A Mixed-methods Study to Explore the Health-related Quality of Life Impact on Caregivers of Children With Hereditary Angioedema

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INTRODUCTION

- Hereditary angioedema (HAE) is a rare, life-threatening genetic disorder that causes recurrent, unpredictable episodes of cutaneous or submucosal swelling.[1–3]
- Pediatric HAE imposes a substantial burden on children and caregivers; even a mild attack causes pain, discomfort, and disfigurement.[1,4,5]
- HAE management is particularly complex in pediatric patients, where treatment options are more limited and the impact on HRQoL extends to caregivers.[6]
- Information on caregiver HRQoL is important to better guide clinical decision-making and address unmet needs of children with HAE and their caregivers.

Objective: This study explored the experience of caring for a child aged 2 to <12 years old with HAE, including the influence of attack frequency on caregiver HRQoL.

METHODS

- This mixed methods study included a quantitative survey and qualitative interviews with caregivers of children aged ≥2 to <12 years old with HAE.
- Caregivers were recruited through HAE patient organizations in the USA, UK, and Canada.
- The survey included demographic and clinical questions, and the Pediatric Quality of Life Inventory-Family Impact Module (PedsQL-FIM).
- Caregivers completed the survey thinking of their own HRQoL in the *past three months* prior to survey completion and retrospectively recalling two three-month periods when their child had the *most* and *least* HAE attacks.
- Interviews were then conducted with the same caregivers to explore the impact of caring on their daily lives, first relating to *overall caregiving experience* (i.e., not associated with a specific time period). They were then asked about the three specific time periods included in the survey.
- Survey data were analyzed descriptively using R; qualitative interview data were analyzed using thematic and content analysis supported by MAXQDA and Excel.

SAMPLE CHARACTERISTICS

- N=17 caregivers completed both the survey and interview, with an additional caregiver completing only the survey (N=18).
- Caregivers were from the USA (n=15/18, 83%), UK (n=2/18, 11%) and Canada (n=1/18, 6%), all were parents to a child with HAE (n=18/18, 100%), and most caregivers had HAE themselves (n=13/18, 72%). Clinical characteristics of the children with HAE are presented in **Table 1.**

Table 1. Clinical characteristics of children with HAE

Characteristic	N, (%)
Child's average monthly attack rate in past 6 months	
0	2 (11%)
1-2	13 (72%)
3-4	3 (17%)
Child's HAE type	
Type 1	18 (100%)
Child treatment use[1]	
Preventative (long-term prophylaxis)	11 (61%)
On-demand (for acute attacks)	15 (83%)
Child's clinical trial participation	
No	15 (83%)
Yes	2 (11%)
Unsure	1 (5.6%)

N, Number of observations. Sample characteristics are provided for the survey sample (N=18). [1]Caregivers could select multiple treatment options.

RESULTS

Experience of caregiving

- Caregivers typically spent on average 18 hours a week providing HAE-related care for their child overall.
- In the past three months, children of the caregivers had an average total of three HAE attacks, 56% (n=10/18) received on-demand and 50% (n=9/18) received long-term prophylaxis (LTP) treatment.
- In the past three months, caregivers most commonly reported preparing and administering HAE medication (n=16/17), educating themselves or others about their child's HAE (n=10/17), monitoring symptoms (n=10/17), and attending or scheduling medical appointments (n=8/17).

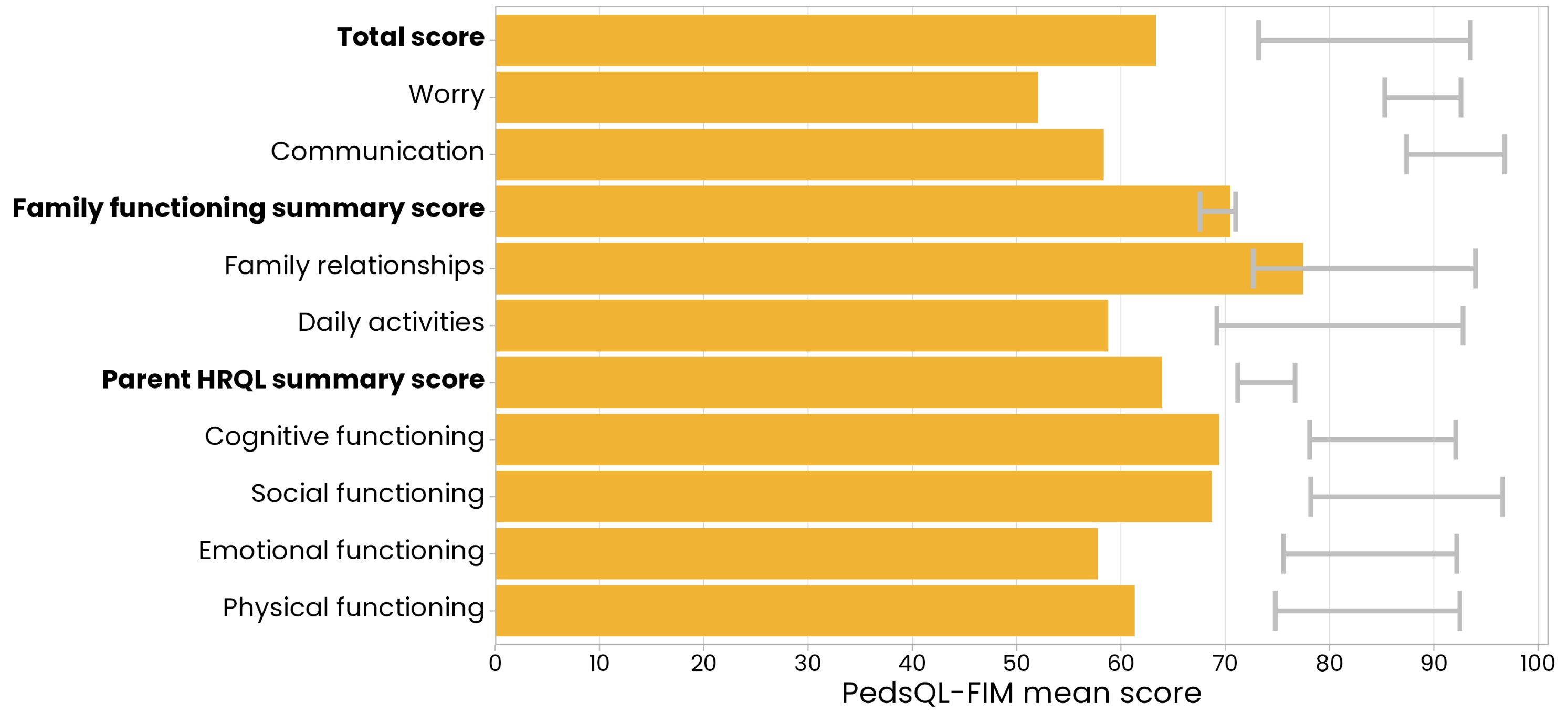
Caregiver HRQoL

- In the past three months, caregivers most commonly reported impact to their emotional wellbeing (n=17/17), particularly anxiety or worry (n=10/17) and stress (n=8/17), their daily activities (n=14/17), particularly work (n=12/17), social lives (n=7/17) and their own physical health (n=7/17).
- Administering LTP treatment was associated with an emotional toll on caregivers.

> *"Primarily on shot days…each one of those days… is the day that affects me the most… it's something that's just not something you enjoy very much, watching your child writhe in pain and discomfort" (US002, no HAE attacks in past three months. Treatment: LTP injectable)*

- Caregivers reported poorer HRQoL across almost all PedsQL-FIM domains in the past three months, compared to parents of healthy children in the literature[7-9] (**Figure 1**).

Figure 1. Caregiver reported PedsQL-FIM in the past three months



Higher score equals better functioning/fewer problems.

Grey lines indicate PedsQL-FIM mean score ranges for caregivers of healthy children from the USA in the literature[7-9]

Yellow bars represent mean PedsQL-FIM scores from the current study.

Influence of child's HAE attack frequency on caregiving

- A greater proportion of children of the caregivers received on-demand treatment in the three-month period of most attacks (n=10/18, 56%) compared to the three-month period of least attacks (n=4/18, 22%).
- Periods of most attacks (mean total attacks = 4.61) were, compared to periods of least attacks (mean total attacks = 1.00), particularly associated with: monitoring potential symptoms (n=9/17 vs n=5/17), providing additional help for their child (such as with eating and drinking [n=8/17 vs n=1/17], self-care [n=8/17 vs n=3/17] and physical support [n=4/17 vs n=0/17]); providing emotional support for their child (n=8/17 vs n=3/17), and supporting medical intervention (n=7/17 vs n=1/17).

> *"I gave more emotional support just based on what he needed, like I felt like he needed at the time, at that time he was kinda struggling with, you know, "Why me?"…I could tell he was struggling, you know, so … I paid more attention I guess …like to see if I thought he was getting depressed" (US010, 3 HAE attacks in three-month period of most attacks)*

> *"There wasn't anything that I needed to do outside of just normal parenting, because she wasn't having any attacks, so everything was "normal". So, life was good, right? No attacks, no stomach issues, no complaining of anything, no medication was needed." (US003, no HAE attacks in three-month period of least attacks)*

- However, even in the period of least attacks, caregivers described a continued need for support; most frequently mentioned activities were preparation or administration of treatment (n=9/17), scheduling or attending medical appointments (n=8/17), and educating themselves or others about their child's HAE needs (n=7/17).

> *"We had a letter from the consultant explaining what has to be done, in case of if swelling happens in limbs…And obviously the teachers are also worried about it, so we had to have a few separate meetings…I guess maybe it's just like a day or so, so extra…educating the school" (UK001, no HAE attacks in three-month period of least attacks. Treatment: On-demand)*

Influence of child's HAE attack frequency on caregiver HRQoL

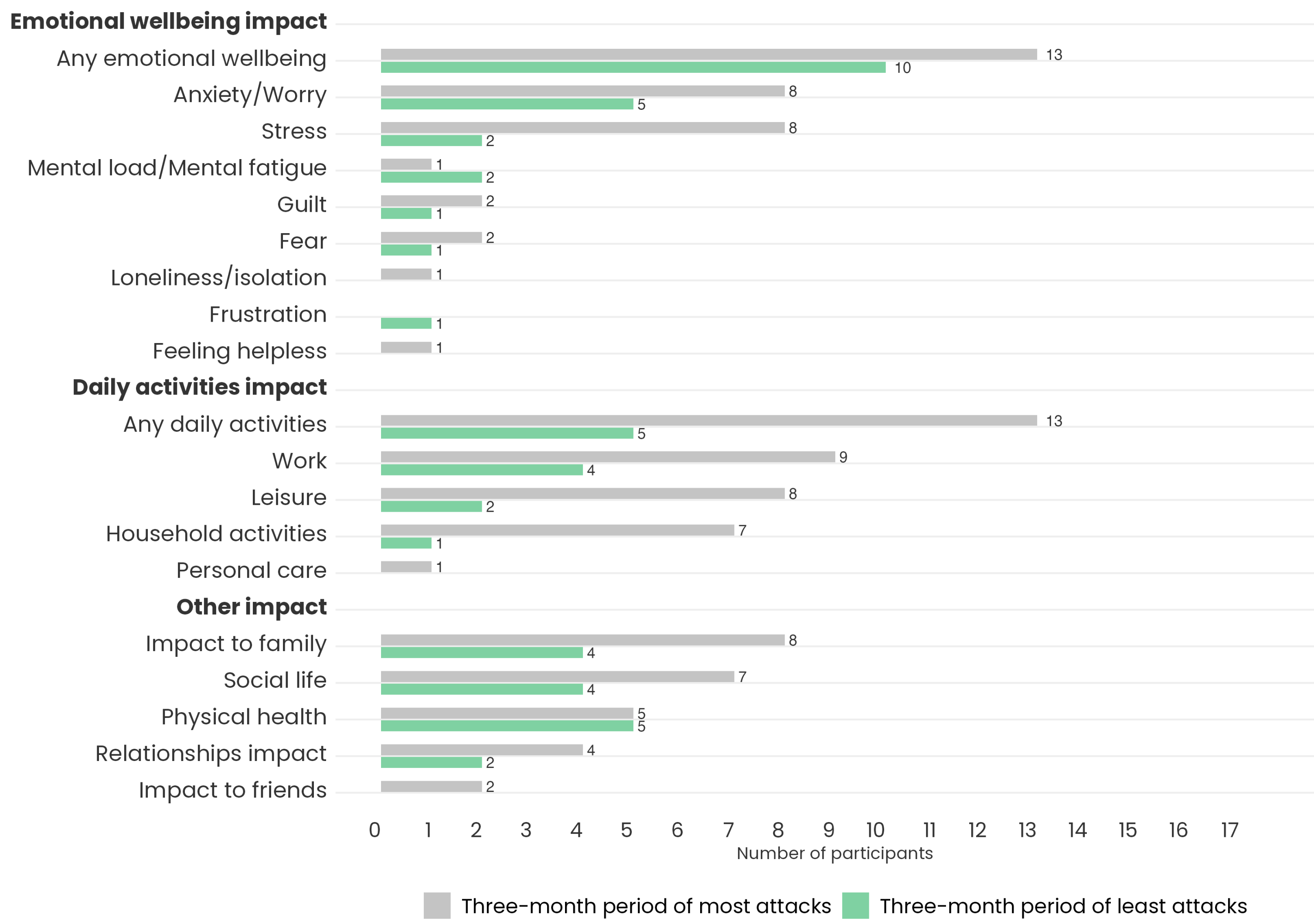
- Periods of most attacks were particularly associated with impacts to caregivers' emotional wellbeing (n=13/17; primarily anxiety/worry, n=8/17, and stress, n=8/17), daily activities (n=13/17), family (n=8/17) and social lives (n=7/17), (**Figure 2**).

> *"There was disruption at work, because I needed to leave work. The focus definitely shifted from one child to the other…my older child…everything…had to stop to focus on him…I wasn't the focus anymore. My daughter wasn't the focus. My husband wasn't the focus. It was just him, and attending to him." (US013, 3 HAE attacks in three-month period of most attacks)*

- Caregivers also experienced impacts to their emotional wellbeing (n=10/17), daily activities (n=5/17), family (n=4/17), social life (n=4/17), and physical health (n=5/17), among other aspects of HRQoL, in periods of least attacks.

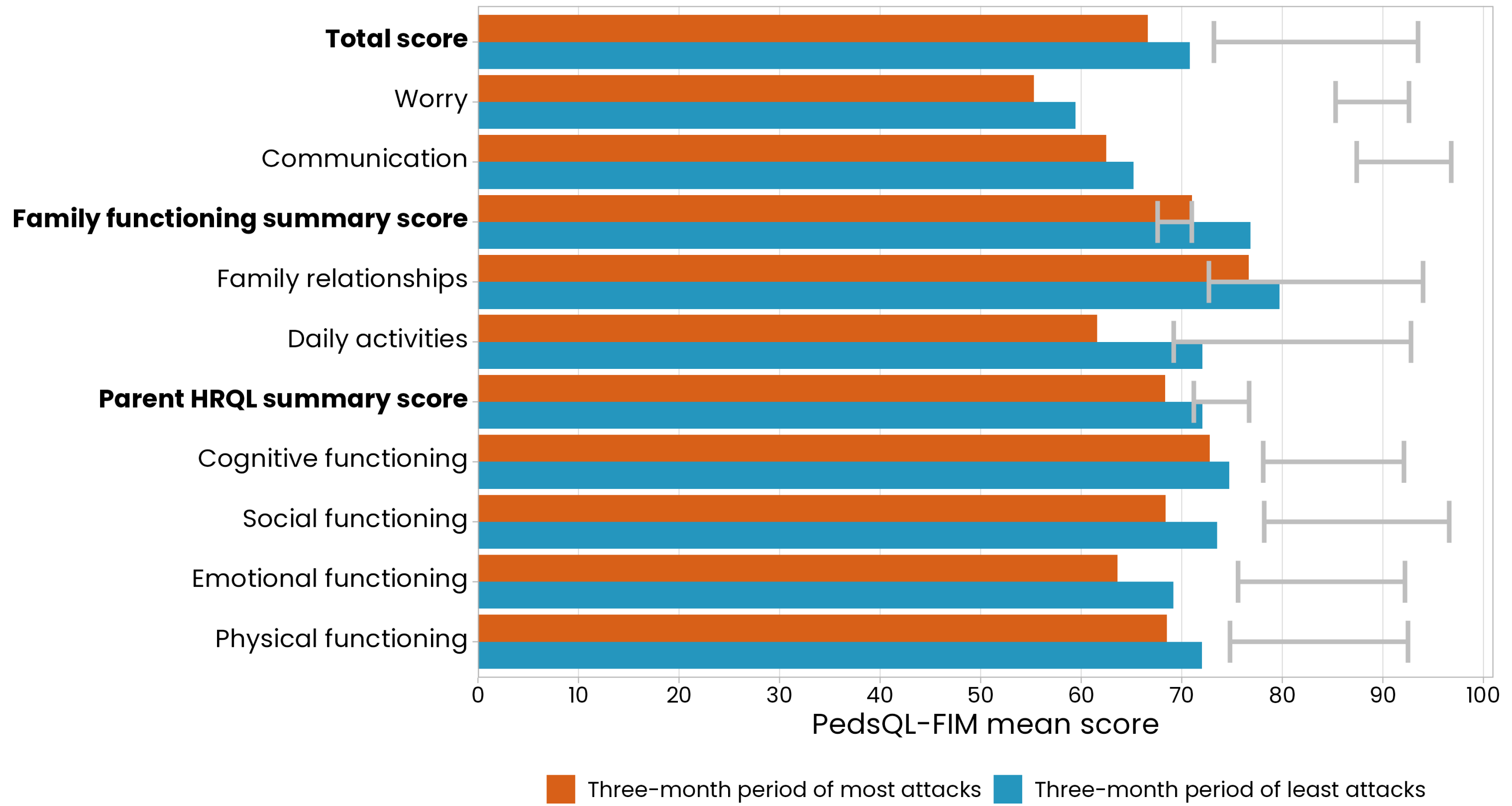
> *"I probably did…lose some sleep during that time, honestly, you know, times that I couldn't, you know, fall asleep at night…, just thinking about it [child's HAE]." (US010, 2 HAE attacks in three-month period of least attacks)*

Figure 2. Qualitative interview data on caregiver-reported HRQoL in periods of most and least HAE attacks



- Caregivers reported poorer HRQoL across all PedsQL-FIM domains in periods of most attacks compared to periods of least attacks, with particular deficits in daily activities (-14.6%), emotional functioning (-8.0%), social functioning (-7.0%), and worry (-7.0%) (**Figure 3**).
- Compared to parents of healthy children described in the literature[7-9], caregivers of children with HAE in this study showed deficits across almost all HRQoL domains, particularly in worry, communication, and emotional functioning, especially during periods of most attacks.

Figure 3. Caregiver reported PedsQL-FIM in periods of most and least HAE attacks



Higher score equals better functioning/fewer problems.

Grey lines indicate PedsQL-FIM mean score ranges for caregivers of healthy children from the USA in the literature[7-9]

Orange and blue bars represent mean PedsQL-FIM scores from the current study.

CONCLUSIONS

1. There is a substantial impact on the HRQoL of caregivers of children with HAE, characterized in particular by anxiety and worry, disrupted routines, emotional wellbeing, and challenges in communicating about their child's health needs.
2. Caregiver HRQoL reported in this study was lower than for parents of healthy children reported in the literature, especially during periods of most attacks.
3. Greater HAE attack frequency in children was associated with a greater negative impact on caregiver HRQoL.

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