Secondary prevention and cognitive function after stroke: a study protocol for a 5-year follow-up of the ASPIRE-S cohort

Daniela Rohde, David Williams, Eva Gaynor, Kathleen Bennett, Eamon Dolan, Elizabeth Callaly, Margaret Large, Anne Hickey

ABSTRACT

Introduction: Cognitive impairment is common following stroke and can increase disability and levels of dependency of patients, potentially leading to greater burden on carers and the healthcare system. Effective cardiovascular risk factor control through secondary preventive medications may reduce the risk of cognitive decline. However, adherence to medications is often poor and can be adversely affected by cognitive deficits. Suboptimal medication adherence negatively impacts secondary prevention targets, increasing the risk of recurrent stroke and further cognitive decline. The aim of this study is to profile cognitive function and secondary prevention, including adherence to secondary preventive medications and healthcare usage, 5 years post-stroke. The prospective associations between cognition, cardiovascular risk factors, adherence to secondary preventive medications, and rates of recurrent stroke or other cardiovascular events will also be explored.

Methods and analysis: This is a 5-year follow-up of a prospective study of the Action on Secondary Prevention Interventions and Rehabilitation in Stroke (ASPIRE-S) cohort of patients with stroke. This cohort will have a detailed assessment of cognitive function, adherence to secondary preventive medications and cardiovascular risk factor control.

Ethics and dissemination: Ethical approval for this study was granted by the Research Ethics Committees at Beaumont Hospital, Dublin and Connolly Hospital, Dublin, Mater Misericordiae University Hospital, Dublin, and the Royal College of Surgeons in Ireland. Findings will be disseminated through presentations and peer-reviewed publications.

INTRODUCTION

Stroke is one of the leading causes of death and disability worldwide, with over half of patients exhibiting signs of cognitive impairment 6 months post-stroke. Deficits in cognitive function are associated with poor functional outcomes, increased vulnerability and poorer quality of life, and can increase disability and levels of dependency, potentially leading to a greater burden on carers and the healthcare system. While there is evidence to support early rehabilitation interventions post-stroke, less is known about the reduction of longer term stroke-related disability. The chronic phase of stroke accounts for a considerable proportion of the total costs of stroke care, with measures to improve long-term outcomes potentially having a substantial impact on the economic burden of stroke.
secondary prevention. However, there are limited longer term follow-up data on patients with stroke, and a lack of information regarding the adequacy of longer term post-stroke secondary prevention. The Action on Secondary Prevention Interventions and Rehabilitation in Stroke (ASPIRE-S) study found a high prevalence of cognitive impairment and cardiovascular risk factors at 6 months post-stroke. While three-quarters of the sample were on antihypertensive therapy, almost two-thirds had blood pressure above the recommended target of 140/90 mm Hg. Similarly, while 95% of patients were on lipid-lowering medications, only approximately three-quarters had total cholesterol or low-density lipoprotein (LDL) cholesterol at European guideline targets.

Medication adherence
Effective secondary stroke prevention is contingent on consistent adherence to prescribed secondary preventive medications. Non-adherence is associated with adverse outcomes, including rehospitalisation, recurring vascular events and death, as well as increased costs of care. However, medication adherence is often poor, with up to 50% of patients discontinuing secondary preventive medications 2 years post-stroke. A recent systematic review reported an estimated rate of non-adherence to secondary preventive medications among stroke survivors of 30.9% (95% CI 26.8% to 35.3%). A number of factors were found to be related to non-adherence in individual studies, including disability, reduced cognitive function, polypharmacy and concerns about treatment. However, this review also noted substantial heterogeneity in the inclusion criteria and definitions and measurements of adherence, with several studies excluding patients with stroke with evidence of cognitive impairment.

Medication adherence and cognitive function
Adherence to medication regimens requires a number of cognitive skills that are affected by cognitive impairment, including instructions for medication taking and accessing and scheduling medications. Suboptimal adherence, in turn, adversely impacts secondary prevention targets, increasing the risk of recurrent stroke and further cognitive decline. However, there is a scarcity of data on longer term treatment continuation and adherence rates in patients with stroke, with several studies of adherence either not including cognitive assessments, or focusing exclusively on adherence to antithrombotic medications by patients with stroke and atrial fibrillation. Further, previous studies of stroke outcomes are limited by relatively short follow-ups and small sample sizes, and may not reflect contemporary outcomes or treatments.

Thus, while secondary prevention may be related to a reduced risk of cognitive impairment in patients with stroke, few studies have examined the association between adherence to secondary preventive medications and cognitive impairment, and it is unclear whether suboptimal adherence affects the risk of later cognitive impairment. Further, there are little data available at present regarding the use of healthcare resources, outcomes and costs post-stroke, or how these may be impacted by cognitive impairment or inadequate secondary prevention. The identification of medication adherence patterns, factors associated with adherence, and the impact on clinical and cognitive outcomes can inform the development of policies and interventions focused on improving medication management. Given the growing health, social and economic burden of cognitive impairment and dementia, longer term follow-up studies are needed to test these associations over extended periods of time.

Aims and objectives
The aim of this study is to profile cognitive function and secondary prevention, including healthcare usage and adherence to secondary preventive medications, at 5 years post-stroke. Specifically, the objectives are:
- To provide a detailed description of cognitive function and secondary prevention, including medication adherence at 5 years post-stroke;
- To investigate risk factor management, including blood pressure and cholesterol control 5 years post-stroke;
- To ascertain rates of recurrent stroke, other cardiovascular events and death in the 5 years post-stroke;
- To explore the prospective associations between cognition, cardiovascular risk factors and adherence to secondary preventive medications from 6 months to 5 years post-stroke;
- To explore levels of agreement between self-reported medication adherence assessed using a validated scale, pill counts and adherence estimates using pharmacy prescription refill data, in this cohort of patients with stroke;
- To explore longer term stroke rehabilitation and healthcare usage, and their associations with cognition and secondary prevention 5 years post-stroke;
- To examine the longer term costs of stroke, in terms of healthcare usage and quality of life, and their association with cognition and secondary prevention 5 years post-stroke.

A secondary aim is to explore carer well-being and the reciprocal associations between changes in cognitive function of patients with stroke and emotional distress and vulnerability in carers or family members.

METHODS AND ANALYSIS
Study design
This is a 5-year follow-up of a prospective observational study of the ASPIRE-S cohort of patients with acute stroke in 2011–2012. A total of 256 patients and their family members or carers were last followed up at
6 months post-stroke. This cohort will be followed up again, 5 years post-stroke (2016–2017), with a comprehensive assessment of clinical and cognitive measures. A detailed health assessment will be conducted, including cognitive function, adherence to secondary prevention and cardiovascular risk factor control. Data will be collected using a combination of clinical and laboratory measurements using standard data collection forms, interviewer and self-completion questionnaires.

Sample size
All participants from the original study will be eligible to participate. On the basis of an estimated rate of attrition of 30% (including death and other loss to follow-up), it is anticipated that c. 180 patients and their family members or carers will be reassessed.

Outcomes
Cardiovascular risk factor control
Secondary prevention will be assessed using a number of clinical measures as part of a health assessment, including height and weight, blood pressure, pulse, anticoagulation, blood analysis and breath analysis (table 1). Analysis of serum total cholesterol, calculated LDL cholesterol and blood glucose will be carried out on all participants. Diabetic patients will also have glycated haemoglobin assessed.

Secondary preventive medications
Reported medications at the time of follow-up will be recorded as part of the interviewer-administered patient questionnaire, and confirmed with prescription refill data where possible.

Medication adherence
There is no consensus on the best measure to define medication adherence. Combining prescription refill data with self-reported measures of adherence is considered essential to capturing the full extent to which patients are (non-)adherent. Thus, adherence to secondary preventive medications will be assessed using a number of methods:

Prescription refills
Participants who are eligible for the General Medical Services (GMS) scheme will be asked for permission to access records of monthly dispensed medications from the Irish Health Service Executive Primary Care Reimbursement Service (HSE-PCRS) database. Access to the GMS scheme, which provides free general practitioner (GP) and hospital visits, and prescription medications at minimal cost, is means-tested for persons aged <70 years, with a substantially higher income threshold for the over 70s, such that over 90% of those over 70 in Ireland are included in the scheme. As a result, members of the scheme are representative of the Irish population of over-70s, but this is not the case for those aged under 70, where women and those in lower socio-economic groups are over-represented. The HSE-PCRS claims database provides details on monthly dispensed medications for each individual in the scheme. Prescription refills provide an objective estimate of medication adherence, circumventing the problem of incorrect self-reporting of medication adherence. Prescription refills can be used to calculate metrics such as the proportion of days covered—the sum of the days supplied for medications within each medication class, divided by the number of days in the study period. This method has been adopted by another recent study on adherence to secondary preventive medications post-stroke.

Self-reported medication adherence
Self-reported medication adherence will be assessed using the Medication Adherence Report Scale (MARS-5), a five-point scale that assesses both intentional and unintentional non-adherence. The eight-item Morisky Medication Adherence Scale (MMAS), which assesses a number of medication-taking behaviours, will also be included.

Pill counts
The research team will conduct pill counts of the remaining tablets in each medication or blister pack, to assess to what extent patients have taken medications as prescribed. In addition to providing a more comprehensive account of medication-taking, the use of several methods to estimate adherence will allow exploration of the levels of agreement between self-reported

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**Table 1** Clinical measures to be collected as part of a health assessment

| Clinical measure | Details |
|------------------|---------|
| Blood pressure   | Three measurements will be taken with the average of the last two readings used for analysis. Twenty-four-hour BP monitoring will also be performed where possible. |
| Pulse            | Where the pulse is found to be irregular, an ECG will be arranged to confirm atrial fibrillation. |
| Anticoagulation  | Record of the last three INR measurements to assess the safety of anticoagulation medication, where relevant. |
| Blood analysis   | To assess serum total cholesterol, HDL cholesterol and calculated LDL cholesterol, glucose and HbA1c. |
| Weight and height| To assess BMI. |
| Breath analysis  | Carbon monoxide monitoring to confirm non-smoking status in former smokers. |

BMI, body mass index; BP, blood pressure; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein; INR, international normalised ratio; LDL, low-density lipoprotein.
medication adherence, pill counts and adherence estimates using pharmacy prescription refill data, which has not previously been reported for patients with stroke.

**Stroke recurrence and other cardiovascular events**
In order to ascertain stroke recurrence or other cardiovascular events, participants will be asked if they have experienced a stroke or other cardiovascular event since the last assessment. Stroke and other cardiovascular event occurrence will also be ascertained from participants’ hospital medical notes, based on recording of diagnosis or other mention in the record.

**Cognitive function**
Cognitive function will be assessed using a number of standardised, validated instruments, including the Montreal Cognitive Assessment (MoCA), the National Institute of Neurological Disorders and Stroke (NINDS) 30 min test battery, and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) (table 2).

**Rehabilitation and healthcare usage**
A number of questions on use of physiotherapy, occupational therapy, psychology, and speech and language therapy in the past 12 months, and the perceived need for these services, will be included in the patient assessment. Questions on healthcare usage, adapted from The Irish Longitudinal Study on Ageing, will also be included. These questions will assess use of GP and nursing services, inpatient and outpatient hospital care, use of mental health services, home help and home care, and meals-on-wheels in the past 12 months. In addition, the Timed Up and Go test, a performance-orientated mobility assessment tool used to identify individuals at increased risk of falls, and a number of questions on falls adapted from the Irish Longitudinal Study on Ageing, will be included.

**Covariates**
A range of demographic information, including age, education, occupational status, marital status and living arrangements, will be collected as part of the patient and family member/carer assessments. The patient assessment will also include questions relating to lifelong learning, social participation and current smoking. Potential barriers to medication adherence will be explored using the Beliefs about Medicines Questionnaire (BMQ), which assesses concerns and perceived necessity of medications. Beliefs of patients with stroke about medicines have been reported to be associated with non-adherence, with non-adherent patients scoring lower on the positive beliefs dimensions of the BMQ (necessity and benefit) and higher on negative beliefs (concern, overuse and harm).

The Frenchay Aphasia Screening Test (FAST) will be used to screen for communication problems that may affect performance on cognitive assessments. Quality of life and health and well-being status will be assessed using the ICEpop CAPability measure for Older people (ICECAP-O), the EQ-5D and the Stroke Specific Quality of Life Scale (SSQOL). Finally, the Nottingham Extended Activities of Daily Living Scale, which assesses activities that may be important to patients with stroke who have been discharged home, and the Vulnerable Elders Scale (VES), a simple function-based tool for identifying older persons who may be at risk of health deterioration, will be included.

**Family member and carer assessments**
In addition to the patient assessment, family members or carers will be asked to complete a family member or carer assessment. This assessment will involve a self-completion questionnaire that includes the IQCODE and the Neuropsychiatric Inventory, Questionnaire Version (NPI-Q) from the NINDS test battery, as well as a number of questions regarding the extent to which patients receive assistance with taking medications. The use of informant report in addition to patient assessments will facilitate triangulation of measures of cognition and increase the validity of the findings. Furthermore, informant report is important in cases where patients receive help from carers with medication taking, as there is a lack of data on factors affecting medication adherence in patients relying on others for medication management.

The family member and carer assessment will also include a measure of anxiety (the Hospital Anxiety and Depression Scale—Anxiety (HADS-A)) and depression (the Centre for Epidemiologic Studies Depression Scale (CES-D)), and vulnerability (VES). These measures

**Table 2  Cognitive assessments**

| Assessment                  | Details                                                                 |
|-----------------------------|-------------------------------------------------------------------------|
| Patient MoCA               | A rapid screening instrument for global cognitive function, which has   |
| NINDS 30 min test protocol | A 30 min neuropsychological assessment battery that includes:         |
| Carer/family member IQCODE | An informant-reported assessment of cognitive function                   |

IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; MoCA, Montreal Cognitive Assessment; NINDS, National Institute of Neurological Disorders and Stroke; NPI-Q, Neuropsychiatric Inventory, Questionnaire Version.
were included in the original ASPIRE-S study, which reported substantial levels of anxious and depressive symptoms among carers, linked to anxiety, depressive symptoms and cognitive impairment in the patients with stroke. By repeating the measures of emotional distress and vulnerability included in the original ASPIRE-S study, we will be able to consider carer well-being over time, and explore the associations between changes in cognitive impairment in patients with stroke and emotional distress and vulnerability in carers or family members.

**Follow-up procedure**

Each potential participant’s consultant physician will be contacted to request permission to contact patients and their GPs. Efforts will be made to identify deceased participants prior to contact being made, using, for example, hospital and GP records, as well as a widely used website of death notifications (RIP.ie). Participants will be sent a study information pack by post, containing a cover letter, patient and family member/carer information leaflet, and a stamped addressed postcard that can be returned by participants wishing to opt out of the study. The cover letter will advise patients and family members that they will be contacted by phone by the research team to discuss their participation in the study, unless they return the postcard or inform their consultant that they do not wish to be contacted.

Participants will then be contacted by phone to discuss the study and to ascertain their interest in participating in the follow-up. If participants agree, a meeting will be arranged with two members of the research team, in the participants’ own home, at a hospital or another location convenient to participants, and written consent will be obtained. In cases where significant cognitive deficits are suspected, either by the patient’s GP or members of the research team conducting the follow-up phone calls, contact will be made with the patient’s family member or carer, who will be requested to be present at the time of interview. The research team will attempt to carry out individual interviews with all patients. Assisted self-interviews, in which the participant can answer most of the questions but requires some help from a family member or carer, may also be used. This procedure has been used by follow-up waves of the Irish Longitudinal Study on Ageing. If a participant is unable to complete an interview (cognitively or physically), the family member or carer will still be eligible to complete the family member/carer assessment.

**Data analysis**

Data will be analysed and reported using descriptive statistics, including means and SDs for normally distributed data, medians and IQRs for non-normally distributed data, and frequencies and percentages, as appropriate. Adjusted associations between medication (non-)adherence, (uncontrolled) cardiovascular risk factors and cognitive function will be assessed using multivariate regression models. The predicted sample size of 180 and an estimated prevalence of cognitive impairment of 50% will permit the inclusion of ~9 variables in multivariate analyses. Covariates that are associated with each outcome at the p<0.10 level will be included in multivariate models. Agreement between measures of medication adherence will be assessed using the κ statistic.

**ETHICS AND DISSEMINATION**

**Treatment of study participants**

Participants will continue to receive standard care throughout the study period from their hospital consultant or GP. If participants become distressed or otherwise unwell during the interview or health assessment, the interview or assessment will be terminated immediately, and the interviewer will call back within 24 hours to see how the participant is. The family member/carer and GP or consultant will be informed that the patient became upset during the course of the interview and, if appropriate, that the patient would like to talk to a member of the medical team. Although potential harm is expected to be minimal, some participants may experience temporary and localised discomfort, mild pain or bruising as a result of venepuncture or blood pressure assessment.

**Dissemination**

Findings from this study will be disseminated through presentations in academic fora and to relevant policymaker, practitioner and stakeholder audiences, and through peer-reviewed publications.

**LIMITATIONS**

This study has a number of limitations, including the reliance on self-report or carer report to ascertain usage of healthcare services. Unfortunately, owing to the complex system of public/private healthcare provision in Ireland, and the lack of universal patient identifiers, there is currently no alternative method available to collect this information. While every effort will be made to follow-up all patients still alive from the original study, patients with more severe cognitive decline may be more likely to be lost to follow-up, which could lead to an underestimation of the prevalence of cognitive impairment in this cohort. Since this is a follow-up study, the sample size will be based on the availability of participants, rather than a statistical power calculation. It is possible that the analyses for some associations of interest will be underpowered. While we will aim to assess and adjust for a number of known confounders, owing to the observational nature of this study, there may be other unknown or unmeasured confounding factors. However, given the fact that longer term follow-up studies of patients with stroke are relatively rare, and no such studies exist in Ireland, recalling this cohort provides a unique opportunity to explore longer term secondary prevention and cognitive function in patients with stroke.
CONCLUSION
Given the potential public health burden of cognitive impairment after stroke, identification of modifiable risk and protective factors to avert or delay cognitive decline is paramount. Delaying cognitive impairment could allow many individuals to reach the end of their natural lifespan before crossing the threshold for dementia. 46 While effective vascular risk factor management through secondary prevention may reduce the burden of post-stroke cognitive impairment, 27 there is a lack of data on longer term treatment continuation and adherence rates in patients with stroke. Similarly, there are currently no Irish data on the costs of cognitive impairment or inadequate secondary prevention post-stroke. This study will provide valuable information on the trajectories of cognitive impairment, medication adherence and cardiovascular risk factors post-stroke, and will indicate how cognitive function and secondary prevention are related to each other, as well as to stroke or other cardiovascular event recurrence and healthcare usage, over time. These findings can help inform future health policy and service planning regarding the longer term management of patients with stroke.

Author affiliations
1Division of Population Health Sciences, Royal College of Surgeons in Ireland, Dublin, Ireland
2Department of Geriatric and Stroke Medicine, Royal College of Surgeons in Ireland and Beaumont Hospital, Dublin, Ireland
3Department of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland
4Department of Geriatric Medicine, Connolly Hospital Blanchardstown, Dublin, Ireland
5Department of Geriatric Medicine, Mater Misericordiae University Hospital, Dublin, Ireland
6Clinical Research Centre, Royal College of Surgeons in Ireland, Beaumont Hospital, Dublin, Ireland

Twitter Follow Daniela Rohde @dannifromdublin

Contributors DR, DW, KB, EG, EC, ED, ML, and AH conceived and designed the study. DR drafted and edited the manuscript. DW, KB, EG, EC, ED, ML, and AH critically revised the manuscript. All authors approved the final draft.

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Competing interests All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: DW is an Advisory Board Member for Boehringer Ingelheim, Daiichi Sankyo, Bristol Myers Squibb and Bayer, and has received personal fees for this outside the submitted work. DW is Speaker Honorarium for Boehringer Ingelheim, and has received personal fees for this outside the submitted work.

Ethics approval This study was approved by the Research Ethics Committees at Beaumont Hospital (ref. 16/28), Connolly Hospital Blanchardstown (28/11/2016) and the Royal College of Surgeons in Ireland (REC 13SE5).

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REFERENCES
1. McElwaine P, McCormack J, Harbisson J, on behalf of the National Stroke Programme Audit Steering Group IHF, and HSE. National stroke audit. Dublin Irish Heart Foundation and HSE, 2015.
2. Mellon L, Brewer L, Hall P, et al. Cognitive impairment six months after ischaemic stroke: a profile from the ASPIRE-S study. BMC Neurol 2015;15:31.
3. Brainin M, Tuomilehto J, Heiss WD, et al. Post-stroke cognitive decline: an update and perspectives for clinical research. Eur J Neurol 2015;22:229–38, e13–6.
4. AtteIh S, Mellon L, Hall P, et al. Implications of stroke for caregiver outcomes: findings from the ASPIRE-S study. Int J Stroke 2015;10:918–23.
5. Wolfe CD, Crichton SL, Heuschmann PU, et al. Estimates of outcomes up to ten years after stroke: analysis from the prospective South London Stroke Register. PLoS Med 2011;8:e1001033.
6. Srin S, Horgan P, Sexton E, et al. The future cost of stroke in Ireland: an analysis of the potential impact of demographic change and implementation of evidence-based therapies. Age Ageing 2013;42:299–306.
7. Allan LM, Rowan EN, Firbank MJ, et al. Long term incidence of dementia, predictors of mortality and pathological diagnosis in older stroke survivors. Brain 2011;134(Pt 12):3716–27.
8. Douin A, McKevitt C, Emmett ES, et al. Long-term effects of secondary prevention on cognitive function in stroke patients. Circulation 2013;128:1341–8.
9. Richard E, Jongstra S, Soinnen H, et al. Healthy ageing through internet counselling in the elderly: the HATICE randomised controlled trial for the prevention of cardiovascular disease and cognitive impairment. BMJ Open 2016;6:e010806.
10. Hankey GJ. Secondary stroke prevention. Lancet Neurol 2014;13:178–94.
11. Brewer L, Mellon L, Hall P, et al. Secondary prevention after ischaemic stroke: the ASPIRE-S study. BMC Neurol 2015;15:216.
12. Van Schaik SM, Van den Berg-Vos RM, Weinstein HC, et al. Limited efficacy of a long-term secondary prevention program in ischemic stroke and transient ischemic attack patients. J Stroke Cerebrovasc Dis 2015;24:1378–82.
13. Murphy SJ, Coughlan CA, Tobin O, et al. Continuation and adherence rates of initially prescribed intensive secondary prevention therapy after Rapid Access Stroke Prevention (RASP) service assessment. J Neurol Sci 2016;361:13–18.
14. Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: its importance in cardiovascular outcomes. Circulation 2009;119:3028–35.
15. Kronish IM, Ye S. Adherence to cardiovascular medications: lessons learned and future directions. Prog Cardiovasc Dis 2013;55:590–600.
16. Glader EL, Sjölander M, Eriksson M, et al. Persistent use of secondary preventive drugs declines rapidly during the first 2 years after stroke. Stroke 2010;41:397–401.
17. Al AShaikeh S, Quinn T, Dunn W, et al. Predictive factors of non-adherence to secondary preventative medication after stroke or transient ischaemic attack: a systematic review and meta-analyses. Eur Stroke J 2016;1:65–75.
18. Campbell NL, Boustani MA, Skopolja EN, et al. Medication adherence in older adults with cognitive impairment: a systematic evidence-based review. Am J Geriatr Pharmacother 2012;10:165–77.
19. Bushnell CD, Olson DM, Zhao X, et al. Secondary preventive medication persistence and adherence 1 year after stroke. Neurology 2011;77:1182–90.
20. O’Carroll R, Whittaker J, Hamilton B, et al. Predictors of adherence to secondary preventative medication in stroke patients. Ann Behav Med 2011;41:383–90.
21. Sjölander M, Eriksson M, Glader E-L. Inequalities in medication adherence to statin treatment after stroke: a nationwide observational study. Eur Stroke J 2016;1:101–107.
22. Björk P, Renlund H, Svensson P-J, et al. Warfarin persistence among stroke patients with atrial fibrillation. Thromb Res 2015;136:744–8.
23. Crichton SL, Bray BD, McKevitt C, et al. Patient outcomes up to 15 years after stroke: survival, disability, quality of life, cognition and mental health. J Neurol Neurosurg Psychiatry 2016;87:1091–8.
24. Wren MA, Gillespie P, Smith S, et al. Towards earlier discharge, better outcomes, lower costs: stroke rehabilitation in Ireland. Dublin: Economic and Social Research Institute, 2014.

25. Sanfélix-Gimeno G, Rodríguez-Bernal CL, Hurtado I, et al. Adherence to oral anticoagulants in patients with atrial fibrillation—a population-based retrospective cohort study linking health information systems in the Valencia region, Spain: a study protocol. BMJ Open 2015;5:e007613.

26. Richardson K, Kenny RA, Peklar J, et al. Agreement between patient interview data on prescription medication use and pharmacy records in those aged older than 50 years varied by therapeutic group and reporting of indicated health conditions. J Clin Epidemiol 2013;66:1308–16.

27. Hansen RA, Kim MM, Song L, et al. Comparison of methods to assess medication adherence and classify nonadherence. J Clin Hypertens (Greenwich) 2009;43:413–22.

28. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. Psychol Health 1999;14:1–24.

29. Morisky DE, Ang A, Krousel-Wood M, et al. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich) 2008;10:348–54.

30. Nasreddine ZS, Phillips NA, Bedirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53:695–9.

31. 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;37:2220–41.

32. Jorm AF, Jacomb PA. The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): socio-demographic correlates, reliability, validity and some norms. Psychol Med 1989;19:1015–22.

33. Podsiadlo D, Richardson S. The timed “Up & Go”: a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991;39:142–8.

34. Sjölander M, Eriksson M, Glader EL. The association between patients’ beliefs about medicines and adherence to drug treatment after stroke: a cross-sectional questionnaire survey. BMJ Open 2013;3:e003551.

35. Endertby PM, Wood VA, Wade DT, et al. The Frenchay Aphasia Screening Test: a short, simple test for aphasia appropriate for non-specialists. Int Rehabil Med 1987;8:166–70.

36. Grewal I, Lewis J, Flynn T, et al. Developing attributes for a generic quality of life measure for older people: preferences or capabilities? Soc Sci Med 2006;62:1891–901.

37. EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. Health Policy 1990;16:199–208.

38. Williams LS, Weinberger M, Harris LE, et al. Development of a stroke-specific quality of life scale. Stroke 1999;30:1362–9.

39. Nouri F, Lincoln N. An extended activities of daily living scale for stroke patients. Clin Rehabil 1987;1:301–5.

40. Saliba D, Elliott M, Rubenstein LZ, et al. The Vulnerable Elders Survey: a tool for identifying vulnerable older people in the community. J Am Geriatr Soc 2001;49:1691–9.

41. De Simoni A, Mant J, Sutton S. Adherence to medication in stroke survivors dependent on caregivers. Br J Gen Pract 2015;65:e789–e91.

42. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361–70.

43. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.

44. Nolan A, O’Regan C, Dooley C, et al. The over 50s in a changing Ireland: economic circumstances, health and well-being. Dublin: The Irish Longitudinal Study on Ageing, 2014.

45. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. Am J Epidemiol 2007;165:710–18.

46. Lautenschlager NT, Anstey KJ, Kurz AF. Non-pharmacological strategies to delay cognitive decline. Maturitas 2014;79:170–3.