

Title: The sequence effect in time trade-off elicitation.

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1 Abstract

2 **Background:** Most valuation experiments include only a few health states related to a specific
3 condition. We tested the sequence effect in time trade-off elicitation, i.e. the value given to a
4 particular health state would be higher when the previous health state elicited was a milder health
5 state as compared to a worse health state. **Methods:** 54 nurses enrolled prospectively were
6 randomly assigned to one of two sequence valuation strategies: a 'mild-to-moderate' sequence
7 from chronic low back pain to asthma, or a 'severe-to-moderate' sequence from permanent
8 impairments after stroke to the previous asthma. **Results:** Time trade-off values of the initial
9 disease stages were 0.87(std 0.18) for chronic low back pain and 0.45(std 0.12) for moderate
10 permanent impairments after stroke. The value of severe asthma was significantly higher in the
11 'mild-to-moderate' than in the 'severe-to-moderate' evaluation sequence (0.84 vs. 0.72, $p < 0.04$).
12 **Conclusion:** The sequence effect revealed in our experiment is in line with other findings
13 showing framing effects and violations of procedure invariance in health state valuation.
14
15
16 **Keywords:** procedure invariance; sequence effect; order effect; time trade-off; QALY; DALY

17

18 Introduction

19 Quality-Adjusted Life Years (QALYs) take into account both the number of years lived in a
20 particular condition and the relative severity of a year lived in that condition. QALYs have been
21 recommended to measure effectiveness of health interventions in cost-effectiveness analysis.¹
22 The number of published cost-utility analyses relying on QALYs increased exponentially with
23 time.² However there is no gold standard method to elicit the relative severity of year lived in a
24 particular condition. Various valuation methods have been developed following rational theories
25 of riskless or risky choice (time trade-off and standard gamble, respectively).³ Whatever the
26 valuation method, respondents are expected to maximize some subjective measure associated
27 with each health state and thus to reveal their preferences for health states.

28
29 A basic assumption of rational theories of choice is the principle of invariance. It states that the
30 relation of preference between health states should not depend on the description of the options
31 (framing invariance) nor on the method of elicitation (procedure invariance). Without stability
32 across equivalent descriptions and equivalent elicitation procedures, respondents' preferences
33 cannot be represented as maximizing some subjective measure. A few experiments have
34 addressed this issue in health economics. Within a given valuation method, framing invariance
35 was not supported by various types of health state description,⁴⁻⁷ nor when reference anchor
36 varied from perfect health to death.^{4,7-9} Procedure invariance was not found in time trade-off
37 and standard gamble methods when respondents completed a written questionnaire or were
38 interviewed with props¹⁰ or by means of a computer,¹¹ nor when usual ping-pong search
39 procedure was challenged by a top-down titration.¹²

40

41 Most valuation experiments include only a few health states related to a specific condition.¹³ We
42 hypothesized that the value of a particular health state is not independent from the health state
43 valued previously, e.g., the value given to a particular health state would be higher when the
44 previous health state was a milder health state as compared to a worse health state. In this paper,
45 we looked for this sequence effect in time trade-off elicitation with a randomized trial design.

46

47 Material and Methods

48 Study design

49 We defined two sequence valuation strategies. In the ‘mild-to-moderate’ sequence valuation
50 strategy, participants valued successively a mild disease stage, i.e. chronic low back pain, a
51 moderate disease stage related to asthma, and the mild disease stage again. In the ‘severe-to-
52 moderate’ sequence valuation strategy, participants valued successively a severe disease stage,
53 i.e. moderate permanent impairments after stroke, the previous moderate reference disease stage
54 related to asthma, and the severe disease stage again. Participants were randomly assigned to
55 either sequence valuation strategies. Our main hypothesis was that the value of the reference
56 moderate disease stage would be higher in the ‘mild-to-moderate’ than the ‘severe-to-moderate’
57 valuation strategy, i.e. a sequence effect.

58

59 Population

60 We selected an homogenous group regarding both knowledge of health conditions elicited and
61 willingness to participate in valuation experiments. Thus we enrolled prospectively French nurses
62 following a MPH course during the spring 2001 (Ecole Montsouris, Paris).

63

64 Disease stages' descriptions

65 The disease stages' descriptions were taken among 28 disease stages covering 13 diseases and
66 validated in the European Disability Weights project by external health care professionals and
67 public health experts.¹⁴ All disease stages were described on a sheet with the name of the disease
68 at the top, the position of the selected disease stage among the other stages, a brief clinical

69 description and a health state profile, i.e. EQ-5D extended with a cognitive dimension.¹⁵⁻¹⁷ We
70 selected the three disease stages based on their individual unambiguous ranking in the European
71 Disability Weights project:¹⁴ chronic low back pain, severe asthma, moderate permanent
72 impairments after stroke received overall time trade-off values of 0.87, 0.80, and 0.58,
73 respectively (n=232). Their presentation is shown in **Figure 1**.

74

75 Valuation method

76 After a course on health economics, nurses were asked to participate in a short elicitation
77 exercise. They were interviewed by a single interviewer (MS) following a standardized elicitation
78 protocol. After presentation of the first health state (either chronic low back pain in the ‘mild-to-
79 moderate’ sequence valuation strategy, or moderate permanent impairments after stroke in the
80 ‘severe-to-moderate’ sequence valuation strategy), a time trade-off was used with the following
81 features: a fixed 40 years life-expectancy; a fixed gain formulation (e.g. ‘do you prefer to live 30
82 years in full health over living 40 years in the described health state?’); and a ping-pong
83 elicitation procedure starting by the extreme anchors (i.e., full health and death) to check for
84 understanding.

85

86 Statistical analysis

87 Disease stage values were computed on a scale from zero (death) to unity (full health) by
88 dividing by 40 the number of years for which respondent was indifferent. With the risk of a type
89 I error at 5 percent (one-sided test) and the risk of a type II error at 20 percent, the required
90 sample size was 50 nurses to show a sequence effect of 0.1 on the mean value of the reference
91 moderate disease stage (with standard deviation of 0.1). We used the Student t test to compare

92 the value of the reference moderate disease stage between the 'mild-to-moderate' and the
93 'severe-to-moderate' groups. Other binary data were compared by a chi-square test or Fisher's
94 exact test. Significance was attributed at the 5% level, and data were analysed with SAS 8.0
95 (SAS Institute, Cary NC).

96

97 Results

98 Fifty-four nurses were approached to participate in the elicitation experiment. After the
99 presentation of the first health state to be valued, all nurses showed a correct understanding of the
100 time trade-off method as indirectly shown by their answers to the trade-off with reference
101 anchors. However, one third of the nurses were unwilling to trade-off years in the ping-pong
102 elicitation questions (41% in the ‘severe-to-moderate’ strategy group and 26% in the ‘mild-to-
103 moderate’ strategy group, $p=0.25$). For the 36 nurses who were willing to trade-off years, mean
104 age (40.3 (std 5.4)) and gender (80% females) did not differ significantly between the two
105 valuation strategy groups.

106 **Table 1** shows that the valuation pattern of the three health states followed the predicted pattern
107 from the European Disability Weights project with increasing severity from chronic low back
108 pain, severe asthma, to moderate permanent impairments after stroke. Our main hypothesis about
109 sequence effect in time trade-off elicitation was supported by our experiment, i.e. the mean
110 value of severe asthma was significantly higher in the ‘mild-to-moderate’ valuation group (0.84
111 (std 0.2)) than in the ‘severe-to-moderate’ valuation group (0.73 (std 0.18)) ($t_{35} = -1.80$, $p < 0.04$).
112 The valuation group effect remained significant when adjusting on age and gender in ANOVA.
113 Finally, there was almost no change in the value given to the initial health state when it was
114 elicited again at the end of the elicitation exercise (0.88 in chronic low back pain and 0.46 in
115 moderate permanent impairments after stroke).

116

117 Discussion

118 QALYs are increasingly used in cost-effectiveness analysis and are recommended by the Panel
119 on Cost-Effectiveness Analysis in Health and Medicine since 1996.¹ However, the question
120 remains whereas the 'Q' is simply revealed by elicitation exercises or actually constructed during
121 the process of elicitation. The former approach relies on strong assumptions, i.e. individual
122 preferences are well formed, complete, and stable.^{18,19} As shown by our study, the value of a
123 second health state in a evaluation sequence was affected by the sequence effect with a
124 significantly higher value in the 'mild-to-moderate' than in the 'severe-to-moderate' health state
125 valuation strategy. The sequence effect revealed in our experiment is in line with other findings
126 showing framing and procedure invariance in health state valuation.^{4-8,10-12}

127
128 To the best of our knowledge, our experiment is the first to show the sequence effect in health
129 economics. Had we used a valuation strategy comprising only two health states, results would
130 have signified an order effect. That is, the values given to states A and B depend on the
131 evaluation sequence, A-B or B-A. The only study dealing with order effects in health state
132 valuation actually controlled for order effects rather than studied them.²⁰ In that study, 55
133 patients with early-stage breast cancer had to value their actual health state and a radiotherapy
134 scenario at different times of their disease (before, during and after radiotherapy). There was no
135 significant order effect but it may be explained by the clear overlap of the two health state values
136 (e.g. 0.94 and 0.89 before radiotherapy, respectively). Outside health economics, order effects in
137 preference judgments were evidenced by willingness-to-pay for options previously shown to
138 produce joint-versus-separate preference reversals.²¹

139
140 An intuitive explanation of the sequence effect is that respondents do not have any clue of health
141 state values a priori, and that they construct their values during the process of elicitation. In order
142 to prepare her first health state elicitation, the respondent has to generate a representation for the
143 health state considered. When valuing the next health state, she uses the same representation,
144 “considering” it is still relevant. Several indirect arguments could sustain this explanation: the
145 health state elicited first in the sequence valuation strategy (i.e. chronic low back pain in the
146 ‘mild-to-moderate’ sequence or moderate permanent impairments after stroke in the ‘severe-to-
147 moderate’ sequence), differs not only by health-related quality of life dimensions but also the
148 vital prognosis; respondents took a longer time to value the first health state than the second one;
149 and there was almost no change in the value given to the initial health state when it was elicited
150 again at the end of the elicitation exercise.

151
152 The sequence effect may be seen as an extension of the well-known anchoring effect, where
153 response is biased toward any value, even if it is arbitrary, that the respondent is induced to
154 consider as a candidate answer. In our experiment, respondents anchor themselves on their first
155 estimation of health state value without any anchor provided by the interviewer. Several theories
156 have been proposed to explain anchoring bias, such as anchoring and adjustment,²² and the
157 selective accessibility model.²³ Future research could look for feasible debiasing strategies in the
158 sequence of health state valuation even if previous experiments showed the robustness of
159 anchoring effects in other economic areas.^{24,25} It would also be of interest to compare the
160 sequential process of valuation described in our experiment with an end-of-sequence process of
161 valuation where all health states would be presented and ranked initially, as psychometric

162 experiments showed that relative ratings on a Visual Analogue Scale depend on the set of stimuli
163 proposed to the respondent.²⁶

164
165 We found far from easy to offer a theoretical framework that accounts for the sequence effect.
166 According to Prospect theory,^{8,27} respondents evaluate outcomes as changes from a reference
167 point, and they value generally losses as more serious than equivalent gains. In our experiment, if
168 respondents had taken the first health state as a reference point, then they should have given more
169 weight to the loss of the 'mild-to-moderate' sequence than to the gain of the 'severe-to-moderate'
170 sequence of valuations. However our results showed a reversed pattern with the value of the
171 moderate health state pulled "up" toward the mild health state in the former sequence and "down"
172 toward the severe health state in the latter sequence. A plausible explanation is that our moderate
173 health state was too close to the mild health state as the absolute value difference in the 'mild-to-
174 moderate' sequence (0.04) was much smaller than in the 'severe-to-moderate' sequence (0.28).
175 The sequence effect found in our experiment should be retested with other moderate health states
176 distributed over the range of values between the mild and the severe health states to check if the
177 sequence effect was related to the particular health states used in our study or if it is a general
178 phenomenon. In addition, predictions from Prospect theory could have been checked if we had
179 elicited all three health states in both sequence valuation strategies with, e.g., the expected value
180 of the severe health state in the 'mild-to-moderate' evaluation sequence lower than in the 'severe-
181 to-moderate' sequence.

182
183 Our study has some limitations. We found an unexpectedly high refusal rate in willingness to
184 trade longevity for health quality in our French convenient sample who had nonetheless both a

185 high level of education and the knowledge of the conditions elicited. We decided to exclude from
186 analysis those nurses who refused to trade-off years of life as it is usually done in valuation
187 experiments. However, the sequence effect would have become not significant if we had imputed
188 a value of 1 for those missing data, i.e. the mean value of severe asthma would be 0.88 and 0.84
189 in the ‘mild-to-moderate’ and the ‘severe-to-moderate’ valuation groups, respectively ($t_{53}=-0.87$,
190 $p=0.19$). Of particular interest is the higher refusal rate in those presented with the severe health
191 state first (41% vs. 26%). It may be related to the unwillingness to trade-off survival and quality
192 of life in those who suffer from severe and life-threatening diseases. This phenomenon was found
193 in patients affected by severe conditions,²⁸ and in individuals eliciting hypothetical scenarios as
194 in our experiment.²⁹ Follow-up discussions were consistent with this phenomenon. In particular
195 many nurses said that they would not trade any year of life as they have young children. This
196 high refusal rate to trade-off years of life should be replicated in a second study with a different
197 sample, e.g., with unmarried nurses with no children or older women whose children have grown.
198 Alternatively, Chapman et al. suggested the use of an impersonal elicitation questionnaire to
199 avoid this phenomenon.²⁸ More broadly, the very few cost-effectiveness analyses that relied on
200 real French valuation experiments may reflect difficulties to translate the Anglo-Saxon QALY
201 concept into the French health-care system (in fact only two over 125 studies collected in the
202 French cost-effectiveness analyses database).³⁰

203
204 We found that the sequence effect could significantly affect the results of a health state valuation
205 experiment. Indeed the value of severe asthma decreased by 0.11 points on a 0-1 scale from the
206 ‘mild-to-moderate’ sequence to the ‘severe-to-moderate’ sequence valuation strategy. This new
207 procedure effect could be added to other procedure effects,¹⁰⁻¹² framing effects,⁴⁻⁸ logical

208 inconsistencies,^{31,32} or internal inconsistency,³³ found in health state valuation methods that
209 all show that health states values are poorly constructed values. The recognition of these failures
210 of invariance should contribute to a new conception of judgment and choice in which preferences
211 are often constructed, not merely revealed, in the process of elicitation, and their measure could
212 follow a 'building code'.³⁴ Otherwise, the sequence effect may contribute to the difficulties in
213 comparing constructed values from various studies addressing different conditions or even within
214 a single condition at different stages.^{35,36}

215

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218

219

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Table 1: Valuation of three disease stages in the 'mild-to-moderate' and the 'severe-to-moderate' valuation groups, mean(std)

Disease stage	Mild-to-moderate	Severe-to-moderate
Chronic low back pain	0.88 (0.18)	NA
Severe asthma	0.84 (0.20)	0.73 (0.18)
Moderate permanent impairments after stroke	NA	0.45 (0.12)

NA: Non applicable.

Stroke

STR

Acute incident plus rehabilitation phase

Mild permanent impairments after stroke

Moderate permanent impairments after stroke

Severe permanent impairments after stroke



Patient with permanent impairments in movement, speech and memory after incomplete recovery from a stroke more than one year ago.

- Some problems in walking about
- Some problems with washing or dressing self
- Some problems with performing usual activities (*e.g. work, study, housework, family or leisure activities*)
- Moderate pain or discomfort (*in this case, discomfort*)
- Moderately anxious or depressed
- Some problems in cognitive functioning (*e.g. memory, learning ability, concentration, comprehension*)

Asthma

AST

Mild asthma

Moderate asthma

Severe asthma



Patient who has at least two attacks of severe shortness of breath a year, that each confine them to their home for one week or may lead to hospitalisation, despite adequate therapy. Between attacks the patient has limited exercise capacity, needs to take daily preventive medication and has to avoid provocative situations (e.g., smoke, dust and strong perfumes).

Health status outside attacks:

- Some problems in walking about
No problems with washing or dressing self
- Some problems with performing usual activities (e.g. work, study, housework, family or leisure activities)
- Moderate pain or discomfort (in this case, discomfort)
- Moderately anxious or depressed
No problems in cognitive functioning (e.g. memory, learning ability, concentration, comprehension)

Low Back Pain

LBP

Acute low back pain

Chronic low back pain ←

Patient with radiating pain low in the back, limited in sitting and to a smaller extent in walking; patient is generally restricted in all physical activities; standard pain relieving treatment is provided.

- Some problems in walking about
- Some problems with washing or dressing self
- Some problems with performing usual activities (e.g. work, study, housework, family or leisure activities)
- Moderate pain or discomfort (in this case, pain)
Not anxious or depressed
No problems in cognitive functioning (e.g. memory, learning ability, concentration, comprehension)