

- Growth hormone deficiency (GHD) in children causes a decreased growth rate and a markedly reduced final adult height. Treatment for GHD is given as subcutaneous injections.
- Research has shown that the current burden of illness for both children and caregivers is substantial.¹ However, to our knowledge, the impact of GHD treatment on health-related quality of life (HRQoL) has not been investigated using time trade-off (TTO) methodology.
- This study aimed to investigate the impact of some of the most important aspects of GHD treatment on HRQoL using TTO surveys in the UK and Canada.

Pain-Free Injections for Growth Hormone Deficiency (GHD) Improve Quality of Life: A Time Trade-Off (TTO) Study in the UK and Canada

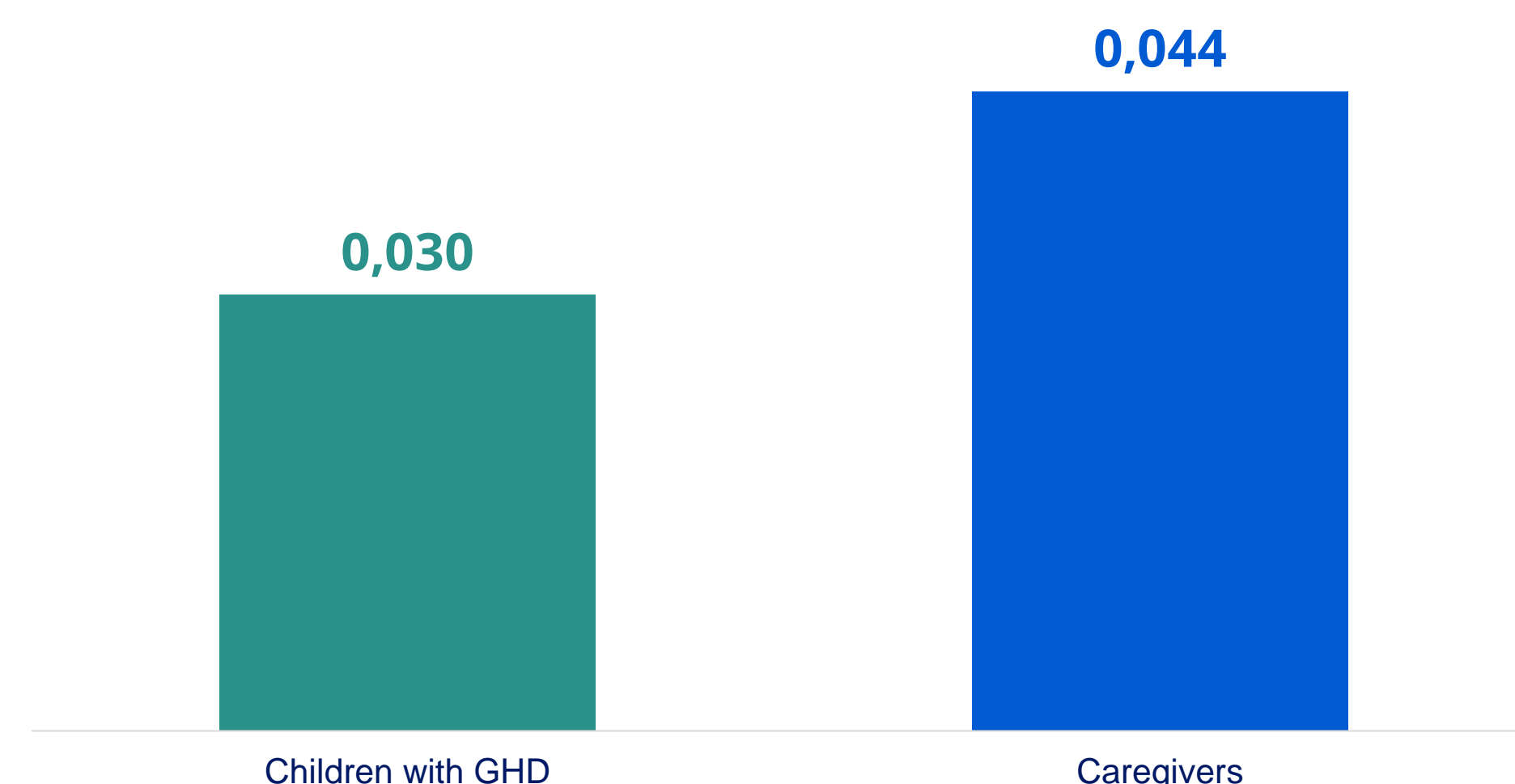


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Utility gain for avoiding injection pain



Using GH treatment options which do not involve injection pain is expected to result in higher HRQoL among both children with GHD and their caregivers

- TTO methodology was used to estimate health utilities through two online surveys (S1 and S2) completed by the adult (18+ years) general population in the UK and Canada.
- In S1, respondents evaluated health states as if they took injections themselves. This survey was used as a proxy for children with GHD.
- In S2, respondents evaluated health states as if they gave injections to a child with GHD. Only respondents with a child under the age of 15 years were included in S2.
- Respondents were excluded if they did not meet the inclusion criteria or finish the survey (Table 1).
- The following treatment aspects were evaluated: injection frequency, device complexity, needle visibility, injection pain and storage possibilities using eight different health states (Table 2).

Table 1 Overview of respondents in S1 & S2

	S1		S2	
	UK	Canada	UK	Canada
Respondents, n	1,341	1,228	4,227	4,350
Included in analysis, n (%)	1,025 (76)	1,001 (82)	1,017 (24)	1,011 (23)
Mean age, years	46.9	47.2	41.3	40.1
Women, %	52	51	53	57

Table 2 Overview of health states included in the study

Health state	1	2	3	4	5	6	7	8
Injection frequency	Weekly	Weekly	Weekly	Daily	Weekly	Daily	Weekly	Weekly
Device complexity	Less	Less	Less	Less	More	Less	More	Less
Needle visibility	Visible	Visible	Invisible	Visible	Invisible	Visible	Invisible	Visible
Injection pain	No	Yes	No	No	No	No	No	No
Storage possibilities	Fridge	Fridge	Fridge	Fridge	Fridge	RT	RT	RT <72h

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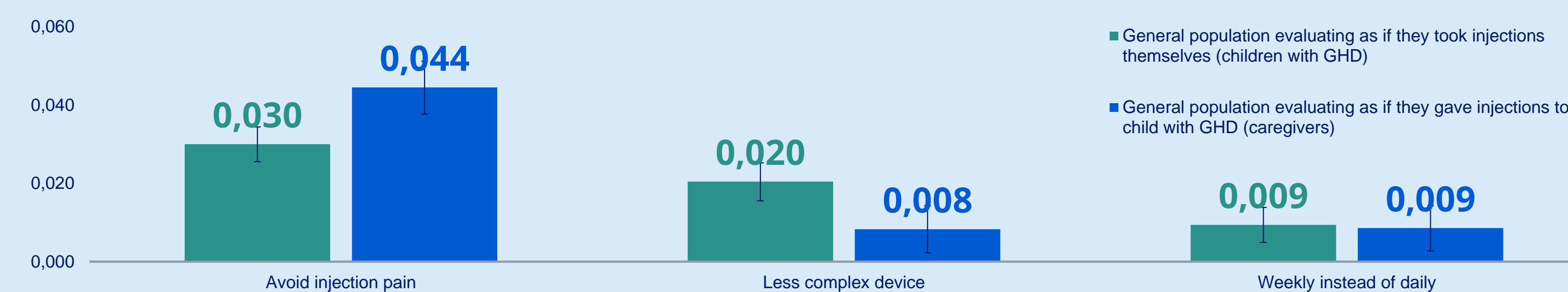
General population evaluating as if they took injections themselves (S1)

- Avoiding injection pain was associated with a significant utility gain of 0.030 in both countries (CI 95% UK: 0.025–0.036, p<0.001, Canada: 0.023–0.036, p<0.001, aggregated: 0.026–0.035, p<0.001).
- A less complex device and a lower injection frequency were also preferred in the UK and Canada (UK: 0.019 (CI 95% 0.013–0.026, p<0.001) and 0.009 (CI 95% 0.004–0.015, p=0.001), Canada: 0.023 (CI 95% 0.016–0.030, p<0.001) and 0.010 (CI 95% 0.003–0.017, p=0.008)). Using aggregated data, a less complex device was associated with a significant utility gain of 0.020 (CI 95% 0.016–0.025, p<0.001), and weekly injections were associated with a significant utility gain of 0.009 (CI 95% 0.005–0.014, p<0.001).
- There was no significant impact of needle visibility (UK: 0.004, p=0.202, Canada: 0.004, p=0.213) or of different combinations of storage possibilities in any of the countries

General population evaluating as if they gave injections to a child with GHD (S2)

- Avoiding injection pain was associated with a significant utility gain of 0.039 (CI 95% 0.030–0.048, p<0.001) in the UK and 0.050 (CI 95% 0.040–0.060, p<0.001) in Canada. Using aggregated data, the utility gain was 0.044 (CI 95% 0.038–0.051, p<0.001).
- A less complex device and a lower injection frequency were preferred in Canada (0.010 (CI 95% 0.001–0.020, p=0.036) and 0.013 (CI 95% 0.005–0.022, p<0.001)). In the UK, these results were not significant (0.007 (CI 95% -0.0003–0.015, p=0.058) and 0.004 (CI 95% -0.004–0.011, p=0.366)). Using aggregated data, a less complex device was associated with a significant utility gain of 0.008 (CI 95% 0.002–0.014, p=0.006), and weekly injections were associated with a significant utility gain of 0.009 (CI 95% 0.003–0.014, p=0.003).
- There was no significant impact of needle visibility (UK: 0.002, p=0.585, Canada: -0.009, p=0.059). For different combinations of storage possibilities, there were inconsistent but mostly not significant results in both countries.

Figure 1 Health state utility gain elicited using S1 & S2



Positive sign favors the first health state presented; negative sign favors the second. N (S1) = 1.408/674/741. N (S2) = 1.106/568/572.

- Earlier research has identified several challenges when evaluating HRQoL among children.^{2,3,4} Thus, Rowen et al. (2022) has described it as preferable to use the general population's own perspective when eliciting utilities for children.⁵ When using an adult population as a proxy for children, Rowen et al. (2020) have previously suggested that QALY weighting or deliberation could be applied.³ However, there are currently no clear guidelines regarding QALY weighting, hence the suggested approach should be used with caution.
- Findings in S1 were almost identical in the UK and Canada. In S2, they varied more, e.g., injection frequency only had a significant impact on caregivers in Canada. However, when using aggregated data, the utility gain of weekly injections was significant. Additionally, results from a recent randomized study indicate that weekly injections are associated with a lower treatment burden compared to daily injections for both children with GHD and their caregivers.⁶

- This study finds that several aspects of the GHD treatment are burdensome and have an impact on HRQoL. These findings support earlier evidence about the burden of treatment.
- Based on the results, treatment options without 1) injection pain, 2) a time-consuming and complex injection device and 3) daily injections are expected to result in higher HRQoL among children with GHD as well as their caregivers.
- Choosing the right treatment for children with GHD not only results in higher HRQoL but could potentially also lead to a higher treatment compliance over time. Thus, these findings underline the importance of choosing the most appropriate treatment of GHD for both the children themselves and their caregivers.
- In the future, the utility values found in this study can be used to estimate the real value of GHD treatments which seem similar regarding clinical benefits. Additionally, the values can be used in future cost-effectiveness analyses.