DOI: 10.1017/cjn.2024.303
This is a manuscript accepted for publication in *Canadian Journal of Neurological Sciences*.
This version may be subject to change during the production process.

DOC screen completion time reflects executive function, speed of processing and fluency

Sajeevan Sujanthan, HBSc[1]*, Alisia Southwell, MPH[1]*, Tera Armel, HBSc[1], Elaine Xing, HBSc[1], Arunima Kapoor, MSc[1], Xiao Yu Eileen Liu, MSc[1], Krista L. Lanctot, PhD[2,3,4], Nathan Herrmann, MD[2,3,4], Brian J. Murray, MD[1,2,3], Kevin E. Thorpe, MMath[4,5], Megan L. Cayley, BScN[1], Michelle N. Sicard, MSW[1], Karen Lien, MD[1], Demetrios J. Sahlas, MD, MSc[6,7,8], Richard H. Swartz, MD, PhD[1,3,4,9]

[1]Department of Medicine (Neurology), Sunnybrook Health Sciences Centre, Toronto
[2]Department of Psychiatry, Sunnybrook Health Sciences Centre, Toronto
[3]Hurvitz Brain Sciences Research Program, Toronto
[4]University of Toronto, Toronto
[5]St Michael's Hospital, Applied Health Research Centre of the Li Sha Shing Knowledge Institute, Toronto
[6]McMaster University, Hamilton
[7]Department of Medicine (Neurology), Hamilton Health Sciences Centre, Hamilton
[8]Hamilton General Hospital, Toronto
[9]Heart and Stroke Foundation Canadian Partnership for Stroke Recovery

*The first two authors contributed equally to this work

Corresponding Author: Dr. Richard H. Swartz, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Toronto, ON, Canada, M4N 3M5, Phone: 416-480-4866 e-mail: rick.swartz@sunnybrook.ca Fax: 416-480-4552

Short Title: DOC screen time as a measure of executive function

Email Address:

Sajeevan Sujanthan – sajeevan.sujanthan@mail.utoronto.ca
Alisia Southwell – alisia.bonnick@mail.utoronto.ca
Tera Armel – 15ta20@queensu.ca
Elaine Xing - elaine.xing@mail.utoronto.ca
Arunima Kapoor - aru.kapoor@gmail.com
Xiao Yu Eileen Liu - Eileen_148@hotmail.com
Krista L. Lanctot - krista.lanctot@sunnybrook.ca
Nathan Hermann - Nathan.Herrmann@sunnybrook.ca
Brian J. Murray - brian.murray@sunnybrook.ca
Kevin E. Thorpe - kevin.thorpe@utoronto.ca
Megan L. Cayley - megan.cayley@uhn.ca
Michelle N. Sicard - michelle@tuesdayafternoon.net
Karen Lien - karenlien90@hotmail.com
Demetrios Sahlas - sahlas@mcmaster.ca
Richard H. Swartz - rick.swartz@sunnybrook.ca
Keywords: Stroke, cognition, depression, sleep apnea, executive function

Authorship:

SS – Formal analysis, writing – original draft, writing – reviewing and editing

AS – Data collection, formal analysis, writing – original draft

TA – Formal analysis, writing – original draft

EX – Formal analysis, writing – original draft

AK – Formal analysis, writing – original draft

XL - Formal analysis, writing – original draft

KLL - Resources, supervision, writing – review and editing

NH - Resources, supervision, writing – review and editing

BJM - Resources, supervision, writing – review and editing

KET - Resources, supervision, writing – review and editing

MLC – Data collection, writing – review and editing

MNS – Data collection, writing – review and editing

KL – Data collection, writing – review and editing

DS - Resources, supervision, writing – review and editing

RHS – Funding, conceptualization, resources, supervision, writing – original draft, writing – reviewing and editing

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

Abstract

Background: The Depression, Obstructive sleep apnea, and Cognitive impairment (DOC) screen assesses three post-stroke comorbidities, but additional information may be gained from the time to complete the screen. Cognitive screening completion time is rarely used as an outcome measure.

Objective: To assess DOC screen completion time as a predictor of cognitive impairment in stroke/TIA clinics.

Methods: Consecutive English-speaking stroke prevention clinic patients consented to undergo screening and neuropsychological testing (n=437). DOC screen scores and times were compared to scores on the NINDS-CSC battery using multiple linear regression (controlling for age, sex, education and stroke severity) and receiver operating characteristic (ROC) curve analysis.

Results: Completion time for the DOC screen was 3.8 ± 1.3 minutes. After accounting for covariates, completion time was a significant predictor of speed of processing (p=0.002, 95% CI: -0.016 to -0.004), verbal fluency (p<0.001, CI: -0.012 to -0.006) and executive function (p=0.004, CI: -0.006 to -0.001), but not memory. Completion time above 5.5 minutes was associated with a high likelihood of impairment on executive and speed of processing tasks (likelihood ratios 3.9-5.2).

Conclusions: DOC screen completion time is easy to collect in routine care. People needing over 5.5 minutes to be screened likely have deficits in executive functioning and speed of processing - areas commonly impaired, but challenging to screen for, after stroke. DOC screen time provides a simple, feasible approach to assess these under-identified cognitive impairments.

Data Access: Data is not available to share publicly, as patients did not consent to public data release.

Clinical Trials Registration Identifier: NCT02363114

Clinical Trials URL: https://clinicaltrials.gov/ct2/show/NCT02363114

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

Introduction

Stroke is the leading cause of neurological disability in adults[1] and survival after stroke is increasing.[2–4] In addition to physical post-stroke deficits,[5] approximately 30 to 50% of stroke survivors are affected by each of **d**epression, **o**bstructive sleep apnea (OSA), and **c**ognitive impairment (DOC).[6–9] These DOC comorbidities are all associated with poorer functional outcomes,[10] and an increased risk of mortality.[11]

The DOC screen was developed as a feasible and valid tool to screen and stratify stroke patients into high, intermediate, and low risk groups for DOC comorbidities to facilitate detection and management in high-volume stroke clinic settings.[12] The screen is efficient, yet designed to maintain the construct validity of a delayed recall task. Eighty-nine percent of patients in stroke prevention clinics are able to complete the tool in <6 minutes (mean=4.2 minutes, SD=1.5).[12] In validation studies, the cognitive component of the DOC score is helpful to quickly stratify people into "cognitively normal", "cognitively impaired" and "need more assessment" groups, compared to more detailed cognitive testing.[12]Although the DOC completion time was originally collected as a way to assess feasibility, practitioners can record this measure when administering the DOC screen in clinical settings. Several studies have reported the average time taken to complete other well-known cognitive screens as feasibility demonstrations, including the Montreal Cognitive Assessment (MoCA; means ranging from 9.5 minutes – 11 minutes)[13,14] and the Mini Mental State Examination (MMSE; means ranging from 8 minutes – 13.4 minutes).[14,15] However, few studies have assessed the utility of using a cognitive screen's completion time as a metric to evaluate underlying cognitive abilities, such as executive functioning.

Executive dysfunction and delays in speed of processing are the most commonly reported cognitive impairments after stroke. The DOC screen specifically examines mood symptoms, cognitive (executive, memory and abstraction) dysfunction and OSA/fatigue – all of which could be associated with cognitive or psychomotor slowing.[16]

Aim

Screen completion time is an immediately available metric, requiring no additional effort from either patients or clinicians, that might reflect executive function. The objective of this study was to determine whether completion time for the DOC screen is a reliable reflection of cognitive dysfunction and whether a single completion time cut-point could indicate cognitive impairment.

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

Methods

All patients were recruited from the DOC feasibility and validity study.[12] This study included English speaking (or English fluent) patients newly referred to stroke prevention clinics between April 23rd, 2012 and April 30th, 2014 (n=1504) who could complete the screen independently (with the administrator, but without third party support). We excluded patients with severe aphasia, severe motor dysfunction (unable to hold a pen and draw a clock) and patients who were not fluent in English. Each eligible participant was administered the DOC screen (**Figure 1**) as a brief screen of depression, obstructive sleep apnea (OSA) and cognitive impairment. All DOC screens were timed from the beginning of the memory registration (first task) until the end of the 5-word free recall (final task). Chart abstractions by trained research members captured demographic and clinical data on all participants from patient charts using previously published and validated methods.[17,18]

To reduce sampling bias, all consecutive patients from stroke prevention clinics who completed the DOC screen were asked to complete more detailed neuropsychological assessments, including a cognitive battery and formal mood assessments as outlined in the DOC feasibly study.[12] All patients who completed the detailed assessments provided written informed consent. Only the site PI could access the information that could identify individual participants, all the other authors were given anonymized study ID that was created upon the completion of the informed consent process. A complete list of all mood and cognitive assessments completed as part of the DOC study is reported elsewhere.[12] In this analysis, cognition was assessed using the 30-minute neuropsychological battery recommended by the NINDS-CSN.[19] This cognitive battery consists of the: Controlled Oral Word Association Test (phonemic fluency), Animal Naming task (semantic fluency), California Verbal Learning Test (CVLT), Digit Symbol Coding, and Trail Making Tests (TMT-A and TMT-B). All scores were normalized (z-score or scaled score) for age using age-matched norms from each respective test manual. CVLT and Animal Naming were also education-standardized.[20,21] The study was approved by the Sunnybrook Research Ethics Board (approval number SUN-2312).

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows version 24. Descriptive statistics, including means and standard deviations, were calculated for age, screen completion time, and number of years of education.

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

Multivariable linear regression analyses of the relationship between time-to-completion and NINDS-CSC standardized scores

To assess whether screen time reflects cognitive function, independent linear regression models were used to examine the association between DOC completion time and the scaled or z-scores of all neuropsychological subtests. Data from all participants were used in the regression models. A sensitivity analysis was performed using a complete case approach to assess whether missing variables affected the models. All models controlled for age, education, modified Rankin Score (mRS) and sex. Due to the established relationship between the DOC cognitive sub-scores and detailed cognitive assessments,[12] we also controlled for the DOC-Cognition score in all models. To adjust for multiple (7) linear regressions, Bonferroni correction (0.05/7 = 0.0071) was used to define significance at $p < 0.007$ for all analyses.

ROC and logistic regression analyses to identify cutoffs associated with high likelihood of cognitive impairments:

To identify whether a single cut point (in seconds) for screen time could be found with high specificity and likelihood ratios for cognitive impairment, receiver operating characteristic (ROC) curves were used. ROC analyses were run for each neuropsychological assessment significantly associated with the DOC screen completion time. A logistic regression with screen time completion (as a continuous variable) and the cognitive impairment classification on the NINDS-CSN assessments was applied to the ROC curves. The classification of cognitive impairment of NINDS-CSN was defined as scores >2.0 standard deviations from expected norms, on 2 or more cognitive tasks. This required participants to have completed all tests in the detailed cognitive battery, thus a complete case approach was used for all ROC analyses. First, a single, specific cut-point (time in seconds) was defined based on the ROC curve output for patients with an overall classification of impaired on the NINDS-CSN battery. The cut-point was pre-specified to have 95% specificity for cognitive impairment. This cut-point was then applied to ROC curves from each individual assessment and evaluated using likelihood ratios (LR).

Results

437 patients completed the cognitive and mood gold standard assessments within a maximum of 3 months of screening, with the average time interval of 3 days[22] (Supplemental Table 1). 213 (48.7%) participants were male, the mean (± standard deviation) age was 62.7 ± 15.6 years, and the mean years of education was 15.6 ± 3.9 years (**Table 1**). 387 patients were able to complete

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

all assessments in the battery; 13.7 % of those were classified as impaired based on the NINDS-CSN classification. The DOC screen completion mean was 3.8 ± 1.3 minutes (range: 1.9-9.6 minutes).134 (31%) patients had an ischemic stroke, 138 (32%) had a probable/possible TIA, and the remainder (37%) were diagnosed with other conditions (**Table 1**). Non-stroke/TIA diagnoses included patients referred with possible stroke symptoms, but whose further investigations revealed alternative diagnoses, as well as patients without specific stroke/TIA symptoms referred for either vascular risk reduction or assessment of incidental abnormal imaging findings.

We performed linear regressions with DOC screen completion time (in seconds) as a predictor for each neuropsychological assessment score (**Table 2**). In all models we controlled for age, sex, years of education, screening score of cognitive function (DOC-Cognition score), and overall function (mRS). All regression models for screen completion time were significant ($p < .001$) (Supplemental Table 2). Additionally, model summaries showed that screen completion time was a significant predictor ($p < 0.005$) of: verbal fluency semantic score (95% Confidence Interval (CI) of Beta-coefficient from linear regression: -.006 to -.001), verbal fluency phonemic Score (95% CI: -.018 to -.006), Digit Symbol Coding (95% CI: -.016 to -.004) and the Trail Making Tests (TMT-A 95% CI: -.017 to -.005; TMT-B 95% CI: -.016 to -.004). In all cases, these were negative correlations (i.e., longer completion times correlated with poorer cognitive scores). DOC screen completion time was not a significant predictor of memory performance on the CVLT Short Delay Free Recall (p=.713, 95% CI: -.003 to .002) or the CVLT Long Delay Free Recall (p=.790, 95% CI: -.002 to .003). Results did not differ in the sensitivity models with complete case data (see Table 2 compared to Supplemental Table 3 with complete case data). Neither DOC mood and apnea screening scores, nor SCID-D or polysomnogram scores were associated with DOC screen completion time in any multivariable regression.

Using the single cut-off point approach on the overall cognitive impairment ROC curve (Figure 2, Table 3A), the point with 95% specificity for cognitive impairment was 332.5 seconds. When this time was applied to ROC models for each individual cognitive task (Table 3B), the same cut-point had high specificity on all executive and speed of processing tasks. The area under the curve was greater than 0.7 for all executive and speed of processing tasks. Likelihood ratios for predicting abnormal results on executive and speed of processing tasks ranged from four to six – that is, people taking more than 332.5 seconds to complete the DOC

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

screen were 4-6 times more likely to have severe cognitive impairment on executive and speed of processing tasks than those with faster completion times (see Table 3). Scatterplots demonstrating the predicted probability of impairment on each domain by completion time, derived from the logistic regression analysis can be found in the supplemental material.

Discussion

Several studies[23] have shown that post-stroke cognitive impairments can be separated into independent cognitive factors including language, memory and executive function, with deficits in executive functioning and speed of processing being the most common.[24] Screening tests for executive function and speed of processing are limited and rarely used in routine clinical care. These results demonstrate that DOC screen completion time is an independent predictor of executive function (semantic fluency,[25] TMT-B[26]), speed of processing (Digit symbol coding,[27] TMT-A and B[28]) and verbal fluency[29] after stroke, even after controlling for age, sex, education, DOC-Cognition score and stroke severity. Completion time did not predict CVLT scores, a verbal test primarily affecting verbal memory (learning/registration and recall).[30] Verbal fluency, while reflecting language function, is also reflective of executive function.[31] Moreover, we have demonstrated that a 332.5 second (roughly 5.5 minutes) cut-off has 95% specificity and high likelihood ratios for predicting both overall cognitive and executive function impairment. This can be used as a quick and easily obtainable measure to identify people at risk for impairment on executive and speed of processing tasks. Certainly, other timed tasks, whether pen-and-paper (like Trails) or digital (e.g. Creyos), can be used to assess executive and speed of processing deficits in detail; however, detailed cognitive batteries are too onerous for routine clinical use. Simply timing the DOC screen as it is administered provides additional information, beyond the actual DOC cognitive screening score, that can flag people at high risk of having multi-domain cognitive impairment and executive/speed of processing dysfunction.

A few notable neuropsychological measures have used completion time to assess specific cognitive functions. For instance, Trail Making Tests (TMTs) are a set of widely accepted timed neuropsychological measures that provide insight into executive abilities.[28] Processing speed is highly associated with performance on TMT Part B (a task reflecting attention and executive functions such as set shifting), and with performance on TMT Part A (which is more closely related to motor speed and attention).[26,32,33] Similarly, Woods et al. discovered that a patient's question completion time on self-paced questionnaires could be used as a measure of executive

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

functioning.[34] Question completion time measures processing and decision-making speeds, providing insight into motivation, effort, and cognitive ability that is not measured by existing tests.[34] These studies support the notion that timed measures may be useful as a measure of executive dysfunction in addition to their use as screening instruments. The findings presented in our study correspond well to those reported by Woods et al. Their analysis showed that complex tasks, akin to our DOC-Cognitive tasks, were strongly related to executive function and processing speed. Their neuropsychological tests (including TMT-B and Digit Span) also correlated significantly with self-paced question completion time. Their research process was similar to ours, wherein completion time was compared to existing screens to validate completion time as a metric; both studies suggest that completion time of self-paced complex assessments may be valid markers of executive function.

Few studies use completion time of a neuropsychological screening tool as a cognitive marker. Most timed tasks examine processing speed directly (e.g. Trails, Symbol-digit modalities test[35]) and have been studied in clinical settings, for example for HIV induced cognitive dysfunction[36,37] and in Multiple Sclerosis.[38,39] However, these types of tasks are more detailed and time consuming, and while they can be performed in clinic in isolation, they are more often done as part of larger batteries. In contrast, screening tasks like the MoCA or MMSE are not routinely timed when applied in clinical settings. By simply timing the DOC screen, in addition to the information generated by the screen on mood, apnea and cognitive function, the time taken to complete the entire screen is itself an indirect measure that can highlight people at risk for cognitive impairment, especially executive, speed of processing and attentional issues. Moreover, executive function deficits are not often assessed in stroke patients; these deficits are subtle, challenging to test for, and often go unrecognized.[24] The NINDS-CSC battery is recommended as a research battery, but it requires a trained administrator, and at least 30 minutes per person plus scoring. This is not feasible for routine clinic use. The DOC screen, in contrast, takes less than 5 minutes, can be performed by clinical staff (students, administrative assistances, nurses and physicians) and can help to highlight people at risk for impairments in mood, apnea and cognition.

The interpretation of our findings is limited by our sample population. Compared to the total number of patients who were asked to volunteer from the stroke prevention clinic (n=1504), consenting participants (n=437) tended to be slightly younger and with slightly milder

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

neuropsychological deficits (healthy participant bias).[12] However, our sample also included a wide range of patients across the full spectrum of severity. As expected from stroke/TIA clinic samples, 62% had a diagnosis of stroke and/or TIA, and the rest had alternative diagnoses common in stroke prevention clinics (mimics, multiple vascular risk factors, abnormal imaging). This heterogeneity reflects the pragmatic nature of the screening and its broad generalizability to the population of patients referred to stoke prevention clinics. TIA patients are well recognized to share similar long-term risk profiles[40] and are also at risk for cognitive impairment,[41] compared to those with imaging confirmed strokes. While the strongest associations to DOC completion were with tests of executive function, processing speed and verbal fluency, other domains that were less well represented in the NINDS-CSC battery could also impact screen completion time. For example, visuospatial function was not specifically assessed in the NINDS-CSC battery; and while language function could also affect completion time, there was no relationship with score on the California Verbal Learning Task (a verbal memory task). Since many tasks have more than one cognitive construct underlying them (e.g. phonemic and semantic fluency tasks each require language, attention and executive functions), DOC screen time cannot be considered a reflection of only one underlying domain. However, the tasks associated with DOC screen time all share underlying cognitive constructs of attention, executive dysfunction and/or speed of processing. The relationship between DOC completion time and gold standard testing was found across a range of severity from normal function to severely impaired. It should also be noted that there is not a single perfect cut-off score for DOC completion time that indicates executive dysfunction. To facilitate clinical utility, and because this is intended as a screen in high-volume clinics, we chose to explore a cut-off with high specificity so clinicians could be confident there was a high likelihood of true cognitive impairment beyond this time; however, this cut-off will have a low sensitivity and will miss some people with cognitive impairments. Previous work has already established that the DOC-Cognition score can also be a sensitive screen, effectively ruling out cognitive impairment in people who score highly.[12] Finally, it is important to note that although screen completion time may be a useful tool to identify people at risk for executive dysfunction, it is still not equivalent to a detailed neuropsychological assessment.

Conclusion

Clinical cognitive screening tools have not commonly used completion time as a metric. We

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

aimed to determine whether the DOC screen completion time could provide clinically relevant information on patients' cognitive function. DOC screen completion time reflects executive function, speed of processing and verbal fluency. When administering the DOC screen, completion time requires no additional time or patient burden to collect. This convenience is vital in busy stroke prevention clinic settings, where there is minimal time for detailed cognitive assessments. Exploring whether screen time can act as a predictor of future outcomes would provide further support the utility of this measure in clinical settings.

Acknowledgments

We would like to acknowledge the DOC participants who volunteered their time for the study.

Sources of Funding

This study was supported by CIHR (Grant Ref No. 137038) and HSF (Project No. 000392). RHS received salary support for research from an Ontario Clinician Scientist (Phase II) Award from the HSF Canada and from the Department of Medicine (Neurology) at Sunnybrook and University of Toronto. In-kind support for data storage was provided by the Ontario Brain Institute and the Ontario Neurodegenerative Disease Research Initiative (ONDRI).

Disclosures

RHS reports ownership shares in FollowMD Inc., a virtual vascular risk reduction clinic. None of the other authors have any conflicts of interest to disclose.

Data Availability

DOC screening for mood, cognition and apnea was performed in stroke prevention clinics under waiver of consent. Patients provided written consent to undergo detailed cognitive testing and to relate their screening results to the detailed neuropsychological testing. However, public release of data was not part of the patient consent.

Non-Standard Abbreviations and Acronyms

CVLT – California Verbal Learning Test

DOC – Depression, Obstructive Sleep Apnea, Cognitive Impairment

MMSE – Mini Mental State Examination

MoCA – Montreal Cognitive Assessment

OSA – Obstructive Sleep Apnea

QCT – Question Completion Time

TMT – Trail Making Test

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

References

1. Feigin VL, Nichols E, Alam T, et al. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol*. 2019;18(5):459-480. doi:10.1016/S1474-4422(18)30499-X
2. Lakshminarayan K, Berger AK, Fuller CC, et al. Trends in 10-Year Survival of Patients With Stroke Hospitalized Between 1980 and 2000. *Stroke*. 2014;45(9):2575-2581. doi:10.1161/STROKEAHA.114.005512
3. Rodríguez-Castro E, López-Dequit I, Santamaría-Cadavid M, et al. Trends in stroke outcomes in the last ten years in a European tertiary hospital. *BMC Neurol*. 2018;18(1):164. doi:10.1186/s12883-018-1164-7
4. Waziry R, Heshmatollah A, Bos D, et al. Time Trends in Survival Following First Hemorrhagic or Ischemic Stroke Between 1991 and 2015 in the Rotterdam Study. *Stroke*. 2020;51(3):824-829. doi:10.1161/STROKEAHA.119.027198
5. Verstraeten S, Mark R, Sitskoorn M. Motor and Cognitive Impairment after Stroke: A Common Bond or a Simultaneous Deficit? *Stroke Research & Therapy*. 2016;1(1).
6. Herrmann N, Seitz D, Fischer H, et al. Detection and treatment of post stroke depression: results from the registry of the Canadian stroke network. *Int J Geriatr Psychiatry*. Published online 2011:n/a-n/a. doi:10.1002/gps.2663
7. Johnson KG, Johnson DC. Frequency of sleep apnea in stroke and TIA patients: a meta-analysis. *J Clin Sleep Med*. 2010;6(2):131-137.
8. Patel MD, Coshall C, Rudd AG, Wolfe CDA. Cognitive Impairment after Stroke: Clinical Determinants and Its Associations with Long-Term Stroke Outcomes. *J Am Geriatr Soc*. 2002;50(4):700-706. doi:10.1046/j.1532-5415.2002.50165.x
9. Kapoor A, Lanctôt KL, Bayley M, et al. "Good Outcome" Isn't Good Enough. *Stroke*. 2017;48(6):1688-1690. doi:10.1161/strokeaha.117.016728
10. Kapoor A, Lanctot KL, Bayley M, Herrmann N, Murray BJ, Swartz RH. Screening for Post-Stroke Depression and Cognitive Impairment at Baseline Predicts Long-Term Patient-Centered Outcomes After Stroke. *J Geriatr Psychiatry Neurol*. 2019;32(1):40-48. doi:10.1177/0891988718819859
11. Swartz RH, Bayley M, Lanctôt KL, et al. Post-stroke depression, obstructive sleep apnea, and cognitive impairment: Rationale for, and barriers to, routine screening. *International Journal of Stroke*. 2016;11(5):509-518. doi:10.1177/1747493016641968

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

12. Swartz RH, Cayley ML, Lanctôt KL, et al. The “DOC” screen: Feasible and valid screening for depression, Obstructive Sleep Apnea (OSA) and cognitive impairment in stroke prevention clinics. Romigi A, ed. *PLoS One*. 2017;12(4):e0174451. doi:10.1371/journal.pone.0174451
13. Lees RA, Hendry BA K, Broomfield N, Stott D, Larner AJ, Quinn TJ. Cognitive assessment in stroke: feasibility and test properties using differing approaches to scoring of incomplete items. *Int J Geriatr Psychiatry*. 2017;32(10):1072-1078. doi:10.1002/gps.4568
14. Barnay JL, Wauquiez G, Bonnin-Koang HY, et al. Feasibility of the cognitive assessment scale for stroke patients (CASP) vs. MMSE and MoCA in aphasic left hemispheric stroke patients. *Ann Phys Rehabil Med*. 2014;57(6-7):422-435. doi:10.1016/J.REHAB.2014.05.010
15. Molloy DW. *Standardised Mini-Mental State Examination (SMMSE): Guidelines for Administration and Scoring Instructions*.; 2014.
16. Schrijvers D, Hulstijn W, Sabbe BGC. Psychomotor symptoms in depression: A diagnostic, pathophysiological and therapeutic tool. *J Affect Disord*. 2008;109(1-2):1-20. doi:10.1016/j.jad.2007.10.019
17. Hall R, Khan F, O’Callaghan C, et al. *Ontario Stroke Evaluation Report 2013: Spotlight on Secondary Stroke Prevention and Care*.; 2013.
18. Kapral MK, Fang J, Hill MD, et al. Sex Differences in Stroke Care and Outcomes. *Stroke*. 2005;36(4):809-814. doi:10.1161/01.STR.0000157662.09551.e5
19. Hachinski V, Iadecola C, Petersen RC, et al. National Institute of Neurological Disorders and Stroke–Canadian Stroke Network Vascular Cognitive Impairment Harmonization Standards. *Stroke*. 2006;37(9):2220-2241. doi:10.1161/01.STR.0000237236.88823.47
20. Tombaugh T. Normative Data Stratified by Age and Education for Two Measures of Verbal Fluency FAS and Animal Naming. *Archives of Clinical Neuropsychology*. 1999;14(2):167-177. doi:10.1016/S0887-6177(97)00095-4
21. Delis DC, Kramer JH, Kaplan E, Ober BE. *California Verbal Learning Test | Second Edition*. Second. The Psychological Corporation; 2000.
22. Swartz RH, Cayley ML, Lanctôt KL, et al. The “DOC” screen: Feasible and valid screening for depression, Obstructive Sleep Apnea (OSA) and cognitive impairment in stroke prevention clinics. *PLoS One*. 2017;12(4):e0174451. doi:10.1371/JOURNAL.PONE.0174451
23. Swartz RH, Stuss DT, Gao F, Black SE. Independent Cognitive Effects of Atrophy and Diffuse Subcortical and Thalamico-Cortical Cerebrovascular Disease in Dementia. *Stroke*. 2008;39(3):822-830. doi:10.1161/STROKEAHA.107.491936

24. Zinn S, Bosworth HB, Hoenig HM, Swartzwelder HS. Executive function deficits in acute stroke. *Arch Phys Med Rehabil*. 2007;88(2):173-180. doi:10.1016/J.APMR.2006.11.015
25. Maseda A, Lodeiro-Fernández L, Lorenzo-López L, Núñez-Naveira L, Balo A, Millán-Calenti JC. Verbal fluency, naming and verbal comprehension: three aspects of language as predictors of cognitive impairment. *Aging Ment Health*. 2014;18(8):1037-1045. doi:10.1080/13607863.2014.908457
26. Arbuthnott K, Frank J. Trail Making Test, Part B as a Measure of Executive Control: Validation Using a Set-Switching Paradigm. *J Clin Exp Neuropsychol*. 2000;22(4):518-528. doi:10.1076/1380-3395(200008)22:4;1-0;FT518
27. Deloire MS, Bonnet MC, Salort E, et al. How to detect cognitive dysfunction at early stages of multiple sclerosis? *Multiple Sclerosis Journal*. 2006;12(4):445-452. doi:10.1191/1352458506ms1289oa
28. Muir RT, Lam B, Honjo K, et al. Trail Making Test Elucidates Neural Substrates of Specific Poststroke Executive Dysfunctions. *Stroke*. 2015;46(10):2755-2761. doi:10.1161/STROKEAHA.115.009936
29. Whiteside DM, Kealey T, Semla M, et al. Verbal Fluency: Language or Executive Function Measure? *Appl Neuropsychol Adult*. 2016;23(1):29-34. doi:10.1080/23279095.2015.1004574
30. JACOBS M, DONDERS J. Criterion validity of the California Verbal Learning Test-Second Edition (CVLT-II) after traumatic brain injury. *Archives of Clinical Neuropsychology*. 2007;22(2):143-149. doi:10.1016/j.acn.2006.12.002
31. Aita SL, Beach JD, Taylor SE, Borgogna NC, Harrell MN, Hill BD. Executive, language, or both? An examination of the construct validity of verbal fluency measures. *Appl Neuropsychol Adult*. 2019;26(5):441-451. doi:10.1080/23279095.2018.1439830
32. MacPherson SE, Cox SR, Dickie DA, et al. Processing speed and the relationship between Trail Making Test-B performance, cortical thinning and white matter microstructure in older adults. *Cortex*. 2017;95:92-103. doi:10.1016/j.cortex.2017.07.021
33. Fishman KN, Ashbaugh AR, Swartz RH. Goal Setting Improves Cognitive Performance in a Randomized Trial of Chronic Stroke Survivors. *Stroke*. 2021;52(2):458-470. doi:10.1161/STROKEAHA.120.032131
34. Woods DL, William Yund E, Wyma JM, Ruff R, Herron TJ. Measuring executive function in control subjects and TBI patients with question completion time (QCT). *Front Hum Neurosci*. 2015;9(MAY). doi:10.3389/FNHUM.2015.00288

35. Zaidi KB, Rich JB, Sunderland KM, et al. Methods for Improving Screening for Vascular Cognitive Impairment Using the Montreal Cognitive Assessment. *Can J Neurol Sci*. 2020;47(6):756-763. doi:10.1017/CJN.2020.121
36. Davis HF, Skolasky RL, Selnes OA, Burgess DM, McArthur JC. Assessing HIV-associated dementia: Modified HIV dementia scale versus the grooved pegboard. *AIDS Reader*. 2002;12(1):29-31+38.
37. Van Harten B, Courant MNJ, Scheltens P, Weinstein HC. Validation of the HIV Dementia Scale in an Elderly Cohort of Patients with Subcortical Cognitive Impairment Caused by Subcortical Ischaemic Vascular Disease or a Normal Pressure Hydrocephalus. *Dement Geriatr Cogn Disord*. 2004;18(1):109-114. doi:10.1159/000077818
38. Ezegbe C, Zarghami A, van der Mei I, Alty J, Honan C, Taylor B. Instruments measuring change in cognitive function in multiple sclerosis: A systematic review. *Brain Behav*. 2023;13(6):e3009. doi:10.1002/BRB3.3009
39. Wishart M, Everest MR, Morrow SA, Rose J, Shen L, Feinstein A. Establishing the consistency of a voice recognition symbol digit modalities test analogue. *Mult Scler*. 2023;29(13):1676-1679. doi:10.1177/13524585231199321
40. Edwards JD, Kapral MK, Fang J, Swartz RH. Long-term morbidity and mortality in patients without early complications after stroke or transient ischemic attack. *Can Med Assoc J*. 2017;189(29):E954-E961. doi:10.1503/cmaj.161142
41. Pendlebury ST, Wadling S, Silver LE, Mehta Z, Rothwell PM. Transient Cognitive Impairment in TIA and Minor Stroke. *Stroke*. 2011;42(11):3116-3121. doi:10.1161/STROKEAHA.111.621490

Figure 1: The **D**epression, **O**bstructive sleep apnea (OSA), and **C**ognitive impairment (DOC) screen (freely available for download at www.docscreen.ca).

DOC SCREEN PART 1

Date: _____

Patient of: _____

Completed by:
☐ RN
☐ MD
☐ RA

Language:
☐ English 1st language
☐ ESL, fluent
☐ ESL, not fluent

Sex:
☐ M
☐ F

Unable to complete due to:
☐ Language
☐ Aphasia/Dysphasia
☐ Unable to translate
☐ Motor
☐ Vision
☐ Too ill
☐ Other: _____

Resides at:
☐ Home
☐ Nursing Home/ LTC/CCC
☐ Inpatient rehab facility
☐ Retirement Home
☐ Other Residential Facility
☐ No Fixed Address
☐ UTD

Education: highest grade (1-13) _____ # of undergraduate years _____ # of graduate years _____

Systolic BP: _____

Diastolic BP: _____

Height: _____

Weight: _____

Waist/Hip Circumference: _____/_____

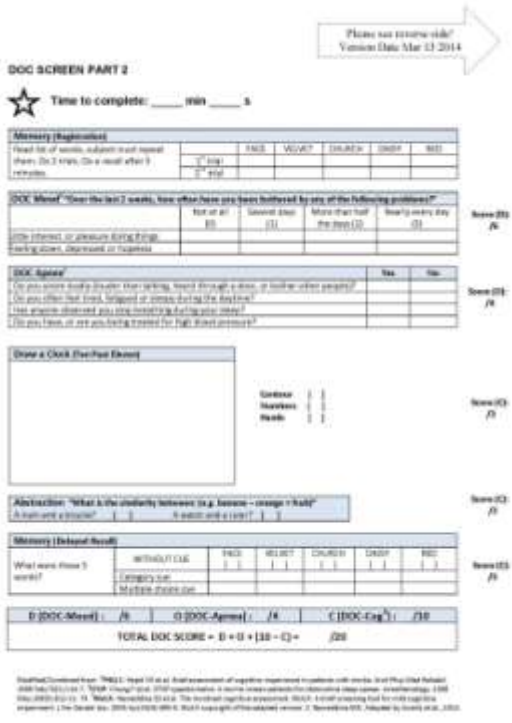
Modified Rankin Scale: _____

0 – No symptoms.
1 – No significant disability despite symptoms; able to carry out all usual duties and activities.
2 – Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance.
3 – Moderate disability; requiring some help, but able to walk without assistance (**with or without cane or walker**).
4 – Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance.
5 – Severe disability; bedridden, incontinent and requiring constant nursing care and attention.

Clinical Frailty Scale: _____

1 – Very fit - Robust, active, energetic, well-motivated and fit
2 – Well - Without active disease, but less fit than those in 1
3 – Well, with treated comorbid disease - Disease symptoms well controlled
4 – Apparently vulnerable - Not dependent, but common complaints about being 'slowed up' or having disease symptoms
5 – Mildly frail - Limited dependence for IADLs
6 – Moderately frail - Help required for both IADLs/ADLs
7 – Severely frail - Completely dependent on others for ADLs, or terminally ill

Please see reverse side!
Version Date: Mar 13 2014



Please see reverse side!
Version Date: Mar 13 2014

DOC SCREEN PART 2

Time to complete: _____ min _____ s

Memory (Registration)

Read list of words, subject must repeat them. Do 3 trials. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED
	1st trial					
	2nd trial					

DOC Mood "Over the last 2 weeks, how often have you been bothered by any of the following problems?"

	Not at all (0)	Several days (1)	More than half the days (2)	Nearly every day (3)
Little interest or pleasure doing things				
Feeling down, depressed or hopeless				

Score (D): /6

DOC Apnea

	Yes	No
Do you snore loudly (louder than talking, heard through a door, or bother other people)?		
Do you often feel tired, fatigued or sleepy during the daytime?		
Has anyone observed you stop breathing during your sleep?		
Do you have, or are you being treated for high blood pressure?		

Score (O): /4

Draw a Clock (Two-Step Eleven)

Contour [ ]
Numbers [ ]
Hands [ ]

Score (C): /3

Abstraction: "What is the similarity between (e.g. banana – orange = fruit)"

A train and a bicycle? [ ] A watch and a ruler? [ ]

Score (C): /2

Memory (Delayed Recall)

What were those 5 words?	WITHOUT CUE	FACE	VELVET	CHURCH	DAISY	RED
		[ ]	[ ]	[ ]	[ ]	[ ]
	Category cue					
	Multiple choice cue					

Score (D): /5

D [DOC-Mood] : /6	O [DOC-Apnea] : /4	C [DOC-Cog] : /10
TOTAL DOC SCORE = D + O + [10 – C] =		/20

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

Table 1: Demographics for participants completing detailed cognitive and neuropsychological assessments (n = 437).

Variables	**Mean (SD)**
Age (years)	62.7 (15.6)
Education (years)	15.6 (3.9)
DOC screen completion time (s)	227.8 (76.6)
Language	**n (%)**
English	363 (83.1)
English Second Language	74 (16.9)
Sex (female)	51.3%
Most Responsible Diagnosis	
Undetermined Diagnosis	4 (.9)
Abnormal CT/MRI Scan	21 (4.8)
Asymptomatic Carotid Artery Disease	4 (0.9)
Definite Ischemic Stroke	121 (27.7)
Definite TIA	54 (12.4)
Hemorrhage ICH	17 (3.9)
Hemorrhage IVH	1 (0.2)
Hemorrhage SAH	4 (0.9)
Hemorrhage SDH	1 (0.2)
Other Non-Vascular	96 (22)
Other Vascular	14 (3.2)
Possible/Query Ischemic	13 (3.0)
Possible/Query TIA	84 (19.2)
Sinovenous Thrombosis	3 (0.7)
Modified Ranking Scale (mRS)	
0	230 (52.6)
1	113 (25.9)
2	69(15.8)
3	19 (4.3)
4	2 (.5)
Missing	4 (.9)

† TIA = transient ischemic attack, ICH = intracerebral hemorrhage, IVH = intraventricular hemorrhage, SAH = subarachnoid hemorrhage, SDH = subdural hemorrhage, CT = Computed Tomography, MRI = Magnetic Resonance Imaging

DOC = **D**epression, **O**bstructive sleep apnea (OSA), and **C**ognitive impairment

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

Table 2: Linear Regression results showing the effect of the DOC screen completion time on individual neuropsychological assessments.

Measure	Test	B-value	Sig.	95% Confidence Interval	
				Lower Bound	Upper Bound
Executive Function	Semantic Fluency (Z-score)	-.004	**.004**	-.006	-.001
Language (verbal fluency)	Phonemic Fluency (Scaled Score)	-.012	**< .001**	-.018	-.006
Speed of Processing	Digit Symbol Coding (Scaled Score)	-.010	**.002**	-.016	-.004
Motor & Speed of processing	TMT-A (Scaled Score)	-.011	**< .001**	-.017	-.005
Executive function & Speed of processing	TMT-B (Scaled Score)	-.010	**.002**	-.016	-.004
Memory	CVLT Short Delay Free Recall (Z-score)	.000	.713	-.003	.002
	CVLT Long Delay Free Recall (Z-score)	.000	.790	-.002	.003

*all models controlled for by age, sex, years of education, DOC-Cognition score and modified Rankin Scale (mRS)

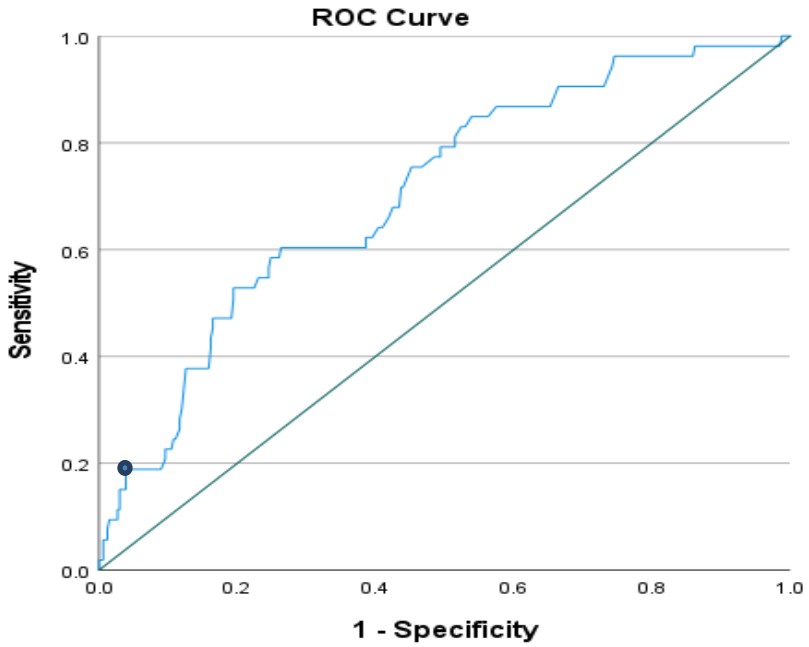
†significant results bolded and set at $p < 0.007$

† TMT = Trails Making Test, CVLT = California Verbal Learning Test,

DOC = **D**epression, **O**bstructive sleep apnea (OSA), and **C**ognitive impairment

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

Figure 2 – Receiver Operating Characteristic (ROC) curve, model for overall cognitive impairment with a **cut-off set at 95% specificity**.



Area Under the Curve	**0.706**
Error	**0.037**
Confidence Interval	**.633 - .779**

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press

Table 3 – Receiver Operating Characteristic (ROC) model outputs comparing DOC screen completion time with full neuropsychological assessments, with a cut off set at **332.5 seconds (95% specificity) obtained from the model for overall cognitive impairment.**

	Cut-off – Time (seconds)	**Specificity**	**Sensitivity**	**Area Under the Curve (AUC)**	**Likelihood Ratio (LR+)**
A) Impairment ROC regression (>2 standard deviations from expected norms on 2 or more tasks)					
Impaired/not	332.5	0.95	0.19	0.706	**3.7**
B) ROC regressions for each task					
Phonemic fluency	332.5	0.93	0.27	0.735	**3.7**
Semantic fluency	332.5	0.94	0.30	0.763	**4.7**
Digit Symbol	332.5	0.92	0.4	0.788	**5.1**
Trails A	332.5	0.94	0.28	0.737	**4.8**
Trails B	332.5	0.95	0.30	0.762	**5.9**

† Trails = Trails Making Test

DOC = **D**epression, **O**bstructive sleep apnea (OSA), and **C**ognitive impairment

https://doi.org/10.1017/cjn.2024.303 Published online by Cambridge University Press