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Screening and follow-up care for cognitive and emotional problems after TIA and ischemic stroke: a national survey among neurologists in the Netherlands

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Abstract

Background: After stroke, many patients experience cognitive and/or emotional problems. While national guidelines recommend screening for these problems, actual screening rates might be limited.

Objective: This study aimed to examine the clinical practice at neurology departments regarding screening, information provision and follow-up care for cognitive and emotional problems after TIA and ischemic stroke.

Methods: A nationwide, cross-sectional, online survey was conducted between October 2018 and October 2019 among neurologists in all hospitals in the Netherlands.

Results: Neurologists in 78 hospitals were invited to join the survey, and 52 (67%) of them completed it. Thirty-one (59%) neurologists reported that screening for cognitive problems after TIA and ischemic stroke was mostly or always performed. When cognitive screening was performed, 42 (84%) used validated screening instruments. Twenty-nine (56%) of the respondents reported that screening for emotional problems was mostly or always performed. When emotional screening was performed, 31 (63%) reported using validated screening instruments. Timing of screening and information provision was highly variable, and the majority reported that there was no protocol for follow-up care when cognitive or emotional problems were found.

Conclusions: This study demonstrates that clinical practice at neurology departments is highly variable regarding screening, information provision and follow-up care for cognitive and emotional problems in patients after TIA or ischemic stroke. Approximately half of the participating neurologists reported that screening was performed only sometimes or never for cognitive and emotional problems after TIA and ischemic stroke.

Keywords

Screening, cognition, depression and anxiety, stroke, rehabilitation, survey

Strengths and limitations of this study

- A detailed overview is provided of the current clinical practice at neurology departments with regard to screening for cognitive and emotional problems after TIA or ischemic stroke.
- Multiple opportunities are identified to further optimize the clinical practice of screening and care for cognitive and emotional problems after stroke.
- Neurologists in all Dutch hospitals were invited to participate and a satisfactory percentage completed the survey.
- Being a survey study, the results might deviate from the actual clinical practice, for example due to social desirability.
- This study focuses on the views of neurologists and their teams, which might underestimate the true screening rates for cognitive and emotional problems.

Introduction

Stroke is a leading cause of disability worldwide.(1) After stroke, many patients experience cognitive and/or emotional problems,(2-6) which affect their quality of life and participation.(7-11) Therefore, national guidelines recommend screening and care for cognitive and emotional problems after stroke.(12-15) The Dutch guideline recommends

screening all stoke patients for cognitive problems, using the Montreal Cognitive Assessment (MoCA) rather than the Mini Mental State Examination (MMSE), and referral to rehabilitation services when cognitive problems are present.(15) With regard to emotional problems, multiple screening instruments are considered suitable, namely the Hospital Anxiety and Depression Scale (HADS), the Beck Depression Inventory (BDI), the Symptom CheckList (SCL-90) subscale for depression, and the Hamilton Depression Scale (HDS).(15) When emotional problems are present, psychotherapy or pharmacotherapy should be considered.(15) Previous studies in the United Kingdom found that compliance with the guidelines is low as regards screening for cognitive and emotional problems after transient ischemic attack (TIA) and ischemic stroke.(16, 17) In the Netherlands, in general, stroke patients are admitted to a stroke unit in the acute phase, where a neurologist functions as treating physician. From the stroke unit, patients are discharged home, to a rehabilitation centre or to a nursing home. If patients are discharged home, they are followed-up at the outpatient clinics of the neurology department.

This study aimed to investigate the current clinical practice of screening for cognitive and emotional problems after TIA and ischemic stroke at neurology departments in hospitals in the Netherlands. This study examined: (1) if patients with TIA or ischemic stroke are screened for cognitive and emotional problems, (2) if so, which screening instruments are used, (3) when screening is performed, (4) whether patients receive information regarding the presence and nature of cognitive and emotional problems and (5) what kind of follow-up care is delivered when cognitive and/or emotional problems are present.

Materials and Methods

Study design and participants

A nationwide, cross-sectional, online survey was conducted in the Netherlands between October 2018 and October 2019. Neurologists in all Dutch hospitals with an inpatient neurology ward were invited to participate in this survey. For every neurology department, one neurologist with experience of stroke care was asked to complete the survey about screening and care for cognitive and emotional problems after TIA and ischemic stroke at their department. The neurologist was allowed to forward the survey to another neurologist, a nurse practitioner or a physician assistant within the same department with experience of stroke after-care.

The data supporting the findings of this study are available from the corresponding author upon reasonable request. Ethical approval for this study was waived by the local ethics committee of OLVG Amsterdam. All data were handled in accordance with the EU General Data Protection Regulation 2016/679.

Development and content of the survey

The survey was developed by a multidisciplinary team, including a clinical neuropsychologist, a rehabilitation physician, two vascular stroke neurologists and a resident in neurology. A data manager verified the content and structure after the survey had been built in the web-based system Castor EDC.(18)

The survey was divided into two parts: one part about screening and follow-up care for cognitive consequences after TIA and ischemic stroke, and the second part about screening and follow-up care for emotional consequences. Both parts included 10 multiple choice questions, resulting in 20 questions in total (see Table 2 and Table 3). The number of answer options ranged from two to nine. The multiple choice questions were formatted either as

single-answer multiple choice questions (only one answer allowed) or as multiple-answer multiple choice questions (multiple answers allowed).

Survey administration

All neurologists received an invitation by email to participate in this online survey. Non-respondents received up to two subsequent emails. If the questionnaire was not completed after invitation by email, the neurologist was contacted by telephone. Participants completed the survey independently online, using a computer. Data were collected anonymously.

Statistical analysis

The results of the survey were analysed using descriptive statistics. For single-answer multiple choice questions, all answer options were recorded as percentages of the total number of respondents. For multiple-answer multiple choice questions the following analysis was performed. First, a dichotomous dummy variable was computed for each potential answer option. The options of the dummy variables were 'marked' or 'not marked' for each answer option. All answer options were then recorded as percentages of 'marked', divided by the total number of respondents. IBM SPSS version 22.0 was used for analyses.

Patient and public involvement

Patients or the public were not involved in the design, conduct or reporting of this research.

Results

Response rate and characteristics of the participants

Of the neurologists in 78 Dutch hospitals who were invited to join the survey, 52 (67%) completed the survey. The characteristics of the respondents are shown in Table 1. Nineteen (37%) participants were female, and the median age was 45 years (interquartile range: 40 – 57); seven (15%) were working at a university hospital, 44 (87%) in a large general hospital (more than 100 stroke patients per year) and one (2%) in a small general hospital (less than 100 stroke patients per year). Of the non-respondents, one (4%) was working at a university hospital, 25 (96%) at a large general hospital and none at a small general hospital.

Screening for cognitive problems after TIA and ischemic stroke

The various items regarding screening for cognitive problems in patients after TIA or ischemic stroke are shown in Table 2. Of the respondents, 31 (59%) reported that patients were mostly or always screened for cognitive problems after TIA or ischemic stroke, while 21 (41%) said that patients were sometimes or never screened. When screening for cognitive problems was performed, 42 (84%) stated that validated screening instruments were used. When screening instruments were used, the most commonly used instruments were the MoCA (n = 35; 84%), the Mini-Mental State Examination (MMSE) (n = 21; 50%) and the Checklist for Cognitive and Emotional Consequences following Stroke (CLCE-24) (n = 6; 14%). The timing of screening for cognitive problems varied greatly among the hospitals: 31 (62%) screened during hospital admission and 19 (38%) at a follow-up visit between 4-8 weeks after TIA or ischemic stroke. Fourteen (27%) stated that they screened at multiple time points. According to the participants, the majority of patients received some form of information about possible cognitive problems after TIA or ischemic stroke during admission or at follow-

up visits, but 19 (37%) reported that no written information was provided at all. When cognitive problems were observed, it was the local neurologist, nurse practitioner or physician assistant, or the rehabilitation physician, who acted as the treating physician in most cases. Thirty-nine of the participants (75%) stated that they did not have a guideline or protocol for follow-up care in case of cognitive problems after TIA and ischemic stroke. The reasons for referral to specialized care varied considerably among the hospitals: 36 (69%) referred patients based on cognitive complaints, 36 (69%) based on cognitive disorders, 30 (58%) based on positive screening results and 14 (27%) based on deviant results during a neuropsychological examination.

Screening for emotional problems after TIA and ischemic stroke

Table 3 shows the survey responses for the items about screening for emotional problems. According to 29 (56%) of the participants, patients were mostly or always screened for emotional problems after TIA or ischemic stroke at their hospital. When patients were screened, 31 (63%) used validated screening instruments. When screening instruments were used, the most commonly used instrument was the Hospital Anxiety and Depression Scale (HADS) (n = 27; 87%). Screening for emotional problems was performed at variable time points, but mostly during hospital admission (n = 14; 29%) or at a follow-up visit between 1 – 4 weeks after discharge (n = 21; 43%). Fifteen percent of the participants reported that patients were screened at multiple time points. According to 22 (61%) of the participants, information about the possible emotional sequelae was given to most or all patients, and according to 21 (40%), written information was mostly or always given. According to the respondents, 42 (81%) of the hospitals had no guideline or protocol for follow-up care for emotional problems after TIA and ischemic stroke. When emotional problems arose, it was

mostly the neurologist who acted as the treating physician (n = 30; 58%), followed by the nurse practitioner or physician assistant (n = 27; 52%), the rehabilitation physician (n = 23; 44%) or the patient's general practitioner (n = 16; 31%). Indications for referral to specialized care were emotional complaints (n = 37; 71%), clinical suspicion of an emotional disorder (n = 31; 60%) and positive screening results (n = 14; 27%).

Discussion

Our nationwide survey in the Netherlands found a wide variety as regards screening at neurology departments for cognitive and emotional problems in patients after TIA or ischemic stroke. While a small majority of the participants reported screening for cognitive and emotional problems was performed in most or all patients with TIA or ischemic stroke, the others did so only sometimes, or never. When patients were screened, the most commonly used instruments for cognitive problems were the MoCA and the MMSE, and for emotional problems the HADS. Screening for cognitive and emotional problems was performed at various time points, and information provision was highly variable. The vast majority of respondents indicated that their hospital lacked a protocol or a guideline for follow-up care for cognitive and emotional problems after stroke.

A strength of this study is that neurologists in all Dutch hospitals with a neurology ward were invited to participate, and that a satisfactory percentage of invited clinicians actually completed the survey. A limitation of this study is its design as a survey, which might not accurately reflect current clinical practice, for example due to social desirability. In addition, we focused on the views of the neurologists and their teams. This might underestimate the true screening rates for cognitive and emotional problems, since part of this care might be provided by, for example, general practitioners or rehabilitation physicians.

National guidelines recommend screening for cognitive and emotional problems in all stroke patients. Nevertheless, almost half of the respondents reported that they only sometimes, or even never, screened patients for cognitive and emotional problems after TIA or ischemic stroke, which is in accordance with the findings of other studies.(12-17, 19) Previous studies found considerable practice variation for other aspects of stroke care as well, such as secondary prevention and mobilization after stroke.(20, 21) Studies have identified multiple barriers to the implementation of evidence-based guidelines in clinical practice.(22, 23) With regard to screening for cognitive and emotional problems after stroke, multiple factors might explain the low rates of routine screening. First, there are numerous screening tools for cognitive and emotional problems, and they can be time-consuming and may be difficult to use for patients with language barriers or disabilities such as aphasia, hearing loss or vision loss.(24) Second, insufficient time, training and expertise of clinicians might further limit routine screening, as well as the lack of a protocol for follow-up care when a screening turns out to be positive.(19, 22-24) Third, stroke care predominantly focuses on secondary prevention, which might overshadow the importance of screening for cognitive and emotional problems.

Remarkably, when screening for cognitive problems was performed, 50% of our respondents who used screening instruments reported using the MMSE. However, two reviews have demonstrated that the MMSE is not sufficiently sensitive to the cognitive consequences of stroke, as it was originally designed to screen for the presence of dementia.(15, 25, 26) It is recommended to use the MoCA as a screening instrument for cognitive disorders in patients with stroke.(15, 26) When patients were screened for emotional problems after stroke, the vast majority of the respondents said they used the HADS, as has been recommended.(15)

Apart from screening, information provision and follow-up care for cognitive and emotional problems were also highly variable in our study, and most respondents reported that a

protocol for follow-up care was lacking. Nonetheless, cognitive and emotional problems are very common after stroke, and a previous evaluation among patients identified information provision after stroke as a major target for improvement.(27) Moreover, patients' evaluations underline the importance of the cognitive and emotional sequelae, and patients even rated these consequences as among the top 10 of research priorities in stroke.(28) Fortunately, attention is increasingly being drawn to the cognitive and emotional consequences of stroke, and screening rates seem to be increasing.(29) Still, our results suggest that further improvement is possible and, in our opinion, desirable. Therefore, we recommend to perform screening for all patients after stroke for cognitive and emotional problems with validated screening instruments such as the MoCA and HADS, respectively. In our opinion, the additional use of stroke-specific patient-reported screening instruments that measure subjective cognitive complaints and a wider spectrum of emotional problems will provide even better and valuable insights into the consequences of stroke. An example of such an instrument is the Checklist for the Detection of Cognitive and Emotional Consequences After Stroke (CLCE-24). Additionally, we recommend that such screenings should be performed by health care professionals with experience in screening for cognitive and emotional problems, and with sufficient time to use appropriate screening instruments. In our opinion, these screenings can be performed in primary care, in hospitals or in rehabilitation centres. However, to ensure that all patients are actually screened, it is important to have clear agreements embedded in the collaborative network of stroke care. Furthermore, guidance for stroke patients with proven cognitive and emotional problems can be further optimized by implementing local protocols for follow-up care. Follow-up care for cognitive problems can include referral to a rehabilitation physician for treatment such as cognitive rehabilitation.(30) With regard to follow-up care for emotional problems, psycho-education, psychotherapy and pharmacotherapy can be considered.(15)

In conclusion, this study indicates that stroke care practice at neurology departments in the Netherlands is highly variable with regard to screening, information provision and follow-up care for cognitive and emotional problems in patients after TIA or ischemic stroke. Almost half of the respondents reported that they only sometimes or never screened for cognitive and emotional problems after TIA and stroke. Therefore, in order to optimize stroke care, screening rates should be improved and should include suitable screening instruments and a protocol for follow-up care.

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Declarations

Conflicting interests: The authors declare that they have no competing interests

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Informed consent: Informed consent was not sought for this study because participants were not subjected to procedures and because the questions were not regarded as confrontational or time-consuming.

Ethical approval: Ethical approval for this study was waived by the local ethics committee of OLVG Amsterdam. This study was completed in accordance with the Helsinki Declaration as revised in 2013.

Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Contributorship: RvdB, CH, VK, JS and AV were involved in the conception of the study design. RvdB, VK and JS were involved in participant recruitment. JS was involved in researching the literature, gaining ethical approval and data analysis. JS wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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Table 1. Characteristics of respondents and non-respondents

Characteristic	Respondents, n= 52	Non-respondents, n = 26
Female sex (%)	19 (37)	-
Age, median (interquartile range)	45 (40 – 57)	-
Neurologist (%)	49 (94)	-
Nurse practitioner or physician assistant at the neurology department (%)	3 (6)	-
Type of hospital		
University (%)	7 (15)	1 (4)
Large general (%)	44 (87)	25 (96)
Small general (%)	1 (2)	0 (0)

369 **Table 2. Screening for cognitive problems after TIA and ischemic stroke**

	Item	Answer options	n	(%)
1.	**Are patients screened for cognitive problems?**	Always	8	(15)
		Mostly	23	(44)
		Sometimes	19	(37)
		Never	2	(4)
2.	**Are validated screening instruments used? ***	Yes	42	(84)
		No	8	(16)
3.	**Which screening instrument(s) is / are used?** † ‡	MoCA	35	(83)
		MMSE	21	(50)
		CLCE-24	6	(14)
		Other	4	(9)
4.	**When does screening take place? * ‡**	During hospital admission	31	(62)
		< 1 week after discharge	2	(4)
		1 – 4 weeks after discharge	5	(10)
		4 – 8 weeks after discharge	19	(38)
		>8 weeks after discharge	14	(28)
5.	**Do patients receive information about possible cognitive problems?**	Always	15	(28)
		Mostly	25	(48)
		Sometimes	12	(23)
		Never	0	(0)
6.	**Do patients receive written information about possible cognitive problems?**	Always	13	(25)
		Mostly	13	(25)
		Sometimes	7	(14)
		Never	19	(37)
7.	**Do caregivers receive information about possible cognitive problems?**	Always	13	(25)
		Mostly	23	(44)
		Sometimes	15	(29)
		Never	1	(2)
8.	**Reasons for referral to specialized care ‡**	Cognitive complaints	36	(69)
		Clinical suspicion of cognitive disorders	36	(69)
		Abnormal screening results	30	(58)
		Abnormal results during neuropsychological examination	14	(27)
9.	**Who is the treating physician for cognitive problems? ‡**	Neurologist	35	(67)
		Resident in neurology	3	(6)
		Nurse practitioner or physician assistant	23	(55)
		Rehabilitation physician	30	(58)
		Psychologist	6	(12)
		Geriatrician	8	(15)
		Nursing home doctor	6	(12)
		General practitioner	16	(31)
		Occupational therapist	5	(10)
10.	**Does your hospital have a protocol or**	Yes	12	(23)

guideline for follow-up care for cognitive problems?	No	39	(75)
	Missing	1	(2)

MoCA: Montreal Cognitive Assessment; MMSE: Mini-Mental State Examination; CLCE-24: Checklist for Cognitive and Emotional Consequences following Stroke.

* Items 2 and 4 were only asked if item 1 had been marked 'Always', 'Mostly' or 'Sometimes'.

† Item 3 was only asked when item 2 had been marked 'Yes'.

‡ These items allowed multiple answers and were analysed accordingly, see 'Statistical Analysis' paragraph; consequently, the sum of the percentages is not 100%.

376 **Table 3. Screening for emotional problems after TIA and ischemic stroke**

	Item	Answer options	n	(%)
1.	**Are patients screened for emotional problems?**	Always	10	(19)
		Mostly	19	(37)
		Sometimes	20	(39)
		Never	3	(6)
2.	**Are validated screening instruments used? ***	Yes	31	(63)
		No	18	(37)
3.	**Which screening instrument(s) is / are used? † ‡**	HADS	27	(87)
		CLCE-24	4	(13)
		HDRS	1	(3)
		BDI	1	(3)
		SIGEB	2	(6)
4.	**When does screening take place? * ‡**	During hospital admission	14	(29)
		< 1 week after discharge	1	(2)
		1 – 4 weeks after discharge	13	(27)
		4 – 8 weeks after discharge	21	(43)
		>8 weeks after discharge	12	(25)
5.	**Do patients receive information about possible emotional problems?**	Always	11	(21)
		Mostly	21	(40)
		Sometimes	18	(35)
		Never	2	(4)
6.	**Do patients receive written information about possible emotional problems?**	Always	9	(17)
		Mostly	12	(23)
		Sometimes	12	(23)
		Never	19	(37)
7.	**Do caregivers receive information about possible emotional problems?**	Always	8	(15)
		Mostly	13	(25)
		Sometimes	12	(23)
		Never	19	(37)
8.	**Reason for referral to specialized care ‡**	Emotional complaints	37	(71)
		Clinical suspicion of emotional disorders	31	(60)
		Abnormal screening results	14	(27)
9.	**Who is the treating physician for emotional problems? ‡**	Neurologist	30	(58)
		Resident in neurology	3	(6)
		Nurse practitioner or physician assistant	27	(52)
		Rehabilitation physician	23	(44)
		Psychiatrist	1	(2)
		Psychologist	14	(27)
		Geriatrician	5	(10)
		General practitioner	16	(31)
10.	**Does your hospital have a protocol or guideline for follow-up care for emotional problems?**	Yes	9	(17)
		No	42	(81)
		Missing	1	(2)

HADS: Hospital Anxiety and Depression Scale; CLCE-24: Checklist for Cognitive and Emotional Consequences following Stroke; HDRS: Hamilton Depression Rating Scale; BDI: Beck Depression Inventory; SIGEB: Assessment tool for long-term Consequences After Stroke (*'Signaleringsinstrument voor de lange termijn Gevolgen van een Beroerte'*)(31)

* Items 2 and 4 were only asked when item 1 had been marked 'Always', 'Mostly' or 'Sometimes'.

† Item 3 was only asked when item 2 had been marked 'Yes'.

‡ These items allowed multiple answers and were analysed accordingly, see 'Statistical Analysis' paragraph; consequently, the sum of the percentages is not 100%.

Checklist for preparing the report of a survey

1. Burns et al., A guide for the design and conduct of self-administered surveys of clinicians, CMAJ. 2008 Jul 29; 179(3): 245–252. doi: 10.1503/cmaj.080372

2. Huston P. Reporting on surveys: information for authors and peer reviewers. CMAJ 1996;154:1695-704

Abstract	
Is the objective clearly stated?	Yes, see subhead 'Objectives', page 3.
Is the design of the study stated?	Yes, see subhead 'Methods', page 3.
Is the study setting well described?	Yes, see subhead 'Methods', page 3.
Is the survey population described?	Yes, see subhead 'Methods', page 3.
Are the outcome measures identified?	Partly, we described to conduct a survey, see subhead 'Methods', page 4, but a full explanation on all different items was not considered suitable for the abstract.
Are the main results clearly reported?	Yes, see subhead 'Results', page 3.
Are the conclusions appropriate?	Yes, the conclusion answers the objective and is in line with the results. See subhead 'Conclusion', page 4.
Introduction	
Is the problem clearly stated?	Yes, see paragraph 'Introduction', page 4-5.
Is the pertinent literature cited and critically appraised?	Yes, see paragraph 'Introduction', page 4-5.
Is the relevance of the research question explained?	Yes, see paragraph 'Introduction', page 5.
Is the objective clearly stated?	Yes, see paragraph 'Introduction', page 5.
Methods	
Is the study design appropriate to the objective?	Yes, neurologists in all hospitals in the Netherlands were invited to participate, therewith enhancing its generalizability. As we did not intend to measure change over time, a cross-sectional survey sufficed.
Is the setting clearly described?	Yes, see subhead 'Study design and participants', page 6.
Are the methods described clearly enough to permit other researchers to duplicate the study?	Yes, see subhead 'Study design and participants', page 6. Moreover, all items of the questionnaire are displayed in Table 2 and Table 3, page 18 – 21.
Is the survey sample likely to be representative of the population?	Yes, neurologists in all hospitals in the Netherlands were invited to participate. The response rate was acceptable (67%)[1] and responders were spread across the country. No further inclusion or exclusion criteria were applied.
Is the questionnaire described adequately?	The questionnaire is described in paragraph

	'Development and content of the survey', page 6-7. All items of the questionnaire are displayed in Table 2 and Table 3, page 18 – 21.
Have the validity and reliability of the questionnaire been established?	Face validity was tested by a multidisciplinary team, including a clinical neuropsychologist, a rehabilitation physician, two vascular stroke neurologists and a resident in neurology. As the questionnaire was specifically developed for this purpose only, further testing for validity and reliability was not considered feasible.
Was the questionnaire administered in a satisfactory way?	Yes, the survey was administered online in a web-based system called Castor EDC. We ensured that all potential respondents had access to electronic mail. A data manager verified the content and structure after the survey had been built. Non-respondents received up to two subsequent emails.
Are the statistical methods used appropriately?	Yes, descriptive analyses were used to display the results. Only the results of multiple-answer multiple choice questions were transformed, as is described in paragraph 'Statistical analysis', page 7.
Results	
Do the results address the objective?	Yes, the results address the current clinical practice of screening for cognitive and emotional problems after TIA and ischemic stroke at neurology departments in hospitals in the Netherlands, see paragraph 'Results', page 7 – 10.
Are all respondents accounted for?	Yes, the total number of surveys sent is considered as well as the number of respondents and non-respondents.
Are the results clearly and logically presented?	Yes, the results in the Results section follow a clear logic and follow the same structure as Table 2 and Table 3. Only important (selected) results are shown in text.
Are the tables and figures appropriate?	Yes, both tables support the findings in text and show all items of the questionnaire in order to increase transparency.
Are the numbers consistent in the text and the tables?	Yes.
Discussion	
Are the results succinctly summarized?	The results are summarized in the first section of the 'Discussion', see page 10.
Are the implications of the results stated?	The implications are stated and discussed on page 11.
Are other interpretations considered and refuted?	The limitation section considers other possibilities for low screening rates.
Are appropriate conclusions drawn?	A conclusion is drawn in the last section of the

	'Discussion' that answers the objective and is supported by the results shown in text and tables.

1. *Sierles FS. How to do research with self-administered surveys.* Acad Psychiatry *2003;27:104-13*

BMJ Open

Screening and follow-up care for cognitive and emotional problems after transient ischemic attack and ischemic stroke: a national, cross-sectional, online survey among neurologists in the Netherlands

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Screening and follow-up care for cognitive and emotional problems after transient ischemic attack and ischemic stroke: a national, cross-sectional, online survey among neurologists in the Netherlands

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Abstract

Background: After stroke, many patients experience cognitive and/or emotional problems. While national guidelines recommend screening for these problems, actual screening rates might be limited.

Objective: This study aimed to examine the clinical practice at neurology departments regarding screening, information provision and follow-up care for cognitive and emotional problems after TIA and ischemic stroke.

Methods: A nationwide, cross-sectional, online survey was conducted between October 2018 and October 2019 among neurologists in all hospitals in the Netherlands.

Results: Neurologists in 78 hospitals were invited to join the survey, and 52 (67%) of them completed it. Thirty-one (59%) neurologists reported that screening for cognitive problems after TIA and ischemic stroke was mostly or always performed. When cognitive screening was performed, 42 (84%) used validated screening instruments. Twenty-nine (56%) of the respondents reported that screening for emotional problems was mostly or always performed. When emotional screening was performed, 31 (63%) reported using validated screening instruments. Timing of screening and information provision was highly variable, and the majority reported that there was no protocol for follow-up care when cognitive or emotional problems were found.

Conclusions: This study demonstrates that clinical practice at neurology departments is highly variable regarding screening, information provision and follow-up care for cognitive and emotional problems in patients after TIA or ischemic stroke. Approximately half of the participating neurologists reported that screening was performed only sometimes or never for cognitive and emotional problems after TIA and ischemic stroke.

Keywords

Screening, cognition, depression and anxiety, stroke, rehabilitation, survey

Strengths and limitations of this study

- A detailed overview is provided of the current clinical practice at neurology departments with regard to screening for cognitive and emotional problems after TIA or ischemic stroke.
- Multiple opportunities are identified to further optimize the clinical practice of screening and care for cognitive and emotional problems after stroke.
- Neurologists in all Dutch hospitals were invited to participate and a satisfactory percentage completed the survey.
- Being a survey study, the results might deviate from the actual clinical practice, for example due to social desirability.
- This study focuses on the views of neurologists and their teams, which might underestimate the true screening rates for cognitive and emotional problems.

Introduction

Stroke is a leading cause of disability worldwide.(1) After stroke, many patients experience cognitive and/or emotional problems,(2-6) which affect their quality of life and participation.(7-11) Therefore, national guidelines recommend screening and care for cognitive and emotional problems after stroke.(12-15) The Dutch guideline recommends screening all stoke patients for

cognitive problems, using the Montreal Cognitive Assessment (MoCA) rather than the Mini Mental State Examination (MMSE), and referral to rehabilitation services when cognitive problems are present.(15) With regard to emotional problems, multiple screening instruments are considered suitable, namely the Hospital Anxiety and Depression Scale (HADS), the Beck Depression Inventory (BDI), the Symptom CheckList (SCL-90) subscale for depression, and the Hamilton Depression Scale (HDS).(15) When emotional problems are present, psychotherapy or pharmacotherapy should be considered.(15) Previous studies in the United Kingdom found that compliance with the guidelines is low as regards screening for cognitive and emotional problems after transient ischemic attack (TIA) and ischemic stroke.(16, 17) In the Netherlands, in general, stroke patients are admitted to a stroke unit in the acute phase, where a neurologist functions as treating physician. From the stroke unit, patients are discharged home, to a rehabilitation centre or to a nursing home. If patients are discharged home, they are followed-up at the outpatient clinics of the neurology department.

This study aimed to investigate the current clinical practice of screening for cognitive and emotional problems after TIA and ischemic stroke at neurology departments in hospitals in the Netherlands. This study examined: (1) if patients with TIA or ischemic stroke are screened for cognitive and emotional problems, (2) if so, which screening instruments are used, (3) when screening is performed, (4) whether patients receive information regarding the presence and nature of cognitive and emotional problems and (5) what kind of follow-up care is delivered when cognitive and/or emotional problems are present.

Materials and Methods

Study design and participants

A nationwide, cross-sectional, online survey was conducted in the Netherlands between October 2018 and October 2019. Neurologists in all Dutch hospitals with an inpatient neurology ward were invited to participate in this survey. In the Netherlands only neurologists, and no other specialists, act as treating physicians at stroke units. For every neurology department, one neurologist with experience of stroke care was asked to complete the survey about screening and care for cognitive and emotional problems after TIA and ischemic stroke at their department. The neurologist was allowed to forward the survey to another neurologist, a nurse practitioner or a physician assistant within the same department with experience of stroke after-care.

The data supporting the findings of this study are available from the corresponding author upon reasonable request. Ethical approval for this study was waived by the local ethics committee of OLVG Amsterdam. All data were handled in accordance with the EU General Data Protection Regulation 2016/679.

Development and content of the survey

The survey was developed by a multidisciplinary team, including a clinical neuropsychologist, a rehabilitation physician, two vascular stroke neurologists and a resident in neurology. A data manager verified the content and structure after the survey had been built in the web-based system Castor EDC.(18)

The survey was divided into two parts: one part about screening and follow-up care for cognitive consequences after TIA and ischemic stroke, and the second part about screening and follow-up care for emotional consequences. Both parts included 10 multiple choice questions, resulting in 20 questions in total (see Table 1 and Table 2). The number of answer options

ranged from two to nine. The multiple choice questions were formatted either as single-answer multiple choice questions (only one answer allowed) or as multiple-answer multiple choice questions (multiple answers allowed).

Survey administration

All neurologists received an invitation by email to participate in this online survey. Non-respondents received up to two subsequent emails. If the questionnaire was not completed after invitation by email, the neurologist was contacted by telephone. Participants completed the survey independently online, using a computer. Data were collected anonymously.

Statistical analysis

The results of the survey were analysed using descriptive statistics. For single-answer multiple choice questions, all answer options were recorded as percentages of the total number of respondents. For multiple-answer multiple choice questions the following analysis was performed. First, a dichotomous dummy variable was computed for each potential answer option. The options of the dummy variables were 'marked' or 'not marked' for each answer option. All answer options were then recorded as percentages of 'marked', divided by the total number of respondents. IBM SPSS version 22.0 was used for analyses.

Patient and public involvement

Patients or the public were not involved in the design, conduct or reporting of this research.

Results

Response rate and characteristics of the participants

Of the neurologists in 78 Dutch hospitals who were invited to join the survey, 52 (67%) completed the survey. The characteristics of the respondents are shown in Table 3. Nineteen (37%) participants were female, and the median age was 45 years (interquartile range: 40 – 57); seven (15%) were working at a university hospital, 44 (87%) in a large general hospital (more than 100 stroke patients per year) and one (2%) in a small general hospital (less than 100 stroke patients per year). Of the non-respondents, one (4%) was working at a university hospital, 25 (96%) at a large general hospital and none at a small general hospital.

Screening for cognitive problems after TIA and ischemic stroke

The various items regarding screening for cognitive problems in patients after TIA or ischemic stroke are shown in Table 1. Of the respondents, 31 (59%) reported that patients were mostly or always screened for cognitive problems after TIA or ischemic stroke, while 21 (41%) said that patients were sometimes or never screened. When screening for cognitive problems was performed, 42 (84%) stated that validated screening instruments were used. When screening instruments were used, the most commonly used instruments were the MoCA (n = 35; 84%), the Mini-Mental State Examination (MMSE) (n = 21; 50%) and the Checklist for Cognitive and Emotional Consequences following Stroke (CLCE-24) (n = 6; 14%). The timing of screening for cognitive problems varied greatly among the hospitals: 31 (62%) screened during hospital admission and 19 (38%) at a follow-up visit between 4-8 weeks after TIA or ischemic stroke. Fourteen (27%) stated that they screened at multiple time points. According to the participants,

the majority of patients received some form of information about possible cognitive problems after TIA or ischemic stroke during admission or at follow-up visits, but 19 (37%) reported that no written information was provided at all. When cognitive problems were observed, it was the local neurologist, nurse practitioner or physician assistant, or the rehabilitation physician, who acted as the treating physician in most cases. Thirty-nine of the participants (75%) stated that they did not have a guideline or protocol for follow-up care in case of cognitive problems after TIA and ischemic stroke. The reasons for referral to specialized care varied considerably among the hospitals: 36 (69%) referred patients based on cognitive complaints, 36 (69%) based on cognitive disorders, 30 (58%) based on positive screening results and 14 (27%) based on deviant results during a neuropsychological examination. All respondents from university hospitals (100%) reported to use validated screening instruments when a screening was performed, whereas 35 respondents from general hospitals (83%) reported to use validated screening instruments when screening was performed. Apart from the use of validated screening instruments, screening for cognitive problems after TIA and ischemic stroke was overall comparable between university and general hospitals.

Screening for emotional problems after TIA and ischemic stroke

Table 2 shows the survey responses for the items about screening for emotional problems. According to 29 (56%) of the participants, patients were mostly or always screened for emotional problems after TIA or ischemic stroke at their hospital. When patients were screened, 31 (63%) used validated screening instruments. When screening instruments were used, the most commonly used instrument was the Hospital Anxiety and Depression Scale (HADS) (n = 27; 87%). Screening for emotional problems was performed at variable time points, but mostly during hospital admission (n = 14; 29%) or at a follow-up visit between 1 – 4 weeks after

discharge (n = 21; 43%). Fifteen percent of the participants reported that patients were screened at multiple time points. According to 22 (61%) of the participants, information about the possible emotional sequelae was given to most or all patients, and according to 21 (40%), written information was mostly or always given. According to the respondents, 42 (81%) of the hospitals had no guideline or protocol for follow-up care for emotional problems after TIA and ischemic stroke. When emotional problems arose, it was mostly the neurologist who acted as the treating physician (n = 30; 58%), followed by the nurse practitioner or physician assistant (n = 27; 52%), the rehabilitation physician (n = 23; 44%) or the patient's general practitioner (n = 16; 31%). Indications for referral to specialized care were emotional complaints (n = 37; 71%), clinical suspicion of an emotional disorder (n = 31; 60%) and positive screening results (n = 14; 27%). Apart from the timing of screening, screening for emotional problems after TIA and ischemic stroke was overall comparable between university and general hospitals.

Discussion

Our nationwide survey in the Netherlands found a wide variety as regards screening at neurology departments for cognitive and emotional problems in patients after TIA or ischemic stroke. While a small majority of the participants reported screening for cognitive and emotional problems was performed in most or all patients with TIA or ischemic stroke, the others did so only sometimes, or never. When patients were screened, the most commonly used instruments for cognitive problems were the MoCA and the MMSE, and for emotional problems the HADS. Screening for cognitive and emotional problems was performed at various time points, and information provision was highly variable. The vast majority of respondents indicated that their hospital lacked a protocol or a guideline for follow-up care for cognitive and emotional problems after stroke. These results were comparable between university and general hospitals.

A strength of this study is that neurologists in all Dutch hospitals with a neurology ward were invited to participate, and that a satisfactory percentage of invited clinicians actually completed the survey. A limitation of this study is its design as a survey, which might not accurately reflect current clinical practice, for example due to social desirability. In addition, we focused on the views of the neurologists and their teams. This might underestimate the true screening rates for cognitive and emotional problems, since part of this care might be provided by, for example, general practitioners or rehabilitation physicians. Besides, in the current questionnaire, no distinction was made between TIA and ischemic stroke. While patients with TIA and ischemic stroke receive comparable follow-up treatment in the Netherlands, it is not known whether the results of the current paper differ between TIA and ischemic stroke.

National guidelines recommend screening for cognitive and emotional problems in all stroke patients.(12-15) Nevertheless, almost half of the respondents reported that they only sometimes, or even never, screened patients for cognitive and emotional problems after TIA or ischemic stroke. Our findings focussed on the clinical practice in the Netherlands and are in accordance with international studies, viz. from the United Kingdom and Canada, which also showed low compliance rates with guideline recommendations to screen for cognitive and emotional problems after stroke.(15-17, 19, 20) Since cognitive and emotional problems after stroke are universal, these low compliance rates might hinder optimal treatment of the consequences of stroke internationally. Therefore, it is important to identify and overcome barriers for screening. Studies have identified multiple barriers to the implementation of evidence-based guidelines in clinical practice.(21, 22) With regard to screening for cognitive and emotional problems after stroke, multiple factors might explain the low rates of routine screening. First, there are numerous screening tools for cognitive and emotional problems, and they can be time-consuming and may be difficult to use for patients with language barriers or disabilities such as aphasia, hearing loss or vision loss.(23) Second, insufficient time, training and expertise of

clinicians might further limit routine screening, as well as the lack of a protocol for follow-up care when a screening turns out to be positive.(19, 21-23) Third, stroke care predominantly focuses on secondary prevention, which might overshadow the importance of screening for cognitive and emotional problems.

Remarkably, when screening for cognitive problems was performed, 50% of our respondents who used screening instruments reported using the MMSE. However, two reviews have demonstrated that the MMSE is not sufficiently sensitive to the cognitive consequences of stroke, as it was originally designed to screen for the presence of dementia.(15, 24, 25) It is recommended to use the MoCA as a screening instrument for cognitive disorders in patients with stroke.(15, 25) When patients were screened for emotional problems after stroke, the vast majority of the respondents said they used the HADS, as has been recommended.(15)

Apart from screening, information provision and follow-up care for cognitive and emotional problems were also highly variable in our study, and most respondents reported that a protocol for follow-up care was lacking. Nonetheless, cognitive and emotional problems are very common after stroke, and a previous evaluation among patients identified information provision after stroke as a major target for improvement.(26) Moreover, patients' evaluations underline the importance of the cognitive and emotional sequelae, and patients even rated these consequences as among the top 10 of research priorities in stroke.(27) Fortunately, attention is increasingly being drawn to the cognitive and emotional consequences of stroke, and screening rates seem to be increasing.(28) Still, our results suggest that further improvement is possible and, in our opinion, desirable. Therefore, we recommend to perform screening for all patients after stroke for cognitive and emotional problems with validated screening instruments such as the MoCA and HADS, respectively. In our opinion, the additional use of stroke-specific patient-reported screening instruments that measure subjective cognitive complaints and a wider spectrum of emotional problems will provide even better and valuable insights into the

consequences of stroke. An example of such an instrument is the Checklist for the Detection of Cognitive and Emotional Consequences After Stroke (CLCE-24). Additionally, we recommend that such screenings should be performed by health care professionals with experience in screening for cognitive and emotional problems, and with sufficient time to use appropriate screening instruments. In our opinion, these screenings can be performed in primary care, in hospitals or in rehabilitation centres. However, to ensure that all patients are actually screened, it is important to have clear agreements embedded in the collaborative network of stroke care. Furthermore, guidance for stroke patients with proven cognitive and emotional problems can be further optimized by implementing local protocols for follow-up care. Follow-up care for cognitive problems can include referral to a rehabilitation physician for treatment such as cognitive rehabilitation.(29) With regard to follow-up care for emotional problems, psycho-education, psychotherapy and pharmacotherapy can be considered.(15)

In conclusion, this study indicates that stroke care practice at neurology departments in the Netherlands is highly variable with regard to screening, information provision and follow-up care for cognitive and emotional problems in patients after TIA or ischemic stroke. Almost half of the respondents reported that they only sometimes or never screened for cognitive and emotional problems after TIA and stroke. Therefore, in order to optimize stroke care, screening rates should be improved and should include suitable screening instruments and a protocol for follow-up care.

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Declarations

Conflicting interests: The authors declare that they have no competing interests

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Informed consent: Informed consent was not sought for this study because participants were not subjected to procedures and because the questions were not regarded as confrontational or time-consuming.

Ethical approval: Ethical approval for this study was waived by the local ethics committee of OLVG Amsterdam. This study was completed in accordance with the Helsinki Declaration as revised in 2013.

Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Contributorship: RvdB, CH, VK, JS and AV were involved in the conception of the study design. RvdB, VK and JS were involved in participant recruitment. JS was involved in researching the literature, gaining ethical approval and data analysis. JS wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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373 **Table 1. Screening for cognitive problems after TIA and ischemic stroke**

	Item	Answer options	n	(%)	University hospital (n = 7)	General hospital (n = 45)
1.	**Are patients screened for cognitive problems?**	Always	8	(15)	0	8
		Mostly	23	(44)	5	18
		Sometimes	19	(37)	2	17
		Never	2	(4)	0	2
2.	**Are validated screening instruments used? ***	Yes	42	(84)	7	35
		No	8	(16)	0	8
3.	**Which screening instrument(s) is / are used?** † ‡	MoCA	35	(83)	6	29
		MMSE	21	(50)	3	18
		CLCE-24	6	(14)	2	4
		Other §	4	(9)	0	4
4.	**When does screening take place? * ‡**	During hospital admission	31	(62)	5	26
		< 1 week after discharge	2	(4)	0	2
		1 – 4 weeks after discharge	5	(10)	1	4
		4 – 8 weeks after discharge	19	(38)	3	16
		>8 weeks after discharge	14	(28)	2	12
5.	**Do patients receive information about possible cognitive problems?**	Always	15	(28)	2	13
		Mostly	25	(48)	2	23
		Sometimes	12	(23)	3	9
		Never	0	(0)	0	0
6.	**Do patients receive written information about possible cognitive problems?**	Always	13	(25)	2	11
		Mostly	13	(25)	1	12
		Sometimes	7	(14)	1	6
		Never	19	(37)	3	16
7.	**Do caregivers receive information about possible cognitive problems?**	Always	13	(25)	0	13
		Mostly	23	(44)	4	19
		Sometimes	15	(29)	3	12
		Never	1	(2)	0	1
8.	**Reasons for referral to specialized care ‡**	Cognitive complaints	36	(69)	5	31
		Clinical suspicion of cognitive disorders	36	(69)	5	31
		Abnormal screening results	30	(58)	3	27
		Abnormal results during neuropsychological examination	14	(27)	2	12
9.	**Who is the treating physician for cognitive**	Neurologist	35	(67)	4	31
		Resident in neurology	3	(6)	1	2

	problems? ‡	Nurse practitioner or physician assistant	23	(55)	3	20
		Rehabilitation physician	30	(58)	5	25
		Psychologist	6	(12)	0	6
		Geriatrician	8	(15)	1	7
		Nursing home doctor	6	(12)	1	5
		General practitioner	16	(31)	2	14
		Occupational therapist	5	(10)	0	5
10.	**Does your hospital have a protocol or guideline for follow-up care for cognitive problems?**	Yes	12	(23)	2	1
		No	39	(75)	5	44
		Missing	1	(2)	0	

MoCA: Montreal Cognitive Assessment; MMSE: Mini-Mental State Examination; CLCE-24: Checklist for Cognitive and Emotional Consequences following Stroke.

* Items 2 and 4 were only asked if item 1 had been marked 'Always', 'Mostly' or 'Sometimes'.

† Item 3 was only asked when item 2 had been marked 'Yes'.

‡ These items allowed multiple answers and were analysed accordingly, see 'Statistical Analysis' paragraph; consequently, the sum of the percentages is not 100%.

§ Other screening instruments included the Cambridge Cognitive Examination (CAMCOG) (n = 1), the Symbol Digit Modalities Test (SDMT) (n = 1), the Assessment tool for long-term Consequences After Stroke (SIGEB) (n = 1) and a neuropsychological examination (n = 1).

Table 2. Screening for emotional problems after TIA and ischemic stroke

	Item	Answer options	n	(%)	University hospital	General hospital
1.	**Are patients screened for emotional problems?**	Always	10	(19)	1	9
		Mostly	19	(37)	3	16
		Sometimes	20	(39)	3	17
		Never	3	(6)	0	3
2.	**Are validated screening instruments used? ***	Yes	31	(63)	6	25
		No	18	(37)	1	17
3.	**Which screening instrument(s) is / are used? † ‡**	HADS	27	(87)	6	21
		CLCE-24	4	(13)	0	4
		HDRS	1	(3)	0	1
		BDI	1	(3)	0	1
		SIGEB	2	(6)	0	2
4.	**When does screening take place? * ‡**	During hospital admission	14	(29)	0	14
		< 1 week after discharge	1	(2)	0	1
		1 – 4 weeks after discharge	13	(27)	4	9
		4 – 8 weeks after discharge	21	(43)	1	20
		>8 weeks after discharge	12	(25)	2	10
5.	**Do patients receive information about possible emotional problems?**	Always	11	(21)	1	10
		Mostly	21	(40)	3	18
		Sometimes	18	(35)	3	15
		Never	2	(4)	0	2
6.	**Do patients receive written information about possible emotional problems?**	Always	9	(17)	0	9
		Mostly	12	(23)	2	10
		Sometimes	12	(23)	3	9
		Never	19	(37)	2	17
7.	**Do caregivers receive information about possible emotional problems?**	Always	8	(15)	0	8
		Mostly	13	(25)	3	10
		Sometimes	12	(23)	2	10
		Never	19	(37)	2	17
8.	**Reason for referral to specialized care ‡**	Emotional complaints	37	(71)	5	32
		Clinical suspicion of emotional disorders	31	(60)	4	27
		Abnormal screening results	14	(27)	2	12
9.	**Who is the treating physician**	Neurologist	30	(58)	5	25

	for emotional problems? ‡	Resident in neurology	3	(6)	1	2
		Nurse practitioner or physician assistant	27	(52)	4	23
		Rehabilitation physician	23	(44)	3	20
		Psychiatrist	1	(2)	0	1
		Psychologist	14	(27)	1	13
		Geriatrician	5	(10)	1	4
		General practitioner	16	(31)	1	15
10.	**Does your hospital have a protocol or guideline for follow-up care for emotional problems?**	Yes	9	(17)	2	7
		No	42	(81)	5	37
		Missing	1	(2)	0	1

HADS: Hospital Anxiety and Depression Scale; CLCE-24: Checklist for Cognitive and Emotional Consequences following Stroke; HDRS: Hamilton Depression Rating Scale; BDI: Beck Depression Inventory; SIGEB: Assessment tool for long-term Consequences After Stroke (*'Signaleringsinstrument voor de lange termijn Gevolgen van een Beroerte'*)(30)

* Items 2 and 4 were only asked when item 1 had been marked 'Always', 'Mostly' or 'Sometimes'.

† Item 3 was only asked when item 2 had been marked 'Yes'.

‡ These items allowed multiple answers and were analysed accordingly, see 'Statistical Analysis' paragraph; consequently, the sum of the percentages is not 100%.

Table 3. Characteristics of respondents and non-respondents

Characteristic	Respondents, n= 52	Non-respondents, n = 26
Female sex (%)	19 (37)	-
Age, median (interquartile range)	45 (40 – 57)	-
Neurologist (%)	49 (94)	-
Nurse practitioner or physician assistant at the neurology department (%)	3 (6)	-
Type of hospital		
University (%)	7 (15)	1 (4)
Large general (%)	44 (87)	25 (96)
Small general (%)	1 (2)	0 (0)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	**Page 1/ line 1-3**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	**Page 3/ line 29 – 50**
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	**Page 4 – 5 / line 69 – 86**
Objectives	3	State specific objectives, including any prespecified hypotheses	**Page 5 / line 87 – 93**
Methods			
Study design	4	Present key elements of study design early in the paper	**Page 6 / line 97 – 98**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	**Page 6 - line 97 – 105 Page – 7 / line 116 – 128**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	**Page 6 / line 98 – 105**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	**Page 6 – 7 – line 112 – 122**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	**Page 6 – 7 / line 112 – 128**
Bias	9	Describe any efforts to address potential sources of bias	**Page 11 / line 217 - 225**
Study size	10	Explain how the study size was arrived at	**Page 6 / line 98 - 100**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	**Page 7 / line 131 - 137**

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	**Page 7 / line 131 - 137**
		(*b*) Describe any methods used to examine subgroups and interactions	**NA**
		(*c*) Explain how missing data were addressed	**NA**
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	**NA**
		(*e*) Describe any sensitivity analyses	**NA**
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	**Page 8 / line 144 – 150 & Page 17, Table 1**
		(b) Give reasons for non-participation at each stage	**Page 17, Table 1**
		(c) Consider use of a flow diagram	**NA**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	**Page 8 / line 144 – 150 & Page 17, Table 1**
		(b) Indicate number of participants with missing data for each variable of interest	**Page 17, Table 1**
Outcome data	15*	Report numbers of outcome events or summary measures	**Page 17 – 19, Table 1, Table 2, Table 3**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	**Page 17 – 19 Table 1, Table 2, Table 3**
		(*b*) Report category boundaries when continuous variables were categorized	**NA**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	**NA**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	**NA**
Discussion			
Key results	18	Summarise key results with reference to study objectives	**Page 10 – 11 / line 204 - 214**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any	**Page 11 / line**

		potential bias	**217 - 225**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	**Page 11 – 13 / line 226 – 278**
Generalisability	21	Discuss the generalisability (external validity) of the study results	**Page 11 / line 217 - 225**
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	**Page 14 / line 291 - 292**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.