Patients’ Utilities for Cancer Treatments: A Study of the Chained Procedure for the Standard Gamble and Time Tradeoff

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Objective. Temporary health states cannot be measured in the traditional way by means of techniques such as the time tradeoff (TTO) and the standard gamble (SG), where health states are chronic and are followed by death. Chained methods have been developed to solve this problem. This study assesses the feasibility of a chained TTO and a chained SG, and the consistency and concordance between the two methods. Patients and methods. Seventy female early-stage breast cancer patients were interviewed. In using both chained methods, the temporary health state to be evaluated was weighed indirectly with the aid of a temporary anchor health state. The patients were asked to evaluate their actual health states, a hypothetical radiotherapy scenario, and a hypothetical chemotherapy scenario. Results. Sixty-eight patients completed the interview. The use of the anchor health state yielded some problems. A significant difference between the means of the TTO and the SG was found for the anchor health state only. For the other health states, the results were remarkably close, because the design avoided some of the bias effects in traditional measurements. Conclusion. The feasibility and the consistency of the chained procedure were satisfactory for both methods. The problems regarding the anchor health state can be solved by adapting the methods and by the use of a carefully chosen anchor health state. The chained method avoids biases present in the conventional method, and thereby the TTO and the SG may be reconciled. Moreover, there are several psychological advantages to the method, which makes it useful for diseases with uncertain prognoses. Key words: utility assessment; time tradeoff; standard gamble; breast cancer; chemotherapy; radiotherapy. (Med Decis Making 1998;18:391–399)

Cancer treatments, such as radiotherapy and chemotherapy, may improve the life expectancy or quality of life of patients with cancer, but can also cause serious side effects. Therefore, it is necessary to study not only the effects of these treatments on the life expectancies of cancer patients, but also their effects on the patients’ quality of life. Furthermore, it is important to examine the preferences and valuations of patients with regard to these treatments. Patients’ preferences are relevant to the process of decision making on an individual level and to decision analyses on a collective level. In addition, they can be used to improve patient information about various treatments.

Usually, health states are temporary and change over time. Temporary health states are particularly important for patients whose life expectancies are short and who face relatively long periods of treatment, as is the case for patients undergoing palliative chemotherapy for breast cancer. Hence it is important to measure the utilities of these temporary health states as precisely as possible.

Utility assessment serves to measure patient preferences. The utility approach uses one or more scaling methods to assign numerical values, utilities, on a scale from 0, anchored as death, to 1, anchored as complete health. The three measurement instruments most commonly applied are the visual analog scale (VAS), the time tradeoff (TTO), and the standard gamble (SG).

The TTO and the SG in their conventional forms measure utilities for chronic health states preferred
to death. They are not suitable for the measurement of temporary health states, as the following example illustrates. If the valuation of a temporary health state, say, a chemotherapy treatment, is measured by means of a conventional TTO, the patient has to trade off a chemotherapy treatment for a specified period of time, followed by death, against perfect health during a shorter period, followed by death. In fact, this does not constitute a realistic choice, and furthermore the evaluation of the chemotherapy treatment may be influenced by the subsequent death.

Instead of using the conventional methods, utilities for temporary health states can be measured with a chained procedure introduced by Torrance. With this method, the temporary health state to be evaluated is not weighed directly against perfect health and death, but is weighed indirectly with the aid of an intermediate anchor health state. The temporary health state is followed by the life expectancy in good health. So far as we know, only one published study explicitly describes the measurement of temporary health states using a chained SG. Utilities elicited by chained SG were significantly greater than, but highly correlated with, rating scale values.

A chained SG has been used in a number of studies for the measurement of chronic health states. In these studies all considered health states are lifelong. The studies by Llewellyn-Thomas et al., Rutten-van Molken et al., and Bleichrodt found higher utilities by means of the chained SG than by means of the conventional SG. Possible explanations offered by Llewellyn-Thomas et al. are a framing effect and the possibility that some of the health states are considered worse than death. Rutten-van Molken et al. gave as a possible explanation that patients’ utilities for a particular health state are influenced by the outcome of the gamble, and in particular by the description of the severe reference state. Bleichrodt proposes a framing effect, imprecision of preference, and probability weighting.

We have found one study of the elicitation of utilities for chronic health states by means of the chained TTO. In this study, the chained TTO utilities were lower than the conventional TTO utilities. Verhoef gave three explanations for this observation: a method-order effect, anchoring and adjustment, and salience of attributes.

Because there has been little research on the measurement of temporary health states by means of the chained methods, additional experience is needed in the adaptation and use of these methods. This article reports on a study of the feasibility of a chained TTO and a chained SG to measure utilities for temporary health states in an early-stage breast cancer population. The study will lead to greater methodologic insight into the procedures.

**Methods**

**PATIENTS**

Early-stage breast cancer patients who had completed primary treatment (lumpectomy or mastectomy) were interviewed just before starting radiotherapy treatment. Exclusion criteria were: prior experience with chemotherapy or radiotherapy, metastatic disease, a diagnosis of ductal carcinoma in situ, and inability to speak Dutch. Of the 109 eligible patients, 39 (36%) refused to participate, mostly for reasons of difficulties in the process of coping with their disease. The remaining patient group consisted of 70 women.

The patients were initially approached for study entry by their attending physicians, who explained the purpose of the study and provided information in writing. A few days later the patients were invited by one of the interviewers to participate in the study.

**DEVELOPMENT OF THE SCENARIOS**

Two treatment scenarios (adjuvant radiotherapy and adjuvant chemotherapy) were developed on the basis of the literature and of the experience of medical oncologists, radiotherapists, and patients. The scenarios contained effects of the treatments on physical, psychological, and social dimensions, following the World Health Organization (WHO) definition of health.

The use of the chained procedure requires an anchor health-state scenario that can be evaluated either as a temporary health state or as a chronic health state. We opted for a hypothetical "hospitalization, caused by a serious accident," because this situation is one that we felt most patients had probably not experienced but could imagine. We did not use an anchor health-state scenario based on breast cancer, for example metastatic disease, because we considered this too threatening for the patients.

For the proper use of the chained procedure, a specific ranking in health states is required, with good health as the best outcome, the temporary health state as second-best, the anchor health state as worse than the temporary health state, and, finally, death as the worst outcome.

To avoid confusion, we decided on a period of six months for all hypothetical scenarios (hospitalization, chemotherapy, radiotherapy) and for the actual health-state scenario. Applied to the radiotherapy scenario, this results in a six-week radiotherapy treatment followed by four and a half months of possible side effects. See the appendix for descriptions of the health-state scenarios.

The qualities of life in the periods following the temporary health states had to be the same for all

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health states. To be realistic, this had to be life after the diagnosis of breast cancer. Therefore, all temporary health states (including good health) comprised surgery for breast cancer in the past, but no requirement for further treatment and a good quality of life. The good health-after-breast-cancer state was sufficiently close to perfect health to be evaluated as equal to 1.

UTILITY MEASURES

To measure utilities of temporary health states, Torrance' proposed the chained TTO method. We adapted this method to our study as shown in figure 1. Here, the value of a temporary health state Q is related to an anchor health state A (the hospitalization scenario) and to the best state (good health). The patient is offered two alternatives. Alternative 1 is the temporary health state Q for the specified duration t, which in our case is six months, followed by good health for the rest of one's life. Under the usual QALY assumptions, alternative 1 comprises a loss of health equal to t·(1 − hQ), where hQ indicates the utility of temporary health state Q and good health has utility 1.

Alternative 2 is the anchor health state for a duration x shorter than the temporary health state Q, followed by good health for the rest of one's life. Time x is varied until the respondent expresses no preference for either of the two alternatives. The induced loss of health then is x·(1 − hA), where hA is the utility of the anchor health state. Equality to the loss of health of the first alternative leads, by algebraic manipulation, to the following preference value for the temporary health state Q:

\[ h_Q = 1 - \frac{(1 - h_A) \cdot x}{t} \]

If the preference value for the temporary health state is to be related to the 0 (death) − 1 (good health) scale, the utility hA of the anchor health state can be measured in the second step of the procedure by the conventional TTO for chronic states (see figure 2). The length of the anchor health state in the second step of the TTO was set to three months, which seemed a plausible average of patients' indifference points, and was compared with good health. In the special case where the utility for the anchor health state (hA) is zero, we have hQ = 1 − x/t.

Using the chained SG, the preferences for temporary health states can be measured in relation to the anchor health state (see figure 3). Temporary health state Q, in our case during six months, followed by good health, is measured in comparison...
with the best state (good health) and the anchor health state (state A), both for six months, followed by good health. A probability p is elicited such that the patient is indifferent between temporary health state Q and a gamble yielding a p chance at good health and a \((1 - p)\) chance at anchor health state A. In the following calculations, we adopt the usual QALY assumptions. We do not incorporate the health values after six months because they are common terms that cancel out of the equation. Now state Q for t (=six months) has value \(t' h_q\), and the gamble has value \(t' [p' 1 + (1 - p) h_A]\). Dropping the common factor t then yields:

\[ h_q = p + (1 - p) h_A \]

If the utility of the temporary health state Q is to be related to the \(0\) (death) \(-\ 1\) (good health) scale, the value \(h_q\) of the anchor health state must be measured in the second step of the procedure by the conventional SG for chronic states (see figure 4). The length of the anchor health state was set to six months, the duration of all temporary health states, and compared with good health and death. In the special case where the utility for the anchor health state \(h_A\) is zero, we have \(h_q = p\).

**STUDY PROCEDURE**

At the beginning of the interview, the patients provided sociodemographic information and clinical data on the date and the type of surgery and the date of diagnosis. Next, utilities were elicited for the patients' actual health states, the radiotherapy scenario, the chemotherapy scenario, and the anchor health state. During the assessment of the chained methods, the patients were repeatedly instructed that each temporary health state had a six-month time frame, followed by good health for the rest of one's life. It was also pointed out to the patients that in the radiotherapy scenario the six-week treatment was followed by four and a half months of possible side effects. Specially constructed TTO and SG boards were used to indicate the six-month time frame and to facilitate the elicitation of the utilities for the patients.

Utilities were elicited in a "ping-pong" fashion. By means of the TTO, the patient first chose between six months in the anchor health state versus six months in the temporary health state to be evaluated, both followed by good health for the rest of the patient's life. If the patient preferred the health state to be evaluated, the duration of the anchor health state was set to one month, and if necessary to one day. If the patient preferred the one-month anchor health state, the duration was set to five months, and so on. Preferences were elicited to a precision of half a week.

By means of the SG, the patient chose between a certainty of six months in the temporary health state to be evaluated and a gamble with a 50% chance of good health for six months and a 50% chance of the anchor health state for six months. All health states were followed by good health for the rest of the patient's life. Depending on the stated preference, the chance of good health was set to 90% or 10% and the corresponding chance of the anchor health state to 10% or 90%, respectively, and so on. Preferences were elicited to a precision of 1%. The TTO was administered before the SG.

Upon the completion of the interview, the patients were asked whether the interview had been upsetting to them and whether they had found it difficult. Other patient comments about the interview were recorded. Patients were interviewed by one of three trained interviewers, generally in the patients' homes. Quality control of the interviewing was achieved by random taping of the interviews and detailed discussion of the tapes by the interviewers.
ANALYSES

The feasibilities of the chained TTO and the chained SG were evaluated by the numbers of interviews that were broken off, by the numbers of missing answers, and by the patients' comments on whether they had been upset by the questions or whether they had found the methods difficult.

Consistency was evaluated using the rank order of the health states. If two methods demonstrate consistent results, then they agree on which state is assigned the highest preference, which the second highest, which the third highest, and which the lowest by a particular respondent. If two states are equivalent in one method but not the other, then this rank order is also regarded as agreement.\(^8\)

Means and standard deviations of utilities are presented. To study concordance, differences between mean utilities elicited by TTO and by SG were examined with paired t-tests and confidence intervals were given. To assess the degrees to which TTO utilities where related to SG utilities at the individual level, we calculated Spearman correlation coefficients.

### Results

#### DESCRIPTION OF THE PATIENT GROUP

The demographic and clinical characteristics of the patients are listed in table 1. The ages of the 70 women ranged from 33 to 82 years (median 57 years). Chemotherapy was not part of the treatment plan for any of the patients at the time of the interview, and no patient had had prior experience with radiotherapy or chemotherapy.

#### FEASIBILITY OF THE CHAINED PROCEDURE

Two interviews (3%) were broken off: one because the patient’s partner had recently died and she was still coping with her bereavement, the other because the patient got upset by the utility question regarding the second step of the TTO. There were 39 missing answers (7%) out of a total of 560 utility questions (four health states by two methods for 70 patients). The distribution of the missing answers is shown in table 2. Of the 39 missing answers, 28 (5% of all utility questions) were due to: refusal (18), difficulties with the method (8), and the fact that the respondent was not able to choose between the proposed options (not due to indifference; 2). Eleven answers (2% of all utility questions) were missing because of interviewer mistakes (3) or unexpected interruptions that led to lack of time (8).

The number of missing answers in the SG (26) is twice as large as the number of missing answers in the TTO (13). This difference is mainly due to the fact that the SG appeared to be too difficult (=8 missing answers) for two patients.

Most of the missing answers occurred for the chemotherapy scenario, followed by the anchor health state. Three patients found thinking about chemotherapy too threatening. Two patients refused to answer the questions concerning the valuation of the anchor health state. Thirteen patients (19%) reported that the interview had been upsetting to them. For these patients, the most threatening aspect had been thinking about chemotherapy, which was mentioned by five patients. The second most threatening aspect had been the second step of the procedure, the valuation of the anchor health state. Three patients had found this upsetting, probably because it considered a short-term chronic health state (six months), followed by death. Sixty-one patients were asked...
whether they had found the interview difficult. Forty-two patients (69%) stated that the interview had been rather (25%) or somewhat (44%) difficult for them. Twenty-four patients reported having had difficulties with choosing between the proposed options, and six patients, with thinking about chemotherapy.

In administering the chained methods, two problems in the valuation of the health states were encountered. Contrary to our expectation, one third of the patients (n = 24, 34%) preferred the anchor health state (the hospitalization scenario) to the chemotherapy scenario in the TTO evaluation.* This means that the hospitalization scenario is no longer suitable as an anchor health state, so utilities could not be computed for these patients. For the SG evaluation this was the case for four patients (6%).

A second problem concerned the valuation of the anchor health state. Forty-one patients (59%) recorded a valuation of zero for the anchor health state by TTO and 25 patients (36%) by SG.† It is possible that for some of these patients, the value would have been negative if negative values had been allowed. The chained methods of Torrance were, however, not developed for that situation. In addition, negative utilities and health states worse than death are controversial, and therefore are often not permitted or are set to zero.5-9,11 For a study of negative utility, see Patrick et al.8 For these reasons, we have not considered negative utilities. An extension of the method to allow for utilities below the anchor-health-state utilities is proposed in the discussion. It can be expected that such an extension would, on average, produce somewhat lower utilities for temporary health states.

CONSISTENCY AND CONCORDANCE BETWEEN METHODS

On the individual level, consistent rank orders for the four health states were found for 50 (89%) patients of the total of 56 patients who had no missing answers.

Table 3 shows the mean utilities and standard deviations for the temporary health states on a scale ranging from 0 (death) to 1 (good health).

The mean utilities recorded for the TTO and the SG are almost identical, with slightly higher scores for the TTO for the radiotherapy scenario, and lower scores for the chemotherapy scenario and the anchor health state. Notice that the mean utility for the chemotherapy scenario was based on the 35 patients who preferred chemotherapy to the anchor health state with both the TTO and the SG. For the subjects preferring the anchor health state to chemotherapy (TTO: n = 24; SG: n = 4) we have incomplete data, so their utilities for chemotherapy have not been calculated.

A pairwise t-test revealed a significant difference between the two methods for the anchor health state only [p < 0.01, 95% CI = (0.13, 0.28)]. The other temporary health states did not show a significant difference: actual health state [p = 0.88, 95% CI = (-0.03, 0.04)]; radiotherapy scenario [p = 0.46, 95% CI = (-0.07, 0.03)]; chemotherapy scenario [p = 0.90, 95% CI = (-0.10, 0.11)]. The larger confidence interval for chemotherapy can be explained by the fact that fewer subjects (n = 35) were involved.

Spearman correlation coefficients between the TTO and the SG measurements for the various health states ranged from 0.31 to 0.44, with an exception of 0.20 for the actual health state.

Discussion

FEASIBILITY

The chained methods seem feasible, considering that only two of the patients stopped the interview and there were only 5% missing answers due to refusal to answer or difficulties with the method. The majority of patients did consider the interview difficult, but considering the low level of education of our patient group and their lack of experience with utility measurement, this seems plausible. Besides, it did not lead to a substantial amount of missing data.
The number of patients declining participation was rather high (36%). This may be explained by the fact that the patients had only recently learned they had breast cancer and were still coping with the diagnosis. Another reason could be the fact that the first interview had to take place shortly after the invitation was issued, before the start of the radiotherapy treatment, so the patients had little time (one to three days) to decide about participation and to prepare for the interview.

**ANCHOR HEALTH STATE PREFERRED TO TEMPORARY HEALTH STATE**

The chained method developed by Torrance is based on the assumption that the temporary health state is preferred to the anchor health state. Hence, to follow his method as closely as possible, we have not calculated utilities for patients who did not satisfy that requirement. We now suggest an extension of his method by means of which utilities can also be measured for such patients. Instead of shortening the time in the anchor health state, it can be prolonged. Nine months in the anchor health state could, for example, be equal for the patient to six months in the health state to be evaluated, for instance chemotherapy. For the computation of the utilities, the same formula can then be applied as described for the chained TTO, namely:

\[ h_q = 1 - (1 - h_a) \times x/t \]

For the SG, adaptation results in switching the options. The gamble consists of the health state to be evaluated and good health. The certain option is now the anchor health state. An adaptation of the formula is then required:

\[ h_q = (h_a - p)/(1 - p) \]

Adapting the TTO and the SG in this way can result in the assessment of health states worse than death. Recent studies of health states worse than death are those of Patrick et al. and Rutten-van Molken et al.

**CONCORDANCE BETWEEN TTO AND SG**

The results show that the mean utilities found with the chained TTO and the chained SG are most identical. The only exception pertains to the anchor health state, which had a significantly higher utility by means of the SG (p < 0.01). In the second step of the chained methods, the anchor health state is redefined as a chronic health state of short duration and measured according to the conventional methods. The observation that in our study the utility for the anchor health state was higher by means of the SG is thus in agreement with results from other studies comparing valuations for chronic health states by means of a conventional TTO and a conventional SG. This difference has usually been attributed to the difference between risky and riskless utilities.

The agreement between the utilities for the chained TTO and the chained SG is contrary to the common finding in the literature mentioned above. We think that our method has avoided a number of distorting factors that are present with conventional measurements. We next explain how we avoided, first, a bias downwards such as occurs with conventional TTO measurements, and second, two biases upwards, as occur in conventional SG measurements.

A distorting factor in conventional TTO measurements is that the TTO calculations assume linear utility and thus risk neutrality (zero discounting) for life duration. In reality, people are risk-averse, valuing close years more than remote years. They are therefore willing to trade off more life years in the conventional TTO than risk neutrality can explain, leading to an underestimation of utilities for health states. In our study, the TTO method concerned only periods of six months. Utility of life duration is approximately linear over such short periods, and risk neutrality holds to a good approximation. We thus avoided the downwards bias.

For the conventional SG method, research has shown three major systematic biases, all enhancing risk aversion and the overestimation of utility. The first and major bias concerns framing and loss aversion: with the conventional SG method, subjects tend to focus on the riskless health-state outcome, which becomes their "status quo." They perceive the healthy outcome in the gamble as a gain and the death outcome as a loss. In general, people tend to pay more attention to losses than to gains ("loss aversion"). That implies the well-known overattention to the death outcome in the SG and hence an overestimation of risk aversion. In our study, the temporary health states were followed by good health for the rest of one's life. In that case, it would seem natural that patients would take good health as their status quo, and that all outcomes in the SG would be perceived as losses. Then there is no more overattention of the worst outcome as compared with the best outcome due to loss aversion, so loss aversion no longer distorts the measurement.

The fact that with our SG measurement all outcomes were perceived as losses had an additional effect on a second distorting factor of the conventional SG, i.e., probability transformation. Many studies have demonstrated that subjects do not evaluate probabilities linearly but in general transform them by underweighting moderate and high probabilities, while small probabilities are typically over-
weighted. Probability transformation seems to be a major cause of deviations from expected utility. It has mostly been studied in relation to gains, where it enhances risk aversion. For losses, probability transformation seems to enhance risk seeking rather than risk aversion. That again suggests that the utilities elicited with our SG measurement are lower than those commonly found. A third bias in conventional SG questions concerns "contingent weighting." It is induced by the fact that with the SG method, subjects should provide answers in terms of probabilities. Hence they tend to pay much attention to the probabilities and relatively less to the outcomes. They thus tend to overvalue the certainty of the riskless outcome in the SG, again enhancing risk aversion. We expect that effect to be as strong using our approach as with the conventional approach. The effect leads to violations of transitivity, and explains why the anchor health state is judged similar to death more often in step 2 of the TTO (59%) than in step 2 of the SG (36%).

Whereas we have avoided some systematic biases, differences will of course remain at the individual level. The nonsystematic biases effective in the different measurements are strong and unrelated, and therefore no high correlations can be expected for different utility measurements. It is well known that individual measurements of value and utility are prone to many distortions and high unreliability. For instance, Torrance' states "Thus, single individual measurements are not particularly precise" (page 26), and "Fortunately, the imprecision of individual measurements and the considerable differences among individuals can be ameliorated by taking the mean of a large group of subjects" (page 27). Tversky and Kahneman, in their introduction of new prospect theory, discuss the point repeatedly: "Although the overall pattern of preferences is clear, the individual data, of course, reveal both noise and individual differences. . . . It should be noted that prospect theory implies the pattern demonstrated in table 4 within the data of individual subjects, but it does not imply high correlations across subjects" (pp. 306–308).

In summary, we have avoided one downwards bias of conventional TTO questions (nonlinear utility for life years) and two upwards biases of conventional SG questions (loss aversion and probability transformation). One bias of conventional SG questions (contingent weighting) that commonly enhances risk aversion similarly does so in our study. Probability transformation may in fact have enhanced risk seeking rather than risk aversion in our SG questions. Thus, it may have neutralized the effect of contingent weighting to some degree. On the whole, we think that both our TTO and our SG utilities were less biased than would have been the case with the conventional methods. As a result, they did not differ systematically.

PSYCHOLOGICAL ADVANTAGES OF THE CHAINED METHODS FOR TEMPORARY HEALTH STATES

A major psychological advantage of the chained method is that it is not necessary to explicitly mention a specific life expectancy, as in the case for the TTO for chronic health states. It is sufficient to state "for the rest of your life." This is an advantage if one does not want to upset a patient, or when the life expectancy is unknown, which commonly occurs in oncology. Of course, it may still be made explicit, if matters of life expectancy are germane to the preference elicitation. Second, the chained method may be less threatening to patients because with the TTO the patient is not confronted with trading off life years in return for gaining perfect health. With the SG the possibility of immediate death is replaced by the anchor health state.

Conclusion

The chained methods seem feasible for the measurement of temporary health states. The role of the anchor health state is central in the chained method. The selection of suitable anchor health states, broadly applicable and comparable across different contexts, is an important subject for future study. For measuring temporary health states worse than the anchor health state, a slight adaptation of the methods is needed; this will be elaborated in a future study. The chained methods have psychological advantages. First, it is not necessary to mention a specific life expectancy, and, second, the chained method may be less threatening to patients because death is replaced by the anchor health state. We found no systematic difference between the chained TTO utilities and the chained SG utilities, possibly because we avoided a number of biases known to affect the conventional methods.

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References


APPENDIX

Descriptions of the Health State Scenarios

Actual health state

Physical Possible symptoms or limitations to everyday activities
Psychological Emotions, moods
Social Possible limitations in work, leisure activities, sport or social contacts

Radiotherapy scenario

Daily hospital visit for radiotherapy treatment over a period of six weeks

Physical Skin reactions (warm, red breast and dry skin), general fatigue and listlessness
Psychological Feelings of anxiety, worry about one’s future health
Social Limitations to work or other daily activities, restrictions on leisure activities

Chemotherapy scenario

During six months one or two hospital visits per three weeks for chemotherapy treatment via an infusion

Physical Nausea, fatigue, hair loss, difficulty in carrying out strenuous activities, frequent need to rest
Psychological Dissatisfaction with one’s body
Social Limitations to work or other daily activities, restrictions on social activities

Anchor health-state scenario hospitalization after a serious accident

Physical Body almost entirely in plaster, being barely able to move, get out of bed, wash, dress or go to the toilet
Psychological Anxiety and depression for longer or shorter periods
Social Being dependent on others for almost everything, e.g., fetching things, for social contact being dependent on those who come to visit