Disease Progression in Niemann-Pick Disease Type C Across the Lifespan: Functuoinal Decline by Domain and Reporting Perspective

Mobility, swallowing, speech, fine motor, and cognition differences in adult self-report vs caregiver-report cohorts

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Background / Rationale

Niemann-Pick disease type C (NPC) is a rare, progressive neurodegenerative disorder characterized by highly variable functional decline. Disease progression often affects multiple domains, including mobility, swallowing, speech, fine motor function, and cognition, with patterns influenced by age and disease stage. Patient- and caregiver-reported data provide complementary insight into real-world progression and may differ by reporting perspective, particularly in pediatric populations or more advanced disease.

Primary Objective:

To characterize disease progression patterns across key functional domains and compare impairment distributions across adult self-report, adult caregiver-report, and pediatric caregiver-report cohorts.

Methods

This cross-sectional analysis summarizes responses from an international NPC survey (N=103; 15 countries). Participants were stratified into three cohorts: **adult self-report (n=12)**, **adult caregiver-report (n=41)**, and **minor caregiver-report (n=49)**. Functional status was assessed across domains including walking/mobility, swallowing, speech, fine motor function, and cognition. Results were summarized descriptively using proportions across severity categories.

Results

Mobility Adults completing the survey for themselves showed higher preservation of walking ability compared with caregiver-reported cohorts, including a greater proportion reporting **no walking problems**. Pediatric patients demonstrated greater functional limitation, with higher proportions requiring **assistance or wheelchair use**, consistent with earlier and more severe mobility decline in minors.

Swallowing impairment differed substantially by cohort, with caregiver-reported groups, particularly pediatric patients, showing greater distribution across more severe swallowing categories. Adult self-report responses indicated greater preservation overall, suggesting swallowing decline may be more prominent or more readily observed in caregiver-reported populations.

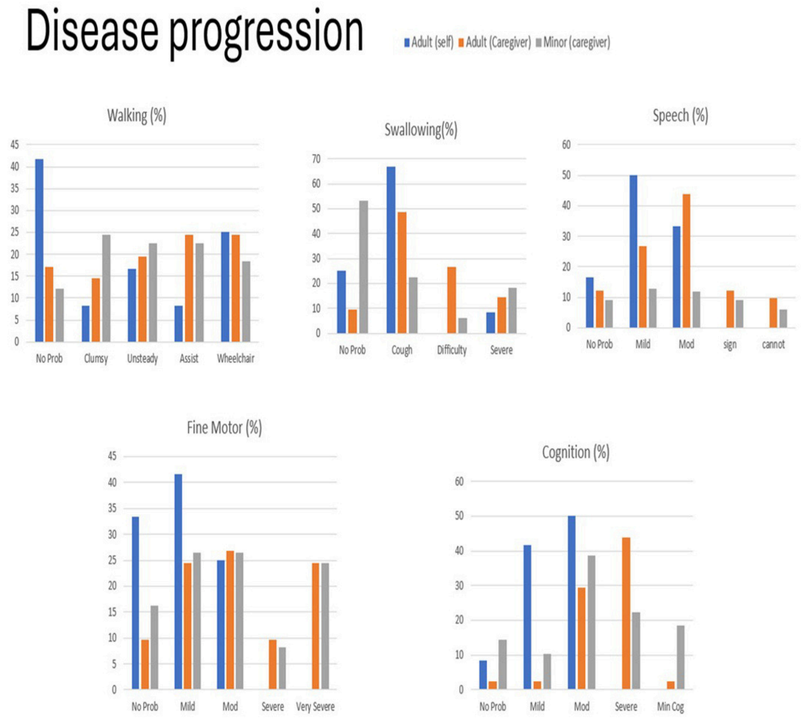
Speech difficulties were more frequently represented in caregiver-reported cohorts and were more evenly distributed across mild-to-moderate impairment categories. Pediatric caregiver reports showed greater representation of advanced speech limitations (including reliance on signing or inability to communicate), consistent with broader progression in minors.

Fine motor impairment was common across all cohorts, with adult self-report indicating higher proportions in the mild range, whereas caregiver-reported cohorts demonstrated a broader spread across moderate-to-severe impairment. Pediatric caregiver reports showed the widest distribution, suggesting early and progressive functional impact on fine motor ability.

Cognitive impairment was present across cohorts, with caregiver reports capturing a wider range of moderate-to-severe impairment compared with adult self-report. Pediatric caregiver reporting indicated meaningful cognitive burden early in the disease course, with a proportion of children reported as having minimal cognition, highlighting severe neurodegenerative progression in a subset.

Survey Respondents

	Adult (>18y) (Self) (n=12)	Caregiver of Adult (n=41)	Caregiver of Minor (<18y) (n=49)
Age of Individual with NPC	38.2y	35.2y	9.8y
Age at Diagnosis (mean, IQR)	29, IQR=30.3	24.3, IQR=10.8	4.2, IQR=6.2
Sex of Individual with NPC	50% F	46% F	41%F
Sex of Respondent	---	73% F	82% F
Age of Respondent	---	61.4	41.1
Diagnosed before Birth	0	0	1
Neurologic Symptoms	92%	100%	92%



Future Directions

Future studies should incorporate longitudinal follow-up to quantify progression rates and domain sequencing, validate survey-reported function against standardized clinician-rated measures, stratify analyses by age of onset and diagnosis to refine progression phenotypes, and evaluate concordance between self- and caregiver-reported outcomes over time.

Results and Conclusions

Across all functional domains, **adult self-report respondents consistently reported higher preserved function** compared with caregiver-reported cohorts. Caregiver-reported adults and minors demonstrated broader impairment distributions across mobility, swallowing, speech, fine motor, and cognition. Pediatric caregiver reports most frequently reflected **earlier and more severe** functional decline, consistent with an accelerated progression phenotype among individuals diagnosed in childhood. These findings underscore that disease progression in NPC differs meaningfully across the lifespan and that reporting perspective influences the apparent severity distribution.

To learn more:

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