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ORIGINAL COMMUNICATION

Factors associated with long-term functional outcomes and psychological sequelae in Guillain–Barre syndrome

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Abstract To examine factors impacting long-term health-related outcomes in survivors of Guillain–Barre syndrome (GBS). Seventy-six consecutive patients with definite GBS admitted to the Royal Melbourne Hospital (1996–2009) were reviewed in the neurorehabilitation clinics. They underwent a structured interview designed to assess the impact of GBS on their current activity and restriction in participation using validated questionnaires: Functional Independence Measure (FIM), Perceived Impact of Problem Profile (PIPP) and Depression Anxiety Stress Scale (DASS). Their sociodemographic and disease severity data were obtained from the medical record. The 76 patients [60% male, mean age 56 years, median time since GBS 6 years (range 1–14 years)] showed good functional recovery (median motor FIM score 90). However, 16% reported moderate to extreme impact on their ability to participate in work, family, and social activities; and 22% substantial impact on mood, confidence and ability to live independently. More reported moderate to extreme depression (18%), anxiety (22%) and stress (17%) compared with the normative Australian population (13%). Factors associated with poorer current level of functioning and wellbeing included: females, older patients (57+ years), acute hospital stay (>11 days), those treated in intensive care and those discharged to rehabilitation. No associations were found between the Medical Research Council (MRC) Motor Scale Rating scores at admission, nor time since GBS diagnosis (≤6 vs. >6 years) on outcomes used. Conclusion: GBS is complex and requires long-term management of psychological sequelae impacting activity and participation.

Keywords Guillain–Barre syndrome · Rehabilitation · Functional Independence Measure · PIPP · Depression Anxiety Stress Scale

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Introduction

Guillain–Barre syndrome (GBS) is an acute demyelinating polyradiculopathy due to inflammation of the peripheral nerves and nerve roots which can cause severe motor deficits (symmetrical ascending paralysis), autonomic dysfunction and respiratory failure [1–3]. GBS has a worldwide annual incidence of 1–2 per 100,000 [4, 5]. It can occur at any age, and is common between ages 30 and 50 years with a reported male preponderance [6]. Approximately, 3% of patients may die of complications in the acute phase of GBS [7], up to 25% require artificial ventilation (involvement of respiratory and bulbar muscles), and 20% may have residual permanent severe disability, with deficits in ambulation or require ventilator assistance 12 months later [8].

Recovery from GBS can be prolonged up to 2 years [8]. The distal motor weakness, sensory impairment and psychological problems can result in persistent disability [3, 9–11]. Although the majority of GBS survivors (75%) have a good outcome (the ability to walk independently) [12], the impact of GBS on activities of daily living, work, social activities and quality of life (QoL) is considerable at 2 years after onset and persists beyond this time [13]. One study [14] ($n = 70$) reported that, despite 90% of GBS survivors making a complete functional recovery, 5 years later 27% still had to make substantial changes in their job, hobbies or social activities. Further, a reduction in leisure and social activities was found in 44% of GBS survivors ($n = 116$) [14], and 62% report ongoing detrimental impact upon their (and carers') lives 3–6 years later [15].

With advances in medical care and increased life expectancy issues related to health, wellbeing and participation become increasingly important. A recent report of factors impacting short-term outcomes (6 months) after GBS [16] suggests that female gender, mechanical ventilation, work and tendency to depression are associated with a lower QoL, emotional reactivity and social isolation. The objective of this study, therefore, is to examine factors associated with residual disability and restriction in participation over a long term, including functional outcomes and psychosocial sequelae in GBS survivors in an Australian community cohort.

Methods

Participants and setting

This study was part of a prospective rehabilitation outcomes research program for GBS survivors at the Royal Melbourne Hospital (RMH), a tertiary referral centre in Victoria, Australia, approved by its ethics committee. The RMH GBS program provides acute neurological and rehabilitative care for inpatients and in ambulatory settings to minimize activity limitation and enhance participation.

Participants in this study were recruited from the 157 consecutive patients admitted to RMH for acute care between 1996–2009 with the ICD Code (G61.0) for GBS as primary diagnosis (first admission only). The RMH Access Database was used for cross-indexing of diseases from the Patient Administrator System (HOMER) of Hospital Information Systems, Department of Health Victoria, Australia. The source of these patients was a pool of persons residing in the community, referred to the RMH from public and private medical clinics across greater Melbourne in Victoria. All patients were aged >18 years and fulfilled standard diagnostic criteria for GBS as defined by the National Institute of Neurologic Disorders and Stroke clinical criteria [17] and assessed by an independent neurologist at the RMH. These patients resided in the community (area of greater Melbourne <60 km radius), and had known limitations in their neurological status (including mobility) at admission and discharge from RMH.

Data collection

At the time of recruitment 122 (of 157) patients listed on the RMH GBS Database were eligible for this study due to entry criteria. All were invited by mail to participate in the study, and the 76 who consented were recruited for the project (flow chart Fig. 1). All interviews (45 min each) were conducted by two trained research assistants and clinical assessment by one physician.

Measurement

The International Classification of Functioning, Disability and Health [18] was used as a conceptual basis for choice of best outcomes for measurement.

GBS-related measures

Information extracted from the medical record included: sociodemographic data, total hospital length of stay (LOS) for acute, subacute and intensive care (and duration of ventilation). The signs and symptoms at admission and at discharge from the RMH were motor, sensory and autonomic dysfunction; cranial nerve and sphincter involvement. The electrophysiological data and treatments received were noted.

Measures of impairment

The Medical Research Council (MRC) scale graded muscle power (0 = no contraction, 5 = normal power).

Measures of activity and functioning

The Functional Independence Measure (FIM) [19] assessed function (activity) and need for assistance (assessed by a physician). The FIM motor section has 13 items that assess level of function in four subscales: self-care, transfers, locomotion and sphincter control. Each item is rated on a scale of 1–7 (1 = total assistance, 5 = needs supervision, 6 = modified independence, 7 = independent). The score reflects burden of care in each area measured. FIM has good reported reliability and validity.

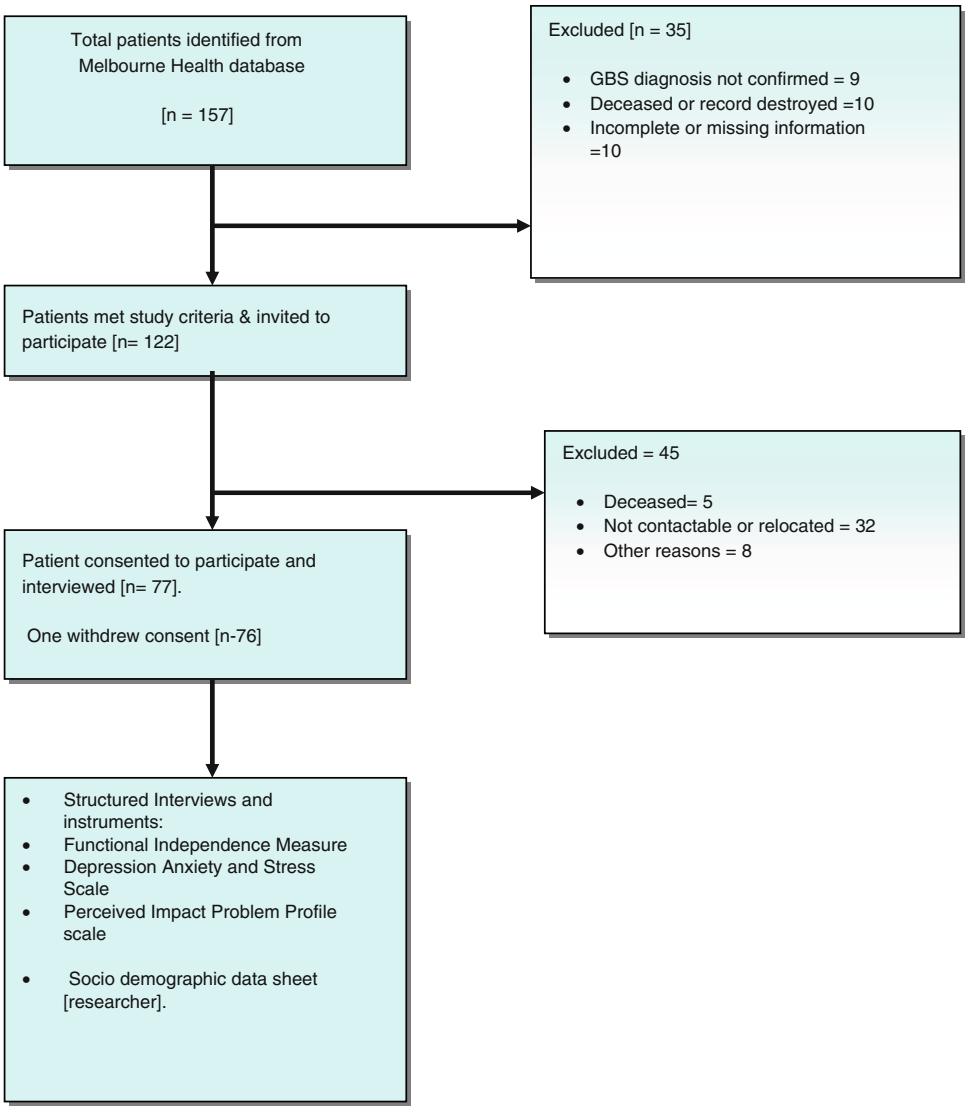

Fig. 1 Flow chart of recruitment process

Measures for participation and quality of life

The Depression Anxiety Stress Scale-21 (DASS-21) [20] consists of three 7-item self-report scales designed to measure the negative emotional states of depression, anxiety and stress. Participants rate the extent to which they experienced each state over the past week on a 4-point Likert rating scale. Sub-scale scores are derived by totalling the scores, and multiplying by two to ensure consistent interpretation with the longer DASS 42-item version. It has good internal consistency.

The Perceived Impact of Problem Profile (PIPP) [21] is a 23-item scale containing five subscales (mobility, self-care, relationships, participation and psychological well-being) designed to assess the impact associated with a health condition. For each item, respondents are asked to rate 'how much impact have your current health problems had on (item of function or activity)' using a 6-point scale ('no impact' and 'extreme impact'), with high scores indicating greater impact.

Statistical analyses

A series of analyses were conducted to describe the current level of function and wellbeing of participants and to identify those factors associated with scores on the FIM, PIPP and DASS subscales. Given the skewed distributions, continuous predictor variables (age, LOS, time since diagnosis) were split at the median to form approximately equal groups for comparison. Non-parametric analyses (Mann–Whitney U tests) were used to compare scores across groups. Although a substantial number of univariate analyses were conducted, increasing the likelihood of a Type 1 error, it was decided to report all p values above

0.05 as significant. This was consistent with the descriptive nature of the study to ensure all potentially important predictors of the long-term sequelae of GBS were identified.

Results

Sample characteristics

The 76 patients [60% male, mean age 56 years, median time since GBS 6 years (range 1–14 years)] had a median acute hospital stay of 10 days (IQR 7–16), 22% were admitted to intensive care with a median stay of 5 days (IQR 3–18) (see Table 1). Electrophysiological studies during the acute episode confirmed demyelinating (54%) and axonal neuropathy (4%), while the remaining patients had mixed patterns. Approximately 60% of participants had pain of multifactorial origin (included non-nociceptive neuropathic pain and pain due to mechanical issues). The report of bladder (13%) and bowel (12%) difficulties (urinary urgency/frequency and constipation) was higher than expected. Although steroid use in not effective in GBS, this information is included given the historical nature of some of the treatment data.

Current level of functioning, participation and psychological wellbeing

Participants reported minimal change in their physical function since GBS. As expected, most individuals reported good levels of functional independence indicated by the high median values on the FIM motor subscales (see Table 2). Although median scores on the PIPP subscales were low (indicating low levels of impact), participant scores extended across the full range of possible scores. Over 16% of GBS survivors reported moderate to extreme impact of their current health condition on their ability to participate in work, family, leisure and social activities. On the PIPP psychological subscale, 22% of participants recorded scores above the midpoint of the scale indicating substantial impact on satisfaction with life, mood, confidence, and the ability to live independently.

Compared with a normative sample of the Australian population, a higher percentage of participants reported moderate, severe or extreme levels of depression, anxiety and stress. While 13% of the normative sample [20] recorded scores in the moderate to extreme categories, in the current sample the corresponding value was 18.4% for the depression scale, 22.4% for the anxiety scale, and 17.1% for the stress scale (see Table 2).

Table 1 Demographic and disease characteristics of sample ($n = 76$)

Characteristic	Statistic
Gender	
Female	30 (39.5%)
Male	46 (60.5%)
Age	
Median	56.0 (IQR: 39.2, 71.7)
Range	19–90
Years since diagnosis	
Median	6.0 (IQR: 2.9, 10.0)
Range	1–13.8
Length of stay—acute (days)	
Median	10.0 (IQR: 7.0, 16.5)
Range	1–135
Intensive care admission	
Yes	17 (22.4%)
No	59 (77.6%)
Intensive care length of stay (days) ($n = 18$)	
Median	5.0 (3.0, 18.5)
Range	2–104
Pain	
Yes	46 (60.5%)
No	30 (39.5%)
Facial weakness	
Yes	25 (32.9%)
No	51 (67.1%)
Dysarthia	
Yes	15 (19.7%)
No	61 (80.3%)
Dysphagia	
Yes	12 (15.6%)
No	64 (84.2%)
Opthalmoplegia	
Yes	11 (14.5%)
No	65 (85.5%)
Urinary problems (urgency, frequency, nocturia)	
No	63 (82.9%)
Yes	13 (17.1%)
Bowel problems (constipation)	
No	64 (84.2%)
Yes	12 (15.8%)
Autonomic Dysfunction	
Yes	8 (10.5%)
No	51 (89.5%)
Plasma Exchange	
Yes	17 (22.4%)
No	59 (77.6%)
Intravenous Immunoglobulin	
Yes	60 (78.9%)

Table 1 continued

Characteristic	Statistic
No	16 (21.1%)
Steroids (intravenous, oral)	
Yes	7 (9.2%), 9 (11.8%)
No	69 (90.8%), 67 (88.2%)
Discharge destination	
Community	35 (46.1%)
Rehabilitation	34 (44.7%)
Acute care	7 (9.2%)

Factors associated with current level of functioning and wellbeing

Mann–Whitney *U* tests were used to compare the two levels of each predictor variable across each of the measures of function and well-being.

Gender Statistically significant differences were identified between males and females on the DASS scales (DASS: depression $p < 0.001$, anxiety $p = 0.02$, stress $p = 0.01$), three of the PIPP scales (PIPP: psychological scale $p = 0.02$, self-care $p = 0.05$, participation $p = 0.02$) and two of the FIM scales (motor $p = 0.04$, self-care $p = 0.03$). Females reported lower levels of functional independence, higher levels of depression, anxiety, and stress, and greater impact.

Age Older participants (57+ years) recorded significantly lower levels of functional independence (FIM: self-care $p = 0.008$, motor $p = 0.03$), and higher impact scores (PIPP: self-care $p = 0.001$, relationship $p = 0.03$).

Time since diagnosis The sample was divided into two approximately equal groups based on time since diagnosis (≤6 years vs. >6 years). There were no statistically significant differences between these groups on the FIM, PIPP or DASS scales.

Clinical severity indicators

- *ICU admission:* Those requiring an ICU admission recorded higher scores on the PIPP subscales [self-care ($p = 0.03$), participation ($p = 0.03$)].
- *LOS acute:* A comparison of scores for patients with less than, versus more than, 10 days, LOS in acute care showed significant differences on three of the PIPP subscales (PIPP: self-care $p = 0.04$, mobility $p = 005$, participation $p = 0.04$), and the FIM subscales [mobility ($p = 0.03$, motor ($p = 0.04$)]. LOS exceeding 11 days was associated with lower FIM scores and higher impact scores.
- *MRC Motor Scale Rating:* There was no significant difference in scores for patients with 'one or more' severe ratings on any of the four MRC motor domains (left and right arm and leg) versus those who reported 'no' severe rating.
- *Discharge destination:* Patients discharged to the community recorded higher FIM motor scores ($p = 0.04$) than those discharged to a rehabilitation facility.

Discussion

This is the first report of factors associated with long-term outcomes (median >6 years) for persons with GBS residing in the community. The GBS survivors made good functional recovery (median motor FIM score = 90) consistent with other studies [16, 22–25]. Participants reported residual neurological deficits (motor and sensory) [9, 16, 26] and minimal change in their physical status in relation to time elapsed since GBS. This is similar to other reports [17, 25] that suggest that, at 2–3 years after GBS, there is no substantial expectation of recovery. The report of ongoing pain (mixed patterns), autonomic dysfunction, including urinary urgency and constipation [4], were beyond the scope of this study and need further exploration. GBS survivors may develop detrusor hyperactivity over time which may persist many years after GBS (personal communication—Prof C Fowler National Hospital for Neurology and Neurosurgery UK); however, currently there are no long-term studies of bladder dysfunction in the GBS population. In the current study 16% of GBS survivors reported moderate to extreme impact on participation in work, family, leisure and social activities, and substantial impact (22%) on satisfaction with life, mood, confidence, and ability to live independently (PIPP subscales). These are consistent with reports of participatory limitation (work, social and recreational activity, family life, caregiver stress, activities of daily life) in other GBS cohorts [13, 15, 16, 22, 25].

Previously anxiety, depression and brief episodes of reactive psychosis were reported in GBS in high dependency units, associated with severe GBS requiring ventilation, quadriparesis and cranial nerve involvement [27]. This has not been well studied over the long term in GBS survivors. Although studies report a positive correlation of depression with patient psychosocial status [28], depression was not reported as a major factor causing psychosocial difficulty in the GBS population [25]. Other reports suggest that those with GBS and complete physical

Table 2 Descriptive statistics for subscales of the Functional Independence Measure (FIM), Perceived Impact of Problem Profile (PIPP) and Depression Anxiety Stress Scale (DASS)

Scale	Statistics	
FIM ($n = 75$)		
self-care	Md = 42.0 IQR: 41.0, 42.0 Range 25–42	
Sphincter	Md = 14.0 IQR: 14.0, 14.0 Range 2–14	
Mobility	Md = 35.0 IQR: 33.0, 35.0 Range: 15–35	
Motor	Md = 90.0 IQR: 87.0, 91.0 Range: 42–91	
PIPP ($n = 75$)		
self-care	Md = 1.0 IQR: 1.0, 1.0; Range 1–5; Score above midpoint 3 (3.9%)	
Mobility	Md = 1.1 IQR: 1.0, 2.0; Range 1–6; Score above midpoint 7 (9.2%)	
Participation	Md = 1.2 IQR: 1.0, 2.6; Range 1–6; Score above midpoint 11 (15.1%)	
Relationship	Md = 1.0 IQR: 1.0, 1.0; Range 1–6; Score above midpoint 4 (5.3%)	
Psychological	Md = 1.4 IQR: 1.0, 3.0; Range: 1–6; Score above midpoint 16 (21.1%)	
DASS ($n = 76$)		
Depression	Md = 2.0 IQR: .0, 10.0 Range 0–40	
Anxiety	Md = 4.0 IQR: .0, 8.0 Range 0–28	
Stress	Md = 6.0 IQR: 2.0, 16.0 Range 0–34	
DASS clinical classifications	Current sample	Normative sample (%)
Depression		
Normal (0–9)	55 (72.4%)	78
Mild (10–13)	7 (9.2%)	9
Moderate (14–20)	8 (10.5%)	8
Severe (21–27)	2 (2.6%)	3
Extreme (28+)	4 (5.3%)	2
Anxiety		
Normal (0–7)	51 (7.1%)	78
Mild (8–9)	8 (10.5%)	9
Moderate (10–14)	10 (13.2%)	8
Severe (15–19)	2 (2.6%)	3
Extreme (20+)	5 (6.6%)	2
Stress		
Normal (0–14)	55 (74.3%)	78
Mild (15–18)	6 (8.1%)	9
Moderate (19–25)	6 (8.1%)	8
Severe (26–33)	3 (4.1%)	3
Extreme (34+)	4 (5.4%)	2

Md median, *IQR* Interquartile range

FIM Functional Independence Measure, *PIPP* Perceived Impact of Problem Profile, *DASS* Depression Anxiety Stress Scale

recovery or minimal residual deficits show impaired psychosocial functioning [22, 25], including altered emotional reactions, sleep disturbance, social isolation and low energy levels [16]. Participants in this study, with a median time since diagnosis of 6 years, reported ongoing psychological distress, in contrast to a previous study suggesting that psychological distress, anxiety and depression occur more frequently in the earlier recovery phase [29]. More GBS participants in the current study recorded moderate to extreme levels of depression (18%), anxiety (22%), and stress (17%) compared with the normative Australian population (13%), similar to a Dutch health status report [25]. This has important clinical implications for long-term monitoring, education, support and counselling of GBS survivors (and their families).

Restricted activity alone explains only a minor part of the variance of health-related QoL [25] as many factors may influence QoL. Consistent with other reports [16, 22, 23], this study identified gender and age as factors associated with lower level of current function and greater impact. Women in this study had higher depression, anxiety and stress levels, tended to stay home and led more

restricted lives. This gender bias, however, needs further study. Similar to other reports [16, 22, 26], those treated in intensive care with severe GBS showed greater impact on QoL, and those with longer acute hospital stay (>11 days) recorded lower function and higher impact scores [22]. No association was found between the MRC Motor Scale Rating scores (at admission to acute hospital), nor time since GBS diagnosis (≤6 vs. >6 years). As expected, those discharged to the community had higher functional scores than those discharged to rehabilitation. Almost 40% of all GBS patients require inpatient rehabilitation (especially those requiring ventilatory support and the more disabled). Although there is some evidence to support multidisciplinary GBS rehabilitation for improved physical and QoL outcomes [16, 30], a further systematic review is currently underway [31].

The GBS survivors in this study are similar to those in other studies in terms of age, gender, disease severity and treatment [16, 22, 24]. They did, however, have a shorter LOS in both acute and intensive care compared with other reports [23, 24]. These variations may be due to differences in Australian healthcare and service delivery, and availability of ambulatory programs within the community setting. Further research is currently underway on data for GBS survivors using the Australian Rehabilitation Outcomes Centre (AROC)—a national dataset from 160 accredited public and private rehabilitation facilities across Australia over the last 8 years [32].

Shorter term studies after GBS (up to 2 years) report the prevalence of residual deficits ranging from 16 to 54% of patients [22, 33, 34]. The variation in reported outcomes of GBS may reflect insensitive and varied outcome measurement used in this population. Previous measures used to evaluate neuropathies were biased towards disability (e.g. Rankin scale, Hughes scale) [33, 35], and not participation. The International Classification of Functioning, Disability and Health (ICF) [18] provides a framework for describing the impact of disease at the level of impairment, limitation in activity and participation. Recently, patient reported problems due to GBS were linked with categories of ICF [36] to highlight the patient perspective, and an expert consensus meeting identified the preliminary ICF 'Core' set for GBS (short list of clinically relevant ICF categories) that needs to be addressed in multidisciplinary care settings [37]. These in the future may enable more comprehensive measurement of participatory issues in this population.

Some caution needs to be exercised in the interpretation of the group comparisons conducted in this study due to the substantial number of univariate statistical analyses undertaken, with no adjustment to the alpha value used to indicate statistical significance. This study was intended as a preliminary descriptive study, with the aim to identify possible factors that may have an impact on long-term outcomes. Further research using larger studies and more sophisticated multivariate analyses will need to be undertaken to extend these findings. This study utilized a relatively small sample in a tertiary regional metropolitan region which may limit the generalizability and validity of these findings. The GBS survivors in this study, however, are similar to GBS patients in other cohorts in terms of their gender, disease severity and course. This study provides longitudinal information, including information from the GBS participants in the community. The participants had strict inclusion criteria and were listed in a database of people with GBS admitted to the RMH and who agreed to participate in research projects. In an attempt to reduce recall bias, all questions were limited in the main to the current situation. Medical records were used to confirm participant self report**.** This method of information gathering has potential information bias. Problems not included within the domains of the outcome measures used were not able to be identified, the measures used, however, were broad and expansive. We acknowledge that other factors may have impacted depression and anxiety in GBS participants and were not studied. More research into ongoing pain and bladder and bowel dysfunction in GBS survivors is also needed.

GBS is a challenging condition requiring integrated long-term management. The factors associated with long-term functional and psychological sequelae in GBS survivors in this study have important implications for the treating clinicians and need to be explored in larger and different GBS cohorts. The GBS ICF 'Core' set [37] may enable clinicians to provide targeted care in multidisciplinary care settings, and focus on participatory issues in this patient population.

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Conflict of interest statement None.

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