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Published in:
Haemophilia

DOI:
10.1111/j.1365-2516.2004.00954.x

2004

Haemophilia (2004), **10,** 527–541 DOI: 10.1111/j.1365-2516.2004.00954.x

Willingness to pay for on-demand and prophylactic treatment for severe haemophilia in Sweden

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Summary. The objective of the present paper was to provide an estimate of the benefits of on-demand and prophylaxis treatment strategies for severe haemophilia in monetary terms. Using the contingent-valuation method, which simulates a missing market by asking people about their willingness to pay (WTP), we asked a representative sample ($n = 609$) of the Swedish population if they would be willing to pay a specific amount (bid) so that patients with severe haemophilia could receive on-demand treatment and another bid for prophylactic treatment. Different respondents were offered different bids and the bid vector ranged from 71 Euro cents to EUR 130. The order of the bid questions was randomized so that half of the respondents were asked first about their WTP for on-demand treatment, and then about their WTP for prophylaxis, while the order was reversed for the other half of the respondents. The mean estimated WTP (year 2002) was EUR 39 (95% CI 31–47) for on-demand and EUR 65 (95% CI 55–73) for prophylaxis. Our sensitivity analysis showed that the ranking of the two treatment alternatives was robust in that the WTP was greater for prophylaxis in all possible subsets. The point estimates of WTP varied somewhat in subsets defined by individual characteristics, but confidence intervals always overlapped that of the main results. The WTP for on-demand and prophylaxis exceeded the calculated cost of treatment per taxpayer of providing on-demand and prophylactic treatment, respectively, based on our previous results [1].

Keywords: cost-benefit analysis, economic evaluation, on-demand, prophylaxis, willingness to pay

Introduction

The treatment of patients with severe haemophilia in the industrialized world offers a choice between two main strategies, on-demand and prophylaxis. We have reported elsewhere that the average annual cost of prophylactic treatment is nearly three times as great as that of on-demand treatment according to data from Sweden and Norway [1]. However, prophylaxis also gives better health-related outcomes and quality of life [2–8]. Hence, a systematic evaluation of both benefits and costs is required in order to rank the strategies.

Previous studies have quantified health benefits either in terms of specific single effects (number of haemorrhages avoided, Pettersson score of joints, work days lost, etc.) [3,4,7], or by aggregating a range of multiple health effects into a single index (such as quality-adjusted life-years – QALYs) [6,8]. These quantifications of benefits may then be related to the costs of the respective treatments. Single-effect benefits produce cost-effectiveness ratios used in cost-effectiveness analysis (CEA), while index measures produce cost-utility ratios used in cost-utility analysis (CUA) [9,10]. CEA would be sufficient for the ranking of strategies if benefits were indeed one-dimensional and possible to express in a common metric. Should they be multi-dimensional, however, a CUA would be preferred to the CEA, as cost-utility

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Accepted after revision 29 June 2004

ratios offer a more comprehensive benefit measure [9–11].

However, both CEA and CUA measure costs and benefits in different units, a fact that confines the investigator to assessing ratios. In a priority-setting perspective, where a decision-maker needs an assessment of the value of haemophilia treatment in relation to other healthcare programmes [1,11,12], such a ratio will not by itself provide sufficient information on whether a healthcare programme is worthwhile or not. First, cost-effectiveness ratios are insufficient, as different outcome measures are relevant for different programmes. Secondly, cost-utility ratios for a limited number of healthcare programmes will inform about the ranking of *these* alternatives, but are unable to tell whether any, or all, of the programmes provide quality and length of life enough to be implemented. Moreover, even if cost-utility ratios were available for all healthcare programmes, they would only be sufficient for the ranking of healthcare programmes within a fixed budget [13]. In a changing world with new medical technologies developing, such a fixed-budget perspective should be challenged.

If, instead, benefits are measured in the same (monetary) units as costs, it enables the investigator to perform a cost-benefit analysis (CBA) and to compare treatment strategies and healthcare programmes in terms of their *net benefits* [10]. One advantage of this approach is that any programme with a positive net benefit (benefits exceed costs) is worthwhile and should be implemented, whereas a negative net benefit would imply a discontinuation of the programme. Another advantage is that the theoretical requirements for comparing people's valuation of different kinds of health-benefits are less strict for CBA than for CUA, because money, unlike QALYs, can be transferred from one person to another [14]. Moreover, CBA is not limited to the fixed-budget perspective [9–12]. Thus, there are several strong arguments for estimating the benefits of on-demand and prophylaxis treatment in monetary terms. Patient fees cannot be used for this purpose, however, as third-party payment systems are a characteristic feature in healthcare finance.

The objective in this study was to estimate the benefits of on-demand and prophylaxis treatment for severe haemophilia in Sweden, using the contingent-valuation method to estimate willingness to pay in a representative sample of the adult population. The rationale for asking the general population, rather than patients only, was that (i) the high treatment costs of severe haemophilia calls for some kind of insurance solution; (ii) unregulated private insurance will fail, as a risk-related premium, corresponding to the average cost of treatment, would be prohibitive for most people; and hence (iii) costs of treatment need to be covered through some mandatory/regulated (private or social) insurance where costs of treatment are shared by the general population. Hence we were asking the respondents about their willingness to pay for someone else's healthcare consumption. Analyses of the act of giving up own consumption in order to further someone else's consumption may be found in the literature under the heading altruism [15,16]. To our knowledge, the alternative methods for economic evaluation (CEA and CUA) today do not provide options for incorporating these altruistic aspects that may be important motives for resource allocation to and within the healthcare sector.

The obtained monetary measure of benefits is then used together with our previous cost estimates [1], to provide a comprehensive CBA of the two main strategies for treating severe haemophilia.

Materials and methods

Contingent-valuation method

A contingent-valuation study simulates a missing market by asking people hypothetical questions about their willingness to pay (WTP) for a commodity. The valuation is then conditioned on the good being obtainable only if WTP covers the costs of production, and on the respondent thus losing the opportunity to consume other goods for an amount equal to their stated WTP [10,17,18]. The method is theoretically valid (i.e. individual characteristics and other factors affect WTP according to what would be expected) [19–22]. It also has convergent validity (i.e. it produces results similar to those of other valuation techniques or results that differ from those obtained by other methods in a predictable way) [22–28].

To make the choice situation resemble market decisions as much as possible and to minimize potential problems of non-responses, strategic bias, protest answers and anchoring bias, we used the dichotomous-choice form of contingent valuation, where each respondent is given one *bid* only per treatment (would you pay EUR x so that patients with severe haemophilia can get prophylactic/on-demand treatment; yes or no) [10,18]. Even so, there is still a hypothetical element involved, and experimental studies have shown that the probability of being willing to pay a hypothetical bid may exceed the probability of actually buying the good at that

price [25,29–34]. However, this potential bias could be addressed by investigating the degree of certainty in the yes responses. Thus, there is no significant difference between the probability of obtaining an 'absolutely certain' yes response and the probability of observing an individual actually buying the good at that price [26].

The CV method has been applied in the valuation of a number of goods and services where competitive market prices do not exist. Examples of studies in health care include WTP for enrolment in an asthma management programme [26] and for antenatal care [35]; as well as for priority setting between two life-saving healthcare programmes and hip operations [36]. The WTP for risk reductions in various areas has been estimated: influenza [37], common cold [38], cigarettes [39] and safety [40]. There is also a large literature on the valuation of environmental resources [18,41].

Study population

Our study population came from a household panel, constituting a representative sample of Swedish households and run by the market research company GfK Sverige AB. Using a pilot study as a basis, we calculated that we needed 600 completed interviews in order to have a statistically sufficient number of respondents answering each bid and also to be able to conduct sensitivity analyses. For this purpose, we made an age- and sex-stratified random selection of 1080 individuals from the panel.

Study design and data collection

Respondents were first recruited by telephone (Appendix A). After agreeing to participate, they received a letter with a presentation of the aims of the study as well as two pages of background information based on our own previous results [2] and the international literature. As the respondents could not be assumed to have any prior information about haemophilia or its treatments, the information included the fact that haemophilia is congenital, the problems caused by the disease (painful haemorrhages etc.), descriptions of the two available treatment strategies and their consequences (see Appendices B and C). An interviewer then called back within a few days for the interview. The computer-assisted telephone interview opened with a short (standard) recapitulation of the background information provided in the letter (Appendix D). Interviews took place from 30 November 2002 to 15 January 2003 with an interruption for Christmas holidays (21 December–7 January).

Before launching the final study, a pilot study was conducted. It had two aims: (i) to test the design of the questionnaire (comprehensibility, acceptability of the questions, etc.) and (ii) to obtain information about the relevant bid vector (where ideally everyone would be willing to pay the lowest bid none the highest bid). Following that, we made some changes in the ordering of questions and the wording of some questions. We also stretched the bid vector (Table 1) so that the highest bid would exceed SEK 1000 (EUR 118), which was assumed to be a psychological level.

Table 2 presents the selection and dropouts in the final study. Only 14% (of the 1080) actually declined participation in the study, while interviewers did not need to or were not able to get in contact with 29%. Young people were oversampled due to their comparatively high dropout ratio. In other respects, the distribution of the dropouts in terms of gender, marital status, income and size of household did not diverge from that of the general population.

Table 3 presents the full set of questions. Respondents were first asked for their WTP out of their annual income for the provision of on-demand and prophylactic treatment, respectively, for all patients with severe haemophilia in Sweden (questions 1

Table 1. Bid vector with a fifth of the respondents allocated to each group and pair of bids. Half of each group were offered the high bid first and the other half the lowest bid first. Equivalently, half of each subgroup were offered on-demand first and the other half prophylaxis first. Respondents were offered bids in Swedish Kronor.

	Swedish kronor annually		Euro annually	
Group	Low bid	High bid	Low bid	High bid
1	6	9	0.71	1.07
2	30	60	3.55	7.10
3	80	150	9.47	17.76
4	250	500	29.60	59.20
5	800	1100	94.71	130.23

Exchange rate year 2000; SEK 100 = EUR 11.84.

Table 2. Telephone recruitment, full interviews and dropouts.

	Selected	Dropouts	Total
Telephone recruitment	1080		
Declined participation		112	
No contact*		159	
Letters sent			809
Declined participation at interview		42	
No contact*		158	
Complete interviews			609

*No contact includes respondents who were not contacted as their age/sex-subgroup was full.

Table 3. Questions in the telephone interview.

No.	Question	Answer
	I will now ask you how *you* value the two treatment methods. Before you answer, please imagine that, if you answer 'yes', your annual income would be reduced by the specified amount	
1	Would you pay SEK *x* annually from your income so that patients with severe haemophilia could obtain prophylactic treatment?	Yes/no
2	How sure are you that you consider the prophylactic treatment to be worth SEK *x*?	Absolutely certain/fairly certain
3	Would you pay SEK *y* annually from your income so that patients with severe haemophilia could obtain on-demand treatment?	Yes/no
4	How sure are you that you consider the on-demand treatment to be worth SEK *y*?	Absolutely certain/fairly certain
5	Which one of the described treatments do you think is best for people with severe haemophilia?	Prophylaxis/on-demand
6	What factors do you think are important for your choice of treatment? (follow-up: something else? Yet something more?)	Own words
7	Did you have any previous knowledge about haemophilia?	Yes/no
8a	Do you yourself have haemophilia? (version asked of men)	Yes/no
8b	Do you yourself have von Willebrand's disease? (version asked of women)	Yes/no
9	Do you have any family member or close relative with a haemophilia-related disease?	Yes/no
10	Do you know anyone else or have a distant relative with a haemophilia-related disease?	Yes/no
11	Man or woman?	(Never asked, only registered by the interviewer)
12	How many children under the age of 16 are there in the household?	0, 1, 2, 3, 4, 5 or more
13	What is your main occupation? Are you at the moment…	Entrepreneur Gainfully employed Student Retired Other (state what)
Only persons active in the labour market were asked questions 14–17		
14	Are you employed by…	The private sector The local government sector The government sector
15	How many hours do you work in an ordinary week?	Integer
16	Do you consider your occupation as belonging to the category of…	Blue-collar workers White-collar workers
17	Do you have a management position?	Yes/no
18	Were you gainfully employed before you became a student/retired/other (automatically repeating the answer from Q13)	Yes/no
Only persons who answered yes to question 18 were asked questions 19–21		
19a	Before you became a student/retired/other (automatically repeating the answer from Q13), did you work in…	Private sector Local government sector Government sector
19b	Do you consider your last occupation as belonging to the category of…	Blue-collar workers White-collar workers
20	Did you have a management position at your last job?	Yes/no
21	As a last question I wonder how much your family's total income is per month before taxes? (in SEK)	<6000 6000–8999 9000–11 999 12 000–14 999 15 000–17 999 18 000–20 999 21 000–23 999 24 000–26 999 27 000–29 999 30 000–39 999 40 000–49 999 50 000–59 999 60 000–79 999 80 000–99 999 >100 000

Annual average exchange rate year 2000; SEK 100 = EUR 11.84.

and 3) and the degree of certainty in the answer (questions 2 and 4). Only 'absolutely certain' yes-responses were considered as true yes responses in the estimation of the WTP.

Question 5 in Table 3 allowed for an analysis of whether respondents were consistent in their answers. Comments to question 6 were used to investigate whether respondents had accepted our framework, interpreted the choice situation as intended, and what factors had influenced their decisions. Finally, data on individual characteristics, generated by questions 7–21 in Table 3, were used to test for theoretical validity. Table 4 shows the descriptive statistics of the data.

Table 4. Descriptive statistics for the 609 respondents.

Variable	Proportion
Man	0.49
Age 20–29	0.19
Age 30–39	0.20
Age 40–49	0.20
Age 50–59	0.20
Age 60 and over	0.20
Monthly household income below EUR 2131	0.21
Monthly household income EUR 2131–3552	0.29
Monthly household income EUR 3553–4736	0.26
Monthly household income over EUR 4736	0.23
Active in the labour market	0.67
Student	0.08
Retired	0.20
Working/worked in private sector	0.52
Manager	0.38
Health care and social costs important aspects when choosing treatment strategy	0.31
Health and quality-of-life important aspects when choosing treatment strategy	0.79
Willing to pay prophylaxis bid	0.85
Absolutely certain would be willing to pay prophylaxis bid among those who agreed to pay ($n = 516$)*	0.77
Willing to pay on-demand bid	0.67
Absolutely certain would be willing to pay on-demand bid among those who agreed to pay ($n = 409$)*	0.58
Absolutely certain willing to pay for prophylaxis (second bid) if previously willing to pay for on-demand (first bid) ($n = 118$)*	0.94
Absolutely certain willing to pay for on-demand (second bid) if previously willing to pay for prophylaxis (first bid) ($n = 185$)*	0.57
Prophylaxis bid first	0.50
On-demand bid first	0.50

Continuous variables	Mean	SD
Bid for prophylaxis (in EUR)	35.70	43.09
Bid for on-demand (in EUR)	35.40	42.77

*Proportion of relevant subsample who received the question or else fulfilled criteria indicated.

Theoretical framework and statistical analysis

Following standard procedures for the estimation of WTP in a dichotomous choice framework, we assume that individual preferences can be represented by 'indirect utility functions' as defined in random utility theory [18 (ch. 5), 42]. Thus, when the interviewer asked, 'Would you pay EUR x so that patients with severe haemophilia can get prophylactic (on-demand) treatment', the respondent was assumed to compare his own utility of patients obtaining prophylactic (on-demand) treatment *and* him paying the bid x, with a status quo level (no treatment and no payment). If the respondent's utility level with treatment (and after paying x) was higher, he would agree to pay, otherwise not [18]. Using standard assumptions [18], the probability (P) of saying 'yes' can be modelled as

$$P = \left(1 + \mathrm{e}^{-(a+bx)}\right)^{-1}, \tag{1}$$

where x is the bid offered and a and b are the coefficients to be estimated. Following [5,43–45], we used logistic regressions where only the bid and a constant were included as independent variables to estimate Eq. (1). The expected WTP was then calculated by integrating the estimated probability of being willing to pay a specific bid over the range of bids:

$$\begin{aligned} E(WTP) &= \int_{l}^{u} \left(1 + \mathrm{e}^{-\left(\hat{a}+\hat{b}x\right)}\right)^{-1} \mathrm{d}x \\ &= u - l - \frac{1}{\hat{b}}\left(-\ln\left(\frac{\left(1 + \mathrm{e}^{-\left(\hat{a}+\hat{b}u\right)}\right)}{\left(1 + \mathrm{e}^{-\left(\hat{a}+\hat{b}l\right)}\right)}\right)\right), \end{aligned} \tag{2}$$

where l is the lower and u the upper limit of integration. Equation (2) does not include a negative WTP, i.e. we exclude the existence of malevolent behaviour. Our bid interval provided the figures for l (71 Euro cents) and u (EUR 130) in Eq. (2). The estimate of WTP was conservative (possibly underestimated) in the sense that it did not account for any positive WTP outside our bid interval. Confidence intervals were obtained by bootstrapping (a method for obtaining measures of statistical precision when no formula is otherwise available) [46].

Sensitivity analysis

We explored the sensitivity of our results with respect to (i) the degree of certainty in the yes

responses, (ii) anchoring effects and (iii) individual characteristics. As the probability of being willing to pay a hypothetical bid may exceed the probability of actually buying the good at that price, we analysed whether the inclusion of answers from respondents who were not absolutely certain that they would pay the given amount had any statistically significant effects on our estimated WTP.

Anchoring bias refers to a possible influence of information that, on theoretical grounds, should not have an effect; for instance, that the value of the quality of life should not be influenced by the cost to obtain this quality of life in itself. In particular, the first bid offered could be seen as an example of such irrelevant information that might affect the probability of agreeing to the second bid. To investigate this, we randomized respondents into 10 subgroups of equal size. Five of these groups got the highest bid first and the other five groups got the lowest bid first (Table 1 shows the bid pairs employed). We also randomized the order of questions 1–2 and 3–4 in Table 3, so that the highest bid would be randomly attributed to either treatment strategy. Consequently, 50% of the respondents considered a bid for prophylaxis first and the other 50% a bid for on-demand treatment first.

Anchoring bias may result in either too high or too low an estimate. The presence and size of the effect were determined by investigating whether there were statistically significant differences in the estimated mean WTP using, respectively, first bids only, and second bids only, for each strategy.

The sensitivity of our results with respect to individual characteristics (income, age, gender, etc.) was analysed by incorporating them as additional explanatory variables in the logistic regression and checking whether they had the theoretically predicted effects on the probability of agreeing to pay (theoretical validity). We would, for instance, expect that the size of the bid would have a negative effect, and that having haemophilia in the family or among friends would have a positive effect on the probability to agree to pay. A higher household income would also be expected to increase the probability, while the number of children in the family would be expected to reduce the probability at a given household income [18].

Results

Figure 1 illustrates graphically the predicted probability of WTP for on-demand and prophylactic treatment. As expected, the probability of agreeing to pay decreases with bid size. The predicted probability of agreeing to pay the lowest/highest bid was 50/14% (on-demand) and 72/27% (prophylaxis). Hence, our bid range did not exhaust the WTP. The point estimates of mean WTP were EUR 39 (on-demand) and EUR 65 (prophylaxis); based on absolutely certain first bids (the highlighted first row, Table 5). These estimates were significantly different from each other ($P < 0.01$).

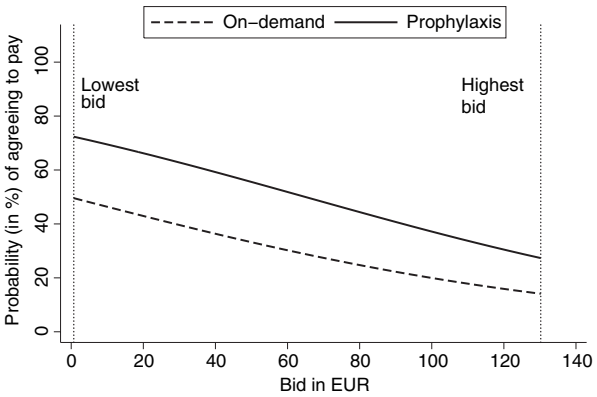

Fig. 1. Predicted probability of agreeing to pay the offered bid for on-demand and prophylaxis.

Sensitivity analysis

Table 5 reports the estimated WTP in the full sample and in subsets. For on-demand treatment, there was no statistically significant difference between the estimated WTP when using the absolutely certain yes answers to first bids (Table 5, row 1; the conservative estimate, highlighted), and when using the absolutely certain yes answers to second bids (row 2). Hence, there was no anchoring effect. For prophylaxis, on the contrary, the WTP estimated from the answers to first bids was significantly lower than that estimated from answers to second bids. This led us to choose the estimate based on first bids only. Finally, when all answers to first bids (i.e. both the absolutely certain and the fairly certain yes answers; row 4) were used, the estimates were substantially higher than our conservative estimates for both treatment strategies.

The estimated WTP varied somewhat in different subsamples of individual characteristics (Table 6). Comparing these figures with our conservatively estimated WTP for the two treatment strategies, we found that the confidence intervals in Tables 5 and 6 overlap indicating that differences in point estimates were not statistically significant at conventional levels. However, there was some tendency that

Table 5. Willingness to pay for on-demand and prophylactic treatment (in EUR). Main result (highlighted) based on only absolutely certain responses (first row). Anchoring bias may be investigated using the WTP estimates of the second row. Hypothetical bias may be investigated using the WTP estimates of the fourth row.

	On-demand		Prophylaxis	
Group	WTP (95% CI)	*n*	WTP (95% CI)	*n*
Absolutely certain, first bids only	**39 (31–47)**	302	**65 (55–73)**	307
Absolutely certain, second bids only	39 (31–47)	307	82 (73–91)	302
Absolutely certain, first and second bids	39 (33–44)	609	73 (67–80)	609
All yes answers, first bids only	76 (67–85)	302	104 (91–111)	307

Table 6. Willingness to pay for on-demand and prophylactic treatment in subsamples with different individual characteristics based only on first bids and absolutely certain yes-responses.

	On-demand		Prophylaxis	
Group	WTP (95% CI)	*n*	WTP (95% CI)	*n*
Monthly household income				
Over EUR 4736	39 (21–57)	69	64 (46–80)	73
Below EUR 2131	24 (8–39)	64	57 (35–77)	65
Knowledge about haemophilia				
Prior	41 (29–55)	123	77 (61–91)	123
No prior	37 (27–47)	363	58 (46–68)	184
Demographics				
Men	40 (29–51)	152	61 (48–74)	148
Women	32 (22–42)	150	68 (55–80)	159
Age 20–39	30 (18–42)	114	62 (48–75)	124
Age 50 and over	37 (26–49)	122	66 (51–80)	126
Occupational characteristics				
Management position	40 (27–53)	120	62 (47–77)	111
Working/worked in the private sector	48 (36–60)	146	61 (48–73)	168
Working/worked in the public sector	29 (19–39)	156	68 (55–81)	139

people with low income, and people working in the public sector, valued on-demand treatment lower than other respondents. The highest point estimate of WTP for prophylaxis came from people with prior knowledge of haemophilia.

The results from the logistic regressions (Table 7) show that the size of the bid, whether it was the first bid (on-demand), and whether the respondent had agreed to pay the bid offered for the first treatment were all important determinants of whether respondents would be willing to pay the offered bid. Individual characteristics such as age and occupational characteristics were less influential. The effect of monthly household income was not significant.

We also asked people what treatment they considered to be the best for the patients and what factors that were important for their choice (questions 5 and 6 in Table 3). Prophylaxis was considered to be the best treatment by 97%. Looking at what aspects were important for their choice, 59% considered patient health to be important and 43% included quality of life aspects. Note that respondents were allowed to answer freely and were not given a range of alternatives to choose from. The analysts assigned categories afterwards. Formulations like 'they [the patients] don't have to feel the pain of haemorrhages' and 'better quality of life and [patients] feeling safe in daily activities' were typical. This focus on other people's health and well-being may be taken as support for the fact that the respondents were not purely selfish, and accordingly may have a positive WTP for the health of others.

A considerable number of people (24%) also noted that preventive measures on the whole would be a better choice. Even those who mentioned factors associated with allocation of resources [sickness absence (18%) and costs to the healthcare sector and/or society at large (19%)], appeared to incorporate an alternative explanation for our (high) stated WTP. The reasoning then went: '…[if I am going to pay for treatment of this patient group,] I want it to be cost-effective and prophylaxis appears to be considerably more successful'. Note that the background information revealed no information on the costs of treatment, only on treatment and outcome (Appendix C). The only 'price' information was then the bids offered in questions 1 and 3 in Table 3.

Table 7. Logistic regression of absolutely certain yes-responses on individual and bid characteristics. Columns contain odds ratios.

Variable	On-demand		Prophylaxis	
	Starting model	Last model	Starting model	Last model
Bid on-demand	0.99***	0.99***		
Bid prophylaxis			0.99***	0.99***
On-demand bid first	5.82***	5.65***	0.81	
Willing to pay for prophylaxis in first bid†	10.67***	10.35***		
Willing to pay for on-demand in first bid†			12.57***	10.94***
Monthly household income EUR 2131–3 552†	0.88		0.83	
Monthly household income EUR 3553–4736†	1.43		0.83	
Monthly household income over EUR 4736†	1.03		0.59	
Age 30–39†	0.60	0.50**	1.19	
Age 40–49†	1.18		1.20	
Age 50–59†	1.84		0.96	
Aged 60 and over†	1.44		0.82	
Man†	1.00		1.03	
Number of children	1.41**	1.32*	0.93	
Haemophilia in the family or among friends†	1.51		1.29	
White-collar profession†	1.30		1.35	
Working/worked in private sector†	1.86**	1.77**	0.86	
Management position†	1.06		0.65*	0.63*
Number of observations	609	609	609	609
Percentage correctly predicted	69.29	68.47	70.61	69.29
Log-likelihood this model	−341.62	−348.40	−337.82	−341.17
Log likelihood model no variables	−407.04	−407.04	−393.58	−393.58
χ^2	130.83	117.27	111.53	104.81
Pseudo R^2	0.16	0.14	0.14	0.13

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.
†Dummy variable; 1 if characteristic, else 0.

Discussion

We have reported elsewhere that the average predicted annual cost of treatment was EUR 51 832 per patient on on-demand treatment and EUR 146 118 per patient on prophylaxis (year 2000 prices) [1].

Hence a CBA has to account for the fact that haemophilia treatment is an example of healthcare provision involving a considerable annual cost per patient. In order to solve the problem of financing health care in general, and expensive health care in particular, countries in the industrialized world resort to some kind of insurance solution, private or social, where insurance buyers (taxpayers) share the costs. In addition to the actual organization of healthcare financing, the literature on altruism [47] [15,16] led us to conjecture that only asking patients about their valuation of their own treatment using contingent valuation and WTP, would underestimate *society's* value of haemophilia treatment. There are a number of reasons why non-haemophiliacs might want to pay for haemophilia treatment, although they themselves will not use the treatment directly: (i) helping others gives pleasure also to the donor; (ii) for moral reasons (duty to help); (iii) because they expect it ensures future assistance should they themselves need health care (reciprocal altruism; which is basically an egoistic motive), or (iv) for other reasons [15,16].

Consequently, we rejected a study design asking patients about their WTP for their own treatment because it would not catch potential altruistic WTP. Instead, we chose a design where we asked a representative sample of the Swedish population whether they were willing to pay a specific amount so that patients with severe haemophilia would obtain on-demand treatment and another specific amount for prophylaxis.

Our approach then amounted to estimating the average WTP in the general population (potential

taxpayers) and comparing it with each taxpayer's share of the total cost of haemophilia treatment by splitting the latter equally on 7.0 million registered taxpayers out of 8.9 million inhabitants in Sweden 2002. The cost per taxpayer framework is relevant in the Swedish setting where health care is tax-financed. However, cost sharing with non-haemophiliacs would also be relevant in any setting where insurance premiums were *not* related to individual risk but reflected an average expected cost per insured, and cost-sharing with the general population would then correspond to mandatory insurance.

The total cost of treatment for patients with severe haemophilia in Sweden, given that there are 254 persons (spring 2003) with severe haemophilia, would then be EUR 13.8 million if all were treated on-demand and EUR 38.8 million if all had prophylaxis (year 2002 costs calculated using consumer price index from Statistics Sweden that indicated a 4.6% increase in prices between years 2000 and 2002). Translating this into a cost per taxpayer resulted in EUR 1.97 (95% CI 1.69–2.26) for on-demand treatment and EUR 5.56 (95% CI 4.94–6.17) for prophylaxis. Hence, the conservative estimates of the mean WTP for haemophilia treatment in our sample of representative taxpayers, EUR 39 (on-demand) and EUR 65 (prophylaxis), indicated substantial positive net benefits for both treatments.

Taken at face value, this study (i) gives support for both treatment strategies (in comparison with no treatment), since the estimated mean WTP exceeded costs of treatment; and (ii) gives firm support for prophylactic treatment, as the additional cost per taxpayer of prophylactic treatment (EUR 3.59) was covered more than sevenfold by the additional WTP (EUR 65-EUR 39 = EUR 26). Moreover, points (i) and (ii) hold for all possible subsets of the data and the estimated mean WTP was several times greater than the actual cost.

There is convincing evidence that the results are reliable. True, people had to answer hypothetical questions in a telephone interview. However, we used a scientifically well-tested [18] and frequently applied [26,35–41] study design, checked our specific construction in a pilot study, used a representative sample of the Swedish population, and employed professional interviewers. We also explored the sensitivity of our results to hypothetical bias and anchoring effects and, by analysing the effects of individual characteristics, we investigated their theoretical validity. Both design and analysis support the conclusion that we can be confident with the results.

We found that WTP estimated from all answers was significantly higher than WTP estimated from absolutely certain yes answers only. One explanation may be that people like to feel nice and generous, the 'warm glow' effect [18]. However, this desire may be satisfied by an actual contribution of less magnitude than the stated WTP. This may explain that the probability of observing a hypothetical yes answer to a given bid has been found to be larger than the probability of people actually buying a good for the same amount in experimental studies [29,32]. Nevertheless, as our results were based on 'absolutely certain' yes answers only, the potential warm glow effect has been minimized (note also that Blumenschein *et al*. [26] found no statistically significant differences between the probability of observing an absolutely certain hypothetical yes answer and the probability of observing people actually buying the good at a given price).

Our analysis also indicated that there was an anchoring effect for prophylaxis but not for on-demand treatment. However, as our main result was based on answers to first bids only, this anchoring effect cannot have influenced the results.

We also had a high proportion of absolutely certain yes-answers at the highest bid (EUR 130), 10% for on-demand and 48% for prophylaxis in raw data. Ideally, to obtain a definite estimate of the total willingness-to-pay, everyone should agree to pay the lowest bid and none the highest bid. Our conservative estimates were in fact the areas under the respective probability curves in Fig. 1 (i.e. we have no information regarding probabilities for bids below 71 Euro cents, or above EUR 130.23). Hence, they underestimate the mean WTP for both treatments.

Although point estimates of WTP for on-demand and prophylaxis were lower for low-income people, these differences were not statistically significant (Table 6) and income did not have a statistically significant effect on the probability to agree to pay following in the logistic regression analysis (Table 7). The lack of statistical significance may partly be explained by the fact that the bid vector did not exhaust the respondents' WTP and that if we had included bids well exceeding EUR 130, the income effect may have been significant.

We also expect that the average WTP for haemophilia treatment would be different in a country with another level of income and the assumption would then be that, all else equal, a higher income would be associated with a higher WTP. Other differences between countries, for instance with respect to organization of society in general and healthcare

financing and production in particular, could also affect the stated WTP. For comparison, Swedish GDP per capita was ranked number 13 in 2002 (using purchasing power parities) among the 30 OECD countries, at about the same level as the UK, France and Germany, while the GDP per capita in the US was 33% greater.

It is also possible that the perceptions of the effect of having a reduced level of health on, for instance, opportunities to participate in the labour market or on performing daily activities would affect the average WTP. Our follow-up questions indicated that such aspects were important to our respondents. The results may then not be directly transferable to countries with a different organization of society. In the environmental field, cultural and socio-economic effects have been suggested to explain remaining differences between Europe and the US in average WTP for the preservation of wetlands areas when differences in purchasing power parities had been accounted for [18].

Our study was designed as a *marginal* analysis of people's WTP for one specific healthcare programme. The implicit assumption was then that the respondents answered the WTP questions considering that they had the income they had, and in other respects made the consumption choices they made. We explicitly reminded them that they should consider an yes-answer as a reduction in their annual income corresponding to the bid offered. This resembled the ordinary purchasing situation, where the choice of one good implies that one has to give up other possible consumption. Moreover, it is rare that all consumption choices are made at the same time, so the fact that we only asked about treatment of one disease does not rule out the possibility that the respondents also made intertemporal comparisons of alternative uses of resources. Still, a potential concern could be that people's stated WTP reflected attitudes that would not be stable if at the same time they had also been asked to consider several healthcare programmes or other uses of money [48]. However, first, such effects would not change the ranking of on-demand and prophylactic treatment strategies. Secondly, we note that the net benefit was considerable (and likely to have been underestimated) for both treatments. Hence, even if respondents might have reduced their WTP for haemophilia treatment, if they had been confronted with yet another healthcare programme, this reduction would have to be quite substantial in order to result in negative net benefits for either of the haemophilia strategies.

The results of a CBA are not directly comparable with those of a CUA as the latter includes fewer dimensions of potential benefits than the former. However, from a policy point of view, it may still be interesting to comment on our results vis-à-vis the simulation results in Miners *et al.* [49]. Those results indicated that primary prophylaxis would be cost-effective for haemophilia B but not for haemophilia A based on simulation of factor concentrate use, probability of surgery and lost production and imputed values of QALYs. The authors commented that the data input available for the simulation was in some cases rather crude and obtained from different sources, for instance the QALY values for primary prophylaxis were assumed to equal that of patients with mild or moderate haemophilia, and factor consumption was derived based on assumptions on keeping factor activity levels from falling below 1 IU dL^{-1} at all times. The latter assumption together with the assumed decay rates of factor VIII and factor IX were probably driving the twice as high, simulated cost of prophylactic treatment for haemophilia A compared with that for haemophilia B, and consequently the different results on cost-effectiveness.

In our data on actual resource use based on a 11-year panel of 156 patients in Norway and Sweden [1,2] we found that the factor concentrate consumption for haemophilia A was only on average 11% higher than for haemophilia B for prophylactic treatment and 38% higher than for haemophilia B for on-demand treatment. We believe that the reason behind our different results in terms of policy recommendation are to be found in (i) the fact that the CBA incorporated non-health-related benefits of treatment; and (ii) the fact that, in Miners *et al.*, several assumptions had to be made concerning the link between factor consumption and its consequences in terms of health-related quality of life. Our study was based on actual, observed variations in resource use and outcome, and on the stated willingness of the general population to pay for the two treatment strategies.

In conclusion, patients on prophylaxis have significantly better health outcome (measured in days lost from work or school, in-hospital episodes, reconstructive surgery, use of special equipment, etc.) than patients treated on-demand [2], but the costs of prophylaxis are considerably higher [1]. This study showed that even the most conservative estimates of WTP in Sweden exceeded by far the costs, given the present prices, for on-demand and prophylaxis as described from Norway and Sweden, respectively [1]. In other words, our results indicate that providing

patients with severe haemophilia with either on-demand or prophylaxis will increase societal welfare. Furthermore, net benefits (estimated WTP – cost per taxpayer) were greater for prophylaxis.

Acknowledgements

The authors would like to thank Anders Glomstein [Institute for Rare Diagnoses, Oslo (formerly Institute for Hemophilia)], Sam Schulman (Karolinska University Hospital, Stockholm) and Lilian Tengborn (Sahlgrenska University Hospital, Gothenburg) for their crucial assistance in part I of this project where costs of on-demand and prophylactic treatment were assessed.

Financial support was received from Aventis Behring GmbH, Bayer, Baxter, Octapharma and Wyeth/Genetics Institute, and from funds managed by county council Region Skane (Stefan Lethagen and Erik Berntorp). However, none of the sponsors was involved in any of the analyses nor did they influence the conclusions of the research.

Appendix A: telephone recruitment

Hello, this is [name]. I am calling you from GfK in Lund. I would like to talk to [name of respondent].

You participate in one of GfK's panels and you have now been selected to participate in the present survey. We are conducting a survey on behalf of Lund University Centre for Health Economics. Your telephone number has been randomly selected from GfK's household panel. The survey concerns your attitudes to two different treatment strategies for the disease severe haemophilia. No prior knowledge of the subject is required. It is your opinion that is of interest. If you agree to participate in the survey, your household will gain 100 GfK points. You will first receive an introductory letter from Lund University together with an introductory text on the two treatment strategies. A few days later, we will phone you and ask a couple of short questions. The telephone interview will take 10 min at the most.

Appendix B

Dear respondent,

We are all concerned about health and health care. For some health problems there are several treatment strategies where the effects differ. One example is severe haemophilia treatment for which one could follow either a strategy of attempting to prevent haemorrhages from occurring (prophylaxis), or a strategy of trying to stop them as soon as possible when they occur (on-demand treatment). As you can see in the presentation below, the two strategies differ in their consequences. We would like to know how people value these differences. Your answer may be important for the choice of treatment for this disease.

Our survey is conducted in cooperation with GfK in Lund and our interviewer will call you on the phone in a few days' time. Participation in the survey is of course completely *voluntary*. You have been selected by pure chance and you will not be contacted again. The data will be treated as *strictly confidential*, and all responses are deidentified so that they are totally anonymous before use. We do not need to know who you are to conduct the study, but we do need your opinion.

Our interviewer will ask you whether you think the respective treatment strategies are worth the suggested amounts, and which one of them you believe is the best. You do not need to fill in any forms, but we ask you to read and keep the presentation for the interview.

If you choose to participate, GfK will grant you 100 points. If you prefer not to participate or be contacted by our interviewer, we ask you to call (name of contact person, phone number of contact person, E-mail address of contact person) Monday–Friday, between 9.00 and 16.00 hours.

If you have any questions you are welcome to contact any one of us (Monday–Friday, between 9.00 and 16.00 hours).

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Appendix C: evaluation of treatment for severe haemophilia

Haemophilia is a congenital disease that affects men. It is caused by deficiency of a substance (coagulation factor) needed for the clotting of blood. Severe haemophilia implies that the patient experiences haemorrhages, often in the joints, that can occur without any apparent reason. The haemorrhages are painful and lead to a gradual destruction of the joints and finally to disability. If the haemorrhages are severe, or if they occur in the brain, the patient may

die. The disease can, however, be treated, and there are two main strategies: (i) *on-demand treatment* and (ii) *prophylactic treatment*.

On-demand treatment

On-demand treatment implies that the patient is given injections with coagulation factor as soon as a haemorrhage occurs, or when the patient is at risk of bleeding (i.e. in connection with surgery or tooth extractions). The patient himself may administer the injections at home. The aim of on-demand treatment is to stop haemorrhages as soon as possible. Thereby the patient will suffer less pain and a slower destruction of joints than if the disease had been left untreated.

Prophylactic treatment

Prophylactic treatment implies that the patient is given injections of factor concentrate on a regular basis (one to three times weekly). The patient can also administer these injections at home. The aim of prophylactic treatment is to prevent the occurrence of haemorrhages. If successful, this strategy could reduce the patient's exposure to pain and joint destruction even further.

Effects of prophylactic and on-demand treatment

Several clinical studies show that both on-demand and prophylactic treatment reduce the risk of joint destruction and disability, as well as increasing the life expectancy of patients (although it is uncertain whether life expectancy increases equally under both treatment strategies). The studies have also shown that prophylactic treatment can prevent haemorrhages almost completely. Thus, patients with prophylactic treatment experience substantially less pain, have fewer days lost from school or work, run a smaller risk of undergoing surgery, smaller risks of disability, and do not have to refrain from physical activity to the same extent as patients on on-demand treatment. We found similar results when we investigated what had happened to patients with severe haemophilia during the period 1989–99. As seen from Figs 1 and 2, 41% of the patients on *on-demand treatment* had experienced one major surgical procedure (arthrodeses, prostheses implantation, etc.), and 20% had experienced more than one. The corresponding figures for patients on *prophylactic treatment* were, respectively, 9% and 2%.

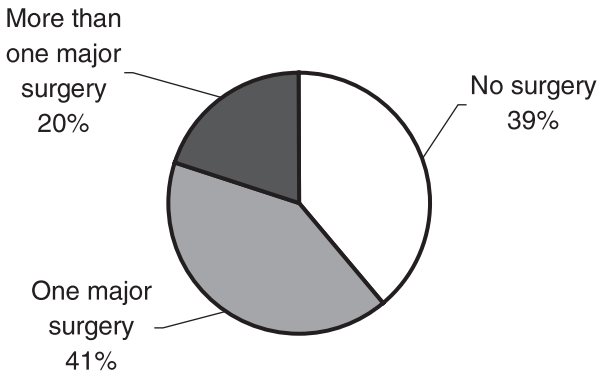

Fig. a1. On-demand

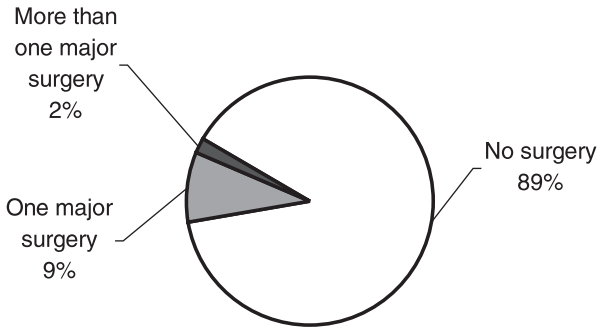

Fig. 2. Prophylaxis

We also found that 25% of the patients on *on-demand treatment* had been granted part- or full-time early retirement, that 16% of them had had at least one long period of sickness-absence (longer than 6 months), and that 21% of them were using wheelchairs. Of the patients on *prophylactic treatment*, 8% had been granted part- or full-time early retirement, 4% had experienced at least one long period of sickness-absence, and 6% were using wheel chairs (Fig. 3 below).

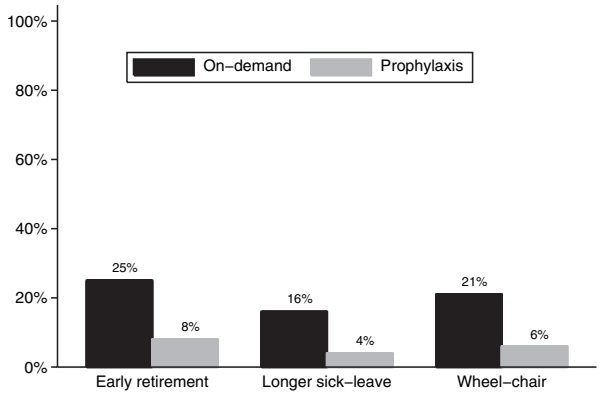

Fig. 3.

Thus, the two treatment strategies seem to give different results. We would like to know how this affects your evaluation of them. Our interviewer will therefore ask you if you are prepared to pay a specified amount, per year, to enable patients with severe haemophilia to receive prophylactic treatment, and another specified amount to enable patients with severe haemophilia to receive on-demand treatment. Other randomly selected persons will be asked to respond to other amounts. Before answering, we ask you to consider that, in case you accept the bid, your annual income will be reduced by the corresponding amount.

Thank you for your participation.

Appendix D: telephone interview

Hello, I am [name] and I am calling you from GfK in Lund. I would like to talk to [name of respondent].

A colleague of mine here at GfK called you a couple of days ago and you agreed to participate in a survey that we are conducting. Recently you have also received a letter from Lund University Centre for Health Economics concerning two treatment strategies for severe haemophilia. As we agreed, I would now like to ask you to answer a few questions. The interview will take 10 min at the most. Before we start, I would like to inform you that participation is voluntary and that you may choose to terminate the interview whenever you like. GfK will register your answers but you will remain completely anonymous for our client, Lund University Centre for Health Economics. Answers will only be kept as table entries. Could we begin the interview?

To help you remember the two treatment alternatives I shall read parts of the information you received in the letter.

Haemophilia is a congenital disease that only affects men. It is caused by a deficiency of a substance (coagulation factor) needed for the clotting of blood. Severe haemophilia implies that the patient has haemorrhages, often in the joints, which can occur without apparent reason. The haemorrhages are painful and will gradually lead to destruction of the joints and to disability. If the haemorrhages are severe, or if they occur in the brain, the patient may die. However, the disease can be treated and there are two ways of doing it: on-demand treatment and prophylactic treatment.

On-demand treatment implies that the patient receives injections of the coagulation factor when a haemorrhage occurs or when doctors assume that the patient will bleed (for example during operations). These injections can be administered by the patient himself at home. The purpose of on-demand treatment is to stop the haemorrhage as soon as possible. This implies that the patient will be exposed to less pain and that the joints will not be destroyed as quickly as if the disease had been untreated.

Prophylactic treatment implies that the patient receives extra coagulation factor through regular injections, one to three times weekly, administered by the patient himself at home. The purpose of this is to prevent haemorrhages from occurring. Thereby the risk of pain and joint destruction because of haemorrhages could be reduced even further.

Both treatment strategies lead to a considerable increase in length of life. Both treatments also reduce the risk of joint destruction and disability. There are however other differences. Several clinical studies have shown that prophylactic treatment may almost prevent haemorrhages entirely. They have also shown that patients with prophylactic treatment have less pain, fewer sick days, run a smaller risk of having an operation, a smaller risk of disability, and do not have to refrain from physical activity to the same extent as patients on on-demand treatment.

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