Health and Quality of Life Outcomes

RESEARCH

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Patient-reported outcomes and daily activity assessed with a digital wearable device in patients with paroxysmal nocturnal hemoglobinuria treated with ravulizumab: REVEAL, a prospective, observational study

Elizabeth A. Griffiths[1], Jae S. Min[2], Wei-Nchih Lee[2], Jeffrey C. Yu[3], Yogesh Patel[3], Karl-Johan Myren[4] and David Dingli[5*]

Abstract

Background Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, chronic blood disorder. Symptoms such as fatigue can have a substantial impact on patients' physical activity levels, sleep, quality of life, and work productivity. Ravulizumab treatment can reduce thrombosis risk, improve survival and quality of life, and reduce fatigue in PNH, but information is limited on how it impacts sleep and physical activity. Here, data on resting heart rate, daily physical activity, and sleep in ravulizumab-treated patients with PNH were passively collected via a digital wearable activity-tracking device and patient-reported outcome (PRO) data were collected via weekly surveys in the same cohort.

Methods REVEAL was a 32-week prospective observational cohort study in individuals with PNH receiving ravulizumab in the USA. A wrist-worn Fitbit™ collected data on resting heart rate, daily step count, and sleep duration from eligible patients. Patients also completed the following electronic weekly surveys: Functional Assessment of Chronic Illness Therapy (FACIT) – Fatigue, Patient-Reported Outcomes Measurement Information System (PROMIS) Global Physical Health, PROMIS Global Mental Health, PROMIS Sleep-Related Impairment and Sleep Disturbance, and Work Productivity and Activity Impairment Questionnaire – Specific Health Problem (WPAI-SHP). Data collected from the activity trackers and surveys were compared against US general population values reported in the literature.

Results Twenty-eight ravulizumab-treated patients were included (median age: 34 years; 54% female). PRO scores were within US general population normative values, including FACIT-Fatigue (40.0), PROMIS Global Physical Health (51.0), Global Mental Health (51.0), Sleep-Related Impairment (50.0), and Sleep Disturbance (49.0). Similarly, mean resting heart rate (67 bpm), daily step count (7476), and sleep duration (7.7 h) were within the range of US general population values. Daily step count was positively correlated with PROMIS Global Physical and Mental Health scores.

Conclusions This was the first study to use digital monitoring technology to collect data on physical activity and sleep in patients with PNH. The findings indicate that ravulizumab treatment enables patients with PNH to achieve activity levels (heart rate, sleep duration, step count) and quality of life that are comparable to those

*Correspondence:
David Dingli
Dingli.David@mayo.edu
Full list of author information is available at the end of the article

of the US general population. A weak positive correlation was identified between patient-reported physical and mental health and daily physical activity levels.

Keyword Paroxysmal nocturnal hemoglobinuria, Health-related quality of life, Fatigue, Patient-reported outcomes

Plain language summary

Why did we perform this research?

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, chronic, progressive and potentially life-threatening blood disorder. It is characterized by red blood cell destruction within blood vessels (known as intravascular hemolysis) and white blood cell and platelet activation which may lead to blood clots, kidney damage and other complications. The disease can cause symptoms such as tiredness, stomach pain, and difficulty swallowing, resulting in poor quality of life for patients. Ravulizumab is an approved treatment for PNH that works by binding to a protein in the immune system known as complement component 5. Although clinical trials have shown that ravulizumab reduces thrombosis risk, improves survival and improves the quality of life of patients with PNH, its impact on their sleep, physical and mental health, and ability to work needs further research.

How did we perform this research?

This study observed a small group of patients who were receiving ravulizumab for the treatment of PNH over a period of 32 weeks. The aim of this study was to understand patient experiences of their tiredness, sleep, physical and mental health, and ability to work. Patients completed weekly questionnaires about their experiences, and also wore a Fitbit™ device every day during the study period, which recorded real-time data on their heart rate, steps, and sleep patterns. The results of the questionnaires and the Fitbit™ data were then compared with the values for the US general population.

What were the findings of this research and what are the implications?

Patients with PNH treated with ravulizumab had quality of life and activity levels (tiredness, sleep, and physical and mental health) within the range of the healthy US general population.

Background

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, chronic, and potentially life-threatening blood disorder resulting from acquired somatic mutations in the *PIGA* gene, causing uncontrolled activation of the terminal complement pathway [1, 2], The disease is characterized by intravascular hemolysis and activation of white blood cells and platelets, resulting in anemia, increased risk of thromboembolic events, organ damage (particularly to the kidneys, lungs, and heart), and premature death [1]. The incidence of PNH is estimated to be 0.08–0.35 per 100,000 person-years [3, 4], and prevalence ranges from 12–20 per million people worldwide [5, 6].

The symptoms of PNH are wide-ranging and include fatigue, abdominal pain and dysphagia, [2], all of which can negatively affect quality of life (QoL) and work productivity. Fatigue is one of the most commonly reported symptoms. Fatigue can be severe in untreated patients with PNH and has been shown to affect several aspects of patients' lives including mental health and activity levels [2, 7]. In PNH, fatigue is not directly correlated with hemoglobin levels or anemia, but chiefly arises as a consequence of nitric oxide scavenging by free hemoglobin released during intravascular hemolysis [8–10]. In addition to fatigue, nitric oxide depletion at the tissue level can cause symptoms such as abdominal pain, difficulty swallowing due to esophageal spasm, and erectile dysfunction [9].

Ravulizumab is a complement component 5 (C5) inhibitor administered via intravenous infusion that provides immediate, complete, and sustained inhibition of C5, a key component in the terminal complement pathway, thus ensuring control of intravascular hemolysis [11–13]. In the USA, ravulizumab is the current standard of care for patients with PNH [14].

Patient-reported outcomes (PROs) in PNH have been described in the context of prospective clinical trials. These have shown that improved QoL and reduced fatigue are associated with treatment with ravulizumab [15, 16]. However, longitudinal real-world data, outside the controlled setting of a therapeutic clinical trial, on sleep patterns, physical and mental health, daily activity, and work productivity are currently limited. With consumer wearable technology becoming more widespread, there are increasing opportunities to study disease through continuous patient monitoring and passive data collection. Previous studies have used data from consumer wearable devices to study chronic pain in daily life [17], depression [18], and to describe population-level response to influenza-like illness [19]. However, the extent to which these data relate to PROs in PNH is not yet understood.

The objective of the REVEAL study was to evaluate data on resting heart rate, physical activity, sleep collected via

a digital wearable activity-tracking device from patients with PNH on ravulizumab therapy in the USA and to understand how passively-collected data relates to PRO data collected via surveys in the same cohort.

Methods

Study design

REVEAL was a 32-week prospective, non-interventional observational cohort study in adult individuals with PNH on maintenance therapy with ravulizumab (Ultomiris®, Alexion Pharmaceuticals Inc.) or eculizumab (Soliris®, Alexion Pharmaceuticals Inc.). The study was conducted virtually, and participants were able to complete all study tasks at home.

Patients with PNH in the USA were recruited from various sources, including patient advocacy organizations, healthcare professionals, and Alexion's OneSource Patient Assistance Program. Potential participants who were interested in participating in the study took an online screening survey to determine eligibility. Patients were eligible for inclusion if they had a diagnosis of PNH, were aged 18 years or older and were receiving ravulizumab (8-week infusion schedule) or eculizumab (2-week infusion schedule). In addition, patients were required to live in the USA, be able to speak, read and understand English, and own and use a smartphone with Apple™ iOS 11 or Android™ OS 7.0 or higher. Full inclusion and exclusion criteria are shown in Appendix 1: Table S1. Patients electronically completed a baseline survey which collected information on demographic and baseline characteristics, medication usage, and infusion schedule (Appendix 1: Table S2).

Activity assessments and PRO surveys

Eligible participants were sent a wrist-worn Fitbit™ (Fitbit™ Charge 3, San Francisco, CA, USA) through which the following data were passively collected during the study period: resting heart rate, daily step count, and sleep pattern.

Patients completed the following electronic surveys each week during the 32-week study period to provide data on fatigue, sleep quality and disturbance, and physical and mental health (full data collection schedule shown in Appendix 2: Table S2):

- Functional Assessment of Chronic Illness Therapy (FACIT) – Fatigue, a 13-item questionnaire, developed to assess fatigue and validated in patients with chronic illnesses, with items covering feelings of fatigue, tiredness and weakness, and the impact of fatigue on ability to perform daily and social activities [20–22]. It is scored on a scale of 0–52, with lower scores indicating worse fatigue.
- Patient-Reported Outcomes Measurement Information System (PROMIS) Global Physical Health Short Form and PROMIS Global Mental Health Short Form, both 2-item questionnaires that assess participants' physical and mental health over the previous 7 days, and are shorter, psychometrically validated variants of the PROMIS Global Physical and Mental Health scales [23]. For PROMIS measures, raw survey scores are calibrated against the US general population (which has a mean [standard deviation, SD] score of 50 [10]) to generate a standardized score ranging from 0 to 100. For the physical and mental health scales, higher scores relative to the general population represent better physical and mental health.
- PROMIS Sleep-Related Impairment and Sleep Disturbance Short Form, two 4-item questionnaires that assess sleep quality over the past 7 days [24]. Raw survey scores are calibrated to generate a standardized score from 0–100. Higher scores relative to the general population (mean score of 50) represent worse sleep-related impairment and disturbance.
- Work Productivity and Activity Impairment Questionnaire – Specific Health Problem (WPAI-SHP), a 6-item questionnaire that yields four types of scores based on absenteeism (work time missed), presenteeism (impairment at work/reduced effectiveness at work), work productivity loss, and activity impairment [25]. WPAI outcomes are expressed as impairment percentages (0–100%), with higher numbers indicating greater impairment and less productivity.

Ethical approval and informed consent

The study protocol, informed consent form, recruitment materials, and participant materials were reviewed and approved by the Western Institutional Review Board (approval number: 20211134). All patients provided informed consent prior to participation in the study. Patients were informed that participation in the study was voluntary and that all data collected would be deidentified. Participants were compensated for study participation and survey completion and were able to keep the Fitbit™ activity trackers at study completion.

Data analysis

The primary endpoints were correlations between activity data (resting heart rate, daily step count, and sleep) and PRO scores, including fatigue, sleep, and QoL. A moderate correlation (Pearson's correlation coefficient, *r*) between the PROs and the passively measured activity data was hypothesized; in particular, between sleep duration and PROMIS sleep measures and FACIT-Fatigue.

An absolute value of $r < 0.10$ was interpreted as negligible correlation, 0.10–0.39 as weak correlation, 0.40–0.69 as moderate correlation, and > 0.70 as strong correlation [26]. Statistical significance testing for Pearson's correlation coefficient was performed at the study cohort level (in which PRO and activity data were aggregated for all participants based on relative weekly time-indexing). Exploratory analyses were performed to descriptively evaluate results against US general population normative values, and to explore PRO scores and activity data before and after infusion.

To ensure sufficient data for meaningful interpretation, analyses were only performed for cohorts of more than 5 patients; since only 5 eculizumab-treated patients were enrolled, this cohort was excluded from analysis. Data collected from the baseline and weekly surveys were descriptively reported for the ravulizumab-treated cohort. Because survey data were collected on a weekly basis, the data collected via the activity trackers were aggregated per person over the same week, so that aggregates of activity data were aligned with the PRO scores. Results are reported as the average of all measurements collected over the 32-week study period.

The minimum number of consecutive hours of device wearing required to qualify as passive data collection was 10 h/day. Daily resting heart rate was calculated by Fitbit™ by measuring heart rate when sleep was detected (if worn during sleep), or by measuring heart rate detected throughout the day while inactive (if not worn during sleep). Daily sleep duration was calculated based on the main night-time sleep detected, not including naps. The daily number of steps was calculated as the sum of all steps taken while the participant was not asleep. The PRO and activity data from these patients with PNH were compared against US general population normative values reported in the literature.

Participants were required to complete and return the electronic PRO surveys within 24 h of receipt. Participants who did not submit information on time were sent reminders via email, text messages push notification, or phone call; these patients remained in the study regardless of whether they submitted data in a timely manner.

Table 1 Baseline characteristics and demographics of ravulizumab-treated patients enrolled in REVEAL

	Ravulizumab-treated patients (*N* = 28)
Age, years, median (IQR)	34 (28–38)
Female, n (%)	15 (54%)
Ethnicity, n (%)	
Hispanic or Latino	3 (11%)
Not Hispanic or Latino	25 (89%)
Race, n (%)	
White	24 (86%)
Black or African American	2 (7.1%)
Asian	1 (3.6%)
Other	2 (7.1%)
Body mass index, kg/m^2, median (IQR)	26.2 (23.3–28.8)
Highest level of education, n (%)	
High school graduate, diploma, or the equivalent	1 (3.6%)
Some college or no degree	6 (21%)
College graduate, associate, or bachelor's degree	8 (29%)
Graduate degree	12 (43%)
Doctorate degree	1 (3.6%)
Annual household income, n (%)	
Less than $25,000	4 (14%)
$25,000–34,999	1 (3.6%)
$35,000–49,999	3 (11%)
$50,000–74,999	2 (7.1%)
$75,000–99,999	7 (25%)
$100,000–149,999	7 (25%)
$150,000 or more	2 (7.1%)
Prefer not to answer	2 (7.1%)
Age at symptom onset, years, median (IQR)	27 (21–30)
Age at diagnosis, years, median (IQR)	28 (21–34)
Clone size, %, median (IQR)	69 (35–94)
Hemoglobin level, g/dl, median (IQR)	11.15 (10.60–12.55)
Lactate dehydrogenase level, U/L, median (IQR)	226 (187–266)
Blood transfusions in the past 3 months, n (%)	
0	27 (96%)
1–10	1 (3.6%)
11–20	0 (0%)

IQR interquartile range, *PNH* paroxysmal nocturnal hemoglobinuria, *SD* standard deviation

Results

Baseline demographics and clinical characteristics

In total, 28 ravulizumab-treated patients were enrolled in the study (Table 1). The median age of ravulizumab-treated patients was 34 (interquartile range [IQR]: 28–38) years, and 54% were female. The majority of patients were non-Hispanic and White and were highly educated. A wide range of household incomes were represented (Table 1).

Twelve patients (44%) were on a maintenance dose of ravulizumab 3300 mg, five patients (19%) were on 3000 mg, and one patient (3.7%) was on 3600 mg; 10 patients did not know their dose. All patients were on an 8-week ravulizumab infusion schedule. At baseline, ravulizumab-treated patients had a median lactate

dehydrogenase level of 226 U/L and a median hemoglobin level of 11.15 g/dl. In the 3 months prior to baseline, 96% of patients had no blood transfusion.

PRO scores

Over the 32-week study period, 82% of PRO surveys were completed and returned by patients within the given timeframe. PRO scores reported by patients treated with ravulizumab were within the normal range for the US general population (Fig. 1). Across the 32-week study period, the mean (SD) FACIT-Fatigue score in ravulizumab-treated patients was 40.0 (9.0); in the US general population, means of 44.7 and 43.7 have been reported for 30–39 year-old males and females, respectively [27], In ravulizumab-treated patients, PROMIS Global Physical and PROMIS Global Mental Health scores were 51.0 (7.0) and 51.0 (8.0), respectively, while US normative values for those aged 18–34 years have been reported as 51.6 and 48.5, respectively [28]. For PROMIS – Sleep-Related Impairment and PROMIS – Sleep Disturbance, scores were 50.0 (9.0) and 49.0 (6.0), respectively, which were comparable to the US general population norm for both measures of 50.0 [28].

Work impairment was evaluated in 23 patients. Mean (SD) overall work impairment from the WPAI-SHP was 22.0% (25) for ravulizumab-treated patients; in a sample of the US general population, a WPAI of 17.0% was reported in patients aged 30–39 years [29].

Activity data

The Fitbit™ data collection rate over the study period was 81% (i.e., on 81% of days, patients wore their devices for at least 10 h). The mean (SD) resting heart rate was 67 (8) bpm (Fig. 2), which was close to the US general population normative value for resting heart rate of 65.5 bpm [30]. The mean (SD) daily number of steps was 7476 (3164); in the US general population a mean (SD) of 7271 (1553) steps per day has been reported [31]. The mean (SD) duration of sleep over the study period was 7.7 (1.3) hours, which is within the range of normative values reported for the US general population (7.2 [1.0] hours) [32].

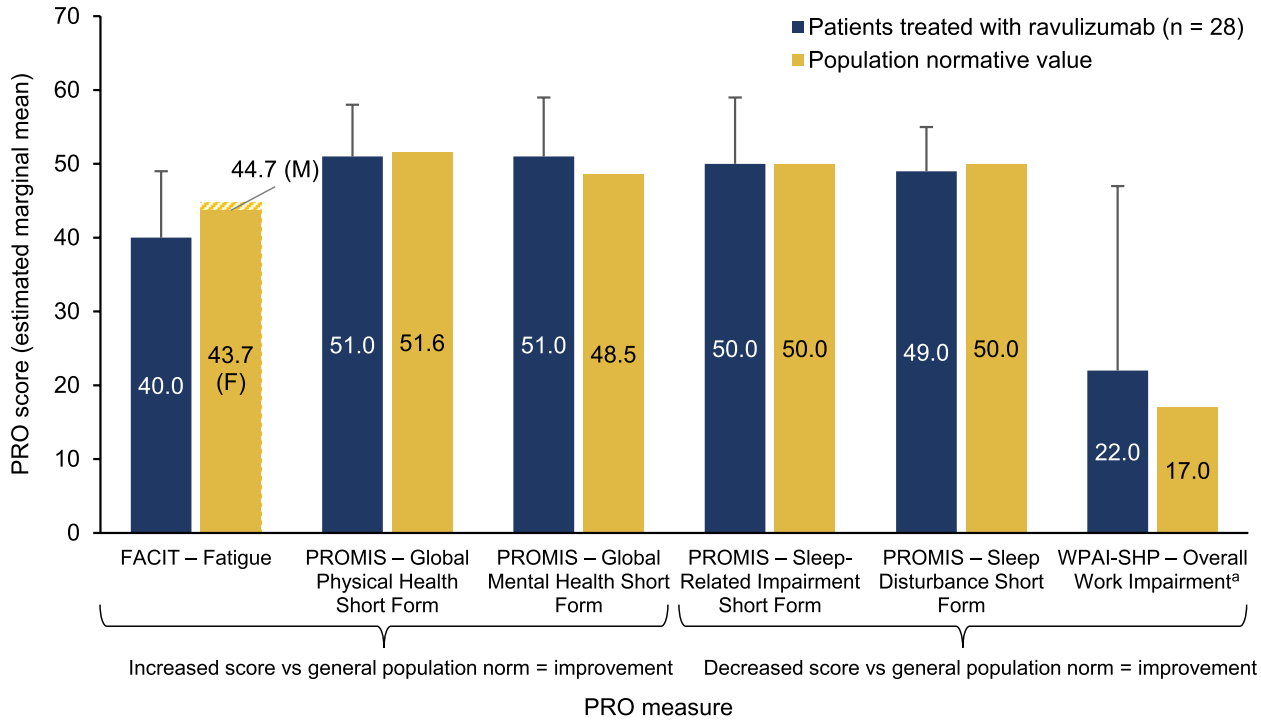

Fig. 1 Summary of PRO measures in patients with PNH treated with ravulizumab compared with the US general population. *FACIT* Functional Assessment of Chronic Illness Therapy, *F* females, *M* males, *PRO* patient-reported outcome, *PROMIS* Patient-Reported Outcomes Measurement Information System, *WPAI-SHP* Work Productivity and Activity Impairment Questionnaire – Specific Health Problem. Values were collected longitudinally for each participant and estimated marginal means across multiple observations per participant are shown; error bars represent standard deviation. Population normative values are 43.7 (females) and 44.7 (males) for FACIT – Fatigue [27], 48.5 for PROMIS Global Mental Health Short Form (subpopulation norm for age category 18–34 years), 51.6 for PROMIS Global Physical Health Short Form (subpopulation norm for age category 18–34 years), 50.0 for PROMIS sleep measures [28], and 17.0 for WPAI [29]. [a]Five patients in the ravulizumab group were not working

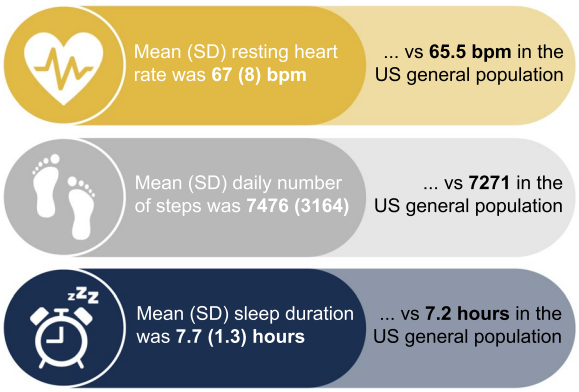

Fig. 2 Passively collected data in the REVEAL ravulizumab-treated cohort compared with the US general population. *bpm* beats per minute, *SD* standard deviation, *vs* versus

Resting heart rate for the ravulizumab cohort was similar on the day of infusion (66.8 [7.9] bpm) and in the 2 days before or after infusion (Fig. 3a). On the day of infusion, a slightly lower mean (SD) number of steps was recorded (6313 [4183]), but step count was comparable on the 2 days before or after infusion (Fig. 3b). There was also a slight decrease in sleep duration on the day of infusion to 7.5 (1.6) hours, but this increased to 8.3 (1.9) hours on the day after infusion (Fig. 3c).

Summary of correlations between activity data and PRO scores

Correlation between activity data and PRO scores are reported in Appendix 3: Table S3. In patients receiving ravulizumab, a higher number of daily steps showed weak positive correlation with PROMIS Global Physical Health (correlation coefficient $[r] = 0.119$; minimum false discovery rate $[q] < 0.05$) and PROMIS Global Mental Health scores ($r = 0.124$; $q < 0.05$). A lower resting heart rate showed weak positive correlation with PROMIS – Global Physical Health score ($r = 0.117$; $q < 0.05$). Increased sleep duration showed weak positive correlation with a better WPAI-SHP score ($r = 0.126$; $q < 0.05$). No meaningful correlations were identified between other activity measures or PRO scores ($r < 0.10$).

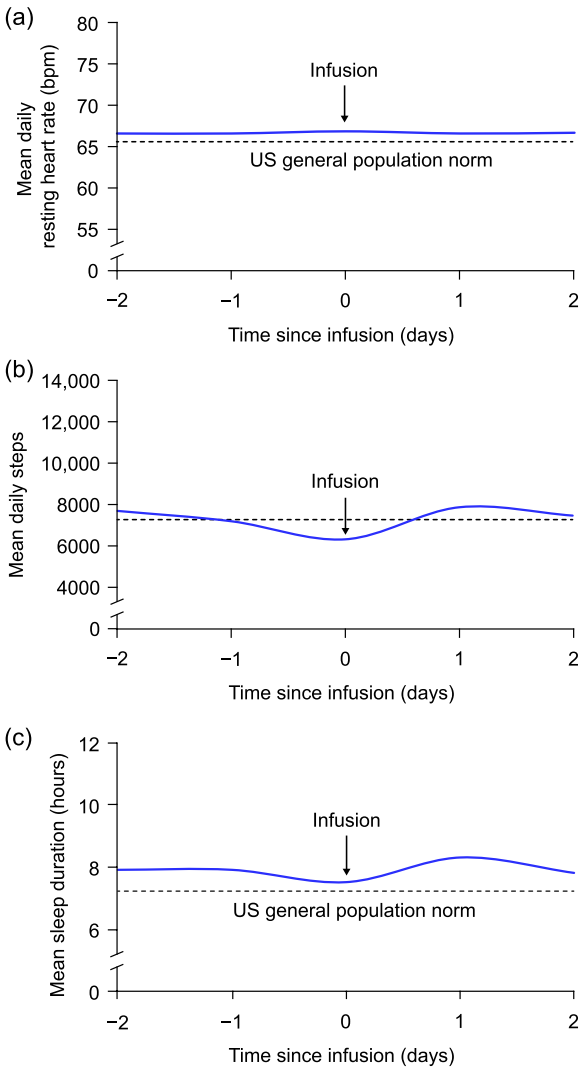

Fig. 3 Outcomes from −2 to + 2 days around infusion in patients with PNH treated with ravulizumab ($N = 28$). **a** Resting heart rate. **b** Daily step count. **c** Sleep duration. *bpm* beats per minute, *PNH* paroxysmal nocturnal hemoglobinuria, *SD* standard deviation, dashed lines represent US general population normative values. Data presented as locally estimated scatter plot smoother. Four patients were excluded from the analysis: two patients who withdrew and two who were considered to be outliers (daily number of steps > 2 SD from the mean). General population normative values: resting heart rate, range 50–80 bpm (mean 65.5 bpm) [30]; daily step count, 7271 [31]; sleep duration, mean (SD), 7.2 (1.0) hours [32]

Discussion

PNH is a debilitating disease, and the symptoms in untreated patients significantly affect QoL [2, 33]. The REVEAL study recruited 28 ravulizumab-treated patients with PNH and evaluated their daily activity via a digital device tracker and their QoL via electronic PRO surveys over a period of 32 weeks. To our knowledge, this is the first study to use digital monitoring technology to longitudinally evaluate outcomes in patients with PNH. The findings from the REVEAL study show that ravulizumab-treated patients with PNH who achieve good disease control (primarily indicated by lactate dehydrogenase levels within the near-normal range) demonstrate physical and mental health, fatigue, resting heart rate, daily activity, and sleep parameters that are within the range of US general population norms.

PRO scores collected for patients with PNH were compared with US general population normative values reported in the literature. A previous analysis of untreated patients with PNH reported mean FACIT-Fatigue scores of 33.4–35.9 [34], and another reported a score of 24 [33]. These low scores indicate a high general level of fatigue in untreated patients with PNH. In the current study of ravulizumab-treated patients, the mean FACIT-Fatigue score of 40.0 indicates fatigue levels consistent and comparable with the normative values reported for the US general population of individuals aged 30–39 years of 44.7 (for males) and 43.7 (for females). A previous study using patient data from the International PNH Registry estimated that a change in FACIT-Fatigue score of at least 5 was considered to be 'clinically important' in PNH [35]; the difference in the REVEAL cohort versus US general population is below this value, indicating that ravulizumab-treated patients with controlled disease do not have excess fatigue.

Where possible, this study conducted comparisons with age-matched cohorts. For PROMIS Global Physical and Global Mental Health measures, age-specific subpopulation norms were available [28], enabling comparison of the REVEAL cohort (median age 34 years) with a population of a similar age. A systematic review of studies estimating a meaningful change in PROMIS measures identified a threshold of between 2 and 6 points to indicate a minimal important change [36]. For PROMIS Physical Health and sleep measures, differences between the REVEAL cohort and general US population were < 2.0 points, indicating similarity to the US general population. For PROMIS Mental Health, the score in the REVEAL cohort was 51.0 vs 48.5 in the US general population (a difference of 2.5 points), indicating slightly better mental health in the REVEAL cohort, although given the small sample size this should be interpreted with caution.

To the authors' knowledge, this is the first study to look at the association between PRO scores and activity levels in PNH. For most measures, no correlation was identified between the PRO survey responses and activity data (Table S3). It was anticipated that sleep duration would correlate with both PROMIS sleep measures and with FACIT-Fatigue, but in all instances, correlation was negligible ($r = -0.017$ and $r = 0.051$ for PROMIS sleep measures and $r = -0.066$ for FACIT-Fatigue). This may be because fatigue scores, sleep scores and sleep duration in the ravulizumab-treated cohort were similar to those in the general US population. A lower resting heart rate and a higher daily step count during ravulizumab treatment were positively, albeit weakly, correlated with increased QoL (as measured using PROMIS Global Mental and Physical Health scores), and increased sleep duration showed weak positive association with better work productivity (measured using the WPAI-SHP). These findings show that in some instances PRO scores can reflect activity levels in patients with PNH, but further investigation and additional data collection are needed to support this point.

Using a digital activity-tracking device to monitor patient activity continuously enabled the evaluation of PNH symptoms in a novel, objective way and limited any potential perception bias that may be associated with survey data. The adherence rate (81%) for device wearing over the study period was high, which supports the feasibility of performing real-world digital health studies in patients with PNH. The longitudinal study design, including use of continuous monitoring and collection of weekly survey data, enabled evaluation of PRO and activity data over a long-term period. The use of continuous monitoring via the activity tracker also enabled collection of data on patient activity levels in relation to the day of ravulizumab infusion. This revealed some changes in both step count and sleep duration around the day of infusion. There was a numerical decrease in step count on the day of infusion compared with the days preceding and after the day of infusion, which likely reflects the minimum infusion time of 30–55 min for patients receiving maintenance ravulizumab doses of 3000–3600 mg [37]. Similarly, the slight decrease in sleep duration on the day of infusion may be related to disruption to the patients' daily life because of the infusion visit.

Evaluating the impact of PNH on work productivity is important, especially because the diagnosis of PNH is often rendered during the most productive years of life (consistent with the median age for diagnosis in this cohort of 28 years). Although the work impairment score was numerically higher (indicating greater impairment) in the REVEAL ravulizumab-treated cohort (22.0%) compared with individuals in the US general population aged 30–39 (17.0%), it is still considered to be within normal ranges, particularly as previous studies have estimated a minimal clinically important difference in the WPAI to be 15–20% in patients with psoriasis or psoriatic arthritis [38, 39]. Conversely, a previous cross-sectional survey found that work impairment in ravulizumab-treated patients with PNH was higher than in REVEAL, with 30.2% experiencing work productivity impairment [40]. Differences in study design are likely to contribute to the variance between our findings and prior reports; for instance, REVEAL studied patients over a 32-week period, and the survey-based study evaluated only a single time point for each patient. Patients in REVEAL were also considerably younger (median age: 34 years) than those in the aforementioned survey study (mean age: 48 years), which may explain some of these differences.

There are some limitations to the present study. First, owing to the lack of age- and sex-matched data, conclusions relating to comparisons against US general population normative values may be limited, although the REVEAL results were compared with individuals of a similar age within the general population when this data was available in the literature. Second, there is potential selection bias, because patients who were satisfied with treatment may have been more likely to participate. The patients in this study had generally good disease control, as indicated by lactate dehydrogenase levels within population normal ranges, and the fact that they were largely transfusion-independent. Therefore, findings from this study may not be applicable to patients managed in a broader population. Third, the PRO scores and data regarding baseline demographics and clinical characteristics were self-reported by participants and therefore may be prone to bias. Both the passively collected activity data and the self-reported data were within US general population ranges, indicating that the survey findings accurately reflected patients' experience. Finally, given the relatively small sample size, the data may not be representative of the wider PNH population; given that this was the first use of digital monitoring technology in this rare condition, it was expected that the sample size would be limited. The small sample size also precluded formal statistical comparisons.

Conclusion

The findings from REVEAL indicate that patients with PNH treated with ravulizumab reached quality of life scores (tiredness, sleep, and physical and mental health) that were within the range of the healthy US general population. A weak association was identified between patient-reported physical and mental health and daily physical activity levels; given the majority of PROs showed negligible correlation with activity levels, this is an area that needs further investigation. The study also supports the use of wearable devices for the collection of activity data in clinical trials for such patients.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12955-024-02279-2.

Additional file 1: Table S1. Full inclusion and exclusion criteria.

Additional file 2: Table S2. Study data collection schedule.

Additionsal file 3: Table S3. Correlation between PRO and activity data.

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Authors' contributions

EAG, JSM, WNL, JCY, YP, KJM, and DD made substantial contributions to study conception and design; EAG, JSM, WNL, JCY, YP, KJM, and DD contributed to analysis and interpretation of the data; EAG, JSM, WNL, JCY, YP, KJM, and DD drafted the article or revised it critically for important intellectual content; EAG, JSM, WNL, JCY, YP, KJM, and DD provided final approval of the version of the article to be published.

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Availability of data and materials

Alexion will consider requests for disclosure of clinical study participant-level data provided that participant privacy is assured through methods like data de-identification, pseudonymization, or anonymization (as required by applicable law), and if such disclosure was included in the relevant study informed consent form or similar documentation. Qualified academic investigators may request participant-level clinical data and supporting documents (statistical analysis plan and protocol) pertaining to Alexion-sponsored studies. Further details regarding data availability and instructions for requesting information are available in the Alexion Clinical Trials Disclosure and Transparency Policy at https://alexion.com/our-research/research-and-development. Link to Data Request Form: https://alexion.com/contact-alexion/medical-information.

Declarations

Ethics approval and consent to participate

The study protocol, informed consent form, recruitment materials and participant materials were reviewed and approved by the Western Institutional Review Board. All patients provided informed consent to participate in the study. Participation in the study was voluntary, and patients were free to withdraw at any time.

Consent for publication

Not required.

Competing interests

Elizabeth A. Griffiths receives honoraria/grant support and/or has relationships with AbbVie, Alexion, AstraZeneca Rare Disease, American Society of Hematology, Apellis, The Aplastic Anemia and MDS International Foundation, Celgene/BMS, CTI BioPharma, Genentech, MediCom Worldwide, Novartis, Physician Educational Resource, PicnicHealth, Taiho Oncology, and Takeda Oncology. Jae S. Min was an employee of and owned stock options in Evidation Health, Inc. at the time of the study. Wei-Nchih Lee is an employee of and owns stock options in Evidation Health, Inc. Jeffrey C. Yu, Yogesh Patel and Karl-Johan Myren are employees of and shareholders in Alexion, AstraZeneca Rare Disease. David Dingli receives honoraria from Alexion, AstraZeneca Rare Disease, Apellis, GSK, Janssen, Novartis, Osseum, Roche, Sanofi, and Takeda.

Author details

[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA. [2]Evidation Health, San Mateo, CA, USA. [3]Alexion, AstraZeneca Rare Disease, Boston, MA, USA. [4]Health Economics and Outcome Research, Alexion Pharmaceuticals, Inc., Stockholm, Sweden. [5]Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA.

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