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Are Limitations in Physical Function Relevant and Important Concepts to Assess in Patients on Antithrombotic Therapy for Cardiovascular Conditions?

Kathleen W. Wyrwich,[1] Amy Clark,[2] John Fastenau,[3] Ellen O'Brien,[4] Amiee Kang,[1,*] Priyanka Gaitonde,[1] Eric Chan,[5] Brandon Becker,[1] Mona Martin[2]

[1]Bristol Myers Squibb, Lawrenceville, NJ, USA; [2]Evidera, Bethesda, MD, USA; [3]Janssen Research & Development, LLC, a Johnson & Johnson Company, Raritan, NJ, USA; [4]Janssen Global Services, LLC, a Johnson & Johnson Company, Horsham, PA, USA; [5]Janssen Global Services, LLC, a Johnson & Johnson Company, Raritan, NJ, USA.

*Presenting author.

BACKGROUND

- Thromboembolic cardiovascular diseases are the leading cause of death worldwide, with heart disease and stroke responsible for >19 million deaths annually[1]
  - Acute coronary syndrome (ACS), stroke (including secondary stroke), and atrial fibrillation (AF) are among the greatest contributors of thromboembolic cardiovascular disease–related deaths and disability and cause substantial financial and emotional burdens to patients and their caregivers[1-8]
- Antiplatelet therapy is indicated in ACS and secondary stroke prevention (SSP) while anticoagulants are indicated in cardioembolic stroke prevention for patients with AF
- Content-valid patient-reported outcome (PRO) assessments for antithrombotic treatment studies are needed
- The reported impact of thromboembolic cardiovascular diseases on health-related quality of life includes physical function limitations (PFLs). There is a need to establish content validity of the selected questionnaires that address prior stroke (PS), ACS, and AF to ensure they are fit for the purpose of assessing novel antithrombotic therapies in these patient populations[9]

OBJECTIVE

- This qualitative study evaluated the content validity of standard physical function (PF) assessment tools in patients with self-reported PS, ACS, or AF who use antithrombotic therapies to understand the patient perspective on interference in daily functioning and how much of that interference patients attribute to their antithrombotic therapy

METHODS

- Individual qualitative interviews were conducted via telephone with patients in the United States, United Kingdom, Germany, and Japan
- Patients were recruited to participate in, gave consent to, and were scheduled for interviews by a recruitment vendor (Global Perspectives) using existing databases, social networks, and clinician referral networks
- Interviews were conducted by trained qualitative research interviewers at Evidera using a video conference platform (Microsoft Teams) and lasted for an average of 90 minutes
- Audio files were transcribed and coded using ATLAS.ti software
- Concept codes were used to organize patient expressions by similarity of content and prepare the data for thematic analysis
- Three standardized scales that assessed PF were discussed during interviews: Patient-Reported Outcomes Measurement Information System (PROMIS; 3 PF bank [PFB] items), PROMIS-10 (single global daily activities item), and PROMIS-29 (5-item PF subscale)

CONCLUSIONS

- **Physical function limitations (PFLs) are relevant to patients with prior stroke (PS), ACS, or AF on current antithrombotic therapy**
- **All 3 PRO instruments examined have adequate content validity from a relevance standpoint**

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Disclosures

KWW was an employee of Bristol Myers Squibb at the time of the study. AC and MM are employees of Evidera. JF was an employee of Janssen Research & Development, LLC, a Johnson & Johnson Company at the time of the study. EO and EC are employees of Janssen Global Services, LLC, a Johnson & Johnson Company, and may hold stock in Johnson & Johnson. AK, PG, and BB are employees of and may hold stock in Bristol Myers Squibb.

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RESULTS

- A total of 66 adult patients were interviewed across the 4 countries (**Table 1**)
- The mean age was 60.3 years, and 56.1% of patients were female (**Table 2**)
- Most of the patients were married (60.6%), 33.3% had a high school/technical school (or equivalent) education or less, and 30.3% were retired (**Table 2**)
- A total of 48 (72.7%) patients were currently taking "blood thinners" (28.0% within the last 6 months)

Table 1. Patient Recruitment by Country and Condition

Patients, n	ACS (n = 23)	PS (n = 20)	AF (n = 23)	Total (N = 66)
US	6	6	6	**18**
UK	5	6	6	**17**
Germany	6	2	5	**13**
Japan	6	6	6	**18**
			Total interviews	**66**

Table 2. Patient Demographic Information

Characteristic	US (n = 18)	UK (n = 17)	Germany (n = 13)	Japan (n = 18)	Total (N = 66)
Age, years					
Mean (SD)	61.3 (7.3)	57.5 (15.1)	61.2 (13.0)	61.3 (11.1)	**60.3 (11.7)**
Gender, n (%)					
Male	3 (16.7)	8 (47.1)	6 (46.2)	12 (66.7)	**29 (43.9)**
Female	15 (83.3)	9 (52.9)	7 (53.8)	6 (33.3)	**37 (56.1)**
Marital status, n (%)					
Single, never married	0	2 (11.8)	1 (7.7)	2 (11.1)	**5 (7.6)**
Living with partner	0	3 (17.6)	1 (7.7)	0	**4 (6.1)**
Married	9 (50.0)	10 (58.8)	8 (61.5)	13 (72.2)	**40 (60.6)**
Divorced	5 (27.8)	1 (5.9)	0	1 (5.6)	**7 (10.6)**
Widowed	4 (22.2)	1 (5.9)	3 (23.1)	2 (11.1)	**10 (15.2)**
Highest level of education, n (%)*					
High school/technical school (or equivalent) or less	0	0	5 (38.5)	17 (94.4)	**22 (33.3)**
Vocational school, some college, graduate school, or certification	18 (100)	16 (94.1)	8 (61.5)	1 (5.6)	**43 (65.2)**
Employment status, n (%)*					
Employed full time or part time	1 (5.6)	10 (58.8)	6 (46.2)	10 (55.6)	**27 (40.9)**
Retired	7 (38.9)	4 (23.5)	5 (38.5)	4 (22.2)	**20 (30.3)**
Unable to work	4 (22.2)	0	0	0	**4 (6.1)**

SD, standard deviation.
*Other categories are not shown.

- All 66 (100%) patients reported performing the physical activities on the questionnaires; 46 (69.7%) reported having difficulty doing those activities
  - Seventeen (37.0%) of the 46 patients attributed this difficulty to their antithrombotic therapy. No differences were seen between the PS, ACS, or AF patient subgroups (**Table 3**)
  - Doing chores, walking, and exercising were among the top impacts identified by patients as their "worst" ones related to their "blood thinner" (**Table 4**)
- While all 3 populations reported experiences that made the PRO items relevant to them, the AF population tended to show greater numbers of symptoms/impacts that matched item content (**Table 5**)

Table 3. Summary of Activity Difficulties and Attribution to "Blood Thinner" by Country and Condition

	All patients (N = 66) reported doing the physical activities asked about in the PROs that were discussed during the interview				Of patients who reported doing the activities (N = 66), 46 (69.7%) reported having difficulty with the physical activities asked about in the PROs				Of patients who had difficulties doing the physical activities (N = 46), 17 (37.0%) attributed those difficulties to their "blood thinner"			
Country	**ACS, n**	**PS, n**	**AF, n**	**Total, n (%)**	**ACS, n**	**PS, n**	**AF, n**	**Total, n (%)**	**ACS, n**	**PS, n**	**AF, n**	**Total, n (%)**
US (n = 18)	6	6	6	**18 (27.3)**	5	4	6	**15 (32.6)**	1	1	2	**4 (23.5)**
UK (n = 17)	5	6	6	**17 (25.8)**	5	4	5	**14 (30.4)**	1	3	2	**6 (35.3)**
Germany (n = 13)	6	2	5	**13 (19.7)**	4	2	4	**10 (21.7)**	3	1	1	**5 (29.4)**
Japan (n = 18)	6	6	6	**18 (27.3)**	2	3	2	**7 (15.2)**	1	0	1	**2 (11.8)**
Total (N = 66), n (%)	23 (34.8)	20 (30.3)	23 (34.8)	**66 (100)**	16 (34.8)	13 (28.3)	17 (37.0)	**46 (100)**	6 (35.3)	5 (29.4)	6 (35.3)	**17 (100)**

Table 4. Impacts Identified by Patients as Their "Worst" Ones Related to Their "Blood Thinner"

Impact	Impact identified as their "worst," n (%)	Example quotation describing what makes it their "worst"
N	**66**	
Household tasks/ chores impacted	3 (4.5)	*The household chores, sometimes I do struggle… cleaning and like tidying up and stuff because I sometimes can hurt myself doing that… so I try not to do that as much or get help.*
Walking impacted	2 (3.0)	*The fact that I can't walk long distances anymore… the heart condition has already been cured… it is probably because of the treatment… But I can't stop taking the blood thinner.*
Exercise and sports affected	2 (3.0)	*It does limit some of the physical activities that I was a participant in. As I mentioned earlier, it limits me from cycling, which also has an impact on my physical health since I can't partake in that exercise activity.*

Other categories (including emotional impacts) are not shown.

Table 5. Relevance of Item Content to Patient Experience With Their Condition

PROMIS-29 PF subscale		**ACS (n = 23)**	**PS (n = 20)**	**AF (n = 23)**
Are you able to do chores such as vacuuming or yard work?	Household tasks/chores impacted Physical mobility/function affected Shortness of breath	9 (45) 4 (20) 10 (50)	9 (39) 2 (9) 20 (87)	12 (52) 5 (22) 15 (65)
Are you able to go up and down stairs at a normal pace?	Physical mobility/function affected Shortness of breath	4 (20) 10 (50)	4 (20) 20 (87)	4 (20) 15 (65)
Are you able to go for a walk of ≥15 minutes?	Walking impacted Exercise and sports affected Shortness of breath	6 (30) 7 (35) 10 (50)	8 (34) 7 (30) 10 (50)	8 (34) 14 (61) 10 (50)
Are you able to run errands and shop?	Errands/shopping impacted Shortness of breath	9 (5) 10 (50)	9 (4) 10 (50)	9 (4) 10 (50)
PFB items		**ACS (n = 23)**	**SSP (n = 20)**	**SPAF (n = 23)**
Does your health now limit you in doing housework or jobs around the house? **PFB46**	Household tasks/chores impacted Physical mobility/function affected Shortness of breath	9 (45) 4 (20) 10 (50)	9 (39) 2 (9) 20 (87)	12 (52) 5 (22) 15 (65)
Does your health now limit you in going for a short walk (<15 minutes)? **PFB49**	Walking impacted Exercise and sports affected Shortness of breath	6 (30) 7 (35) 10 (50)	8 (34) 7 (30) 10 (50)	8 (34) 14 (61) 10 (50)
Does your health now limit you in going outside of the home, for example to shop or visit a doctor's office? **PFB54**	Errandss/shopping impacted Driving affected Shortness of breath	9 (5) 5 (25) 10 (50)	9 (4) 3 (13) 10 (50)	9 (4) 3 (13) 10 (50)
PROMIS-10 PF global		**ACS (n = 23)**	**SSP (n = 20)**	**SPAF (n = 23)**
To what extent are you able to carry out your everyday physical activities, such as walking, climbing stairs, carrying groceries, or moving a chair?	Household tasks/chores impacted Physical mobility/function affected Walking impacted Exercise and sports affected Shortness of breath	9 (45) 4 (20) 6 (30) 7 (35) 10 (50)	9 (39) 2 (9) 8 (34) 7 (30) 20 (87)	12 (52) 5 (22) 8 (34) 14 (61) 15 (65)

SPAF, stroke prevention in atrial fibrillation.
Response scale (PROMIS-29 PF subscale): Without difficulty, with little difficulty, with some difficulty, with much difficulty, unable to do.
Response scale (PF item bank and PROMIS-10 PF global): Not at all, a little, moderately, mostly, completely.
Recall period: None (this is a real-time assessment).
Blue indicates ≥50% of the subgroup population was affected by the symptom/impact.

SUMMARY

- Study results showed some level of support for each of the 3 PRO assessment options, but for different reasons. More patients found the more specific items to be easier to answer than the broader global items. Some patients found the more global items simpler and easier to understand. There was not one scale that stood out as substantially better than the others in terms of understandability or meaningfulness to the patients interviewed. Therefore, we conclude that all 3 of these PRO instruments will work from a relevance standpoint, but the different options do offer different advantages and drawbacks
  - The PROMIS-29 is a tested scale that also addresses other important domains, but the PF items are all "capacity" items and ask patients to speculate on what they can do and not what they actually do
  - The PFB items ask about "health limiting you" instead of capacity. This makes them better items from an item-construction sense, but they are limited to the construct of PF
  - The PROMIS-10 offers the advantage of being quite brief and has some published support for performance, but the items (including the 1 PF item) are large global items with multiple examples of tasks and activities. While easy to understand, these single items are broad and not very specific to the key areas of difficulty for a given condition