

EXPERT  
REVIEWS

# Parent preference in Switzerland for easy-to-use attributes of growth hormone injection devices quantified by willingness to pay

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Sustained treatment adherence, usually over long periods of time, is critical to the success of growth hormone (GH) therapy. However, adherence rates are often poor which may result in suboptimal clinical outcomes. The type of device used by patients to administer their GH can influence adherence. Offering patients a choice of device maximizes the chance of adherence to treatment. Multiple factors will influence a patient's choice of device, depending on individual priorities. This study evaluated the most preferred features of GH injection devices by parents using a web-based questionnaire and as assessed by their willingness to pay for specific device features. The results show that parents are willing to pay for device features facilitating ease of use.

**KEYWORDS:** adherence • easy to use • growth hormone • injection devices • willingness to pay

For children with short stature due to growth hormone (GH) deficiency (GHD), Turner syndrome or born small for gestational age, treatment with GH enables most to achieve an adult height as close to their genetic height potential as possible and within the normal population range [1]. One factor influencing height outcome is compliance and adherence to GH treatment. As GH must be injected daily over a period of several years, an inconvenient and sometimes distressing process, adherence issues [2] and avoidance of therapy [3] may be frequently observed. Treatment effectiveness appears to be closely associated with adherence [2,4,5]. Among 177 children and adolescents receiving GH, the overall estimated rate of non-adherence was 66% (73/110) [2] with significantly greater linear growth reported in patients with good adherence than in those who missed injections ( $p < 0.05$ ). Poor adherence can arise for several inter-related reasons including the patient's perspective of their treatment and

consequences of missing injections, as well as device-related factors, such as ease of use and injection pain [6].

Although training in good injection technique may help limit injection pain and discomfort [7], pen injection devices and needle-free devices have aimed to further improve ease of use, and reduce injection pain and discomfort [8]. Offering patients an informed choice of treatments and devices meeting a broad range of requirements and individual preferences may impact positively on adherence [4,9–12] and so improve outcomes.

The aim of this study was to investigate device-specific features that may affect adherence to treatment and treatment outcome. The most preferred features of GH injection devices and GH administration were evaluated using the parents' willingness to pay (WTP) as a method to quantify preference, as determined using discrete choice experiment (DCE) methodology [13].

**Table 1. Choice scenarios concerning growth hormone administration and technical aspects of growth hormone injection devices: attributes and levels.**

Attribute	Level
<i>GH administration</i>	
Who can give the injection?	The device can be operated by grown ups and children $\geq 6$ years old The device can be operated by grown ups and children $\geq 10$ years old
How should the device be stored?	Refrigerator Room temperature or refrigerator
Does the device require instructions before it can be used safely?	Yes No
How often can the child see the injection needle?	Always visible Never visible The injection needle can be visible or not visible
Price per month	CHF 20 CHF 50 CHF 150
<i>Technical aspects of GH administration</i>	
Does the device confirm dose delivery?	Yes No
Does the medication require mixing?	Yes No
Is it prefilled or does it require manual loading of cartridges?	Pre-filled Cartridge
Is it operated manually or electronically?	Manual Electronic
Price per month	CHF 20 CHF 50 CHF 150
In January 2012, CHF 20 = €16.5; CHF 50 = €41.2; CHF 150 = €123.5. GH: Growth hormone.	

## Patients & methods

### Participants

The study was conducted in Switzerland in January 2012 by an independent consultancy company, Incentive (Holte, Denmark). Study participants were contacted through an existing database; an online research panel owned by an independent research company, Panelbase (Hexham, UK [101]). Members who sign up for the research panel are rewarded €2–4 for their participation in each relevant market research survey. Eligible study participants were German-speaking parents who had children without GHD, and who were considered representative of the national population (as validated by household income

analysis). Parents were chosen as they form the majority of society and the questionnaire topic was relevant. Parents have been used to elicit responses in similar studies regarding decisions that affect children's welfare or treatment [14,15]. All eligible respondents selected one of their children as the basis for answering questions in the survey, answering as they related to this child with the pretext that the child had GHD. Using a focal child for participants to direct their questionnaire responses is a commonly used method in DCE studies [16]. All responses were made in an anonymous manner.

### Study design

A closed-design, web-based questionnaire was used to collect data. Participants were sent a link by email to gain access to the questionnaire. The questionnaire was created to fit a standard computer screen with 1–2 questions on each page. To go from one page to the next, respondents pressed the 'Next' button. Respondents could review their answers by using the 'Back' button. The design of questionnaire ensured that respondents could only complete it once.

This study was undertaken following International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Good Research Practice for Conjoint analysis checklist [17].

The questionnaire was subdivided into three sections concerning: the respondents' children, choice scenarios on features of the administration of GH treatment and technical aspects of GH injection devices (TABLE 1), and background questions on height and household income.

After answering section 1, participants completed the rest of the questionnaire based on the assumption that one of their children, selected at random, was diagnosed with GHD requiring GH therapy. Respondents were provided with background information on GHD and its treatment.

A DCE was used to identify the most preferred features of GH injection devices. DCE provides a systematic assessment of patient preferences using an attribute-based measure of benefit based on the assumption that a healthcare intervention can be described by its attributes and that an individual's valuation of that intervention depends on the levels of those attributes. Within a DCE, choices are made between two or more hypothetical treatment options with the resultant choice revealing an underlying utility function [13,18]. Conjoint analysis was used to estimate the relative importance of different attributes, the trade-offs between these attributes and preference for features of the GH devices [19].

In this study, respondents were given the choice between two different hypothetical treatment options (A and B). Treatment attributes were subdivided into general administration of GH and technical aspects of GH injection devices (TABLE 1). The selection of attributes and their levels was developed by Incentive, in collaboration with Novo Nordisk, and was informed by a literature review and qualitative interviews with experts in the field to determine the most important features of GH injection devices that are currently available. Excluded were features related to pain, for example, pain associated with needle prick

or type of injection fluid, as these were considered too complex to describe in the questionnaire. Information cited in the questionnaire was unbranded. To reduce the number of combinations to a more manageable size, a balanced and orthogonal factorial design was used [20]. Using this procedure, 18 different scenarios were generated from which parents were able to choose. An example choice question on GH administration from the electronic questionnaire is presented in APPENDIX A. The inclusion of a cost (or price) attribute in DCE allows estimation of the participant's WTP for desirable attributes. In this study, costs cited were for 1 month of treatment and were considered as out-of-pocket, not covered by insurance, and independent of current healthcare payments [14]. Switzerland has a capped patient co-pay system; some cases may be 100% reimbursed if the disease is acknowledged as a birth defect.

Each participant received six choice questions on the administration of GH and six choice questions on the technical aspects of GH devices. To ensure that respondents understood the concept of trading-off, a test question was included in the questionnaire. The test question asked respondents to choose between two treatment options with one being clearly better than the other. Respondents who failed the test question were excluded from the study [21].

### Statistical analysis

Only fully completed questionnaires were evaluated (142/172) (FIGURE 1). Data collected were validated, by checking for consistency and errors, and descriptive statistics were calculated for all questions. Frequency tables were generated for discrete answer categories. All statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA).

As each question in the questionnaire included a choice of options of which only one could be selected, conditional logit regression was employed to analyze the effect of the attribute levels on the parents' preferences for device features.

The WTP for the attribute levels was calculated by the method of Lancaster [22].

Confidence limits for WTP cannot be derived directly from the parameter estimates of the conditional logit estimations because WTP is calculated as the ratio between two stochastic variables. For this reason, bootstrapping was used (bootstrapping assumes that the data are a random sample of the whole population). Confidence intervals for the WTP results were calculated using 10,000 iterations as recommended by Barker [23]. Data are presented as mean (95% CI).

## Results

### Participants

Of 331 people who were initially contacted, 142 complete questionnaires were analyzed (FIGURE 1).

Of the 142 respondents whose questionnaires were assessed in this study, all had healthy children and 62% (88/142) were female. The average age of respondents was 40.2 years (male, 43.0; female, 38.4) and 59% (84/142) were employed; 76% (41/54) males and 49% (43/88) females. The ages of the selected children were: <5 years of age (n = 37; 26%), 5–9 years

of age (n = 37; 26%); 10–14 years of age (n = 43; 30%) and 15–18 years of age (n = 25; 18%). Overall, 56% (80) of the selected children were boys, 44% (62) were girls.

### Background information on height

Participants were asked to answer several background questions on their child's height and on their perception of the importance of their child's height (TABLE 2).

Most (89%; 127/142) parents knew their child's height, with this being assessed regularly and at least annually in the majority of cases (83%; 118/142). All parents were knowledgeable regarding their own child's height with respect to that of their peers. Over half (57%; 81/142) of parents felt that it was very important or important for their child to be of a similar height to their peers, although 31% (44/142) had no strong views on whether or not it was important for their child to achieve a height that was similar to that of their peer group.

### Willingness to pay

Respondents ascribed a positive value to all attributes tested concerning the general and technical aspects of GH administration (TABLE 1). The monthly WTP values (CHF, euros) attributed to specific features tested are shown in FIGURE 2, ranked according to the value (WTP). The most important device features, in terms of WTP per month, were to avoid mixing the medication (CHF 89 [95% CI: 70–112], €77) and being able to store the medication at room

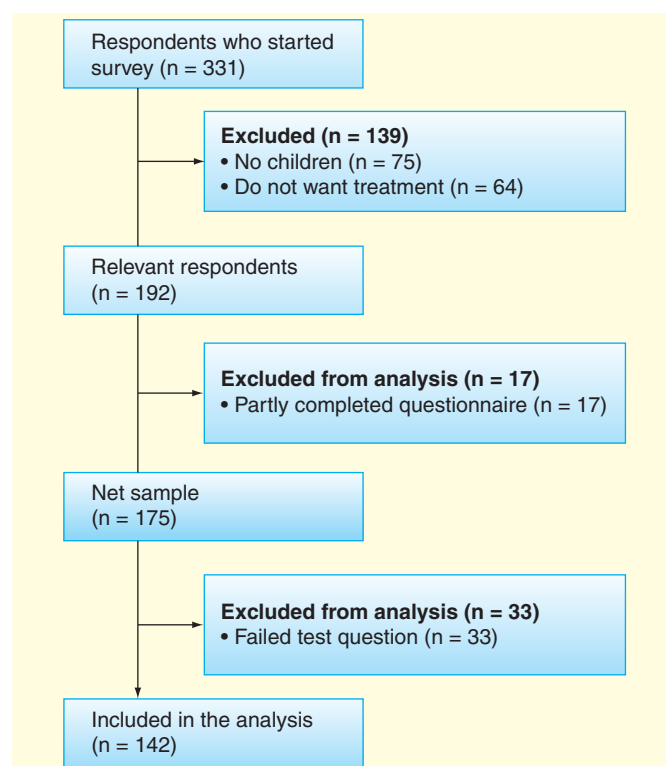


Figure 1. Respondents in the study.

**Table 2. Respondents' answers to questions regarding their focus on their child's height.**

	Male parents (n = 54)	Female parents (n = 88)	Entire cohort (n = 142)
<i>Knowledge of height (n; %)</i>			
Know specific height	42 (78)	85 (97)	127 (89)
Know range of height	54 (100)	88 (100)	142 (100)
Know height compared with other children	54 (100)	88 (100)	142 (100)
<i>How often has the height of the child been monitored from the time he/she was 2 years old? (n; %)</i>			
Every 3 months or more often	8 (15)	8 (9)	16 (11)
Every 6 months	10 (20)	18 (20)	28 (20)
Every year	30 (56)	44 (50)	74 (52)
Less than every year	1 (2)	9 (10)	10 (7)
Almost never	2 (4)	4 (5)	6 (4)
Do not know	2 (4)	5 (6)	7 (5)
<i>Who has monitored the height of the child? (more than one response is allowed) (n; %)</i>			
I have	20 (37)	43 (49)	63 (44)
My spouse has	19 (35)	14 (16)	33 (23)
Our family doctor has	15 (28)	20 (23)	35 (25)
Our child's doctor has	39 (72)	58 (66)	97 (68)
Other healthcare professionals have	1 (2)	3 (3)	4 (3)
Other	1 (2)	2 (2)	3 (2)
No one has	0	2 (2)	2 (1)
<i>How important is it for you that your child achieves at least the average height of his or her peers? (n; %)</i>			
Very important	5 (9)	13 (15)	18 (13)
Important	22 (41)	41 (47)	63 (44)
Neither	17 (31)	27 (31)	44 (31)
Less important	9 (17)	6 (7)	15 (11)
Not at all important	1 (2)	1 (1)	2 (1)

temperature over refrigerated storage (CHF 81 [95% CI: 62–107], €70). Least important to respondents was the option of the device being electronically operated compared with manually operated, although there was a slight preference for electronic versus manual operation (CHF 15 [95% CI: 2–29], €13). In comparison with these lowest ranked device features, the most preferred attributes, 'no mixing required' and 'room temperature storage', were ranked 5.9-

and 5.4-fold higher, respectively. The option for the needle to be either visible or not visible compared with being always visible, was also ranked highly (CHF 64 [95% CI: 42–91], €55) (4.3-fold higher than the lowest ranked attribute). With regards to technical aspects of the delivery device, respondents showed a preference for confirmation of dose delivery (CHF 59 [95% CI: 43–79], €51), ease of use (can be used without instruction), pre-filled rather than needing manual loading of cartridges and for the device to be able to be used safely by a child >6 years of age. These features were ranked as 3.9-, 1.2- and 1.2-fold higher, respectively, than the lowest ranked attribute.

The effect of the age and sex of the child on the reported WTP values was assessed but was not shown to have a significant effect on the results.

## Discussion

The overall aim of this study was to determine injection device-specific factors that may improve treatment adherence and effectiveness. Patient preferences for specific attributes of injection devices that may help make the injection process easier are, therefore, important. By understanding parents' views of GH treatment devices, healthcare providers may be able to develop targeted interventions to improve adherence to GH treatment [24].

The results of this WTP analysis demonstrate that parents are willing to pay up to CHF 89 (€77) each month for the most preferred injection device attributes, 5.9-times more than for the lowest rated attributes. Highest value was placed on device features associated with ease of use, such as 'no mixing required' and 'room temperature stable', which had a five- to sixfold higher value than the lowest ranked feature, electronic versus manual operation. This is consistent with data from a web-based survey of 61 patients and 239 caregivers that reported mixing GH medication and storage of GH (need for refrigeration) was considered burdensome by more than one-third of respondents [25]. Indeed, problems with storage of GH while away from home or traveling was the most frequently cited reason for missing a dose.

Patient preference for GH device characteristics has been assessed in several studies [11,26–32]. Findings in the present study are in agreement with these studies that showed patients place high value on products that are easy to use, ready mixed and easy to store [11,26–28,30,31,33].

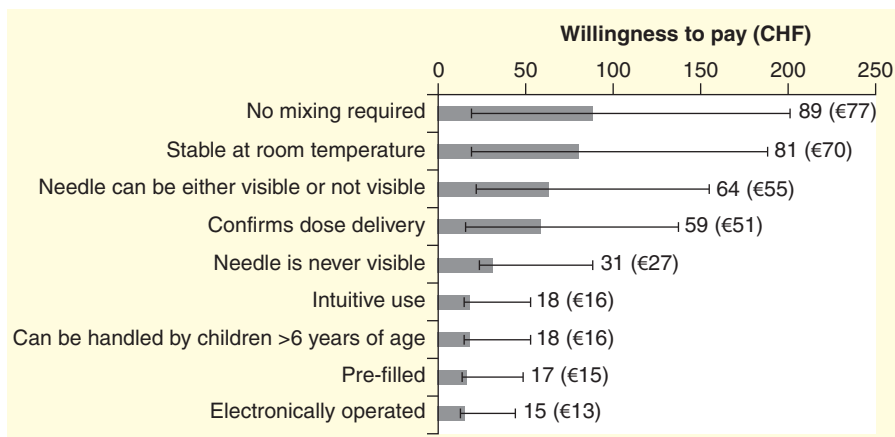
Also rated highly in the present study, and approximately fourfold higher than the lowest ranked attribute, was the ability to have the needle visible or not visible, as well as confirmation of dose delivery. For some patients, even looking at a needle may provoke anxiety, which may escalate to needle phobia with repeated exposure [3]. A hidden needle and auto-injector were among the most preferred features of a GH injection device in the conjoint analysis reported by Ahmed *et al.* [26]. In an open-label, multicenter study that assessed acceptability of an electronic GH injection device among patients, factors including display of the remaining



drug in the cartridge, pre-programmed dosing, automatic needle insertion and on-screen instructions, were regarded as ‘very useful’ by patients [28,31].

Discomfort with injections, the burden associated with storage of GH products, misperceptions about the consequences of missed GH doses, dissatisfaction with treatment results and inadequate contact with healthcare providers are among the reasons reported in studies that have evaluated factors that may adversely affect treatment adherence [5–7,25,34]. Continuously working on a stable patient–physician relationship and strengthening the motivation to self-treat by providing the patient with a clear understanding of their disease, the projected length of treatment, realistic treatment goals and the benefits of adherence [35] may be highly influential in determining the success of treatment and encourage good treatment adherence [7]. Enabling patients to manage their own disease and involving them in decisions affecting their treatment can also contribute to good treatment adherence [36]. Included in this strategy might be help and support in selecting the most appropriate GH injection device for an individual patient [9]. Studies suggest that patients are more likely to adhere to a GH treatment regimen if they have some choice in the injection device [4,12] enabling them to select a device that fits their lifestyle and individual needs [9]. A retrospective observational study of pediatric patients with GHD showed that lack of choice of GH injection device was positively associated with reduced height velocity [4].

As all respondents in this study had a healthy child, and were therefore unfamiliar with dealing with healthcare professionals with regards to their child’s growth issues, and had no previous experience with GH injection devices, the views expressed in the study are considered unbiased and not based on previous experience. By selecting their own child to base their responses on, participants were able to project the described situation to their own life to substantiate their opinion; this helped to make the questions as realistic for the respondent as possible. Evidence suggests that respondents with healthy children are more likely to base their decisions on cognitive processing strategies and normative beliefs compared with parents with children who have the illness under investigation, who may have emotions that play a role in decision-making [37]. Parents of children with GHD, or other GH-treated growth disorders, could, however, be expected to be more informed about the condition and have practical experience regarding features of GH devices. For example, the expectation that needle-free devices might make GH injections more bearable for children is not necessarily borne out in ‘real-life’ as bruising, pain, redness and soreness may be associated



**Figure 2. Monthly willingness to pay values (CHF [Euros; €]) for features of growth hormone devices related to general administration and technical aspects of administration.** The average exchange rate CHF to € during January 2012 was 1 CHF = €0.8623. Data are shown as the point estimate (95% CI).

with needle-free as well as needled devices [32,38]. In addition, as borne out by the observation that while 57% of parents in this study felt it was important for their child to achieve at least the height of their peers the remaining 43% had no strong views (31%), or thought that this was less important or not important (12%), parents of children with short stature could be expected to have much stronger views on their child’s height and the importance of being of a similar height to their friends.

Although DCEs are increasingly used in health services research, one potential limitation with this methodology can be sensitivity of the results to the choice of attributes presented because it is only possible to indicate trade-offs in relation to the attributes selected. It is therefore critical that the attribute selection process involves a wide range of opinion makers. This was included at the design stage of the present study and specific product information was deliberately omitted from the questionnaire. A further limitation of the study is that it was not possible to assess if WTP and parent preferences were stable over time. A drop in adherence may occur with increasing duration of treatment: long-term users may be less enthusiastic or less motivated about adhering to treatment than those new to treatment, who may be more diligent [4,39]. Furthermore, the study only evaluated device features and did not consider other aspects of medical therapy such as long-term outcomes.

## Conclusions

Participants were willing to pay for specific features of GH injection devices, placing a high monetary value on device features associated with ease of use and those features likely to impact daily life, such as the ability to store the product at room temperature and a ready-to-use, liquid formulation. It could be expected that devices with more preferred features would be favored over those with fewer preferred features. Ultimately, a more desirable treatment outcome could be expected to result from improved treatment adherence. Matching

patients' preferences with the most appropriate injection device to suit their circumstances and lifestyle may play a part in enabling better treatment adherence, resulting in a more satisfactory height gain and an adult height within the normal population range.

### Expert commentary

Currently, administration of GH by patients and parents may be achieved using a variety of device types including syringes with needles, injection pen, auto-injector, needle-free injector or an electronic injection device. Comparison of different injector types has shown that different aspects of each device type are favored by users, suggesting that multiple factors influence a patient's choice of device, depending on their individual priorities. Treatment adherence may be affected by the type of device used by a patient [40] and adherence may be improved among patients offered a choice of device [4,11]. To make an informed choice, patients need to have had relevant information on the pros and cons of each device type. Reducing the treatment burden by providing the patient with an easy-to-use device matched to their lifestyle choices and individual needs, may improve clinical outcome through improved adherence.

### Five-year view

Developments in GH delivery devices have aimed to reduce the physical and psychological stress of daily injections.

Further innovations aimed to improve the injection process and aid adherence may help to improve treatment outcome. Poor compliance, however, remains problematic, providing a strong rationale for developing a long-acting GH formulation. Despite the fact that endogenous GH secretion in healthy humans is pulsatile, current evidence supports that prolonged exposure to GH, either as an infusion or via a long-acting GH formulation can provide similar efficacy to daily injections. Over the next few years, it can be expected that clinical data will become available to support the development of a safe and effective long-acting GH for replacement therapy.

### Financial & competing interests disclosure

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### Key issues

- Adherence to growth hormone (GH) therapy, as with many chronic medical conditions requiring long-term therapy, is frequently poor.
- Non-adherence to GH therapy undermines clinical outcomes.
- Multiple issues may influence treatment adherence including patient- and product-related factors.
- Developments in GH delivery devices have aimed to simplify administration.
- The range of choice of GH injection devices offers physicians the opportunity to individualize treatment and maximize adherence.
- This study demonstrates that parents prefer device features that are associated with ease of use.
- Providing patients with easy-to-use devices may improve treatment adherence.

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**Website**

- 101 Panelbase.  
[www.panelbase.net/](http://www.panelbase.net/)



**Appendix A. Example of scenario pair presented to participants.**

	Option A	Option B
Who can give the injection?	Adults and children >10 years of age	Adults and children >6 years of age
How is the device stored?	Either room temperature or refrigerator	Refrigerator
Are instructions necessary to use the device properly?	Yes	No
Is the needle visible to the child?	Never visible	Always visible
Price per month (CHF)	30	100
RESPONSE (please choose one of the following four options)		
I prefer option A		
I possibly prefer option A		
I possibly prefer option B		
I prefer option B		
In January 2012, CHF 30 = €26; CHF 100 = €86.		