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**Assessing Health-Related Quality-of-Life in  
Prenatal Diagnosis  
Comparing Chorionic Villi Sampling and Amniocentesis:  
A Technical Report**

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## ABSTRACT

**Objectives.** To assess the health-related quality-of-life (HRQL) effects of chorionic villi sampling (CVS) and genetic amniocentesis (GA) prenatal diagnosis, including factors related to both the processes and the outcomes.

**Study Design.** The HRQL of one hundred twenty six women participating in a randomized controlled clinical trial of CVS versus GA in Toronto and Hamilton, Ontario was assessed in four interviews at weeks 8, 13, 18, and 22 of pregnancy. Statistical analyses included analysis of variance, repeated measures analysis of covariance, chi-square, Fisher's exact test, Student's t-tests, and paired t-tests.

**Results.** Utility scores for patients undergoing CVS exceeded those for GA patients at week 18 ( $p = 0.04$ ). Utility scores for hypothetical health states did not differ significantly by trial arm.

**Conclusions.** CVS results in slightly improved HRQL relative to GA during the second trimester of pregnancy. This advantage needs to be weighed against the high disutility patients attach to infrequent outcomes associated with pregnancy losses, equivocal diagnoses, and diagnostic inaccuracy.

**Key Words.** Prenatal diagnosis; health-related quality of life; genetic amniocentesis; chorionic villi sampling; utility scores.



## INTRODUCTION

Chorionic villi sampling (CVS) is one of two established modalities for obtaining biologic samples for prenatal diagnosis. CVS is performed between 10 and 12 weeks gestation; results can be available within two weeks. Genetic amniocentesis (GA) is performed between 15 and 17 weeks of gestation; the results may not be available until 20 weeks gestation. Because diagnosis is available sooner after the test is performed and earlier in pregnancy with CVS than genetic amniocentesis, a potential advantage of CVS is a reduction in the duration of anxiety and stress for reproductive couples. An additional potential health-related quality of life (HRQL) advantage of CVS is the ability to terminate the pregnancy during the first trimester (with a decreased risk of complication to the woman) prior to fetal movement or public awareness (Blumberg, Golbus, Hanson, 1975; Borelli, Bender, Puck, et al., 1984; Bryce, Bradley, and McCormick, 1989; Caccia, Johnson, Robinson, and Barna, 1991; Evers-Kiebooms, Swerts, and van den Berghe, 1988; Fava, Kellner, Nichelacci, et al., 1982; Fava, Tambini, Michelacci, et al., 1983; Finley, Varner, Vinson, et al., 1977; Ganiats, 1996; Heckerling and Verp, 1991, 1994; Heckerling, Verp and Hadro, 1994; Kolker, 1989; Hook and Willey, 1981; Kuppermann, Shiboski, Feeny, et al. 1997; Lippman, Perry, Mandel, and Cartier, 1985; McCormack, Rylance, MacKenzie, and Newton, 1990; McGovern, Goldbert and Desnick, 1986; Modell, Ward, and Fairweather, 1980; Modell, Ward, Rodeck, et al., 1984; Mooney and Lange 1991, 1993; Perry, Vekemans, Lippman, et al., 1985; Robinson, Garner, Olmstead et al., 1988; Scriver, Bardanis, Cartier, et al., 1984; Verp and Heckerling, 1995). Disadvantages of CVS include elevation in the risk of miscarriage and slight increase in the risk of maternal infection (Canadian Collaborative CVS-ACT Group, 1989; Lippman, Tomkins, Shime, et al., 1992; Rhoads, Jackson, Schlesselman, et al., 1989; MRC Working Party on the Evaluation of Chorion Villus Sampling, 1991). CVS is also associated with lower diagnostic accuracy and a higher rate of equivocal diagnosis (Lippman, Tomkins, Shime, et al., 1992). There have also been reports of limb reductions associated with CVS (D'Alton and DeCherney 1993; Rodeck, 1993). In addition, CVS samples do not provide information for testing for neural tube defects.

Given the potential advantages and disadvantages of CVS, it is not obvious that the overall health-related quality of life (HRQL) for women undergoing CVS will be greater than that for women undergoing GA. Because approximately half of spontaneous abortions (SA) that occur between the ninth and twelfth weeks of pregnancy involve a chromosomally abnormal fetus (Mikkelsen, 1985; Simoni, Ginelli, Cuoco, et al., 1986; Yamamoto and Watanabe, 1979), the rate of detection of abnormalities using CVS exceeds that of GA (4.6% versus 2.4% reported in the preliminary report of the Canadian Collaborative CVS-ACT Group, 1989; 5.6% versus

3.4% in the final Canadian trial results reported in Lippman, Tomkins, Shime, et al., 1992; in the U.S. study, results for aneuploidy were 1.8% versus 1.4%, Rhoads, Jackson, Schlesselman, et al., 1989; results in the European trial were 5.6% versus 3.9%, MRC Working Party on the Evaluation of Chorion Villus Sampling, 1991). If the guilt and psychic costs of a therapeutic abortion (TA) exceeds those associated with a SA by a wide enough margin, CVS could reduce the HRQL for women receiving the procedure even if CVS were as safe and as accurate as GA. Guilt from having chosen a higher-risk procedure may also adversely affect the HRQL associated with CVS (Robinson, Carr and Wright, 1991).

This paper describes results from HRQL assessments conducted within a randomized controlled clinical trial of CVS versus GA. (Obstetric and cytogenetic results from the overall trial are reported in Lippman, Tomkins, Shime, et al., 1992.) The focus is on women who utilize prenatal diagnosis for late maternal age indications. Several measures of HRQL were employed to cover the range of issues including the consequences of miscarriages, terminations for genetic indications, diagnostic inaccuracy, and anxiety.

## METHODS

### Design

The study was an ancillary study completed in conjunction with a multi-center trial of CVS and GA conducted in 11 centers across Canada (Lippman, Tomkins, Shime et al., 1992). In the multi-center trial, designed to answer safety and accuracy issues surrounding CVS, eligible and consenting patients were randomized to receive CVS or GA. Randomized patients from two of these centers were enrolled concurrently into the Health-Related Quality-of-Life study. The HRQL study did not begin, however, until the final quarter of the main trial.

### Patients

Patients enrolled at the two centers in the larger trial were contacted for participation in the HRQL study after randomization. Patients were considered eligible for the HRQL study according to the following criteria:

- i) age > 35 at EDC (expected date of confinement);
- ii) ability to complete the HRQL interview (i.e., speak and read English); and
- iii) informed consent for participation in HRQL study obtained.

The study received the ethics approval of McMaster University, Chedoke-McMaster Hospitals, and the Toronto General Hospital. All respondents provided informed consent.

One hundred sixty-one women were contacted to participate in the HRQL study from October 1987 to September 1988. Of these, 29 initially refused to participate (18%). Reasons for refusals were documented and included: work commitments, no interest in the HRQL study and illness of family members. Patients who initially refused received a second request and 11 patients agreed to participate following this second request, reducing the final refusal rate to 11%. (Clarification of the nature of the HRQL study may have led to agreement from those who initially refused.) An analysis of the information available about those who refused suggests that there were no demographic differences between the refusal group and participants.

Demographic information for patients enrolled in the HRQL study revealed that the two arms of the study were evenly matched in terms of age, percentage married, education level, and other factors. No statistically significant differences were found. Overall, the patients were a well-educated and affluent group. Patient demographic characteristics are summarized in Table 1.

## Preference Measures

The focus of the study was on the HRQL effects of CVS and GA. Quality of life is a multi-dimensional concept that includes dimensions such as the material standard of living, health status, cultural amenities, recreational facilities, and air and water quality. Although these factors are important in affecting people's overall quality of life, most are unlikely to be affected by interventions in health care. Thus, for evaluative purposes in health care, the focus is on health-related quality of life which includes health status and the desirability of the variety of health status conditions associated with the health-care program (Guyatt, Feeny, and Patrick 1993).

In the context of prenatal diagnosis a number of specific aspects of HRQL warrant attention. These include anxiety, the effects of being tested and waiting for test results, the effects of pregnancy losses, and the effects of diagnostic inaccuracy. The impact of the two prenatal diagnostic procedures on the HRQL of patients was measured in two ways: through the use of an instrument for assessing anxiety and through utility assessment. Results from the anxiety assessments, using a portion of the State-Trait Anxiety Inventory, are reported separately. The utility approach was employed to examine a number of the HRQL effects of prenatal diagnosis (Torrance, 1976; Torrance, 1986; Torrance, 1987; Torrance and Feeny, 1989; Feeny and Torrance, 1989). In this approach, the effects of anxiety reduction are integrated with the effects of other consequences of prenatal diagnosis to obtain an estimate of the overall effects on HRQL.

In the "utility" approach to measuring HRQL, subjects reveal their preferences about particular health states on a scale in which dead has the anchor value of 0.0 and full healthy life has the anchor value of 1.0. (Utility is the technical term for cardinal preference scores measured under conditions of uncertainty.) The utility approach has its foundation in the theory of decision-making under uncertainty (von Neumann and Morgenstern, 1944). This same foundation underlies many models of clinical and medical decision-making (Feeny and Torrance, 1989). For the purposes of this evaluation, an important characteristic of this approach is that it allows the measurement of preferences for all relevant health outcomes, including respondents' "rate of time preference" and risk attitudes. In the context of prenatal diagnosis, there are many possible branches in the decision tree that may be partially described by various temporary (i.e., process) and chronic (i.e., outcome) health states. By combining measures of the utility of each state with data on the frequency and duration of each state, the expected utility of each diagnostic test may be estimated in terms of quality-adjusted life years.

There are two major reasons for measuring the preferences of pregnant women seeking prenatal diagnosis for short-term health states. First, a major advantage of CVS over GA is that



most women experience a reduction in the duration of anxiety resulting from earlier knowledge of a negative test result (i.e., being reassured that the fetus is free of detectable abnormalities at week 12 versus week 20 of pregnancy). Second, anticipation of undergoing the test itself and, in particular, waiting for the results also heighten anxiety; these periods are temporary in nature. Therefore expected differences between the two procedures include the degree and duration of anxiety while awaiting the results of genetic testing (Blumberg, Golbus and Hanson, 1975; Finley, Varner, Vinson, et al., 1977; Borelli, Bender, Puck, et al., 1984; Perry, Vekemans, Lippman, et al., 1985; Tabor and Jonsson, 1987). For CVS, the period of anxiety lasts for approximately 7 weeks: from the time the pregnancy is confirmed (about week 6) to the time the genetic test results are communicated to the patient (about weeks 12 to 14). For GA, the period of heightened anxiety is approximately 13 weeks: from week 6 until weeks 18 to 20. The expected difference in duration of heightened anxiety between individuals in the two trial arms, therefore, would be approximately six weeks.

The long-term or chronic consequences of prenatal diagnosis testing and pregnancy include a wide variety of outcomes. In cases where positive test results lead to a therapeutic abortion, outcomes of the two procedures may differ (Blumberg, Golbus and Hanson, 1975; Adler, 1980). Differences in the sensitivity of CVS and GA as diagnostic tests would lead to differences in the number of undetected chromosomally abnormal children (i.e., births associated with false negative results). Similarly, the two tests may lead to different numbers of therapeutic abortions of healthy fetuses (i.e., abortions associated with false positive results).

On the basis of an examination of the process and possible outcomes of prenatal diagnosis, the estimated frequency of each outcome, and the expected importance of each outcome, a set of health states were selected for utility measurement (Feeny and Torrance, 1989). The list of states appears in Tables 2 and 3, for temporary and chronic health states respectively. Health-state descriptions were prepared for each of these. Each health-state description describes the approximate timing during the pregnancy as well as the salient features of the health state. All patients were asked to provide preference measures for each of the short-term (temporary) and long-term (chronic) states. The full set of health-state descriptions, as presented to patients, appear in Appendix 1. Patients were also asked to consider their own current health and provide preference measures for the HRQL that they were experiencing at that time, the quality of their subjectively-defined current state (SDCS) of health.

In the utility approach the respondent is asked to weigh all the pros and cons to provide a single score which reflects their strength of preference for being in a particular health state.

Operationally, the preference measurement interviews consisted of two stages. Subjects were first asked to rate states on a Feeling Thermometer (FT). The FT is a vertical visual analogue scale. (Some investigators classify it as a form of category scaling; see Patrick and Erickson 1993, pp 162-164.) The top of the FT at 100 was labelled as “Most Desirable”, and the bottom at 0 was labelled as “Least Desirable”. This exercise served to introduce the health states to patients and provides information about the relative desirability of health states from the perspective of patients. The scores obtained from the FT represent value scores. Value scores are preference scores measured under conditions of certainty. The rankings from the FT were used in the next stage of measurement: the standard gamble. The standard gamble is the classic method, in the fields of economics and decision analysis, of measuring cardinal preferences under conditions of uncertainty. Standard gamble scores are utility scores.

The standard gamble was presented to respondents through the use of a prop called the Chance Board (Furlong et al., 1990). In the standard gamble, the respondent is asked to choose between two alternatives: one uncertain and one certain. The two alternatives included three health states which were ranked earlier by the subject on the FT. Alternative 1 is described as uncertain and consists of the most preferred health state and the least preferred health state of the three states. As an example, using FT results from one patient interview, Alternative 1 presented the most preferred state as being the birth of a healthy baby (C9) and the least preferred state as being the birth of a Down syndrome baby after receiving a normal test result (C7). There is a probability “ $p$ ” of living in the most preferred health state and a probability “ $1-p$ ” of living in the least preferred health state. Alternative 2 is described as being certain (100% chance) of living in an intermediately ranked health state. Using FT results from the patient interview described above, Alternative 2 health state was the detection of a fetal abnormality and termination of the pregnancy during week 11 (C1). During a series of questions, probability “ $p$ ” is varied to determine the probability “ $p$ ” for which the respondent is indifferent between the two alternatives. This “indifference probability” provides an interval-scale preference measure, called a utility score. Utility scores are generally reported on a scale defined such that 0.00 is the utility of dead and 1.00 is the utility of “Perfect Health”. Health states of a chronic duration were measured on this “dead - perfect health” continuum, and positive linear transformation was used to transform scores for temporary states onto this conventional scale.

Transformation of scores for health states of a temporary duration was necessary because the notion of a health state of “temporary death” was considered unbelievable. It was necessary, therefore, to select an anchor state of a temporary nature that would clearly be least desirable to most respondents. To avoid upsetting respondents, the health state chosen was

removed from the context of pregnancy (Table 2, T13; Appendix 1, T13). This temporary, low-anchor state was then measured in a standard gamble with dead and perfect health to produce a score for this health state on the conventional 0 - 1 scale. All temporary health state scores were then linearly transformed, using the low-anchor score, to produce scores on the conventional 0 - 1, dead-healthy, scale.

To reduce both the length of interview and respondent burden, we obtained direct utility measures (via the standard-gamble technique) on only a portion of the health states. Utility scores for the remaining health states were imputed using an equation that estimated the relationship between measured utility (Chance Board) and measured value (Feeling Thermometer) scores. Details on the estimation of the exponential function for this imputation are provided in Appendix 2.

### **Assessment Schedule**

Interviews were conducted in patients' homes by trained professional interviewers. Although interviewers were not informed as to which diagnostic procedure each patient had been randomized, blinding was difficult to maintain because patients sometimes revealed to the interviewer the procedure that they had undergone.

Patients were interviewed four times during the course of their pregnancy because levels of anxiety varies over the term of the pregnancy (Fava, 1982 and Fava, 1983), and because health states of a temporary duration vary over the course of pregnancy. It was desirable to elicit patients' preferences for hypothetical temporary health states at or about the time each state would occur naturally and, because context is an important factor in the measurement of health state preferences, it was also desirable to elicit preference measures for the subjectively-defined current health state of each patient in the context of the relevant set of hypothetical states. For example, health states occurring in the first trimester of pregnancy were evaluated by patients at the first assessment, when patients were in weeks 8 - 12 of pregnancy.

Patients were interviewed upon entry into the study (weeks 8-12); at approximately week 13 (when results were expected to be known by the patients who had CVS); at approximately week 18 (when subjects who had amniocentesis were still awaiting their results); and at approximately week 22 (when the prenatal diagnosis results were available to subjects in both arms of the trial). Respondents were instructed to evaluate their current state on three occasions during their pregnancy. On each of these occasions patients were also asked to provide preference scores for a number of hypothetical health states of temporary duration. Patients' subjec-

tively-defined state (T14) was defined as a temporary state and was measured at weeks 8, 13 and 18 (assessments 1, 2 and 3). Although it would have been desirable to measure the subjective state at week 22 as well, to do so would have complicated the interview considerably because it would have introduced the need to assess the patient's temporary health state within an interview otherwise designed to assess chronic health states. Instead, utility measurement at week 22 was focussed exclusively on the hypothetical chronic health states.

Patients completed the Spielberger State Anxiety Questionnaire (Spielberger, Gorsuch, Lushene 1970) at all four interviews. Eight temporary health states (T1, T2, T3, T5, T9, T12, T13, T14 - the SDCS) were assessed at the Week 8 interview; 10 temporary health states were assessed at Week 13 (states T1, T2, T3, T5, T6, T8, T9, T12, T13, T14); 8 temporary health states were assessed at Week 18 (states T4, T7, T8, T10, T11, T12, T13, T14); and 12 chronic health states (C1-C12) were assessed at Week 22. An additional state, dead, was assessed during week 22 interviews. The order of presentation of health states was not randomized. At each session subjects first evaluated the hypothetical health states, then their subjectively-defined current health state, and then completed the Spielberger State Anxiety Questionnaire.

## Recruitment

Adequate sample size (see Statistical Analyses Section) was difficult to obtain for a variety of reasons. First, when we began entering patients into the HRQL study in October, 1987, the main trial was scheduled to cease patient randomization and enrolment in January, 1988. Second, as noted earlier, a small number of patients initially refused to participate.

To augment patient accrual, it was decided to contact enrolled patients in the main trial who were past 12 weeks gestation and therefore not available for the full set of four interviews. In addition, funding was obtained to support continued randomization at the two centers participating in the HRQL study. During the main trial, women with late maternal age indication for prenatal diagnosis could obtain CVS in Canada only by agreeing to be randomized (to CVS or GA) within the trial. Following cessation of entry of patients into the main trial, patients seeking CVS in the areas served by the HRQL study centers, Toronto and Hamilton, could still only obtain CVS by agreeing to be randomized. CVS on demand was, however, available at centers in the U.S. and at some other Canadian centers, and it is possible that not all available patients in the two regions were recruited for the HRQL study. It is, therefore, important to assess the two cohorts of enrollees (those recruited during the main trial and those recruited during follow-up) for any differences in their characteristics or preferences.

Not all patients completed all four interviews because some patients were recruited past 12 weeks gestation and some patients were unable to complete a full set of scheduled interviews due to personal time constraints or illness or other circumstances. In addition, some patients agreed to an interview after initially refusing to participate. Finally, two patients withdrew from the HRQL study after participation in one interview, citing time constraints as a barrier to further participation. One-hundred and twenty five women contributed at least one interview. In total, 79 patients completed assessments at Week 8; 87 at Week 13; 108 at Week 18; and 126 at Week 22.

## **Statistical Analyses**

The study was designed to estimate the HRQL effects of prenatal diagnosis and to test several hypotheses. The first hypothesis is that patients in the CVS arm would experience earlier and more rapid declines in anxiety than patients in the GA arm. This should be reflected in results from the State section of the Spielberger State-Trait Anxiety Inventory (reported elsewhere) and in utility assessments for T14, the subjectively-defined current health state (reported here). The second hypothesis was that because patients were randomized to CVS or GA, their preference scores on hypothetical states should not differ significantly. It was calculated that a minimum of 75 patients per trial arm would be required to provide 80 per cent power to detect a difference of 0.10 (or larger) between mean utility scores. When there was more than one set of data available to perform a test of the second hypothesis, the data set that had undergone the least amount of transformation was used. Thus some tests are done on data on the Perfect Health - Disease State scale rather than the conventional Perfect Health - Dead scale.

Chi-square and Fisher's exact test were used to test for differences in demographic characteristics among groups. A repeated measures analysis of covariance (ANCOVA) of preference scores for the subjectively-defined health state (measured at weeks 8, 13 and 18) was conducted to test for differences in HRQL between CVS and GA groups. To ensure that baseline differences would not account for differences during other assessment periods, Week 8 value scores were treated as a covariate. Trends in anxiety levels and subjective health state scores across assessments were also examined. The Student's t-test was used to examine differences in utility scores for T14 between groups and paired t-tests were used to examine changes in utility scores for T14 between interviews. To determine differences due to time of recruitment (i.e., pre or post main trial recruitment cessation), an analysis of variance using time of recruitment as a factor was conducted on all health state scores. Similarly for hypothetical health states, differences due to time of assessment (weeks 8, 13, or 18) were examined using an analysis of variance.

## RESULTS

### Preference Scores for Subjectively Defined Current Health State

For the overall ANCOVA test of differences between groups in value scores for the subjectively defined health state there were 66 subjects who each contributed scores at all three assessments. The overall difference in subjective state value scores between groups was not significant ( $F_{1,66} = 1.12$ ;  $p = 0.29$ ) when scores for Week 8 were included as a covariate. Mean subjective-state values are reported in Table 4. Student's t-tests did not detect statistically significant differences ( $p > 0.4$ ) between mean value scores by group at weeks 8 and 13. For week 18, however, the mean value score of the CVS group was 0.06 greater than the mean value score of the GA group ( $p = 0.04$ ).

Paired t-tests were conducted for changes in scores from interview to interview. The paired t-test results for the subjective-state value scores appear in Table 5. There was no statistically significant difference in the subjective state value scores in the GA arm from week 8 to week 13 ( $p > 0.1$ ), from week 13 to week 18 ( $p > 0.3$ ), or from week 8 to week 18 ( $p > 0.2$ ). For the CVS group, however, subjective state value scores increased over time. The difference between Week 8 and 13 was significant ( $p < 0.02$ ); the difference between week 8 and 18 was also significant ( $p < 0.01$ ), although the difference between week 13 and week 18 was not significant ( $p > 0.1$ ).

### Preference Scores for Hypothetical Temporary Health States

Directly measured temporary health state utility scores appear in Table 6. No statistically significant differences between groups were detected (week 8,  $p = 0.82$ ; week 13,  $p = 0.30$ ; week 18,  $p = 0.75$ ). In spite of the lack of statistical significance, there may nonetheless be a trend for higher utility scores for GA patients. Analysis of variance detected no statistically significant differences in mean value scores for GA and CVS in weeks 8 ( $p = 0.05$ ), 13 ( $p = 0.79$ ), and 18 ( $p = 0.83$ ). Similarly there were no significant differences by week of pregnancy ( $p = 0.52$ ). Directly measured value scores for all of the temporary health states are presented in Table 7. Imputed utility scores from the exponential function (see Appendix 2) are shown in Table 8.

### Preference Scores for Hypothetical Chronic Health States

Utility scores for chronic states (40 years duration) were obtained in interviews conducted at week 22. These health states are hypothetical in nature. Almost all patients proceeded to health state C9, the most desirable outcome, birth of a healthy baby. The mean directly

measured utility scores for chronic health states (measured using the standard gamble technique) are presented in Table 9. Mean value scores for all chronic health states appear in Table 10. An ANOVA detected no significant difference ( $p > 0.6$ ) in value scores by group. There does, however, appear to be a trend toward higher utility scores for GA patients. Utility scores for all chronic health states, imputed using the value scores and the exponential function (see Appendix 2), are presented in Table 11.

Chi-square and Fisher's exact tests (not shown) indicated that there were no differences in demographic characteristics by time of recruitment or by arm of the trial. An ANOVA was performed to determine if there were any significant differences in mean utility scores due to time of recruitment: before versus after January 31, 1988 when randomization for the main trial ended. No significant differences in mean utility scores were detected (week 8,  $p = 0.75$ ; week 13,  $p = 0.21$ ; week 18,  $p = 0.53$ ; week 22,  $p = 0.98$ ).

## DISCUSSION

There are two major findings. First, CVS is associated with higher HRQL while undergoing prenatal diagnosis (significant difference at week 18). Second, women found the negative long-term outcomes of testing, which are more frequently associated with CVS than amniocentesis, to be quite burdensome.

We had expected to find clear differences between the CVS and GA groups in both the anxiety and subjective state value scores. For the subjective state value scores, the observed differences are most apparent at week 18 of pregnancy: on average the HRQL of CVS patients is better than that reported by GA patients. This is to be expected because at week 18 the difference between the experience in both arms is most obvious. Patients in the CVS arm have received their test results while patients in the GA arm have received the test but not the results. (In the original design of the study we had expected to observe a similar difference between GA and CVS at Week 13. We had assumed that by Week 13 CVS patients would have received their test result and would therefore have experienced an increase in HRQL. In practice, however, many patients had not received their test result by Week 13.) For the anxiety scores, a statistically significant difference between groups was also detected at Week 18.

There is a lack of congruence between the results from the ANCOVA analyses and those relying on t-tests or paired t-tests. Three considerations are important in interpreting these differences. First, the sample sizes for the ANCOVA analyses were smaller; thus the statistical power to detect differences was low. Second, the differences in subjective utility between the two groups were small further exacerbating the lack of power issue. Third, although the differences between the two groups at week 8 were not statistically significant, there was a trend in favour of the CVS group both in the subjective state value and anxiety scores. When this difference at baseline is taken into account by the ANCOVA, the importance of the differences in favour of CVS at later weeks (like week 18) is diminished. Thus differences between CVS and GA are significant at week 18 using the t-test but insignificant when using the ANCOVA. The difference at week 8 may reflect random measurement error. One could speculate, however, that the difference may reflect a true underlying difference between the two groups at week 8. Many patients agreed to participate in the trial because they wanted access to CVS; at the time CVS was only available, for late maternal age indications, through the trial. Thus it is unlikely that preference for modality was equally distributed between the two arms of the trial. If more patients wanted CVS than wanted GA, then at week 8, more CVS patients would have been satisfied with the outcome of randomization than GA patients would have been. (Week 8 inter-



views took place after patients learned the arm of the trial to which they had been randomized.) The higher level of satisfaction of CVS patients might then have been reflected in their preference scores thus reducing later increases in health-related quality of life for the CVS group.

An examination of the value scores for the temporary hypothetical states reveals neither significant differences by trial arm nor by week of pregnancy. We had not expected differences in scores of hypothetical health states by trial arm. Although there were no statistically significant differences by trial arm, a trend towards GA patients assigning higher preference scores to hypothetical health states is apparent in the data. One could speculate that because GA was the established procedure and therefore women had less reason to worry about it, their general outlook was more favourable and thus they rated the states higher than CVS women did. Evidence in favour of this interpretation is, however, weak. Week-to-week improvements in mean preference scores for subjectively-defined current health states (T14) favour CVS versus GA, and at week 18 CVS scores are higher than GA scores.

We were uncertain whether current health states would influence the scoring of hypothetical, but related, health states. Value scores for the five hypothetical states assessed at both weeks 8 and 13 appear to have been stable. The hypothetical chronic health state value scores did not differ statistically by trial arm; this is as expected.

Mean value scores by group for the subjectively-defined current health state (T14) ranged from 0.77 to 0.85 over the week 8 through week 18 period (Table 4). Mean value scores for the corresponding hypothetical states (T1-T4) ranged from 0.50 to 0.62. Women appear to have rated their own health-related quality of life as being preferable to the hypothetical health-state description that was designed to have corresponded to health states they were experiencing during the process of prenatal diagnosis.

It is important to examine the relationships among the mean scores for health states describing an early pregnancy termination (C1), a late pregnancy termination (C2), a miscarriage unrelated to any test (C4), a false positive (C3) and a false negative (C7). The scores for these states can all be compared using the value scores (Table 10) or imputed utility scores (Table 11). The mean scores indicate that a miscarriage unrelated to a test (C4) was preferred to a first trimester therapeutic abortion for a genetic indication (C1) which was in turn preferred to a second trimester therapeutic abortion (C2). Interestingly the consequences of diagnostic inaccuracy, false positives (C3) and false negatives (C7), were considered as being approximately equal and rates as being much worse than a miscarriage or termination. This is particularly

important given the evidence that diagnostic inaccuracy is more common with CVS than GA (Lippman, Tomkins, Shime, et al, 1992). The low scores associated with the birth of a child with Down Syndrome (C8), a false negative test (C7), and a false positive test (C3) may suggest that the underlying goal of patients is the birth of a healthy baby. (Similar results are found in Kuppermann et al. 1999.) Thus the two most important factors that contribute to HRQL for women seeking prenatal diagnosis for late maternal age are the avoidance of the birth of a chromosomally abnormal child and the avoidance of the termination of a healthy fetus. The timing of procedures is of secondary importance.

Although the utility scores reported here were obtained in the context of a trial comparing CVS and GA, the health-state descriptions that were evaluated include a number of states that are more generally applicable to prenatal diagnosis. The generalizability of the utility scores is enhanced by the lack of statistically significant differences by trial or week of pregnancy. Thus the descriptive results are of relevance to evaluations of the health-related quality of life impacts of maternal serum alpha-fetoprotein screening programs, transabdominal chorionic villi sampling, early amniocentesis, and other prenatal diagnostic tests, including the introduction of tests based on molecular genetic techniques.

The inclusion of HRQL instruments in the trial comparing CVS and GA produced important new information that complement the assessment of clinical outcomes. Evidence about the effects of prenatal diagnosis on women undergoing it has implications for the provision of prenatal diagnostic services and genetic counselling. If women attach great disutility to the consequences of diagnostic inaccuracy, there may be implications about the types of information that should be included in genetic counselling in order to enable women to select the modality most consistent with their preferences. Similarly, rates of miscarriage and the extent to which pregnancies are “replaced” are important considerations. Evidence on the value that women place on the outcomes produced by prenatal diagnostic programs should be crucial in formulating clinical and public policies for prenatal diagnosis. Both the utility and psycho-social HRQL instruments performed well in the trial. Investigators concerned with prenatal diagnosis should seriously consider the inclusion of HRQL assessments in their studies.

Finally, as hypothesized, the results indicate a modest temporary advantage in favour of CVS. This short term gain, however, needs to be seen in light of the substantial disutility associated with diagnostic inaccuracy that while infrequent, does occur at a higher rate with chorionic villi sampling than genetic amniocentesis.

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**Table 1**  
**Patient Demographic Characteristics**

	GA (n = 61)	CVS (n= 65)
Age (in years)	37.8 (2.2) *	37.6 (1.9) *
% with children	75.4	76.9
% married or common-law	93.4	100
% with income > \$40,000	78.7	86.2
Education:		
% with no university	37.7	24.6
% with some university	14.8	24.6
% with bachelor degree(s)	26.2	18.5
% with post-graduate		
degree(s)	9.8	26.2
% with other	11.5	6.2

Legend:

\* mean (standard deviation)

**Table 2**  
**Temporary Health States**  
(duration assessed: one week)

Code	Health State Label	Assessment
T1	In week 9; waiting for prenatal diagnosis test.	Weeks 8, 13
T2	In week 14; waiting for prenatal diagnosis test.	Weeks 8, 13
T3	Test performed in week 10; waiting for results.	Weeks 8, 13
T4	Test performed in week 16; waiting for results.	Week 18
T5	Abnormality detected; terminate pregnancy in week 11.	Week 8, 13
T6	Miscarriage at weeks 10-12; suspect due to test at week 10.	Week 13
T7	Abnormality detected; terminate pregnancy in week 20.	Week 18
T8	Miscarriage in weeks 12-16; unlikely to be related to test at week 10.	Weeks 13, 18
T9	Miscarriage in weeks 10-16; no test.	Weeks 8, 13
T10	Pregnancy loss at weeks 16-18; suspect due to test at week 16.	Week 18
T11	Pregnancy loss after week 18; unlikely to be related to test.	Week 18
T12	Continuing in a normal pregnancy.	Weeks 8, 13, 18
T13	HOME/RADIATION/CHEMO... (i.e., disease state).	Weeks 8, 13, 18
T14	Your Present Health State (i.e., subjectively-defined current health state).	Weeks 8, 13, 18

Note: See Appendix 1 for full health state descriptions.



**Table 3**

**Chronic Health States**  
(duration assessed: 40 years)

Code	Health State
C1	Abnormality detected; pregnancy terminated in the 11th week.
C2	Abnormality detected; pregnancy terminated in the 20th week.
C3	Abnormality reported; terminated pregnancy; told results were incorrect.
C4	Miscarriage in weeks 10-16; no test.
C5	Miscarriage; suspect due to test.
C6	Pregnancy loss after week 20; unlikely to be related to test.
C7	Test reported normal; birth of Down syndrome baby; test results incorrect.
C8	No test available; birth of Down syndrome baby.
C9	Birth of healthy baby.
C10	HOME/RADIATION/CHEMO... (i.e., disease state).
C11	Risk of abnormality; choose not to become pregnant.
C12	Death.

Note: See Appendix 1 for full health state descriptions.

**Table 4**  
**Value Scores for Subjectively-Defined Current Health States**

Mean (standard deviation)

ASSESSMENT	GROUP _____		
	GA _____	CVS _____	OVERALL
WEEK 8	0.77 (0.20)	0.77 (0.13)	0.77 (0.17)
WEEK 13	0.82 (0.16)	0.82 (0.17)	0.82 (0.16)
WEEK 18*	0.79 (0.19)	0.85 (0.17)	0.82 (0.18)

\* t-test of difference between trial groups for this assessment is statistically significant ( $p = 0.038$ ).

Notes:

Scores are on the Perfect Health (T12) = 1.00 to Disease State (T13) = 0.00 scale.

Sample sizes are as follows.

Week 8:  $n = 41$  for GA;  $n = 38$  for CVS; total  $n = 79$ .

Week 13:  $n = 40$  for GA;  $n = 47$  for CVS; total  $n = 87$ .

Week 18:  $n = 55$  for GA;  $n = 53$  for CVS; total  $n = 108$ .

**Table 5**

**Differences in Value Scores Between Assessment Weeks  
for Subjectively-Defined Current Health States**

ASSESSMENT WEEK	GA Group		CVS Group	
	Difference in mean scores	t - statistic	Difference in mean scores	t - statistic
WEEK 13 - WEEK 8	0.03	0.90	0.06	2.20*
WEEK 18 - WEEK 13	-0.01	-0.32	0.03	1.28
WEEK 18 - WEEK 8	0.02	0.55	0.08	2.28*

\*Statistically significant (  $p < 0.05$  ).

**Table 6**

**Directly Measured Utility Scores for Temporary Health States**  
Mean (standard deviation)

**WEEK 8**

Health State	GA	Group CVS	Overall
T3	0.93 (0.12)	0.89 (0.21)	0.91 (0.17)
T5	0.78 (0.23)	0.66 (0.32)	0.72 (0.28)
T9	0.79 (0.24)	0.73 (0.28)	0.76 (0.26)

**WEEK 13**

Health State	GA	Group CVS	Overall
T3	0.96 (0.06)	0.90 (0.17)	0.93 (0.13)
T5	0.83 (0.23)	0.70 (0.28)	0.76 (0.27)
T9	0.86 (0.22)	0.76 (0.25)	0.81 (0.24)

**WEEK 18**

Health State	GA	Group CVS	Overall
T4	0.94 (0.10)	0.89 (0.17)	0.92 (0.14)
T7	0.80 (0.20)	0.66 (0.33)	0.73 (0.28)
T13	0.43 (0.36)	0.31 (0.34)	0.37 (0.35)

Notes: Week 8: n = 37 for GA; n = 35 for CVS; total n = 72.  
Week 13: n = 36 for GA; n = 45 for CVS; total n = 81.  
Week 18: n = 49 for GA; n = 50 for CVS; total n = 99.

Utility scores are on the conventional Perfect Health = 1.00  
to Dead = 0.00 scale, linked by the chronic state score  
for the Disease State.

**Table 7**  
**Directly Measured Value Scores for Temporary Health States**

State	Measured Value *
T1	0.62
T2	0.50
T3	0.60
T4	0.58
T5	0.23
T6	0.24
T7	0.15
T8	0.30
T9	0.30
T10	0.23
T11	0.26

\* The measured value scores reported are means of pooled scores from the interviews conducted in weeks 8, 13 and 18 on the perfect health = 1.0 to disease state = 0.0 scale.

**Table 8**  
**Imputed Utility Scores for Temporary Health States**

State	Imputed Utility _ Scores _____	Mean Directly Measured _ Utility Scores _
T1	0.94	-
T2	0.89	-
T3	0.94	0.93
T4	0.93	0.91
T5	0.67	0.74
T6	0.69	-
T7	0.59	0.71
T8	0.75	-
T9	0.74	0.80
T10	0.67	-
T11	0.70	-
T13		0.38

Note: Value scores from which the utility scores are imputed are from Table 7; methods of imputation are described in Appendix 2. Utility scores are on the conventional Perfect Health = 1.00 to Dead = 0.00 scale.

**Table 9**

**Directly Measured Utility Scores for Chronic Health States at Week 22**  
 Mean (standard deviation)

Health State	Group		
	GA	CVS	Overall
C1	0.86 (0.21)	0.81 (0.29)	0.83 (0.26)
C2	0.81 (0.25)	0.76 (0.29)	0.78 (0.27)
C4	0.87 (0.20)	0.83 (0.25)	0.85 (0.23)
C7	0.58 (0.34)	0.48 (0.35)	0.53 (0.35)
C10	0.44 (0.36)	0.32 (0.33)	0.37 (0.35)

Notes:

n = 56 for GA; n = 65 for CVS; total n = 121.

Utility scores are on the conventional  
 Perfect Health = 1.00 to Dead = 0.00 scale.

**Table 10**

**Value Scores for Chronic Health States**  
Mean Score (standard deviation)

Health State_	GA_____	Group CVS_____	Overall__
C1	0.50 (0.25)	0.47 (0.28)	0.48 (0.27)
C2	0.39 (0.24)	0.36 (0.24)	0.37 (0.24)
C3	0.17 (0.16)	0.20 (0.18)	0.19 (0.17)
C4	0.48 (0.24)	0.52 (0.26)	0.50 (0.26)
C5	0.38 (0.20)	0.40 (0.23)	0.39 (0.22)
C6	0.39 (0.20)	0.44 (0.25)	0.42 (0.23)
C7	0.18 (0.16)	0.20 (0.20)	0.19 (0.18)
C8	0.25 (0.19)	0.24 (0.22)	0.24 (0.21)
C9*	1.00 (n.a.)	1.00 (n.a.)	1.00 (n.a.)
C10	0.12 (0.15)	0.10 (0.14)	0.11 (0.15)
C11	0.43 (0.25)	0.42 (0.30)	0.43 (0.28)
C12**	0.00 (n.a.)	0.00 (n.a.)	0.00 (n.a.)

Notes:

These value scores are on the conventional Perfect Health = 1.0 to  
Dead = 0.0 scale.

\* - C9 is the upper anchor state of the scale with a defined utility of 1.0.

\*\* - C12 is the lower anchor of the scale with a defined utility of 0.0.

n.a. - not applicable (utility score was not measured but defined by the scale).

n = 56 for GA; n = 65 for CVS; total n = 121.



**Table 11**

**Imputed Utility Scores for Chronic Health States**

Health _State_	Imputed _Utility_	Directly Measured _Utility_
C1	0.85	0.83
C2	0.74	0.78
C3	0.45	-
C4	0.87	0.85
C5	0.75	-
C6	0.79	-
C7	0.45	0.53
C8	0.55	-
C10	0.28	0.37
C11	0.79	-

Notes:

Utility scores are imputed using overall value scores from Table 10 and methods of imputation described in Appendix 2.

Utility scores are on the conventional Perfect Health = 1.00 to Dead = 0.00 scale.



## Appendix 1 Health-State Descriptions

In this Appendix each health state is presented using a two-character code, a short descriptive label, and a detailed health state description. Each health state is identified using a code consisting of a letter (T for temporary; C for chronic) and a number (1-14 for temporary, 1-12 for chronic) corresponding to the list of states in Tables 2 and 3. The health state identification code was printed on the back of each description.

A short descriptive label was printed only on the arrow that went with each card and the arrow was used by the respondent to indicate the score on the visual analog scale. The short descriptive labels appear below in block capitals.

The full text of each health-state description is presented below, using the exact wording presented to respondents of the prenatal diagnosis patient survey. (Modestly revised versions of these descriptions were presented to male and female respondents participating in the survey of general population couples.) Each full description appeared on the front face of a card (4 inches by 5 inches in size) that was handed to respondents for them to read. Coloured stripes along the left-hand edge of each card (colour on each card noted in parentheses following two-character code) helped respondents identify similar health state descriptions and underlining of text (represented by underlined wording in the descriptions below) helped respondents identify key differences among health state descriptions.

### Temporary Health State Descriptions

T1 (pink)

IN WEEK 9; WAITING FOR PRENATAL DIAGNOSIS TEST

You are in week 9, about 2 months, of your pregnancy and you have decided to have a test to determine if the baby has a chromosomal abnormality. The test will not occur for at least another week. Your pregnancy is still private; only those whom you have told are aware of it. Although you have been reassured by your physician, you may have lingering concerns about the effects of the test on yourself or the baby and about the possibility of a miscarriage. You may also be thinking about whether or not to terminate the pregnancy if the test indicates that the baby is abnormal. Think about spending the next week in this situation.

T2 (pink)

IN WEEK 14; WAITING FOR PRENATAL DIAGNOSIS TEST

You are in week 14 (a little over 3 months) of your pregnancy and have decided to have a test to determine if the baby has a chromosomal abnormality. The test will not occur for at least a week. It is no longer easy for you to hide your pregnancy. Although you have been reassured by your physician, you may have lingering concerns about the effects of the test on yourself or the baby and about the possibility of a miscarriage. You may also be thinking about whether or not to terminate the pregnancy if the test indicates that the baby is abnormal. Think about spending the next week in this situation.

T3 (orange)

TEST PERFORMED IN WEEK 10; WAITING FOR RESULTS

You are in week 10 (about 2 months) of your pregnancy and have just had a test to determine if the baby has a chromosomal abnormality. Your pregnancy is still private; only those whom you have told are aware of it. The test results will not be available for at least a week. The test procedure itself went well. It involved some mild discomfort but you were able to resume

normal activities the same day. In spite of reassurance, you may be concerned about what effect the procedure may have had on yourself or the baby and about the possibility of a miscarriage. You may also be thinking about whether or not to terminate the pregnancy if the test indicates that the baby is abnormal. Think about spending the next week in this situation.

T4 (orange)

TEST PERFORMED IN WEEK 16; WAITING FOR RESULTS

You are in week 18 (about 4 months) of your pregnancy and have had a test to determine if the baby has a chromosomal abnormality. It is no longer easy for you to hide your pregnancy and you may have felt the baby move. It takes four weeks for the results to become available; you have already waited two weeks and have two more weeks to wait. The test procedure itself went well. It involved some mild discomfort but you were able to resume normal activities the same day. In spite of reassurances, you may be concerned about what effect the procedure may have had on yourself or the baby and about the possibility of a miscarriage. You may also be thinking about whether or not to terminate the pregnancy if the test indicates that the baby is abnormal. Think about spending the next week in this situation.

T5 (yellow)

ABNORMALITY DETECTED; TERMINATE PREGNANCY IN WEEK 11

You received the results of a test which determined that the baby had a chromosomal abnormality and you decided to terminate the pregnancy. The procedure to terminate the pregnancy was performed at week 11 (about 2 months) of your pregnancy; it required a day in hospital and was performed under general anaesthetic. The procedure took about 10 minutes to perform. You went home the same day and were able to resume normal activities within one or two days. Following the procedure you may have experienced feelings of depression, mild tearfulness, sadness, lethargy and a sense of loss. You have experienced these feelings for two weeks and they may persist for two more weeks. Think about spending the next week in this situation.

T6 (green)

MISCARRIAGE AT WEEKS 10-12; SUSPECT DUE TO TEST AT WEEK 10

You suffered a miscarriage 2 weeks ago. You had had a test at week 10 (about 2 months) of your pregnancy to determine whether or not the baby had a chromosomal abnormality. There were some problems with the test procedure itself, but the results indicated the baby was normal. You are not certain of the cause of the miscarriage, but you suspect it might be due to the procedure. You may experience feelings of guilt for having undergone the procedure and for the loss of your pregnancy. You may feel depressed and experience feelings of sadness because you could not carry the baby to term. You have experienced these feelings for two weeks and they may persist for two more weeks. Think about spending the next week in this situation.

T7 (yellow)

**ABNORMALITY DETECTED; TERMINATE PREGNANCY IN WEEK 20**

You received the results of a test which determined that the baby had a chromosomal abnormality and you decided to terminate the pregnancy. The procedure to terminate the pregnancy was performed at week 20 (about 4 months) of your pregnancy. A drug was injected into the uterus, causing labour to begin. The time from the beginning to the end of the procedure was about 20 hours and you were awake during this time. You spent up to 2 days in hospital for the procedure and you may have seen the fetus at the time of delivery. You may be experiencing feelings of grief, depression or loss, particularly if you had felt the baby move during the pregnancy. Think about how you might feel telling your family and friends about the termination of your pregnancy. You have experienced these feelings for two weeks and they may persist for two more weeks. Think about spending the next week in this situation.

T8 (green)

**MISCARRIAGE IN WEEKS 12-16; UNLIKELY TO BE RELATED TO TEST AT WEEK 10**

You suffered a miscarriage two weeks ago. You were in weeks 12-16 (about 2 to 3½ months) of your pregnancy. You had had a test some weeks ago to determine whether or not your baby had a chromosomal abnormality. The test went well and the results indicated that the baby would be normal. Your physician assures you that it is unlikely that the miscarriage was related to the test procedure. You may experience periods of depression and disappointment at the loss of your pregnancy. You may have to deal with feelings of sadness because you could not carry the baby to term. You have experienced these feelings for two weeks and they may persist for two more weeks. Think about spending the next week in this situation.

T9 (green)

**MISCARRIAGE IN WEEKS 10-16; NO TEST**

You suffered a miscarriage two weeks ago. You were in weeks 10-16 (about 2 to 3½ months) of your pregnancy. No tests or procedures were performed that could have caused this loss. You may experience periods of depression and disappointment at the loss of your pregnancy. You may have to deal with feelings of sadness because you could not carry the baby to term. You have experienced these feelings for two weeks and they may persist for two more weeks. Think about spending the next week in this situation.

T10 (purple)

**PREGNANCY LOSS AT WEEKS 16-18; SUSPECT DUE TO TEST AT WEEK 16**

You suffered a pregnancy loss two weeks ago. You had had a test in week 16 (about 3½ months) of your pregnancy to determine whether or not the baby had a chromosomal abnormality. There were some problems with the test procedure itself, but the results indicated the baby was normal. You are not certain of the cause of the loss, but you suspect it might be due to the procedure. You may experience feelings of guilt for having undergone the procedure and for the loss of your pregnancy. You may feel depressed and experience feelings of remorse because you were unable to carry the baby to term. You have experienced these feelings for two weeks and they may persist for two more weeks. Think about spending the next week in this situation.

T11 (purple)

**PREGNANCY LOSS AFTER WEEK 18; UNLIKELY TO BE RELATED TO TEST**

You suffered a pregnancy loss two weeks ago. You were in the second half (past 4 months) of your pregnancy. You had had a test some weeks before to determine whether or not your baby had a chromosomal abnormality. The test went well and the results indicated the baby would be normal. Your physician assures you that it is unlikely that the pregnancy loss was related to the test procedure. You may experience feelings of sadness and loss, particularly because you had felt the baby move. You may experience feelings of guilt and/or remorse because you were unable to carry the baby to term. You have experienced these feelings for two weeks and they may persist for two more weeks. Think about spending the next week in this situation.

T12 (black)

**CONTINUING IN A NORMAL PREGNANCY**

You are between the ages of 35 and 40 and continuing in a wanted pregnancy. The prenatal diagnosis test and all other tests indicate that everything is normal. You have no more than the usual anxieties and worries which most women experience in this condition. The pregnancy is progressing normally. Think about spending the next week in this situation.

T13 (red)

**HOME/RADIATION/CHEMOTHERAPY/INJECTIONS/FEVER, PAIN, VOMITING/NO WORK OR SCHOOL/BALD**

You have a disease which periodically requires intensive treatment for one week. At the end of this treatment you will feel healthy and well. Sometime in the future your disease may flare up again and require further treatment, but for now, please consider a one week period during which you are receiving the treatment for this disease. You will live at home for this week but visit the hospital each day for painless radiation to your head.

Over the course of the week you will receive a needle into a muscle on one occasion and a needle into your spine to inject drugs on an additional occasion. During the treatment week you will be able to walk and engage in moderate leisure activities, but you will be unable to attend work or school.

You will have a few fevers, a fairly sore mouth, and a few stomach aches. You can also expect to vomit frequently, and to lose all of your hair. You will be embarrassed by your baldness and swollen face. This will be a fairly stressful time for your family. Think about spending the next week in this situation.

T14 (blue)

**YOUR PRESENT HEALTH STATE**

I would like you to think about your present health - - the way you have felt for the past week. Think about how your present state of health and how your feelings affect your work, your social life, your home life and your happiness.

### **Descriptions Used in Chance Board for third & final standard gamble question at week 18**

A - (placed in left-hand pocket of Choice A)

You have a disease that periodically requires intensive treatment. No one can predict the course of the disease. In the future, you may remain healthy, you may become disabled by the disease, or you may die. Consider a one-week period during which you are having no problems with the disease. You are feeling healthy and well and lead a normal life. Imagine spending the next week in this situation.

B - (placed in Choice B pocket in Chance Board)

You have a disease that periodically requires intensive treatment for one week. Otherwise, when the disease is not bothering you, you are fairly healthy and lead a normal life. No one can predict the course of the disease. In the future, you may remain healthy, you may become disabled by the disease, or you may die. Consider a one-week period during which you are receiving the treatment for this disease. You will live at home for this week but visit the hospital each day for painless radiation to your head.

Over the course of the week you will receive a needle into a muscle for one occasion and a needle into your spine to inject drugs on an additional occasion. During this week you will be able to walk and engage in moderate leisure activities, but you will be unable to attend work or school.

You will have a few fevers, a fairly sore mouth, and a few stomach aches. You can also expect to vomit frequently, and to lose all of your hair. You will be embarrassed by your baldness and swollen face. This will be a fairly stressful time for you and your family. Think about spending the next week in this situation.

Death - (placed in right-hand pocket of Choice A)

Imagine that sometime within the next week you will die of natural causes, without pain, in your sleep.

## Chronic Health State Descriptions

### C1 (yellow)

#### ABNORMALITY DETECTED; PREGNANCY TERMINATED IN THE 11th WEEK

In the 11th week (about 2 months) of your pregnancy you received the results of a test which indicated that your baby was abnormal. You decided to terminate the pregnancy. It has been more than 4 weeks since the procedure. Your initial feelings have subsided and your life has returned to normal. You may experience periods of sadness and loss and perhaps depression. You are, however, secure in the knowledge that the decision not to have an abnormal child was the best one for you. If you found yourself in that situation with a future pregnancy, you would make the same decision. Think about living the rest of your life with the knowledge of this experience.

### C2 (yellow)

#### ABNORMALITY DETECTED; PREGNANCY TERMINATED IN THE 20th WEEK

In the 20th week (about 4 months) of your pregnancy you received the results of a test that indicated that your baby was abnormal. You decided to terminate the pregnancy. It has been more than 4 weeks since the procedure. You were no longer able to hide your pregnancy; your family and friends may have been aware of your decision. Your initial feelings have subsided and your life has returned to normal. You may experience periods of sadness and loss and perhaps some depression. You are, however, secure in the knowledge that your decision not to have an abnormal child was the best one for you. If you found yourself in that situation in a future pregnancy, you would make the same decision. Think about living the rest of your life with the knowledge of this experience.

### C3 (blue)

#### ABNORMALITY REPORTED; TERMINATE PREGNANCY, TOLD RESULTS WERE INCORRECT

Your pregnancy was terminated after receiving the results of a test that indicated that the baby was abnormal. Since that time you have been told that the test results were incorrect and the baby was, in fact, normal. Think about your feelings and reactions to this information. You may experience periods of sadness and loss and perhaps depression. You may regret your decision to have the test and to terminate the pregnancy. Think about living the rest of your life with the knowledge of this experience.

### C4 (green)

#### MISCARRIAGE IN WEEKS 10-16; NO TEST

It has been at least 4 weeks since you suffered a miscarriage. You were in weeks 10-16 (about 2 to 3½ months) of the pregnancy. No tests or procedures were performed that could have caused this loss. Your initial feelings have subsided and your life has returned to normal. You may experience periods of sadness and loss and perhaps depression. Think about spending the rest of your life with the knowledge of this experience.



C5 (green)

MISCARRIAGE; SUSPECT DUE TO TEST

It has been at least 4 weeks since you suffered a miscarriage. You had a test early in the pregnancy to determine whether or not the baby had a chromosomal abnormality. There were some problems with the procedure itself, but the results indicated the baby was normal. You are not certain of the cause of the miscarriage, but you suspect it might be due to the procedure. Your initial feelings have subsided and your life has returned to normal. You may regret your decision to have the test. You may experience periods of sadness and loss and perhaps depression. Think about spending the rest of your life with the knowledge of this experience.

C6 (green)

PREGNANCY LOSS AFTER WEEK 20; UNLIKELY TO BE RELATED TO TEST

It has been at least 4 weeks since you suffered a pregnancy loss. You had a test during the pregnancy to determine whether or not your baby had a chromosomal abnormality. The test went well; results indicated the baby would be normal. After the test and in the second half of your pregnancy, you suffered a pregnancy loss. Your physician assured you that it was unlikely that the pregnancy loss was related to the test procedure. Your initial feelings have subsided and your life has returned to normal. You may experience periods of sadness and loss and perhaps depression, particularly because you had felt the baby move. Think about spending the rest of your life with the knowledge of this experience.

C7 (pink)

TEST REPORTED NORMAL; BIRTH OF DOWN SYNDROME BABY; TEST RESULTS INCORRECT

In spite of testing during your pregnancy which indicated that your baby would be normal, you have given birth to a baby affected with Down syndrome. Typically Down syndrome children are mentally retarded, and some have physical abnormalities as well. Some of these children undergo treatment to correct defects such as bowel or heart abnormalities. They often have colds, infections and pneumonia more frequently than other children. In the past some parents placed their Down syndrome children in institutional care; however these days there exists community support so that this is seldom necessary. Some Down syndrome children eventually are capable of earning income, but rarely can live independently. Even in favourable cases you will want to make arrangements for long-term care, that is when your child is fully grown and can live in a group home or other community facility. At times many parents feel stressed with the additional responsibilities of caring for their Down syndrome child, in spite of their positive feelings about the child. Many parents experience feelings of distress and sadness at having a child with special needs. However, families are capable of including their Down syndrome child in all the ordinary activities in which families engage, such as travel and sports. Some parents find hidden strengths in themselves and appreciate the special rewards in nurturing and caring for such special children. Think about your feelings toward the failure of the test to detect the abnormality. Think about spending the rest of your life as the parent of a Down syndrome child.

C8 (pink)

**NO TEST AVAILABLE; BIRTH OF DOWN SYNDROME BABY**

During your pregnancy you were not able to have a test to determine if the baby had a chromosomal abnormality (prenatal diagnosis). You have given birth to a baby affected with Down syndrome. Typically Down syndrome children are mentally retarded, and some have physical abnormalities as well. Some of these children undergo treatment to correct defects such as bowel or heart abnormalities. They often have colds, infections and pneumonia more frequently than other children. In the past some parents placed their Down syndrome children in institutional care; however, these days there exists community support so that this is seldom necessary. Some Down syndrome children eventually are capable of earning income, but rarely can live independently. Even in favourable cases you will want to make arrangements for long-term care, that is when your child is fully grown and can live in a group home or other community facility. At times many parents feel stressed with the additional responsibilities of caring for their Down syndrome child, in spite of their positive feelings about the child. Many parents experience feelings of distress and sadness at having a child with special needs. However, families are capable of including their Down syndrome child in all the ordinary activities in which families engage, such as travel and sports. Some parents find hidden strengths in themselves and appreciate the special rewards in nurturing and caring for such special children. Think about spending the rest of your life as the parent of a Down syndrome child.

C9 (black)

**BIRTH OF HEALTHY BABY**

You have given birth to a healthy baby. You face the usual joys and challenges of parenting. Think about how this will affect the rest of your life and how you will feel.

C10 (red)

**HOME/RADIATION/CHEMOTHERAPY/INJECTIONS/FEVER, PAIN, VOMITING/NO WORK OR SCHOOL/BALD**

You have a disease which flares up about once every four or five weeks. These flare-ups are severe and require intensive treatment for one week. Otherwise, when the disease is not bothering you, you are fairly healthy and lead a normal life. For the treatment week,, you will live at home but you must visit the hospital each day for painless radiation to your head. You will receive a needle into a muscle on one occasion and a needle into your spine to inject drugs on an additional occasion during the week. During the treatment week you will be unable to attend work or school. Because of treatment you will have occasional fevers, a fairly sore mouth, occasional stomach aches, vomiting and hair loss. You may be embarrassed by your baldness and swollen face. The treatment period will be fairly stressful for you and your family, but, after the treatment week, you feel healthy and well. Think about spending the rest of your life alternating periods of treatment and periods during which you are fairly healthy.

C11 (orange)

**RISK OF ABNORMALITY; CHOOSE NOT TO BECOME PREGNANT**

You have just been informed that you have an increased risk of delivering a chromosomally abnormal baby. You and your spouse have decided not to attempt to become pregnant rather than risk having a chromosomally abnormal child. Think about how this will affect the rest of your life.

C12 (pale blue)

**DEATH**

Imagine that sometime within the next week you will die of natural causes, without pain, in your sleep.



## Appendix 2 Estimation of Exponential Functions

In order to reduce the cognitive burden and duration of preference elicitation interviews, direct utility scores were not obtained for all health states. Instead a two-stage measurement strategy was used. First, value scores (preference scores measured under certainty using the Feeling Thermometer, a visual analog scale) were obtained for all states. Second, utility scores (preference scores measured under uncertainty) were obtained for a sub-set of states using the Chance Board, a visual aid which presents the classic standard gamble method for measuring utility scores.

There is a well known relationship between value and utility scores. Torrance (1976) has shown that an exponential function can be used to transform value scores into utility scores. The exponential function takes the following general form:

$$(1-u_i) = (1-v_i)^\alpha$$

where  $u_i$  is the utility score for state  $i$ ,  $v_i$  is the value score for state  $i$ , and  $\alpha$  is the exponent of the exponential function. (In the decision analysis literature this exponential function is referred to as a power function; the parameter of the function,  $\alpha$ , does not have the same meaning as in conventional statistical testing where it represents the probability of a type I error.)

Two separate exponential functions, one for the set of temporary health states and one for the set of chronic health states, were estimated. (There were no statistically significant differences between  $\alpha$  estimates based on each of week 8, 13, and 18 temporary state scores; the temporary health state measurements were then pooled to increase the precision of the overall estimate of  $\alpha$ .) The estimates reported here were based on a linear regression of the natural logarithm of the person-mean disutility scores on the natural logarithm of the person-mean disvalue scores with the intercept term forced to zero (in order to conform to the functional form of the exponential function). (A disutility score for a state is equal to one minus the utility score for that state; a disvalue score is one minus the value score for that state. A person-mean observation was defined such that the mean value and mean utility score for each health state and each assessment week were treated as separate observation points.)

The estimated exponent for the exponential function from the five temporary health states (on the perfect health = 1.0, disease state (T13) = 0.0 scale) was 2.45 (standard error of estimate = 0.17;  $R^2 = 0.75$ ). The estimated exponent from the exponential function for the five chronic health states (on the conventional perfect health = 1.0, dead = 0.0 scale) was 2.86 (standard error of estimate = 0.14;  $R^2 = 0.94$ ). These results are consistent with previous estimates of  $\alpha$  (Torrance, 1976).

These estimated power functions provide a reasonably accurate method for imputing utility scores for states which were not included in the standard gamble/chance board portion of the interviews. The temporary and chronic versions of the power function were used to impute the utility scores shown in Tables 8 and 11.



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Paper 00-04

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Prenatal Diagnosis Comparing Chorionic  
Villi Sampling and Amniocentesis:  
A Technical Report**

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