Unraveling Fatigue in Hemodialysis Patients

Citation for published version (APA):

Brys, A. DH., Stifft, F., Van Heugten, C. M., Bossola, M., Gambaro, G., & Lenaert, B. (2020). Unraveling Fatigue in Hemodialysis Patients: comparing retrospective reports to real-time assessments with an mHealth Experienced Sampling Method. *Journal of Pain and Symptom Management*, 60(6), 1100-1108.e2. <https://doi.org/10.1016/j.jpainsymman.2020.06.042>

Document status and date:

Published: 01/12/2020

DOI:

[10.1016/j.jpainsymman.2020.06.042](https://doi.org/10.1016/j.jpainsymman.2020.06.042)

Document Version:

Publisher's PDF, also known as Version of record

Document license:

Taverne

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

Original Article

Unraveling Fatigue in Hemodialysis Patients: Comparing Retrospective Reports to Real-Time Assessments With an *mHealth* Experienced Sampling Method

Astrid D.H. Brys, MD, Frank Stiff, MD, Caroline M. Van Heugten, PhD, Maurizio Bossola, MD, Giovanni Gambaro, MD, PhD, and Bert Lenaert, PhD

Faculty of Psychology and Neuroscience (A.D.H.B., C.M.V.H., B.L.), Department of Neuropsychology and Psychopharmacology, Maastricht University, Maastricht; Division of Nephrology (A.D.H.B., F.S.), Department of Internal Medicine, Zuyderland Medical Centre, Sittard-Geleen, The Netherlands; Divisione di Nefrologia (A.D.H.B.), Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma; Università Cattolica del Sacro Cuore (A.D.H.B., M.B., G.G.), Roma, Italy; School for Mental Health and Neuroscience (C.M.V.H., B.L.), Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht; Limburg Brain Injury Centre (C.M.V.H., B.L.), Maastricht, The Netherlands; Hemodialysis Unit (M.B.), Università Cattolica del Sacro Cuore, Rome; and Division of Nephrology (G.G.), University Hospital of Verona, Verona, Italy

Abstract

Context. Fatigue is prevalent among hemodialysis (HD) patients and associated with depressive mood. To advance our understanding of its etiology and develop appropriate treatments, reliable measurement instruments are needed. However, conventional fatigue and mood questionnaires are prone to bias because of their retrospective nature and may misrepresent or overestimate actual symptom experience (i.e., the so-called memory-experience gap). Experience sampling methodology (ESM) overcomes this limitation through repeated real-time assessments in patients' natural environment, thereby providing reliable and ecologically valid data.

Objectives. We investigated to what extent retrospective symptom reporting accurately represents real-time experiences of fatigue and mood in HD patients using an ESM mobile Health application (PsyMate™; smartHealth GmbH, Luxembourg).

Methods. Forty HD patients used the PsyMate for one week to assess real-time fatigue and mood. In addition, they retrospectively evaluated their symptom experience completing end-of-day and end-of-week questionnaires as well as the conventional Fatigue Severity Scale and Hospital Anxiety and Depression Scale.

Results. Results of real-time observations ($N = 1777$) showed that fatigue and mood varied *between* and *within* individuals. Retrospective end-of-week fatigue evaluation was significantly higher than the average real-time fatigue score; $t(38) = 3.54$, $P = 0.001$, and $d = 0.57$. Fatigue Severity Scale and Hospital Anxiety and Depression Scale correlated moderately to strong with the average ESM score for fatigue and mood: $r = 0.66$ and $r = 0.77$, respectively.

Conclusion. Retrospective fatigue assessment may lead to overestimation of real-time symptom experience. ESM provides detailed insight and personalized information about symptom experiences, which may be crucial for the design of more targeted and personalized interventions for fatigue and mood problems in HD patients. *J Pain Symptom Manage* 2020;60:1100–1108. © 2020 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

Key Words

mHealth, ESM, measurement instrument, fatigue, depressive symptoms, hemodialysis

Address correspondence to: Astrid D.H. Brys, MD, Hemodialysis Unit, Università Cattolica del Sacro Cuore, Largo A. Gemelli, 8, 00168 Rome, Italy. E-mail: astrid.brys@unicatt.it

Accepted for publication: June 25, 2020.

Introduction

Fatigue, with a prevalence range of 40%–80%, is one of the most prioritized outcomes among hemodialysis (HD) patients and greatly impacts their health-related quality of life.^{1,2} Among biological, psychological, and social variables under investigation, so far only a solid association between fatigue and depressive mood has been demonstrated.^{3–5} Moreover, reliable measurement instruments to assess fatigue in HD patients are lacking.⁴ This further impedes the development of appropriate therapies.

Conventional measurement instruments, such as the commonly used Fatigue Severity Scale (FSS), are limited in their clinical applicability in that they only provide a general picture of fatigue severity without giving detailed insight in diurnal variations and related factors in daily life, which may contribute to variability in fatigue. In addition, their reliability to measure symptom fluctuation over time may be questionable as there is report of a high level of faked compliance because of backfilling of retrospective paper diaries.⁶ Perhaps even more importantly, conventional questionnaires are prone to memory bias because of their retrospective nature and may therefore misrepresent actual symptom experience. For instance, retrospective symptom reports have been shown to overestimate actual symptom experience in various clinical populations (i.e., the so-called memory-experience gap).⁷ Furthermore, symptom recall may be influenced by symptom variability and intensity during recall as well as by emotional states at the time of recall or during symptom experiences. Longer time intervals between symptom experience and recall may also affect accuracy. Accurate recall may be further impacted by cognitive heuristics used by patients, such as the peak-end effect where more importance is given to more intense or more recent experiences.^{8,9}

The experience sampling methodology (ESM) resolves these constraints by repeatedly measuring symptoms and potential contributing factors, such as behavioral, psychological, and social variables, in-the-moment (i.e., momentary) and in patients' natural environments in the flow of daily life.¹⁰ In a way, ESM captures the film rather than an instantaneous photograph of patients' symptom experiences in daily life. Therefore, ESM not only allows to identify informative variability in symptoms and factors related to that variability but also overcomes ecological and recall bias. Moreover, digitalized ESM, such as an ESM mobile Health (*mHealth*) application, using time stamps may reduce faked compliance and can be easily integrated in patients' daily lives.⁶

Because conventional retrospective questionnaires are often used to inform diagnostic and therapeutic decisions, it is relevant to better understand how retrospective symptom reports correspond to actual day-to-day experiences. Previous studies comparing ESM and retrospective questionnaires for symptoms, such as pain, fatigue, or dyspnea in somatically ill subjects (e.g., rheumatoid arthritis, stroke, irritable bowel syndrome), psychiatric patients (e.g., schizophrenia), and healthy individuals, have shown that retrospective symptom reports often overestimate the intensity of the experienced symptoms, which support the aforementioned memory-experience gap.^{8,9,11–14} Moreover, some studies demonstrated a peak-end effect for retrospective pain evaluation but not (consistently) for fatigue. Furthermore, a number of studies investigated fatigue and its course in HD patients' daily life using an ESM technique.^{5,15–18} They mainly showed that fatigue is dynamic, changes over time, and may be determined by mood or contextual variables, such as activities, social company, or location. However, none of these studies reported a comparison between momentary assessments and conventional retrospective evaluation of fatigue.

Therefore, we designed a study to investigate the relationship between momentary assessments and retrospective reporting of fatigue in HD patients. To this end, we collected real-time symptom reports using an *mHealth* ESM application during seven consecutive days; as well as retrospective symptom reports during the same period at the end of every day and finally at the end of the week. This allowed us to investigate the time period after which differences (if any) between momentary and retrospective reports occur. In addition, we collected the FSS and Hospital Anxiety and Depression Scale (HADS) to assess to what extent conventional retrospective evaluation of fatigue and mood correlated to real-time assessments; and whether individuals scoring below or above these conventional measures' cutoff scores also differed in their symptom experience in daily life.

The primary aim of this study was to investigate how retrospective reports and conventional measurement instruments for fatigue and mood correspond to the actual day-to-day symptom experiences. The secondary aim was to explore which aspect of momentary fatigue and mood is best captured by retrospective evaluation: the average, the highest level (peak) or the most recent score (end). Finally, we explored to what extent mood may be related to a memory-experience gap in fatigue experience in HD patients given that previous research showed a positive relationship between negative affect and subjective symptom reporting.¹⁹

Materials and Methods

Study Population and Design

Between July and August 2019, patients receiving HD for at least six months at the HD units of Zuyderland Medical Center in Sittard and Heerlen, The Netherlands, were enrolled in this prospective observational study. Exclusion criteria were younger than 18 years, insufficient understanding of the Dutch language compromising participation in the study based on clinical judgment, patients unable to handle the *mHealth* application independently because of hearing problems, vision problems or insufficient (cognitive) skills based on clinical judgment by the attending physician, patients with diagnosed dementia, chronic fatigue syndrome, fibromyalgia, or actual instability of their clinical condition requiring hospitalization. All patients gave written informed consent, and the study protocol was approved by the institutional review board (medical ethical committee of Zuyderland Medical Center [METCZ20190078]) and registered NCT04049773 (clinicaltrials.gov).

Symptom Assessment

Experience Sampling Method. To assess real-time fatigue and mood (e.g., feeling cheerful, relaxed, satisfied, or confident to express positive affect and feeling anxious, down, irritable, or powerless as an expression of negative affect, respectively) in daily life, a digital ESM was used by means of the PsyMate™ (smartHealth GmbH, Luxembourg). The PsyMate is a user-friendly smartphone-based *mHealth* application

developed by Maastricht University and Maastricht UMC+ (www.psymate.eu) to implement ESM in clinical practice.²⁰

During seven consecutive days, the PsyMate gave 10 auditory (beep) signals at random time points throughout the day between 6.30 AM and 10.30 PM. Beeps were separated by at least 15 minutes. At each beep, patients were requested to complete a short self-report questionnaire of 25 items on their smartphone including statements about momentary fatigue and mood, using a seven-point Likert scale ranging from one (not at all) to seven (very much) (Appendix Table 1; Fig. 1). Whenever patients gave a score of two or higher to the general statement *I feel tired*, two additional questions were presented: *I feel mentally tired* and *I feel physically tired*. Fifteen minutes after each beep signal, the questionnaire was shut down and registered as missing data if it was not filled in. The administered set of questions was based on a preset questionnaire applied in previous studies, using the PsyMate application in other clinical populations.^{21–23} These studies demonstrated good internal consistency of the items to measure mood and self-reported symptoms. They also demonstrated the capacity of the PsyMate to capture between and within person's variability of symptoms, mood, and behavior over time.

Retrospective Electronic Questionnaires. Patients completed a short self-report morning and end-of-day questionnaire in the PsyMate application as soon as they woke up or prior going to bed, respectively,

Fig. 1. PsyMate interface representation of experience sampling methodology questionnaire.

during the same week. In these questionnaires, patients retrospectively evaluated, on a seven-point Likert scale, their sleep quality during the previous night and overall experienced fatigue and mood during the preceding day, respectively (e.g., *Overall, I felt tired today*; *Overall, I felt tense today*) (Appendix Table 2).

Retrospective Paper Questionnaires

On the last study day, patients completed a paper questionnaire that was visually identical to the electronic PsyMate interface but now requested participants to retrospectively evaluate their fatigue (general, mental, and physical) during the past seven days. Moreover, patients completed conventional retrospective questionnaires measuring fatigue, anxiety, and depressive symptoms.

The FSS is a nine-item questionnaire assessing fatigue severity in daily life during the past week and uses a seven-point Likert scale. The total score is calculated by averaging the scores of the individual item responses. Individual item scores can range from 1 to 7 (no to maximum fatigue). A total FSS score of ≥ 4 is considered as indicative of problematic fatigue.²⁴ The FSS is one of the most frequently used instruments to evaluate fatigue in renal patients.⁴

The HADS is developed to assess depressive symptoms and anxiety during the past week in somatically ill patients.²⁵ Both subscales for depression and anxiety range from 0 to 21. Scores of ≥ 8 possibly indicate a clinical depression or anxiety disorder. The HADS has been validated in HD patients.^{26,27}

Baseline Data and Laboratory Measurements

Demographical, clinical, and laboratory data were obtained from computerized medical records at the hospital.

HD Treatment

Conventional HD technique was used except for four patients who were on hemodiafiltration. Participants underwent dialysis treatment with bicarbonate dialysate three times weekly either in sessions during daytime (three to four hours) or at night (six to seven hours). Arterial blood flow was 300–400 mL/minute during daytime treatment and 150–200 mL/minute during overnight dialysis. Dialysis rate flow was 400–600 mL/minute for day treatment and 300 mL/minute overnight. Most patients received regular treatment with recombinant human erythropoietin, antihypertensive medications, vitamin D analogues, as well as phosphate and potassium binders.

Study Procedure

The general procedure has been previously described in detail.¹⁸ In brief, after a briefing session, patients used the PsyMate application for one week to rate their momentary fatigue and mood as well as the retrospective morning and end-of-day questionnaires. Retrospective paper questionnaires were completed at the end of the study week during patients' regular HD treatment (Fig. 2).

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp, Armonk, NY). Data are reported as mean $\pm$ SD or median (range) as appropriate. Each participant received a maximum of 70 momentary PsyMate questionnaires during the entire study week (seven days of 10 beeps). For each patient, three indices of momentary fatigue were calculated from these data: 1) the *average fatigue score* of all completed ESM observations to capture average momentary fatigue; 2) the *average fatigue score on the last day* to capture most recent momentary fatigue; and 3) the *maximum fatigue score* during the entire study week to capture peak momentary fatigue. The same three indices were calculated for negative affect (i.e., average score of feeling anxious, down, irritable, and powerless). To investigate differences between retrospective and momentary fatigue reports, paired samples t-tests were used to compare patients' average ESM fatigue score with their average retrospective end-of-day fatigue score and their retrospective end-of-week fatigue score, respectively. To assess whether patients with an FSS score or an HADS score indicative of possible clinical significant fatigue or depression or anxiety disorder, respectively, had a higher average score of momentary fatigue or negative affect, independent-samples t-tests were used with a score of four (FSS) and eight (HADS subscale) as specified cut point. To investigate which index of momentary fatigue or negative affect best corresponded to the total score of the conventional retrospective FSS and HADS questionnaires, respectively, correlation analyses were carried out. Finally, linear regression analysis (backward stepwise method; 0.05 significance level) was carried out to explore potential predictors of the difference between momentary and retrospective reports.

A sample size of 34 participants was required to detect a medium or larger effect size (Cohen's $d \geq 0.50$) with alpha error probability of 0.05 and power of 80% regarding our first study aim. Moreover, ESM data have multilevel structure, with observations (Level 1) nested within individuals (Level 2). The richness of data obtained by conducting multiple

Fig. 2. Study procedure flowchart.

observations nested within individuals allowed to carry out reliable statistical estimations in relatively small samples.

Results

Sample Characteristics

Forty-two patients (33 males; 77.5%) enrolled in this study. Two patients were excluded from the analyses conform ESM guidelines because they completed less than 30% of all PsyMate questionnaires.²⁸ The mean age of our sample was 64.35 (SD = 13.69) years. Table 1 reports demographical and clinical characteristics. A total of 1777 ESM PsyMate questionnaires were completed, averaging to 44 of 70 questionnaires per patient (63% compliance and 97% completion rate). The average number of completed ESM questionnaires per day was 254 (range 236–300). The median time needed to complete one ESM questionnaire was 1:21 minutes (interquartile range 1:09–2:29). One patient did not complete the end-of-day ESM questionnaires. Another patient did not return the end-of-week retrospective paper questionnaires.

Momentary Fatigue and Mood Assessments. At the level of the ESM questionnaires, average momentary fatigue on a 1–7 scale was 3.36 (SD = 1.97; range 1.00–7.00). Patients responded two or higher to the general statement *I feel tired* in 1209 completed ESM questionnaires, which means that patients indicated to experience at least some fatigue in 68% of all momentary observations. Average physical fatigue was 4.26 (SD = 1.61; range 1.00–7.00), and average mental fatigue was 2.71 (SD = 1.60; range 1.00–7.00). The large SDs and range of observed fatigue scores indicate substantial variability in fatigue scores *between* patients. Moreover, fatigue scores also varied considerably *within* individuals over time. This is reflected by within-individual SDs (i.e., variation in the fatigue scores of the same individual) and the large variability therein. The mean within-individual SD of fatigue was 1.04 (SD = .52; range 0.00–2.50). Average momentary positive and negative affect score was 5.32 (SD = 1.30; range 1.00–7.00) and 1.75 (SD = 1.01; range 1.00–6.50), respectively. The mean within-individual SD for positive and negative affect was 0.67 (SD = .33; range 0.00–2.10) and 0.46 (SD = .28; range 0.00–1.31), respectively. Again, this

indicates that mood varied *between* as well as *within* patients. The average momentary negative affect score correlated significantly with the average momentary fatigue score ($r = 0.63$; $P \leq 0.001$). Average sleep quality was 4.92 (SD = 1.83; range 1.00–7.00).

Retrospective Fatigue and Mood Assessments. Mean fatigue scores on the retrospective end-of-day and end-

Table 1
Participants' Baseline Characteristics (N = 40)

Characteristics	Mean $\pm$ SD (Range)/n (%)
Demographical & clinical characteristics	
Age (yrs)	64.4 $\pm$ 13.7 (34–84)
Sex (male)	31 (77.5)
BMI (kg/m ²)	27.9 $\pm$ 5.9
Charlson Comorbidity Index	2.7 $\pm$ 1.6 (0–6)
Primary kidney disease	
Hypertension	8 (20)
Glomerulonephritis	2 (5)
Diabetes	13 (32.5)
Interstitial nephritis	0 (0)
Polycystic kidney disease	6 (15)
Other/unknown	11 (27.5)
Dialysis vintage (months)	49 $\pm$ 47
Diuresis/residual urine output	14 (35)
Diuresis/residual urine output (mL/24 hours) ^a	1044 $\pm$ 687
Interdialytic weight gain (kg) ^b	1.6 $\pm$.7
UF rate mL/hour/kg (n = 34) ^c	4.35 $\pm$ 2.23
Anuric patients (n = 26)	4.50 $\pm$ 2.34
Nonanuric patients (n = 8)	3.87 $\pm$ 1.93
Day HD treatment (n = 25)	4.82 $\pm$ 2.34
Night HD treatment (n = 9)	3.06 $\pm$ 1.28
HD access	
Arteriovenous fistula	30 (75)
Arteriovenous graft	3 (7.5)
Central venous catheter	7 (17.5)
Dialysis group (dialysis hours/treatment)	
Morning (3.5–5.0 hours)	18 (45)
Afternoon (4.0 hours)	8 (20)
Evening (4.0 hours)	4 (10)
Night (7–7.25 hours)	10 (25)
Laboratory characteristics	
SpKt/V	1.6 $\pm$.3
Hemoglobin (mmol/L)	7.0 $\pm$.6
Serum albumin (g/L)	39.8 $\pm$ 3.4
Serum creatinine (μ mol/L)	922.8 $\pm$ 260.8
Serum urea (mmol/L)	23.6 $\pm$ 4.9
Parathyroid hormone (pmol/L)	37.8 $\pm$ 26.6
Calcium (mmol/L)	2.3 $\pm$.1
Phosphorus (mmol/L)	1.7 $\pm$.5
C-reactive protein (mg/L)	9.4 $\pm$ 9.8

BMI = body mass index; UF = ultrafiltration; HD = hemodialysis; spKt/V = urea clearance.

^aExcluding anuric patients (n = 26).

^bIn patients with target weight (n = 34).

^cExcluding patients without UF.

of-week questionnaires were 3.44 (SD = 1.84; range 1.00–7.00) and 3.82 (SD = 2.02; range 1.00–7.00), respectively. The average FSS score was 4.99 (SD = 1.17; range 2.10–7.00). Thirty (77%) patients had an FSS score of four or higher, potentially indicative of clinically significant fatigue.²⁴ The average HADS depression subscale score was 4.15 (SD = 3.81; range 0.00–16.00) and 4.54 (SD = 3.63; range 0.00–14.00) for the anxiety subscale. Eight patients (21%) scored eight or higher on the HADS depression subscale, and nine individuals (23%) scored eight or higher on the HADS anxiety subscale, indicating the possible presence of a depressive or anxiety disorder, respectively.²⁵

Comparison Between Momentary Ratings and Retrospective Questionnaire Scores. Retrospective end-of-week fatigue scores (mean [M] = 3.82; SE = 0.32) were, on average, higher than the mean of patients' momentary fatigue scores during the preceding study week (M = 3.31; SE = 0.26). This difference of 0.51 (95% CI [0.22, 0.80]) was statistically significant $t(38) = 3.54$, $P = 0.001$, and represented an effect size of $d = 0.57$. The average retrospective end-of-day fatigue score for each individual (M = 3.42; SE = 0.24) was also higher than the average momentary fatigue scores during the entire study week (M = 3.29; SE = 0.16). However, this difference of 0.13 (95% CI [−0.12, 0.38]) was not significant, $t(38) = 1.07$, $P = 0.291$, and $d = 0.17$.

Patients with an FSS ≥ 4 had an average momentary fatigue score during the entire study week (M = 3.64; SE = 0.31) that was significantly higher compared with subjects with an FSS score of <4 (M = 2.22; SE = 0.25); $t(31.457) = 3.56$, $P = 0.001$, and 95% CI (0.61, 2.24).

Patients with an HADS depression subscale of ≥ 8 had an average negative affect score during the entire study week (M = 2.74; SE = 0.24) that was significantly higher compared with patients with an HADS depression score of <8 (M = 1.46; SE = 0.12); $t(10.808) = 4.67$, $P = 0.001$, and 95% CI (0.67, 1.87). Likewise, patients with an HADS anxiety subscale of ≥ 8 had an average negative affect score during the entire study week (M = 2.75; SE = 0.30) that was significantly higher compared with individuals with an HADS anxiety score of <8 (M = 1.42; SE = 0.10); $t(9.826) = 4.20$, $P = 0.002$, and 95% CI (0.62, 2.04).

ESM Indices and Retrospective Questionnaires. Table 2 reports correlations between the conventionally used retrospective FSS and HADS and the ESM indices of momentary fatigue and negative affect, respectively. Correlations are strongest for the average of all momentary fatigue and negative affect scores.

Potential Predictors of the Fatigue Memory-Experience Gap.

The difference between end-of-week fatigue ratings and the average of momentary fatigue scores during the preceding study week did not significantly correlate with the average of ESM negative affect scores during the study week, ($r = 0.09$; $P = 0.583$). In a multiple linear regression analysis, neither maximum or average ESM negative affect score, nor maximum or average ESM fatigue score, gender or age predicted the difference between retrospective end-of-week fatigue score and the average of momentary fatigue scores (all P s > 0.05).

Discussion

This is the first study investigating to what extent retrospective reports for fatigue and mood in HD patients correspond to their moment-to-moment and day-to-day symptom experiences assessed with an experience sampling method in an *mHealth* application.

First, our results may suggest that HD patients' retrospective evaluation of fatigue symptoms overestimates their real-time symptom experience. These results are in line with previous studies reporting a memory-experience gap for symptoms, such as fatigue and pain, in other clinical populations.^{9,11–14} Our results showed that the memory-experience gap increased as time passed between retrospective symptom evaluation and actual symptom experience. This accords with the theoretical position that momentary assessments and retrospective memory reports may draw information from different sources, resulting in potentially discrepant response patterns. Momentary symptom assessments may primarily reflect information from an experiencing self in a here-and-now context.⁷ In contrast, retrospective reports rely on information from our autobiographical episodic memory, where experiences from a proximal past are processed. It has been suggested that information from this remembering self may prioritize functionality over accuracy in reflecting on past experience.²⁹ For instance, remembering situations in which fatigue was higher or at its peak may be more useful (or functional) than remembering every single moment of a certain experience. As such, autobiographical memories of symptom experience may be biased to experiences that are more relevant to guide future behavior, rather than accurately represent the past experience.²⁹ Furthermore, information about experiences in a more distal past may be influenced by semantic memory, which reflects personal beliefs and views on health and disease in general (e.g., I am always tired and there is nothing I can do about it).⁷ Understanding how symptom experiences are processed and consolidated in memory may help to elucidate the

Table 2
Pearson Correlations Between Total Scores of the FSS and HADS on the One Hand and Indices for Real-Time Momentary Fatigue and Negative Affect Feelings on the Other Hand, Derived From Data Collected Using ESM (N = 39)

Questionnaire	Average ESM Fatigue	Average ESM Fatigue Last Day	Maximum ESM Fatigue
FSS			
<i>R</i>	0.66	0.65	0.53
CI	0.49, 0.80	0.47, 0.80	0.28, 0.71
<i>P</i>	<0.001	<0.001	0.001
<i>N</i>	39	39	39
	Average ESM Negative Affect	Average ESM Negative Affect Last Day	Maximum ESM Negative Affect
HADS			
Depression subscale			
<i>R</i>	0.74	0.74	0.59
CI	0.57, 0.89	0.57, 0.88	0.36, 0.79
<i>P</i>	<0.001	<0.001	<0.001
<i>N</i>	39	39	39
Anxiety subscale			
<i>R</i>	0.77	0.75	0.68
CI	0.55, 0.90	0.52, 0.89	0.41, 0.83
<i>P</i>	<0.001	<0.001	<0.001
<i>N</i>	39	39	39

FSS = Fatigue Severity Scale; HADS = Hospital Anxiety and Depression Scale; ESM = experience sampling methodology; CI = bias corrected and accelerated bootstrap 95% CIs.

discrepancies observed between momentary and retrospective reports of symptom experience. The memory-experience gap for fatigue symptoms observed in this study sample was not related to negative affect or cognitive heuristics, such as a peak-end effect. Neither could fatigue severity, negative affect, age nor gender predict the memory-experience gap for fatigue in this HD population. Future research might consider investigating the relationship with cognitive capacity or catastrophizing about symptoms.³⁰ However, to the extent that momentary assessments and retrospective memory reports do indeed reflect information from different sources (i.e., experiencing vs. remembering self), which may have a different function (e.g., accuracy vs. guidance of future behavior) explaining discrepancies between memory and experience may not be necessary all together. Alternatively, it is possible that participants completed less surveys on days or moments when they felt worse because of the potential burden associated with completing multiple surveys a day. This might then result in an underestimation of symptom severity based on ESM reports. Future ESM studies could benefit from the inclusion of a poststudy interview to assess this potential bias.

Second, correlation coefficients of the FSS and HADS with the averages of momentary assessments of fatigue and mood ranged from 0.66 to 0.77. These correlations show that conventionally used retrospective measurement instruments are moderately to strongly related to daily life experience of fatigue and mood in HD patients. However, we found that momentary fatigue and mood scores varied *between* as well as *within* individuals over time. This within-individual variability in fatigue and mood over time

cannot be captured by conventional retrospective questionnaires. Nevertheless, this type of information may be especially relevant to design and implement personalized interventions. That is, insight in diurnal symptom patterns and factors related to these patterns may be crucial for effective treatment of fatigue. For instance, fatigue may be lower during certain types of activities for some individuals but higher for others or may be temporally related to changes in mood for some but not for others. Such highly personalized information provided by ESM may be crucial for successful alleviation of symptoms. For instance, in a recently conducted randomized controlled trial in depressed outpatients, ESM-derived personalized feedback led to a significant and clinically relevant decrease of depressive symptoms.³¹

Taken together, momentary and retrospective symptom assessments may reflect different types of information. Therefore, they may complement rather than replace each other and can be used for different types of outcomes. For instance, diagnostic decision making and treatment follow-up may benefit more from ESM-based self-reports as they enable to capture moment-to-moment symptom variation and provide insights in related contextual variables (e.g., location, activity, company, time of day), which may be used as entry points for tailored and personalized interventions. In contrast, retrospective symptom assessment may be more relevant when the focus of interest is understanding treatment adherence or patients' illness behavior.^{7,32}

Major strengths of this study include the use of an *mHealth* application to collect reliable and ecologically valid data, with a 15-minute time frame to control for

faked compliance and reduce potential recall bias; and the comparison of momentary assessments with an *mHealth* ESM and conventionally used retrospective questionnaires. Limitations include a potential selection bias because of a certain level of cognitive capacities needed to use the *mHealth* application. Moreover, careful item selection and reduction of questions may further reduce patients' burden. Promisingly, preliminary work to develop a valid and reliable patient-reported outcome measure for fatigue in HD patients that takes into account different dimensions of fatigue in HD patients has been done in 2016 by the Standardized Outcomes in Nephrology initiative's working group for fatigue in HD patients.³³ When such a patient-reported outcome measure would be incorporated in an *mHealth* ESM, it may have the potential to become a valid and reliable measurement instrument to accurately assess fatigue in HD patients. As such, it may provide concrete entry points to develop personalized and targeted interventions to alleviate fatigue symptoms and improve HD patients' quality of life. Finally, this study may have a restricted representativeness because of the imbalance between male and female participants, notwithstanding a gender imbalance of 60% men receiving HD in European countries, including The Netherlands.³⁴

In conclusion, we found that retrospective symptom evaluation led to higher fatigue reporting relative to real-time momentary fatigue experiences. Moreover, momentary assessments of fatigue and mood revealed important variance in symptoms between individuals and within individuals (over time), which cannot be captured by conventional retrospective measurement instruments. Therefore, we recommend that future research investigating fatigue in HD patients and variability therein in daily life should make use of the ESM rather than—or at least in addition to—retrospective measurement instruments.

Disclosures and Acknowledgments

The authors gratefully thank the patients, involved in this study, and the renal teams of Zuyderland Medical Center in Sittard-Geleen and Heerlen for assistance with recruitment and data collection. This research received no specific funding/grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors declare no conflicts of interest.

References

1. Jhamb M, Argyropoulos C, Steel JL, et al. Correlates and outcomes of fatigue among incident dialysis patients. *Clin J Am Soc Nephrol* 2009;4:1779–1786.

2. Urquhart-Secord R, Craig JC, Hemmelgarn B, et al. Patient and caregiver priorities for outcomes in hemodialysis: an international nominal group technique study. *Am J Kidney Dis* 2016;68:444–454.
3. Jhamb M, Weisbord SD, Steel JL, Unruh M. Fatigue in patients receiving maintenance dialysis: a review of definitions, measures, and contributing factors. *Am J Kidney Dis* 2008;52:353–365.
4. Artom M, Moss-Morris R, Caskey F, Chilcot J. Fatigue in advanced kidney disease. *Kidney Int* 2014;86:497–505.
5. Brys ADH, Lenaert B, Van Heugten CM, Gambaro G, Bossola M. Exploring the diurnal course of fatigue in patients on hemodialysis treatment and its relation with depressive symptoms and classical conditioning. *J Pain Symptom Manage* 2019;57:890–898.e4.
6. Stone AA, Shiffman S, Schwartz JE, Broderick JE, Hufford MR. Patient compliance with paper and electronic diaries. *Control Clin Trials* 2003;24:182–199.
7. Van den Bergh O, Walentynowicz M. Accuracy and bias in retrospective symptom reporting. *Curr Opin Psychiatry* 2016;29:302–308.
8. Walentynowicz M, Bogaerts K, Van Diest I, Raes F, Van den Bergh O. Was it so bad? The role of retrospective memory in symptom reporting. *Health Psychol* 2015;34:1166–1174.
9. Schneider S, Stone AA, Schwartz JE, Broderick JE. Peak and end effects in patients' daily recall of pain and fatigue: a within-subjects analysis. *J Pain* 2011;12:228–235.
10. Shiffman S, Stone AA, Hufford MR. Ecological momentary assessment. *Annu Rev Clin Psychol* 2008;4:1–32.
11. Lenaert B, Neijmeijer M, van Kampen N, van Heugten C, Ponds R. Poststroke fatigue and daily activity patterns during outpatient rehabilitation: an experience sampling method study. *Arch Phys Med Rehabil* 2020;101:1001–1008.
12. Mujagic Z, Leue C, Vork L, et al. The Experience Sampling Method—a new digital tool for momentary symptom assessment in IBS: an exploratory study. *Neurogastroenterol Motil* 2015;27:1295–1302.
13. Ben-Zeev D, McHugo GJ, Xie H, Dobbins K, Young MA. Comparing retrospective reports to real-time/real-place mobile assessments in individuals with schizophrenia and a nonclinical comparison group. *Schizophr Bull* 2012;38:396–404.
14. Friedberg F, Sohl SJ. Memory for fatigue in chronic fatigue syndrome: the relation between weekly recall and momentary ratings. *Int J Behav Med* 2008;15:29–33.
15. Abdel-Kader K, Jhamb M, Mandich LA, et al. Ecological momentary assessment of fatigue, sleepiness, and exhaustion in ESKD. *BMC Nephrol* 2014;15:29.
16. Riis J, Loewenstein G, Baron J, et al. Ignorance of hedonic adaptation to hemodialysis: a study using ecological momentary assessment. *J Exp Psychol Gen* 2005;134:3–9.
17. Horigan AE, Barroso JV. A comparison of temporal patterns of fatigue in patients on hemodialysis. *Nephrol Nurs J* 2016;43:129–138. 148; quiz 39.
18. Brys A, Stiff F, van Heugten C, et al. mHealth based experience sampling method to identify fatigue in the context of daily life in hemodialysis patients. *Clin Kidney J* 2020. In press.

19. Van Diest I, De Peuter S, Eertmans A, et al. Negative affectivity and enhanced symptom reports: differentiating between symptoms in men and women. *Soc Sci Med* 2005; 61:1835–1845.
20. Myin-Germeys I, Birchwood M, Kwapil T. From environment to therapy in psychosis: a real-world momentary assessment approach. *Schizophr Bull* 2011;37:244–247.
21. Lenaert B, Colombi M, van Heugten C, et al. Exploring the feasibility and usability of the experience sampling method to examine the daily lives of patients with acquired brain injury. *Neuropsychol Rehabil* 2019;29:754–766.
22. Wichers M, Peeters F, Rutten BP, et al. A time-lagged momentary assessment study on daily life physical activity and affect. *Health Psychol* 2012;31:135–144.
23. Oorschot M, Lataster T, Thewissen V, et al. Emotional experience in negative symptoms of schizophrenia—no evidence for a generalized hedonic deficit. *Schizophr Bull* 2013;39:217–225.
24. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol* 1989;46:1121–1123.
25. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361–370.
26. Loosman WL, Siegert CE, Korzec A, Honig A. Validity of the hospital anxiety and depression scale and the beck depression inventory for use in end-stage renal disease patients. *Br J Clin Psychol* 2010;49:507–516.
27. Untas A, Aguirrezabal M, Chauveau P, et al. Anxiety and depression in hemodialysis: validation of the hospital anxiety and depression scale (HADS). *Nephrol Ther* 2009;5: 193–200. [in French].
28. Delespaul PAEG. Assessing schizophrenia in daily life: The experience sampling method. Maastricht, The Netherlands: Maastricht University, 1995.
29. Conway MA, Pleydell-Pearce CW. The construction of autobiographical memories in the self-memory system. *Psychol Rev* 2000;107:261–288.
30. Lukkahatai N, Saligan LN. Association of catastrophizing and fatigue: a systematic review. *J Psychosom Res* 2013; 74:100–109.
31. Kramer I, Simons CJ, Hartmann JA, et al. A therapeutic application of the experience sampling method in the treatment of depression: a randomized controlled trial. *World Psychiatry* 2014;13:68–77.
32. Horne R, Chapman SC, Parham R, et al. Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: a meta-analytic review of the necessity-concerns framework. *PLoS One* 2013;8:e80633.
33. Nair D, Finkelstein FO. Toward developing a patient-reported outcome measure for fatigue in hemodialysis. *Am J Kidney Dis* 2019;74:151–154.
34. Kramer A, Pippas M, Noordzij M, et al. The European Renal Association—European Dialysis and Transplant Association (ERA-EDTA) registry annual report 2015: a summary. *Clin Kidney J* 2018;11:108–122.

Appendix Table 1
ESM PsyMate: Questions

Domain	Item	Scale Type
Mood	1. I feel cheerful	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	2. I feel relaxed	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	3. I feel satisfied	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	4. I feel anxious	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	5. I feel down	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	6. I feel confident	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	7. I feel irritable	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	8. I feel powerless	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	9. I am worrying	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
Context activity	10. What am I doing (just before the beep)?	Doing nothing; resting; undergoing HD treatment; watching TV; reading; listening to music; Internet or social media; work; household; self-care; eating or drinking; having a conversation; relaxing; something else
	11. And also?	Resting; undergoing HD treatment; watching TV; reading; listening to music; Internet or social media; work; household; self-care; eating or drinking; having a conversation; relaxing; something else
	12. And ... ?	Resting; undergoing HD treatment; watching TV; reading; listening to music; Internet or social media; work; household; self-care; eating or drinking; having a conversation; relaxing; something else
	13. I can do this well	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	14. This is difficult for me	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	15. I would rather be doing something else	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
Context location	16. Where am I?	At the HD unit, at home; at family's/friend's place; at work; public space; transport; somewhere else
Context social	17. Who am I with?	No one; health care professional; partner; family living in; family outliving; friends; colleagues; acquaintances; strangers
	18. And also?	Health care professional; partner; family living in; family outliving; friends; colleagues; acquaintances; strangers
	19. And ... ?	Health care professional; partner; family living in; family outliving; friends; colleagues; acquaintances; strangers
Fatigue	20. I feel tired	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	Branched questions when feeling tired >1	
	20a. I feel mentally tired	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	20b. I feel physically tired	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
Physical	21. I am suffering from a headache	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	22. I am suffering from muscle cramps	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	23. I am suffering from pain in bones or joints	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	24. I am suffering from itch	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	25. I am suffering from restless legs	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	26. I have been physically active before the beep	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	27. I have been mentally active before the beep	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
General	28. This beep disturbed me	Seven-point scale (1 <i>not at all</i> to 7 <i>very much</i>)

ESM = experience sampling methodology; HD = hemodialysis; TV = television.

Questions about momentary activities, contextual aspects, and physical symptoms are not discussed in the present article but can be found in Ref. 18.

Appendix Table 2
ESM PsyMate Retrospective Questionnaires

Domain	Item	Scale Type
Morning questionnaire		
Sleep—night rest	1. I slept well	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very good</i>)
	2. How long did it take before I felt asleep yesterday evening	0 to five minutes; five to 15 minutes; 15–30 minutes; 30–45 minutes; 45 minutes—one hour; one to two hours; two to four hours; more than four hours
	3. How often did I wake up last night	One time; two times; three times; four times; five times; and more than five times
	4. I feel rested	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	5. I feel tired	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	Branched questions when feeling tired >1	
Fatigue	5a. I feel mentally tired	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	5b. I feel physically tired	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
End-of-day questionnaire	6. I do not look forward to this day	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	General	
	1. Today was an ordinary day	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	2. Without the application, I would have done other things today	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	Fatigue	
	3. Overall, I felt tired today	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	4. Overall, I felt mentally tired today	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	5. Overall, I felt physically tired today	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	Mood	
	6. Overall, I felt good today	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	7. Overall, I felt tense today	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	8. Overall, I have been worrying today	Seven-point Likert scale (1 <i>not at all</i> to 7 <i>very much</i>)
	Medication	
	9. Today, I took my medication	Seven-point scale (1 <i>nothing</i> to 7 <i>everything</i>)

ESM = experience sampling methodology.