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CUES AND CLUES PREDICTING PRESENCE OF SYMPTOMS OF DEPRESSION IN STROKE SURVIVORS

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ABSTRACT

Aims and Objectives

To investigate to what extent self-reported cues about lack of treatment or concerns about inadequate health care from stroke survivors were associated with symptoms of depression.

Background

Stroke survivors are prone to depression, thus any easily available cues which may inform health care workers about patients' mental well-being are potentially important. This study investigates whether two such cues – Cue 1 the subjectively reported lack of access to rehabilitation, and, more generally, Cue 2 an expressed concern that their health care needs may not be adequately met – may be clinically relevant to be on the outlook for.

Design

A cross-sectional survey of stroke survivors three months after discharge from a stroke unit.

Methods

Analysis of data on stroke-survivors, collected at three months after discharge from a hospital's stroke unit, by means of a mailed questionnaire. Descriptive statistics for the sample population were computed, and a binary logistic model fitted to estimate the impact of subjectively perceived lack of rehabilitation and subjectively reported low confidence in the health care system on symptoms of depression as measured by the Hospital Anxiety and Depression Scale.

Results

The percentage of patients reporting the presence of symptoms of depression three months post-discharge (22.6%) was consistent with the main body of literature on this subject. Both cues investigated had a significant ($p < 0.05$) and elevated odds ratio (OR) –Cue 1 OR = 4.7 (1.3— 18.4) and Cue 2 OR = 2.8 (1.2— 6.4) respectively – for showing symptoms of depression in our population.

Conclusion

Health care workers who come in contact with stroke survivors who report having missed out on rehabilitation or express concern that their care needs may not be adequately met by their access to health care should ensure that the patients' mental well-being is being duly monitored, and should consider further investigation for depression.

Relevance to clinical practice

Health care workers who come into contact with stroke survivors should pay attention to patients' remonstrance of access to rehabilitation, or concerns about adequacy of received care, as these might constitute cues for the presence of symptoms of depression.

What does this paper contribute to the wider global clinical community?

- Easily recognized cues indicating possible symptoms of depression are identified.
- Emphasizes the usefulness of paying attention to detail in communication during clinical encounters.

INTRODUCTION

Stroke can be defined as a sudden onset of a focal or global disturbance in brain-function caused by disrupted blood flow in the brain, with symptoms persisting for more than 24 hours or leading to death (Hatano, 1976; Mendis et al., 2011; WHO 2015). When the ischemic disturbance of cerebral function is transient and does not inflict infarction, the stroke is defined as a *transient ischemic attack (TIA)*.

Every year, more than fifteen million people worldwide experience a stroke; in excess of six million of these strokes are fatal, more than five million persons are left permanently disabled. Globally, stroke is one of the leading causes of death: it is the estimated second largest cause of death for persons above the age of 60, and the fifth major cause of death of those between 15 and 60 years of age (Mendis et al., 2011; World Heart Federation, 2015).

This paper presents the results of a research study that investigates to what extent self-reported cues from stroke survivors about perceived lack of rehabilitation and expressed concern that their health care needs may not be adequately met is associated with symptoms of depression, and thus if these cues could indicate that further measures should be taken to ensure the mental well-being of the stroke survivor.

BACKGROUND

The bidirectional relationship between depression and chronic conditions is well documented (Wells KB et al., 1989; Stordal et al., 2003; Moussavi et al., 2007; J. Katon, 2011). That is depression may cause somatic illness and impaired function, and disease may cause depression. Higher age is also in itself positively correlated with risk of developing clinical depression, and women are at a double risk compared with their male peers (Cole and Dendukuri, 2003; Gaete and Bogousslavsky, 2008; Luppa et al., 2012). Furthermore, depression is a common sequela to stroke (Sagen et al., 2010; Ayerbe et al., 2013a, 2013b), and symptoms of *post-stroke depression (PSD)* may develop immediately following the stroke (Fure et al., 2006). Prevalence of depression in stroke survivors may be up to 30% (Ayerbe et al., 2013b; Hackett and Pickles, 2014), and symptoms of depression often last for more than 5 years (Ayerbe et al., 2013a; Lincoln et al., 2013). The severity of the stroke, in terms of the loss of bodily function and the need for help in *activities of daily living* (ADL), increases the risk of developing PSD. As in the general population, female stroke survivors have been reported to have an increased risk, but results are not consistent (Kouwenhoven et al., 2011; Kutlubaev & Hackett, 2014). Depression three months post-stroke is associated with a Modified Rankin Scale score (Robinson & Spalletta 2010) greater than 2. A pre-existing history of depression is also known to increase the risk of PSD in some studies (Ayerbe et al., 2013b; Kutlubaev and Hackett, 2014). Because it is documented that short-term mortality is increased in depressed stroke patients (Robinson and Spalletta, 2010), that patients with underlying somatic illness tend to somatize the symptoms of depression (Kirmayer et al., 1993; Steinbrecher et al., 2011), and that many patients do not mention their psychological distress during consultations (Maguire, 1985), a focus on cues indicating PSD early is important. Therefore, any diagnostic aid helping to identify PSD is potentially important in a clinical setting (Ginkel et al., 2013, 2012).

In two review articles (Ryan et al., 2005; Zimmermann et al., 2007) the need to be aware of which *cues and concerns* to look for in order to detect emotional distress and other psychiatric disturbances is highlighted. These reviews report that most previous studies have studied cancer patients, or patients in primary health care consultations. None of the studies we identified investigated a cohort

of stroke survivors. Or, as Lussier & Richard put it: "*During a consultation, there are often numerous cues from patients that indicate they have more to say than what has been said outright, but time constraints prevents doctors from exploring them all. Doctors have to make choices."(Lussier & Richard, 2009 p. 121).* Certainly, this applies not only to doctors, but to all health care professionals.

In this paper we investigate whether a patient's expressed concern about a perceived missed opportunity for rehabilitation following a stroke, or a concern about the adequacy of the health care system's ability to provide adequate care for them, can be interpreted as a cue for symptoms of depression in stroke survivors. That is: *is there evidence that expressed concerns about the adequacy of post-stroke health care or rehabilitation are cues predicting symptoms of depression?*

METHODS

Data

This study uses data collected as part of a project investigating the delivery of health services to Norwegian patients during the pre-, peri-, and post-hospital phases of a stroke at the Akershus University hospital (Ahus) in Norway (*Norwegian Stroke – Paths of Treatment (NOR-SPOT)*). Ahus is a major acute care hospital, with a catchment area of 500,000 unselected patients from the Oslo greater metropolitan area. All suspected acute stroke cases in adults (18 years of age and above) are routinely admitted to the 28-bed specialized *stroke unit (SU)*. All patients admitted to the SU during the period from February 15th 2012 to March 15th 2013 were included in the NOR-SPOT cohort.

Patients were classified as either *transient ischemic attack (TIA)*, *cerebral infarction (INF)*, *intracerebral haemorrhage (ICH)* or as *other* (including traumatic ICH and subarachnoidal haemorrhage) by neurologists. Furthermore, medical information (stroke sub-type, previous stroke or depression) was compiled by the neurologists. Variables on *length of stay (LOS)*, age and sex were retrieved from the electronic patient journal system.

Three months after discharge from the SU, patients with a stroke diagnosis (TIA, INF or ICH) received a postal follow-up questionnaire. The 3-month follow-up questionnaire included information about NOR-SPOT and instructions on how to complete and return the questionnaire. For patients who were above the age of 80 years or who had not been discharged to their own home, a caregiver was contacted by telephone prior to sending out the questionnaire to help ensure that the questionnaire reached the patient. In the case of severe disability the caregiver was also encouraged to help the patient complete the questionnaire.

All questionnaires were entered into a Microsoft Access database, which permits exportation of data to most statistical software, by a dedicated research assistant.

Ethics

The NOR-SPOT project is an in-hospital venture investigating the paths of treatment of the hospital's patients without any deviation from standard practices, and has been classified as a quality-assurance project by the *Regional Ethics Committee (REK)* of the hospital's jurisdiction. Therefore, and in accordance with REK's recommendation, ethical approval was sought with the Privacy Ombudsman at Ahus (Approval number 11-076.) Furthermore, all respondents were informed about the project in the cover letter accompanying the questionnaire, and asked to return the 3-month questionnaire only if they consented to the information being used for research on stroke survivors' treatment paths and health related quality of life.

Variables and measures

The Hospital Anxiety and Depression Scale (HADS) is an instrument for (self-) assessment of symptoms of anxiety and/or depression. The instrument is comprised of two subscales – HADS-A and HADS-D – measuring the two underlying constructs (Zigmond & Snaith, 1983). The questionnaire is reliable and valid, and is used with in- and out-patients in both somatic and psychiatric settings, as

well as with the general population (Herrmann, 1997; Bjelland et al., 2002; Roberge et al., 2013). The HADS has 7 questions for each of the two subscales, and each question provide 4 alternatives graded from 0 to 3, yielding a maximum sum-score of 21 on each subscale. The HADS was included in the 3-month follow-up questionnaire. For our study we only analyzed the depression subscale, and employed a dichotomized variable, using the recommended cut-off of a score of ≥ 8 to indicate symptoms of depression (Zigmond & Snaith, 1983; Bjelland et al., 2002). For respondents with up to two missing items of the seven depression items on the HADS instrument, the average value of the five or six completed items were imputed for the missing values. In accordance with established practice, respondents with three or more missing items were excluded from further analysis (Morris and Coyle, 1994).

The modified Rankin Scale (mRS) is a simple and well-validated stroke-specific instrument for assessment of dependence with ADL in stroke populations. Patients are scored from 0—5, where 0 represents *no problems* and 5 represents *total dependency*. The score is often dichotomized into *good outcome* (mRS = 0—2) vs. *poor outcome* (mRS = 3—5) (Salter et al., 2005; Banks and Marotta, 2007). Even though assessment by a trained rater is always preferable, the relatively straightforward scoring system appears to be well-suited for self-assessment when used in analyses as a dichotomized variable (Lindley et al., 1994; Eriksson et al., 2007). The mRS in the questionnaire was a standard Norwegian translation, amended with explanatory texts for each mRS category 0—5. Respondents circled the most appropriate alternative. In all analyses the mRS score was dichotomized into *good outcome* and *poor outcome* as described above. For three responders, a value of 0 was imputed for a missing mRSD observation on the basis of a reported full-function according to Barthel ADL index[*].

[*] The Barthel ADL index is a general ADL instrument which was not analyzed separately here.

Cue 1 – Self-reported rehabilitation and desire for rehabilitation. The 3-month follow-up questionnaire contained the following two questions[†]:

1. *I have had an admission to a rehabilitation facility*
2. *I wanted to have an admission to a rehabilitation facility*.

The possible answers were *yes*, *no*, and *uncertain*. From these answers we defined a dichotomous variable called *perceived missed rehabilitation (PMR),* defined as 1 when the respondent reported the combination *no—yes* to the preceding two questions and 0 otherwise. That is, PMR is a dummy-variable for a reported self-perceived discrepancy between the need for, and the access to, rehabilitation. The variable was computed as 0 for patients who had responded only to question 1 with a *Yes* (because these would be coded as a 0 regardless their answer to question 2), and similarly for those who had responded only to question 2 with a *No*. For eight respondents a PMR-value was imputed after manual inspection of the questionnaires: seven respondents who had answered *Yes* to question 2, and had also specified the number of days they had spent in a rehabilitation facility in a later questionnaire field (not analyzed here) the PMR variable was coded as 0; for one respondent who had answered *No* to question 2 and had hand-written "nothing was offered to me" on the rehabilitation page of the questionnaire, the PMR variable was coded as 1.

Remark to Cue 1

While patients diagnosed with a TIA will only very rarely be referred to a rehabilitation facility, their answers to these questions are analyzed here because the expressed lack of access may still be a cue for symptoms of depression. Furthermore, many TIA patients receive a follow-up appointment following a TIA, during which such a cue might be picked up on by health care professionals.

[†] The assertions, in Norwegian language, were: *"Jeg har hatt opphold på en rehabiliteringsinsitituspon" and "Jeg ønsket opphold på en rehabiliteringsinstitusjon."*

Cue 2 – Self-reported adequacy of help from the public health care services. In the 3-month follow-up questionnaire, the respondents were asked to qualify the following assertion[‡]:

> *I receive enough help from the public health care system to be able to manage. (If you do not need any help you can answer 'Yes').*

The possible answers were *yes*, *no* or *uncertain*. A dichotomous variable called *inadequate help dichotomized (IHD),* was defined as 1 for the response *no*, and 0 otherwise. That is, IHD is a dummy-variable for a self-perceived discrepancy between care needed and care provided by the public health services.

Remark to Cue 2

To interpret *Cue 2*, some basic facts about Scandinavian health care systems are necessary: there is government-funded universal coverage. In practice this means that post-stroke care is provided by the public health care system. According to the WHO[§] *European health for all database*, in Norway in 2012 the public expenditure on health accounted for 85.1% of total health expenditures; out-of-pocket payments accounted for 13.1% of the total expenditures, revealing that only an estimated 1.8% of expenditures were reimbursements from e.g. health insurance (with similar figures for Denmark and Sweden) – see also Hofmann for a recent description of the "Scandinavian model" (Hofmann, 2013). This is to say: when a Scandinavian citizen makes a qualifying assertion about the *public* health care system, the person is making a qualifying assertion about *the* health care system. As such, we assume in this paper that an expressed concern that the public health care system is not able to adequately cater to one's needs, is (most likely) a concern that this need will not be fulfilled at all.

[‡] The question, in Norwegian language, was: *"Hjelpen jeg får fra det offentlige helsevesenet er tilstrekkelig til at jeg klarer meg. (Dersom du ikke har behov for hjelp kan du svare **Ja**.)"*

[§] URL: http://data.euro.who.int/hfadb/ (accessed March 6th 2015)

Socio-demographic and stroke-specific variables: Age and sex of all respondents. Furthermore, the type of stroke (TIA, ICH, INF), and the *length of stay (LOS)* at the SU were collected. Ideally, we would have included a measure of the severity of the stroke, for example NIHSS score at arrival. The NIHSS-score is a variable in our data set, but had too many missing variables to be useful for analysis.

Previous history of depression (PD): A dichotomous variable coding *known history of depression*. This variable was coded by either a nurse or a neurologist, based on anamneses and/or available medical records (e.g. additional diagnoses).

Previous cerebrovascular accident (PCVA): a dichotomous variable coding for a known previous stroke. The variable was quality assured in like manner to the PD-variable.

Statistical methods

The statistical software R version 3.0.1 (2013-05-16) was used for statistical analysis (R Core Team, 2015).

We computed descriptive statistics for our sample in order to assess face validity of the data and to ensure that the data were appropriate for the subsequent regression modeling (ensuring sufficient event-per-variable ratio). Tests for differences of means or associations (Fisher's exact with mid-p correction for the dichotomous variables sex and mRSD; two sample t-test for equality of mean) were computed for the depressed and the non-depressed.

To investigate our main research question – testing whether the two cues predict symptoms of depression with statistical significance – we fitted a binary logistic regression model to the data with HADS-D score of ≥ 8 as the dependent variable. The initial specification included predictors for age,

sex, mRSD, PD, PCVA, and dummy variables for type of stroke. Furthermore, the LOS was included as a proxy for severity of the stroke. To assess the appropriateness of using LOS as a proxy for severity, we computed Spearman coefficients for the correlation between LOS and NIHSS-at-arrival for the entire NOR-SPOT cohort (including 450 non-responders to the 3-month questionnaire, but excluding fatalities). The predictor variables were included to correct for commonly studied risk factors for post stroke depression (Gaete and Bogousslavsky, 2008; Ayerbe et al., 2013b; Hackett and Pickles, 2014; Kutlubaev and Hackett, 2014).

The appropriateness of the data for regression modeling was assessed by standard methods, in particular with respect to an appropriate event per variable ratio (Peduzzi et al., 1996). The native `glm(family="binomial")`-function was used for the binary logistic regression. A model including all confounders was fitted to assess the statistical significance of our two main predictors (the two cues). A final model was fitted without the non-significant ($p \geq 0.05$) confounders to obtain the most reliable odds ratios and confidence intervals when presenting the results.

We also computed descriptive statistics and performed basic tests of associations (Fisher's exact with mid-p correction for dichotomous variables sex and mRSD; two sample t-test for equality of mean) for groups of patents with positive cues – that is with either PMR = 1 or IHD = 1. Similarly, we computed Fisher's exact *p*-values for association between the two cues.

A simple sensitivity analysis was performed to investigate to what extent our main result is sensitive to the chosen cut-off value for the dichotomized HADS-D variable; a second linear regression model with raw HADS-D-score as a continuous variable was fitted to the data.

A rudimentary non-responder analysis was carried out to investigate to what extent our sample (responders to the NOR-SPOT's 3-month questionnaire) can be said to be representative for Norwegian stroke survivors. For this analysis we computed descriptive statistics along our main variables of study, to see if responders and non-responders differed significantly. In this analysis, we also included *mortality between 3 and 12 months after discharge* (that is, a dummy-variable indicating whether a patient who was alive three months after discharge, was still alive twelve months

after discharge) as a proxy for morbidity at three months after discharge[**]. Also, a dummy indicating that the patient had been *discharged to a nursing home* was included.

RESULTS

A total of 1144 unique patients were discharged from the SU with a stroke diagnosis during the NOR-SPOT inclusion period, of which 853 patients had a questionnaire mailed to them three months later; the 291 who did not receive a questionnaire were either deceased (168), refused to receive (18), or had an unclear diagnosis at the time of mailing the questionnaire[††] (105). Of these 853 questionnaires a raw return rate of 425 (49.8%) was obtained, of which 393 (92.5%) had valid HADS-D data. Of these 11 (2.8%) had two missing HADS items and 16 (4.1%) had one missing HADS item and therefore imputed values were used for the computation of the HADS-D score.

Descriptive statistics for the 393 respondents with valid HADS-D score are summarized in Table 1. The results are stratified by the main outcome variable of this study, that is symptoms of depression – as operationalized by a *HADS-D score* ≥ 8 – with *p*-values from simple tests for differences between the respondents with symptoms of depression and those without symptoms of depression:

22.6% of the patients had a HADS-D score of 8 or above, and thus were classified as showing symptoms of depression. The univariate associations with this outcome, which were statistically significant, were mRSD ($p < 0.001$), PMR ($p = 0.002$), IHD ($p < 0.001$), type of stroke ($p = 0.015$) and LOS ($p = 0.001$).

[**] Because our study is concerned with the predictive value of patients' cues, this variable is not included in other analyses for obvious reasons.

[††] The neurologists confirming the diagnoses were not always able to complete this task within the three months from discharge. Due to the wording in the questionnaire, it was deemed very important that no one without a verified stroke diagnosis received them.

Regression analysis

For our main hypothesis test we fitted a binary logistic regression model with a dichotomized HADS-D score as the dependent variable (with cut-off ≥ 8 as recommended by Bjelland et. al. (2002) and Stordal et. al. (2003)), and with predictors age; sex; LOS (see also the next paragraph); PCVA; PD; dummy-variables for TIA, infarction and ICH; mRS-defined *poor* versus *good* outcome; and PMR and IHD – the two latter being our main variables of study. The variables included were chosen in order to correct for some of the most important known risk factors for symptoms of depression, while keeping the event per variable ratio at an acceptable level.

With respect to using LOS as a proxy for severity, inspection of the data revealed an (unsurprising) interaction with Age. We therefore computed Spearman coefficients for the correlation between LOS and NIHSS-at-arrival for five year age-brackets: these ranged from 0.47— 0.66 which suggests that LOS may be considered a reasonable proxy for severity if the interaction with age is included in the model. Therefore, the interaction Age*LOS was included in the initial regression model described in the preceding paragraph. All the Age, LOS and Age*LOS coefficients were statistically insignificant.

The predictors with significant ($p < 0.05$) coefficients were mRSD ($p < 0.000$), PMR ($p = 0.017$), and IHD ($p = 0.015$); a final regression model retaining the significant predictors (controlling for age and sex) was fitted (table 2). The odds ratios from the final model were mRSD 5.2 (95CI = 2.5— 11.1). Both cues investigated had a significant ($p < 0.05$) and elevated odds ratio – Cue 1 4.7 (95CI 1.3— 18.4) and Cue 2 2.8 (95CI 1.2— 6.4) respectively – for showing symptoms of depression in our population.

To investigate to what extent the results reported in Table 2 are sensitive to the chosen cut-off value for depression of HADS-D ≥ 8 , we specified a linear regression model with the final set of predictors (age, sex, mRSD, PMR and IHD), but with HADS-D depression score as a continuous variable; the result was consistent with the binary logistic specification (the same predictors were significant – not reported) and indicates that the results from the main model are not strongly dependent upon the chosen cut-off value for the HADS-D variable.

Sub-analyses of the patients with positive cues

Only 15 (3.8%) patients reported missed rehabilitation, and 39 patients (9.9%) reported a concern about inadequate help. Still, the regression models detected significant effects from both the cues on the odds ratio for simultaneously reporting symptoms of depression. Descriptive statistics and results of basic tests of associations (Fisher's exact with mid-p correction for dichotomous variables Sex and $mRSD$; two sample t-test for equality of mean) are presented in Table 3, and show no particular discernible patterns for this group. The exception is the association between IHD and $mRSD$, which means a correlation between low function and a tendency to rate the health care received as inadequate ($p < 0.001$). Furthermore, we see that there is only a non-significant association ($p = 0.068$) between those who reported $PMR = 1$ and those who reported $IHD = 1$.

Non-responder analysis

Neither mean age (responders 70.8 vs. non-responders 71.4; $p = 0.468$), nor sex (responders 58.3% males vs. non-responders 56.0% males; $p = 0.489$) differed from the cohort as a whole. Mean LOS was identical (6.3 days). The distribution of stroke type is also non-significant between the two groups. However, two variables were highly significantly correlated with non-responses (both $p < 0.001$): *mortality between 3 and 12 months after discharge* and *being discharged to a nursing home*. The 3-to-12 month mortality was 12.8% amongst the non-responders, compared to 5.3% amongst the responders. Also, 19.8% of the non-responders had been discharged to a nursing home, while this was true of 9.0% of the responders.

DISCUSSION

This study investigated to what extent two subjectively expressed concerns about post-stroke care was correlated with symptoms of depression as measured by the HADS depression subscale. Cue 1 we can dub a *concern about missed opportunity for recovery*, while Cue 2 may be thought of as a *concern*

about future access to adequate health care[‡‡].

We found that a small group of 15 stroke survivors reported a discrepancy between their perceived desire for, and their reported access to, rehabilitation (Cue 1), and that this subgroup have a statistically significant and markedly higher probability (OR = 4.7) of also reporting symptoms of depression. Based on our data, we cannot say whether or not the cause of this perceived discrepancy is that the patients were in fact denied indicated treatment. These patients might have restricted access to rehabilitation because of low motivation stemming from an underlying depression, or, conversely, they might report missed rehabilitation because they have recently become depressed. As seen in Table 3, there is little support for drawing any further conclusions about this group of responders, other than that they more often report symptoms of depression.

The somewhat larger group of 39 stroke survivors who reported a concern that the public health services would not adequately meet their needs for care now or in the future (Cue 2), also exhibited an elevated odds ratio (OR = 2.8) of reporting symptoms of depression. This cue was also strongly associated with lowered independence in ADL as measured by the mRSD variable; an independent predictor of symptoms of depression. It is plausible that concerns for adequate health care increase with a deteriorating level of physical function and independence in ADL. We cannot say if these responders have good reason to worry about inadequate future health care. Perhaps their symptoms of depression are partly caused by this concern. On the other hand, an underlying depression might be the cause of this worry. Many other possible causal pathways may explain this finding, and we shall not speculate more here, but only remark that the relationship between depression and loss of function is likely bi-directional, and may reinforce each other (Wells KB et al., 1989).

It is also interesting to note that we did *not* find a statistically significant association between the two cues. One possible interpretation of this is that the two cues pick up on different underlying causes of symptoms of depression. For example, one might conjecture that Cue 1 is associated with a feeling of unrealized potential, while Cue 2 is associated with a feeling of helplessness or concern for the future.

[‡‡] Recall the **Remark on Cue 2** in the **METHODS** section.

However, their association might be underestimated because the $PMR = 1$ group is small. In conclusion, while it cannot be ruled out, we have not found support for redundancy between the two cues studied here, and thus health care professionals should be aware of both cues.

There were no surprising findings regarding the depression incidence (22.6%) of our respondents. This figure is somewhat lower than previously reported depression incidence for stroke survivors in Norway (36.3 %) (Stordal et al., 2003). Ayerbe et al. reported a PSD-prevalence of 29%, at each follow-up point in a meta-study based on 50 previously published studies on the topic (Ayerbe et al., 2013b). Similar to our findings, Townend et al. reported a 21% prevalence rate of depression three months after discharge (Townend et al., 2007). However, Townend et al.'s study was based on a HADS-D score > 8, and with patients with either cognitive dysfunction or aphasia excluded from the study population and so is not directly comparable to our results. Furthermore, we have included TIA patients. Our findings, as well as the main body of literature, suggest that the severity of the stroke impacts the risk of developing PSD. Hence, a slightly lower prevalence of symptoms of depression might be expected.

The most important predictor of HADS-D ≥ 8 in our cohort is *poor function* measured by an mRS-score of above 2. This result is in accord with both common sense and the main body of literature on the subject (Fure et al., 2006; Robinson & Spalletta, 2010; Naess et al., 2010; Kouwenhoven et al., 2011; Ayerbe et al., 2013b). A previously history of depression was, somewhat surprisingly, not statistically significantly associated with HADS-D ≥ 8 in our data. This predictor obtained a p–value of 0.07 in the initial logistic regression model. However, PD was only positive for 11 respondents, and there is no reason to interpret this as negating previous findings of an PD—PSD association since this variable was not the main focus of our study, and might also be underreported.

Ryan et al. suggest many strategies for incorporating looking for cues and concerns in clinical consultations with patients with cancer (Ryan et al., 2005). These methods appear appropriate also in encounters with stroke survivors. We encourage the clinical practice of looking for cues for the mental well-being of stroke survivors.

It is recommended that patients displaying symptoms of depression according to a scoring/screening instrument undergo more thorough testing by health care professionals in order to adequately diagnose them (Carson et al., 2000; Gaete & Bogousslavsky, 2008). It is clear that this is also important for stroke survivors, who are known to be susceptible to depression, and who also present with many of the known risk factors for depression. An interesting field of research, tangent to ours, is that of so-called *ultra-brief screening tools* for symptoms of depression (Ryan et al., 2012; Ginkel et al., 2012, 2013). This field is concerned with reliably detecting symptoms of depression with as few questions as possible. These studies are concerned with developing standardized and validated screening tools which nevertheless contain only very few questions (only two in some tools.) As expected the trade-off between sensitivity and specificity is a main concern here. With sufficiently high sensitivity a low specificity can be acceptable when the cost of the initial screening is kept minimal while at the same time the potential health benefit is substantial. We believe that disease specific cues can be of great value as *a help-question* to such ultra-brief tools, as have been demonstrated by (Ryan et al., 2012).

Strengths and limitations

Ideally we would have included *arrival NIHSS* as a measure of the severity of the stroke. Unfortunately, this variable was ruled out due to excessive missingness. Therefore LOS was included in the analyses as a proxy for the severity of the stroke. While not entirely satisfactory, the correlation (0.287) of LOS with arrival-NIHSS indicated a positive relationship between severity and LOS. Furthermore, included in the analysis is mRS-data at three months, which may also indicate stroke severity to some degree.

Another limitation is the probable bidirectional relationship between function and depression and depression and self-reporting. Several studies (Dennis et al., 2000; J. Katon, 2011; Kirmayer et al., 1993; Kutlubaev & Hackett, 2014; Naess et al., 2010; Wells KB et al., 1989) indicate that depression both causes somatic morbidity and somatization, and, vice versa, that depression is most likely to

some extent caused by somatic morbidity. Therefore, it is fair to suspect that the strong correlation reported here between mRS outcome and symptoms of depression might be inflated by depressed patient reporting a worse mRS outcome than would a trained mRS-scorer. Of course, these bidirectional relationships may bias our result in other ways as well.

The relatively low response rate is a possible limitation of our study. The result from the non-responder analysis is interpreted as support for the claim that our responders are fairly representable for their cohort, albeit with some under-representation for the most severely morbid stroke-survivors. While the prevalence of depression might be underestimated here, the patients not well represented in our study – the severely ill and the institutionalized – should have their mental health closely monitored in any case (Langan et al., 2013; Stanners et al., 2014).

CONCLUSIONS

An expressed discrepancy between the availability of and the desire for rehabilitation in stroke survivors (Cue 1) is an important cue that the patient may be exhibiting symptoms of depression. The same applies to an expressed worry about the prospect of receiving adequate health care (Cue 2.) Therefore, health care workers who come in contact with stroke survivors or TIA patients who express such concerns should ensure that the patient's mental well-being is adequately monitored. Further research will be needed in order to determine the generalizability of these cues, and to investigate causal pathways.

RELEVANCE TO CLINICAL PRACTICE

Health care workers who come into contact with stroke survivors should pay attention to patients' remonstrance of access to rehabilitation, or concerns about adequacy of received care, as these might constitute cues of possible depression.

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TABLES

Table 1.—Descriptive statistics of sample with valid HADS-D data; stratified by HADS-D score below and above cut-off value of 8.

	HADS-D < 8	**HADS-D** $\geq$ **8**	Total		
n	304 (77.4%)	89 (22.6%)	393	(100%)	
Age	70.8 (SD12.4)	73.5 (SD12.1)	71.4	(SD12.4)	$p = 0.062$†
LOS	5.9 (SD 4.6)	7.8 (SD 5.1)	6.3	(SD 4.8)	$p = 0.001$†
Sex					
Female	134	41	175	(44.5%)	$p = 0.740$‡
Male	170	48	218	(55.5%)	
Total	304	89	(393)		
mRS					
Missing			80	(20.4%)	
Good (0—2)	219	38	257	(65.4%)	$p < 0.001$‡
Poor (3—5)	27	29	56	(14.2%)	
Total	246	67	(313)		
PMR					
Missing			22	(5.6%)	
No	282	74	356	(90.6%)	$p = 0.002$‡
Yes	6	9	15	(3.8%)	
Total	288	83	(371)		
IHD					
Missing			28	(7.1%)	
No	265	61	326	(83.0%)	$p < 0.001$‡

Yes	20	19	39	(9.9%)	
Total	285	80	(365)		
Type of Stroke					
TIA	88	16	104	(26.5%)	
INF	192	58	250	(63.6%)	p =0.015§
ICH	24	15	39	(9.9%)	
Total	304	89	(393)		
PCVA					
No	247	70	317	(80.7%)	$p = 0.582$‡
Yes	57	19	76	(19.3%)	
Total	304	89	(393)		
PD					
No	298	84	382	(97.2%)	$p = 0.097$‡
Yes	6	5	11	(2.8%)	
Total	304	89	(393)		

† p-value computed with native `t.test()`-function providing a Welch Two Sample t-test.

‡ p-value computed with `oddsratio()`-function from the R library psych with mid-p correction on 2x2 table of non-missing values.

§ p-value computed with native `fisher.test()`-function.

PMR - Perceived Missed Rehabilitation; IHD – Inadequate Help Dichotomized; LOS - Length of stay; PCVA - Previous cerebrvascular accident; PD -Previous Depression; mRSD – modified Rankin Scale score Dichotomized; HADS-D – Hospital Anxiety and Depression Scale Depression subscale; TIA – Transient Ischemic Attack; INF – INFarction; ICH – IntraCerebral Haemorrhage

Table 2.—Logistic regression model summary: stroke survivors' HADS-D score (dichotomized to 1 for HADS-D ≥ 8).

Predictor	β	OR	(95%CI)	*p*
Intercept	-2.427	-	-	.019
mRSD (1 = poor)	1.656	5.240	(2.503—11.105)	.000
PMR (1 = perceived missed)	1.552	4.721	(1.260—18.357)	.021
IHD (1 = inadequate help)	1.019	2.770	(1.171—6.420)	.018
Age	0.007	1.007	(0.980—1.035)	.620
Sex	-0,280	0.757	(0.388—1.478)	.411

Model diagnostics:

Goodness-of-fit test	χ^2	*df*	*p*
Hosmer & Lemeshow	5.481	8	.705
	Res.dev	*df*	*p*
Pearson's Residual Deviance	232.640	271	.956

Cox and Snell R^2 = .154. Nagelkerke R^2 = .242, Tjur's D = .190, Gini's R^2 =.194, Pearson's squared = .186

AIC (only significant predictors) = 244.64 vs. AIC (full model) = 248.98

PMR - Perceived Missed Rehabilitation; IHD – Inadequate Help Dichotomized; mRSD – modified Rankin scale dichotomized; HADS-D – Hospital Anxiety and Depression Scale Depression subscale

Table 3. —Descriptive statistics for the subgroups defined by the two cue-variables PMR and IHD.

				Sex		mRSD	
PMR	IHD=1	LOS[§]	Age[§]	Male	Female	0	1
0	34	6.3	71.1	199	157	234	50
1	4	7.3	72.5	6	9	8	5
IHD	PMR=1						
0	10	6.1	71.1	185	141	221*	37*
1	4	7.3	74.2	20	19	19*	16*

[§]Mean values for subgroups.

* The Fisher exact test for the association between mRSD and IHD was significant ($p < 0.001$); all other associations and differences of means were insignificant.

PMR - Perceived Missed Rehabilitation; IHD – Insadequate Help Dichotomized; mRSD – modified Rankin Scale score Dichotomized; LOS – Length Of Stay (days)