

# Caregiver burden in amyotrophic lateral sclerosis: a cross-sectional investigation of predictors

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**Abstract** The objective of the study was to investigate whether cognitive and behavioural impairment in Amyotrophic Lateral Sclerosis (ALS) contributes to caregiver burden, and whether carer burden affects patient outcome. Thirty-three dyads of incident patients with ALS and their primary caregivers ( $n = 33$ ) completed a series of measures to determine cognitive and behavioural profiles, (patients) and carer burden (carers) to investigate the psychological impact of ALS, and the impact of behavioural change since the onset of ALS. Caregivers were divided into high- and low-burden groups using previously established norms. High burden in carers was associated with significantly higher apathy ( $p = 0.009$ ), disinhibition ( $p = 0.005$ ), and executive dysfunction ( $p = 0.015$ ) in

patients. Regression analyses for burden confirmed significant predictors such as change in apathy ( $r = 0.390$ ,  $F = 5.19$ ,  $p = 0.03$ ), disinhibition ( $r = 0.530$ ,  $F = 11.32$ ,  $p = 0.002$ ), and executive dysfunction ( $r = 0.372$ ,  $F = 4.66$ ,  $p = 0.039$ ), with total behaviour change contributing to 31 % of caregiver burden ( $r = 0.563$ ,  $F = 4.17$ ,  $p = 0.015$ ). Total distress as measured by the Hospital Anxiety and Depression Scale was also a significant predictor of caregiver burden, contributing to 38.5 % of variance ( $r = 0.621$ ,  $F = 18.79$ ,  $p < 0.000$ ). Caregiver burden did not affect survival ( $p = 0.496$ ). Caregiver burden in ALS is modulated by patient's cognitive and behavioural status, but does not significantly impact patient survival.

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## Introduction

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder of an unknown aetiology, limited treatment, with a rapidly progressive and fatal trajectory. ALS leads to progressive neurodegeneration and paralysis with death from respiratory failure within 3 years of symptom onset in the majority of patients [1].

Caregiver burden has been reported to be a consequence of physical impairment worsening congruently with disease trajectory [2], although recent reports also implicate cognitive, behavioural and neuropsychiatric symptoms as significant factors contributing to caregiver burden [3–6]. It has been suggested that caregivers' psychological status may influence the mental and physical outcome of patients

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[6–10]. However, few studies have collectively considered the triad of impairments known to occur in ALS, i.e. behavioural impairment, cognitive impairment and deteriorating physical condition.

Up to 50 % of ALS patients exhibit cognitive and behavioural impairment [10]. Behavioural symptoms preceding motor features are of clinical relevance, with the most commonly reported change in ALS patients being apathy, present in up to 60 % of ALS patients [11], followed by disinhibition [12]. Behavioural impairment increases carer burden, however, the impact of highly burdened caregivers on patient survival has not yet been established.

Through detailed neurocognitive assessment of patients with ALS, cross-sectional clinical interviews and assessment with their primary caregiver, we sought to further characterize factors contributing to caregiver burden, including behaviour, cognitive status, and physical condition and to determine whether high levels of burden influenced patient survival.

## Methods

Participants were recruited as part of an ongoing longitudinal population-based investigation into the heterogeneous cognitive profile of people with ALS, previously described in detail [1, 5, 13]. ALS patients recruited to this sub-study ( $n = 33$ ) of carer burden were diagnosed with probable, or definite ALS, according to the revised El Escorial Criteria [14]. In all patient cases, their primary caregivers were interviewed once during recruitment ( $n = 33$ ), over a 3-month recruitment period. Exclusion criteria included history of neurologic conditions that could affect cognition (such as major hemispheric stroke), alcohol dependence syndrome, and/or the use of high-dose psychoactive medications. Neuropsychological and clinical data were collected through hospital assessments and home visits.

Information on cognitive status, behavioural status, and physical progression was obtained through direct evaluation of ALS patients, and semi-structured interviews with their primary caregiver. The neuropsychological performance of patients with ALS was compared with a cohort of age-, sex- and education-matched healthy controls, as described previously [5]. Abnormal performance on any task was defined as a score that is two standard deviations below the control mean. Extensive details of the neuropsychological battery, clinical data, and method for categorizing cognitive impairment have been described in detail previously [13], and supplementary information relating to the neuropsychological tests can be seen in Table 1. Measurements of caregiver burden were undertaken with the patients and caregiver dyads ( $n = 33$ ).

The Zarit Burden Interview (ZBI [15]) was used to assess subjective caregiver burden, where a score  $\geq 24$  indicates burden [16]. For the purpose of this study, caregivers with a score of  $\geq 24$  were categorically defined as being in the ‘burdened’ group, with more psychometric information regarding the scale available [17].

The McGill Quality of Life Questionnaire Single-Item Scale (MQOL-SIS [18]) specified the patient’s perceived quality of life over the past 2 days, scoring 0–10, with higher scores being indicative of greater quality of life.

Behaviour was assessed using the Frontal Systems Behaviour Scale (FrSBe [19]), a self- and proxy-report behaviour questionnaire associated with fronto-striatal circuitry, which measures Apathy, Disinhibition and Executive Dysfunction. The Hospital Anxiety and Depression Scale (HADS) [20, 21] was administered, as a statistically reliable measure composed of two subscales measuring Depression (HADS-D) and Anxiety (HADS-A).

Patients’ survival data were captured by the Irish ALS register, as previously described [1, 5].

This study was granted ethical approval from Beaumont Hospital Medical Research Ethics Committee. Informed written consent was obtained from all participants in this study ( $N = 66$ ).

## Statistical analysis

Comparisons of descriptive variables were made using independent sample *t* test, and simple linear regressions were employed to investigate significant predictors of caregiver burden. According to power calculations, our sample per group met requirements to detect robust significance, with Bonferonni analyses used to correct for multiple comparisons.

The distribution of the data was homoscedastic for principal-dependent variables. All tests were set to an alpha value of 0.05. Statistical analyses were performed using SPSS [22] version 21.

## Results

Information relating to caregiver–patient dyads is summarized cumulatively and subcategorized based on whether the patient’s caregiver was experiencing high or low burden. The patients (19 men, 59.4 %) had a mean age of 63.99 years ( $SD \pm 9.2$  years; range 39–77), a mean duration of symptoms of 30.13 months ( $SD \pm 18.22$  months), and a mean Amyotrophic Lateral Sclerosis Functional Rating Scale (revised) score of 36.63 ( $SD \pm 7.79$ ). Primary caregivers (11 men, 34.4 %) had a mean age of 58.17 ( $SD \pm 11.1$ ; range 35–83); 26 were cohabiting spouses (81.3 %), 4 were children (12.4 %), and 2 were other

**Table 1** Supplementary details of the neuropsychological battery [5]

Executive dysfunction	Impairment that is two SD below the mean for healthy controls on at least two executive tasks
Stroop colour-word test	(a) Priming trial: patients presented with a multicoloured list of colour names and asked to read as many words as they can in 2 min. (b) Inhibitory trial: a similar list is presented, but colour names (e.g. 'blue') are printed in an ink colour not denoted by the name (e.g. red). Correct responses in two minutes are recorded Non-executive factors (including bulbar disability) contribute equally to both trials. The difference in scores between the two trials represents the number of responses 'lost' due to the delay imposed by the extra executive demands in the inhibitory trial
Brixton spatial anticipation test	A rule attainment-based task whereby the rule in operation, cannot be identified by any perceptually salient aspect of the stimuli. It consists of pages showing the same basic array of 10 circles set in two rows of five, with each circle numbered from one to 10. The changes in position are governed by a series of simple rules, which vary without warning
Backward digit span	A measure of auditory attention and working memory. This test is composed of trials where examinees are read strings of digits and are asked to repeat them back aloud. The length of the digit strings is incrementally increased over successive trials
Category fluency	Patients were asked to name as many animals as they could think of in 1 min (spoken only)
Phonemic verbal fluency	Written/spoken, number of words starting with letter 'S' generated in 5 min and number of four letter words starting with letter 'C' generated in 4 min. Verbal Fluency Index used to adjust for disability
Memory dysfunction	Impairment that is two SD below the mean for healthy controls on at least four* of the parameters highlighted using +
Logical memory (LM)	+LM1 (immediate recall), +LM2 (delayed recall) and +LM retention (retention)
Verbal paired associate (VPA)	+VPA1 (immediate recall), +VPA2 (delayed recall) and +VPA retention (retention)
Auditory delayed recognition task	+Sum of total recognition scores on logical memory and verbal paired associates
California verbal learning tests	+Total of five trials, +short delay free recall (immediate recall) +long delay free recall (delayed recall)
Rey–Osterrieth complex figure test	Non-verbal memory: parameters used: +immediate and +delayed recall trials
Language dysfunction	
Boston Naming Test	Impairment that is two SD below the mean for healthy controls on this task
Visuo-spatial dysfunction	
Rey–Osterrieth complex figure test	Impairment that is two SD below the mean for healthy controls on copy trial of this task

relatives (6.3 %). Some patients received additional care other than from their primary caregiver, approximately 8.55 h ( $\pm 8.01$  h) per week. For additional demographic, clinical and stratified group data, please refer to Tables 2 and 3.

The mean ZBI score for all caregivers, regardless of level of burden, was 21.62 ( $SD \pm 14.0$ ). Subgroup analysis into those scoring above and below 24 revealed 2 main groups. The 'Low-Burden' group reported a mean burden score of 12.75 ( $SD \pm 7.35$ ), whereas the 'High-Burden' group reported a mean burden score of 37.6 ( $SD \pm 8.66$ ). Considering burden as the grouping variable, a significant difference in subjective burden was observed ( $p < 0.001$ ).

Caregivers had a mean anxiety score of 7.35 ( $SD \pm 4.02$ ), as measured by the HADS-A. There was a significant difference noted between groups with mean anxiety scores of 5.86 ( $SD \pm 3.37$ ) and 9.88 ( $SD \pm 2.84$ ) for the low-burdened caregivers and high-burdened caregivers, respectively ( $p = 0.007$ ). No significant differences were noted on the HADS-D subscale between the high-

burdened caregivers and low-burdened caregivers, with scores of 2.20 ( $SD \pm 2.14$ ) and 3.88 ( $SD \pm 2.84$ ), respectively ( $p = 0.133$ ). Combining the HADS-A and HADS-D subscales creates a reliable 'Total Distress score' (HADS-T), and in this cohort there were significant differences between the burdened groups ( $p = 0.015$ ). The relationship between the HADS and the ZBI was also investigated. Greater distress scores were positively correlated with subjective symptoms of burden, congruent with previous studies (ZBI\*HADS-A:  $r = 0.360$ ; ZBI\*HADS-D,  $r = 0.301$ ; ZBI\*HADS-T,  $r = 0.383$ ).

### Behaviour and burden

Caregivers were dichotomized based on their ZBI score, and using the FrSBe relative change in apathy ( $p = 0.009$ ), disinhibition ( $p = 0.005$ ), executive dysfunction ( $p = 0.015$ ) and total behaviour ( $p = 0.001$ ) we noted. The higher burden patient group showed greater mean changes from baseline in apathy (25 vs 12), disinhibition (10 vs 2)

**Table 2** Demographic, clinical and interview data

ALS patients ( <i>N</i> = 33)	Total patient	Low burden <i>n</i> = 22	High burden <i>n</i> = 11	<i>p</i>
Males <i>n</i> (%)	19 (59.4)	13 (61.9)	6 (54.5)	0.317
Age at assessment <i>y</i> ( $\pm$ sd)	63.99 (9.2)	65.80 (6.71)	60.5 (12.5)	0.228
Years of education <i>x</i> ( $\pm$ sd)	11.5 (3.11)	11.5 (3.15)	11.45 (3.1)	0.777
Spinal onset <i>n</i> (%)	22 (66.6)	14 (63.63)	8 (72.7)	0.803
ALSFRS-R <i>x</i> ( $\pm$ sd)	36.63 (7.79)	36.95 (7.74)	36.0 (8.24)	0.749
Onset-assessment month ( $\pm$ sd)	30.13 (18.22)	26.5 (13.95)	36.1 (23.9)	0.173
Primary caregivers ( <i>N</i> = 33)	Total caregiver	Low burden <i>n</i> = 22	High burden <i>n</i> = 11	<i>p</i>
Males <i>n</i> (%)	11 (32.35)	7 (31.81)	4 (36.36)	0.162
Mean age at interview <i>y</i> (%)	58.17 (11.1)	66.05 (6.79)	60.5 (11.9)	0.265
Families w/children <i>n</i> (%)	10 (31.2)	3 (14.3)	7 (63.6)	0.072
External assistance <i>x</i> ( $\pm$ sd)	8.55 (8.01)	6.12 (4.32)	10.16 (9.8)	0.094

**Table 3** Additional participant characteristics

Neuropsychiatric and burden measures	Total caregiver	Low burden <i>n</i> = 22	High burden <i>n</i> = 11	<i>p</i>
HADS: anxiety	7.35 (4.02)	5.86 (3.37)	9.88 (2.84)	<b>0.007</b>
HADS: depression	2.77 (2.37)	2.20 (2.14)	3.88 (2.84)	0.133
HADS: distress	10.06 (5.93)	8.06 (5.03)	13.7 (5.47)	<b>0.015</b>
ZBI	21.62 (14.00)	12.75 (7.35)	37.6 (8.66)	N/A
McGill QoL-SIS	6.90 (1.77)	6.91 (1.67)	6.5 (2.42)	0.674
Hours of care provided per day	8.30 (7.45)	5.96 (7.27)	9.93 (7.09)	0.875
Supervision	7.63 (7.37)	5.2 (5)	7.89 (7.85)	0.436
Dressing	0.861 (0.51)	0.75 (0.43)	1 (0.612)	0.563
Feeding	1.33 (0.750)	1.66 (1.15)	1.37 (0.47)	0.661
Toileting	0.625 (0.541)	0.125 (0.176)	1 (0.5)	0.107
Other	2.58 (2.05)	1.5 (1.32)	3 (2.82)	0.463
Medical	1.50 (0.70)	2.00	1.00	N/A
Housekeeping	2.12 (1.35)	2 (0.816)	1.00	N/A
Transportation	1.33 (0.57)	1.00	1.5 (0.707)	N/A

Bold values are statistically significant ( $p < 0.05$ )

and executive function (9 vs 2). The mean total behaviour change, according to caregivers, from before onset of ALS to the time of testing was increased due to the aforementioned subtests (15 vs 6).

The ZBI was itemized to identify variables associated with increased caregiver burden (see Table 4). Caregivers who experienced higher burden, as indicated through their ZBI scores, stated that the patients with ALS asked for more help that they may need ( $p = 0.033$ ), or that the caregiver's personal time was being consumed by caregiving ( $p = 0.014$ ). Caregivers report that stress was significantly increased due to caring for the patient ( $p = 0.002$ ). High-burden caregivers further reported that they felt more frustrated and strained ( $p = 0.003$ ), and angry around their family members ( $p = 0.013$ ). Feelings of impaired social life ( $p = 0.013$ ) and personal privacy ( $p = 0.020$ ) were significantly more intense in high-

burdened caregivers, and they felt that their relative was dependent on them ( $p = 0.005$ ), with an uncertain future ( $p < 0.000$ ).

High-burdened caregivers expressed concern that they were the only person on whom the patient could depend for support ( $p = 0.002$ ), that they would not be able to care for the patient indefinitely, ( $p = 0.022$ ), and that they wished they could leave the care of their relative to someone else ( $p = 0.029$ ). Overall, when the dichotomized groups were specifically asked about the severity of burden experienced, the high-burden group reported that they had lost control of their lives ( $p = 0.004$ ).

Caregiver burden was not influenced by the efficacy of the caregiving ( $p = 0.069$ ), whether caregivers felt they were doing enough ( $p = 0.093$ ), uncertainty about what to do for their relative ( $p = 0.191$ ) or financial implications ( $p = 0.593$ ). Furthermore, caregiver burden was not

**Table 4** ZBI Questions and endorsement

ZBI question	Total caregiver <i>N</i> = 33	Low burden <i>n</i> = 22	High burden <i>n</i> = 11	<i>p</i>
Do you feel that your relative asks for more help than he/she needs?	1.73 (0.647)	1	1.86 (0.690)	0.033*
Do you feel that because of the time you spend with your relative that you do not have enough time for yourself?	1.95 (0.780)	1.78 (0.833)	2.50 (0.548)	0.014*
Do you feel stressed between caring for your relative and trying to meet other responsibilities for your family or work?	2.37 (1.11)	2.09 (1.13)	2.78 (1.09)	0.002**
Do you feel embarrassed over your relative's behaviour?	1.40 (0.548)	1	1.50 (0.707)	0.295
Do you feel angry when around your relative	1.82 (0.728)	2 (0.707)	1.71 (0.756)	0.013*
Do you feel that your relative currently affects our relationship with other family members or friends in a negative way	1.80 (0.789)	2.50 (0.707)	1.75 (0.957)	0.254
Are you afraid what the future holds for your relative	2.92 (0.977)	2.45 (0.820)	3.22 (0.833)	<0.000**
Do you feel your relative dependent on you	2.80 (1)	2.58 (0.996)	3.33 (0.866)	0.005*
Do you feel strained when you are around your relative	2 (0.679)	1.75 (0.5)	2.29 (0.756)	0.003*
Do you feel your health has suffered because of your involvement with your relative	2 (0.707)	–	2.33 (0.577)	0.088
Do you feel that you do not have as much privacy as you would like because of your relative	2.10 (1.19)	2	2.29 (0.756)	0.020*
Do you feel that your social life has suffered because you are caring for you relative	2.19 (1.07)	2 (1.22)	2.33 (0.577)	0.013*
Do you feel uncomfortable about having friends over because of your relative	1.75 (0.957)	1.50 (0.707)	2.5 (1.37)	0.414
Do you feel that your relative seems to expect you to take of him/her as if you were the only one s/he could depend on?	2.60 (1.05)	1.75 (957)	2.33 (1.11)	0.002**
Do you feel that you do not have enough money to take care of your relative in addition to the rest of your expenses	2.07 (0.829)	1.83 (0.753)	2 (1.41)	0.593
Do you feel that you will be unable to take care of your relative much longer	1.83 (0.937)	1.33 (0.577)	2.75 (0.886)	0.022*
Do you feel you have lost control of your life since your relative's illness	2.40 (1.13)	2.33 (1.52)	2.50 (0.837)	0.004*
Do you wish you could leave the care of your relative to someone else	2.09 (1.22)	1.50 (0.707)	2.29 (0.951)	0.029*
Do you feel uncertain about what to do about your relative	2.20 (1.13)	2 (1.41)	2.25 (1.16)	0.191
Do you feel you should be doing more for your relative	2.27 (1.14)	1.67 (0.577)	2.60 (1.51)	0.093
Do you feel you could do a better job caring for your relative	2.36 (1.02)	1.67 (0.577)	2.80 (1.30)	0.069
Overall, how burdened do you feel in caring for your relative?	1.86 (0.774)	1.56 (0.527)	2.22 (0.833)	0.006*

\*  $p \leq 0.05$ ; \*\* adjusted sig.  $p \leq 0.002$ 

associated with concern relating to patient behaviour in terms of feeling embarrassed ( $p = 0.295$ ), or being uncomfortable when socializing with friends ( $p = 0.414$ ) or family ( $p = 0.254$ ), and denied that their health had been adversely affected due to their involvement in caring for their relative ( $p = 0.088$ ).

### Predictors of caregiver burden and distress

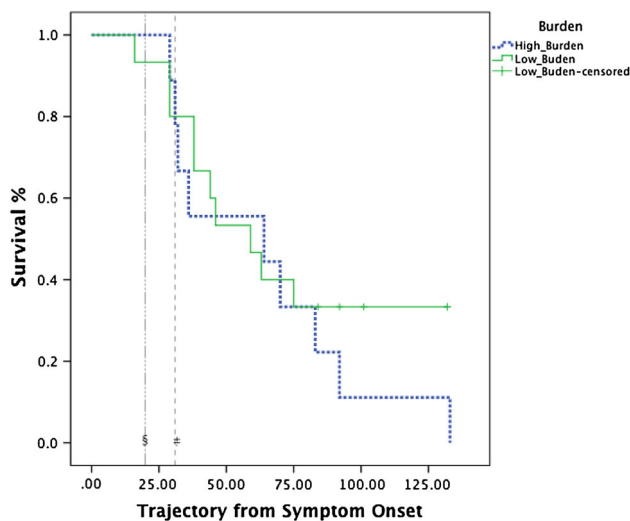
Significant neuropsychological predictors of burden were associated with increased mean change of apathy ( $r = 0.390$ ,  $F = 5.19$ ,  $p = 0.03$ ), disinhibition ( $r = 0.530$ ,  $F = 11.32$ ,  $p = 0.002$ ), and executive dysfunction ( $r = 0.372$ ,  $F = 4.66$ ,  $p = 0.039$ ), with the total change in behaviour contributing to 31 % to caregiver burden ( $r = 0.563$ ,  $F = 4.17$ ,  $p = 0.015$ ). The HADS-T score is a further factor contributing to caregiver burden, contributing to 38.5 % of variance ( $r = 0.621$ ,  $F = 18.799$ ,  $p < 0.000$ ).

Caregiver quality of life (QoL-SIS;  $r = 0.382$ ,  $F = 3.76$ ,  $p = 0.065$ ), patient age ( $r = 0.235$ ,  $F = 1.57$ ,  $p = 0.220$ ), total hours caring ( $r = 0.311$ ,  $F = 3.21$ ,  $p = 0.083$ ), cognitive status ( $r = 0.016$ ,  $F = 0.007$ ,  $p = 0.933$ ), and patients' level of functioning as defined by the ALSFRS-R ( $r = 0.183$ ,  $F = 1.034$ ,  $p = 0.317$ ) did not significantly contribute to caregiver burden. Lastly, the gender of patients was not found to be a significant contributory factor ( $r = 0.128$ ,  $F = 0.497$ ,  $p = 0.486$ ).

### Does caregiver burden affect patient survival?

Dichotomized groupings based on the ZBI did not affect survival time (log rank test  $p = 0.496$ ; see Fig. 1 for Kaplan–Meier Survival Plots). Considering a low participant cohort, linear contrast analytic modelling was conducted to determine whether an increased sample size would produce an alternate outcome of this analysis. Using this analysis,





**Fig. 1** Survival plot, § Mean time of diagnosis, ±mean time of ZBI

we predict that higher burden in caregivers would not affect survival rates of patients ( $p = 0.138$ ).

## Discussion

The purpose of this study was to examine factors associated with caregiver burden in patients with ALS, and to determine whether high caregiver burden in the context of established disease influenced patient survival. Previous cross-sectional studies have found patients' level of disability, especially with spinal onset ALS, and depression were factors yielding the strongest correlation with caregivers' burden [3]. Our findings are consistent with these findings for low mood, anxiety and total distress. Our findings are congruent with studies of caregiver burden in other chronic neurologic disorders.

Behavioural symptomatology is not routinely assessed in a systematic manner [3], and accurate profiling may enhance interventions specific to caregivers whom experience higher levels of burden. Interestingly, patients and caregivers reported similar levels of behavioural change after the onset of ALS. The caregivers who experience higher burden report lower scores than caregivers within the low-burden category, and this may reflect a difference in the manifestation of behavioural change. This could be investigated by future research, through qualitative means. The present study has demonstrated that patient behaviour is a major factor to be considered when investigating caregiver burden.

Our data suggest that behavioural change is of great importance as a mediator of caregiver burden. Considering the rapidly progressive and devastating physical features of ALS, comprehensive behavioural phenotyping, with

detailed evaluation of social cognitive and executive processes, is required to further elucidate and understand the burden–behaviour relationship.

Notwithstanding, survival analysis suggests that a patient's disease trajectory, and ultimately survival, is not negatively associated with higher levels of caregiver burden. However, considering models used with other patient cohorts, skills training and symptom management may be of considerable benefit in reducing caregiver burden.

Our study has several limitations. Due to the small sample, results from regression analyses should be considered exploratory, alongside the survival analysis. Secondly, these findings may apply only at particular states of the illness, as this study was cross-sectional in design, albeit in patients with established illness and moderate disability. A longitudinal follow-up of caregiver wellbeing, cognitive status of patients, detailed investigation of patient support, and intervention evaluation is required to determine whether caregiver burden shifts as the disease progresses.

In conclusion, our study has shown that caregiver burden is higher in dyads in which the patient has evidence of behavioural impairment.

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**Conflicts of interest** Nothing to declare.

**Ethical standard** This research has received ethical approval from Beaumont Hospital Medical Research Ethics review team, and written consent was obtained from all participants.

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