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PURPOSE

This study aims to capture burden-of-disease experiences of persons with spinocerebellar ataxia (PWSCA) and their caregivers.

BACKGROUND

- Spinocerebellar ataxias (SCAs) are a group of dominantly inherited, ultra-rare, progressively debilitating neurodegenerative disorders that currently have no treatments that can stop or slow disease progression.^{1,5}
- PWSCA experience loss of motor coordination, including gait disturbances, loss of balance, and associated falls, as well as cognitive impairment and difficulty with speech and swallowing, all of which worsen over time.^{1,4,6-9}
- Furthermore, SCA can significantly disrupt mental and social well-being and overall quality of life (QOL).
- Of the more than 40 distinct genotypes that comprise SCAs, genotypes 1, 2, 3, and 6 are the most common.^{2,10}
- Lived experiences of PWSCA offer essential insights regarding care and treatment. More data regarding these experiences are needed to better understand the impact of SCA over time, identify potential therapeutic goals, and determine optimal modalities for providing care to PWSCA.¹¹
- This global study describes burden-of-disease experiences of PWSCA, including those with SCA1, SCA2, SCA3, and SCA6 and their caregivers.

CONCLUSIONS

- Data from this global, cross-sectional, mixed-methods study involving PWSCA (convenience sample) highlight the significant burden that gross motor challenges (including loss of enjoyable activities, impaired mobility, lack of balance, and falls) have on QOL.
- Mean summary scores for physical and mental components of the SF-36 were numerically lower in PWSCA across all 4 SCA types, and lowest in PWSCA3, compared to the general population. PWSCA3 also were most likely to be wheelchair-bound.
- In follow-up surveys, 53 of 70 participants (75.7%) reported experiencing at least 1 fall during the past year. Among PWSCA3, 81.2% experienced at least 5 falls in the past year. Most participants indicated that fear of falls affected their daily lives.
- The majority of participants reported that they would find an approved medication that slowed or stabilized the progression of SCA to be "extremely meaningful." Furthermore, most PWSCA3 and PWSCA6 rated falling as an outcome of an approved therapy "extremely important."
- "If I was not so fearful of falls (and the potential damage that the fall may inflict on me), this could open up a steadily closing door in my activities." (PWSCA3)
- "To have medication available would improve the life of myself and my family. I constantly worry about the future. We are not able to plan because I don't know how my health will be." (PWSCA6)

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Table 1. Participant Attrition

	n
Total number of people who visited the RSVP site, gave consent, and provided some information	347
People excluded because they did not complete the SF-36 or modified Klockgether Functional Staging of Ataxia measurement, did not provide proof of disease, or lacked proof of disease sufficient for enrollment	161
Completed phase 1 of the study	186
o Caregivers	3
o Patients	183
Completed phases 1 and 2 of the study	80
o Caregivers	3
o Patients	77
Follow-up surveys related to falls and/or desired therapeutic outcomes	
o Contacted for survey	77
o Completed survey	70
o Caregivers	2
o Patients	68

Table 2. Demographic Data and SF-36 Scores for Study Participants Who Completed Phases 1 and 2

	SCA1 (n = 20)	SCA2 (n = 20)	SCA3 (n = 20)	SCA6 (n = 20)	P value
Female / male	14 / 6	10 / 10	12 / 8	10 / 10	
Mean age (yrs) (range)	50.2 (28.0–75.0)	45.5 (26.9–74.3)	52.6 (31.6–73.9)	64.5 (48.9–86.0)	
Mean age (yrs) at first clinical suspicion	43.9	35.8	41.6	56.2	
Mean age (yrs) at genetic diagnosis	45.1	40.2	45.4	58.2	
Geography					
Americas	14	13	14	12	
Europe and UK	6	5	5	6	
Asia	0	2	0	0	
Africa/Middle East	0	0	0	0	
Australia	0	0	1	2	
Mean SF-36 Scores					
SF-36 physical summary	44.7*	42.8*	36.7*	40.7*	0.11
SF-36 mental summary	47.8*	47.5*	45.4*	48.7*	0.85
SF-36 physical functioning	52.4*	50.8*	32.9*	39.0*	0.14
SF-36 role, physical	66.5*	65.5*	37.8*	51.3*	0.02†
SF-36 bodily pain	79.6*	72.4*	59.3*	79.9*	0.05†
SF-36 general health	50.8*	49.8*	50.3*	54.0*	0.93
SF-36 vitality	54.3*	41.8*	43.4*	45.4*	0.38
SF-36 social functioning	67.8*	68.4*	55.3*	63.8*	0.44
SF-36 role, emotional	78.1*	78.1*	61.4*	74.2*	0.21
SF-36 mental health	66.1*	67.9*	63.4*	70.5*	0.82

*n = 77 in phase 2 because data from caregivers of 1 PWSCA1, 1 PWSCA2, and 1 PWSCA3 were excluded.

†p < .05.

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METHODS

Study Participants and Recruitment

- To be eligible for participation in this study, individuals were required to have symptomatic SCA1, SCA2, SCA3, or SCA6 and proof of disease.
 - Proof of SCA was confirmed by laboratory testing (68.8%), medical record (14.0%), or physician communication (17.2%).
- Surveys were conducted in English, French, German, or Portuguese with patients or caregivers. Caregivers and spouses of PWSCA participated if the PWSCA either was currently living but had difficulty speaking or had passed away within the 2 years prior to study initiation.
- Participants were predominantly recruited from the US, the UK, Canada, Australia, France, Germany, and Brazil through the Coordination of Rare Diseases at Stanford (CoRDS) Registry, National Ataxia Foundation, Ataxia UK, and the Engage Health EnCompass® database.
- The study consisted of 2 phases. The targeted total sample size for phase 1 was 100. A subset of individuals was selected from phase 1 to participate in qualitative semi-structured interviews during phase 2. Quota sampling, purposive sampling, and saturation analysis were used to ensure a representative sample of SCA types and to increase the probability that the data collected in the study were representative of patients with SCA1, SCA2, SCA3, and SCA6. Initially, the study sought to obtain input from 15 PWSCA and/or caregivers representing each SCA type (SCA1, SCA2, SCA3 and SCA6) (quota sampling). Persons who volunteered to participate and provided proof of disease were scheduled for interviews (convenience sampling). After themes were coded by 2 independent coders and a saturation analysis was conducted to determine the saturation of themes, an additional 5 persons were sought for each SCA type, with priority given to those residing outside the US (purposive sampling). The targeted total sample size for phase 2 was 60.
- All participants who spoke English or German and completed phases 1 and 2 were invited to take part in follow-up surveys.
- This poster reports data from participants who completed both phase 1 and phase 2 of the study as well as those who completed the follow-up surveys.

RESULTS

Participant Disposition

- 347 individuals accessed the online site and provided preliminary information, including consent. Of these individuals, 161 were excluded due to failure to complete the modified Klockgether Functional Staging of Ataxia questionnaire or the SF-36 assessment, lack of proof of disease, or proof of disease that was deemed insufficient for study enrollment (Table 1).
- 186 individuals participated in phase 1; 80 individuals, including 3 caregivers (2 caregivers for 2 PWSCA who died and 1 parent of a PWSCA), participated in both phase 1 and phase 2 (Table 1).
- 77 participants were contacted to complete a follow-up survey pertaining to their experiences with falls and/or desired therapeutic outcomes, of whom 70 (90.9%) completed survey questionnaires (Table 1).

Demographics

- There was equal representation of all 4 SCA types (n = 20 for each SCA type). Caregivers represented 1 PWSCA1, 1 PWSCA2, and 1 PWSCA3; no caregivers of PWSCA6 participated in the study (Table 2).
- Among participants, 57.5% were female.
- Mean age ranged from 45.5 to 64.5 years. PWSCA2 were the youngest population and the youngest at diagnosis; PWSCA6 were the oldest population and the oldest at diagnosis (Table 2).
- The majority of participants were from the Americas, including 45 (56.3%) from the US (Table 2).

SF-36 by SCA Type

- Mean SF-36 physical and mental summary scores were numerically lower compared to the general population for all SCA types and were lowest in PWSCA3 (Table 2).
- PWSCA3 reported significantly lower scores for bodily pain and physical role subscales than did participants with other SCA types.

Functional Status by SCA Type

- 2 PWSCA were deceased at the time of data gathering. Therefore, functional status, as measured by the modified Klockgether Functional Staging of Ataxia questionnaire, was chronicled for 78 of 80 PWSCA (Figure 1).
- The majority of participants (94.6%) were ambulatory.
- PWSCA3 were most likely to be wheelchair-bound, and PWSCA6 were most likely to need a walking aid.

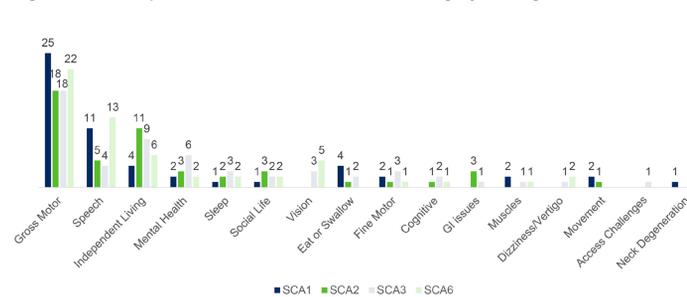
Relation Between Functional Status and SF-36

- There was a direct linear correlation between scores on the modified Klockgether Functional Staging of Ataxia assessment and the physical component summary of the SF-36 (R² = .472).

Figure 1. Functional Status by SCA Type

Legend: SCA1 (dark blue), SCA2 (green), SCA3 (light blue), SCA6 (purple)

Figure 2. Most Important Disease-Related Burden Category Among Persons With SCA



Legend: SCA1 (dark blue), SCA2 (green), SCA3 (light blue), SCA6 (purple)

Figure 3. Number of Falls by SCA Type in the Past Year

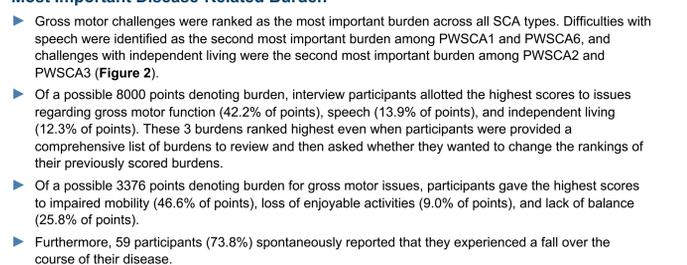


Figure 4. Impact of Fear of Falling on Lives of PWSCA

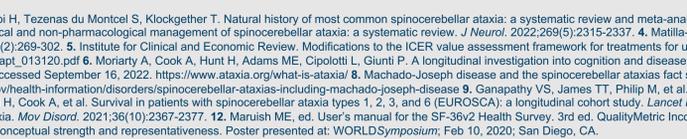


Figure 5. Most Important Disease-Related Burden

Figure 6. Most Important Disease-Related Burden

Figure 7. Most Important Disease-Related Burden

Study Design

- Phase 1: Secured Online Quantitative Assessments**
 - Participants provided demographic data, completed a modified version of the Klockgether Functional Staging of Ataxia questionnaire (a physician-administered tool that assesses SCA functional status, modified with patient-friendly language), and completed the SF-36® QOL measure via a secure, HIPAA/508/GDPR-compliant, multilingual online portal.
 - The SF-36v2 utilizes norm-based scoring with a linear T-score transformation method such that each of the health domain scores and summary components have a mean of 50. Scores below or above 50 reflect scores below and above those of the 2009 US general population, respectively. Scores lower than 50 represent a lower QOL than that in the general US population.¹²
 - Post-hoc ANOVAs of SF-36 scores were performed to calculate nominal P values comparing values between SCA types, where P < .05 indicated a statistically significant difference (Excel 2016, Version 2308, Microsoft Corporation).
 - The relationship between participants' self-assessment of functioning using the modified Klockgether Functional Staging of Ataxia scale and physical health measured by the SF-36 was evaluated using linear correlation coefficients (Excel 2016, Version 2308, Microsoft Corporation).
 - Given the self-reporting nature of the SF-36 assessment, only PWSCA were invited to complete the SF-36 QOL and associated measurements; caregivers were excluded.
 - Phase 2: Semi-Structured Qualitative Interviews**
 - Trained interviewers conducted 90-minute, semi-structured telephone interviews with participants in the participant's native language. Interviews consisted of open- and closed-ended questions regarding disease burden. All questions were derived from a comprehensive review of the medical literature and discussions with both disease experts and leaders of patient support organizations.
 - Skip logic was used to ensure that participants were only asked questions that pertained to them. Participants had the option to abstain from any question or discontinue the study at any time.
 - In an unaided fashion, participants were first asked to list and rank disease-related burdens that were important to them, using scores of 0-100 points.
 - Afterwards, participants were asked about symptoms associated with SCA, which were drawn from PROM-Ataxia, the medical literature, and transcripts of prior patient-focused meetings.
 - This qualitative methodology has previously been described and used in other forums.¹³
 - Follow-Up Surveys**
 - Follow-up questionnaires were shared with participants to better understand their desired therapeutic outcomes and experiences related to falls.
 - Participants chose to complete the follow-up survey online, by phone, or via both methods.
 - If a participant did not previously report having a fall, they received a questionnaire that excluded questions pertaining to experiences with falls.
- The study received institutional review board (IRB) and ethics approval from WCG IRB prior to initiation and again prior to the administration of follow-up surveys. Participants provided consent in their native language via the online portal prior to engaging in study activities.

Falls

- In follow-up surveys, 53 out of 70 participants (75.7%) reported experiencing at least 1 fall over the course of the past year. Among PWSCA3, 81.2% experienced at least 5 falls in the past year.
- In total, 53 participants experienced 2850 falls over the past year. Falls in PWSCA3 represented 71.5% of all falls reported (Figure 3).
- The majority of injuries resulting from falls (2280, 99.2%) were minor (including broken tooth, cuts or lacerations, bumps and bruises, swelling, muscle pain/discomfort, and limited range of motion). However, there were 17 emergency room visits and 1 hospital admission reported for fall-related injuries.
- Participants reported that falling resulted in increased reliance on others and changes in their daily routines.
- Many participants reported that fear of falling impacted their daily life; this included fear of injury, slower movement, and increased concentration on not falling. On a scale of 1 to 10, with 10 denoting extreme impact, 30 of the 53 participants who experienced a fall (56.7%) rated the impact of fear of falling as 6 or higher, 36 (67.9%) rated this factor as 5 or higher, and 46 (86.8%) rated it as 2 or higher. The mean score was highest in PWSCA6 (Figure 4).

Figure 3. Number of Falls by SCA Type in the Past Year

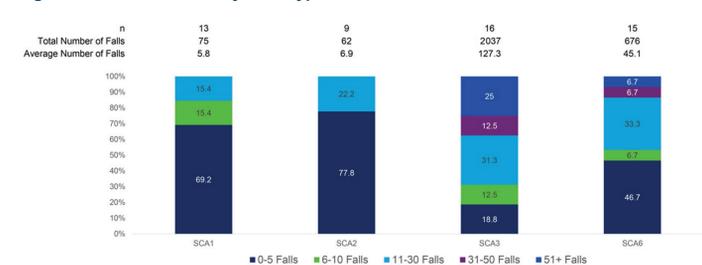
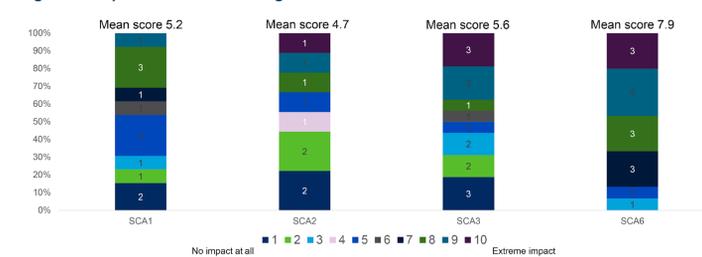


Figure 4. Impact of Fear of Falling on Lives of PWSCA



Desired Therapeutic Outcomes

- When asked to describe a specific impact (other than a cure) that they wished to see from a potential therapy developed for their type of SCA, most participants (47, 67.1%) desired that the therapy would address issues regarding mobility, speech, or balance.
- In the follow-up survey, the majority of participants (64, 91.4%) reported they would find an approved medication that slowed or stabilized disease progression as "extremely meaningful" (5 on a scale of 0-5).
 - In particular, the majority of PWSCA3 and PWSCA6 (≥50% in each group) rated the importance of falling as an outcome of an approved therapy as 10, or "extremely important" on a scale of 1-10.
- Participants reported that a medicine that slowed or stabilized disease progression would provide hope as well as the ability to maintain their daily physical activities and QOL and, as a result, potentially improve their mental well-being.

Table 3. Illustrative Quotes Regarding Disease Burden, Falls, and Desired Therapeutic Outcomes

Disease Burden	"I don't want to be perfect. I just want to do things normally without too much difficulty. I don't want to ask for help. It's a very hard condition to deal with—debilitating. They should find a solution as quickly as possible." (PWSCA2)
Falls	"I have been cautioned by my doctors not to fall, as my symptoms get worse after each one and I do not recover to the point where I was previously. I need someone to help me go up a curb or step if there is no rail or if I can't find a cutout in the sidewalk. I have to think about where to sit in places like theaters or church because I need to be able to get there safely and stand back up. It is becoming harder to remain independent out of my home." (PWSCA1)
Fear of Falling	"I am extremely careful to NOT fall. I use a walker frequently, go up and down stairs 1 step at a time, etc. My daily life consists of BEING CAREFUL to avoid falls." (PWSCA6)
Therapeutic Outcomes	"It would be amazing to have a drug that slowed the progression of this disease. Knowing I have it [SCA] and now waiting for symptoms to develop has impacted my mental health. Having the ability to slow/stop this would allow me to live a normal and hopefully carefree life to the fullest." (PWSCA6)

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