# CKDL5 deficiency disorder (CDD): caregiver's perception of clinical symptoms, disease management and its impact on quality-of-life

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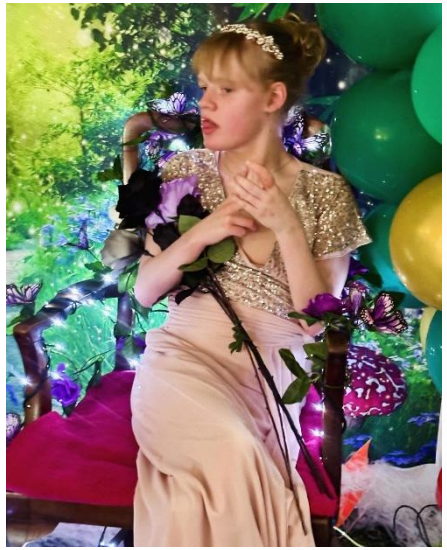
Study sponsored by Orion in collaboration with Marinus (now Immedica)

## CONTEXT

- CDKL5 Deficiency Disorder (**CDD**) is an ultra-rare genetic condition
- Incidence : **2,36 / 100,000** births
- Prevalence : <2000 cases in the US, <3000 cases in EU4
- CDD is a recent disease :
  - first described in 2004 as a variant of Rett syndrome,
  - established as a separate condition in **2013**
- CDD is a developmental epileptic encephalopathy condition causing severe developmental delay, epileptic seizures, important psychomotor impairment with limited communication skills from the first months of life
- High symptoms and care load for patients and families
- Limited data on the burden for caregivers/ families, and their perception of the disease and its management



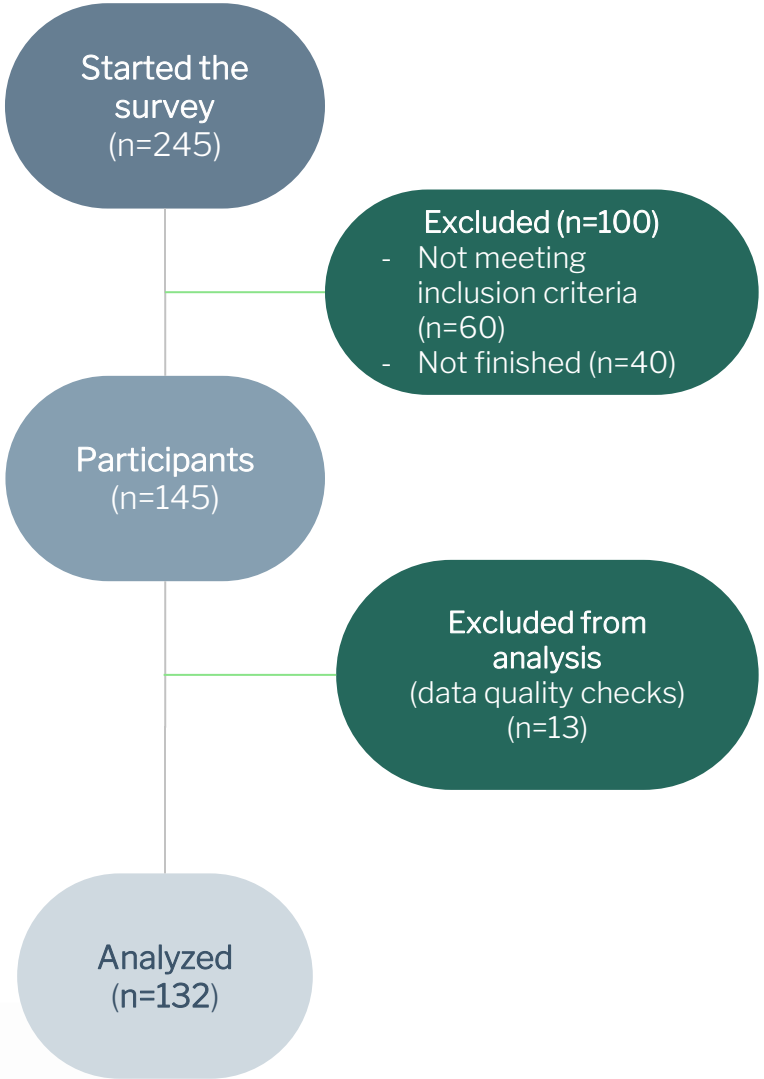
**Amber aged 20 (UK)**

## OBJECTIVE

- Better understand the burden of CDD on both patients and their family from the perspective of caregivers

# Study design

- Cross-sectional international self-administered online survey via Carenity online patient platform
- Caregivers were invited to complete an online 40-question survey translated in 12 languages
- Questionnaire was designed in collaboration with an internation panel of experts: researchers, doctors and parents of persons with CDD from patient associations
- Patients' HR-QoL from caregivers' perspective assessed using **EQ-5D-5L Proxy version 1** tool (specifically adapted to caregivers and digital)
- Data collection : 7 months (May to Dec 2023)




## RECRUITMENT

- Recruitment via Social media targeted campaigns and Patient Advocacy Organisations

CDKL5 ALLIANCE

EpiCARE

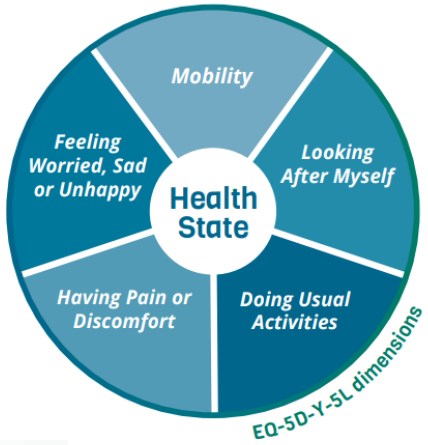
## INCLUSION CRITERIA

- Adult (≥18 y) caregivers of a person with CDD, confirmed by genetic testing
- Legal representant or guardian of the person with CDD
- Having given an electronic informed consent prior to participation



carenity part of EvidentIQ

# Methodology: EQ5D-5L user guide




## SCORING THE DESCRIPTIVE SYSTEM

- 1 level for each dimension
- Health is defined by the combining one level from each dimension
- Conversion of the 5-digit code in a **EQ-5D index value** using value sets of each country/region
- Value sets are based on the preference in the general population.

**EQ-5D-5L**

**Please select the ONE box that you think best describes the person's health TODAY.**
**You should not answer on behalf of the person, but rather rate the person's health as you see it.**

**MOBILITY**
- [x] No problems in walking about
- [ ] Slight problems in walking about
- [ ] Moderate problems in walking about
- [ ] Severe problems in walking about
- [ ] Unable to walk about

**SELF-CARE**
- [ ] No problems washing or dressing him/herself
- [x] Slight problems washing or dressing him/herself
- [ ] Moderate problems washing or dressing him/herself
- [ ] Severe problems washing or dressing him/herself
- [ ] Unable to wash or dress him/herself

**USUAL ACTIVITIES** *(e.g. work, study, housework, family or leisure activities)*
- [ ] No problems doing his/her usual activities
- [ ] Slight problems doing his/her usual activities
- [x] Moderate problems doing his/her usual activities
- [ ] Severe problems doing his/her usual activities
- [ ] Unable to do his/her usual activities

**PAIN / DISCOMFORT**
- [ ] No pain or discomfort
- [ ] Slight pain or discomfort
- [ ] Moderate pain or discomfort
- [x] Severe pain or discomfort
- [ ] Extreme pain or discomfort

**ANXIETY / DEPRESSION**
- [ ] Not anxious or depressed
- [ ] Slightly anxious or depressed
- [ ] Moderately anxious or depressed
- [ ] Severely anxious or depressed
- [x] Extremely anxious or depressed

Levels of perceived problems are coded as follows:

- Level 1 is coded as a '1'
- Level 2 is coded as a '2'
- Level 3 is coded as a '3'
- Level 4 is coded as a '4'
- Level 5 is coded as a '5'

5-digit code : **12345**

- Index value for a French = **0.116**
- Index value for a Spanish = **0.201**
- Index value for a Japanese = **0.522**

# Methodology: EQ5D-5L user guide

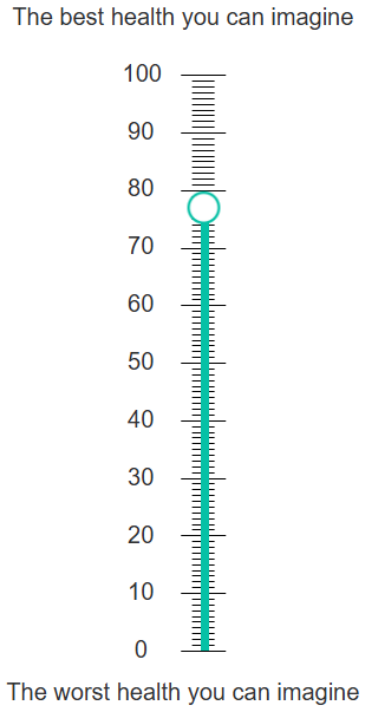
## SCORING THE VAS

- 1 score for general health TODAY

- We would like to know how good or bad you think the person's health is TODAY.
- You will see a scale numbered from 0 to 100.
- 100 means the best health you can imagine. 0 means the worst health you can imagine.

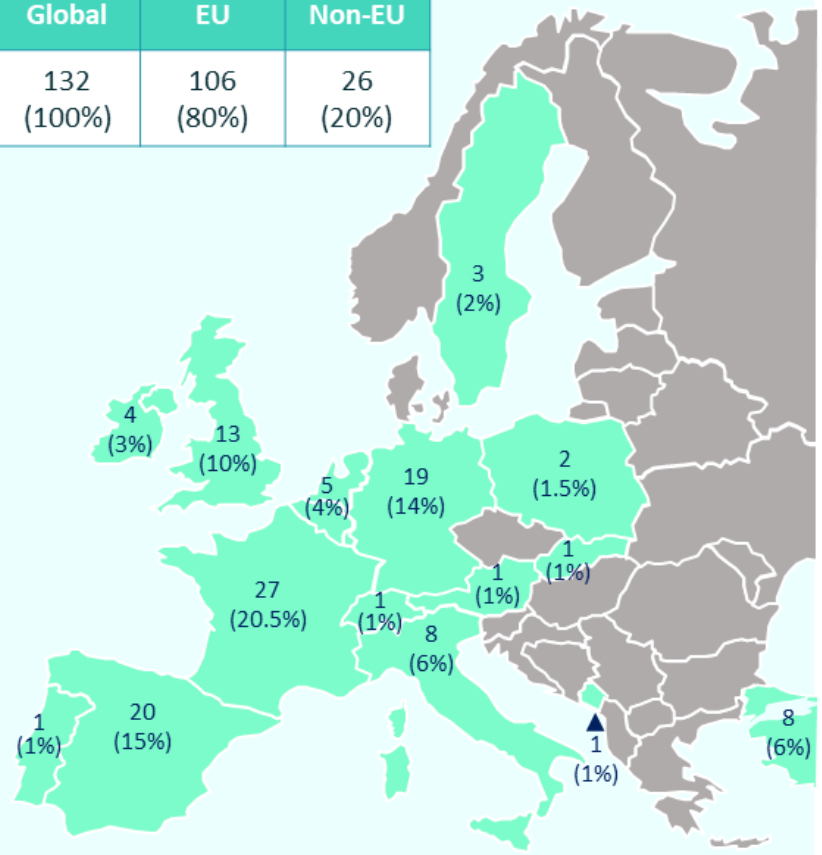
- Please indicate on the scale how you think the person's health is TODAY.

THE PERSON'S HEALTH TODAY **77**



# Sociodemographic profile of caregivers & patients

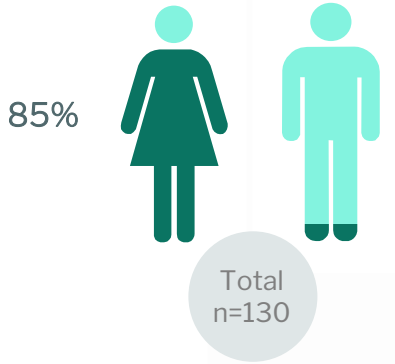
| Respondents | Global | EU | Non-EU |
|---|---|---|---|
| Number (percentage) | 132 (100%) | 106 (80%) | 26 (20%) |




Other Countries, 26 (21%): US, 2 (1.5%); Australia, 1 (1%)
LATAM, 15 (11%): Argentina, 3 (2%); Bolivia, 1 (1%); Chile, 1 (1%); Colombia, 1 (1%); Peru, 5 (4%); Mexico, 2 (1.5%); Uruguay, 2 (1.5%)

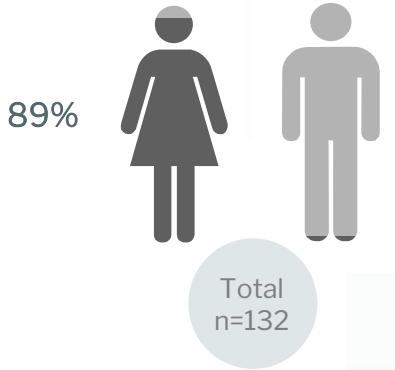
## CAREGIVERS

- **All were parents of a CDD patient**
- Median age = **41** years
- Most of them (64%) **did not work** or work partially due to the disease (mostly impacted in France: 74%)

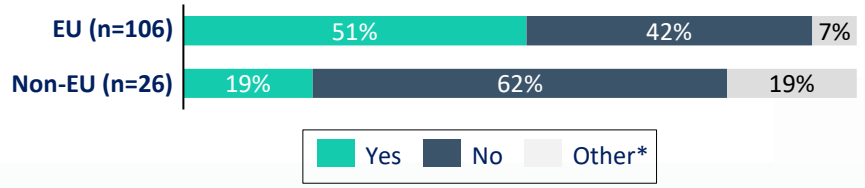



## CDD PATIENTS

- Ratio woman/man 4:1
- Their median age was **9** years
- Non-European patients younger than Europeans



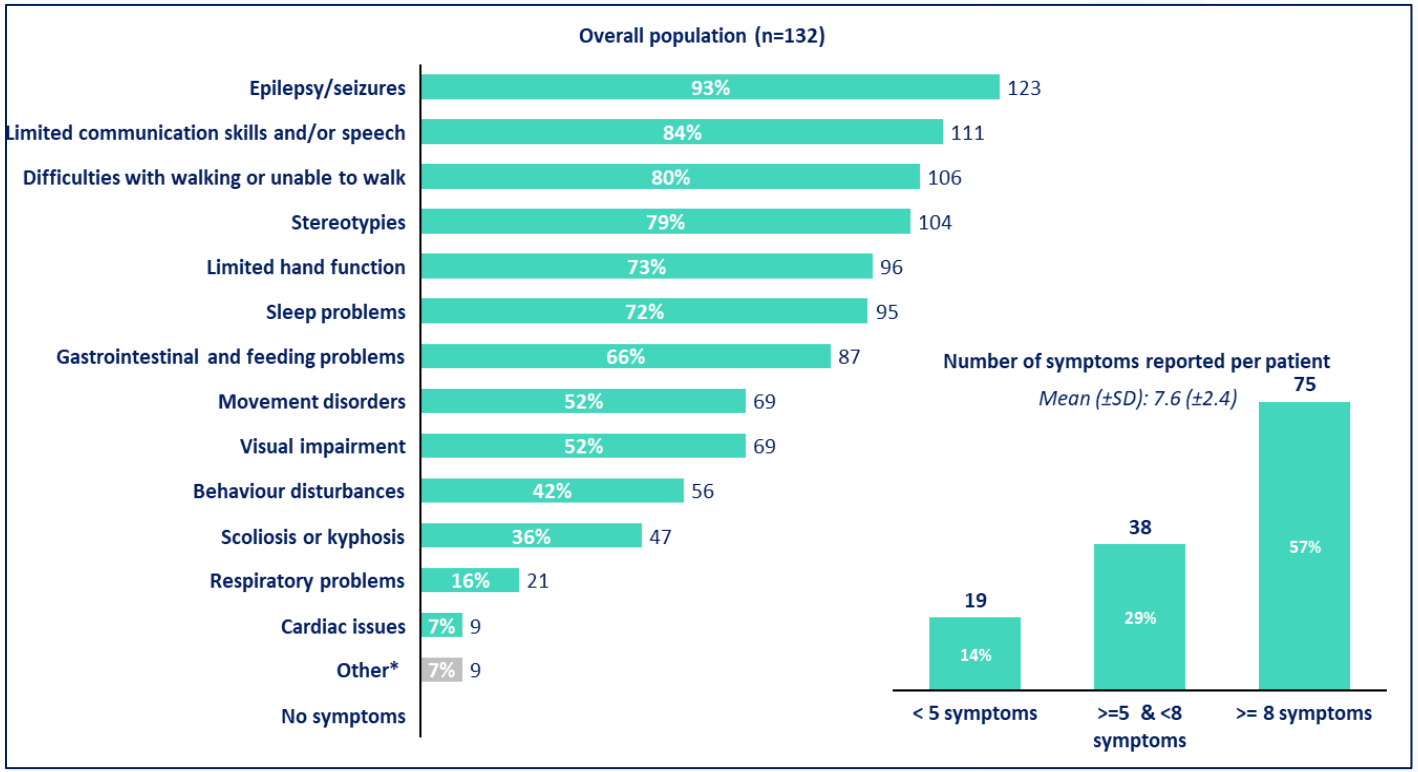

- **Access to a medical center specialized in CDD:**

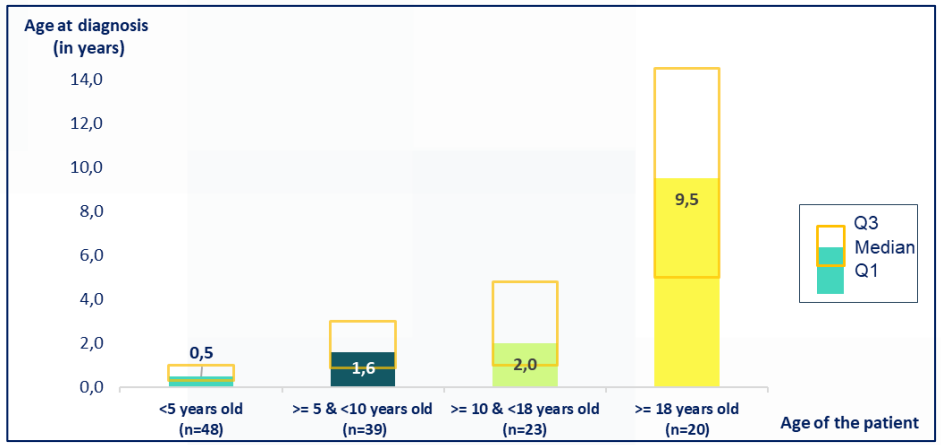


# Medical profile of patients

**Medical profile of CDD patients in line with epidemiological data:**

- Early onset of seizures (median age : **2 months**)
- **Multiple types** of seizures (major motor, spasms, myoclonic, HTSS)
- High seizure **frequency** (one or more a day for 66% patients)
- **Impaired development** with limited communication, difficulties with walking, stereotypies, limited hand functions
- Median age at diagnosis (=1y) increases with the age of the patients, reflecting **improved diagnosis**




**Care & treatments:**

- 97% of patients received antiseizure medication(s)
- Treatments vary across countries ( no Vagus Nerve Stimulation out of EU)
- Multidisciplinary care gets poorer when patients become **adults**

# Patients HR-QoL perceived by caregivers

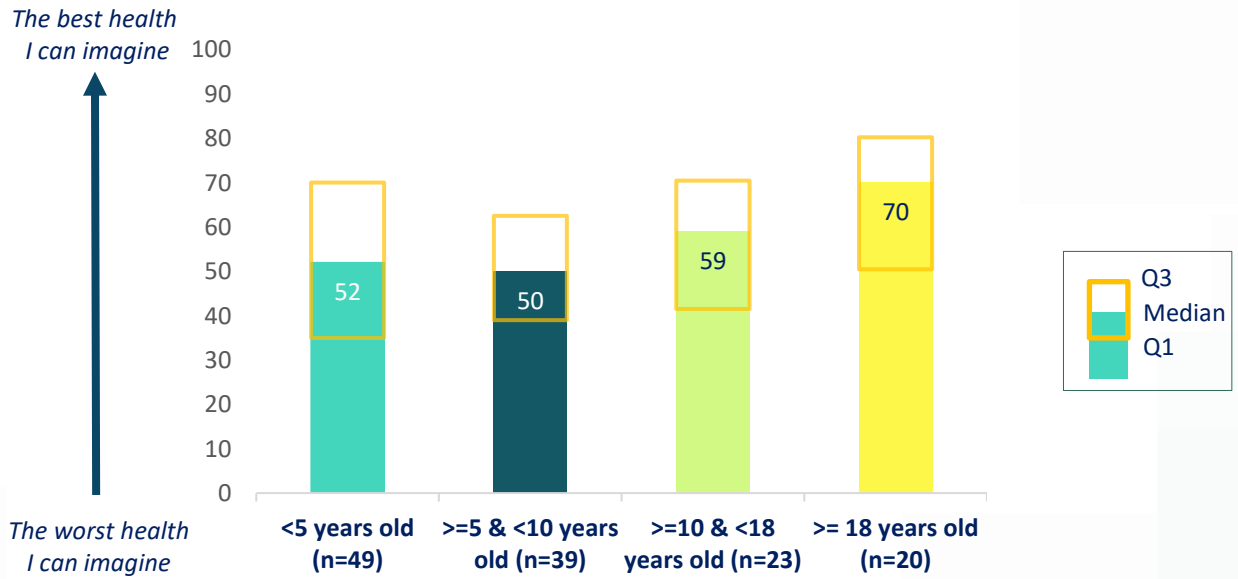
## BY DIMENSION & SEVERITY LEVEL

- Patients are severely affected by CDD, mainly in their mobility (walking about), self-care (washing or dressing themselves) and usual activities (going to school, hobbies, sports, playing, doing things with family and friends)
- **Adults are less affected in their mobility (35% unable to walk)**
- Very low **index value** for the global population: **0.18**
- Negative index value reported by 17 participants, indicating **a state worse than death.**

| | EQ-5D-5L DIMENSION | | | | |
|---|---|---|---|---|---|
| | Mobility | Self-care | Usual Activities | Pain/discomfort | Anxiety/ Depression |
| Level 1 (no problems) | 5% | 1% | 1% | 24% | 42% |
| Level 2 (slight problems) | 7% | 2% | 2% | 34% | 31% |
| Level 3 (moderate problems) | 9% | 2% | 5% | 27% | 20% |
| Level 4 (severe problems) | 12% | 4% | 14% | 11% | 5% |
| Level 5 (Extreme problems/ Unable to do) | 67% | 91% | 78% | 5% | 2% |

## HEALTH TODAY (VAS)

- Poor Health reported by caregivers
- Better overall health reported for adults

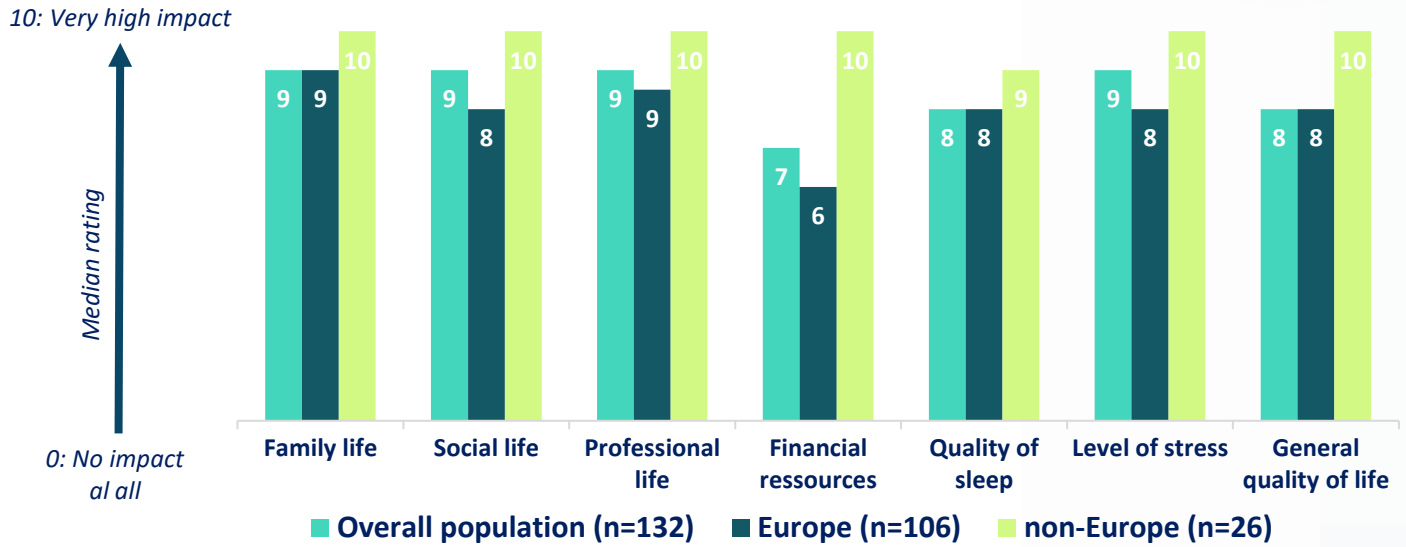


# Burden for Caregivers

## IMPACT OF CDD ON CAREGIVERS'LIFE

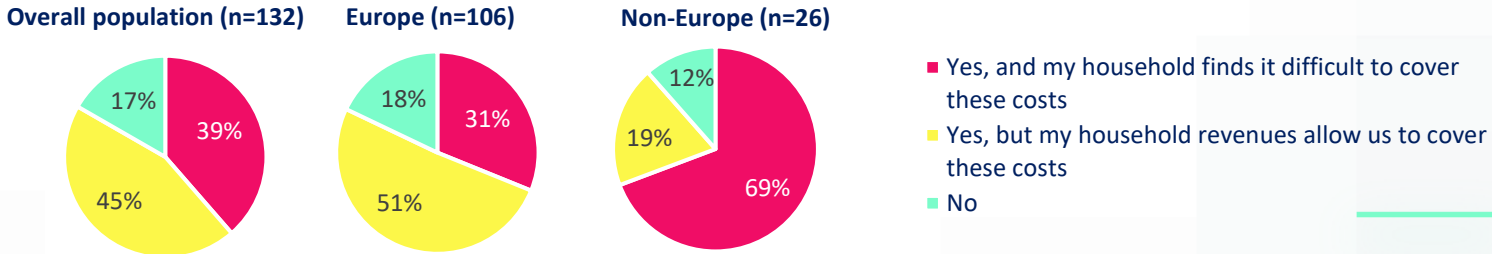
- High impact of CDD on all aspects of caregivers' life
- Very high **financial impact** for Non-European participants
- Smallest financial impact in France (median rating : 5/10)

=> Better coverage in Europe




## OUT OF POCKET COST DUE TO THE DISEASE

- **84%** declared having out-of-pocket costs from managing the disease (alternative therapies, indirect costs and non-pharma treatments)
- A majority of Non-EU participants reported **difficulties** to cover these costs.



# Conclusion

## KEY FINDINGS

- Improvement of **CDD diagnosis** at young age but poor care of adults
- **Poor HR-QoL** for patients (worth than death in some cases)
- Important impact on caregivers' life, including **professional and financial impact**
- Differences between regions regarding diagnosis, care and treatments

## LIMITATIONS

- Low number of respondents per country / region
- Data self-reported by caregivers, no medical records
- Voluntary participation to this online survey : overrepresentation of most severely affected patients with internet access

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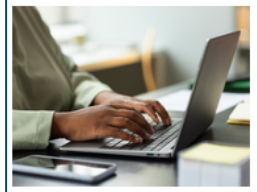

**Caregivers' Perceptions of Clinical Symptoms, Disease Management, and Quality of Life Impact in Cases of Cyclin-Dependent Kinase-Like 5 Deficiency Disorder: Cross-Sectional Online Survey**

Sam Amin[1]; Carol-Anne Partridge[2]; Helen Leonard[3]; Jenny Downs[3]; Helen Allvin[4]; Valentine Ficara[5]; Emilie Pain[5]; Minna A Korolainen[4]

## PERSPECTIVES

- Successful recruitment for an ultra-rare and recent disease, with the support of **patient associations**
- Development of an instrument (**EQ-5D-5L Proxy version1**) that could be used in future studies transversal or longitudinal