Association between patient outcomes and key performance indicators of stroke care quality: a systematic review and meta-analysis

Urimubenshi G[1,2]

Langhorne P[1]

Cadilhac DA[3,4]

Kagwiza NJ[2]

Wu O[5]

1) Institute of Cardiovascular and Medical Sciences, University of Glasgow, UK
2) College of Medicine and Health Sciences, University of Rwanda, Rwanda
3) Stroke and Ageing Research, School of Clinical Sciences at Monash Health, Monash University, Clayton, Australia
4) The Florey Institute Neuroscience and Mental Health, Heidelberg, University of Melbourne, Vic, Australia
5) Institute of Health and Wellbeing, University of Glasgow, UK

Corresponding author:

Gerard Urimubenshi

Level 2, New Lister Building

Glasgow Royal Infirmary

Glasgow

G31 2ER

United Kingdom

Email: g.urimubenshi.1@research.gla.ac.uk

ABSTRACT

Introduction: Translating research evidence into clinical practice often uses key performance indicators (KPIs) to monitor quality of care. We conducted a systematic review to identify the stroke KPIs used in large registries, and to estimate their association with patient outcomes.

Method: We sought publications of recent (January 2000-May 2017) national or regional stroke registers reporting the association of KPIs with patient outcome (adjusting for age and stroke severity). We searched Ovid Medline, EMBASE and PubMed and screened references from bibliographies. We used an inverse variance random effects meta-analysis to estimate associations (odds ratio; 95% Confidence Interval) with death or poor outcome (death or disability) at the end of follow up.

Findings: We identified 30 eligible studies (324,409 patients). The commonest KPIs were swallowing/nutritional assessment, stroke unit admission, antiplatelet use, brain imaging, anticoagulant use, lipid management, deep vein thrombosis prophylaxis and early physiotherapy/mobilization. Lower case fatality was associated with stroke unit admission (OR 0.79; 0.72-0.87), swallow/nutritional assessment (OR 0.78; 0.66-0.92), antiplatelet (OR 0.61; 0.50-0.74) or anticoagulant use (OR 0.51; 0.43-0.64) for ischemic stroke, lipid management (OR 0.52; 0.38-0.71), and early physiotherapy or mobilization (OR 0.78;

0.67-0.91). Reduced poor outcome was associated with adherence to swallowing/nutritional assessment (OR 0.58; 0.43-0.78) and stroke unit admission (OR 0.83; 0.77-0.89). Adherence with several KPIs appeared to have an additive benefit.

Discussion: Adherence with common KPIs was consistently associated with a lower risk of death or disability after stroke.

Conclusion: Policy makers and health care professionals should implement and monitor those KPIs supported by good evidence.

Keywords

Stroke, indicator, care quality, patient outcome

INTRODUCTION

In recent years there have been concerted efforts to develop and implement clinical practice guidelines for the management of patients with acute stroke (1). Clinical guidelines are written to promote diagnostic or therapeutic interventions applicable to the majority of patients in most circumstances. However, the use of guideline recommendations for individual patients has traditionally been left to the discretion of individual clinicians (2). A recognised approach to assist the translation of research evidence into clinical practice is to monitor the quality of care using standardized performance indicators (3) also called quality indicators, process of care measures or key performance indicators (KPIs). Performance indicators are standards of care that imply that health care professionals are providing inadequate care if eligible patients do not receive that standard of care. Performance indicators can be used to monitor the adherence to current guidelines, and support the transfer of new evidence into everyday clinical practice (4).

There are now numerous stroke interventions that have been shown to improve patient outcomes in research trials; admission to specialized stroke units, use of intravenous thrombolysis, mechanical thrombectomy, antiplatelet drugs, anticoagulants, and management of fever, hyperglycaemia, and swallowing dysfunction for selected patient groups (5-9). However, application into routine practice is challenging and regular monitoring is important (10). Ideally, implementation of clinical evidence can be demonstrated using a range of stroke KPIs, which offer proxy measures for ideal care being delivered. In turn this would lead to evidence of better patient outcomes (11).

In a previous systematic review of the association between stroke quality (performance) indicators and patient-centered outcomes, out of 14 studies that met the eligibility criteria; nine had mostly positive associations, whereas five reported little or no association with a lower risk for mortality, disability, medical complications, stroke recurrence, or patient dissatisfaction (12). A limitation of this review was the exclusion of stroke unit care as a performance indicator. With the ongoing developments in clinical guidelines and quality indicators for monitoring the application of these guidelines (10,13), we believe that there is a need for up-to date comprehensive information on KPIs for stroke care.

We aimed to conduct a systematic literature review to identify the KPIs that have been described in stroke care and to summarise their association with patient outcomes. We intend that information gathered from this review will provide decision makers and health care professionals with information on reliable and meaningful KPIs that can be implemented to improve outcomes post stroke.

METHODS

This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (14). This review was registered in Prospero Database (CRD42016050798).

Search strategy

Searching sources were Ovid Medline, Embase and PubMed databases, and relevant references from screening the bibliographies of the initial articles included in the search.
We used Medical Subject Headings (MeSH) and all subheading terms including “stroke”, “cerebrovascular accident”, “cerebrovascular disease”, “cerebrovascular disorders”, “brain hemorrhage”, “intracranial hemorrhages”, “brain infarction”, “subarachnoid hemorrhage”, “health care quality”, “quality of health care” “quality indicators, health care”, “quality assurance, health care”, “quality control”, “quality indicator”, “performance indicator”, “register”, “registries”, “clinical audit”, “treatment outcome” , “case fatality rate”, “mortality”, “survival”, “disability”, “functional status”,” hospitalization”, “cost”, “quality

of life", "complication", "hospital discharge" and "stroke recurrence". Our search was restricted to full-text manuscripts published in English from January 1st, 2000 to May 24th, 2017.

The search strategies for different databases are detailed in the *Online Supplement.*

Inclusion criteria: We included national or regional registers that recorded the independent association (after adjusting for at least age and a measure of stroke severity) between the KPIs and stroke patient outcomes, and involved patients from at least three hospitals.

Exclusion criteria*:* We excluded reports that were reviews or did not provide odds ratio (OR), hazard ratio (HR) or rate ratio (RR) data.

Screening and quality assessment

One author (GU) reviewed each title and excluded obviously irrelevant studies. Articles identified as potentially relevant underwent a full review by two authors (GU and PL) to determine if they met the inclusion criteria. In cases of disagreement, final determination was by discussion and consensus.

Data extraction

We used a standardized form to record information on country, main inclusion or exclusion criteria for the recruitment of participants, sample size, stroke severity measure, key performance indicators (KPIs) and outcome(s) reported, and reported results (and 95% confidence interval).

Data analysis

Initially, the identified KPIs and their association with the patient outcomes were categorized on whether the authors reported a significant association between the KPI and patient outcome. There was then a further quantitative analysis (meta-analysis) of the relationship (adjusted for at least age and stroke severity) between the KPIs identified and patient outcomes. Some checking of the consistency of KPIs and outcomes was required with grouping of similar KPIs. For the meta-analysis, we sought information on case fatality and poor outcome (death and disability or requiring support) after stroke.

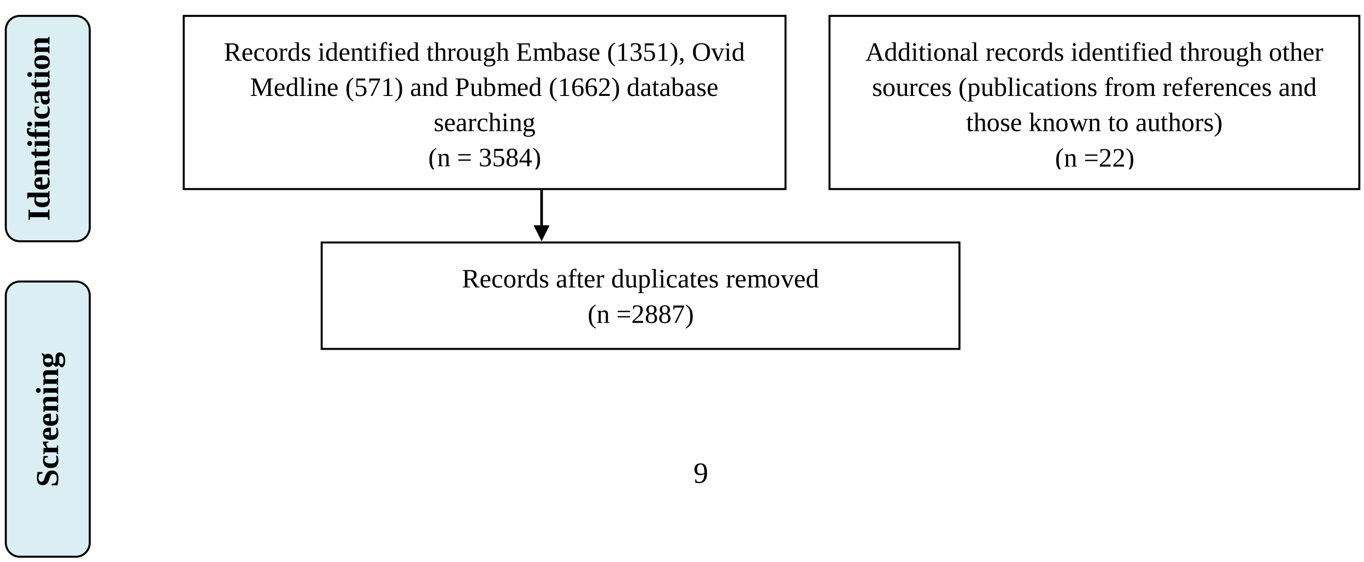
The meta-analysis was done using the Review Manager (version 5.3) software. Log ORs were combined using an inverse variance analysis (random effects model). First, we assumed that HRs and RRs approximate the ORs and performed the primary meta-analysis including all studies reporting on association of KPIs with case fatality and poor outcome.

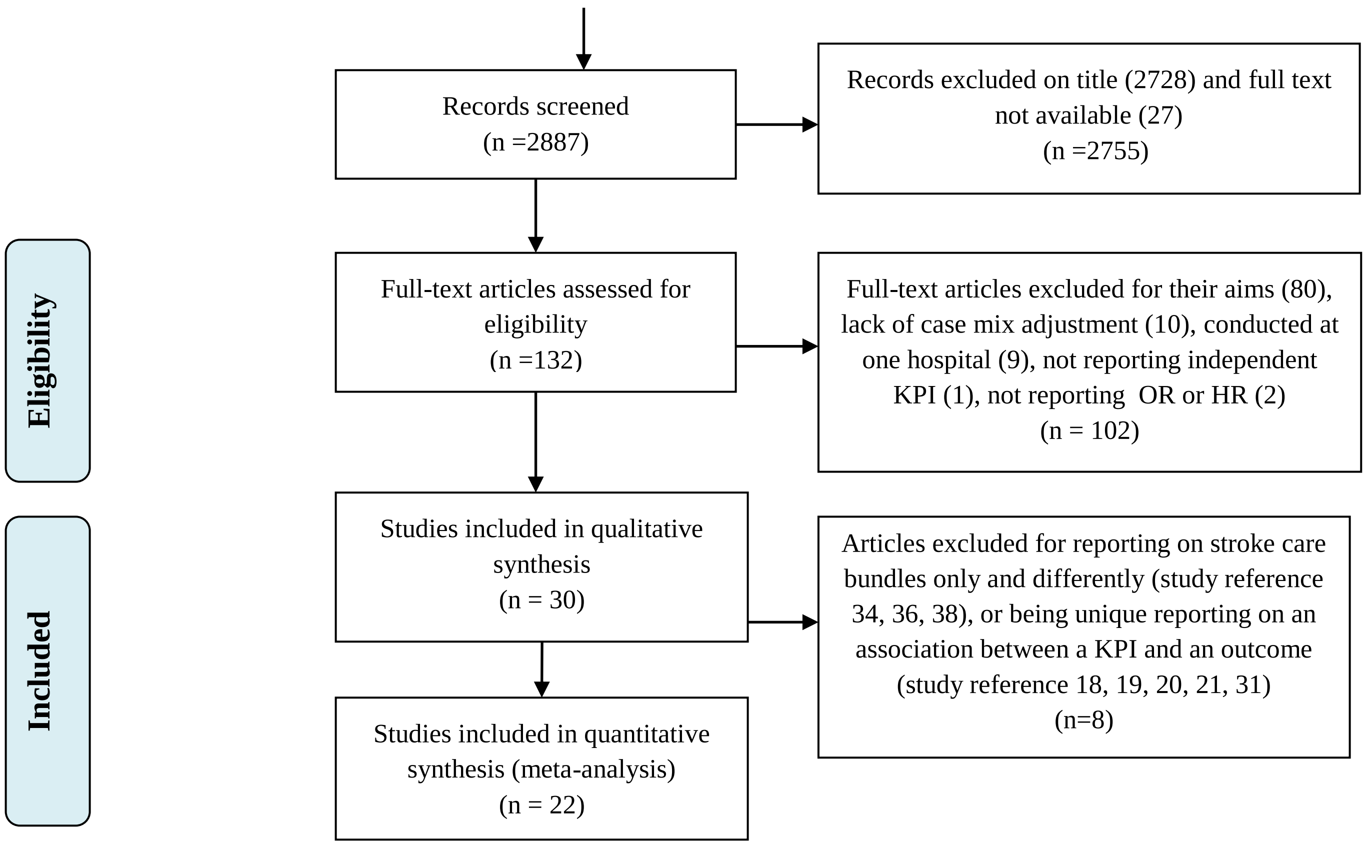
Second, we performed sensitivity meta-analysis by excluding studies that used HR or RR as measures of association.

RESULTS

The review profile is shown in Figure 1. We identified 3606 references from which 30 studies (15-44) were eligible for the qualitative review. Among these, only 22 were eligible for the meta-analysis.

Figure 1: Review profile showing selection of studies





Abbreviations: HR, hazard ratio; KPI, key performance indicator; OR, odds ratio.

Included studies

Table 1 shows the studies considered for our systematic literature review. Most of the included studies (15-29) were conducted in Europe: One European study (15) was multinational (across ten countries), the rest were conducted in Denmark (6), Sweden (2), United Kingdom (3) (one in England and two in Scotland), Italy (1), Spain (1), and Greece

(1). The non-European studies were conducted in the USA, Canada, Chile, Australia, New Zealand, China, Thailand and Taiwan. Two reports from Denmark (17,18) and two from Scotland (24,25) were based on the same datasets but since they provided associations with different outcomes, they were all included in this systematic review.

Table 1: Studies eligible for the systematic literature review

Study	Stroke Type	Stroke Severity Measure	Sample size	Performance Indicator	Patient Outcome	OR/ HR/ RR	95% CI
Europe[15]	SAH excluded	Level of consciousness, incontinence, dysphagia,	1847 (10 countries)	Brain imaging	3-month case fatality	0.7	0.4-1.3
					3-month disability (BI≤18)	1.45	0.39–7.4
				Organized stroke care[a]	3-month case fatality	0.5	0.3-0.8
					3-month disability (BI≤18)	1.3	0.6–1.76
Denmark[16]	Ischemic stroke	SSS	22179(All Danish hospitals)	Anticoagulation treatment	4-year survival	1.91	1.44-2.52
Denmark[17]	SAH excluded	SSS	29573 (40 hospitals)	Specialized stroke unit by 2nd day	90 –day case fatality	0.76	0.69–0.83
				Antiplatelet therapy by 2nd day		0.71	0.62–0.81
				Anticoagulant therapy by 14th day		0.41	0.31–0.52
				CT/MRI scan by first day		1.35	1.24–1.46
				Assessment by a PT by 2nd day		0.81	0.73–0.88
				Assessment by an OT by 2nd day		0.83	0.75–0.91
				Nutritional risk assessment by 2nd d.		0.69	0.61–0.76
				Number of criteria fulfilled			
				1 vs 0		0.94	0.65-1.49
				2 vs 0		0.78	0.54–1.02
				3 vs 0		0.60	0.42–0.78
				4 vs 0		0.61	0.42–0.79
				5 vs 0		0.45	0.31–0.60
				6 vs 0		0.48	0.31–0.65
Denmark[18]	SAH excluded	SSS	2636 (7 stroke units)	Stroke unit (2nd day)	Prolonged LoS	0.71	0.65–0.77
				Antiplatelet (2nd day)		0.80	0.73–0.87
				Anticoagulant (14th day)		0.78	0.62–0.98
				CT/MRI scan (2nd day)		0.82	0.74–0.91
				PT assessment (2nd day)		0.87	0.81–0.93
				OT assessment (2nd day)		0.85	0.80–0.91
				Nutritional risk assessment (2nd day)		0.83	0.77–0.90
				Swallowing assessment (2nd day)		0.78	0.69–0.87
				Constipation risk assessment (2nd day)		0.70	0.63–0.78
				Mobilization (2nd day)		0.67	0.61–0.73
				Intermittent catheterisation (2nd day)		0.77	0.64–0.92
				DVT prophylaxis (2nd day)		0.82	0.71–0.95
				Percentage of criteria fulfilled			
				25%–49% vs 0%–24%		0.77	0.69–0.86
				50%–74% vs 0%–24%		0.67	0.60–0.75
				75%–100% vs 0%–24%		0.53	0.48–0.59
Denmark[19]	All Ischemic strokes	SSS	4292 (All Danish hospitals)	Thrombolysis	1.4 years-mortality	0.66	0.49–0.88
					1.4 years-recurrent stroke	1.05	0.68–1.64
					1.4 years major bleeding	0.59	0.24–1.47

Table 1: Studies eligible for the systematic literature review *Continued*

Denmark[20]	First ever ischemic strokes	SSS	5070 (Aarhus County)	Antidepressants during hospitalization	30-day case fatality	0.28	0.18–0.43
Denmark[21]	All stroke types	SSS	11757 (10 stroke units in 2 counties)	Early admission to a stroke unit	Any medical complication[b] during admission (LoS=13 days)	0.79	0.68–0.92
				Antiplatelet therapy		0.95	0.79–1.15
				Anticoagulant therapy		0.59	0.45–0.76
				CT/MRI scan		1.52	1.35–1.72
				Assessment by a PT		1.10	0.94-1.28
				Assessment by an OT		1.10	0.94–1.27
				Assessment of Nutritional risk		0.87	0.70–1.07
				Swallowing assessment		0.97	0.84–1.11
				Early mobilization		0.43	0.35–0.53
				Percentage of criteria fulfilled			
				25%–49% vs 0%–24%		0.77	0.67–0.88
				50%–74% vs 0%–24%		0.57	0.46–0.70
				75%–100% vs 0%–24%		0.50	0.36–0.68
Sweden[22]	SAH excluded	Level of consciousness	8194 (All hospitals in Sweden)	Stroke unit (Independent before stroke)	2-year case fatality	0.81	0.72-0.92
					2-year functional dependency	0.79	0.66-0.94
Sweden[23]	First ever ischemic strokes	ADLs Function	14 529 (All hospitals in Sweden)	Antiplatelet Therapy	3-month case fatality	0.83	0.68-1.01
				ACE inhibitors Therapy		1.00	0.87–1.14
				Statins Therapy		0.78	0.67–0.91
				Anticoagulants Therapy		0.58	0.44–0.76
UK (England)[24]	Ischaemic stroke	Level of consciousness and neurological deficit	36197 (106 hospitals)	Seen by a stroke consultant or associate specialist within 24 h hours	30-day case fatality	0.88	0.80- 0.97
				Brain scan within 24 hours		0.96	0.86- 1.07
				Bundle 1: seen by nurse and one therapist within 24 hours and all relevant therapists within 72 hours		0.90	0.82-0.99
				Bundle 2: nutrition screening and formal swallow assessment within 72 hours where appropriate		0.76	0.67- 0.87
				Bundle 3: patient's first ward of admission was stroke unit and they arrived there within four hours of hospital admission		0.99	0.90-1.08
				Bundle 4: patient given antiplatelet therapy where appropriate and had adequate fluid and nutrition for first 72h		0.46	0.42-0.50
				Number of criteria fulfilled			
				Quality score 5 or 6 *v* 0-4		0.74	0.66- 0.83

Table 1: Studies eligible for the systematic literature review ***Continued***

UK (Scotland)[25]	All stroke types	SSV	36055 (36 hosp)	Stroke unit on day 0 or 1	6 month case fatality	0.79	0.74–0.85
				Swallow screen on day 0		0.95	0.86–1.04
				Brain scan on day 0		0.95	0.88–1.03
				Aspirin on day 0 or 1		0.54	0.49–0.58
				Number of criteria fulfilled	6 month case fatality		
				0 vs 4		2.26	1.60–3.21
				1 vs 4		1.67	1.45–1.93
				2 vs 4		1.44	1.31–1.59
				3 vs 4		1.17	1.08–1.27
				Number of criteria fulfilled	Discharge to home/usual residence at 6 months		
				0 vs 4		0.70	0.50–0.98
				1 vs 4		0.74	0.65–0.84
				2 vs 4		0.84	0.76–0.91
				3 vs 4		0.91	0.85-0.98
UK (Scotland)[26]	All stroke types	SSV	41692 (36 hosp)	Admission to stroke unit	1-year survival	1.43	2.71-3.56
					6-month discharged home	1.19	1.11-1.28
Italy[27]	All stroke types	Level of consciousness	11572 (424 stroke units and 260 hospitals)	Stroke Unit	2-year case fatality	0.79	0.68–0.91
					2-year death or disability (mRS>2)	0.81	0.72–0.91
					2 year not living at home	0.85	0.74–0.97
Spain[28]	SAH excluded	NIHSS	1767 (47 hospitals)	Brain imaging < 24 hours	1-year case fatality risk for noncompliance	1.4	0.71–2.76
				Screening of dysphagia		1.23	0.88–1.71
				Antiplatelets < 48 h for IS		1.3	0.84–2.02
				Early mobilization		1.54	1.05–2.24
				Assessment of rehabilitation needs		1.48	1.06–2.07
				DVT prevention		0.98	0.60–1.60
				Management of hyperthermia		0.67	0.25–1.79
				Management of hypertension		1.87	1.22–2.86
				Management of dyslipidemia		1.29	0.86–1.93
				Anticoagulants for IS		1.70	0.95–3.05
				Antithrombotics at discharge (IS)		2.79	1.41–5.54
Greece[29]	First-ever acute ischemic stroke	SSS	794 (Different Athenian hospitals)	Statin at discharge	10 year-Case fatality	0.43	0.29-0.61
					10-year stroke recurrence	0.65	0.39-0.97
USA[30]	Ischemic Stroke	NIHSS	1363 (5 hospitals)	Neurology assessment	In-hospital mortality, discharge to hospice, or discharge to a skilled nursing facility	1.13	0.59-2.17
				Swallowing evaluation		0.64	0.43-0.94
				DVT prophylaxis		0.60	0.37-0.96
				Early mobilization		0.69	0.42-1.14
				Blood pressure management		1.00	0.67-1.50
				Fever management		0.71	0.35-1.41
				Hypoxia management		0.26	0.09-0.73

Table 1: Studies eligible for the systematic literature review ***Continued***

USA[31]	All stroke types	Weakness and altered level of consciousness	18017(222 hospitals from 6 States)	Dysphagia screening	Higher risk of pneumonia for no screening	2.15	1.74-2.66
Canada[32]	Ischemic stroke	CNS	3631 (11 hospitals)	OCI[c] 1 vs 0	1-year case fatality	0.69	0.44–1.09
				OCI 2 vs 0		0.39	0.25–0.62
				OCI 3 vs 0		0.40	0.25–0.64
				Antithrombotic therapy		0.33	0.22–0.50
Canada[33]	Intracerebral Haemorrhage Stroke	CNS	2466 (11 hospitals)	Statin use in hospital	6 months case fatality	0.2	0.1–0.3
					Poor outcome (mRS4–6.) at discharge	0.6	0.4–0.9
Canada[34]	Ischemic stroke	CNS	6223 (12 Centres)	OCI[c] 2–3 vs 0–1	30-day case fatality	0.23	0.19-0.28
Chile[35]	Ischemic stroke	Aphasia, hemiplegia, reduced level of consciousness, and speech disturbance	677 (7 hospitals)	Neurological evaluation on admission	30-day case fatality	2.02	0.77-5.30
					In-hospital pneumonia	1.07	0.79-1.44
				Dysphagia screening within 48hours	30-day case fatality	0.52	0.26-1.04
					In-hospital pneumonia	1.58	0.60- 4.15
Australia[36]	SAH excluded	GCS, ability to lift both arms, ability to walk, and urinary incontinence	468 (8 hospitals)	Thorough (n-l≤1)[d] adherence to 15 processes of stroke care[e]	Independent at 28 weeks	1.78	0.93–3.38
					Being at home at 28 weeks	1.69	0.86–3.32
					Alive at 28 weeks	2.10	0.92–4.82
				Complete (n-l≤0) adherence to 15 processes of stroke care	Independent at 28 weeks	2.61	0.96–7.10
					Being at home at 28 weeks	3.09	0.96–9.87
					Alive at 28 weeks	3.22	0.66-15.86
Australia[37]	All stroke types	FIM	2119 (108 Rehabilitations units)	ADLs rehabilitation	Discharged home (Median LoS= 26 days)	1.01	0.33–3.13
				DVT prevention		0.58	0.41–0.81
				Home assessment		6.15	3.70–10.22
				Balance rehabilitation		0.54	0.35–0.83
				Secondary prevention on discharge[f]		1.99	1.12–3.53
				Education to patients[g]		2.37	1.30–4.29
				Discussing post-discharge needs with patients		1.27	0.66–2.43
Australia[38]	All stroke types	Ability to walk on admission	16665 (42 Hospitals)	1 process received vs 0	180-days Case fatality	0.63	0.41-0.97
				2 processes received vs 0		0.46	0.31-0.68
				3 processes received vs 0		0.30	0.18-0.47
				1 process received vs 0	90-180-days Quality of Life (QoL)	12.53	−2.22-27.28
				2 processes received vs 0		16.67	0.30-33.05
				3 processes received vs 0		18.70	1.86-35.55
New Zealand[39]	All stroke types	Age, initial FIM, pre-stroke FIM, and being European	181 (3 hospitals)	Swallowing assessment	1-year Poor outcome (death or moved from home) for swallowing recorded "no"	3.2	0.97-10.7

Table 1: Studies eligible for the systematic literature review ***Continued***

China[40]	Ischemic Stroke	NIHSS	1951 (23 hospitals in 11 major cities of China)	Antiplatelet therapy	1-year case fatality Recurrent cerebrovascular event Functional improvement	0.42 0.58 1.25	0.21–0.86 0.36–0.92 1.02–1.52
China[41]	First ever Ischemic Stroke	NIHSS	7455 (132 hospitals)	Stain use during hospitalization	3-month Case fatality 3-months dependency	0.51 0.95	0.38–0.67 0.81–1.11
China[42]	Intracerebral Haemorrhage Stroke	NIHSS	3218 (132 hospitals)	Stain use during hospitalization	1-year Case fatality 1-year Good functional outcome	0.49 2.04	0.27–0.86 1.37–3.06
Thailand[43]	Ischemic Stroke	NIHSS	1222 (76 hosp)	Stroke unit admission Thrombolysis Aspirin within 48 hours	Poor outcome (mRS 5-6 at discharge) (LoS=4 days)	0.54 0.09 1.25	0.33-0.87 0.03-0.23 0.73-2.15
Taiwan[44]	All stroke types	NIHSS	30599 (39 hospitals)	IV tPA for 2 hours	6-momth functional dependency (mRS≥2)	0.52	0.35-0.76
				Antithrombotics at discharge	6-momth risk of cardiovascular events and death	0.41	0.35-0.47
				Anticoagulation for atrial fibrillation at discharge		0.59	0.44-0.80
				Lipid-lowering agents at discharge		0.94	0.78-1.13

Abbreviations:

ACE, angiotensin-converting enzyme; ADLs, Activities of Daily Living ; BI, Barthel Index; CNS, Canadian neurological scale; CT/MRI, computerized tomography/magnetic resonance imaging; CI, confidence interval; DVT, deep vein thrombosis; FIM, functional independence measure; GCS, Glasgow coma scale; HR, hazard ratio; IS, ischemic stroke; LoS, length of hospital stay; mRS, modified Rankin Scale; NIHSS, national institute of health stroke scale; PT, physiotherapy; OR, odds ratio; OT, occupational therapy; RR, rate ratio; SAH, subarachnoid hemorrhage; SSS, Scandinavian stroke scale; SSV, six simple variable.

[a] Organized stroke care included wards which encompassed multidisciplinary team-working, a physician with an interest in stroke, as well as taking into account the proportion of time spent (>50% of their length of stay) in such an environment. The wards that encompassed organized stroke care included neurology, elderly care, stroke specific unit and intensive care unit.

[b] The complications that were considered in the analysis included pneumonia, urinary tract infection, pressure ulcer, falls, venous thromboembolism, and constipation.

[c] Organized care index (OCI) is a summary score based on the presence of occupational therapy or physiotherapy, stroke team assessment, and admission to a stroke unit. A score of zero indicates that stroke patients received none of these services, and higher scores indicate access to more services. The "organized care" index was classified as having received 0, 1, 2, or 3 services.

[d] n indicates number of applicable processes of care (PoC); i, number of PoC adhered to.

[e] The 15 processes of care consisted of CT scan < 24 h since admission, swallow < 24 h since admission, allied health < 24 h since admission, incontinence addressed, discharged on antiplatelet agent, fever > 38.5 managed, documented premorbid function, documented discharge needs, regular neurology observations for the first 24 h of admission, physiotherapist within 24 h, occupational therapist within 24 h, speech pathologist within 24 h, enteric feeding if nil by mouth > 48 h, aspiration avoidance, and DVT prophylaxis if not ambulant.

[f] Secondary prevention included deep vein thrombosis prophylaxis, discharged on lipid-lowering medication, discharged on blood-pressure–lowering medication, and discharged on antithrombotics.

[g] Education to patients consisted of lifestyle advice, information on sexuality poststroke, information about peer support, information on self-management programs, carer training, and providing contact to patient.

The majority (23/30) of the included studies used prospective recruitment while the rest (25, 26, 28-30, 35, 37) consisted of retrospective audits. Thirteen (16, 19, 20, 23, 24, 29, 30, 32, 34, 35, 40, 41, and 43) included only patients with ischemic stroke, and two (33 and 42) included only patients with intracerebral haemorrhage. The remainder included both ischemic and haemorrhagic stroke. Among those studies that included both types of stroke, six (15, 17, 18, 22, 28, and 36) excluded patients with subarachnoid haemorrhage.

For the association between KPIs and patient outcomes, the majority (22) of the included studies used OR, six studies (16, 19, 23, 29, 38, 40) used HR while the remaining two (17,18) used rate RR. The included studies also used different measures for stroke severity as a case mix variable for adjustment to estimate the independent association between a KPI and a patient outcome. Twenty of the included studies used validated tools including National Institute of Health Stroke Scale (28,30,40-44), Scandinavian Stroke Scale (16-21,29), Canadian Neurological Scale (32-34), Six Simple Variables (25,26), and Glasgow Coma Scale (36), while the remainder used stroke severity proxies such as level of consciousness, incontinence, dysphagia, dysphasia, paralysis, and disability.

Reporting of published KPIs

As there were some variations in data definitions and analysis methods, several assumptions were made to allow easy comparison between the studies:

Swallow/nutritional assessment – This single KPI comprised an assessment of swallowing, dysphagia, and/or nutritional risk. If separate data for both swallow and nutritional risk assessment (18, 21) were reported, we preferentially included data for swallow assessment.

Antiplatelet drugs for ischemic stroke (IS) – Aspirin administration reported in two studies (25, 43) was combined with a KPI for antiplatelet drugs for ischemic stroke reported in seven studies (17, 18, 21, 23, 24, 28, 40).

Early nurse/rehabilitation assessment – This combined indicator of early assessment by a nurse (24) and early assessment of rehabilitation needs (28).

Early physiotherapy/mobilization – This combined five reports of early mobilization (18, 21, 28, 30) with one (17) about early physiotherapy assessment.

Selection of outcome measures

As there were minor variations in the approach to outcome analysis adjustments were made to the reported OR, HR, RR and confidence interval (CI) to allow comparisons between the studies. The *online supplement Table S1* provides a summary of the adjustments made.

Data reported in terms of poor outcome (33, 39, 43), disability (15, 22, 41, 44), death or disability (17, 30), or not returning home (27) post stroke were all combined as a "poor outcome" post stroke. Finally, the results on the association between KPIs and stroke case fatality were categorized at the end of scheduled follow up although the timing of follow up was included in sensitivity analyses.

Key performance indicators

There were 25 reported KPIs in total. The KPIs that were reported by at least a quarter of the eligible studies were swallow/nutritional assessment, stroke unit admission, and antiplatelets for ischemic stroke. One study (18) reported eleven KPIs including hypoxia management, early medical assessment, antidepressant therapy, activities of daily living (ADLs) rehabilitation, home assessment, balance rehabilitation, secondary prevention on discharge, education to patients, discussing post-discharge needs with patients, intermittent catheterization, and constipation risk assessment.

Stroke unit admission was variably defined across the related studies (15,17,18, 21, 22, 24-27,43). Two Danish studies (17,18) defined a “stroke unit” as a hospital department/unit that exclusively or primarily is dedicated to patients with stroke and which is characterized by multidisciplinary teams, a staff with a specific interest in stroke, involvement of relatives, and continuous education of the staff. In the Italian study (27), stroke unit was defined as a hospital ward with dedicated beds (at least 80% stroke admission) and with a dedicated stroke staff (at least one physician and one nurse) who work exclusively in the care of stroke patients.

The online supplement Table S2 provides a list of reported KPIs and their frequencies out of the 30 studies. Table 2 indicates the reported KPIs and their association with patient outcomes.

Table 2: Reported KPIs and their association patient outcomes

1. Reported KPIs and their association with case fatality					
KPI	**Study**	**Treatment time**	**End Follow up period**	**OR/ HR/ RR**	**95% CI**
CT/MRI brain imaging	Europe[15]		3 months	0.70	0.40-1.30
	Denmark[17]	1st day of LoS	3 months	1.35	1.24–1.46
	UK (England)[24]	≤24h	1 month	0.96	0.86-1.07
	UK (Scotland)[25]	day 0	6 months	0.95	0.88–1.03
	Spain[28]	<24h	1 year	0.71	0.36-1.41
Neurological Assessment	Chile[35]	On admission	1 month	2.02	0.77-5.30
Thrombolysis	Denmark[19]		1.4 year	0.66	0.49–0.88
Stroke unit admission	Europe[15]		3 months	0.50	0.30-0.80
	Denmark[17]	2nd day of LoS	3 months	0.76	0.69–0.83
	Sweden[22]		2 years	0.81	0.72-0.92
	UK (England)[24]	≤4h	1 month	0.99	0.90-1.08
	UK (Scotland)[25]	day 0 or 1	6 months	0.79	0.74–0.85
	UK (Scotland)[26]		1 year	0.70	0.65-0.75
	Italy[27]		2 years	0.79	0.68–0.91
Swallow/nutritional assessment	Denmark[17]	2nd day of LoS	3 months	0.69	0.61–0.76
	UK (England)[24]	≤72h	1 month	0.76	0.67- 0.87
	UK (Scotland)[25]	day 0	6 months	0.95	0.86–1.04
	Spain[28]		1 year	0.81	0.58-1.14
	Chile[35]	≤48h	1 month	0.52	0.26-1.04
Antiplatelets for ischemic stroke	Denmark[17]	2nd day of LoS	3 months	0.71	0.62–0.81
	Sweden[23]	-	3 months	0.83	0.68-1.01
	UK (England)[24]	≤72h	1 month	0.46	0.42-0.50
	UK (Scotland)[25]	day 0 or 1	6 months	0.54	0.49–0.58
	Spain[28]	< 48 hours	1 year	0.77	0.50-1.19
	China[40]	LoS	1 year	0.42	0.21–0.86
Anticoagulants for ischemic stroke	Denmark[16]	Acute LoS	4 years	0.52	0.40-0.69
	Denmark[17]	By 14th day	3 months	0.41	0.31–0.52
	Sweden[23]	-	3 months	0.58	0.44–0.76
	Spain[28]		1 year	0.59	0.33-1.05
Blood pressure lowering therapy	Sweden[23]	-	3 months	1.00	0.87–1.14
	Spain[28]		1 year	0.53	0.35-0.82
Hyperthermia management	Spain[28]		1 year	1.50	0.56-4.00
Lipid management	Sweden[23]	-	3 months	0.78	0.67–0.91
	Spain[28]		1 year	0.78	0.52-1.16
	Greece[29]	At discharge	10 years	0.43	0.29-0.61
	Canada[33]	Acute LoS	6 months	0.2	0.1–0.3
	China[41]	LoS	3months	0.51	0.38–0.67
	China[42]	Acute LoS	1 year	0.49	0.27–0.86
DVT Prophylaxis	Spain[28]		1 year	1.02	0.63-1.67
	Canada[32]	Acute LoS	1 year	0.33	0.22–0.50
Early medical assessment	UK (England)[24]	≤24h	1 month	0.88	0.80- 0.97
Early nurse/rehabilitation assessment	UK (England)[24]	≤24h	1 month	0.90	0.82-0.99
	Spain[28]		1 year	0.68	0.48-0.94
Early physiotherapy/mobilization	Denmark[17]	2nd day of LoS	3 months	0.81	0.73–0.88
	Spain[28]		1 year	0.65	0.45-0.95
Occupational therapy assessment	Denmark[17]	2nd day of LoS	3 months	0.83	0.75–0.91
Antidepressant therapy	Denmark[20]	LoS	1 month	0.28	0.18–0.43

Table 2: Reported KPIs and their association patient outcomes ***Continued***

KPI	Study	Treatment time	End of Follow up period	OR/HR/RR	95% CI
2. Reported KPIs and their association with poor outcome					
CT/MRI brain imaging	Europe[15]		3 months	1.45	0.39–7.4
Thrombolysis	Thailand[43]		LoS=4 days	0.09	0.03-0.23
	Taiwan[44]	3h of onset	6 months	0.52	0.35-0.76
Neurological Assessment	USA[30]		LoS	1.13	0.59-2.17
Stroke unit admission	Thailand[43]		LoS=4 days	0.54	0.33-0.87
	Europe[15]		3 months	1.3	0.6–1.76
	Italy[27]		2 years	0.85	0.74–0.97
	UK (Scotland)[26]		6 months	0.84	0.78-0.90
	Sweden[22]		2 years	0.79	0.66-0.94
Swallow/nutritional assessment	Thailand[43]		LoS=4 days	0.54	0.33-0.87
	New Zealand[39]		1 year	0.31	0.09-1.03
	USA[30]		LoS	0.64	0.43-0.94
Antiplatelets for ischemic stroke	China[40]	LoS	1 year	0.80	0.66-0.98
	Thailand[43]	48h	LoS=4 days	1.25	0.73-2.15
Blood pressure lowering therapy	USA[30]		LoS	1.00	0.67-1.50
Hyperthermia management	USA[30]	All episodes	LoS	0.71	0.35-1.41
Hypoxia management	USA[30]	All episodes	LoS	0.26	0.09-0.73
DVT Prophylaxis	USA[30]		LoS	0.60	0.37-0.96
	Australia[37]		26 days	1.72	1.23-2.44
Early physiotherapy/mobilization	USA[30]		LoS	0.69	0.42-1.14
ADLs rehabilitation	Australia[37]		26 days	0.99	0.32-3.03
Home assessment	Australia[37]		26 days	0.16	0.10-0.27
Balance rehabilitation	Australia[37]		26 days	1.85	1.20-2.86
Secondary prevention on discharge	Australia[37]		26 days	0.50	0.28-0.89
Education to patients	Australia[37]		26 days	0.42	0.23-0.77
Discussing post-discharge needs with patients	Australia[37]		26 days	0.79	0.41-1.52
Lipid management	China[41]	Acute LoS	3 months	0.95	0.81–1.11
	China[42]	Acute LoS	1 year	0.49	0.33-0.73
	Canada[33]	Acute LoS	At discharge	0.6	0.4–0.9
2. Reported KPIs and their association with prolonged length of hospital stay					
Stroke unit admission	Denmark[18]	2nd day		0.71	0.65–0.77
Antiplatelets for ischemic stroke	Denmark[18]	2nd day		0.80	0.73–0.87
Anticoagulants for ischemic stroke	Denmark[18]	14th day		0.78	0.62–0.98
CT/MRI brain imaging	Denmark[18]	2nd day		0.82	0.74–0.91
Swallow/nutritional assessment	Denmark[18]	2nd day		0.78	0.69–0.87
Constipation risk assessment	Denmark[18]	2nd day		0.70	0.63-0.78
Early physiotherapy/mobilization	Denmark[18]	2nd day		0.67	0.61–0.73
Occupational therapy assessment	Denmark[18]	2nd day		0.85	0.80–0.91
Intermittent catheterization	Denmark[18]	2nd day		0.77	0.64–0.92
DVT Prophylaxis	Denmark[18]	2nd day		0.82	0.71–0.95

Table 2: Reported KPIs and their association patient outcomes ***Continued***

KPI	Study	Treatment time	End of Follow up period	OR/ HR/ RR	(95% CI)
4. Reported KPIs and their association with medical complications					
CT/MRI brain imaging	Denmark[21]		LoS=13days	1.52	1.35–1.72
Neurological Assessment	Chile[35]	On admission	30 days	1.07	0.79-1.44
Stroke unit admission	Denmark[21]		LoS=13days	0.79	0.68–0.92
Swallow/nutritional assessment	Chile[35]	≤48h	30 days	1.58	0.60- 4.15
	Denmark[21]		LoS=13days	0.97	0.84–1.11
	USA[31]		LoS=5days	0.47	0.38-0.57
Antiplatelets for ischemic stroke	Denmark[21]		LoS=13days	0.95	0.79–1.15
Anticoagulants for ischemic stroke	Denmark[21]		LoS=13days	0.59	0.45–0.76
Early physiotherapy/mobilization	Denmark[21]		LoS=13days	0.43	0.35–0.53
Occupational therapy assessment	Denmark[21]		LoS=13days	1.10	0.94–1.27
Thrombolysis	Denmark[19]		1.4 year	0.59	0.24–1.47
5. Reported KPIs and their association with stroke recurrence					
Antiplatelets for ischemic stroke	China[40]	LoS	12 months	0.58	0.36–0.92
Anticoagulants for ischemic stroke	Taiwan[44]	At discharge	6 months	0.59	0.44-0.80
Lipid management	Taiwan[44]	At discharge	6 months	0.94	0.78-1.13
	Greece[29]	At discharge	10 years	0.65	0.39- 0.97
DVT Prophylaxis	Taiwan[44]	At discharge	6 months	0.41	0.35-0.47
Thrombolysis	Denmark[19]		1.4 year	1.05	0.68–1.64

Abbreviations: ADLs, activities of daily living ; CT/MRI, computerized tomography/magnetic resonance imaging; CI, confidence interval; DVT, deep vein thrombosis; HR, hazard ratio; KPI, key performance indicator; LoS, length of hospital stay; OR, odds ratio; RR, rate ratio.

Association between individual KPIs and lower risk for case fatality at the end of scheduled follow up

The median time of scheduled follow up for the studies reporting on the association between individual KPIs and case fatality was one year; range from one month to 10 years. Significant reductions in case fatality were observed across multiple studies for stroke unit admission (15, 17, 22, 25-27), swallow/nutritional assessment (17,24), antiplatelets for ischemic stroke (17, 40, 24, 25), anticoagulants for ischemic stroke (16, 17, 23), lipid management (23, 29, 33, 41, 42), early nurse/rehabilitation assessment (24,28), early physiotherapy/mobilization (17, 28). In addition, significant associations within single studies were observed for DVT prophylaxis (32) and blood pressure lowering therapy (28).

In contrast, several studies reported wide confidence intervals and no statistically significant association between the reported KPIs and stroke case fatality; stroke unit admission (24), swallow/nutritional assessment (25, 28, 35), antiplatelets for ischemic stroke (23, 28), anticoagulants for ischemic stroke, lipid management (28), DVT prophylaxis (28) and blood pressure lowering therapy (23). Surprisingly, in one study (17) the CT/MRI brain imaging was associated with increased risk of early case fatality (RR: 1.35, 95% CI: 1.24-1.46), while in other studies (15, 24, 25, 28) no evidence for an association of CT/MRI brain imaging and stroke case fatality was found.

Figure 2 summarises the primary meta-analysis results regarding the associations between individual KPIs and stroke case fatality at the end of follow up. The KPIs that were associated with lower risk for case fatality include stroke unit admission (OR: 0.79, 95% CI: 0.72-0.87; I^2=88%), swallow/nutritional assessment (OR: 0.78, 95% CI: 0.66-0.92; I^2=79%), antiplatelets for ischemic stroke (OR: 0.61, 95% CI: 0.50-0.74; I^2=90%), anticoagulants for ischemic stroke (OR: 0.51, 95% CI: 0.43-0.61; I^2=12%), lipid management (OR: 0.52, 95% CI: 0.38-0.71; I^2=80%), and early physiotherapy/mobilization (OR: 0.78, 95% CI: 0.67-0.91; I^2=21%). However, the significant associations of stroke unit admission, swallow/nutritional assessment, antiplatelets for ischemic stroke and lipid management were complicated by substantial heterogeneity (I^2>50%). When analyzed at a fixed time point, swallow/nutritional assessment (OR: 0.72, 95% CI: 0.66-0.79; I^2), antiplatelets for ischemic stroke (OR: 0.64, 95% CI: 0.44-0.93; I^2) and lipid management (OR: 0.64, 95% CI: 0.42-0.97; I^2) were associated with a lower risk for early case fatality (up to three months post stroke), but the heterogeneity was reduced for swallow/nutritional assessment (I^2=1%) only. Stroke unit admission (OR: 0.77, 95% CI: 0.71-0.82; I^2), antiplatelets for ischemic stroke (OR: 0.57, 95% CI: 0.45-0.72; I^2) and lipid management (OR: 0.45, 95% CI: 0.27-0.74; I^2) were associated with lower risk for late case fatality (beyond three months post stroke), but the heterogeneity was reduced for antiplatelets for ischemic stroke (I^2=34%) only.

The meta-analysis showed no evidence for the association between the stroke case fatality and DVT prophylaxis, blood pressure lowering therapy, early nurse/rehabilitation assessment, and CT/MRI brain imaging.

[Insert Figure 2 here]

The sensitivity analysis excluding those that used HR or RR produced results that were similar to those in Figure 2 (data not shown): stroke unit admission (OR: 0.79, 95% CI: 0.71-0.89), swallow/nutritional assessment (OR: 0.82, 95% CI: 0.69-0.98), antiplatelets for ischemic stroke (OR: 0.53, 95% CI: 0.44-0.63), and lipid management (OR: 0.47, 95% CI: 0.30-0.74) remained associated with lower risk for case fatality, and there was no evidence for the association between the stroke case fatality and DVT prophylaxis, early nurse/rehabilitation assessment, and CT/MRI brain imaging.

Significant associations within single studies were observed for thrombolysis (19), early medical assessment (24), OT assessment (17), and antidepressant therapy (20), but there was no evidence for the association between stroke case fatality and hyperthermia management (28), and neurological assessment (35).

Association between individual KPIs and the risk for poor outcome

For studies reporting on the association between individual KPIs and poor outcome the available follow up periods were between four days and two years, with a mean of 282 days.

KPIs that were reported to be associated with the lower risk for poor outcome included thrombolysis (43, 44), stroke unit admission (22, 26, 27, 43), swallowing/nutritional assessment (30, 43), antiplatelets for ischemic stroke (40), DVT prophylaxis (30), and lipid management management (33, 42). However, some studies found no evidence of an association with poor outcome and stroke unit admission (15); swallowing/nutritional assessment (39), antiplatelets for ischemic stroke (43), DVT prophylaxis (37) and lipid management (41).

As summarized in Figure 3, the meta-analysis showed that the KPIs associated with the lower risk for poor outcome were stroke unit admission (OR: 0.83, 95% CI: 0.77-0.89; I^2=15%) and swallowing/nutritional assessment (OR: 0.58, 95% CI: 0.43-0.78, I^2=0%)

while there was no evidence for the association with poor outcome for thrombolysis, antiplatelets for ischaemic stroke, DVT prophylaxis, and lipid management.

[Insert Figure 3 here]

Several individual studies reported significant associations between lower risk for poor outcome and hypoxia management (30); home assessment, secondary prevention on discharge, and education to patients (37). No association with poor outcome was found for CT/MRI brain imaging (15); neurological assessment, blood pressure lowering therapy, hyperthermia management and early physiotherapy/mobilization (30); ADLs rehabilitation, balance rehabilitation and discussing post-discharge needs with patients (37).

All the studies included for the primary meta-analysis about the association of KPIs with poor outcome used ORs, except one Chinese study (40). After excluding that study, antiplatelets for ischemic stroke remained with a single study (43) which showed no association with poor outcome (OR: 1.25, 95% CI: 0.73-2.14).

Association between individual KPIs and relative length of hospital stay

A single Danish study (18), reported that a shorter relative length of hospital stay was associated with stroke unit admission, antiplatelets and anticoagulants for ischemic stroke, CT/MRI brain imaging, early physiotherapy/mobilization, occupational therapy assessment, swallowing/nutritional assessment, and DVT prophylaxis, with rate ratio ranging from 0.67 (0.61–0.73) for early physiotherapy/mobilization to 0.85 (0.80–0.91) for occupational therapy assessment.

Association between individual KPIs and the risk for medical complications and stroke recurrence

Stroke unit admission, anticoagulants for ischemic stroke, and early physiotherapy/mobilization (21), as well as swallow/nutritional assessment (31) were found to be associated with lower risk for medical complications (OR: 0.79; 0.68–0.92; I^2; 0.59, 0.45–0.76; I^2 and 0.43, 0.35–0.53; I^2; 0.47, 0.38-0.57; I^2 respectively). By contrast, CT/MRI brain imaging was associated with a greater risk for medical complications with (1.52, 1.35–1.72; $I^{2)}$ (21). Other studies with wide confidence intervals did not show evidence for the association between the occurrence of medical complications and neurological assessment (35); swallow/nutritional assessment (21, 35); antiplatelets for ischemic stroke, occupational therapy assessment (21); and thrombolysis (19).

KPIs that were reported to be associated with lower recurrence rate for stroke included antiplatelets for ischemic stroke (40), anticoagulants for ischemic stroke and DVT prophylaxis (44), and lipid management (29). However, in one study (21) evidence for the association between lipid management and stroke recurrence was not found (44), and there was no evidence of an association with thrombolysis (19).

Association between adherence to groups of KPIs and the risk for case fatality

Seven studies (17, 24, 25, 32, 34, 36, 38) had consistent findings whereby adherence to a combination of several KPIs ("bundle") was associated with a greater decrease in stroke mortality. A lower risk for poor outcome was also reported when full stroke care bundle was achieved (25, 36). An Australian study (38) also showed that achieving full care bundle was associated with better quality of life at three to six months post stroke. Increased adherence to stroke care KPIs (18) was associated with shorter length of hospital stay (data are not shown in Table 3).

Table 3: Association between the number of KPIs achieved and patient outcomes

	Case Fatality				Poor Outcome				Quality of Life			
Study	**FU Period**	**Number of processes**	**HR**	**95%CI**	**FU Period**	**Number of processes**	**OR/ HR/ RR**	**95%CI**	**FU Period**	**Number of processes**	**OR/ HR/ RR**	**95%CI**
Denmark[17]	3 months	1 vs 0	0.94	0.65-1.49								
		2 vs 0	0.78	0.54–1.02								
		3 vs 0	0.60	0.42–0.78								
		4 vs 0	0.61	0.42–0.79								
		5 vs 0	0.45	0.31–0.60								
		6 vs 0	0.48	0.31–0.65								
UK (England)[24]	1 month	5-6 vs 0-4	0.74	0.66- 0.83								
UK (Scotland)[25]	6 months	0 vs 4	2.26	1.60–3.21	6 months	0 vs 4	1.43	1.02-2.00				
		1 vs 4	1.67	1.45–1.93		1 vs 4	1.35	1.19-1.54				
		2 vs 4	1.44	1.31–1.59		2 vs 4	1.19	1.10-1.32				
		3 vs 4	1.17	1.08-1.27		3 vs 4	1.10	1.02-1.18				
Canada[32]	12 months	OCI 1 vs 0	0.69	0.44–1.09								
		OCI 2 vs 0	0.39	0.25–0.62								
		OCI 3 vs 0	0.40	0.25–0.64								
Australia[36]	6 months	All or n-1	0.48	0.21-1.09	6 months	All or n-1	0.59	0.30-1.16				
		All	0.31	0.06-1.52		All	0.32	0.10-1.04				
Australia[38]	6 months	1 vs 0	0.63	0.41-0.97					3-6 months	1 vs 0	12.5	−2.22-27.28
		2 vs 0	0.46	0.31-0.68						2 vs 0	16.6	0.30-33.05
		3 vs 0	0.30	0.18-0.47						3 vs 0	18.7	1.86-35.55
Canada[34]	1 month	2-3 vs 0-1	0.23	0.19-0.28								

Abbreviations: CI, confidence interval; FU, Follow up; HR, hazard ratio; n, number of applicable processes of care; OCI, Organized care index; OR, odds ratio; RR, rate ratio.

Overall (see *Online Supplement Table 3*), only stroke unit admission, swallow/nutritional assessment, antiplatelets for ischemic stroke, anticoagulants for ischemic stroke, lipid management and early physiotherapy/mobilization were found to be significantly associated with improved outcomes after a meta-analysis of two or more studies. Thrombolysis results were associated with reduced poor outcome in two studies, but the combined analysis was not significant due to substantial heterogeneity. Data were very limited for the outcomes of length of stay, stroke recurrence or medical complications.

DISCUSSION

The publications we have reviewed provide a large and diverse body of evidence on whether quality of care, as measured by adherence with a KPI, is associated with improved clinical outcomes in patients hospitalized with stroke. Our primary meta-analysis indicated that several KPIs including stroke unit admission, swallowing/nutritional risk assessment, antiplatelets for ischemic stroke, anticoagulants for ischemic stroke, lipid management and early physiotherapy/mobilization were associated with a reduction in case fatality or poor outcome.

The strong association of stroke unit care with improved outcomes could be anticipated from a substantial number of RCTs (45). Our review confirms this across a range of studies in routine care. Given the evidence for specialized multidisciplinary stroke unit care in stroke (45), one might also expect to see benefits associated with early nurse or rehabilitation assessment and early medical assessment (24), as well as occupational therapy assessment (17). These indicators lack direct evidence from randomised trials but may possibly be markers for admission to a stroke unit and multidisciplinary stroke care. However, there were no comparable data from many studies about early medical assessment, early nurse or rehabilitation assessment or early occupational therapy assessment for our review.

Our finding of a reduced risk of case fatality after early physiotherapy/mobilization was in accordance with the literature about stroke unit care (45), and some small RCTs (46) but not consistent with recent RCTs of very early mobilisation (47). However, the recent AVERT trial tested mobilisation at an earlier stage than in routine care so the optimal timing of mobilization remains unclear, and very early intensive mobilization within 24 hours may carry some hazard (47).

Our meta-analysis showed that swallow or nutritional assessment was associated with lower risk for both mortality and disability post stroke. This finding was consistent with a randomised controlled trial (9) which found that reinforcement of multidisciplinary management of swallowing dysfunction was significantly associated with lower risk for death or dependency. Thus, swallowing or nutritional assessment may be of paramount importance. The current meta-analysis also showed that early antiplatelet use for ischemic stroke was associated with reduction in case fatality, and this was consistent with the results from a previous systematic review (48) of eight randomized trials. It showed that early antiplatelet therapy was associated with mortality reduction at a final follow-up between one and six months. However, our review showed greater apparent benefit than the 8% reduction in case fatality that was reported in the review of randomised trials (48). However, a recent individual patient data meta-analysis of aspirin trials (49) confirms an important short term benefit of aspirin therapy in preventing recurrent cerebral ischemia and that benefits may be greater than previously estimated. Our meta-analysis finding of a reduced risk of stroke case fatality associated with lipid management was consistent with the results from a meta-analysis (50) of 42 randomised trials.

One major disagreement with the RCTs is that our meta-analysis also showed that early anticoagulant use for ischemic stroke were associated with a reduction in early and late case fatality. However, this finding was not supported by a review (51) of 24 randomized clinical trials. As the studies included in our review were neither randomized nor blinded, the apparent effects of antiplatelets and anticoagulants for ischemic stroke may have been overestimated due to selection bias and incomplete adjustment for confounders. Alternatively KPIs may also reflect other important and unmeasured aspects of care which would not be tested in a well-designed RCT. Additionally, the duration of follow-up for the studies included in our meta-analysis varied between three and 48 months (mean: 16.5 ±21.4 months) while the duration of follow-up in the trials was generally shorter. This short-term follow-up may lead to missing a significant proportion of deaths that occur after one month, and disability is best assessed between three to six months when most of the recovery has taken place (51).

Our review has also identified some areas with inconsistent evidence of the association of KPIs with outcome. Deep vein thrombosis (DVT) prophylaxis was found to be associated with significant benefits in studies in Canada (32) and the USA (30) but not in Spain (28).

However, a meta-analysis of RCTs has failed to show improvements in survival or independence (51).

Regarding thrombolysis, in two studies included for our review (43, 44) thrombolysis was associated with a lower risk for poor functional outcome, and this was consistent with the systematic review of the RCTs (52). However, because of high heterogeneity (I^2=88%) between the two studies reviewed, the summary effect was not statistically significant.

Our review showed that CT/MRI brain imaging and neurological assessment were not associated with any reported patient outcomes. This may be due to several reasons. First, the assessment itself, if not combined with adequate care, is unlikely to show any difference in outcome. For instance, once ischemic stroke is diagnosed with brain imaging, further management by intravenous tissue plasminogen activator was found to be effective. It was however recently reported that only 3% of low-income, 19% of lower-middle-income, 33% of upper-middle-income, and 50% of high-income-countries use it (53). Second, the increased risk of early case fatality (17) and medical complications (21) that were reported after early CT/MRI brain imaging in two Danish studies, was most likely due to reverse causality; patients who deteriorated during the first hours after hospitalization were more likely to receive an early CT/MRI brain imaging, and also had a greater risk of death or medical complications (21). Third, some of the analyses of data may have been hampered by small sample sizes, and lack of statistical power to show the differential benefit.

Adherence to an individual measure in isolation may not have a clinically detectable impact on outcomes, making determination of an effect more difficult (54). However adherence to several KPIs was always associated with improved outcomes.

Strengths and weaknesses

Our systematic review has several strengths including searching a wide range of databases using standardised methodology. Furthermore, the review report was based on the PRISMA guidelines. The studies that were included in our review involved large sample sizes in general, allowing sufficient statistical power and enhancing the external validity of the results. One study (15) was multinational, and 12 studies (16, 17, 19, 22, 23, 27, 37, 38, 41-44) involved nationwide datasets. The remaining studies were conducted regionally with the recruitment of participants from between three (39) to 222 hospitals (31). Additionally we only conducted analyses using data from studies that corrected for patient casemix (age and stroke severity). Our approach to meta-analysis has used a conservative random-effects approach to acknowledge the diversity of studies identified. Finally, we performed a sensitivity analysis to evaluate the robustness of our findings.

We must acknowledge some weaknesses. We did not use any scoring system to assess risk of bias in included studies, but simply included large register studies reporting independent association of KPIs with patient outcomes after adjusting at least two variables including age and stroke severity. Second, the review was based on data from observational studies with different follow-up time periods and designs. Third, although we have only included data that used a multivariable analysis to correct for patient casemix, there remains the possibility that the patient outcomes were influenced by unmeasured or residual confounding factors such as indication bias or factors related to the nonrandomized study design rather than the reported KPIs themselves. Fourthly, our review could be subject to publication bias because our search strategy was limited to electronic databases and references known to the authors, and manuscripts published in English only. Fifth, there is a potential concern about combining results from studies from different settings and using different research methodologies. For instance, there were different measures for stroke severity for case mix adjustment, different models of stroke unit, and different models of implementing or measuring the KPIs. Finally, we were limited to a few studies reporting data on important outcomes such as the length of hospital stay and quality of life, and none of the studies considered the cost of care which is clearly important in a disabling condition such as stroke.

CONCLUSION

Our review found that the most frequently reported KPIs for stroke care were swallow/nutritional assessment, stroke unit admission, antiplatelets for ischemic stroke, CT/MRI brain imaging, anticoagulants for ischemic stroke, lipid management, deep vein thrombosis (DVT) prophylaxis, and early physiotherapy/mobilization. Stroke unit admission and early interventions including swallowing/nutritional risk assessment, antiplatelets for ischemic stroke, anticoagulants for ischemic stroke, lipid management and early physiotherapy/mobilization were all associated with better patient outcomes. Achieving a combination of several KPIs was always associated with a better outcome. Both policy makers and health care professionals should be encouraged to implement the KPIs for stroke management that are reliable and meaningful for regularly monitoring the quality of stroke care. Future research could focus on novel stroke care quality indicators, particularly in the post-acute period.

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The authors declared no conflicting interests

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Informed consent

Not applicable

Ethical approval

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Guarantor

GU and PL

Contributorship

GU and PL conceived the study, researched literature, analyzed data, and 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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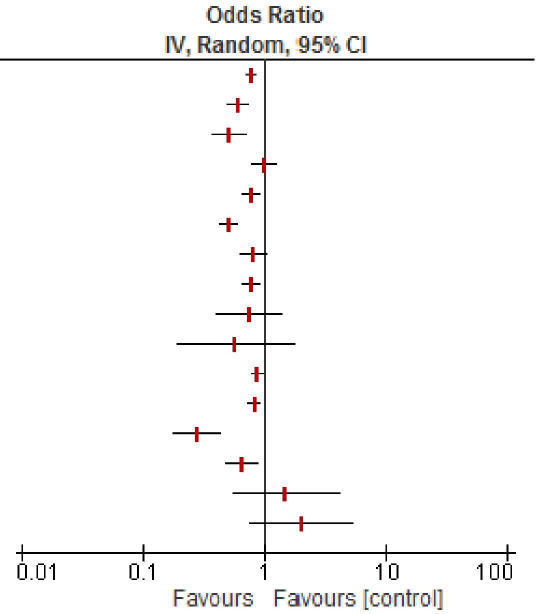
Figure 2: Association between individual KPIs and lower risk for case fatality

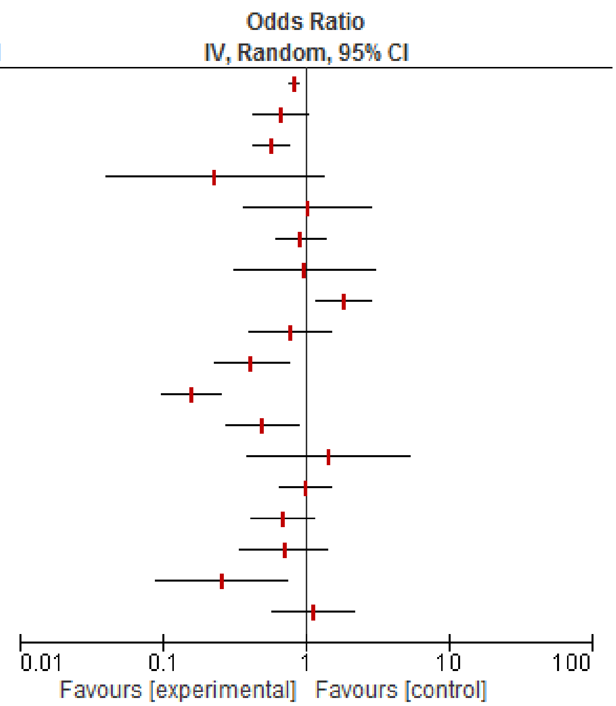
KPI	N studies	N patients	I^2	Odds Ratio IV, Random, 95% CI
Stroke unit admission	7	165130	83%	0.79 [0.72, 0.87]
Antiplatelets for ischaemic stroke	6	120072	90%	0.61 [0.50, 0.74]
Lipid management	6	30229	80%	0.52 [0.38, 0.71]
CT/MRI brain imaging	5	105439	91%	1.00 [0.80, 1.25]
Swallow/nutritional assessment	5	104269	79%	0.78 [0.66, 0.92]
Anticoagulants for ischaemic stroke	4	68048	12%	0.51 [0.43, 0.61]
Early nurse/rehabilitation assessment	2	37964	57%	0.82 [0.64, 1.05]
Early physiotherapy/mobilization	2	31340	21%	0.78 [0.67, 0.91]
Blood pressure lowering therapy	2	16296	88%	0.75 [0.40, 1.41]
DVT prophylaxis	2	5398	92%	0.58 [0.19, 1.77]
Early medical assessment	1	36197		0.88 [0.80, 0.97]
Occupational therapy assessment	1	29573		0.83 [0.75, 0.92]
Antidepressant therapy	1	5070		0.28 [0.18, 0.44]
Thrombolysis	1	4292		0.66 [0.49, 0.89]
Hyperthermia management	1	1767		1.50 [0.56, 4.02]
Neurological assessment	1	677		2.02 [0.77, 5.30]



Abbreviations: CT/MRI, computerized tomography/magnetic resonance imaging; CI, confidence interval; DVT, deep vein thrombosis; I^2, heterogeneity; IV, inverse variance; KPI, key performance indicator; N, number of.

Figure 3: Association between individual KPIs and lower risk for poor outcome

KPI	N studies	N patients	I^2	Odds Ratio IV, Random, 95% CI
Stroke unit admission	5	64527	15%	0.83 [0.77, 0.89]
Lipid management	3	13139	83%	0.67 [0.43, 1.04]
Swallow/nutritional assessment	3	2766	0%	0.58 [0.43, 0.78]
Thrombolysis	2	31821	88%	0.23 [0.04, 1.32]
DVT prophylaxis	2	3482	92%	1.03 [0.37, 2.87]
Antiplatelets for ischaemic stroke	2	3173	57%	0.93 [0.62, 1.39]
ADLs rehabilitation	1	2119		0.99 [0.32, 3.06]
Balance rehabilitation	1	2119		1.85 [1.20, 2.85]
Discussing post-discharge needs	1	2119		0.79 [0.41, 1.52]
Education to patients	1	2119		0.42 [0.23, 0.77]
Home assessment	1	2119		0.16 [0.10, 0.26]
Secondary prevention on discharge	1	2119		0.50 [0.28, 0.89]
CT/MRI brain imaging	1	1847		1.45 [0.39, 5.39]
Blood pressure lowering therapy	1	1363		1.00 [0.67, 1.49]
Early physiotherapy/mobilization	1	1363		0.69 [0.42, 1.13]
Hyperthermia management	1	1363		0.71 [0.35, 1.44]
Hypoxia management	1	1363		0.26 [0.09, 0.75]
Neurological assessment	1	1363		1.13 [0.59, 2.17]



Abbreviations: CT/MRI, computerized tomography/magnetic resonance imaging; CI, confidence interval; DVT, deep vein thrombosis; I^2, heterogeneity; IV, inverse variance; KPI, key performance indicator; N, number of.