

# The Burden of Anxiousness- and Distress-Related Behaviors in Prader-Willi Syndrome

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## Introduction

- Prader-Willi syndrome (PWS) is a rare neurodevelopmental disorder characterized by early childhood-onset hyperphagia and a behavioral phenotype that includes high levels of anxiousness- and distress-related behaviors that can be food- or non–food-related<sup>1</sup>
  - Anxiousness- and distress-related behaviors frequently lead to conflict and temper tantrums that negatively impact the daily functioning and quality of life of individuals with PWS and their families<sup>2</sup>
  - Caregivers have identified the treatment of hyperphagia and anxiety as among the most significant unmet needs in PWS<sup>3</sup>
- Many of the unique signs of anxiousness- and distress-related behaviors commonly observed in PWS (e.g., repetitive questioning) are not among the criteria used to define anxiety disorders in the Diagnostic and Statistical Manual of Mental Disorders 5th edition,<sup>4</sup> and the key triggers for anxiousness and distress common in PWS (e.g., food, schedules, routines, and unexpected change) differ from anxiety-provoking situations of concern to those with anxiety disorders<sup>5</sup>
  - Furthermore, assessments of anxiety used in the general population are typically self-reported, which is not appropriate for those with PWS given the intellectual disability and deficits in social cognition, and most measures include concepts that are not relevant to PWS, and/or do not include aspects of anxiousness that are pertinent in PWS<sup>5</sup>
- The Prader-Willi Anxiousness and Distress Behaviors Questionnaire (PADQ) is a PWS-specific, caregiver-reported assessment that was developed to address these limitations

### The Prader-Willi Anxiousness and Distress Behaviors Questionnaire

- The PADQ is a validated 15-concept caregiver-reported instrument designed to capture the observable signs of anxiousness- and distress-related behaviors that are common among individuals with PWS (**Table 1**)
  - The PADQ total score (range 0–56) is computed based on responses to the first 14 concepts of the measure with each concept scored from 0 ('never') to 4 ('always or almost always'); higher scores indicate greater levels of anxiousness and psychological distress
  - The fifteenth concept is an overall summary of caregivers' observations and is not included in the total score
- The PADQ was developed in collaboration between clinical experts and caregivers of individuals with PWS, who participated in iterative sets of qualitative interviews<sup>5</sup>
  - Caregivers consistently endorsed the concepts on the PADQ and indicated that these concepts comprehensively captured the behaviors associated with anxiousness and distress that were observed in the individuals with PWS for whom they provided care
  - The psychometric properties of the PADQ were subsequently confirmed using data from the phase 3 CARE-PWS trial of intranasal carbetocin (NCT03649477)<sup>6</sup>

Table 1. The PADQ: concepts and scoring system

Concept	Score during past 7 days
1: Ask for excessive details about schedule	0=Never
2: Confirm/review information already knew	1=Rarely
3: Repeat the same or similar question	2=Sometimes
4: Pace/move in agitated way	3=Often
5: Engage in nervous habits	4=Always or almost always
6: Concern when separating from caregiver	
7: Concern about his/her possessions	
8: Engage in self-soothing/comforting	
9: Worried about possible changes in plans	
10: Upset when change happened to plans	
11: Hard time calming down when upset	
12: Emotional outburst something done	
13: Anxious about food	
14: Ask about upcoming meals/snacks	
15: Anxious or distressed in some way	
1–14: Total Score	Total score ranges from 0–56 (higher scores indicate greater levels of anxiety and psychological distress)

PADQ, Prader-Willi Anxiousness and Distress Behaviors Questionnaire

## CONCLUSIONS:

- PADQ concepts and total scores at baseline characterize the high burden of anxiousness in PWS and highlight the important role the PADQ can play in assessing meaningful change due to treatment**
- These findings provide additional context to interpret previously published PADQ results from the CARE-PWS trial, showing patients treated with the 3.2-mg dose of intranasal carbetocin (but not the 9.6-mg dose) achieved significant improvements in anxiousness versus placebo, which were sustained in the 56-week follow-up**

## Results

### Frequency Distribution of Caregiver Responses

#### Individual PADQ Concepts

- Almost all (89%) caregivers reported that individuals with PWS were often (52%) or always/almost always (37%) anxious or distressed in some way during the past 7 days based on their response to item 15 of the PADQ (**Figure 1**)
- Behaviors that were reported as occurring always/almost always by the majority of caregivers included repeatedly asking about meals and snacks (77%), confirming information already known (72%), and food anxiety (71%)
- Notably, all caregivers reported that these behaviors were observed at least sometimes with none indicating that they never or rarely occurred
- Five additional behaviors that were mostly reported as occurring always/almost always were asking excessive details about schedules (71%), repetitive questioning (67%), worry about possible schedule changes (56%), nervous habits like skin picking and finger biting (46%), and upset when schedules/routines changed (35%)
- Less than 4% of caregivers reported that each of these behaviors were never observed
- Other behaviors described as occurring often to always/almost always in more than half the total sample, included engaging in self-soothing/comforting, emotional outbursts, concern about possessions, and difficulty calming down when upset
- Only a small minority (approximately 4% or less) reported that these behaviors were never observed
- Behaviors addressed in the PADQ that were reported to occur least frequently were concern when separating from caregivers and pacing/moving in an agitated manner, which were never observed by 14% and 8% of caregivers, respectively
- However, more than one-third of caregivers still reported that these behaviors were observed often to always/almost always

#### Total PADQ Score

- Total PADQ scores at baseline were in the upper 50th percentile of the scoring range (ie, total score >28) for all but one study participant (118 of 119), indicating that anxiousness- and distress-related behaviors were not only common, but also frequently observed across the entire study sample at baseline (**Figure 2**)

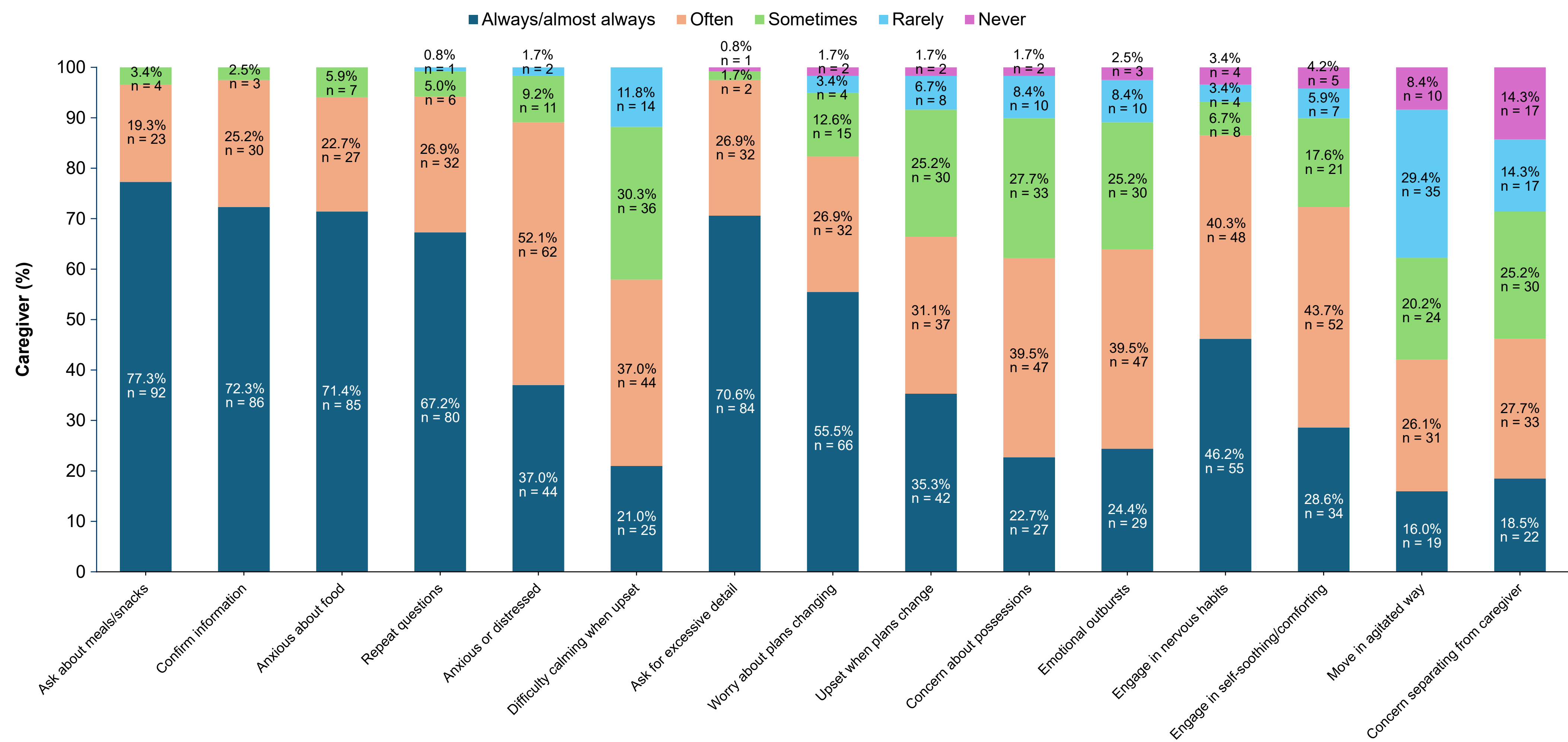
## STUDY OBJECTIVE

- To evaluate the caregiver-reported burden of anxiousness- and distress-related behaviors in PWS using baseline PADQ data from the CARE-PWS study

## Methods

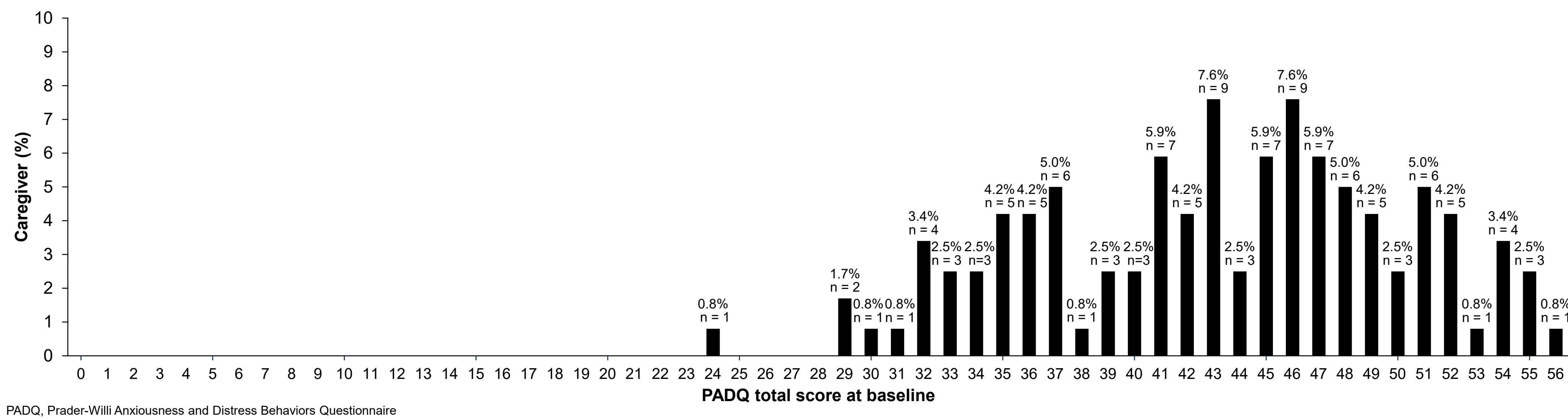
- The phase 3, placebo-controlled CARE-PWS trial investigated the efficacy and safety of intranasal carbetocin (3.2 mg or 9.6 mg, 3 times daily) in 119 participants with PWS aged 7–18 years
- Caregivers were asked to rate the frequency with which they observed the study participants engaging in each of the behaviors encompassed within the PADQ during the past 7 days at baseline (and follow-up time points)
- Descriptive statistics were computed to summarize the data provided by caregivers at baseline

Figure 1. Frequency distribution of PADQ individual concept response at baseline



PADQ concepts are ordered according to the most frequently reported anxiousness- or distress-related behavior (i.e. 'always/almost always', 'often', and 'sometimes')  
PADQ, Prader-Willi Anxiousness and Distress Behaviors Questionnaire

Figure 2. Frequency distribution of total PADQ score reported by caregivers at baseline



PADQ, Prader-Willi Anxiousness and Distress Behaviors Questionnaire

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