 (11)
Widowed	5 (5)
Current Language:	
French	27 (26)
English	64 (62)
Other	12 (12)
Annual household income:	
< $20,000.00	9 (10)
$20,000.00 and < $40,000.00	21 (24)
$40,000.00 and < $60,000.00	26 (30)
> $60,000.00	30 (35)

* Percentages may not sum to 100% due to rounding

Figure 3.1.2 ● Comparison of the discriminant ability of nonpreference-based and preference-based health-related quality of life meaures



Mean difference (95% confidence interval) between scores from healthy participants with dyslipidemia or patients with angina and healthy participants measured on the SF-36 General Health Perception (SF-36 GHP) subscale, the Rating Scale (RS), the Time Trade-Off (TTO) and the conventional and chained Standard Gamble (SG) scales.

Table 3.1.3 ● Mean (median) preference-based and SF-36 General Health Perception subscale scores by study group

	Healthy (n=39)	**Diet (n=35)**	**Angina (n=30)**
SF-36 General Health Perception	83.5 (85.0)	76.7 (75.0)	67.5 (70.0)
Rating Scale	93.7 (95.0)	89.0 (90.0)	81.0 (82.5)
Time Trade-off	92.1 (99.5)	89.6 (95.6)	80.3 (85.0)
Standard Gamble conventional	94.2 (98.5)	94.7 (100.0)	92.4 (98.3)
Standard Gamble chained	98.3 (99.8)	97.9 (100.0)	92.8 (99.0)
First step[¶]:	95.3 (99.0)	90.6 (100.0)	82.6 (93.5)
Second step:	72.8 (79.5)[§]	77.1 (79.5)[§]	51.8 (54.3)[‡]

¶ Probability of *Perfect Health* at the indifference point.

§ Assessment of the hypothetical health state "*Angina*" against a gamble with extreme outcomes (*Perfect Health* and *Immediate Death*)

‡ Assessment of the hypothetical health state "*Heart Failure*" against a gamble with extreme outcomes (*Perfect Health* and *Immediate Death*)

Table 3.1.3 ● Mean (median) preference-based and SF-36 General Health Perception subscale scores by study group

	Healthy (n=39)	**Diet (n=35)**	**Angina (n=30)**
SF-36 General Health Perception	83.5 (85.0)	76.7 (75.0)	67.5 (70.0)
Rating Scale	93.7 (95.0)	89.0 (90.0)	81.0 (82.5)
Time Trade-off	92.1 (99.5)	89.6 (95.6)	80.3 (85.0)
Standard Gamble conventional	94.2 (98.5)	94.7 (100.0)	92.4 (98.3)
Standard Gamble chained	98.3 (99.8)	97.9 (100.0)	92.8 (99.0)
First step[¶]:	95.3 (99.0)	90.6 (100.0)	82.6 (93.5)
Second step:	72.8 (79.5)[§]	77.1 (79.5)[§]	51.8 (54.3)[‡]

¶ Probability of *Perfect Health* at the indifference point.

§ Assessment of the hypothetical health state "*Angina*" against a gamble with extreme outcomes (*Perfect Health* and *Immediate Death*)

‡ Assessment of the hypothetical health state "*Heart Failure*" against a gamble with extreme outcomes (*Perfect Health* and *Immediate Death*)

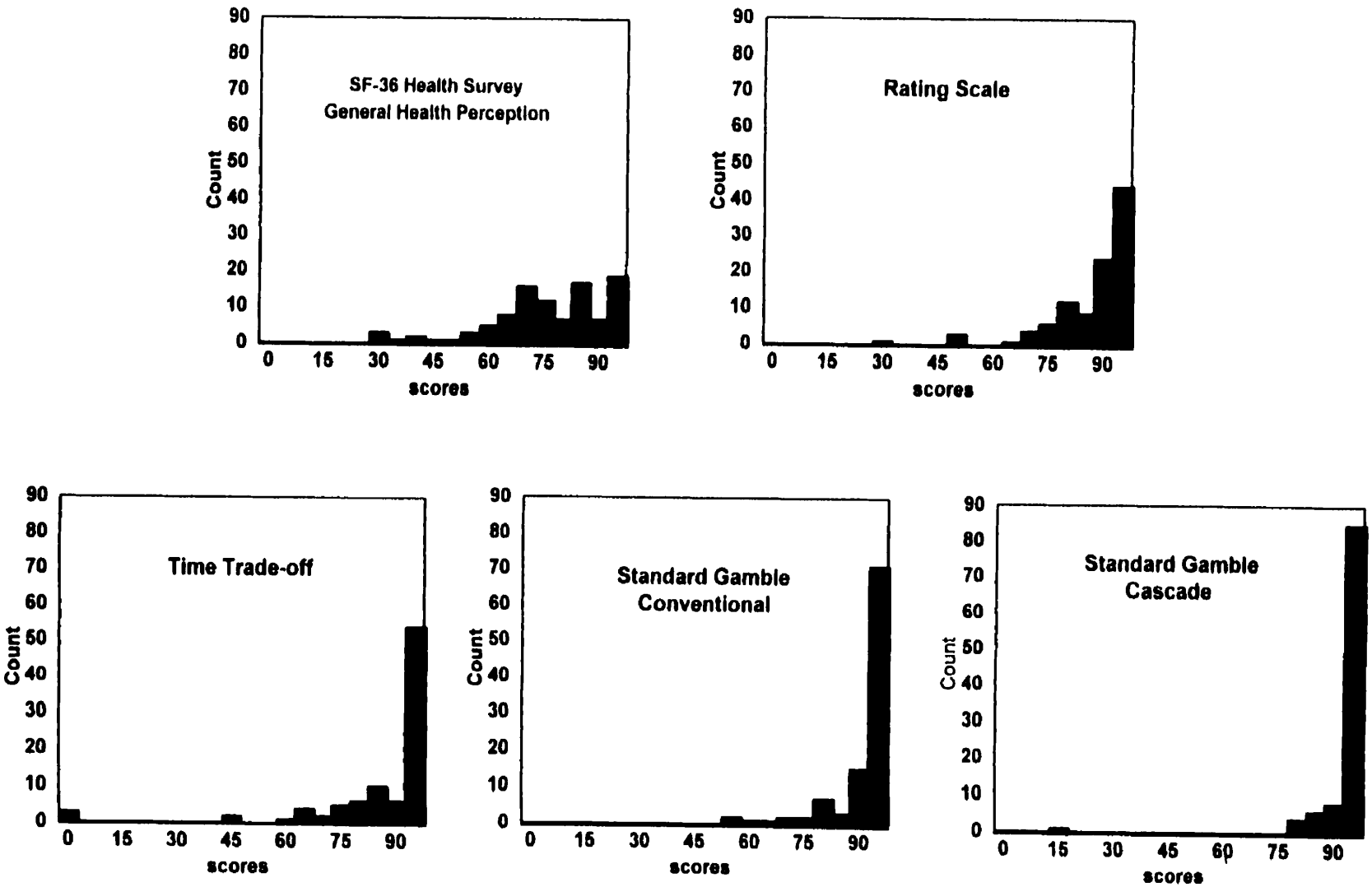
As seen in Figure 3.1.3, a strong ceiling effect was observed on the conventional and the chained SG. The distribution of the chained SG scores was more skewed than the distributions of the conventional SG scores, the non-risky techniques and the SF-36 GHP subscale. We had hypothesised that the use of the chained approach would attenuate the participant's risk aversion when compared to the conventional SG, and would reduce the skewness of the distribution of scores. These results indicate that the chained approach did not attenuate the participant's risk-averse attitude.

We compared the gambling strategy of each participant in the conventional SG and the first step of the chained approach. We had made the hypothesis that, by using a less severe lottery outcome, we would increase the willingness of participants to choose the lottery alternative. We observed that the proportion of participants who did not change their gambling strategy in the conventional and the chained SG was high and equal to 33% for the Angina group and 46% for the Healthy and for the Dyslipidemia groups. In addition, a total of 23% of the participants were less willing to gamble when the worse outcome of the lottery was less severe. This indicates that the majority of the participants did not change their gambling strategy according to our initial prediction.

3.1.5 Discussion

Healthy, Dyslipidemia and Angina participants rated their current health on a conventional and a chained SG, non-risky preference-based scales and the SF-36 GHP subscale. The mean differences between the Healthy and either the Dyslipidemia or the Angina participants on the RS, TTO and the SF-36 GHP subscale suggest that participants in the Dyslipidemia and the Angina groups did not perceive themselves as being as healthy as the participants in the Healthy group. The

Figure 3.1.3 • Histograms of the health-related quality of life measures for the participant's current health (n=104)



conventional SG detected no difference between the Healthy and the Dyslipidemia groups and a small and non significant difference between the Healthy and the Angina groups. The use of the chained approach did not improve the sensitivity of the SG to detect a difference between the Healthy and either the Dyslipidemia or the Angina groups.

The utility associated with dyslipidemia was expected to be very high and probably in the upper 10% of the scale (score > 90). For this reason, we expected the conventional SG to be insensitive to the measurement of such a high utility because of the distortion of probabilities phenomenon. The utility of Angina was reported by others to be below the upper 10% of the scale (score ~ 80). [36,83,147,151,170-172]. Consequently, the use of a conventional SG was not expected to be problematic. Surprisingly, the conventional and the chained SG were both insensitive to the measurement of the utility of angina and suggests that the discriminant ability of SG technique is generally poor.

Because risk attitude is context dependent, we designed the chained SG to reproduce more realistically the participants' attitude when faced with the decision to treat dyslipidemia. Because untreated dyslipidemic subjects have a higher risk of developing a CHD, we replaced the worse outcome of the lottery *immediate death* by *angina*. Contrary to our expectation, changing the *immediate death* outcome by a less severe condition did not increase the willingness of the majority of the participants to gamble. This may be explained by a persistent certainty effect and a misunderstanding of the assessment.

It has been shown that people underweight outcomes that are merely probable in comparison with outcomes that are obtained with certainty. [173] Consequently, most people will choose the sure outcome unless the advantages of the risky choice are considered as substantial. This certainty effect may be so strong that modifying the

severity of the lottery outcome was insufficient to decrease the participant's risk aversion. In real life situations, for people with dyslipidemia, this certainty effect does not exist; treating dyslipidemia does not abolish the risk of having a heart problem but simply reduces it. Techniques such as the SG paired-gamble, which consist of replacing the sure outcome by an other lottery alternative, have been designed to avoid the certainty effect and may be more suitable for the assessment of CHD primary prevention. [166,174]

In addition, although all participants, except four, rated the less severe lottery outcome (*angina or heart* failure) as being better than *immediate death*, 22% of the participants were less willing to gamble when the worse outcome of the SG lottery was less severe. These choices were inconsistent and may reflect the misunderstanding of the chained approach by a substantial proportion of participants.

We conclude that the conventional and the chained SG approached can poorly discriminate groups of participants involved in CHD prevention or treatment. Nonpreference-based and non-risky preference-based scaling techniques appear to be more sensitive and may be the most appropriate scaling techniques to provide quality weights for cost-effectiveness evaluation of CHD prevention strategies.

3.2 Comparing the psychometric properties of preference-based and nonpreference-based health-related quality of life measures in coronary heart disease prevention and treatment

The results of the pilot study performed among the first 104 study participants demonstrated that the chained standard gamble (SG) did not have better discriminant ability than the conventional SG. They also suggested that a substantial proportion of participants missunderstood the chained approach and consequently provided inconsistent answers. For these reasons, we decided to discontinue the use of the chained SG.

We completed a total of 878 interviews with eligible participants, which included the first 104 interviews reported in the previous section . Using the entire study sample, we performed two analyses. The first analysis consisted of comparing the psychometric properties of preference-based and nonpreference-based health-related quality of life (HRQOL) measures. This analysis is reported in section 3.2.

The objective of this analysis was to document the psychometric properties of preference-based measures among healthy populations. Although a few studies have evaluated the psychometric properties of preference-based measures in coronary heart disease population (section 3.2.2), there was, to our knowledge, no empirical data evaluating the psychometric properties of the preference-based measures among healthy populations involved in primary prevention. In addition, comparing the psychometric properties of the preference-based measures can be helpful to identify the most appropriate scaling technique for future QALY analyses of CHD prevention. As described in section 2.3.1.1.4, the choice of the scaling technique is an important methodological issue because preference-based measures are known to vary according to the scaling techniques and consequently the choice of the scaling technique may also influence the cost-effectiveness of dyslipidemia treatment in primary prevention.

Comparing the Psychometric Properties of Preference-Based and Nonpreference-based Health-Related Quality of Life Measures in Coronary Heart Disease Prevention and Treatment

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3.2.1 Abstract

A large survey (n=878) was conducted to compare the psychometric properties of three preference-based and one nonpreference-based health-related quality of life (HRQOL) measures in a population of healthy subjects with and without treatment for dyslipidemia and patients with coronary heart disease (CHD). The reliability of all scaling techniques was similar. Compared to the Time Trade-off (TTO) and the Standard Gamble (SG), the Rating Scale (RS) was the most highly correlated with the different aspects of the HRQOL as measured by the SF-36 Health Survey. In contrast to the SF-36 GHP subscale and the RS, the TTO and the SG had difficulty discriminating CHD patients with various severities of physical disability and were unable to differentiate participants reporting different numbers of health problems. These results confirm findings reported by others suggesting that the TTO and SG scaling techniques have poor discriminant ability. They may not be sufficiently sensitive to measure the impact of primary coronary heart disease prevention strategies on the HRQOL of the participants.

KEY WORDS: Preference-based measures, reliability, validity, cost-effectiveness analysis, coronary heart disease prevention, coronary heart disease, dyslipidemia.

3.2.2 Introduction

Health-related quality of life (HRQOL) is now recognized to be a major end-point in the evaluation of health care programs.[175-177] Moreover, this aspect of medical evaluation is increasingly integrated into cost-effectiveness analysis where the benefits are expressed as the number of quality-adjusted life years (QALYs) gained. In theory, these models are expected to be particularly powerful for the evaluation of primary preventive interventions because they take into account the impact of the intervention on the mortality and the morbidity of participants including the influence of the intervention itself on the HRQOL. In simulation models, the cost-effectiveness of detecting and treating dyslipidemia to prevent coronary heart disease (CHD) has been shown to be extremely sensitive to the potential negative impact of dyslipidemia on the HRQOL and may undermine the beneficial impacts of aggressive interventions. [41,42] However, in practice these models will only be useful if we can measure precisely and accurately the impact of preventive interventions on the HRQOL.

HRQOL can be assessed by using either a nonpreference-based or a preference-based approach.[100] The nonpreference-based approach consists of describing various aspects of the HRQOL, for example, by asking questions about the presence, severity and frequency of symptoms or the ability to perform daily tasks. The SF-36 Health Survey is an example of a nonpreference-based HRQOL questionnaire. It has been validated in general [129] and in various patient populations [71,130-132], and was used to assess CHD treatment[133] and prevention[78] . The General Health Perception (GHP) subscale, representing an overall evaluation of health, has been shown to be sensitive to the detection of low levels of illness in otherwise healthy individuals. [129] However, this subscale does not provide interval scale data [101] and is not preference weighted. For these reasons, it is not suitable for cost-effectiveness analysis. [3]

The preference-based approach consists of asking the respondents to make a judgement about the value of life within a given health state.[102] It measures the strength of preference for health conditions. Preference-based scores are currently used in cost-effectiveness analysis and are particularly useful in allowing allocation of resources in accordance with a population's judgment about a range of health states. The most commonly used preference-based instruments are the rating scale (RS), the time trade-off (TTO) and the standard gamble (SG). A few studies have evaluated the psychometric properties of the preference-based measures in a CHD population.[126,147,151,157,178] Moreover, there are, to our knowledge, no empirical data evaluating the psychometric properties of the preference-based measures in healthy populations involved in primary prevention.

Our study objective was to assess, in a large survey of healthy individuals with and without dyslipidemia, and CHD patients, the psychometric properties of the RS, TTO and SG scaling techniques and to compare them to a nonpreference-based measure, the SF-36 GHP subscale.

3.2.3 Methodology

3.2.3.1 Study population

Between April 1995 and June 1996, we recruited and interviewed outpatients attending cardiology, internal medicine, lipid and hypertension clinics in two University teaching hospitals: The Montreal General Hospital and The Royal Victoria Hospital. Accompanying friends and family members of patients undergoing day surgery, as well as hospital workers from The Montreal General Hospital were also interviewed to provide data on "healthy" individuals. Approval from the Institutional Review Board was obtained from each institution and

participants signed a written informed consent prior to the interview.

Subjects were classified into one of three study groups: 1) Healthy, 2) Dyslipidemia and 3) CHD. The Healthy group consisted of subjects who were not receiving treatment for dyslipidemia. The Dyslipidemia group was composed of healthy subjects undergoing treatment for dyslipidemia through lifestyle changes with or without pharmacotherapy. Subjects included in the CHD group had been diagnosed with angina, myocardial infarction (MI) or/and congestive heart failure (CHF).

To classify each participant into one of the three study groups, we reviewed the hospital charts of all patients attending the hospital clinics and asked each of them to complete a short eligibility questionnaire. Subjects were classified as having a CHD if a diagnosis of angina, MI or CHF was reported on a hospital discharge summary or on a clinic note. The presence of a prescription for nitroglycerin or a loop diuretic was also necessary to document angina or CHF, respectively. Subjects without CHD were classified in the Dyslipidemia group if they reported following a prudent diet prescribed by a physician or taking medication for dyslipidemia. Subjects without CHD and dyslipidemia were classified in the Healthy group.

We included men and women between 30 and 74 years of age who understood French or English. CHD patients needed to be diagnosed at least six months previously and participants with dyslipidemia needed to be on treatment at least one month. In order to control for the effect of comorbid conditions, we excluded pregnant women, all subjects with a temporary illness such as a cold, and Healthy and Dyslipidemia subjects currently trying to quit smoking. In addition, subjects were asked to report any other health problem confirmed by a physician. Subjects in the Dyslipidemia or in the Healthy group who reported symptoms from a comorbid condition in the past four weeks were not eligible for enrollment. We

also asked cardiac patients which health problem had most affected their HRQOL in the past four weeks. They were eligible for participation only if they answered "none" (meaning they had not been bothered by any health problem), a heart disease, or a CHD risk factor such as hypertension or dyslipidemia.

3.2.3.2 Outcome measures

Eligible participants then completed a series of questionnaires. Questionnaires were administered in the following sequence: 1. SF-36 Health Survey; 2. Specific Activity Scale (SAS), for CHD participants only; 3. Medical history; 4. Preference-based HRQOL assessments; 5. Sociodemographic information. Items 2-4 were administered in a face-to-face interview by four trained interviewers and items 1 and 5 were self-administered.

The preference-based assessment of the HRQOL for each patient was obtained using the RS, the TTO, and the SG. The RS was administered first and the order of presentation of the TTO and the SG was randomized. For each technique, participants were first asked to rate a hypothetical health state, blindness, to familiarize themselves with the assessment. Participants read a narrative description, written in the second person, of four health states: *perfect health*, *immediate death*, *blindness* and *present health*. They were told that each health state would last for a specific number of years after which they would die without pain. The duration of each health state was determined based on gender, age and the participant's health condition. For participants in the Healthy and the Dyslipidemia groups, the duration was based on the Canadian age and gender specific mean life expectancy.[169] A shorter duration was used for CHD participants and varied according to the severity of CHD (Table 3.2.1). For those having more than one cardiac condition, the shortest length of time was used. For example, a fifty years old men with angina and CHF

Table 3.2.1 • Health state duration according to age, gender and health status of participants

Age		Health state duration (year)			
Men	Women	Healthy	MI	Angina	CHF
30-34	30-40	50	30	30	20
35-44	41-52	40	20	20	15
45-56	53-63	30	15	15	10
57-63	64-69	20	10	10	5
64-74	70-74	15	10	10	5

would be told to imagine that the health state under evaluation would last until the end of his life, which means for the next 10 years. All preference-based measures varied from 0 to 100, where 100 represented the best possible health state.

RS was administered using a 30 cm feeling thermometer with 100 graduations.[107] The health conditions *perfect health* and *immediate death* were placed by the interviewer at the top (score=100) and the bottom (score=0) of the scale, respectively. Participants were asked to place *blindness* and their *present health* on the thermometer. The value of each health state was determined by the distance between *immediate death* and the health state of interest. Health states considered to be worse than death were given a score of zero. When all the four health states were placed on the thermometer, the participants were allowed to change the location of *blindness* and *present health* if they wished. In addition, we asked them to indicate which health state would be the worst for them: their *present health* or *blindness*.

For the SG, the participants were offered two choices: the health state under evaluation for a specific duration after which they would die without pain (choice A) or a lottery with a probability p of *perfect health* with the same duration after which they would die without pain, and a probability $(1-p)$ of an *immediate death* without pain (choice B). The probability p was changed until the participants were indifferent between the two choices. At the indifference point, the utility of the health state under evaluation was equal to p. We used a visual aid to facilitate the understanding of probabilities where each 1% probability of an *immediate death* was represented by shading one of one hundred (100) faces. [110] The probability p was changed according to a two step ping-pong approach. In the first step, the probability p varied across the lower (0%) and the upper (100%) levels of probabilities with a precision of 10% to identify the indifference point area. In the second step, the probability p was varied within the specific indifference area with a precision of 1%. The smallest

possible risk of *immediate death* with choice B was 1%.

For the TTO, the participants were given the choice between living in *perfect health* for time *t* or living with the health state under evaluation for time *x*, where *t* < x, after which they would die without pain. Time *t* was varied until the participant became indifferent between the two choices. At the indifference point, the value of the health state under evaluation was equal to [(*t*/*x*) x 100]. We used a visual aid similar to the one developed by McMaster group.[107] During the assessment, time *t* was varied in a three step ping-pong approach until the subject became indifferent between the two choices. In the first step, the indifference point area was identified within a five year period. In the second step, time *t* was varied, within the indifference point area, with a precision of one year. Those refusing to give up one year of their life underwent a third step in which they were asked if they would be willing to give up 3, 6 or 9 months of their life.

Participants completed the French or English version of the SF-36 Health Survey evaluating their HRQOL in the past month. It consists of 36 items evaluating eight domains of the HRQOL: general health perception (GHP), physical functioning, role limitations due to physical health problems, role limitations due to emotional problems, social functioning, bodily pain, vitality, and general mental health.[70] For each of the eight subscales, scores vary from 0 to 100, where 100 represents the best possible health. The GHP subscale consists of five items representing an overall evaluation of health, including current health, health outlook, and resistance to illness.[168] Responses from each of those five items are coded from one to five. A simple algebraic sum of responses is computed and transformed into a 0 to 100 scale.

The Specific Activity Scale (SAS) was used to classify cardiac participants by their degree of cardiovascular disability. It is based on the metabolic equivalents of oxygen consumption required for activities a patient actually performs.[179] In a

structured interview, participants were asked if they could perform specific activities and were classified into one of four classes. Participants in class I could perform activities requiring ≥ 7 METS (metabolic equivalents required for jogging or playing basketball) while those in class IV could only complete activities requiring < 2 METS (dressing) and had symptoms at rest. [180] This classification has been shown to be more reproducible and to be more predictive of true exercise tolerance than the New York Heart Association classification.[180] We adapted a European French translation of the SAS (see section 7.1).[181]

Twenty percent of participants were randomized to repeat the interview after three to six weeks to assess the reliability of scores when the scaling techniques were administered to the same participants under the same conditions at two different time periods.

3.2.3.3 Statistical analysis

The reliability of the preference-based measures over time was compared to the SF-36 subscale scores. It was evaluated by computing the mean, the median, and the 95% confidence intervals around the mean and the median at the test and the retest. Because similar results were obtained using the mean and the median, we reported herein only the median scores. At the individual level, we determined the reliability of each measure over time by computing the absolute difference between the test and the retest scores for each participant and by calculating the mean and standard deviation of the absolute difference for each preference-based scaling technique and the SF-36 subscales.

To assess their convergent validity, we computed the Spearman rank correlation between the different preference-based measures as well as between the

SF-36 subscale scores and each preference-based measure. We compared the ability of each preference-based scaling technique and the SF-36 GHP subscale to discriminate cardiac patients with different severities of physical disability and participants with different numbers of health problems. We expected that the average preference-based scores would decrease as the severity of physical disability and number of health problems increased. We combined participants in SAS class III and IV because only one participant was classified into class IV. We also categorized all participants according to their number of health problems. For each stratum we computed the mean, the median, the 10th and the 90th percentiles and the 95% confidence intervals around the mean and the median scores for each of these groups. Again, because we obtained nearly identical results using the mean and the median score, we only reported the median scores.

3.2.4 Results

3.2.4.1 Feasibility

We performed a total of 878 interviews with eligible participants. The sociodemograhic profiles of the participants are reported in Table 3.2.2. Their mean age was 55 years, men and women were almost equally represented, and they reported various levels of education, occupation, marital status, language and income. The face-to-face interviews lasted on average 41 minutes (± sd:13 min). This time was primarily used to administer the preference-based scaling techniques. Sixty-one participants (7%) did not complete all the preference-based measures because they had insufficient time (41), refused to continue (17) or had problems with comprehension (3). A retrospective review of the interviews detected errors in forty-five interviews (5%): the duration of health state did not match with the duration specified by the protocol (17), the sequence of the presentation of choices did not

Table 3.2.2 ● Characteristics of participants

	n (%)*
Sample size	878 (100)
Healthy	307 (35)
Dyslipidemia	251 (29)
Coronary Heart Disease	320 (36)
Age (mean ± sd)	55 ± 12
Gender (male)	482 (55)
Education:	
Secondary school incomplete	170 (20)
Secondary school	211 (24)
C.E.G.E.P. or equivalent	227 (26)
University	258 (30)
Occupation:	
Employed	470 (54)
Unemployed	41 (5)
Retired	289 (33)
Keeping house or student	67 (8)
Current marital status:	
Single	79 (9)
Married	642 (74)
Divorced/ Separated	93 (11)
Widowed	54 (6)
Current Language:	
French	246 (28)
English	462 (53)
Other	163 (19)
Annual household income:	
< $20,000.00	111 (14)
$20,000.00 and < $40,000.00	244 (31)
$40,000.00 and < $60,000.00	173 (22)
> $60,000.00	251 (32)

* Percentages may not sum to 100% due to rounding

correspond with our protocol for the TTO (20) and the SG (2), and six RS measures were not recorded. Ninety-five percent (95%) of the participants identified *blindness* as being worse than their *present health*. For each participant, we compared his or her ranking to the ranking provided by the preference-based scaling techniques. The participant's ranking was consistent with the results of the RS, TTO and SG 99%, 96% and 98% of the time, respectively. These results demonstrate that, although preference-based assessments are feasible in this population, they may be difficult for a few participants and are lengthy to administer for most.

3.2.4.2 Reliability

Among 210 retest interviews scheduled, only 94 (45%) were actually completed as 75 (36%) participants refused to come back for the second interview and 41 (20%) missed the second interview for various reasons. One retest interview was done more than six weeks after the first interview and was excluded from this analysis. The numbers of participants who repeated the second interview were equally distributed across the study groups (Healthy: 28, Dyslipidemia: 32, CHD: 34). The mean (± sd) time between the test and the retest was 33 days (± 6 days).

Among those who were randomized to complete the second interview, we compared those who performed (n=94) and did not perform (n=116) the second interview. The sociodemographic characteristics of the two groups were similar. However, those who repeated the interview were more educated (40% had a university degree versus 28%) and were more likely to be employed (56% versus 46%). Comparing the mean preference-based and SF-36 subscale scores obtained at the first interview suggested that those who completed the second interview reported slightly better health than those who did not perform the second interview. Considering that healthier individuals with better education might be more

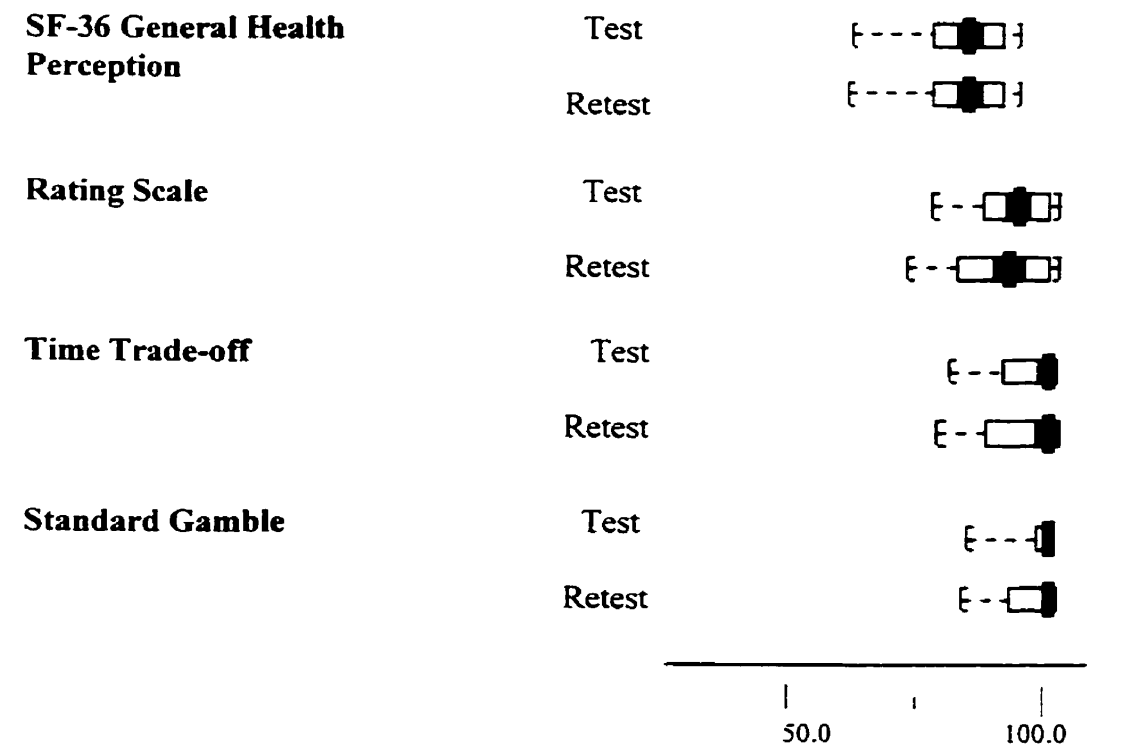
consistent, these results suggest that the low participation rate did not contribute to underestimate the reliability of the preference-based scores.

As seen in Figure 3.2.1, for each preference-based scaling technique and the SF-36 GHP subscale, the point estimates and confidence intervals around the median scores for the participants' present health at the test and the retest were almost identical, indicating no significant difference between the test and the retest. All results were skewed toward the minimum score. The mean absolute difference (± sd) between the test and the retest was very similar for all the scaling techniques and was equal to 8.1 (± 8.8) for the SF-36 GHP subscale; 7.8 (± 11.1) for the RS; 7.7 (± 16.4) for the TTO and 4.9 (± 11.9) for the SG. Seventy five percent (75%) of participants had an absolute difference between the test and the retest equal to 10 units or less for the RS, the TTO and the SF-36 GHP subscale and equal to 6 units or less for the SG. We identified three outliers: two participants had absolute differences greater than 80 units for the TTO, and for one of these participants, the SG also differed by more than 80 units. Overall, these results suggest that scores obtained at the test and the retest are in good agreement for the vast majority of participants and that preference-based measures for the participants' present health were at least as reliable as the SF-36 GHP subscale scores over a three to six week period.

3.2.4.3 Convergent validity

The mean (95% confidence interval) preference-based scores for the participants' *present health* were equal to 84.9 (83.8, 86.0), 88.2 (86.8, 89.6), and 91.6 (90.5, 92.7) when assessed by the RS, the TTO and the SG scaling technique, respectively, confirming that the preference-based measures vary according to the scaling technique.

Figure 3.2.1 ● Reliability (three to six-week interval) of preference-based and SF-36 General Health Perception subscale measures in a subsample of participants (n=94)



Each boxplot was drawn as followed: the dark line in the middle of each box represents the median score; the dark area in each box represents the 95% confidence interval around the median score; the left and right edges of each box represent the 25th and the 75th percentile scores; and the ends of the left and right horizontal lines represent the 10th and the 90th percentile scores.

The correlation between the preference-based measures was moderate and varied from 0.40 to 0.52 (Table 3.2.3). We observed low to moderate correlation coefficients between the SF-36 subscale scores and each of the preference-based measures. Among the three preference-based scaling techniques, the RS was the most highly correlated with the different SF-36 dimensions of HRQOL. The lowest correlation was always obtained with the SG scores.

3.2.4.4 Discriminant ability

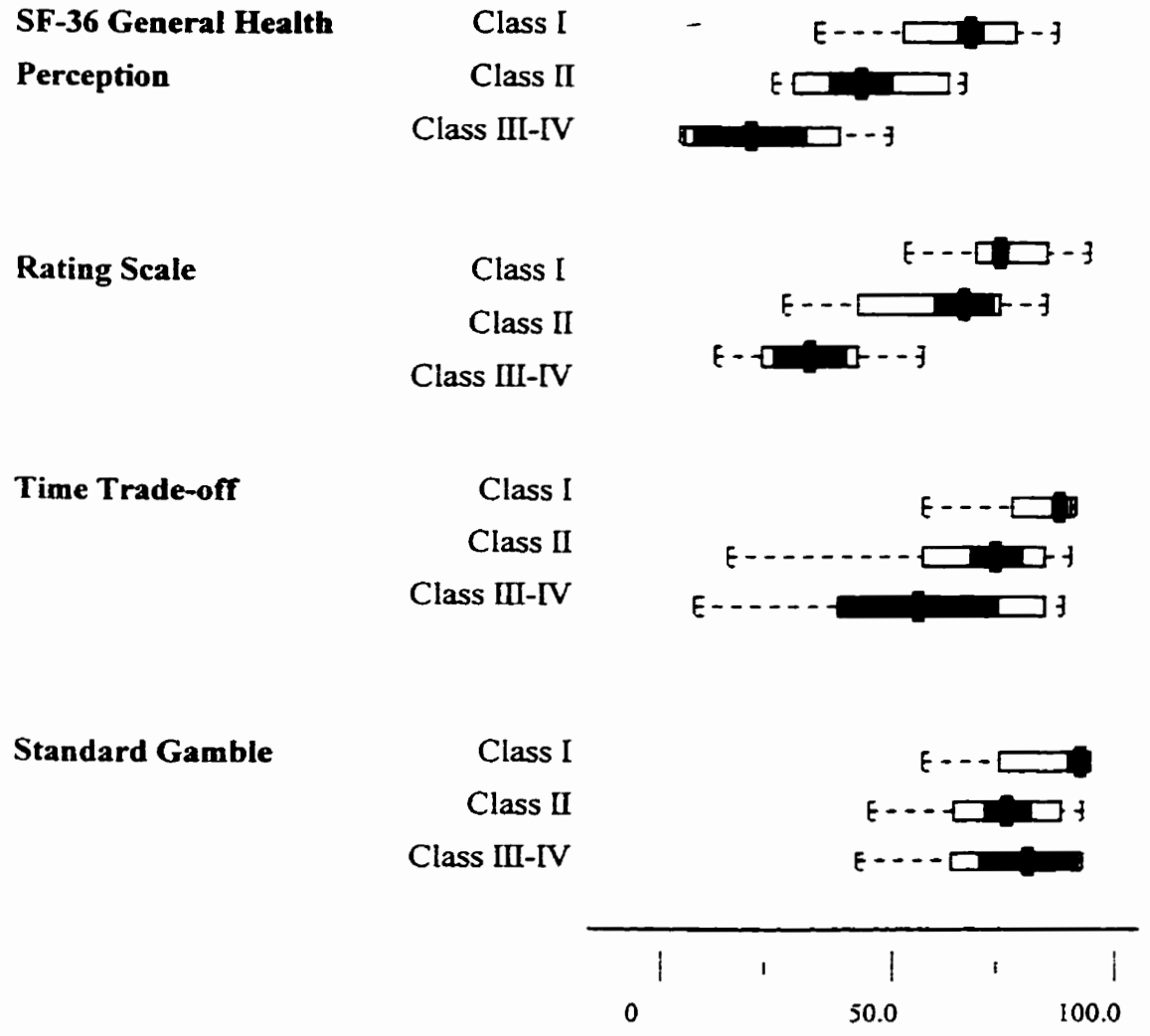
As demonstrated by Figure 3.2.2, the median preference-based and SF-36 GHP scores of cardiac patients decreased with more physical disability as assessed by higher SAS classes. All the scaling techniques were able to differentiate groups of participants in SAS classes I (n=230) and II (n=63) as seen by the absence of overlapping confidence intervals. However, only the SF-36 GHP subscale and the RS were able to differentiate groups of participants in SAS Classes II and III-IV (n=19). The poor discriminant ability of the TTO and SG can be due to the large variability of the scores from patients in Class III-IV and the small number of patients classified in this category.

We also evaluated the ability of each preference-based scaling technique to differentiate groups of participants with none or few health problems. The RS, the TTO and the SF-36 GHP subscale scores decreased with increasing numbers of health problems (Table 3.2.4). The magnitude of the decrement was generally the highest with the SF-36 GHP subscale and the RS and the lowest with the TTO. The median SG scores were equal to 100 for groups of participants reporting fewer than three health problems. In contrast to the RS and the SF-36 GHP subscale, the 95% confidence intervals around the median TTO and SG scores overlapped substantially for the groups reporting fewer than three health problems. Among participants

Table 3.2.3 ● Spearman rank correlation coefficients between preference-based measures of the participants' present health and the SF-36 subscales scores

	Rating Scale	Time trade-Off	Standard gamble
Preference-based measures:			
Rating scale	---	0.46	0.40
Time trade-Off		---	0.52
Standard gamble			---
SF-36 subscales:			
General health perception	0.51	0.36	0.30
Physical functioning	0.44	0.37	0.31
Physical role	0.38	0.32	0.29
Emotional role	0.20	0.19	0.18
Social functioning	0.32	0.25	0.23
Pain	0.27	0.21	0.14
Energy	0.38	0.30	0.19
Mental health	0.31	0.23	0.17

Figure 3.2.2 Distribution of preference-based and SF-36 General Health Perception subscale scores stratified by Specific Activity Scale classes



Refer to Figure 3.2.1 for boxplots description.

Table 3.2.4 • Median (95% confidence interval) preference-based and SF-36 General Health Perception subscale scores by the number of health problems reported by the participants

	Number of health problems reported			
	None (n=168)	One (n=218)	Two (n=205)	Three or more (n=287)
SF-36 General Health Perception	85.0 (83.1, 86.8)	80.0 (77.3, 82.7)	77.5 (75.3, 79.7)	70.0 (66.7, 73.2)
Rating Scale	95.0 (93.8, 96.2)	90.0 (88.0, 91.9)	88.0 (86.3, 89.7)	80.0 (78.6, 81.4)
Time Trade-off	99.5 (98.9, 100.0)	99.0 (97.8, 100.0)	97.0 (95.4, 98.6)	91.0 (88.7, 93.2)
Standard Gamble	100.0 (99.8, 100.0)	100.0 (99.1, 100.0)	100.0 (98.8, 100.0)	94.0 (91.9, 96.0)

reporting fewer than three health problems, the distributions of the TTO and SG scores were very skewed to the left and the majority of scores were larger or equal to 95.0. This ceiling effect may compromise the ability of the TTO and SG to discriminate between groups of participants with few health problems.

3.2.5 Discussion

Preference-based scaling techniques were administered successfully in a population of healthy respondents as well as patients involved in CHD prevention and treatment. The median preference-based measures were as stable as the SF-36 GHP subscale over a three to six week period and the majority of participants reported consistent scores at the test and the retest assessments.

We evaluated the convergence between the preference-based measures to determine to what extent these instruments are measuring the same construct. To maximize the convergence between the scaling techniques we kept constant, for each participant, the health state description and its duration across all preference-based scaling techniques. The mean preference-based score varied according to the scaling technique used: the RS and the SG mean scores were the lowest and highest, respectively. This is in agreement with previous reports. [105,113-115] We found a moderate correlation between the preference-based measures. In the literature, the correlation between these scaling techniques was reported as being low to moderate and varied from 0.22 to 0.65.[105,113,152], which suggests that these three preference-based scaling techniques are not exactly measuring the same construct. As mentioned by Nord [115], we should not be surprised to obtain different answers to different questions. The observed differences can be explained by the consequences and the timing of the consequences associated with each scaling technique and by the participant's risk attitude.

With the RS, respondents are asked to value their present health by simply indicating its location on an interval scale. Contrary to the RS, the TTO and the SG are associated with consequences. The respondents are asked to indicate how much of their current health state they would be willing to give up to gain perfect health. The HRQOL of the current health state is considered to be less than perfect only if the respondents are willing to take an immediate risk of death or are willing to give up some of their life expectancy to avoid it. For this reason, for many individuals, it is more difficult to assign a lower score with the TTO and the SG than with the RS.

The difference between the TTO and the SG may be partly explained by the different timing of the consequences. With the TTO, the number of years of life are sacrificed at the end of the rater's life while, with the SG, the risk of death is immediate. For this reason, the TTO scores tend to be lower than the SG scores.

Finally, in contrast to the TTO, the SG assessment is not only measuring the value of a given health condition but also the risk attitude of the respondent. Because most respondents are risk averse, they tend to choose the gamble alternative only when the probability of perfect health is high. This will also tend to increase the SG scores compared to the TTO.

We also assessed the convergence between the preference-based measures and the SF-36 subscales to determine to what extent preference-based scores are influenced by the various dimensions of the HRQOL. We observed low to moderate correlation between the preference-based scores and the SF-36 subscales. Among the three preference-based scaling techniques, the RS was the most highly correlated with the different dimensions of the HRQOL measured by the SF-36 Health Survey. Very similar findings were reported by Bosch and Hunink.[100] In addition they demonstrated, using multiple regression analysis, that 61%, 28% and 14% of the

total variance of the RS, TTO and SG, respectively, could be explained by the best combination of the SF-36 subscales. Other multiple linear [155,158] and non linear [159,160] regression models have also been unable to explain a large proportion of the SG or TTO scores based on nonpreference-based HRQOL measures. Bosch et al.[100] offered several explanations for the poor correlation between nonpreference-based HRQOL measures and either SG or TTO scores: 1) time preferences and risk attitude may vary among patients; 2) the correlation may be attenuated when a large proportion of the TTO and SG scores are equal or very close to the maximum score (ceiling effect); 3) the importance of the various HRQOL dimension may vary across patients; 4) nonpreference-based HRQOL measures may not measure exactly what they are intended to measure; and 5) the cognitive complexity of the TTO and SG may add additional variability.

We evaluated the ability of the RS, TTO, SG and the SF-36 GHP subscale to discriminate between cardiac patients with different degrees of physical disability and between groups of participants reporting different numbers of health problems. As expected, for each of these scaling techniques, lower scores were associated with more severe physical disability and more numerous health problems. The RS was able to discriminate between all of the groups in our sample. Its discriminant ability was comparable to the SF-36 GHP subscale. The TTO and the SG scaling technique were not able to discriminate cardiac patients in SAS class II and III/IV and groups of participants reporting less than three health problems. These results are in accordance with previous reports.

Nease et al [151], did not detect significant differences between angina patients categorized into the Canadian Cardiovascular Society Class I and II with the TTO and the SG scaling techniques. However, the RS was able to discriminate between groups of angina patients in Class I, II and III/IV. Tsevat et al [147] also found only modest correlation between TTO and functional status in survivors of myocardial

infarction. Among human immunodeficiency virus (HIV)-infected patients, SG scores, in contrast to a nonpreference-based measure, did not discriminate asymptomatic patients, symptomatic patients and patients with acquired immune deficiency syndrome. [161] In another prospective study, among HIV-infected patients at various stage of infection, RS scores were inversely related to disease stage, but TTO scores were generally higher regardless of the disease stage. Over a six month period, nonpreference-based measures indicated deterioration of the HRQOL for patients with acquired immune deficiency syndrome and patients manifesting progression of HIV-infection while TTO scores remained stable.[162] In the Beaver Dam Health Outcome Study [83], the SF-36 GHP subscale was able to differentiate between all groups of participants reporting fewer than three health problems while the confidence intervals (computed from the reported results) around the mean TTO scores of participants reporting one or two health problems overlapped.

The poor discriminant ability of the TTO and the SG can be explained, as suggested by Nease et al. [151], by the fact that people may have different attitudes towards similar health conditions, leading to large variation of the preference-based scores within groups of participants with similar health. In these circumstances, it would be difficult to detect small differences.

A second explanation might be that the discriminant validity of these techniques is affected by an important ceiling effect, where a large proportion of participants rate their present health as being very high on the TTO and SG scales, even when they rate their health as being less than perfect on the RS. In several studies, including this one, high value or utility scores were obtained from respondents affected by serious health conditions such as HIV [162], CHD[151] , intermittent claudication [100] and advanced symptomatic cancer patients [145,182]. This ceiling effect may reduce considerably the ability of these scaling techniques to discriminate between less severely disabled patients.

To better understand how respondents value health states, other types of validity studies were recently undertaken. [183-185] Fowler et al. [185] have demonstrated that for people reluctant to say they would give up any life at all, questions based on the risk of dying or willingness to give up years of life are likely to be poor measures of the values of health states. This would support the hypothesis that the observed ceiling effect is responsible for the poor discriminant ability of the SG and the TTO.

In summary, in a population of healthy and cardiac participants, the reliability of the RS, TTO and SG scaling techniques was similar to the SF-36 GHP subscale. The preference-based measures varied according to the scaling technique used. The RS was the most highly correlated with the various SF-36 subscale scores. The discriminant validity of the SF-36 GHP subscale and the RS was superior to the TTO and SG and suggest that these later techniques may not be sufficiently sensitive to measure the impact of minimal interventions, such as primary coronary heart disease prevention strategies, on the HRQOL of the participants.

3.3 Preference-based health-related quality of life measures in coronary heart disease prevention and treatment

The results of the second analysis, based on the entire study sample (n=878), are reported in section 3.3. The main objective of this analysis was to evaluate the preference-based and the nonpreference-based health-related quality of life measures reported by the healthy participants with and without dyslipidemia treatment and by the cardiac patients, after adjusting for important confounders. We also performed several secondary analyses to better understand the observed differences between the health-related quality of life of healthy participants with and without dyslipidemia.

Health-Related Quality of Life Measures in Coronary Heart Disease Prevention and Treatment

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3.3.1 Abstract

In a large (n=878) multicenter hospital-based cross-sectional survey, we measured the health-related quality of life (HRQOL) of healthy participants with and without treatment for dyslipidemia and patients with coronary heart disease (CHD) using the rating scale (RS), the time trade-off (TTO), the standard gamble (SG) and the SF-36 Health Survey. Participants with dyslipidemia treatment reported a significant 3 points decrement on the SF-36 General Health Perception subscale and the RS when compared to the healthy participants without dyslipidemia. Scores reported by patients with angina and/or a previous myocardial infarction were similar on all scaling techniques. Patients with congestive heart failure reported the lowest scores on all scales. Among dyslipidemia participants, an inverse relationship was observed between the HRQOL and the expected cholesterol level. These results suggest that the impact of dyslipidemia on the participants' HRQOL may be similar to hypertension and significant from a public policy point of view.

KEY WORDS: Health status, health-related quality of life, coronary heart disease prevention, dyslipidemia, angina, myocardial infarction, congestive heart failure

3.3.2 Introduction

Several pharmacoeconomic studies have estimated the cost-effectiveness of detecting and treating dyslipidemia to prevent coronary heart disease (CHD). [25-32,35,36] These analyses were completed assuming that the detection and treatment of dyslipidemia do not directly affect individuals' health-related quality of life (HRQOL). This reflects the fact that there has been little comprehensive assessment of the impact of dietary modifications on HRQOL and lipid medications are reported to be well tolerated.

On the other hand, there is a substantial literature demonstrating that hypertensive individuals report a lower sense of general well-being, greater psychological distress and poorer perceived health status. [48,72,73,75,186,187] Important studies have also found that detecting hypertension can increase illness-related absenteeism and physical disability and decrease time spent in social activities. [49,51,52,54,55,57] Dyslipidemia and hypertension share many characteristics; both conditions are risk factors for CHD, affected individuals generally remain asymptomatic until they develop cardiovascular complications, and lifelong treatments are often required including lifestyle changes, pharmacotherapy, regular medical visits and diagnostic tests. [43] Lifestyle changes may include dietary modification, exercise training, and weight reduction.

As summarised by Brett [84], several aspects of the diagnosis and treatment of dyslipidemia may cause adverse psychologic responses: 1) people may confuse a risk factor with actual disease and consider themselves as unhealthy; 2) the inherent biologic variability of the blood cholesterol level may be a source of frustration and misunderstanding for patients; 3) dietary efforts to reduce the cholesterol level are not uniformly effective and may cause disappointment, confusion, and a sense of failure; 4) confusing messages about the benefits and harms of certain food may be

an additional source of anxiety; 5) and people may be faced with the stressful dilemma between continuing their treatment or stopping their treatment and assuming a greater risk of CHD.

A few studies have been conducted to assess the preference-based HRQOL measures associated with various CHD conditions. [36,83,147,151,170] However, with the exception of the Beaver Dam Outcome Study [83], none of these provided preference-based measures for all CHD conditions required for a cost-effectiveness analysis of CHD prevention and treatment. Furthermore, for the same CHD condition, large variations were observed across studies, possibly attributable to the use of different study populations and different methodologies to assess the HRQOL. For this reason, it is difficult in a cost-effectiveness analysis to combine estimates from different studies. Finally, adequate preference-based measures for dyslipidemia have not been reported so far.

The objective of this study was to provide estimates of the HRQOL of healthy individuals with and without treatment for dyslipidemia and patients with CHD, including angina, previous myocardial infarction (MI) and congestive heart failure (CHF), that could be used in cost-effectiveness analysis of CHD primary prevention.

3.3.3 Methodology

3.3.3.1 Study population

The study population was described in detail elsewhere (section 3.2.3.1.). Briefly, study participants were recruited and interviewed at various outpatients clinics in two University teaching hospitals and among accompanying friends and

family members of patients undergoing day surgery, as well as hospital workers. Subjects were first classified into one of three study groups: 1) Healthy, 2) Dyslipidemia, and 3) CHD. CHD patients were identified through hospital chart review. Subjects without CHD were classified in the Dyslipidemia group if they reported following a prudent diet prescribed by a physician or taking medication for dyslipidemia. Subjects without CHD and dyslipidemia were classified in the Healthy group.

In order to control for the effect of acute comorbid conditions, we excluded pregnant women, all subjects with temporary illness such as a cold or an infection, and Healthy and Dyslipidemia subjects currently trying to quit smoking. In addition, subjects were asked to report any other health problem confirmed by a physician. If they reported at least one other health problem, they were asked: "In the last four weeks, have you had symptoms from any of these health problems?" and "In the last four weeks, which health problem has most affected your quality of life?". Healthy and Dyslipidemia subjects were eligible if they answered *no* to the first question. CHD patients were eligible if their answer to the second question was either *none* (meaning they had not been bothered by any health problem), *CHD* or *a CHD risk factor* (hypertension or dyslipidemia). For example, CHD participants who reported their HRQOL to be mostly affected by arthritis in the past four weeks were excluded from this study. We also used this information to classify participants in one of three comorbidity status classes: 1) no comorbidity: reporting no other health problem; 2) asymptomatic health problem: reporting one or more health problem(s) without symptom in the past four weeks; and 3) symptomatic health problem: reporting one or more health problem(s) with symptoms in the past four weeks.

3.3.3.2 Outcome measures

During the interviews, questionnaires were administered in the following order: 1. SF-36 Health Survey, a generic and nonpreference-based HRQOL questionnaire; 2. Specific Activity Scale (SAS); 3. Medical history; 4. Preference-based HRQOL assessments; and 5. Sociodemographic information. Item 2-4 were administered in a face-to-face interview by one of four trained interviewers and items 1 and 5 were self-administered. Item 2 is not included in this report.

Included in the medical history questionnaire, all participants were asked: "If I were to take a blood sample now, would you expect your cholesterol to be: extremely elevated, very elevated, slightly elevated or normal?". In addition, participants on treatment for dyslipidemia reported how long ago they were first informed that their blood cholesterol was high and their current type of dyslipidemia management. All participants reported their weight and height. Those reporting being on either a diet, an exercise program or pharmacotherapy to control their dyslipidemia indicated, on a four-point or five-point scale, the pleasantness, their compliance and expected efficacy of each type of intervention.

The preference-based assessment of the HRQOL included the rating scale (RS), the time trade-off (TTO) and the standard gamble (SG). Each of these techniques is described in detail in section 3.2.3.2.

3.3.3.3 Statistical analysis

CHD participants were classified into one of seven CHD groups: 1) angina, 2) MI, 3) angina and MI, 4) CHF, 5) CHF and angina, 6) CHF and MI, and 7) CHF and angina and MI. Only 36 CHF patients were included in groups 4 to 7, hence they

were combined into one single CHF group. Patients characteristics and the results from the SF-36 Health Survey were reported combining groups 1 to 3 for convenience.

We compared the Dyslipidemia and the CHD groups against the Healthy group. In order to adjust for important potential confounders, several multivariate linear models were created to describe the preference-based and the SF-36 subscale scores as a function of the study groups and either the participant's age, gender, body mass index or comorbidity. In all models, comorbidity was statistically significant. Similar results were obtained when comorbidity was entered either as a continuous variable (number of comorbid conditions reported by the participant) and as a categorical variable (no comorbidity, asymptomatic comorbidity and symptomatic comorbidity). For all preference-based measures and for most of the SF-36 subscale scores, gender, age and the participant body mass index were not found to be statistically significant covariates. The interaction terms between the study group and either age, gender or the number of comorbid conditions reported were never statistically significant. The body mass index was significant only for the RS and the SF-36 Physical Functioning. However, adjusting for the body mass index did not substantially change the results. Consequently, we computed the mean preference-based and SF-36 subscale scores for each study group after adjusting for the number of comorbid conditions reported by the participants using the least-squares means statement of the Generalized Linear Model from SAS software system for data analysis. We, then, reported the mean scores for participants reporting 1.3 comorbid health conditions, which represented the mean number of comorbid conditions for the entire sample. Ninety-five percent confidence intervals (95% CI) around the adjusted means were computed using the standard error of the mean generated by the least-squares procedure.

We performed several secondary analyses to identify the determinants of the

HRQOL among the dyslipidemia participants using multivariate linear models. In these models, the proportion of the variance of HRQOL explained by the number of comorbid conditions was statistically significant. Again, age and gender were not found to be statistically significant. We reported the adjusted means for participants reporting 1.3 comorbid conditions.

Chi-square test was used to assess the statistical significance of differences between proportions.

3.3.4 Results

We approached a total of 2789 individuals. Among those, 685 (25%) refused to participate (323 were eligible for enrollment but refused after having completed the self-administered questionnaire), 55 were eligible and agreed to participate but left the hospital before the interview, 3 were interviewed twice and we included only the first interview. Finally, 41 subjects were eligible but the recruitment in their study group was closed at the time they were solicited. In addition, 146 subjects were judged unable to perform the interview due to language difficulties. Nine hundred and eighty one (35%) subjects did not comply with one or more eligibility criteria. Reasons for exclusion were: temporary illness (172), pregnancy (4), trying to quit smoking (81), CHF without a loop diuretic medication (2), CHD for less than six months (25), dyslipidemia treatment for less than one month (3), age outside the appropriate range (106), Healthy subjects with symptomatic comorbid conditions (456) and CHD subjects mostly affected by another comorbid health problem (261). A total of 878 interviews were performed, representing 53% of potentially eligible subjects without language difficulties.

3.3.4.1 Characteristics of participants

Important differences were observed between the study groups (Table 3.3.1). Compared to the Healthy group, participants in the Dyslipidemia and the CHD groups were more likely to be older, male and reported more comorbid conditions.

We compared the participants (n=878) to the non-participants (n = 419) who were eligible for enrollment but refused to participate (n=323), left the hospital before the interview (n=55) and were not interviewed because the enrollment was closed in their study group (n=41). The participants and the non-participants groups were similar in terms of age, gender and number of comorbid conditions. The participation rate was similar in the three study groups (66% - 77%). We, therefore, had no evidence that non-participants were different from participants.

3.3.4.2 Preference-based health-related quality of life measures

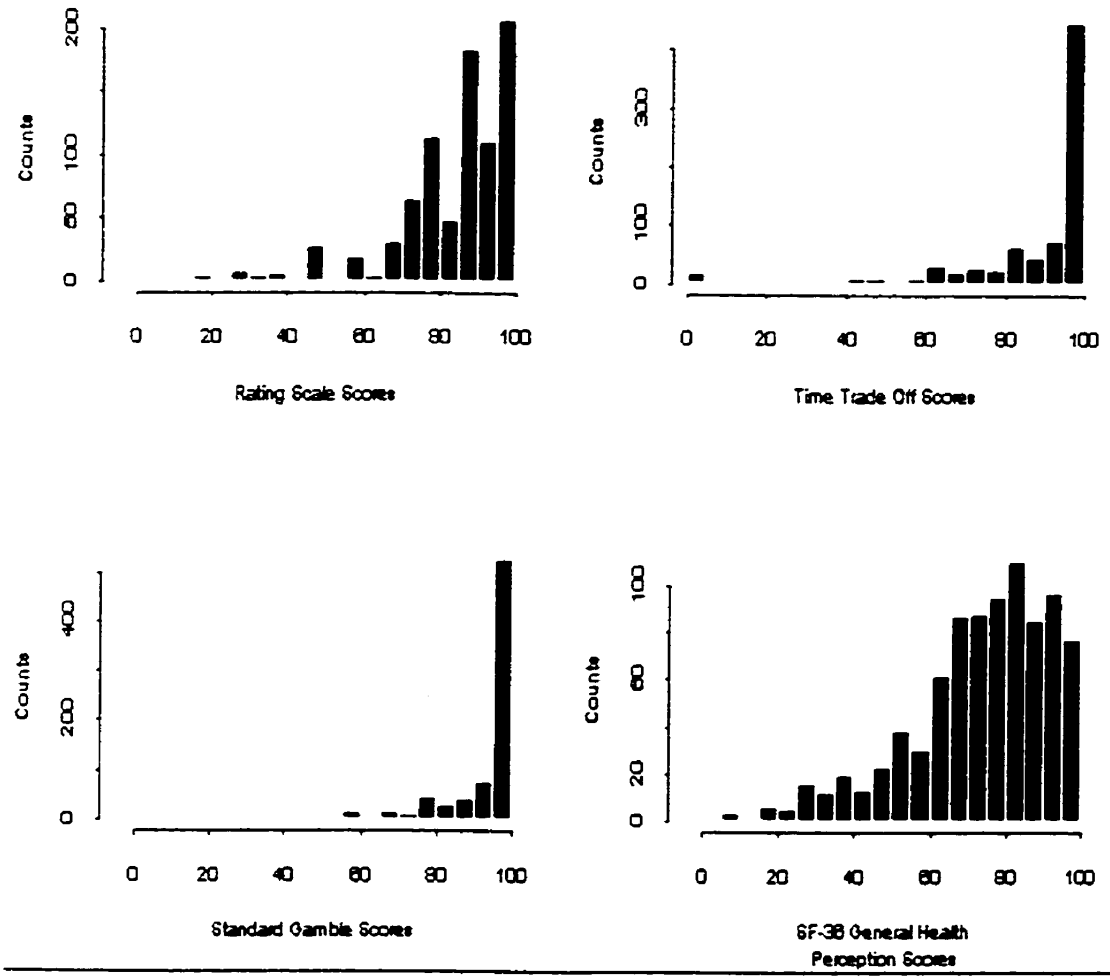
We obtained complete preference-based HRQOL assessment (RS, TTO and SG) from 772 (88%) participants. The histograms of the preference-based measures and the SF-36 General Health Perception (GHP) subscale are presented in Figure 3.3.1. For each scaling technique, the distribution of scores was unimodal and skewed to the left. The skewness was more pronounced for the SG and the TTO where, respectively, 51% and 25% of the scores were equal to the maximum score of 100 compared to 16% and 9% for the RS and GHP subscale scores. The proportion of participants who refused to trade-off their life expectancy (TTO score = 100) varied significantly (p=0.0001) according to the study group and was equal to 38%, 19%, 13% and 3% for the Healthy, the Dyslipidemia, the Angina and/or MI, and the CHF group, respectively. The corresponding proportion of participants who refused to take a risk of death to avoid their present health (SG score = 100) also

Table 3.3.1 ● Characteristics of participants in each study group

Mean Values (± SD)	Healthy	Dyslipidemia	Angina/Myocardial Infarction	Congestive Heart Failure
Age	48 (12)	55 (12)	61 (9)	65 (8)
Gender: n (%) male	100 (33)	149 (59)	213 (75)	20 (55)
Comorbidity status: n (%)				
No other health problem	168 (55)	102 (41)	41 (15)	2 (6)
Asymptomatic health problems	139 (45)	148 (59)	186 (66)	15 (45)
Symptomatic health problems	---*	---*	53 (19)	16 (48)
Number of comorbid conditions	0.7 (1.0)	0.9 (1.0)	2.1 (1.7)	3.1 (1.9)
Body mass index (kg/m^2)	25.2 (4.2)	25.9 (3.5)	27.0 (3.6)	26.3 (5.7)

* subjects with symptomatic comorbid conditions were excluded from this study group

Figure 3.3.1 Histograms of the preference-based measures and the SF-36 General Health Perception subscale



varied significantly (p=0.001) according to the study group and was equal to 61%, 53%, 33% and 8% for the Healthy, the Dyslipidemia, the Angina and/or MI, and the CHF group, respectively. Seventeen (2%) participants rated their present health as being equal to death on the TTO scale. This was relatively high compared to the other scaling techniques where the proportion varied from 0.1% to 0.2%. We performed the analysis with and without these outlier scores. The results of these analyses were similar for all the scaling techniques with the exception of the TTO. We will report the mean TTO scores obtained with and without these outlier observations.

As demonstrated in Table 3.3.2, the adjusted mean RS score of the Healthy group was higher than the mean score of the Dyslipidemia group with a difference of 2.8 units (p=0.02). No differences were detected between these two groups on the TTO and SG scales. After excluding the TTO outlier observations, the adjusted mean of the Healthy group was 1.7 units higher than the Dyslipidemia group (p=0.16). Among the CHD groups, patients with CHF reported the lowest scores on all preference-based scales. Patients diagnosed with angina or MI or with angina and MI, generally reported similar adjusted mean scores on all scaling techniques.

We compared the adjusted mean scores of dyslipidemia participants and patients with angina and/or MI from the two hospitals and found no difference, with the exception of the TTO scores for CHD participants. We concluded that the enrollment site was not a determinant of the preference-based HRQOL among groups of participants recruited at both sites.

Table 3.3.2 • Mean (95% confidence interval) preference-based scores adjusted for the number of comorbid conditions reported by the participants[¶]

	N	Rating Scale	Time Trade-off[§]	Standard Gamble
Healthy	307	90.1 (88.5, 91.7)	89.8 (87.4, 92.2)	94.2 (92.5, 95.9)
Dyslipidemia	251	87.3 (85.6, 89.0)	90.2 (87.7, 92.7)	94.5 (92.5, 96.5)
Angina	115	80.9 (78.4, 83.4)	91.1 (86.4, 93.8)	92.3 (89.4, 95.2)
Myocardial infarction	84	79.9 (76.8, 83.0)	82.9 (78.8, 87.0)	88.0 (84.7, 91.3)
Angina and Myocardial Infarction	85	78.5 (75.4, 81.6)	83.2 (78.9, 87.5)	80.0 (76.7, 83.3)
Congestive Heart Failure	36	59.5 (54.4, 64.6)	78.4 (71.0, 85.8)	77.8 (71.9, 83.7)

¶ adjusted to 1.3 comorbid conditions, the overall sample mean number of comorbid conditions

§ when excluding the Time Trade-off scores equal to zero (n=17) these results were obtained: Healthy: 92.2 (90.4, 94.0), Dyslipidemia: 90.5 (88.5, 92.5), Angina: 92.3 (89.4, 95.2), Myocardial Infarction: 85.6 (82.3, 88.9), Angina and Myocardial Infarction: 85.8 (82.5, 89.1), Congestive Heart Failure: 82.3 (76.4, 88.2)

3.3.4.3 SF-36 Health Survey

Table 3.3.3 provides the adjusted mean and the 95% confidence interval of the SF-36 subscale scores for each study group. The Healthy and the Dyslipidemia groups reported very similar HRQOL on all subscales with the exception of the GHP subscale; the mean score of the Healthy group was 3.3 units ($p=0.02$) higher than the Dyslipidemia group. Compared to the Healthy group, patients diagnosed with angina and/or MI reported significant ($p < 0.05$) lower mean scores on several subscales, namely the GHP, the physical functioning, the role limitations due to physical and emotional problems, the social functioning and the vitality subscales. Patients with CHF reported the worst HRQOL. All their SF-36 subscale mean scores, except the mental health subscale, were significantly ($p < 0.05$) lower than those obtained from the Healthy group.

3.3.4.4 Secondary analysis

We performed several secondary analyses to evaluate if the observed difference between the Healthy and the Dyslipidemia groups could be attributed to residual confounding by comorbidity and to identify the determinants of the HRQOL among dyslipidemia participants.

Adjusting for the number of comorbid conditions may not completely control for the participant's comorbidity. For this reason, we compared Healthy participants reporting no health problem to Dyslipidemia participants reporting no health problem other than dyslipidemia (Table 3.3.4). Overall, participants in this subsample reported slightly better health than participants from the entire sample as seen by the higher mean scores on each scaling technique. The observed differences between the Healthy and the Dyslipidemia groups were similar to those reported from the entire

Table 3.3.3 • Mean (95% confidence interval) SF-36 subscale scores adjusted for the number of comorbid conditions reported by the participants[¶]

	Healthy	Dyslipidemia	Angina/Myocardial Infarction	Congestive Heart Failure
General Health Perception	81.3 (79.4, 83.2)	78.0 (76.0, 80.0)	70.4 (68.4, 72.4)	49.5 (43.8, 55.1)
Physical Functioning	89.7 (87.7, 91.7)	91.0 (88.8, 93.2)	77.6 (75.5, 79.8)	46.7 (40.8, 52.7)
Physical Role	91.5 (88.5, 94.5)	94.3 (91.1, 97.6)	76.3 (73.1, 79.5)	55.6 (46.7, 64.6)
Emotional Role	88.8 (85.5, 92.1)	91.3 (87.8, 94.8)	82.9 (79.4, 86.3)	68.5 (58.8, 78.2)
Social Functioning	90.7 (88.8, 92.6)	91.0 (88.9, 93.1)	87.7 (85.6, 89.7)	70.7 (65.0, 76.3)
Pain	72.5 (69.5, 75.5)	74.7 (71.5, 77.9)	71.4 (68.2, 74.5)	60.5 (51.7, 69.3)
Vitality	72.5 (70.5, 74.4)	71.3 (69.3, 73.4)	66.3 (64.2, 68.3)	55.0 (50.3, 61.7)
Mental Health	78.6 (76.9, 80.4)	79.0 (78.1, 81.8)	78.0 (77.2, 80.8)	73.3 (68.3, 78.4)

¶ Adjusted to 1.3 comorbid conditions, the overall sample mean number of comorbid condition

Table 3.3.4 Mean (95% confidence interval) scores from participants reporting no comorbid condition[¶]

	Healthy (n=168)	**Dyslipidemia** (n=102)
SF-36 General Health Perception	85.6 (83.5, 87.7)	80.5 (77.8, 83.2)
Rating Scale	93.8 (92.2, 95.4)	89.8 (87.8, 91.8)
Time Trade-off[§]	92.4 (89.5, 95.3)	93.8 (90.1, 97.5)
Standard Gamble	96.8 (95.1, 98.5)	95.8 (93.6, 98.0)

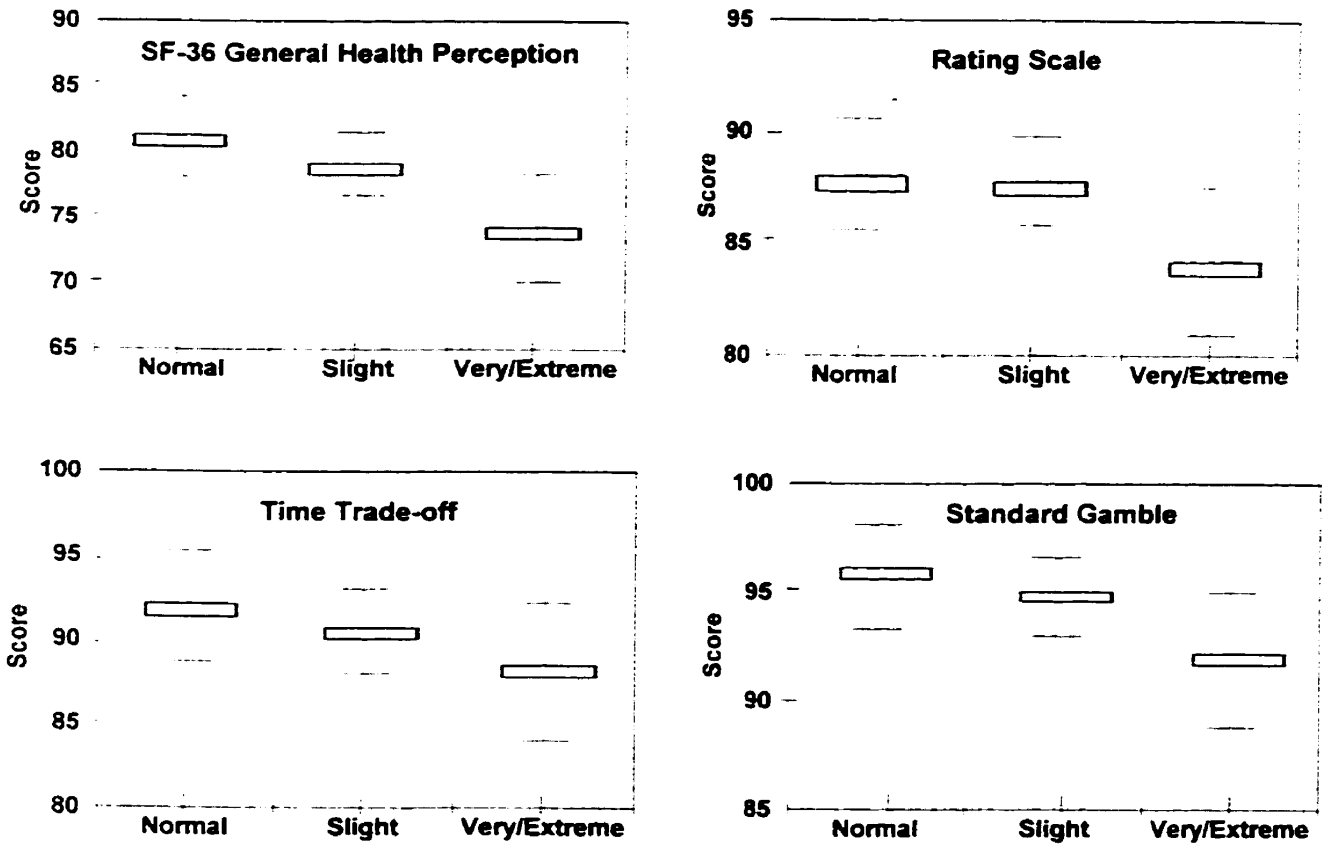
¶ Mean (95% confidence interval) Time Trade-off scores after excluding scores equal to zero (n=6): Healthy: 95.6 (93.6, 97.6), Dyslipidemia: 93.8 (91.3, 96.3)

sample. When compared to the Healthy group, the mean scores from the Dyslipidemia group were 5.1 units and 4.0 units lower on the SF-36 GHP ($p=0.004$) subscale and the RS ($p=0.003$), respectively. There were no significant differences observed on the TTO or the SG scales. Dyslipidemia participants were more likely to be older and male. However, adjusting for age and gender did not substantially change the results.

As an attempt to assess whether the observed decrement of the preference-based HRQOL measures and the SF-36 GHP subscale among the Dyslipidemia group was related to the diagnosis of dyslipidemia, we asked each participant to predict their cholesterol level. Among the participants in the Dyslipidemia group, 2%, 15%, 51% and 29% predicted their cholesterol to be extremely elevated, very elevated, slightly elevated or normal, respectively. The corresponding proportions in the Healthy group were different ($p=0.001$) and equal to 0%, 2%, 13% and 82%, respectively. Although the number of dyslipidemia participants was relatively small in each subgroup, Figure 3.3.2 suggests that the mean preference-based and SF-36 GHP subscale scores from participants expecting their cholesterol level to be very or extremely elevated are lower than those from participants expecting their cholesterol to be normal or slightly elevated.

The scores on the preference-based and the SF-36 GHP scales reported by dyslipidemia participants diagnosed for one year or less were slightly but not significantly lower than those reported from participants diagnosed for more than one year (Table 3.3.5). We also compared the Dyslipidemia participants treated with lifestyle changes only to those on pharmacotherapy (Table 3.3.6). Participants taking dyslipidemia drugs reported slightly lower mean scores on all preference-based scaling techniques and the SF-36 GHP subscale. However, on all scaling techniques, the observed difference was small (about 1 point) and not significant.

Figure 3.3.2 Adjusted mean (95% confidence interval) scores of dyslipidemia participants by their predicted cholesterol level



After adjusting for the number of comorbid conditions, the predicted cholesterol level was significant for the SF-36 General Health Perception subscale (p=0.035) and not significant for the Rating Scale (p=0.088), the Time Trade-off (p=0.362) and the Standard Gamble (p=0.144)

Table 3.3.5 ● Adjusted mean (95% confidence interval) scores for dyslipidemia participants by the time from the first diagnosis of dyslipidemia[¶]

	One year or less (n=45)	More than one year (n=206)
SF-36 General Health Perception	75.2 (71.2, 79.2)	79.6 (77.7, 81.5)
Rating Scale	87.0 (83.7, 90.3)	87.7 (86.2, 89.2)
Time Trade-off	85.3 (81.0, 89.6)	91.3 (89.4, 93.2)
Standard Gamble	92.0 (88.9, 95.1)	95.1 (93.7, 96.5)

¶ Adjusted to 1.3 comorbid conditions, the mean number of comorbid conditions of the entire sample

Table 3.3.6 ● Mean (95% confidence interval) scores adjusted for the number of comorbid conditions of dyslipidemia participants reporting different types of dyslipidemia management[¶]

Dyslipidemia therapy	Rating Scale	Time Trade-off	Standard Gamble	SF-36 General Health Perception
Lifestyle changes only (n=143)	88.1 (86.3, 89.9)	90.6 (88.2, 93.0)	95.1 (93.4, 96.8)	83.4 (81.1, 85.7)
Pharmacotherapy (n=108)	87.0 (85.0, 89.0)	89.7 (87.0, 92.4)	93.9 (91.9, 95.9)	84.3 (81.7, 86.9)

¶ Adjusted to 1.3 comorbid conditions, the mean number of comorbid conditions of the entire sample

Dyslipidemia participants also reported the pleasantness, the perceived efficacy and their compliance with each of their current dyslipidemia therapy. Diet was considered as the most unpleasant intervention, in that 29% of participants rated it as being very unpleasant or unpleasant compared to 13% for pharmacotherapy and 6% for exercise. Participants were also asked to report their perception of the efficacy of each intervention. Again, diet was rated as being the least effective where 42% of participants rated it as being either ineffective or slightly effective compared to 30% for exercise and 15 % for pharmacotherapy. We also asked participants to report their compliance with each intervention; 23% of participants on diet admitted cheating often or continually compared to 14% for those involved in an exercise program and 5% for participants taking dyslipidemia medication. Compared to diet, exercise was perceived as being more pleasant, more efficacious and was associated with better compliance. Among the three interventions, pharmacotherapy was perceived as the most efficacious and had the highest proportion of compliant participants.

3.3.5 Discussion

In a large multicenter hospital-based cross-sectional survey, we asked healthy individuals with and without treatment for dyslipidemia and CHD patients to evaluate their HRQOL using three preference-based scaling techniques and the SF-36 Health Survey. Participants with dyslipidemia treatment did not perceive themselves as being as healthy as participants without dyslipidemia treatment; the observed differences were equal to 3 points on the SF-36 GHP and the RS and were statistically significant. Although the proportion of Dyslipidemia participants willing to sacrifice their life expectancy to avoid their current health was higher than the proportion of Healthy participants, we observed no statistically significant difference between the mean TTO scores of these two groups. On the SG scale, the majority

of the Healthy and the Dyslipidemia participants were unwilling to take any risk of death to avoid their current health and no difference was detected between these two groups. The TTO and SG results were in accordance with previous reports documenting the poor discriminant ability of these scaling techniques. [147,151,161,162].

The observed differences between the healthy participants with and without dyslipidemia, on the RS and the SF-36 GHP subscale, are unlikely to be due to comorbidity. Extensive effort has been made to control for this potential confounder. We excluded participants with symptomatic comorbid conditions, the mean scores were adjusted for the number of comorbid conditions, and we performed a secondary analysis after excluding all participants reporting comorbid conditions. Other potentially important covariables, such as age, gender and the body mass index were not found to modify or to confound the comparison.

Secondary analyses were performed to better document the impact of dyslipidemia on the HRQOL. The majority of the Dyslipidemia participants expected their cholesterol level to be abnormal and a "dose-response" type of relationship was found between the expected cholesterol level and either the SF-36 GHP subscale and the preference-based measures. Preference-based measures did not vary significantly according to the time from the diagnosis of dyslipidemia and the type of dyslipidemia treatment. However, this study sample may not have been sufficiently large to detect such small differences. Participants' opinion about the pleasantness, perceived efficacy and compliance with their current dyslipidemia treatment indicates that diet, exercise and pharmacotherapy may not be equally accepted and tolerated.

Compared to the Healthy group, cardiac patients reported lower scores on all the scaling techniques. Patients diagnosed with CHF reported the lowest mean scores on all scaling techniques. Generally patients with angina and/or a previous MI

reported similar scores.

This study has several strengths. For the first time, the HRQOL associated with CHD conditions and dyslipidemia was assessed in a large sample of individuals using standardized preference-based scaling measures. The psychometric properties of the preference-based instruments in this population were consistent with current literature. [188] In addition, a large "control" group, consisting of healthy participants without dyslipidemia, was included to better judge the impact of dyslipidemia on the HRQOL. Extensive effort was made to control for potential confounders at the design and the analysis stages. However, it is important to mention that the results may be subject to a selection bias due to the fact that the participants were solicited at two university teaching hospitals and at the time of their physician visit. Furthermore, we may have reduced our ability to generalise the results by applying strict eligibility criteria.

The preference-based scores provided by the CHD patients enrolled in this study are consistent with the results reported by others. [36,83,147,151,170] However, to date, very few studies have investigated the impact of detecting and treating dyslipidemia on the HRQOL. Among those that are available, the results have not demonstrated a consistent negative impact of dyslipidemia therapy on HRQOL. Forrow et al. conducted a prospective study on 1052 voluntary participants involved in a cholesterol screening program. [85] Based on their cholesterol level, participants were told they were either at high, moderate or low risk of CHD. They found that people classified as being at high risk had increased worry and concern about health seventeen months after the diagnosis. In other studies, no significant overall negative effect was associated with dyslipidemia. However, these studies had important limitations. Havas et al. investigated whether labelling effects occurred as a result of a community-based screening, education, and referral programs. [43] Their negative results were attributable to the positive and supportive approach taken by the team.

In another screening study, no psychological effects of screening were observed. [87] However, about half of the hypercholesterolemic men did not believe they had hypercholesterolemia despite being told otherwise. In the Beaver Dam Health Outcomes Study, no significant decrement in either the TTO or the Quality of Well Being scores was observed when comparing the HRQOL of participants taking dyslipidemia medication (n=78) with the other participants (n=1356). [90] Again, this study was limited by the small number of dyslipidemic subjects and by the fact that most of the other participants reported other health problems. Clinical trials comparing different types of pharmacotherapy did not capture the impact of labelling healthy people with a diagnosis of dyslipidemia. [93,95]

The significance of our results can be evaluated from a public policy and a patient point of view. Simulations of cost-effectiveness analysis of CHD prevention by the detection and treatment of dyslipidemia have shown that the results vary tremendously according to the estimate of the preference-based HRQOL measures associated with the preventive intervention. [41,42] Consequently, from a public policy point of view, a two to three point decrement is extremely important and could significantly influence the results of a cost-effectiveness analysis. From an individual point of view, a three point reduction of the HRQOL is certainly small but comparable to the negative effects of treating hypertension. Recently, Lawrence et al. [78] evaluated the HRQOL of hypertensive participants from the Beaver Dam study and found that hypertension (n= 1430) was associated with a five point decrement on the SF-36 GHP subscale and the TTO scale. As discussed previously, hypertension has been shown to have a significant psychological and behavioural impact on patients. Similar effects with dyslipidemia remain to be demonstrated.

In summary, this study provides preference-based measures for evaluating the cost-effectiveness of detecting and treating dyslipidemia to prevent CHD and suggests that the impact of dyslipidemia on the participants' HRQOL may be small

but significant from a public policy point of view. Further research should be done confirming these results and elucidating the causes and the consequences of this negative impact on HRQOL.

4. *Summary and conclusion*

4.1 Literature review and study objectives

Pharmacoeconomic analyses of CHD primary prevention interventions suggest that treating dyslipidemia might be cost-effective in specific subgroups of the population. However, these analyses do not take into account the impact of treating dyslipidemia on health-related quality of life (HRQOL). To fully assess the benefits of treating dyslipidemia, it is recommended to use the number of Quality Adjusted Life Years (QALY) as the outcome measure. These are computed by weighting every year of life in a given health state by a quality factor representing the respondent's preference for this health state. By doing so, these analyses incorporate not only the impact of dyslipidemia treatment on mortality but also on HRQOL.

In health economic models, using hypothetical quality weights for dyslipidemia, the cost-effectiveness of treating dyslipidemia is extremely sensitive to the quality weight associated with the preventive intervention itself. For this reason, these models will only be useful if we can accurately measure the impact of preventive interventions on HRQOL.

To better understand the impact treating CHD risk factors can have on the HRQOL, we reviewed and analysed the extensive literature documenting the HRQOL of hypertensives. These studies demonstrated that the detection and

treatment of hypertension may increase absenteeism, and may have a negative psychological impact, such as a lower sense of well-being, greater psychological distress, and poorer perceived health status. This may be explained by the labelling effect and/or the secondary effects of pharmacologic and nonpharmacologic treatments.

A few similar studies were conducted among dyslipidemic individuals. The majority of them did not support the hypothesis that detecting and treating dyslipidemia affect the HRQOL of participants. However, all reported studies had important methodological limitations.

Preference-based measures, obtained by using the RS, TTO and SG scaling techniques, are currently used to assess the preferences for health states and are integrated in cost-effectiveness studies as quality weights.

A few studies were conducted to assess the preference-based HRQOL measures associated with various CHD conditions. However, with the exception of the Beaver Dam Outcome Study, none of these provided preference-based measures for all CHD conditions required for a cost-effectiveness analysis of CHD prevention and treatment. Furthermore, for the same CHD condition, large variations were observed across studies, possibly attributable to the use of different study populations and different methodologies to assess the preference-based measures. For this reason, it would be difficult to combine estimates from different studies in a cost-effectiveness analysis.

We reviewed the methodological aspects of the preference-based scaling techniques in order to adapt these instruments to the measurement of preference-based measures for CHD prevention and treatment. Considering that dyslipidemia has never been shown to affect the HRQOL of participants, individuals experiencing

the health state were considered to be the most appropriate source population. Preference-based measures are sensitive to context dependent variables. Consequently, it was necessary to control these variables by using a standardized methodology. Finally, because a conventional SG, using *perfect health* and *immediate death* as anchors, is not recommended to assess heath states with high utilities, such as dyslipidemia, we decided to conduct a pilot study to assess the feasibility and compare the discriminant ability of a chained SG to a conventional SG, non risky preference-based measures (TTO and RS) and a nonpreference-based measure (SF-36 General Health Perception subscale).

We reviewed the literature evaluating the reliability and validity of the preference-based measures. RS, TTO and SG were reported to have comparable and acceptable reliability and to be, at best, moderately correlated with nonpreference-based HRQOL measures. The discriminant ability of the SG and the TTO was reported to be poor. For this reason, it was important to modify these measures to increase their potential to detect small differences. In SG assessment, this was done by offering to respondents a lottery choice where the smallest probability of the worse outcome was equal to 1% and by using a diagram aid instead of a probability wheel to represent probabilities. For the TTO, respondents refusing to give up one year of their life for *perfect health* were asked if they would be willing to give up a shorter period of time. The shortest period of time was equal to 3 months. Finally, to our knowledge, there have been no empirical data documenting the reliability and validity of the preference-based measures among healthy populations.

This study was, therefore, conducted to:

- Assess, using a standardized methodology, the preference-based HRQOL of patients involved in CHD prevention and treatment.

- Evaluate the psychometric properties of the preference-based scaling techniques among these groups of individuals.

4.2 Methodology

Over a 14 month period, we conducted a large (n=878) cross-sectional survey of healthy individuals with and without treatment for dyslipidemia and CHD patients with angina, MI and/or CHF. We assessed their HRQOL using the SF-36 Healthy Survey, the Specific Activity Scale and three preference-based measures, the RS, the TTO and the SG. Study subjects were recruited at different outpatient clinics at the time of their physician visit, among friends and family members of patients undergoing day surgery, and among hospital workers of two University teaching hospitals in Montréal.

Subjects were classified into one of three study groups: Healthy, Dyslipidemia, and CHD. CHD patients were identified through hospital chart review. Subjects without CHD were classified in the Dyslipidemia group if they reported following a prudent diet prescribed by a physician or taking medication for dyslipidemia. Subjects without CHD and dyslipidemia were classified into the Healthy group.

Strict eligibility criteria were applied to control for the effects of acute and chronic comorbid conditions. We included only Healthy and Dyslipidemia subjects without comorbid conditions or with asymptomatic conditions in the past four weeks.

4.3 Results

4.3.1 Chained SG approach

We compared the ability of a chained SG to a nonpreference-based and three preference-based HRQOL measures to discriminate healthy participants (n= 39) from those on diets for dyslipidemia (n=35) and angina patients (n=30).

- On the RS, the TTO and the SF-36 GHP subscale, participants with dyslipidemia or angina reported lower mean scores than the healthy participants (Figure 3.1.2 and Table 3.1.3). No differences were detected between these groups on a conventional and a chained Standard Gamble (SG) scales.

- The distributions of the conventional and the chained SG scores were very skewed, with the majority of scores being equal or very close to the maximum score (Figure 3.1.3).

We concluded that the discriminant ability of the conventional and the chained SG was poor when compared to nonpreference-based and non-risky preference-based scaling techniques. This may be partially explained by a strong certainty effect and a misunderstanding of the chained approach by some participants.

4.3.2 Psychometric properties of the preference-based measures

We compared the psychometric properties of the preference-based HRQOL measures and the SF-36 Health Survey among our study population composed of

healthy subjects with and without treatment for dyslipidemia and CHD patients.

- The median preference-based measures were as stable as the SF-36 GHP subscale over a three to six week period and the majority of participants reported consistent scores at the test and the retest assessments (Figure 3.2.1).

- Correlation between the preference-based measures and each of the SF-36 subscales varied from poor to moderate (Spearman rank correlation coefficient: 0.14 - 0.51) (Table 3.2.3). Compared to the TTO and the SG, the RS was the most highly correlated with the different aspects of the HRQOL measured by the SF-36 Health Survey.

- In contrast to the SF-36 GHP subscale and the RS, the TTO and the SG were less discriminating among CHD patients with various physical disabilities (Figure 3.2.2) and were unable to differentiate participants reporting different numbers of health problems (Table 3.2.4).

4.3.3 Health-related quality of life associated with CHD prevention and treatment

Compared to the Healthy group, participants in the Dyslipidemia and the CHD groups were more likely to be older, male and report more comorbid conditions. In multivariate linear models, the participants' age, gender and body mass did not explain a significant proportion of the preference-based score variance. However, the participants' comorbidity was always statistically significant.

Consequently, we reported the mean score of each group adjusted for the mean number of comorbid conditions reported by the participants.

The participation rate was relatively low (53%). However, the participants and the non-participants were similar in terms of age, gender and number of comorbid conditions and the participation rate was similar in the three study groups. We, therefore, had no evidence than non-participants were different from participants.

We reported the following results:

- The adjusted mean RS score from participants with dyslipidemia treatment was 2.8 points lower ($p=0.02$) when compared to the healthy participants without dyslipidemia (Table 3.3.2). On the TTO scale, we observed a difference of 1.7 units between these two groups, the mean score of the Dyslipidemia group being lower than the Healthy group. However, this difference was not statistically significant. No difference was detected on the SG scale.

- As seen in Table 3.3.2, the adjusted mean preference-based scores of CHD patients were lower than those reported from the Healthy group. On the RS, those differences were statistically significant for all CHD groups as seen by the absence of overlapping of their 95% CIs. However, on the TTO and the SG scales, there was some overlapping of the 95% CIs of the CHD and the Healthy groups. For each scaling technique, the mean scores obtained from patients with Angina, MI or Angina and MI were similar.

- When compared to the Angina, MI and Angina/MI groups and the

Healthy group, patients with CHF reported the lowest mean preference-based scores (Table 3.3.2). For all preference-based scaling techniques, there was no overlapping of the 95% CIs around the mean scores of the Healthy and the CHF groups.

- On the SF-36 Health Survey, participants in the Healthy and the Dyslipidemia groups reported similar scores on all subscales except for the GHP (Table 3.3.3). The mean GHP subscale score of the Dyslipidemia group was 3.3 points ($p=0.02$) lower than the mean score obtained from the Healthy group.

- Compared to the Healthy group, patients diagnosed with Angina and/or MI reported significantly ($p < 0.05$) lower mean scores on several subscales, including the GHP, the physical functioning, the role limitations due to physical and emotional problems, the social functioning and the vitality subscales (Table 3.3.3).

- CHF patients reported the worst HRQOL on all the SF-36 subscales, except for the mental health subscale (Table 3.3.3).

To assess whether the observed difference between the Healthy and the Dyslipidemia groups could be attributed to residual confounding by comorbidity, we performed a secondary analysis comparing Healthy and Dyslipidemia participants reporting no comorbid conditions.

- In this subsample, participants reported slightly better health than the participants from the entire sample, as seen by higher mean scores on each scaling technique.

- The observed differences between the Healthy and the Dyslipidemia groups were similar to those reported in the entire sample. A difference of 5.1 units (p=0.003) and 4.0 units (p=0.003) were observed on the SF-36 GHP subscale and the RS, respectively (Table 3.3.4). Again, no statistically significant differences were observed on the TTO and the SG scales.

To identify the determinants of the HRQOL among dyslipidemia participants, we compared the adjusted mean score of the dyslipidemia participants stratified by their predicted cholesterol level, type of dyslipidemia treatment and time since their first diagnosis of dyslipidemia. We also reported the participants' evaluation of the pleasantness, perceived efficacy and reported compliance with each type of dyslipidemia treatment.

- The mean preference-based and SF-36 GHP subscale scores from participants expecting their cholesterol blood level to be very or extremely elevated were lower than those from participants expecting their cholesterol to be normal or slightly elevated (Figure 3.3.2). The predicted cholesterol level was a significant predictor of the SF-36 GHP (p=0.035) but was not significant for the RS, TTO and SG.

- The adjusted mean SF-36 GHP subscale, RS, TTO and SG scores were lower for those diagnosed for one year or less compared to those diagnosed for more than one year (Table 3.3.5). However, these differences were not statistically significant.

- Dyslipidemia participants treated by lifestyle changes only (diets, exercise and/or weight loss) reported higher adjusted mean scores than those on pharmacotherapy (Table 3.3.6). Those differences were

not statistically significant.

- Compared to diets, exercise was perceived as being more pleasant, more efficacious and was associated with better compliance. Among the three interventions, pharmacotherapy was perceived as the most efficacious and had the highest proportion of compliant participants.

Although several trends were identified in these secondary analyses, we may not have had a sufficiently large sample to detect such small differences. Participants' opinion about the pleasantness, perceived efficacy and compliance with their current dyslipidemia treatment suggests that diet, exercise and pharmacotherapy might not be equally accepted and tolerated.

4.4 Discussion

4.4.1 Choice of the scaling technique for cost-effectiveness analysis

Preference-based scaling techniques were administered successfully in healthy individuals and cardiac patients. However, they were long to administer (mean time of 41 minutes) and were sometimes difficult for the interviewers and the respondents.

The psychometric properties of the preference-based scaling techniques, among healthy participants with and without treatment for dyslipidemia, and CHD patients, were similar to previous reports. Their reliability was acceptable and the correlations with nonpreference-based HRQOL measures varied from poor to moderate. Although we modified the SG and the TTO assessments to increase their ability to detect small differences, their discriminant ability was still poor compared to the SF-36 GHP subscale and the RS. They had difficulties differentiating CHD patients with different severities of physical disability, CHD patients and Healthy participants, and were unable to distinguish participants reporting different numbers of health problems.

Similar poor discriminant ability of the TTO and the SG were reported previously among CHD patients [151] and patients at different stages of HIV infection. [147,161] There is, however, no consensus regarding the interpretation of this finding. For Nease et al. [151] this reflects the fact that people may have different attitudes toward similar health conditions, leading to **large variation** of the preference-based scores within groups of participants with similar health. In other words, the same condition and symptoms may be valued differently by different people. This creates large variations of preference-based scores within groups and reduces the ability to discriminate between groups. For Nease et al. "the variation in patients' utilities

reflects **true differences** in how patients with similarly severe symptoms feel about those symptoms". They suggest that "guidelines for the management of ischemic heart disease should be based on the preferences of the individual patient rather than on symptom severity alone".

This interpretation can be questioned for two reasons. First, the lack of discriminant ability is not only explained by the large variation of the preference-based scores within groups, but also by the presence of an important ceiling effect. Second, there is no empirical data to support the hypothesis that TTO and SG scores are representative of the respondents true preferences.

In several studies, including this one, high values or utilities were obtained from respondents affected by serious health conditions, such as HIV [162], CHD [151], intermittent claudication [100] and advanced symptomatic cancer patients [145,182]. This ceiling effect may reduce considerably the ability of these scaling techniques to discriminate between less severely disabled patients.

Fowler et al. [185] have indirectly demonstrated that this ceiling effect may be related to the participant's reluctance to give up and may be partially responsible for the poor discriminant ability of the TTO and SG. They described the relationship between the "desire to be resuscitated", the "reluctance to give up" and the respondent's health status, among HIV-infected patients. The desire to be resuscitated was assessed by asking the respondents if they would want to be revived if their heart stopped today. To measure the respondents' reluctance to give up, they asked them if they would want a treatment to extend their life if they would 1) feel nauseous almost all the time, 2) be fed through a tube all the time, 3) be blind, 4) be on a respirator and finally if they would want a treatment that would make them feel worse all the time but might prolong their life. The respondents' health status was evaluated using an overall rating of their health and various self reports of symptoms

and health. They found an inverse relationship between the health status and the desire to be revived. However, this relationship was significant among patients with low reluctance to give up and was not significant for patients with medium and high reluctance to give up.

Although this study did not directly assess the relationship between the participant's health status and TTO and SG scores, it demonstrates that factors other than the respondent health state are considered when questions involving life or death issues are asked. For this reason, "for people reluctant to say they would give up any life at all, questions based on the risk of dying or willingness to give up years of life are likely to be poor measures of the values of health states".

Proponents of the preference-based measures may argue that if people are not willing to give up their life expectancy or are not willing to risk an immediate death to benefit from a better HRQOL, then it may not be appropriate to quality-adjust these health states in a cost-effectiveness study. This would be a convincing argument for using TTO or SG scores as quality weight in cost-effectiveness analyses, only if we could demonstrate that TTO and SG are indicators of the true or actual participants preference. Unfortunately, to our knowledge, there is no empirical data supporting this hypothesis. One study [189], measuring patients' values for future anaesthesia during childbirth, reported that women's preferences during active labour and transition phase of labour were unrelated to their postpartum preferences. Furthermore, the SG and the TTO may not describe adequately true patients preference due to their inability to structure health decisions and to represent decisional processes in a realistic fashion.

For example, in real life situations, treating dyslipidemia does not abolish the risk of dying immediately but reduces the risk of eventually developing or dying from a CHD event. Similarly, the TTO assessment suggests that ignoring dyslipidemia

will automatically reduce the participant's life expectancy. However, in real life, not treating dyslipidemia may simply increase the probability of dying sooner. In a context where preference-based measures have been shown to be influenced by context dependent variables, we may question the ability of these scaling techniques to reproduce the participants' actual preferences.

Finally, in real life situations, important decisions may require time and are often taken after consultations with health professionals, family members and friends. TTO and SG require the respondent to make a decision in a very short period of time without consultations. In this artificial context, it is far from obvious that the measured responses correspond to the patients' actual preferences.

Empirical studies are certainly needed to test the hypothesis that preference-based measures obtained with TTO and SG scaling techniques are good indicators of patients actual preferences. For the present time, the use of simpler preference-based technique more representative of the participants' health status, such as the RS, is justified.

4.4.2 Preference-based measures in CHD prevention

Our results clearly demonstrate that people with Dyslipidemia treatment did not perceive their HRQOL as being as good as the Healthy participants as seen by the results of the SF-36 GHP subscale and the RS. This is unlikely to be due to confounding by age, gender or comorbidity. For the Dyslipidemia participants this may be related to their cholesterol problem, as seen by a "dose-response" type of relationship described between the expected cholesterol level and either the SF-36 GHP subscale and the preference-based measures. It may also be influenced by the time since the diagnosis of dyslipidemia and the type of dyslipidemia therapy.

This study has several strengths. For the first time, the HRQOL of patients with CHD conditions or dyslipidemia was assessed in a large sample of individuals using standardized preference-based scaling measures. The psychometric properties of the preference-based instruments in this population were consistent with current literature. In addition, a large "control" group, consisting of healthy participants without dyslipidemia, was included to better judge the impact of dyslipidemia on the HRQOL. Extensive effort was made to control for potential confounders at the design and the analysis stages.

However, our results may be subject to a selection bias due to the fact that the participants were solicited at two university teaching hospitals at the time of their physician visit. Furthermore, we may have reduced our ability to generalise our results by applying strict eligibility criteria.

From a public health point of view, a two to three point reduction in the HRQOL with dyslipidemia is extremely important and could significantly influence the results of a cost-effectiveness analysis of CHD prevention.

From an individual point of view, a three-point reduction of the HRQOL with dyslipidemia is certainly small but comparable to the negative effects of treating hypertension. As discussed previously, hypertension was associated with significant negative psychological and behavioural effects on patients. Similar effects with dyslipidemia remain to be demonstrated.

In summary, this study provides preference-based measures for evaluating the cost-effectiveness of detecting and treating dyslipidemia to prevent CHD and suggests that the impact of dyslipidemia on the participants' HRQOL may be small but significant from a public policy point of view. Further research should be done confirming these results and elucidating the causes and the impact of this negative

effect on HRQOL.

4.4.3 Advantages and disadvantages of using "standardized" interview strategies to elicit preference-based weights for QALY analyses?

One important aspect of this research was the use of a "standardized" interview strategy to elicit preference-based weights for QALY analyses. We standardized the preference-based assessments across the study groups by using the same measurement strategy, scaling techniques, source population, order of presentation of the scaling techniques, amount of detail and format of the health state descriptions, as well as by using the same interviewing material and visual aids. We also maximized the convergence between the scaling techniques by specifying and keeping constant, for each participant, the duration of the health state under evaluation and its prognosis.

Using standardized procedures increased the internal validity of this study. The preference-based HRQOL measures may be influenced by each of the methodologic issues described above. However, by using a standardized methodology across the study groups we reduced the likelihood of introducing a differential bias. Consequently, we are confident that the observed differences between the study groups can not be attributed to methodologic differences in the preference-based assessments.

The Panel of Cost-Effectiveness in Health and Medicine [3,99,190] recommended the use of standardized methodology to perform cost-effectiveness analysis. They defined the reference case as a standard set of methods and assumptions to be used in cost-effectiveness analyses. The reference case serves as a point of comparison across studies and therefore, increase the ability to compare the cost-effectiveness of

various treatments or programs for different health conditions and illnesses.

In this study, decisions regarding the selection of methodologic issues mentioned above were based on available empirical data and on practical considerations specific to this research project. We did not comply with all the recommendations of the Panel on the Cost-Effectiveness in Health and Medicine. [3,99] For example, the expert panel recommended that preference weights be based on community preferences for the reference case analysis. [3,190] However, for this project, because there were no convincing empirical data supporting the hypothesis that dyslipidemia could negatively impact the HRQOL of diagnosed individuals, it was necessary to first test this hypothesis among individuals with dyslipidemia. For this reason, we used patients as the source population. Compared to a reference case analysis, a cost-effectiveness analysis using the quality weights obtained in this study may overestimate the effectiveness of dyslipidemia treatment (see discussion in section 3).

The expert panels also recommended to use a generic health-state classification system (the decomposed approach as described in section 2.3.1.2) to measure the quality weights. [3] However, as discussed in section 2.3.1.2, in these classification systems, the health-related quality of life aspects relevant to participants with dyslipidemia were either missing or not described with sufficient detail to allow adequate discrimination of healthy participants with and without dyslipidemia treatment. Consequently, we decided to use the holistic approach. It is difficult, however, to predict in what direction choosing an holistic approach may influence the cost-effectiveness ratio when compared to a reference case analysis because only a few studies have compared the results obtained from an holistic and a decomposed measurement strategies. [100, 83]

In conclusion, we improved the internal validity of this study by using a

standardized methodology to measure the quality weights for each health state. This will allow a fair assessment of the incremental cost-effectiveness of detecting and treating dyslipidemia in the primary prevention of CHD. However, because we did not comply with the methodologic criteria of a reference case analysis we may have limited our ability to compare directly the cost-effectiveness of dyslipidemia treatment with those of other reference case studies.

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6. *Appendix I*

6.1 Explicit statement of responsibilities

My thesis committee was composed of Dr. Steven A. Grover (thesis supervisor), Dr. Ann E. Clarke and Dr. Lawrence Joseph. They all reviewed the research proposal, research protocol, interview questionnaires and manuscripts and have made several important suggestions and editorial comments.

Todd Mackenzie, as a PhD student, collaborated to the statistical analysis. More specifically he 1) computed and drew the box plots for the test-retest reliability evaluation (section 3.2), 2) computed the mean absolute difference between the test and the retest (section 3.2), 3) drawn the box plots of the SF-36 General Health Perception subscale and the preference-based measures for patients with different physical disability (section 3.2) and 4) read all three manuscripts and made editorial comments.

Members of The Canadian Collaborative Cardiac Assessment Group* collaborated to this research by allowing us to interview their patients.

Three research assistants, Martine LeConte, Robert Darsigny and Jessica Hand, collaborated in this project by soliciting and interviewing participants and by

---

* Including: LE Cassidy, MD, L Green, MD, D Larochelle, DT P, R Motchula, DT P, J McCans, MD, PJ McLeod, MD, R Repa Fortier, DT P, JA Stewart, MD from The Montreal General Hospital and DW Blank, MD, F Charbonneau, MD, BM Gilfix, MD, M Sami, MD, M. Sherman, MD, and M Smilovitch, MD from the Royal Victoria Hospital, Montreal, Quebec, Canada.

entering and cleaning the data. In addition, Robert Darsigny collaborated in the preparation of computer data entry and cleaning program. Under my supervision, Steven Paquet, a statistician, wrote a computer program to verify the order of presentation of the Time Trade-off and Standard Gamble choices and the computation of the final Time Trade-off and Standard Gamble scores.

My role consisted of:

- Preparing and submitting the research proposal to the Dairy Farmers of Canada to obtain financial support.
- Writing the research protocol.
- Writing the interview questionnaire, including the development and pilot testing of the visual aids to administered the Standard Gamble and the Time Trade-off measures.
- Training and supervising the research assistants.
- Soliciting and interviewing about 30% of the participants.
- Supervising the data entry and cleaning.
- Performing all the statistical analysis with the exception of those done by Todd Mackenzie.
- Writing the manuscripts for publication.
- Writing and submitting this thesis.

You will find attached a list of all co-authors of all three articles and the release form from each of them.

6.2 List of authors

Article No. 1: TITLE: Measuring the impact of primary preventive intervention on the health-related quality of life: can we improve the sensitivity of Standard Gamble?

1. **L. Lalonde**, Department of Epidemiology and Biostatistics, McGill University, and the Division of Clinical Epidemiology, The Montreal General Hospital, Montréal, Québec
2. **Ann E. Clarke**, Department of Medicine, McGill University, and the Department of Clinical Immunology and Allergy, The Division of Clinical Epidemiology, The Montreal General Hospital, Montréal, Québec
3. **Lawrence Joseph**, Department of Epidemiology and Biostatistics and the Department of Mathematics and Statistics, McGill University, and The Division of Clinical Epidemiology, The Montreal General Hospital, Montréal, Québec
4. **Todd Mackenzie**, Department of Mathematics and Statistics, McGill University, Montréal, Québec
5. **Steven A. Grover**, Department of Epidemiology and Biostatistics, Department of Medicine, McGill University, and The Division of Clinical Epidemiology, The Centre for the Analysis of Cost-effective Care, The Division of General Internal Medicine, The Montreal General Hospital, Montréal, Québec
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   DW Blank, MD, F Charbonneau, MD, BM Gilfix, MD, M Sami, MD, M. Sherman, MD, and M Smilovitch, MD from the Royal Victoria Hospital, Montreal, Quebec, Canada.

Article No. 2: TITLE: Comparing the psychometric properties of preference-based and nonpreference-based health-related quality of life measures in coronary heart disease prevention and treatment

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6. **The Canadian Collaborative Cardiac Assessment Group** included:
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Article No. 3: TITLE: Health-related quality of life measures in coronary heart disease prevention and treatment

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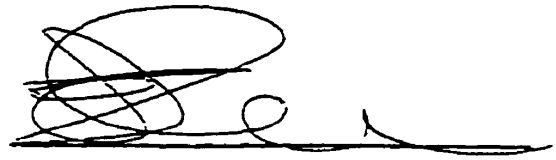
This represents an accurate count of the authors and articles submitted.

Lyne Lalonde, B. Pharm, MSc

Student



Steven A. Grover, MD

Thesis supervisor

6.3 Release forms

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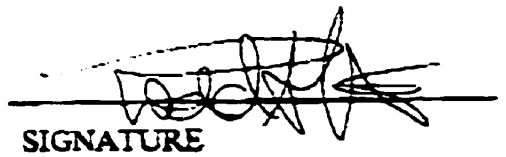

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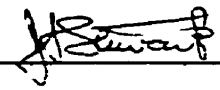

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7. *Appendix II*

7.1 Translation and adaptation of questionnaires

All interviews were conducted in French or in English according to the participant's most familiar language. We used, with permission (see copy of the user agreement in section 7.4), the French and English-Canadian versions of the SF-36 Health Survey. [164]

The Specific Activity Scale (SAS) was available only in English (American) [180] and French (European) [181] versions. We adapted the American version for use in Canada by reporting distances in miles and kilometres and by reporting weight in pounds and kilograms. Adaptation of the French European version to French Canadian was judged necessary to be consistent with Québec "common language". For example, the question "Pouvez-vous passer la serpillière?" was replaced by "Pouvez-vous laver les planchers?".

The health state scenarios used for the Preference-based assessments were first translated from English to French and then from French to English by two bilingual coworkers. The initial and final English versions were compared by a group of three persons and were judged very similar.

Written French and English questionnaires were used to administer the Rating

Scale (RS), the Time Trade-off (TTO) and the Standard Gamble (SG). The English version was very similar to the questionnaire reproduced in the "Guide to design and development of health-state utility instrumentation". [107] The English questionnaire was translated by the investigator (L. Lalonde) and reviewed by the three interviewers.

7.2 Influence of the respondent's first and current language on the Preference-based measures

We assessed the influence of the respondent's first and current language on the Preference-based measures for the hypothetical health state "blindness". The participant's current language (language usually spoken at home) did not explain a statistically significant proportion of the variance of the Preference-based measures for blindness in a subgroup of 522 subjects. [191] The participant's first language (French only, English only, other) explained a statistically significant proportion of the variance of the TTO ($p = 0.0001$) and SG ($p = 0.0001$) scores for blindness. However, the participant's first language explained less than 5% of the TTO or SG variance. The adjusted mean TTO and SG scores from respondents reporting English as their first language were higher (TTO = 0.43 and SG = 0.42) than those obtained from participants reporting French as their first language (TTO = 0.32 and SG = 0.31) and those reporting another language (TTO= 0.28 and SG = 0.30). However, other indicators of cultural differences such as the place of birth, religion or participation in religious services were not significant predictors of Preference-based measures. This analysis provided no evidence for the impact of cultural differences on the Preference-based assessments with the exception of the participant's first language.

Among the entire study sample (n=878), the proportion of participants

reporting English as their first language varied from 34% to 46% (see Table 7.2.1) and represents the largest proportion of participants in each group with the exception of the Congestive Heart Failure group. Among the Congestive Heart Failure group, French was reported as the most common first language. The most frequent current language was English in each study group, with the exception of the Congestive Heart Failure group where French and English were reported by an equal number of participants.

Multivariate linear analyses were created to describe the Preference-based scores as a function of the study group, the number of comorbid conditions reported by participants, the participant's current language and the participant's first language. In these models, the participant's first language explained a statistically significant proportion of the RS variance ($p=0.002$) but was not a significant predictor of the TTO and SG scores. The participant's current language was never found to be statistically significant. As reported in Table 7.2.2, the mean Preference-based scores adjusted for the comorbidity and the participant's first and current language were very similar to the mean scores adjusted for the comorbidity only (Table 3.3.2).

The role of cultural differences in the assessment of Preference-based measures was evaluated in two analyses. The first analysis, evaluating the Preference-based measures for blindness, suggested that cultural differences were not important predictors of Preference-based measures. In these analysis, only the participant's first language was a significant predictor of the TTO and SG scores. In the second analysis, we demonstrated that the participant's first and current language did not confound the observed differences between the Preference-based scores reported by the Healthy, the Dyslipidemia and the coronary heart disease groups. Following these analyses, we felt confident about combining the language groups for presentation in the articles.

Table 7.2.1 • Distribution of the participant's first and current language in each study group

	First language[§]			Current language[¶]		
	French only	English only	Other	French	English	Other
Healthy	93 (30%)	142 (46%)	72 (24%)	84 (27%)	170 (55%)	53 (17%)
Dyslipidemia	58 (23%)	115 (46%)	75 (30%)	52 (21%)	142 (57%)	55 (22%)
Angina and/or Myocardial Infarction	97 (35%)	109 (39%)	74 (26%)	95 (34%)	135 (48%)	50 (18%)
Congestive Heart Failure	18 (51%)	12 (34%)	5 (14%)	15 (43%)	15 (43%)	5 (14%)

§ As assessed by the English question: What is your first language? and the French question: Quelle est la première langue que vous avez apprise?

¶ As assessed by the English question: What language do you usually speak at home? and the French question: Quelle langue parlez-vous habituellement à la maison?

Table 7.2.2 • **Mean valuational scores adjusted for the number of comorbid conditions reported by the participants and the participant's first and current language**

	Rating Scale	Time Trade-off	Standard Gamble
Healthy	89.5	89.4	94.2
Dyslipidemia	86.8	89.7	94.4
Angina and/or Myocardial Infarction	79.5	85.5	87.3
Congestive Heart Failure	59.0	78.0	78.2

7.3 Authorization for using the various questionnaires

Prior to conduct this cross-sectional study, we obtained the authorization to use the French and English Canadian versions of the SF-36 Health Survey, the Specific Activity Scale and the Feeling Thermometer. You will find attached, copy of those authorizations.

McGill

Sharon Wood-Dauphinee, Ph.D., P.T.

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January 23, 1995

Lyne Lalonde, B. Pharm, M.Sc.
Division of Clinical Epidemiology
Montreal General Hospital

Dear Ms. Lalonde,

Thank you for your letter of January 17, 1995 requesting to become a registered user of the French Canadian Version of the MOS 36 Item Short-Form Health Survey (SF-36). As you can see from the attached, I have included the French Canadian Version of the form for your use. I have also included a User Agreement which I have signed. I would ask that you sign it and provide the information requested, make yourself a photostatted copy, and send the signed version off to:

Dr. John E. Ware, Jr.,
The Health Institute - Division of Health Improvement
New England Medical Center Hospitals
Box #345 - 750 Washington St,
Boston, MA 02111 USA

If you are not a registered user of the English form, I also suggest that you request permission to be a registered user for that form. There is no cost associated with this nor do you have to agree to share data. It simply means that they know you are using the form in a study and will provide you with updated material as changes occur in the measure or as new information becomes available about it. In addition, you may want to order a Manual for interpretation and scoring from Barbara Gandek at the same address.

Sincerely,

Sharon Wood-Dauphinee, PhD, PT
Professor
Director, School of Physical and Occupational Therapy
Associate Dean (Rehabilitation Science), Faculty of Medicine

SWD/ph

THE MOS 36-ITEM SHORT-FORM HEALTH SURVEY (SF-36) USER AGREEMENT, French-Canadian Test Version

This Agreement is between New England Medical Center Hospitals, Inc. ("NEMCH") and LYNE LALONDE ("User"). NEMCH hereby grants User a nonexclusive, royalty free, paid up, limited license to use: (1) the French-Canadian test version of the MOS 36-Item Short-Form Health Survey (SF-36™) in an approved format and (2) the documentation for administering and scoring the SF-36 (Basic Scoring Algorithms) based upon the following conditions:

1. User shall not modify, abridge, condense, translate, adapt, recast, or transform the SF-36 or the Basic Scoring Algorithms in any manner or form, including but not limited to any minor or significant change in wording or organization of the SF-36;

2. User shall not reproduce the SF-36 or the Basic Scoring Algorithms except for the limited purpose of generating sufficient copies for its own uses and shall in no event distribute copies of the SF-36 or the Basic Scoring Algorithms to third parties by sale, rental, lease, lending, or any other means;

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In consideration of the rights granted by NEMCH to User hereunder, User agrees to provide NEMCH with a brief annual update regarding whether and for what purpose the SF-36 is used. The term of this User Agreement shall be for a period of one year commencing on the date indicated below provided, however, NEMCH may terminate this User Agreement any time in the event: (i) User fails to submit the annual update to NEMCH regarding its use of the SF-36 and the Basic Scoring Algorithms; or (ii) user breaches any term of this User Agreement. Should NEMCH terminate this User Agreement, User shall immediately cease all use of the SF-36 and the Basic Scoring Algorithms and shall destroy or return all unused copies of the SF-36 to NEMCH. NEMCH retains all rights in the SF-36 and the Basic Scoring Algorithms, including but not limited to all rights under copyright and trademark, not expressly licensed hereunder.

This User Agreement shall be construed and enforced in accordance with the domestic substantive laws of the Commonwealth of Massachusetts without regard to any choice or conflict of laws, rule or principle that would result in the application of the domestic substantive law of any jurisdiction. The rights and obligations of the parties set forth above are subject to all applicable state and Federal law and regulation. Neither party shall be entitled to exercise rights granted to it hereunder if such exercise would violate any applicable state or Federal law or regulation. In addition, no party shall be liable to the other party or to any third person for its breach of this Agreement if such party's satisfaction of its obligation hereunder would put such party in violation of any such applicable state or Federal law or regulation.

FORMAT: ☒ Standard or ☐ Alternate Approved (copy attached)

NEMCH Inc.

BY: _____
John E. Ware, Jr., Ph.D.
Director
International Quality of Life
Assessment Project (IQOLA)

BY: S Wood Dauphinee
Sharon Wood-Dauphinee, Ph.D.
National Principal Investigator

DATE: 3/14/95

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January 17, 1995

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Alvin R. Tarlov, MD
President, Medical Outcomes Trust
20 Park Plaza, Suite 1014
Boston, MA 02116-4313
U.S.A.

Dear Dr. Tarlov:

This letter is to inform you that we will be using the SF-36 Health Survey in a research project designed to assess the cost-utility of dietary prevention of coronary heart disease.

We are planning to measure the utility of dietary prevention and four CHD states (angina, coronary insufficiency, myocardial infarction, and congestive heart failure) by the standard gamble and the time trade-off methods. The SF-36 Health Survey, as well as other instruments, will be used to assess the construct validity of the utility assessment.

The principal investigators of this project are:

Ann Clarke, MD, MS and Steven A. Grover, MD, MPA, FRCPC
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If you need additional information please do not hesitate to contact us.

Sincerely,

Lyne Lalonde, B.Pharm, M.Sc.
Research Coordinator

c.c.: A. Clarke
S.A. Grover

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Alvin R. Tarlov, MD, President

September 9, 1994

Ann Clarke, M.D., MS
Assistant Professor
Department of Medicine
The Montreal General Hospital
1650 Cedar Avenue
Montreal Quebec H3G 1A4
CANADA

Dear Dr. Clarke:

The Medical Outcomes Trust is please to provide the enclosed information about the **SF-36 Health Survey** as requested in your letter dated September 1, 1994.

We are pleased, by this letter, to grant permission to you to use the **U.S., Canadian-English and U.K. versions of the SF-36 Health Survey, as well as the Consumer/Patient Satisfaction Surveys**. Enclosed are copies of both the more commonly used 4-week recall format and the acute 1-week recall format, either of which you may reproduce for your use. Also enclosed is a copy of *How to Score the SF-36 Health Survey*, published by the Medical Outcomes Trust, as well as reprints of publications that may be of interest to you. The scoring algorithms printed in *How to Score the SF-36 Health* Survey should be used for translations of the **SF-36 Health Survey.** Foreign language versions of this document are forthcoming.

If you should decide to use the **SF-36 Health Survey**, we ask that you simply provide us with a brief description of the work for which the instrument will be used and the name of the person in charge of the trial/study, if you have not already done so. The Trust in this way can be informed of progress in the field, be alert to the need for new technology and information, promote standardization, and generally serve to advance the field. We will put you on our mailing list and you will receive copies of the Medical Outcomes Trust Bulletin (enclosed) which is published six times a year, as well as other information.

When reproducing the **U.S. SF-36 Health Survey** please include an identifier as follows:

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When reproducing translations of the **SF-36 Health Survey** please include an identifier as follows:

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If you add any questions to it, as we and other users often do, or embed I in a larger questionnaire, please give the larger questionnaire its own name and indicate the following in small type anywhere on the form including at the end: *This questionnaire includes the SF-36 Health Survey, item numbers X to Y in this questionnaire, Reproduced with permission of the Medical Outcomes Trust, Copyright © 1992.* Foreign language users should change the copyright date to 1994.

If for any reason you change the wording of any part of the **SF-36 Health Survey**, or delete any questions or responses, please do not refer to it as the **SF-36 Health Survey**. This is for purposes of standardization of content, scoring, and labeling. We wish to assure users that the designation **SF-36 Health Survey** refers to the identical instrument and scoring rules in all cases. This will allow comparison of scores across multiple reports.

Two books related to the Medical Outcomes Study and to the **SF-36 Health Survey** have been published commercially. *Measuring Functioning and Well-Being: The Medical Outcomes Study Approach*, Stewart, A.L. and Ware, J.E. Jr., Editors, Duke University Press, 1992; and *SF-36 Health Survey: Manual and Interpretation Guide*, Ware, J.E. Jr., Snow, K.K., Kosinski, M., and Gandek, B., The Health Institute, New England Medical Center, Boston, Massachusetts.

We wish you the best of good fortune in pursuing your goals with the **SF-36 Health Survey**. Please contact us if we can be of further assistance.

Respectfully,

Alvin R. Tarlov
President

Enclosures

BRIGHAM AND WOMEN'S HOSPITAL

Harvard Medical School

Thomas H. Lee, M.D., S.M.
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April 10, 1995

Lyne Lalonde, B. Pharm, M.Sc.
Montreal General Hospital
1650 Cedar Avenue
Montreal, Quebec H3G 1A4

Dear Ms. Lalonde:

Lee Goldman forwarded to me your letter requesting permission to use our version of the Specific Activity Scale. I am enclosing a copy. We do not have a French version. Dr. Goldman indicates to me that there is no problem if you would like to use this form or to translate it.

Yours truly,

Thomas H. Lee, MD

enclosure
/gr

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January 20, 1995

Ms. Lyne Lalonde
Division of Clinical Epidemiology
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(514) 937-6011, ext. 4732
FAX (514) 934-8293

Dear Ms. Lalonde:

RE: Use of Feeling Thermometer in Cost-Utility Analysis for Coronary Heart Disease

Thank you for your letter of January 17, 1995. I am pleased to provide you with permission to use the Feeling Thermometer as described in CHEPA Working Paper 90-9. My colleagues and I would be interested in the results of your preference measurements using the Feeling Thermometer, Time Tradeoff, and Standard Gamble. Good luck in your study!

Sincerely yours,

David Feeny
Professor of Economics and
Clinical Epidemiology and Biostatistics

7.4 Copies of the questionnaires

You will find attached a copy of the French and English Canadian versions of the SF-36 Health Survey, the adapted French and English versions of the Specific Activity Scale, the French and English questionnaires used to administer the RS, TTO and SG, and the Health State Descriptions in French (for the English version of the health state descriptions refer to Table 3.1.1).

N° du sujet	Initiales du sujet	**Hôpital général de Montréal** **Enquête sur l'évaluation de la qualité de vie**
/ / / / /	/ / / /	

SF-36

DIRECTIVES: Les questions qui suivent portent sur votre santé, telle que vous la percevez. Vos réponses permettront de suivre l'évolution de votre état de santé et de savoir dans quelle mesure vous pouvez accomplir vos activités courantes.

Répondez à toutes les questions en suivant les indications qui vous sont données. En cas de doute, répondez de votre mieux.

1. En général, diriez-vous que votre santé est:

(encerclez une seule réponse)

Excellente 1

Très bonne 2

Bonne 3

Passable 4

Mauvaise 5

2. Par comparaison à l'an dernier, comment évaluez-vous, maintenant, votre santé générale?

(encerclez une seule réponse)

Bien meilleure maintenant que l'an dernier 1

Un peu meilleure maintenant que l'an dernier 2

À peu près la même que l'an dernier 3

Un peu moins bonne maintenant que l'an dernier 4

Bien moins bonne maintenant que l'an dernier 5

3. Les questions suivantes portent sur les activités que vous pourriez avoir à faire au cours d'une journée normale. Votre état de santé actuel vous limite-t-il dans ces activités? Si oui, dans quelle mesure?

(encerclez un seul chiffre par ligne)

ACTIVITÉS	Mon état de santé me limite beaucoup	Mon état de santé me limite un peu	Mon état de santé ne me limite pas du tout
a. Dans les activités exigeant un effort physique important comme courir, soulever des objets lourds, pratiquer des sports violents	1	2	3
b. Dans les activités modérées comme déplacer une table, passer l'aspirateur, jouer aux quilles ou au golf	1	2	3
c. Pour soulever ou transporter des sacs d'épicerie	1	2	3
d. Pour monter plusieurs étages à pied	1	2	3
e. Pour monter un seul étage à pied	1	2	3
f. Pour me pencher, me mettre à genoux ou m'accroupir	1	2	3
g. Pour faire plus d'un kilomètre à pied	1	2	3
h. Pour faire plusieurs coins de rue à pied	1	2	3
i. Pour marcher d'un coin de rue à l'autre	1	2	3
j. Pour prendre un bain ou m'habiller	1	2	3

4. Au cours des quatre dernières semaines, avez-vous eu l'une ou l'autre des difficultés suivantes au travail ou dans vos autres activités quotidiennes à cause de votre état de santé physique?

(encerclez un seul chiffre par ligne)

	OUI	NON
a. Avez-vous dû consacrer **moins de temps** à votre travail ou à d'autres activités?	1	2
b. **Avez-vous accompli moins** de choses que vous l'auriez voulu?	1	2
c. Avez-vous été limité(e) dans la **nature** de vos tâches ou de vos autres activités?	1	2
d. Avez-vous eu **de la difficulté** à accomplir votre travail ou vos autres activités (par exemple vous a-t-il fallu fournir un effort supplémentaire)?	1	2

5. Au cours des quatre dernières semaines, avez-vous eu l'une ou l'autre des difficultés suivantes au travail ou dans vos autres activités quotidiennes à cause de l'état de votre moral (comme le fait de vous sentir déprimé(e) ou anxieux(se))?

(encerclez un seul chiffre par ligne)

	OUI	NON
a. Avez-vous dû consacrer **moins de temps** à votre travail ou à d'autres activités?	1	2
b. Avez-vous **accompli moins** de choses que vous l'auriez voulu?	1	2
c. Avez-vous fait votre travail ou vos autres activités avec **moins de soin** qu'à l'habitude?	1	2

6. Au cours des quatre dernières semaines, dans quelle mesure votre état physique ou moral a-t-il nui à vos activités sociales habituelles (famille, amis, voisins ou autres groupes)?

(encerclez une seule réponse)

Pas du tout 1

Un peu 2

Moyennement 3

Beaucoup 4

Enormément 5

7. Au cours des quatre dernières semaines, avez-vous éprouvé des douleurs physiques?

(encerclez une seule réponse)

Aucune douleur 1

Douleurs très légères 2

Douleurs légères 3

Douleurs moyennes 4

Douleurs intenses 5

Douleurs très intenses 6

8. Au cours des quatre dernières semaines, dans quelle mesure la douleur a-t-elle nui à vos activités habituelles (au travail comme à la maison)?

(encerclez une seule réponse)

Pas du tout 1

Un peu 2

Moyennement 3

Beaucoup 4

Enormément 5

9. Ces questions portent sur les quatre dernières semaines. Pour chacune des questions suivantes, donnez la réponse qui s'approche le plus de la façon dont vous vous êtes senti(e).

Au cours des quatre dernières semaines, combien de fois:

(encerclez un seul chiffre par ligne)

	Tout le temps	La plupart du temps	Souvent	Quelquefois	Rarement	Jamais
a. Vous êtes-vous senti(e) plein(e) d'entrain (de pep)?	1	2	3	4	5	6
b. Avez-vous été très nerveux(se)?	1	2	3	4	5	6
c. Vous êtes-vous senti(e) si déprimé(e) que rien ne pouvait vous remonter le moral?	1	2	3	4	5	6
d. Vous êtes-vous senti(e) calme et serein(e)?	1	2	3	4	5	6
e. Avez-vous eu beaucoup d'énergie?	1	2	3	4	5	6
f. Vous êtes-vous senti(e) triste et abattu(e)?	1	2	3	4	5	6
g. Vous êtes-vous senti(e) épuisé(e) et vidé(e)?	1	2	3	4	5	6
h. Vous êtes-vous senti(e) heureux(se)?	1	2	3	4	5	6
i. Vous êtes-vous senti(e) fatigué(e)?	1	2	3	4	5	6

10. Au cours des quatre dernières semaines, combien de fois votre état physique ou moral a-t-il nui à vos activités sociales (comme visiter des amis, des parents, etc.)?

(encerclez une seule réponse)

Tout le temps 1

La plupart du temps 2

Parfois 3

Rarement 4

Jamais 5

11. Dans quelle mesure chacun des énoncés suivants est-il VRAI ou FAUX dans votre cas?

(encerclez un seul chiffre par ligne)

	Tout à fait vrai	Plutôt vrai	Ne sais pas	Plutôt faux	Tout à fait faux
a. Il me semble que je tombe malade un peu plus facilement que les autres	1	2	3	4	5
b. Je suis en aussi bonne santé que les gens que je connais	1	2	3	4	5
c. Je m'attends à ce que ma santé se détériore	1	2	3	4	5
d. Ma santé est excellente	1	2	3	4	5

Subject number	Subject initials	Montreal General Hospital Quality of Life Assessment Survey
/ / / / /	/ / / /	

SF-36

INSTRUCTIONS: This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is:

(circle one)

Excellent 1

Very good 2

Good 3

Fair 4

Poor 5

2. Compared to one year ago, how would you rate your health in general now?

(circle one)

Much better now than one year ago 1

Somewhat better now than one year ago 2

About the same as one year ago 3

Somewhat worse now than one year ago 4

Much worse now than one year ago 5

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

(circle one number on each line)

ACTIVITIES	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
a. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
c. Lifting or carrying groceries	1	2	3
d. Climbing **several** flights of stairs	1	2	3
e. Climbing **one** flight of stairs	1	2	3
f. Bending, kneeling, or stooping	1	2	3
g. Walking **more than a kilometre**	1	2	3
h. Walking **several blocks**	1	2	3
i. Walking **one block**	1	2	3
j. Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(circle one number on each line)

	YES	NO
a. Cut down on the **amount of time** you spent on work or other activities	1	2
b. **Accomplished less** than you would like	1	2
c. Were limited in the **kind** of work or other activities	1	2
d. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(circle one number on each line)

	YES	NO
a. Cut down the **amount of time** you spent on work or other activities	1	2
b. **Accomplished less** than you would like	1	2
c. Didn't do work or other activities as **carefully** as usual	1	2

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

(circle one)

Not at all 1

Slightly 2

Moderately 3

Quite a bit 4

Extremely 5

7. How much bodily pain have you had during the past 4 weeks?

(circle one)

None 1

Very mild 2

Mild 3

Moderate 4

Severe 5

Very severe 6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

(circle one)

Not at all 1

A little bit 2

Moderately 3

Quite a bit 4

Extremely 5

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks -

(circle one number on each line)

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
a. Did you feel full of pep?	1	2	3	4	5	6
b. Have you been a very nervous person?	1	2	3	4	5	6
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
d. Have you felt calm and peaceful?	1	2	3	4	5	6
e. Did you have a lot of energy?	1	2	3	4	5	6
f. Have you felt downhearted and blue?	1	2	3	4	5	6
g. Did you feel worn out?	1	2	3	4	5	6
h. Have you been a happy person?	1	2	3	4	5	6
i. Did you feel tired?	1	2	3	4	5	6

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

(circle one)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

None of the time 5

11. How TRUE or FALSE is each of the following statements for you?

(circle one number on each line)

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
a. I seem to get sick a little easier than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

Échelle d'Activité Spécifique

		Un oui	Non
1.	Pouvez-vous descendre un étage d'escaliers sans vous arrêter?	Allez au #2	Allez au #4
2.	Pouvez-vous transporter quelque chose en montant un étage de 8 marches sans vous arrêter? Ou pouvez-vous: - Jardiner, râteler ou désherber - Faire du patin à roulettes ou danser (foxtrot) - Marcher d'un pas alerte (4 m/h ou 6 km/h) sur un terrain plat	Aller au #3	Classe III
3.	Pouvez-vous transporter au moins 22 livres (10 kg) en montant 8 marches? Ou pouvez-vous: - Transporter des objets lourds (min 80 livres / 35 kg) - Pelleter la neige ou bêcher la terre - Vous adonner à des loisirs tels que le ski, le basketball ou la squash - Jogger ou marcher 5 milles à l'heure (~ 8 km/h)	Classe I	Classe II
4.	Pouvez-vous prendre une douche sans vous arrêter? Ou pouvez-vous: - Changer des draps de lit - Laver les planchers ou les vitres - Étendre du linge - Marcher d'un pas tranquille (2.5 m/h ou 4 km/h) - Jouer aux quilles ou au golf - Pousser une tondeuse à gazon	Classe III	Aller au #5
5.	Êtes-vous capable de vous habiller sans vous arrêter?	Allez au #6	Classe IV
6.	Avez-vous des symptômes lorsque vous mangez, vous tenez debout, êtes calmement assis ou allongé?	Classe III	Classe IV

The Specific Activity Scale

		Any yes	No
1.	Can you walk down a flight of stairs without stopping?	Go to #2	Go to #4
2.	Can you carry anything up a flight of 8 steps without stopping? Or can you: - Garden, rake, or weed - Roller skate, or dance (foxtrot) - Walk at (4 m/h or 6 km/h) on ground level	Go to #3	Class III
3.	Can you carry at least 22 pounds (10 kg) up 8 steps? Or can you: - Carry heavy objects (min 80 pounds / 35 kg) - Shovel snow or spade soil - Do recreational activity such as skiing, basketball, or squash - Jog or walk 5 miles per hour (~8 km/h)	Class I	Class II
4.	Can you shower without stopping? Or can you: - Strip and make beds - Mop floors or clean windows - Hang washed clothes - Walk 2.5 miles per hour (4 km/h) - Bowl or play golf - Push a power lawn mower	Class III	Go to #5
5.	Are you able to get dressed without stopping?	Go to #6	Class IV
6.	Do you have symptoms when eating or standing, sitting or lying relaxed?	Class IV	Class III

N° du sujet	Initiales du sujet	Hôpital général de Montréal Enquête sur l'évaluation de la qualité de vie
/___/___/___/___/	/___/___/___/	

THERMOMÈTRE DES ÉTATS DE SANTÉ

Je vais maintenant vous poser des questions pour connaître votre opinion sur différents problèmes de santé. Pour ce genre de questions il n'y a pas de bonnes ou de mauvaises réponses. Je vais vous poser trois séries différentes de questions.

Pour la première série de questions, je vais vous demander de lire une carte qui décrit un état de santé. Vous devez vous imaginer ce que serait votre vie si votre santé était telle que décrite sur la carte à partir de maintenant et pour les **X** dernières années de votre vie. Je vais alors vous demander d'utiliser un thermomètre spécial pour me dire jusqu'à quel point vous pensez que cet état de santé est bon ou mauvais. Voici le thermomètre.

MONTRER LE THERMOMÈTRE AU RÉPONDANT.

Plus vous pensez qu'un état de santé est bon plus il devrait être haut sur le thermomètre.

INDIQUER AVEC VOTRE DOIGT LA PARTIE SUPÉRIEURE DU THERMOMÈTRE DE 50 À 100.

À l'opposé, plus vous pensez qu'un état de santé est mauvais, plus il devrait être bas sur le thermomètre.

INDIQUER AVEC VOTRE DOIGT LA PARTIE INFÉRIEURE DU THERMOMÈTRE DE 50 À 0.

Je vous demande maintenant de lire la première carte.

DONNEZ AU RÉPONDANT LA CARTE 1 (SANTÉ PARFAITE)

Cette carte décrit un état de santé parfait. C'est le meilleur état de santé que vous puissiez imaginer. Pour cette raison il est placé à l'extrémité la plus élevée du thermomètre. Ce qui à correspond un score de 100.

S'il-vous-plaît voulez-vous lire la deuxième carte.

DONNEZ AU RÉPONDANT LA CARTE 2 (DÉCÈS IMMÉDIAT)

Cette carte décrit un décès immédiat sans douleur. Pour les besoins de notre recherche il s'agit du pire état de santé que vous aurez à juger. Pour cette raison, il est placé à l'extrémité la plus basse du thermomètre. Ce qui correspond à un score de 0.

Je vais maintenant vous demander de lire une carte qui décrit un état de santé particulier. Cette fois je vais vous demander de m'indiquer où se situe cet état de santé sur le thermomètre.

DONNEZ AU RÉPONDANT LA CARTE 3 (ÊTRE AVEUGLE)

Q.1 Imaginez que vous allez vire les **X** dernières années de votre vie avec ce problème de santé. Où placeriez-vous ce problème de santé sur le thermomètre?

1. ___/___
8. NSP
9. NR ou R

Dans la première partie de l'entrevue vous m'avez fait part de vos problèmes de santé.

ÉNUMÉREZ LES PROBLÈMES DE SANTÉ

Je vais vous demander de tenir compte de votre santé en lisant cette carte

DONNEZ LA CARTE 4 (VOTRE SANTÉ ACTUELLE)

Q.2 Pouvez-vous me dire où se situe votre santé au cours des 4 dernières semaines sur le thermomètre?

1. ___/___
8. NSP
9. NR ou R

Q.3 Vous pouvez maintenant voir toutes vos réponses sur le thermomètre. Aimeriez-vous changer une ou plusieurs de vos réponses?

1. Oui — être aveugle: _____ santé actuelle: _____
2. Non
8. NSP
9. NR ou R

Q.4 D'après vous, quel est le pire état de santé?

1. être aveugle
2. santé actuelle
8. NSP
9. NR ou R

N° du sujet	Initiales du sujet	Hôpital général de Montréal Enquête sur l'évaluation de la qualité de vie
/___/___/___/___/	/___/___/___/	

PARI-TYPE

Pour chaque question je vais vous présenter deux choix; A et B. Vous devez me dire si vous préférez le choix A ou B ou si vous croyez que les deux sont égaux.

Le choix A est relativement simple. Il consiste à vivre en étant aveugle à partir de maintenant et pour les **X** prochaines années de votre vie après quoi vous allez mourir sans douleur. Il s'agit d'un choix certain, parce que si 100 personnes choisissent le choix A alors 100 personnes vont vivre en étant aveugle pour les **X** prochaines années après quoi elles vont toutes mourir sans douleur.

Le choix B est plus difficile parce qu'il est risqué. Si vous le choisissez vous pouvez soit vivre avec une santé parfaite pour les prochaines **X** années après quoi vous allez mourir sans douleur ou mourir immédiatement sans douleur. Par exemple, si la probabilité de vivre avec une santé parfaite pour **X** années est de 80% et la probabilité de mourir est de 20% ça signifie que si 100 personnes choisissent le choix B alors 80 vont vivre avec une santé parfaite et 20 vont mourir immédiatement sans douleur.

	Être aveugle	**Santé actuelle**

Imaginez qu'il vous reste **X** années à vivre. Si vous choisissez le choix A, vous allez vivre jusqu'à la fin de votre vie. Si vous choisissez le choix B, vous avez 0 % de chance de vivre avec une santé parfaite et 100% de chance de mourir immédiatement sans douleur.

Q.1 Préférez-vous le choix A ou B ou considérez-vous que les deux sont égaux?

1. A .... **présenter les choix en ordre**
2. B .... **p à ****
3. A = B .... **p à ****
8. NSP .... **p à ****
9. NR ou R .... **commentez et p à proc. section**

** Pour répondre à cette question vous devez regarder les diagrammes. Si 100 personnes choisissent le choix A, elles vont tous vivre avec jusqu'à la fin de leur vie; toutes les figures sont ombragées en gris pâle. Si elles choisissent le choix B, elles vont mourir immédiatement sans douleur parce que la probabilité de mourir immédiatement sans douleur est de 100% et la probabilité de vivre en santé parfaite est de 0%. Comme vous pouvez voir toutes les figures sont ombragées en gris foncé. Ainsi, si vous choisissez A vous allez vivre avec . Si vous choisissez B vous allez mourir immédiatement sans douleur.

Q.2 Si vous prenez en considération ces explications, préféreriez-vous le choix A ou B ou croyez-vous que les deux sont égaux?

1. A .... **présenter les choix en ordre**
2. B .... **p à ****
3. A = B .... **p à ****
8. NSP .... **p à proc. section**
9. NR ou R .... **commentez et p à proc. section**

** Votre réponse indique que pour vous mourir immédiatement sans douleur est mieux que vivre avec jusqu'à la fin de votre vie.

*** Votre réponse indique que pour vous vivre avec a la même valeur que mourir immédiatement sans douleur.

Q.3 Voulez-vous changer votre réponse?

1. Non .... **p à proc. section**
2. Oui .... **p à ****
8. NSP .... **p à proc. section**
9. NR ou R .... **commentez et p à proc. section**

** Cela veut dire que vous préférez le choix A. **PRÉSENTER LES CHOIX EN ORDRE**

ÊTRE AVEUGLE (Probabilité de santé parfaite)

1. _____	5. _____	9. _____	13. _____
2. _____	6. _____	10. _____	14. _____
3. _____	7. _____	11. _____	15. _____
4. _____	8. _____	12. _____	16. _____

SANTÉ ACTUELLE (Probabilité de santé parfaite)

1. _____	5. _____	9. _____	13. _____
2. _____	6. _____	10. _____	14. _____
3. _____	7. _____	11. _____	15. _____
4. _____	8. _____	12. _____	16. _____

	Être aveugle	**Santé actuelle**

Q.4 Mesure de l'utilité?

1. ______
8. NSP
9. NR ou R

		Être aveugle	Santé actuelle
Q.5	**UTILITÉ = 1** Vos réponses indiquent que vous ne voulez pas prendre le risque de mourir immédiatement sans douleur pour éviter de vivre avec [redacted] jusqu'à la fin de votre vie. Ceci est valable même si le risque de mourir immédiatement sans douleur était égale à 1%. Voulez-vous changer votre réponse? 1. Oui ..... **p à Q.9** 2. Non ..... **p à proc. section** 8. NSP ..... **p à proc. section** 9. NR ou R ..... **p à proc. section**		
Q.6	**INDIFFÉRENT** Vos réponses indiquent que si le risque de mourir immédiatement sans douleur était plus grand que **X %** vous préféreriez vivre avec [redacted] jusqu'à la fin de votre vie. Toutefois, si le risque de mourir immédiatement sans douleur était plus petit que **X %** vous préféreriez le choix B pour éviter de vivre avec [redacted] jusqu'à la fin de votre vie. Voulez-vous changer votre réponse? 1. Oui ..... **p à Q.9** 2. Non ..... **p à proc. section** 8. NSP ..... **p à proc. section** 9. NR ou R ..... **p à proc. section**		
Q.7	**PRÉFÈRE A** Vos réponses indiquent que vous refuseriez de prendre **X%** de risque de mourir immédiatement sans douleur pour éviter de vivre avec [redacted] jusqu'à la fin de votre vie. Toutefois, si le risque de mourir immédiatement sans douleur était plus petit que **X %** alors vous accepteriez le choix B. Voulez-vous changer votre réponse? 1. Oui ..... **p à Q.9** 2. Non ..... **p à proc. section** 8. NSP ..... **p à proc. section** 9. NR ou R ..... **p à proc. section**		
Q.8	**PRÉFÈRE B** Vos réponses indiquent que vous accepteriez **X %** de risque de mourir immédiatement sans douleur pour éviter de vivre avec [redacted] jusqu'à la fin de votre vie. Toutefois, si le risque de mourir immédiatement sans douleur était plus grand que **X %** vous préféreriez continuer de vivre avec [redacted] jusqu'à la fin de votre vie. Voulez-vous changer votre réponse? 1. Oui ..... **p à Q.9** 2. Non ..... **p à proc. section** 8. NSP ..... **p à proc. section** 9. NR ou R ..... **p à proc. section**		
Q.9	Quelle est le plus haut risque de mourir immédiatement sans douleur que vous seriez prêt à accepter pour éviter de vire avec [redacted] jusqu'à la fin de votre vie? 1. ___% 8. NSP 9. NR ou R		
Q.10	Si je change votre SANTÉ ACTUELLE pour ÊTRE AVEUGLE, en quoi cela changerait votre volonté d'accepter le choix B? Seriez-vous **LIRE LES TROIS CHOIX** 1. Plus tenté d'accepter le choix B 2. Aussi tenté d'accepter le choix B 3. Moins tenté d'accepter le choix B 8. NSP 9. NR ou R		

N° du sujet	Initiales du sujet	Hôpital général de Montréal Enquête sur l'évaluation de la qualité de vie
/ / / / /	/ / / /	

MÉTHODE DE LA DURÉE DE VIE ÉQUIVALENTE

Nous passons maintenant à une autre série de question. Je vais vous présenter deux choix. Vous devrez me dire lequel vous préférez ou si vous pensez que les deux sont égaux.
Voici les deux choix, celui du haut et celui du bas. Si vous choisissez le choix du haut vous allez vivre en santé parfaite pour les **X** prochaines années après quoi vous allez mourir sans douleur tel qu'indiquer par l'étoile.
Si vous choisissez le choix du bas vous allez vivre en étant aveugle pour les **Y** prochaines années après quoi vous allez mourrir sans douleur tel qu'indiquer par l'étoile.

		Être aveugle	Santé actuelle
Q.1	Préférez-vous de vivre **X** années avec une santé parfaite ou **Y** années avec [redacted] ou croyez-vous que les deux choix sont égaux? 1. Choix du haut (santé parfaite) ..... **présenter les choix en ordre** 2. Choix du bas (être aveugle) ..... **p à **** 3. Haut = bas ..... **p à ***** 8. NSP ..... **répétez et/ou p à proc. section** 9. NR ou R ..... **commentez et p à proc. section**		
**	Votre réponse indique que pour vous **Y** ans avec [redacted] est mieux que **X** ans avec une santé parfaite.		
***	Votre réponse indique que pour vous **Y** ans avec [redacted] a la même valeur que **X** ans avec une santé parfaite.		
Q.2	Voulez-vous changer votre réponse? 1. Non ..... **p à proc. section** 2. Oui ..... **p à **** 8. NSP ..... **p à proc. section** 9. NR ou R ..... **go to next section**		
**	Je comprends maintenant que vous préféreriez vivre **X** ans avec une santé parfaite au lieu de **X** ans avec [redacted]. **PRÉSENTER LES CHOIX EN ORDRE**		

ÊTRE AVEUGLE (Probabilité de santé parfaite)			
1. ____	5. ____	9. ____	13. ____
2. ____	6. ____	10. ____	14. ____
3. ____	7. ____	11. ____	15. ____
4. ____	8. ____	12. ____	16. ____

SANTÉ ACTUELLE (Probabilité de santé parfaite)			
1. ____	5. ____	9. ____	13. ____
2. ____	6. ____	10. ____	14. ____
3. ____	7. ____	11. ____	15. ____
4. ____	8. ____	12. ____	16. ____

		Être aveugle	Santé actuelle
Q.3	Mesure de l'utilité? 1. _____ 8. NSP 9. NR ou R		
Q.4	**UTILITÉ = 1** Vos réponses indiquent que vous ne voulez pas sacrifier aucune des **Y** années de vie qui vous reste pour éviter de vivre avec [redacted]. Voulez-vous changer votre réponse? 1. Oui ..... **p à Q.8** 2. Non ..... **p à proc. section** 8. NSP ..... **p à proc. section** 9. NR ou R ..... **p à proc. section**		

		Être aveugle	Santé actuelle
Q.5	**INDIFFÉRENT** Vos réponses indiquent que pour vous **X** ans en santé parfaite a la même valeur que **Y** ans avec [redacted]. Toutefois,vous préféreriez **X+1** ans en santé parfaite à **Y** ans avec [redacted]. Ceci veut dire que vous seriez prêt à sacrifier **[Y-(X+1)]** des **Y** ans qu'il vous reste à vivre pour éviter de vivre avec [redacted] jusqu'à la fin de votre vie. Voulez-vous changer votre réponse? 1. Oui ..... **p à Q.8** 2. Non ..... **p à proc. section** 8. NSP ..... **p à proc. section** 9. NR ou R ..... **p à proc. section**		
Q.6	**PRÉFÈRE LE CHOIX DU HAUT** Vos réponses indiquent que pour vous **X** ans en santé parfaite est mieux que **Y** ans avec [redacted]. Ceci veut dire que vous seriez prêt à sacrifier **Y-X** des **Y** ans qu'il vous reste à vivre pour éviter de vivre avec [redacted] jusqu'à la fin de votre vie. Voulez-vous changer votre réponse? 1. Oui ..... **p à Q.8** 2. Non ..... **p à proc. section** 8. NSP ..... **p à proc. section** 9. NR ou R ..... **p à proc. section**		
Q.7	**PRÉFÈRE LE CHOIX DU BAS** Vos réponses indiquent que pour vous **Y** ans avec [redacted] est mieux que **X** ans avec une santé parfaite. Toutefois, vous préféreriez **X+1** ans en santé parfaite à **Y** ans avec [redacted]. Ceci veut dire que vous seriez prêt à sacrifier **[Y-(X+1)]** des **Y** ans qu'il vous reste à vivre pour éviter de vivre avec [redacted] jusqu'à la fin de votre vie. Voulez-vous changer votre réponse? 1. Oui ..... **p à Q.8** 2. Non ..... **p à proc. section** 8. NSP ..... **p à proc. section** 9. NR ou R ..... **p à proc. section**		
Q.8	Quelle serait la plus courte durée de vie en santé parfaite que vous seriez prêt à accepter en échange de **Y** ans avec [redacted] ? 1. _____ ans 8. NSP 9. NR ou R		

Q.9 Si je change le choix du bas (**Y** ans avec votre santé actuelle) pour **Y** ans en étant aveugle, en quoi cela changerait-il votre volonté d'accepter le choix du haut? Seriez-vous **LIRE LES 3 CHOIX**

1. Plus tenté d'accepter le choix du haut
2. Aussi tenté d'accepter le choix du haut
3. Moins tenté d'accepter le choix du haut
8 NSP
9. NR ou R

Subject number	Subject initials	Montreal General Hospital Quality of Life Assessment Survey
/ / / / /	/ / / /	

FEELING THERMOMETER

I am going to ask you some questions to determine how you feel about different health problems. There are no good or bad answers. I will ask you three different sets of questions.

For the first set of questions I will ask you to read a card describing a particular health condition. You must imagine what it would be like if your health was as described on the card from now and for the last **X** years of your life. I will then ask you to use a special thermometer in order to tell me how good or how bad you feel a health condition is. This is the thermometer.
SHOW THE THERMOMETER TO THE RESPONDENT

The better you feel a health condition is, the closer it should be to the top of the thermometer.
RUN YOUR FINGER UP THE SCALE FROM 50 TO 100

The worse you feel a health condition is, the closer it should be to the bottom of the thermometer.
RUN YOUR FINGER DOWN THE SCALE FROM 50 TO 0

I will now ask you to read the first card.
SHOW THE FIRST CARD (PERFECT HEALTH)

This card describes perfect health. This is the best health that you can imagine. For this reason, it is placed at the top of the thermometer and has a score of 100.

I will now ask you to read the second card.
SHOW THE SECOND CARD (IMMEDIATE DEATH)

This card describes the worst health. It is an immediate and painless death. For the purposes of our research, it represents the worst health condition we will ask you to judge. For this reason, it is placed at the bottom of the thermometer and has a score of 0.

SHOW THE THIRD CARD (BLINDNESS)

Q.1 Imagine that you will live the last **X** years of your life with this health problem. Where would you place it on the thermometer?

1. ___/___
8. DNK
9. NA or R

In the first part of the interview, you told me about your own health condition.
LIST THE PROBLEMS

I will ask you to consider your own health while reading this card.
SHOW THE FOURTH CARD (YOUR CURRENT HEALTH)

Q.2 Could you tell me where you would place your health in the last four weeks on the thermometer?

1. ___/___
8. DNK
9. NA or R

Q.3 Now that you can see all of your answers, would you like to change any of them?

1. Yes blindness: _____ current health: _____
2. No
8. DNK
9. NA or R

Q.4 According to you, which health condition is the worst?

1. blindness
2. current health
8. DNK
9. NA or R

Subject number	Subject initials	Montreal General Hospital Quality of Life Assessment Survey
/ / / / /	/ / / /	

STANDARD GAMBLE

We will now continue with another set of questions. For each question I will give you two choices - A and B - and I will ask you if you prefer A or B or if you believe that the two choices are equal.

CHOICE A is relatively simple. It consists of living with blindness from now and for the next **X** years, after which you will die without pain. This is a certain choice because if 100 people choose it, they will all live with blindness for the next **X** years and they will all die without pain.

CHOICE B is more difficult because it is a risky choice. If you choose it you may either live in perfect health for the next **X** years after which you will die without pain or you may die immediately without pain. For example, if the probability of living in perfect health for the next **X** years is 80% and the probability of dying immediately is 20%, then if 100 people pick B, 80 people will live in perfect health for the next **X** years and 20 will die immediately.

	Blindness	Current health
Imagine now that you have **X** years remaining in your life. If you choose A, you will live with  until the end of your life. If you choose B, you have 0% chance of living in perfect health until the end of your life and 100% chance of dying immediately without pain.		
Q.1 Do you prefer, A or B, or do you consider both choices equal? 1. A ..... **present the choices in order** 2. B ..... **go to **** 3. A = B ..... **go to **** 8. DNK ..... **go to **** 9. NA or R ..... **comment and go to next section**		
** To answer this question you need to look at the diagrams. If 100 people choose A they will all live with  until the end of their lives: all the faces are shaded in grey. If they choose B they will all die immediately without pain because the probability of dying immediately without pain is 100% and the probability of living in perfect health is 0 %. As you can see all the faces are shaded in dark grey. Therefore, if you choose A you will live with  . If you choose B you will die immediately without pain. Q.2 If you take this into consideration would you prefer choice A or B or do you think that the two choices are equal? 1. A ..... **present the choices in order** 2. B ..... **go to **** 3. A = B ..... **go to ***** 8. DNK ..... **go to the next section** 9. NA or R ..... **comment and go to the next section**		
** Your answer indicates that for you dying immediately without pain is better than living with  until the end of your life. *** Your answer indicates that for you living with  has the same value as dying immediately without pain. Q.3 Would you like to change your answer? 1. No ..... **go to next section** 2. Yes ..... **go to **** 8. DNK ..... **go to next section** 9. NA or R ..... **comment and go to next section** ** This means that you would prefer choice A. **PRESENT THE CHOICES IN ORDER**		

BLINDNESS (Probability of perfect health)				CURRENT HEALTH (Probability of perfect health)			
1. ____	5. ____	9. ____	13. ____	1. ____	5. ____	9. ____	13. ____
2. ____	6. ____	10. ____	14. ____	2. ____	6. ____	10. ____	14. ____
3. ____	7. ____	11. ____	15. ____	3. ____	7. ____	11. ____	15. ____
4. ____	8. ____	12. ____	16. ____	4. ____	8. ____	12. ____	16. ____

	Blindness	Current health
Q.4 Write down the utility measure 1. ____ 8. DNK 9. NA or R		

		Blindness	Current health
Q.5	**IF UTILITY = 1** Your answers indicate that you do not want to take the risk of dying immediately without pain in order to avoid living with [redacted] until the end of your life. This is true even if the risk of dying immediately without pain was equal to 1%. Would you like to change your answer? 1. Yes ..... **go to Q.9** 2. No ..... **go to next section** 8. DNK ..... **go to next section** 9. NA or R ..... **go to next section**		
Q.6	**INDIFFERENT** Your answers indicate that if the risk of dying immediately without pain was higher than **X %** you would prefer to live with [redacted] until the end of your life. However, if the risk of dying immediately without pain was lower than **X %** you would prefer choice B in order to avoid living with [redacted] until the end of your life. Would you like to change your answer? 1. Yes ..... **go to Q.9** 2. No ..... **go to next section** 8. DNK ..... **go to next section** 9. NA or R ..... **go to next section**		
Q.7	**PREFER A** Your answers indicate that you would refuse to take a **X %** risk of dying immediately without pain in order to avoid living with [redacted] until the end of your life. However, if the risk of dying immediately without pain was lower than **X %** you would accept choice B. Would you like to change your answer? 1. Yes ..... **go to Q.9** 2. No ..... **go to next section** 8. DNK ..... **go to next section** 9. NA or R ..... **go to next section**		
Q.8	**PREFER B** Your answers indicate that you would accept a **X %** risk of dying immediately without pain in order to avoid living with [redacted] until the end of your life. However, if the risk of dying immediately without pain was higher than **X %** you would prefer to continue living with [redacted] until the end of your life. Would you like to change your answer? 1. Yes ..... **go to Q.9** 2. No ..... **go to next section** 8. DNK ..... **go to next section** 9. NA or R ..... **go to next section**		
Q.9	What is the highest risk of dying immediately without pain you would be willing to accept in order to avoid living with [redacted] until the end of your life? 1. ____ % 8. DNK 9. NA or R		
Q.10	If I change your current health for BLINDNESS, how this would change your willingness to accept B? Would you be **READ THE 3 CHOICES** 1. More willing to accept B 2. As willing to accept B 3. Less willing to accept B 8. DNK 9. NA or R		

Subject number	Subject initials	Montreal General Hospital Quality of Life Assessment Survey
/ / / / /	/ / / /	

TIME TRADE-OFF

We will now continue with another set of questions. I will present you with two choices and I will ask you which one you prefer or if you believe that the two choices are equal. These are the two choices: the top choice and the bottom choice. If you choose the top choice you will live in perfect health for the next **X** years and then you will die without pain as indicated by the star. If you select the bottom choice you will live with blindness for the next **Y** years and then you will die without pain as indicated by the star.

	Blindness	Current health
Q.1 Would you prefer to live **X** years in perfect health or **Y** years with [redacted] or do you consider the two choices to be equal?		

1. Top choice (perfect health) ..... **present the choices in order**
2. Bottom choice (blindness) ..... **go to ****
3. Top = bottom ..... **go to *****
8. DNK ..... **repeat and/or go to next section**
9. NA or R ..... **comment and go to next section**

** Your answer indicates that for you it is better to live **Y** years with [redacted] than **X** years in perfect health.

*** Your answer indicates that for you living **Y** with [redacted] has the same value as **X** years in perfect health.

Q.2 Would you like to change your answer?

1. No ..... **go to next section**
2. Yes ..... **go to ****
8. DNK ..... **go to next section**
9. NA or R ..... **comment and go to next section**

I understand now that you prefer to live **X** years in perfect health than **Y** years with [redacted].
PRESENT THE CHOICES IN ORDER

BLINDNESS (Probability of perfect health)

1. ____	5. ____	9. ____	13. ____
2. ____	6. ____	10. ____	14. ____
3. ____	7. ____	11. ____	15. ____
4. ____	8. ____	12. ____	16. ____

CURRENT HEALTH (Probability of perfect health)

1. ____	5. ____	9. ____	13. ____
2. ____	6. ____	10. ____	14. ____
3. ____	7. ____	11. ____	15. ____
4. ____	8. ____	12. ____	16. ____

	Blindness	Current health
Q.3 Write down the utility measure		

1. _____
8. DNK
9. NA or R

Q.4 **IF UTILITY = 1** Your answers indicate that you do not want to sacrifice any of your remaining years of life in order to avoid living with [redacted]. Would you like to change your answer?		

1. Yes ..... **go to Q.8**
2. No ..... **go to next section**
8. DNK ..... **go to next section**
9. NA or R ..... **go to next section**

		Blindness	Current health
Q.5	**INDIFFERENT** Your answers indicate that for you **X** years in perfect health has the same value as **Y** years with [redacted]. However, you would prefer **X + 1** years in perfect health to **Y** years with [redacted]. This means that you would be willing to sacrifice **[Y-(X+1)]** of your remaining **Y** years of life in order to avoid living with [redacted]. Would you like to change your answer? 1. Yes ..... **go to Q.8** 2. No ..... **go to next section** 8. DNK ..... **go to next section** 9. NA or R ..... **go to next section**		
Q.6	**PREFER TOP CHOICE** Your answers indicate that for you **X** years in perfect health is better than **Y** years with [redacted]. This means that you would be willing to sacrifice **Y-X** of your remaining years of life in order to avoid living with [redacted]. Would you like to change your answer? 1. Yes ..... **go to Q.8** 2. No ..... **go to next section** 8. DNK ..... **go to next section** 9. NA or R ..... **go to next section**		
Q.7	**PREFER BOTTOM CHOICE** Your answers indicate that for you **Y** years with [redacted] is better than **X** years in perfect health. However, you would prefer **X + 1** years in perfect health to **Y** years with [redacted]. This means that you would be willing to sacrifice **[Y-(X+1)]** of your remaining **Y** years of life in order to avoid living with [redacted]. Would you like to change your answer? 1. Yes ..... **go to Q.8** 2. No ..... **go to next section** 8. DNK ..... **go to next section** 9. NA or R ..... **go to next section**		
Q.8	What would be the fewest number of years in perfect health that you would be willing to accept in exchange for **Y** years with [redacted] ? 1. _____ years 8. DNK 9. NA or R		

Q.9 If I change the bottom choice which is **Y** years with your current health to **Y** years with BLINDNESS how this would change your willingness to accept the top choice? You would be **READ THE 3 CHOICES**

1. More willing to accept the top choice
2. As willing to accept the top choice
3. Less willing to accept the top choice
8 DNK
9. NA or R

Description des états de santé

ÊTRE AVEUGLE

L'année dernière vous êtes devenu aveugle après avoir été exposé à un virus qui est très rare. Vous serez aveugle pour le reste de votre vie. À part le fait d'être aveugle, votre santé est parfaite. Vous n'avez pas besoin de prendre de médicaments ou de suivre une diète. Vous devez voir votre médecin une fois par année pour un examen.

Vous ne pouvez pas faire d'activités qui requièrent la capacité de voir comme le ski, le hockey ou le jardinage. Au travail vous ne pouvez pas faire de tâches qui requièrent la capacité de voir. Vous avez besoin d'aide pour faire des choses telles que l'épicerie. Vos activités sociales avec votre famille, vos amis, vos voisins ou d'autres groupes sont limitées à celles qui n'exigent pas la capacité de voir.

SANTÉ ACTUELLE

Votre santé sera celle que vous avez eu au cours des **4 DERNIÈRES SEMAINES**. Prenez en considération les **problèmes de santé**, les **symptômes** ou les **malaises** que vous avez eu. Considérez également les **médicaments**, la **diète**, les **visites** chez un médecin ou un autre professionnel de la santé et les **tests médicaux** que vous avez eu.

Évaluez de quelle façon votre santé a limité vos activités physiques, votre capacité de travailler, de faire vos activités quotidiennes (prendre soin de vous-même, de votre famille, de votre maison...) et d'avoir des activités sociales avec votre famille, vos amis, vos voisins ou d'autres groupes.

SANTÉ PARFAITE

Votre santé est aussi bonne que vous pouvez l'imaginer. Vous vous sentez toujours très bien et plein d'énergie. Vous n'avez jamais de malaise. Vous n'avez pas besoin de prendre de médicaments ou de suivre une diète. Vous devez voir votre médecin une fois par année pour un examen.

Vous pouvez faire n'importe quel type d'activités physiques. Au travail vous n'êtes pas limité d'aucune façon par votre santé. Votre santé ne limite pas vos activités sociales avec votre famille, vos amis, vos voisins ou d'autres groupes.

DÉCÈS IMMÉDIAT

Vous allez mourir au cours de la semaine prochaine. Votre décès surviendra très rapidement et vous ne souffrirez pas.

Description des états de santé

ANGINE

Environ une fois par mois vous souffrez de douleur à la poitrine accompagnée de palpitations et de difficulté à respirer. Quand vous avez ces symptômes vous placez un comprimé de nitroglycérine sous votre langue et vous vous reposez. Après quelques minutes votre malaise cardiaque disparaît. Vous ne prenez aucun autre médicament. Vous devez suivre une diète spéciale qui contient peu de gras et de cholestérol. Vous devez voir votre médecin à tous les 6 mois pour un examen et des tests.

Vous ne pouvez pas faire d'activités vigoureuses telles que courir ou soulever des objets lourds. Au travail vous ne pouvez pas faire de tâches qui sont physiquement exigeantes. Vos activités sociales avec votre famille, vos amis, vos voisins ou d'autres groupes ne sont pas limitées par votre santé.

DÉFAILLANCE CARDIAQUE

Vous vous sentez faible la plupart du temps. Vous êtes à court de souffle. Vous toussez très souvent et vous vous sentez congestionné. Vos chevilles sont très enflées. Vous avez besoin de vous reposer dans votre lit pendant 2 heures chaque après-midi. Vous prenez 4 différentes sortes de médicaments chaque jour et vous devez suivre une diète très stricte qui est très faible en sel. Vous devez voir votre médecin au moins à tous les 3 mois pour un examen et des tests. Une fois par année vous pouvez avoir besoin d'être hospitalisé parce que vous avez de la difficulté à respirer et que votre médication doit être ajustée.

Vous pouvez marcher lentement mais vous ne pouvez pas courir ou faire un exercice physique intense. Vous n'êtes pas capable de travailler. Il est très difficile pour vous de faire des choses comme l'épicerie ou le jardinage. Vos activités sociales avec votre famille, vos amis, vos voisins ou d'autres groupes sont limitées par votre manque de vitalité.

8. *Appendix III*

8.1 Description of available visual aids for Preference-based instruments

Preference-based health-related quality of life (HRQOL) instruments, such as the Time Trade-off (TTO) and the Standard Gamble (SG), may be difficult to understand for respondents and to administer for the interviewers. To improve the respondent's understanding and facilitate the interviews, visual aids are recommended. [107] In the "Guide to design and development of health-state utility instrumentation" [107], Furlong et al. described in detail the design and assembly of various visual aids available to administer the Rating Scale (RS), the SG, and the TTO.

The RS can be administered by using the Feeling Thermometer. It simply consists of an interval scale, designed as a thermometer, varying from 0 to 100.[107] The lowest endpoint (score = 0) and the highest endpoint (score = 100) represent the worst and the best health state, respectively.

Various visual aids are available to administer the SG: the card deck [107], the chance board [107] and the computerized interview program [110]. The card deck is composed of a series of cards. Two pie charts are drawn on each card. One pie chart is completely shaded and represents the probability of having the health state under evaluation if the respondent chooses the sure outcome. The other pie chart

represents the probability of the worst and the best health state if the respondent chooses the risky alternative. On each card and for each possible answer, the next choice to be displayed is indicated.

The chance board consists of a large board divided in two sections. The upper and the lower sections represent the risky and the sure alternatives, respectively. The probability of occurrence of each health state is represented by probability wheels as described in section 2.3.1.1.

Morss, Lenert and Faustmann [110] have developed a computer program to administer the SG where the probability of each outcome is representing by shading one of one hundred faces.

The TTO board, displayed in the working paper of Furlong et al. [107], consists of a two section board. The upper section describes the preferred health state and its duration. The lower section represents the less desirable health state and its duration. During the interview, the time spent in the preferred health state is varied according to the interview questionnaire.

8.2 Pilot testing of interviewing material and prototypes

Based on the above review of available visual aids, we adapted and constructed various prototypes of visual aids to administer the Preference-based instruments in our study. We adapted the interview's questionnaire of Furlong et al. [107] for this research project. This questionnaire was used to elicit parents' preferences for various health states associated with neonatal intensive care of very low birth-weight infants. [192]

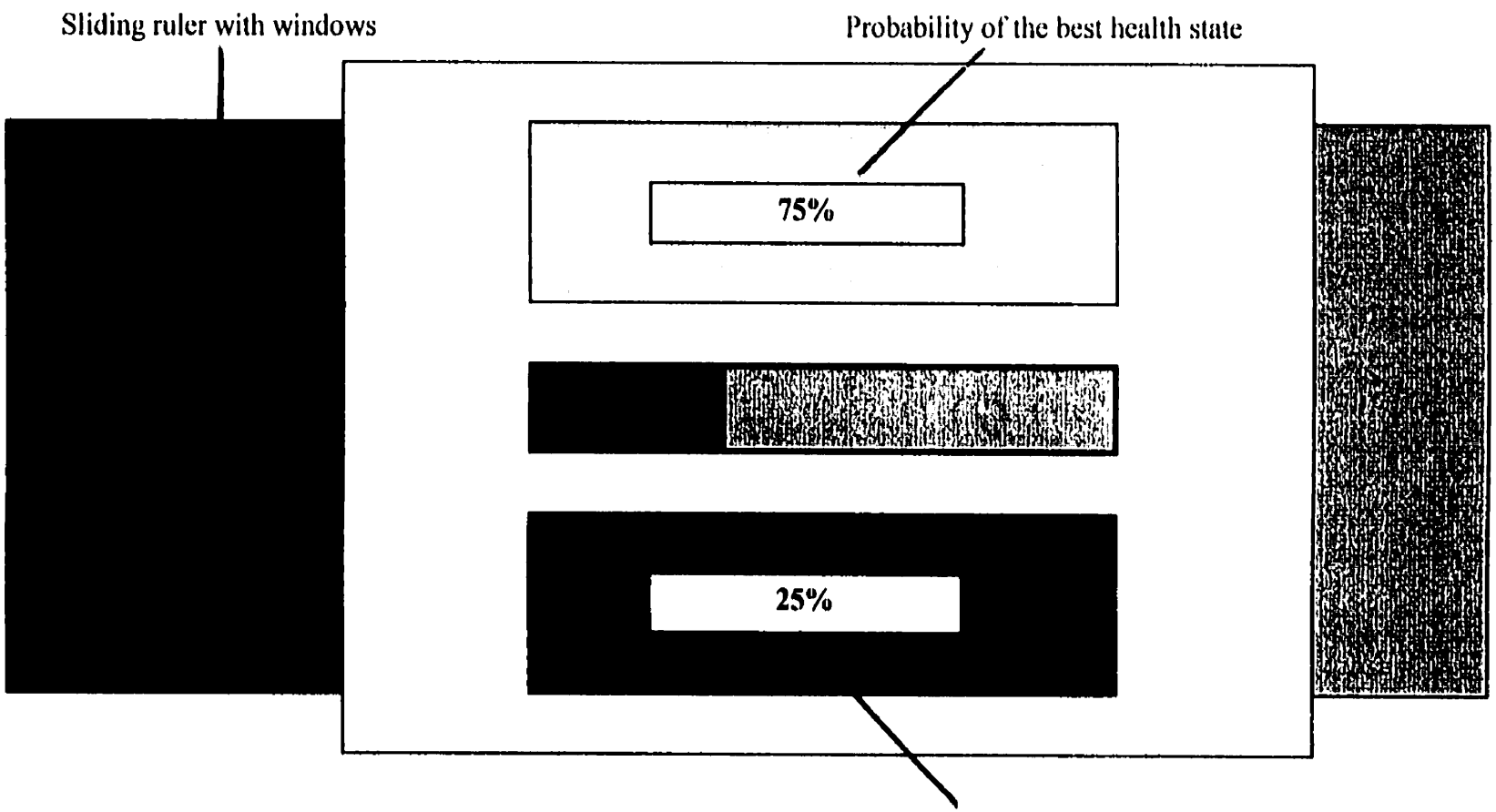
Interviewing material and prototypes of visual aids adapted for our study were

administered in a convenience sample of seven patients with various health conditions. We assessed the participants' understanding of each scaling technique, as well as the ease and time of administration of each scaling technique. We specifically evaluated three hypothetical health states: having both legs paralysed, wearing glasses, and following a low fat diet.

We used a Feeling Thermometer to administer the RS. For the SG assessment, we tested three different approaches to administer this instrument: 1) a two step assessment with "one hundred faces", 2) a two step assessment with a "probability ruler", and 3) a ping-pong approach with "one hundred faces". TTO using a two step approach and a ping-pong approach were also tested. The interview questionnaire for the pilot testing is included in section 8.4. Briefly, the "probability ruler" (Figure 8.2.1) was a colour-coded sliding ruler with windows indicating the probability of the best and the worst health states of the SG risky alternative. The middle section was a schematic display of the probability of the best and the worst health state. The two step approach consisted of assessing the respondent's willingness to take a 1% risk of death or to sacrifice one of their remaining years of life to avoid the health state under evaluation. Those willing to take risk or trade off their life expectancy were asked to specify the highest risk of death they would be willing to take or the lowest number of years of life in *perfect health* they would be willing to accept.

The Feeling Thermometer provided consistent and logical ranking of the various health states. All patients considered low fat diet and wearing glasses as being preferable (higher RS scores) to having their legs paralysed. In addition, the raking of the health states based on the RS scores agreed with the participants' best and worst health states as identified by the questions: "Could you tell me which health problem is the worst?" and "Which one is the best?".

Figure 8.2.1 • **Schematic representation of the probability ruler prototype**



Schematic display of the probability of the Best and the worst health states

SG assessments were more difficult to conduct. Three patients were unable to understand the probability ruler. Problems were also encountered with the two step approach using the "one hundred faces". Most patients reported having difficulties or being uncomfortable indicating the highest risk of death they would be willing to take by blocking out the appropriate number of faces. The ping-pong approach was successfully completed by all participants except one.

One participant was unable to understand the TTO assessments. The remaining participants reported similar scores with the two step and the ping-pong approaches.

We decided to use the Feeling Thermometer for the RS and the ping-pong approach with "one hundred faces" for the SG assessment. In order to be consistent across the scaling techniques, we also selected the ping-pong approach for the TTO assessment.

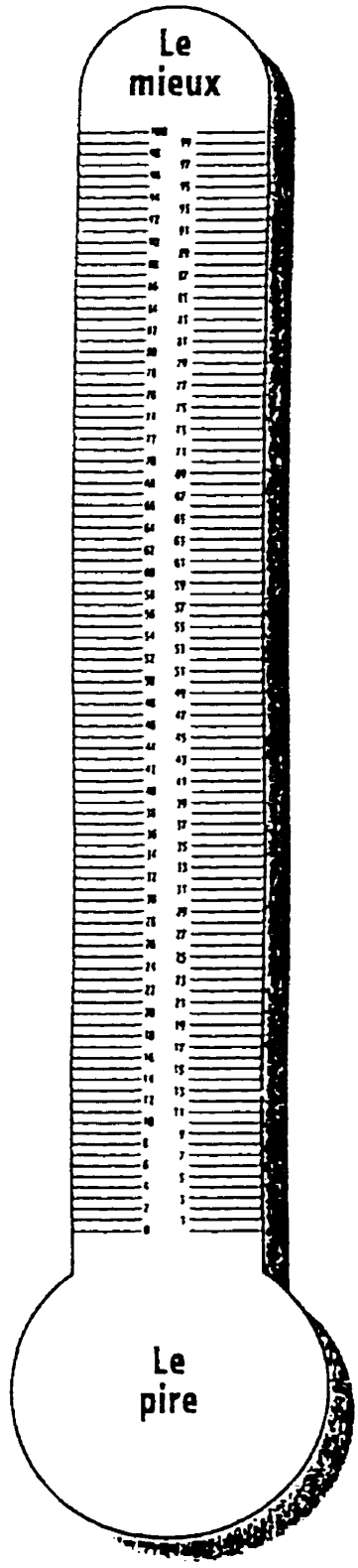
8.3 Description of each instrument

We included the RS, the TTO and the SG instruments in a 8.5 x 14 inches binder. The French and English health state descriptions (see section 3.1.3.2 and section 7.4) were reported on colour coded cards. The worst health state *(immediate death)* was reproduced on a dark shaded card. We used light and medium shading cards to reproduce the best *(perfect health)* and the intermediate *(present health, angina, congestive heart failure, blindness)* health states, respectively.

8.3.1 Feeling Thermometer

We used the Feeling Thermometer to administer the RS. It consisted of a 30 cm thermometer with 100 graduations covered with plastic (see Figure 8.3.1.1).

Figure 8.3.1.1 ● Schematic representation of the French version of the Feeling Thermometer



During the interviews, the interviewer placed the health states *perfect heath* and *immediate death* at the top and the bottom of the scale, respectively. Thereafter, the respondents were asked to indicate, using a non-permanent marker, where they would place the different health states under evaluation on the thermometer.

8.3.2 Standard Gamble

Each SG choice was displayed on a 8.5 x 14 inches sheet covered with plastic (see Figure 8.3.2.1). Each SG choice was described by specifying the health states (with the appropriate colour-code) and their probabilities of occurrence. Probabilities were displayed using numbers and diagrams with one hundred faces. In addition, it also indicated, for each possible respondent's choice, which choice B should be presented next (left bottom part of Choice B).

8.3.3 Time Trade-off

Visual aid for the TTO consisted (see Figure 8.3.3.1) of three sections. The first section identified the health state for each choice. The second and the third sections represented the number of years of life associated with each health state. The star indicated death. The visual aid indicated for each possible answer, the next choice to be presented or the value of the health state under evaluation when the assessment was completed. During the assessment only the third section was changed for each question.

Figure 8.3.2.1 ● **Schematic representation of the Standard Gamble visual aid**

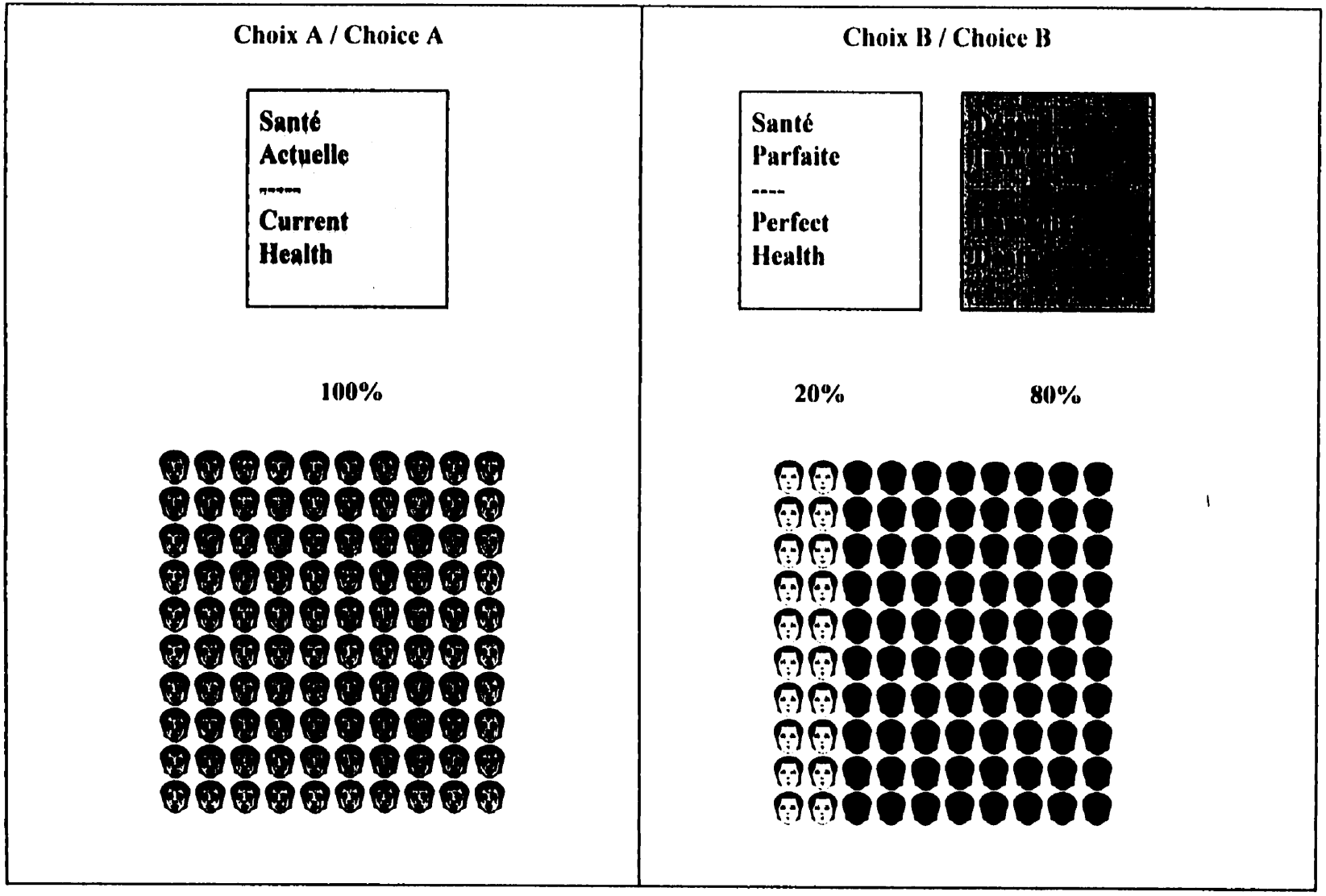
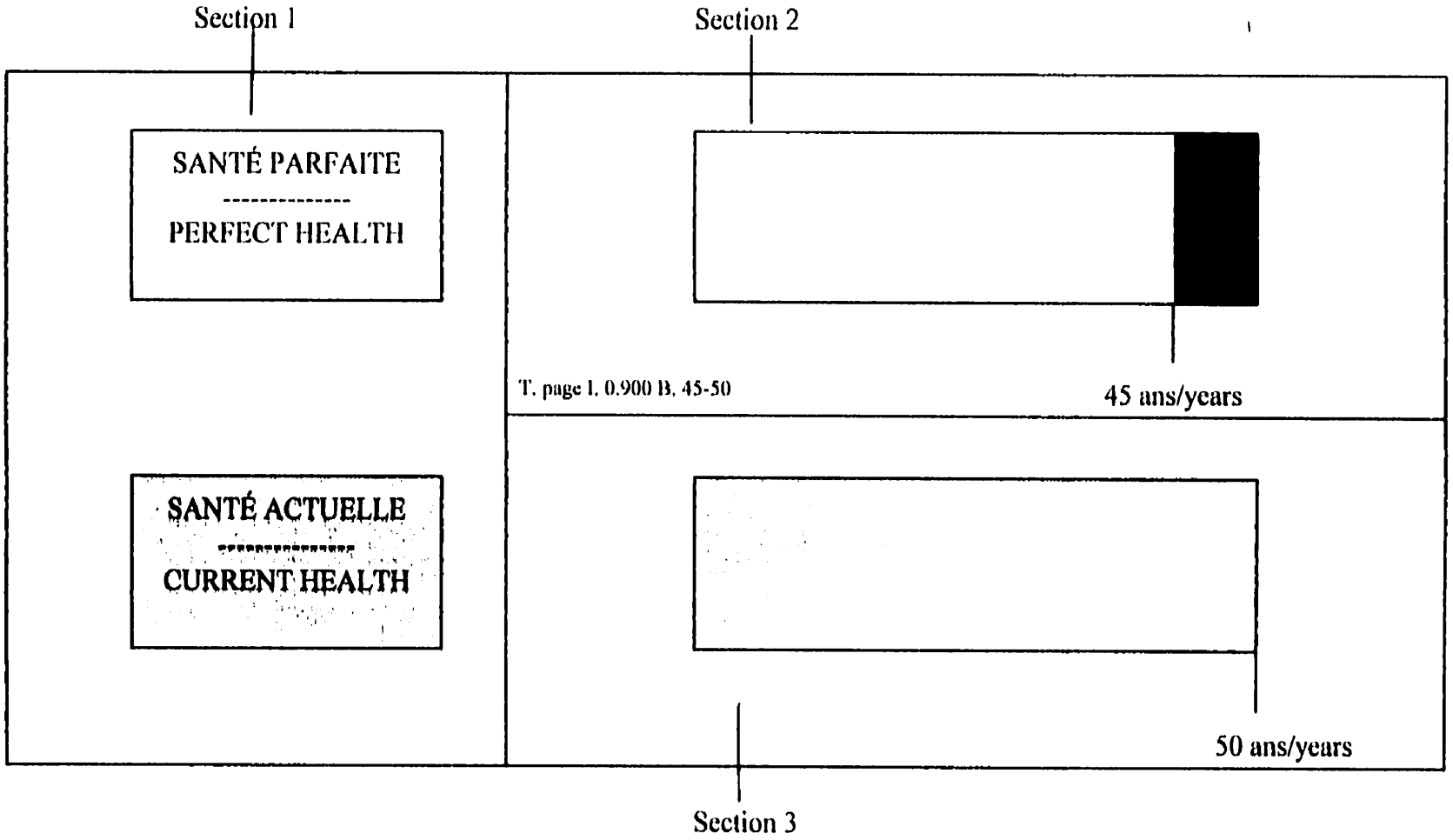


Figure 8.3.3.1 • Schematic representation of the Time Trade-off visual aid



8.4 Interview questionnaire for the pilot testing

INTERVIEW SCHEDULE
Pilot testing

1. INTRODUCTION

We would like to thank you for your participation. The objective of this interview is to compare different techniques to obtain your opinion on various health problems.

All information is confidential and anonymous. Of course, your participation is voluntary, and if we should come to a question you would rather not answer, just let us know and we will skip it.

All the questions deal with matters of opinion. There are no right or wrong answers. You do not have to explain any of your answers, and your answers will not be questioned. All we want is your opinion.

During the interview we will ask you to imagine yourself with different health problems. Your answers should represent what would be best for you if you had this problem. I will ask you five sets of questions.

- 2 -

VALUE ASSESSMENT

Now we will start the first set of questions. In order to make this task a little easier we will use what we call a FEELING THERMOMETER.

DISPLAY THERMOMETER
(Place on table facing Respondent)

We will use this thermometer to measure your feelings on different health problems. It will indicate your preferences, from the best to the worst form of health.

The better you feel a health problem is, the closer it should be to the top of the thermometer.

RUN FINGER UP SCALE FROM 50 TO 100

The worst you feel a health problem is, the closer it should be to the bottom of the thermometer.

RUN FINGER DOWN SCALE FROM 50 TO 0

The highest extremity corresponds to the best form of health. This is perfect health. As written on this card perfect health means health as good as you can imagine.

Display the card "perfect health"

It is represented by the color pink and it is placed at the top of the thermometer.

PLACE A MARK AT THE TOP OF THE FEELING THERMOMETER

The lowest extremity corresponds to the worst form of health. It is immediate death without pain. This is the corresponding card.

Display the immediate death card

It is represented by the color blue and it is placed at the bottom of the thermometer.

PLACE A MARK AT THE TOP OF THE FEELING THERMOMETER

a) **LEGS PARALYSED**

Now I will ask you to imagine yourself with your legs paralysed. Please, read this card.

Allow enough time for the respondent to read the card

Where would you place this health problem on the thermometer?

allow enough time to answer

b) **Wearing glasses**

I will now ask you to read this card describing another health problem.

allow enough time to read the card

Where would you place this health problem on the feeling thermometer?

allow enough time to answer

c) **LOW FAT DIET**

Please read this last card describing you as someone with high cholesterol and on diet.

allow enough time to read the card

Where would you place this form of health on the feeling thermometer?

allow enough time to answer

You have completed the first set of questions. Now that you can see all your answers, are there any changes you would like to make?

PAUSE UNTIL RESPONDENT INDICATES SATISFACTORY COMPLETION OF ANY REVISIONS, THEN RECORD SCORES FOR EACH HEALTH STATE

test: **Could you tell me which health problem is the worst?**

Which one is the best?

UTILITY ASSESSMENT

As you know, every day you make risky choices. For example, each time you cross a street you are at risk of dying from being hit by a car. Nobody can tell you in advance if you will be alive or dead on the other side of the street. However, we know it is more risky to cross a very busy than a very quiet street.

The same is true when you receive a medical treatment, such as an operation. Nobody can tell you in advance if this treatment will cure or kill you. However, we can tell you how risky a treatment is by telling you the probability of dying during the operation and the probability of being cured. For example, we can tell you that the risk of dying following a specific operation is 1%. This means that on average, if 100 people undergo this surgery, 1 will die during the surgery and 99 will be cured and will live in perfect health. This is represented by blocking out one face out of 100 faces. Again, the color pink represents the best outcome, "perfect health" and the color blue the worst outcome "immediate death".

Display the 1 % probability form

If the risk of death with another operation is 10% this means that on average if 100 people undergo the operation 10 will die during the operation and 90 will be cured and will live in perfect health. This is represented by blocking out 10 faces out of 100.

Display the 10% probability form

Can you tell me which treatment is more risky?

allow enough time for the respondent to answer

The second treatment is more risky because on average it kills more people.

3.1 Two steps assessment with "one hundred faces"

We will now start the second set of questions. For each question I will ask you to imagine yourself with a specific health problem. I will then offer you the possibility of undergoing an operation. This operation is risky. If it is successful, you will live in perfect health for the rest of your life. However, if it is not successful you will die without pain during the operation. If you decide to undergo the operation I will ask you the highest risk of dying you would be willing to take.

a) Legs paralysed

Let's assume now that you have been involved in a car accident and your legs are paralysed. This corresponds to the card you have read before. If you don't do anything your legs will remain paralysed for the rest of your life. The doctor offers you the possibility of undergoing an operation. This operation is risky. If it is successful, you will be able to use your legs normally and you will live in perfect health for the rest of you life. If the operation is not successful you will die without pain during the surgery. If the probability of death during the operation was 1% would you be willing to undergo this surgery?

Allow enough time for the respondent to answer
if yes continue
if no go to the next question

IF REFUSE TO GAMBLE: If the risk of death is 1% you would refuse the operation. You would prefer to remain with your legs paralysed for the rest of your life. Is this right?

IF ACCEPT TO GAMBLE: What is the highest risk of death you would be willing to take? To answer this question please block out the appropriate number of faces.

Allow enough time for the respondent to answer

This means that if the risk of death was equal to __ or lower you would be willing to undergo the surgery. However, if the risk of death was higher than __% you would prefer to remain paralysed for the rest of your life. Would you like to change your answer?

Allow enough time for the respondent to answer

b) Wearing glasses

Let's assume now that you need to wear glasses all the time. Again, this corresponds to the description you have read before. If you don't do anything you will continue to wear glasses all the time for the rest of your life. Your doctor offers you the possibility of undergoing an operation. This operation is risky. If it is successfull your vision will become normal, you won't need to wear glasses and you will live in perfect health for the rest of your life. If the surgery is not successful you will die without pain during the operation. If the probability of death during the opereation was 1% would you be willing to undergo this surgery?

Allow enough time for the respondent to answer
if yes continue
if no go to the next question

IF REFUSE TO GAMBLE: This means you would refuse the operation if the risk of death was equal to 1%. You would prefer to wear glasses for the rest of your life. Is this right?

IF ACCEPT TO GAMBLE: What is the highest risk of death you would be willing to take? To answer this question please block out the appropriate number of faces.

Allow enough time for the respondent to answer

This means that if the risk of death was equal to __% or lower you would be willing to undergo the operation. However, if the risk of death was higher than __% you would prefer to continue wearing glasses for the rest of your life. Would you like to change your answer?

Allow enough time for the respondent to answer

c) **Low fat diet**

Lets assume now that you have been on a low fat diet for one year to reduce your cholesterol. This corresponds to the last card you have read previously. If you don't do anything you will be on a diet for the rest of your life. Your doctor offers you the possibility of undergoing an operation. This operation is risky. If it is successful your cholesterol will become normal, you won't need to be on a diet and you will live in perfect health for the rest of your life. If the surgery is not successful you will die without pain during the operation. If the probability of death was 1% would you be willing to undergo this operation?

Allow enough time for the respondent to answer
if yes continue
if no go to the next question

IF REFUSE TO GAMBLE: This means you would refuse the operation if the risk of death was 1%. You prefer to be on a diet for the rest of your life. Is this right?

IF ACCEPT TO GAMBLE: What is the highest risk of death you would be willing to take? To answer this question please block out the appropriate number of faces.

Allow enough time for the respondent to answer

This means that if the risk of death was equal to __ or lower you would be willing to undergo the operation. However, if the risk of death was higher than __% you would prefer to continue bo be on a diet for the rest of your life. Would you like to change your answer?

Allow enough time for the respondent to answer

3.2 Two steps assessment with "the probability ruler"

We will now ask you exactly the same questions but this time instead of blocking out faces you will use a special ruler.

display the RULER

To explain how it works we will do two quick examples together. Let's imagine that you decide to undergo an operation. If the operation is successful you will be cured and you will live in perfect health for the rest of your life. If it is not successful you will die during the operation. Again, the color pink represents the best outcome and the color blue the worst outcome.

Display the choice B

Let's suppose that the probability of being cured is 99% and the probability of dying during the operation is 1%. These probabilities can be represented by setting the pink square at 99% and the blue square at 1%. As you can see almost all the window is pink. This means that the probability of perfect health is much higher then the probability of immediate death.

Display the probability ruler at 99%/1%

If I tell you now that the chance of being cured is 90% and the risk of death is 10% how would you set the ruler?

Display the board and
allow enough time to answer

The pink square needs to be set at 90% and the blue square at 10%. As you can see the probability of death is higher than previously and therefore a larger area of the window is blue.

We will now start the third set of questions.

a) **Legs paralysed**

Let's assume you have been involved in a car accident and your legs are paralysed. If you don't do anything your legs will remain paralysed for the rest of your life. The doctor offers you the possibility of undergoing an operation. This operation is risky. If it is successful you will be able to use your legs normally and you will live in perfect health for the rest of you life. If it is not successful you will die without pain during the surgery.

Display the chance board

If the probability of death was equal to 1%, would you be willing to undergo the operation?

Display the 1% chance of death with the ruler and
Allow enough time for the respondent to answer
if yes continue
if no go to the next question

IF REFUSE TO GAMBLE: This means you would refuse the operation if the probability of death was equal to 1%. You would prefer to remain with your legs paralysed for the rest of your life. Is this right?

IF ACCEPT TO GAMBLE: What is the highest risk of death you would be willing to take? To answer this question please use the ruler.

Allow enough time for the respondent to answer

This means that if the risk of death was equal to __% or lower you would choice the surgery. However, if the risk of death was higher than ___% you would prefer to remain paralysed for the rest of your life. Would you like to change your answer?

Allow enough time for the respondent to answer

b) Wearing glasses

Let's assume now that you need to wear glasses all the time. Your doctor offers you the possibility of undergoing an operation. This operation is risky. If the operation is successful, your vision will become normal, you won't need to wear glasses. You will live in perfect health for the rest of your life. If the surgery is not successful you will die without pain during the operation.

Display the chance board

If the probability of death was equal to 1% would you be willing to undergo the operation?

Display the 1% risk of death and
Allow enough time for the respondent to answer
if yes continue
if no go to the next question

IF REFUSE TO GAMBLE: This means you would refuse the operation if the probability of death was equal to 1%. You would prefer to wear glasses for the rest of your life. Is this right?

IF ACCEPT TO GAMBLE: What is the highest risk of death you would be willing to take? To answer this question please use the ruler.

Allow enough time for the respondent to answer

This means that if the risk of death was equal to __% or lower you would choice the operation. However, if the risk of death was higher than __% you would prefer to continue wearing glasses for the rest of your life. Would you like to change your answer?

Allow enough time for the respondent to answer

c) Low fat diet

Finally, lets assume you have been on a low fat diet for one year to reduce your cholesterol. Your doctor offers you the possibility of undergoing an operation. This operation is risky. If it is successful your cholesterol will become normal, you won't need to be on a diet. You will live in perfect health for the rest of your life. If it is not successful you will die without pain during the operation.

Display the chance board

If the probability of death was 1%, would you be willing to undergo the operation?

Allow enough time for the respondent to answer
if yes continue
if no go to the next question

IF REFUSE TO GAMBLE: This means you would refuse the operation if the probability of death was 1%. You would prefer to remain on diet for the rest of your life. Is this right?

IF ACCEPT TO GAMBLE: What is the highest risk of death you would be willing to take? To answer this question please use the ruler.

Allow enough time for the respondent to answer

This means that if the risk of death was equal to __% or lower you would choice the operation. However, if the risk of death was higher than __% you would prefer to be on a diet for the rest of your life. Would you like to change your answer?

Allow enough time for the respondent to answer

3.3 Ping-pong approach with the "one hundred faces"

We will now start the next set of questions.

Display the board

Like before I will ask you to imagine yourself with a specific health problem. If you don't do anything you will live with this problem for the rest of your life. I will then offer you the possibility of undergoing an operation. The operation will allow you to live with perfect health for the rest of your life. However, there is also a risk of dying without pain during the operation. This time I will tell you in advance the risk of dying during the operation. I wil use a figure like this one to tell you the probability of dying. Here the probability of dying during the operation is 10%. This means that on average if 100 people undergo the operation, 10 will die and 90 will be cured.

I will then ask you if you prefer to live with this health problem for the rest of your life or undergo the operation. If you don't have a preference because you think the two options are equal you tell me.

a) **Legs paralysed**

Display the board

Imagine again that your legs are paralysed. If you don't do anything you will remain paralysed for the rest of your life. Your doctor offer you the possibility of undergoing an operation. If the operation is successful you will be able to use your legs normally and you will live in perfect health for the rest of you life. If it is not successful you will die without pain during the surgery.

If the risk of dying during the surgery was 100%, would you choose to remain paralysed

or to undergo the operation. If you feel the two options are equal choices you tell me.

Ask the same question using the diagram until completion.

IF REFUSE TO GAMBLE: This means you are not be willing to undergo the operation, even if the risk of death was very small. You prefer to remain with your legs paralysed for the rest of your life. Is this right?

IF ACCEPT TO GAMBLE: If I understand well your answer it means that if the probability of death was equal to __% or lower you would prefer the operation. However, if the probability of death was higher than ___% you would prefer continue living with your legs paralysed. Would you like to change your answer?

Allow enough time for the respondent to answer

b) Wearing glasses

Display the board

Let's assume now that you have a bad vision and you need to wear glasses all the time. You may undergo a risky surgery. If it is successful your vision will become normal, you won't need to wear glasses. You will live in perfect health for the rest of your life. If the surgery is not successful you will die without pain during the operation.

If the risk of dying during the surgery was 100%, would you choose to wear glasses for the rest of your life or to undergo the operation? Again, if you feel that undergoing the operation and remaining paralysed are equal choices you tell me.

Ask the same question using the diagram until completion.

IF REFUSE TO GAMBLE: This means you are not be willing to undergo the operation, even if the risk of death was very small. You prefer to wear glasses for the rest of your life. Is this right?

IF ACCEPT TO GAMBLE: If I understand well you answers it means that if the probability of death was equal to ___ % or lower you would prefer the operation. However, if the probability of death was higher than __% you would prefer continue wearing glasses. Would you like to change your answer?

c) **Low fat diet**

Display the board

Lets assume that you have been on a low fat diet for one year to reduce your cholesterol. You may undergo a risky operation. If the operation is successful your cholesterol will become normal, you won't need to be on a diet and you will live in perfect health for the rest of your life. If it is not successful you will die without pain during the operation.

If the risk of dying during the surgery was 100%, would you prefer to remain on diet for the rest of your life or to undergo the operation? If you feel that undergoing the operation and remaining paralysed are equal choices you tell me.

Ask the same question using the diagram.

IF REFUSE TO GAMBLE: This means you are not be willing to undergo the operation, even if the risk of death was very small. You prefer to be on a diet for the rest of your life. Is this right?

IF ACCEPT TO GAMBLE:

If I understand well you answers it means that if the probability of death was equal to _ % or lower you would prefer the operation. However, if the probability of death was higher than __% you would prefer continue to be on a diet. Would you like to change your answer?

TEST QUESTIONS

1. **If the probability of dying during the operation is 10%, what is the probability of being cured?**

2. **Lets assume you had choosen to operation. The operation was successful and you are now cured and in perfect health for the rest of your life.**

   a) **What would be your risk of dying next year in a car accident?**
   0%, 1%, 1/1000, 1/1 million?

   b) **What is your probability of dying from a cancer?**
   0%, 1%, 10%

3.4 TIME TRADE-OFF ASSESSMENT, TWO STEPS APPROACH

We will start another set of questions. You will imagine yourself with a specific health problem. We know that people with this problem live on average another 20 years. After 20 years you will die without pain. This is represented by the blue star. Your doctor offers you the possibility of undergoing an operation. We know this operation will cure you and will allow you to live in perfect health. However, you will live for less than 20 years. If you accept to undergo this operation I will ask you the lowest number of years of life in perfect health you would be willing to accept in exchange of 20 years of life with your health problem. This may seem a little bit confusing but you will understand it better as we go along.

a) **Legs paralysed**

Your legs are paralysed. People like you live on average another 20 years. The doctor offers you the possibility of undergoing an operation. The operation will allow you to use your legs normally and to live in perfect health. However, we know you will live for less than 20 years. If the surgery would allow
you to live 19 years in perfect health instead of 20 years with your legs paralysed, would you be willing to undergo the operation?

Allow enough time for the respondent to answer
if yes, continue
if no, go to the next question

<u>IF REFUSE THE SURGERY:</u> If I understand well you answer it means you would not be willing to sacrifice any of your remaining years of life to avoid living with your legs paralysed. Would you like to change your answer?

<u>IF ACCEPT THE SURGERY:</u> What is the lowest number of years of perfect health you would be willing to accept in exchange of 20 years with your legs paralysed?

Allow enough time for the respondant to answer
and write the answer

If I understand well your answer it means that you would prefer to live ___ years in perfect health than 20 years with your legs paralysed. This means that you would be willing to sacrifice ___ years of your 20 remaining years of life to avoid living with your legs paralysed. Would you like to change your answer?

Allow enough time to answer

b) **Wearing glasses**

You need to wear glasses all the time. People like you live on average another 20 years. The doctor offers you the possibility of undergoing an operation. With this operation your vision will return to normal and you will live in perfect health. However, we know you will live for less than 20 years. If the surgery would allow you to live 19 years in perfect health instead of 20 years with glasses, would you be willing to undergo the operation?

Allow enough time for the respondent to answer
if yes, continue
if no, go to the next question

IF REFUSE THE SURGERY: If I understand well you answer it means you would not be willing to sacrifice any of your remaining years of life to avoid wearing glasses. Would you like to change your answer?

IF ACCEPT THE SURGERY: What is the lowest number of years of perfect health you would be willing to accept in exchange of 20 years with glasses?

Allow enough time for the respondant to answer and write the answer

If I understand well your answer it means that you would prefer to live ___ years in perfect health than 20 years with glasses. This means that you would be willing to sacrifice _ years of your 20 remaining years of life to avoid living with glasses. Would you like to change your answer?

Allow enough time to answer

c) **Low fat diet**

You are on a diet to reduce your cholesterol. People like you live on average another 20 years. The doctor offers you the possibility of undergoing an operation. With this operation your cholesterol will return to normal, you won't need to be on a diet anymore and you will live in perfect health. However, we know you will live for less than 20 years. If the surgery would allow you to live 19 years in perfect health instead of 20 years on a diet, would you be willing to undergo the operation?

Allow enough time for the respondent to answer
if yes, continue
if no, go to the next question

<u>IF REFUSE THE SURGERY:</u> If I understand well you answer it means you would not be willing to sacrifice any of your remaining years of life to avoid being on a diet. Would you like to change your answer?

<u>IF ACCEPT THE SURGERY:</u> What is the lowest number of years of perfect health you would be willing to accept in exchange of 20 years on diet?

Allow enough time for the respondant to answer and write the answer

If I understand well your answer it means that you would prefer to live ___ years in perfect health than 20 years on a diet. This means that you would be willing to sacrifice __ years of your 20 remaining years of life to avoid being on a diet. Would you like to change your answer?

Allow enough time to answer

3.5 TIME TRADE-OFF ASSESSMENT, ping-pong approach

We will now start the last set of questions. I will present you with two choices. I will ask you which one you prefer. If you think the two choices are equal tell me. We will do a quick example together.

Display the TTO board with perfect health versus being blind

These are the two choices. If you choose the first one, at the top, you will live in perfect health. If you choose the second one, at the bottom, you will be blind. The time scale beside each card tells you how long you will live with each of these forms of health. The star indicates the time of death. For example, if you choose the top choice you will live with perfect heath for the next 19 years. After 19 years you will die. If you choose the bottom choice, you will be blind for the next 20 years. After 20 years you will die. Which one do you perfer, 19 years in perfect health or 20 years blind?

Allow enough time for the respondent to answer
if does not understand repeat the previous page
if the respondent understand, continu

a) **Legs paralysed**

We will now start the first question. The top choice represents perfect health. The bottom choice represents your health with your legs paralysed. Again, the time scale besides each health description tells you how long you will live with each form of health. Again, I ask you to tell me if you perfer the top or the bottom choice or if you think the two choices are equal.

Display the TTO board with 20/20

The top choice is 20 years in a perfect health and the bottom choice is 20 years with your legs paralysed. Which one do you prefer?

Allow enough time to answer
if choose perfect health, continue to the next question
if choose legs paralysed continue this section

Again, the question is: Do you perfer to live 20 years in a perfect health or 20 years with your legs paralysed?

Allow enough time to answer
if choose perfect health, continue to next question
if choose legs paralysed, then ask why

I will change the time scale. Now, you have the choice between living 5 years in perfect health or 20 years with your legs paralysed. Which one do you prefer?

Follow the TTO diagram until completion

<u>IF REFUSE 10 VERSUS 20 YEARS:</u> If I understand well you answers you would not be willing to sacrifice any of your remaining years of life to avoid living with your legs paralysed. Would you like to change your answer?

<u>IF UTILITY < 1:</u> If I understand well your answers you are telling me that you would prefer to live ___ years in perfect health than 20 years with your legs paralysed. This means that you would be willing to sacrifice ___ years of your remaining life to avoid living with your legs paralysed. Would you like to change your answer?

b) **Wearing glasses**

I will change the health problem at the bottom. It will now represent 20 years with the

need to wear glasses all the time. The top choice is 20 years in a perfect health.

Display the TTO board with 20/20

Again, I ask you if you perfer the top or the bottom choice or if you think the two choices are equal.

Allow enough time to answer
if choose perfect health, continue to the next question
if choose legs paralysed continue this section

Again, the question is: Do you perfer to live 20 years in a perfect health or 20 years with glasses?

Allow enough time to answer
if choose perfect health, continue to next question
if choose glasses, then ask why

I will change the time scale. Now, you have the choice between living 5 years in perfect health or 20 years with glasses. Which one do you prefer?

Follow the TTO diagram until completion

<u>IF REFUSE 10 VERSUS 20 YEARS:</u> If I understand well you answers you would not be willing to sacrifice any of your remaining years of life to avoid wearing glasses. Would you like to change your answer?

<u>IF UTILITY < 1:</u> If I understand well your answers you are telling me that you would prefer to live ___ years in perfect health than 20 years with glasses. This means that you would be willing to sacrifice __ years of your remaining life to avoid living with glasses. Would you like

to change your answer?

c) **Low fat diet**

Again, I will change the health problem at the bottom. It will now represent 20 years on diet to reduce your cholesterol. The top choice is 20 years in a perfect health. Which one do you prefer? Again if you feel the two choices are equal you tell me.

Allow enough time to answer
if choose perfect health, continue to the next question
if choose legs paralysed continue this section

Again, the question is: Do you perfer to live 20 years in a perfect health or 20 years on diet?

Allow enough time to answer
if choose perfect health, continue to next question
if choose glasses, then ask why

I will change the time scale. Now, you have the choice between living 5 years in perfect health or 20 years on diet. Which one do you prefer?

→	Follow the TTO diagram until completion

<u>IF REFUSE 10 VERSUS 20 YEARS:</u> If I understand well you answers you would not be willing to sacrifice any of your remaining years of life to avoid being on a diet. Would you like to change your answer?

<u>IF UTILITY < 1:</u> If I understand well your answers you are telling me that you would prefer to live ___ years in perfect health than 20 years on diet. This means that you would be willing to sacrifice ___ years of your remaining life to avoid being on a diet. Would you like to change your answer?

3.6 STANDARD-GAMBLE, PING-PONG, TWO CHOICES

This is the last set of questions. Again, I will present you with two choices. I will ask you which one you prefer. If you thisn the two choices are equal tell me.

Display the SG board with the example

This is the two choices. If you choose the first one, on the left, you have 100% chance of living with with a health problem for 20 years. After 20 years you will die without pain. The time of death is indicated by the star. The 100% chance means that if 100 people choose this choice, 100 will live with this health problem for 20 years and will die without pain.

The second choice is on the right. If you choose the second choice you may live in perfect health for 20 years and then die without pain. However, this choice is risky because you may also die immediately without pain. For each question I will tell you the probability of living in perfect health and the probability of dying immediately. In this example, if you select this choice you have 50% chance of living in perfect health for 20 years and then die without pain and you have 50% chance of dying immediately. If 100 people choose this choice 50 will live in perfect health for 20 years and 50 will die immediately without pain. We will go through an example together.

a) Legs paralysed

This is the first choice and this is the second choice. I want you to tell which one you prefer. If you think the two choices are equal tell me.

If you choose the first choice you have 100% chance of having your legs paralysed for the next 20 years. After 20 years you will die without pain. The 100% means that if 100 people choose this choice then 100 will have their legs paralysed for 20 years and will die

without pain.

If you choose the second choice you have 100 % chance of living in perfect health for 20 years and then die without pain. You have 0% chance of dying immedately. This means that if 100 people choose this choice, they will all live in perfect for 20 years and will die without pain.

Now, the question is "Do you prefer the first or the second choice or do you think the two choices are equal"?

Allow enough time for the respondent to answer
If perfer the second choice continue
If perfer the first choice repeat the explanation

I will now change the second choice.

Display page 0

If you choose the second choice you have 0% chance of living in perfect health and 100% chance of dying immediately. The first choice will remain the same. Do you prefer the first or the second choice or you think the two choices are equal?

Display page 90

Now the probability of living 20 years in perfect health is 90% and the probability of dying immediately is 10%. Do you prefer the first or the second choice or you think the two are equal?

Continue until end of SG

b) **Wearing glasses**

We will repeat the same questions.

Display the SG for wearing glasses

This time the first choice consists of wearing glasses for 20 years and then dying without pain. The second choice is risky because you may live in perfect health for 20 years and then die without pain or you may also die immediately without pain. Here the probability of perfect health is 100% and the probability of dying immediately is 0%. Do you prefer the first or the second choice or you think the two choices are equal?

Continue until completion

c) **Diet**

This is the last set of question.

Display the SG board

Now if you choose the first choice you will be on a diet to reduce you cholesterol for the next 20 years. After 20 years you will die without pain. If you choose the second choice you have 100% chance of living in perfect health for the next 20 years and then die without pain and 0% chance of dying immediately without pain. Do you prefer the first or the second choice or do you think the two choices are equal?

Continue until completion

LEGS PARALYSED

Last year I have been involved in a car accident. My health is now as it was before the accident however my legs are paralysed since the accident. They will remain paralysed for the rest of my life. Otherwise my health is good for my age. I have no other disease.

I live in my home. I have to use a wheelchair. I need help to prepare the meals, get dressed, use the bathroom and clean the house. It is hard to go out, especially during the winter.

WEARING GLASSES

I am not able to read or to see something far away without my glasses. I need to wear them all the time. With my glasses my vision is almost perfect. Otherwise, my health is good for someone at my age.

DIET TO DECREASE THE CHOLESTEROL

My cholesterol is high. My doctor told me that if it remains high I may have heart problems later on. To decrease my cholesterol I am on a diet. This diet consists of reducing the amount of fat I take every day. For example, I rarely eat beef or pork. Instead I eat chicken, turkey or fish. I take low fat milk, low fat cheese and I eat less than 4 eggs a week. I need to eat a lot of fruits and vegetables. I will need to follow this diet for the rest of my life.

I follow my diet very closely. Sometimes it is easy but sometimes it is difficult. It is specially hard when I go to restaurants, and on special occasions such as a birthday, Christman and New Year because I cannot eat cookies, cakes, pies and ice cream. If I do I take only a very small portion.

Every year I have a blood test to measure my cholesterol. After one year on diet my cholesterol is lower than it was before but it is still a little bit too high.