Feasibility of electronic patient-reported outcome monitoring with self-instruction and symptom-based warnings in aplastic anemia and paroxysmal nocturnal hemoglobinuria – a pilot study

Sillas Bänziger1, Kimmo Weisshaar2, Reetta Arokoski3, Sabine Gerull4, Jörg Halter5, Alicia Rovo6, Mario Bargietz7, Jeroen Goede8, Yuliya Sentil9, Sabine Valenta10, Jakob R. Passweg1, Beatrice Drexlert1

1Division of Hematology, University Hospital Basel, 4031 Basel, Switzerland; 2Kiulu Health Ltd., Helsinki, Finland; 3Department of Hematology and Central Hematology Laboratory, Inselspital, Bern University Hospital, 3010 Bern, Switzerland; 4Division of Hematology, University Medical Clinic, Kantonsspital Aarau AG, 5030 Aarau, Switzerland; 5Division of Oncology and Haematology, Kantonsspital Winterthur, 8641 Winterthur, Switzerland; 6Nursing Science, Department Public Health, University of Basel, 4056 Basel, Switzerland

INTRODUCTION
Patient reported outcomes (PRO) are defined as any report of the status of a patient’s health condition that comes directly from the patient. PROs can be gathered electronically (ePRO), which has shown to be feasible with high levels of compliance for solid cancer (1, 2). It may not only collect data, but also monitor symptoms and send out messages directly to patients or clinicians if the response meets a pre-defined critical level. In cancer patients, ePROs systems have shown to be useful to flag symptoms which health providers regularly miss or downgrade (3) and several randomized controlled trials have even shown improvement in quality of life and other clinical outcomes compared to standard care (4, 5). It has also been demonstrated that this set-up can improve symptom management, treatment effectiveness, communication and the efficiency of clinical practice (6).

Based on the experience of ePRO systems in solid cancer, aplastic anemia (AA) and paroxysmal nocturnal hemoglobinuria (PNH) patients could be ideal candidates for the use of ePROs. Despite major improvements in therapies in the past decades, AA and PNH patients often remain symptomatic and are prone to disease relapse and severe complications. In this setting symptom-monitoring with ePROs may have the potential to detect life-threatening complications and symptoms earlier, improve the symptom management of patients and promote communication with the medical team. To date, ePROs have not been evaluated for AA and PNH.

This study aimed to examine whether the routine symptom monitoring including self-instructions and a warning system for patients with an ePRO application is feasible in AA and/or PNH in terms of recruitment, compliance, user experience and technical performance including patients’ and clinicians’ perspective.

RESULTS
We asked 14 patients to participate in the study. Five patients were excluded due to a lack of motivation (n=4, 29%) or poor German language skills (n=1, 7%). Nine patients were enrolled, resulting in a recruitment rate of 64%. Median age was 35 years (IQR 29-56), whereby more females (n=6, 67%) than males (n=3, 33%) were included in the study. Five patients were diagnosed with AA, three with PNH and one with overlapping AA/PNH.

A total of 234 weekly reminders were sent and 168 questionnaires completed, resulting in a 72% questionnaire adherence rate. Figure 1 illustrates the monthly adherence rate, showing a decreasing rate from 91% (month 1) to 53% (month 6) over the total study period. Figure 2 demonstrates all reported symptoms for AA and PNH, respectively. A total of 331 symptoms were reported, of which 154 (47%) were classified as mild, 95 (29%) as moderate and 82 (25%) as severe. The most common reported symptom was fatigue in AA (44 entries) as well as in PNH (43 entries). Severe symptoms led to 36 alerts being sent out to the treating physicians. These alerts did not lead to additional physician contacts or admissions of the patients. In addition to the predefined symptom questions, additional symptoms reported were nausea, cough, itching and chest pressure.

Patients did not report any technical problems or concerns on data security. The application was mostly accessed by smartphone (n = 7, 78%). Overall, the usability of the application was rated as “easy to use” while the symptom questionnaire was classified as “easy to understand” by all patients. All patients reported to be satisfied with the app. While 7 patients (78%) would continue to use the app, 2 patients (22%) would stop using it.

The medical team described the application as “easy to use”. More than half of the medical team members (n = 4, 57%) reported a benefit from the tool. The main feedback by the medical team was that the tool should be integrated into the hospital information system and clinic workflow for an optimal usage.

CONCLUSION
• Similar to other ePRO studies (2, 7) patients’ adherence to the weekly symptom questionnaire was good (72%), with the highest rates at the beginning (91%) and a steadily decreasing rate over the six months (to 53%). The main reasons for patients missing entries were forgetting about the application, being too busy or symptom-free.

• The warning system, which sent out an alert to the patients and alerts to the medical team in case of severe symptoms, did not result in additional hospital admissions. This could be explained by the fact that the patients in the study had a long disease history (median duration: 9 years), implying significant experience in managing their symptoms. Consequently, this tool might have a bigger impact on AA/PNH patients in their early disease journey as they learn to better manage their symptoms.

• The user experience was very positive. Most patients and clinicians would continue to use the application and the medical team regarded the tool as a useful addition to the routine management. However, physicians and nurses mentioned the key necessity of integrating the ePRO tool into the hospital information system and standard clinical workflow, as described in previous work (6). This may further improve the communication between the patients and their medical teams and thereby increase patient adherence (8).

• The result can also be seen as a valuable resource to further improve ePRO tools for this patient group but can also be used as an impetus to translate patient-centered workflows to other hematological diseases and provide further support for general implementation of ePRO applications in routine hematologic practice.

• Due to the small sample size, adherence rates may have been overestimated and the symptoms reported cannot be generalized. A randomized controlled trial with a larger patient population is needed to evaluate the impact of ePRO on clinical outcomes of AA and PNH patients.

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Contact:
Beatrice Drexlert MD
Petersgraben 4
4031 Basel
Switzerland
Beatrice.Drexlert@usb.ch
Silas Baenziger
Silas.Baenziger@unibas.ch

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