

## Interventions for the uptake of evidence-based recommendations in acute stroke settings

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## Interventions for the uptake of evidence-based recommendations in acute stroke settings (Protocol)

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[Intervention Protocol]

# Interventions for the uptake of evidence-based recommendations in acute stroke settings

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## ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the effects of implementation interventions for promoting the uptake of evidence-based recommendations in acute stroke unit environments. Secondary objectives are to describe any factors that may modify the effect of implementation interventions; determine factors that may influence the uptake of recommendations in acute stroke units; and determine if single or multifaceted intervention strategies (two or more interventions) are more effective in improving uptake of evidence, patient outcomes, system outcomes or professionals' knowledge, attitudes or intentions in this setting.

## BACKGROUND

Despite research evidence and clinical practice guidelines to direct the clinical management of patients with acute stroke, significant evidence-practice gaps remain (NSF 2015). Many of the evidence-informed recommendations for acute stroke care fit the definition of complex clinical interventions, so they present particular challenges for translation into clinical practice (Redfern 2006).

Strong evidence from previous Cochrane Reviews have supported the use of 'delivery arrangement' interventions to ensure patients presenting with acute stroke receive evidence-informed, co-ordinated care within dedicated stroke units by a specialised multidis-

ciplinary team (EPOC 2016a; Stroke Unit Trialists' Collaboration 2013). Acute care stroke units present unique environments for knowledge translation due to their fast-paced, short-stay nature (usually 5 to 10 days), where co-ordinated multidisciplinary teamwork is the cornerstone to achieving optimal patient outcomes (Langhorne 2002; Seenan 2007; Stroke Unit Trialists' Collaboration 2013). For this Cochrane Review, acute stroke units will include hospital facilities admitting patients immediately after stroke onset to a ward organised to provide specialist care for patients. We will define the different types of acute stroke units to be included based on the characteristics described by the Stroke Unit

[Trialists' Collaboration 2013](#) (see Methods, Types of settings).

Because care within acute stroke units can be variable, efforts to improve care quality within this setting are important. Knowledge translation strategies (barrier identification, education and reminders) have been used successfully to implement evidence-informed clinical protocols in acute stroke units, leading to greater adherence to processes of care, with associated reductions in death and disability for patients receiving care in intervention acute stroke units versus control acute stroke units ([Drury 2014](#); [Middleton 2011](#)).

Strategies to influence health professionals' use of evidence-informed recommendations need to take into account the nature of the desired change in practice, the specific features of the setting, the professionals involved, and the inherent barriers to use of the evidence within the implementation context ([Francke 2008](#); [Grol 2002](#)). Strategies shown to improve uptake of evidence-informed clinical practices in other settings, such as acute cardiac care ([Ting 2007](#)), or even in post-acute stroke settings ([Menon 2009](#)), may not be transferable to acute stroke units. The aim of this Cochrane Review is to assess the effects of implementation interventions to promote the uptake of evidence-based recommendations in acute stroke unit environments.

## Description of the condition

A major cause of death and disability, stroke is defined by the World Health Organization (WHO) as a "neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours" ([Aho 1980](#)). More recently, use of the term has broadened towards a tissue-based definition, which includes evidence of infarct without symptoms ([Sacco 2013](#)). About 80% of strokes are ischaemic in nature (caused by interruption of the blood supply to a particular area in the brain), and the remaining 20% are haemorrhagic (mainly due to rupture of a vessel) ([Sims 2010](#)). Between 20% and 50% of people suffering a stroke die within the first month, depending on the type and severity of the stroke, the age of the patient, comorbidities and the effectiveness of treatment for complications ([WHO 2016](#)). Approximately 65% of survivors have stroke-related disability that reduces their ability to carry out daily living activities unassisted ([Deloitte Access Economics 2016](#)).

## Description of the intervention

This review will focus on implementation interventions, classified in the Cochrane Effective Practice and Organisation of Care (EPOC) taxonomy as delivery arrangements, financial arrangements, governance arrangements and implementation strategies ([EPOC 2016a](#)). The overall aim of these implementation interventions is to increase the uptake of evidence into practice through a

range of approaches. We provide further details of included strategies in the Methods section.

## How the intervention might work

Implementation interventions are contingent on changing multiple behaviours of various health professionals and healthcare managers or of organisational systems ([Cane 2012](#); [Ivers 2014](#); [Johnson 2015](#)). Influencing clinical practice is notoriously difficult, especially in complex settings such as acute stroke units ([Grol 2003](#)). The manner in which specific implementation interventions may bring about improved clinical practice is complicated and still poorly understood. However, success may be more likely when implementation strategies are underpinned by evidence-informed theories or principles of behaviour change ([Abraham 2009](#)), and several relevant theories to frame behaviour change exist ([Graham 2006](#); [Cane 2012](#); [Nilsen 2015](#)). For example, the Theoretical Domains Framework suggests that successful strategies may address one or several of the behaviour change domains identified as barriers to the uptake of evidence, including professionals' roles and identities, decision processes, attitudes and beliefs, knowledge and skills ([Cane 2012](#)). Another theory, the 'knowledge-to-action' cycle, explains that effective clinical practice change is dependent on complex, dynamic knowledge translation processes involving knowledge creation and application ([Graham 2006](#)).

## Why it is important to do this review

In many countries, the provision of evidence-informed treatment for patients with stroke is now a government priority. In addition to the strong evidence for care within an acute stroke unit ([Stroke Unit Trialists' Collaboration 2013](#)), a growing body of evidence is available to guide aspects of acute stroke management, including thrombolysis ([Wardlaw 2014](#)), endovascular clot retrieval ([Rouchaud 2011](#)), the use of aspirin ([Sandercock 2014](#)), and the early identification and management of dysphagia ([Martino 2005](#)). Clinical practice guidelines have been produced in many countries to provide health professionals with ready access to the best evidence for acute stroke management ([Hemphill 2015](#); [Jauch 2013](#); [NSF 2015](#)). Despite recognition of what constitutes the best recommended care, such as administration of aspirin within 24 hours of ischaemic stroke onset, data from clinical registries and audits of clinical practice provide evidence that recommended care is not being optimally provided, even within established acute stroke units ([Abraham 2009](#); [ISWP 2009](#); [NSF 2015](#)). While improved professional performance cannot absolutely guarantee improved patient outcomes, there is an established link between the two. Adherence to evidence-informed recommendations for acute stroke care reduces death and disability ([Cadilhac 2004](#); [Cadilhac 2008](#); [Middleton 2011](#)).

Although monitoring care is important for characterising the problems (i.e. care gaps) (Cadilhac 2013; Cadilhac 2016), this information alone will have limited effects on adoption of evidence-informed recommendations in the absence of implementation strategies to influence professional practice (Davies 2010). However, little guidance exists on the effectiveness of various implementation strategies directed at professionals or organisations, to improve the provision of recommended processes of care in acute stroke units. Such units are considered as providing the ultimate 'package' of recommended care for patients with stroke, and patients who receive stroke unit care have better outcomes than those who do not (Stroke Unit Trialists' Collaboration 2013). However, large variation in performance and gaps in practice remain (Middleton 2016). There is currently little available evidence on the implementation interventions that can guide better care in acute stroke units. The identification of successful interventions to bring about clinical practice improvements should lead to improved health outcomes for patients, reduced healthcare costs and reduced social costs related to long-term disability.

## OBJECTIVES

To assess the effects of implementation interventions for promoting the uptake of evidence-based recommendations in acute stroke unit environments. Secondary objectives are to describe any factors that may modify the effect of implementation interventions; determine factors that may influence the uptake of recommendations in acute stroke units; and determine if single or multifaceted intervention strategies (two or more interventions) are more effective in improving uptake of evidence, patient outcomes, system outcomes or professionals' knowledge, attitudes or intentions in this setting.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

The review will consider randomised trials, cluster-randomised trials, non-randomised trials, controlled before-after studies with at least two intervention sites and two control sites, interrupted time series, and repeat measures studies (where there is a clearly defined point in time when the intervention occurred and at least three data points before and three after the intervention).

## Types of participants

### Health professionals

We will include studies that describe care provided by health professionals providing direct services to patients admitted with acute stroke, working within acute stroke units (see Types of settings). Included participants will be licensed, registered healthcare providers, such as nurses, physicians, pharmacists, physiotherapists, occupational therapists, speech pathologists, dietitians, social workers, psychologists and radiographers.

### Patients

We will include studies assessing care provided in acute stroke units within the first seven days poststroke onset, in all types of ischaemic and haemorrhagic strokes. We will include studies evaluating care in participants drawn from mixed diagnostic groups including stroke, but only where it is clearly possible to extract the separate results for people with stroke.

### Types of settings

Eligible acute stroke units will be those that admit patients with acute stroke (usually within hours of onset), and where a multidisciplinary team, including specialist nursing staff based in a discrete ward, cares exclusively for stroke patients. We will use the Stroke Unit Trialists' Collaboration 2013 hierarchy of stroke service organisation to define and compare 'more-organised' versus 'less-organised' acute stroke services. The hierarchy in descending order from most organised is as follows (Stroke Unit Trialists' Collaboration 2013).

1. Acute stroke units that accept patients acutely but discharge early (usually within 7 days); these appear to fall into three broad subcategories:

- i) 'intensive' model of care, with continuous monitoring, high nurse staffing levels, and the potential for life support;
- ii) 'semi-intensive', with continuous monitoring, high nurse staffing but no life support facilities; and
- iii) 'non-intensive', with none of the above.

2. Comprehensive (i.e. combined acute and rehabilitation) stroke units that accept patients acutely, but also provide rehabilitation for at least several weeks if necessary.

To differentiate our review from the ongoing Cochrane Review by Cahill (in press) on evidence implementation in stroke rehabilitation settings, we will exclude settings described by Stroke Unit Trialists' Collaboration 2013 as rehabilitation stroke units that accept patients after a delay, usually of seven days or more, and that focus on rehabilitation.

Where insufficient detail is available in publications to determine the type of setting, we will contact authors.

## Types of interventions

We will include interventions aimed at enhancing the uptake of evidence-informed recommendations in acute stroke units and bringing about changes in the behaviour of healthcare professionals, stroke services or both. These will include, among others, delivery arrangements, financial arrangements, governance arrangements and implementation strategies, as defined by EPOC taxonomy (EPOC 2016a). Examples of interventions include creating new multidisciplinary teams or triage systems or changing facilities (delivery arrangements); using targeted financial incentives or insurance schemes (financial arrangements); changing the scope of practice or instituting policies for regulating training by health professionals (governance arrangements); and using reminders, audit and feedback, or local opinion leaders (implementation strategies).

We will exclude one specific 'delivery arrangement' intervention that Cochrane Reviews have already explored and is known to be highly effective, namely, organised care provided in dedicated stroke units (Stroke Unit Trialists' Collaboration 2013).

Comparison: in randomised trials, cluster-randomised trials, non-randomised trials, and controlled before-after studies, we will include studies that compare an intervention with either an inactive control (i.e. usual practice) or an active control intervention (i.e. passive information provision only).

## Types of outcome measures

We will include studies with analysable data for any objective measure of the following outcomes.

### Primary outcomes

1. Quality of care (as measured by health professionals' performance in terms of adherence to recommended practice or process of care). For example, the uptake or increase in:

- i) recommended diagnostic procedures or assessments;
- ii) acute medical interventions;
- iii) interventions to prevent complications;
- iv) patient-centred goal setting;
- v) early rehabilitation interventions;
- vi) prescribing patterns for secondary prevention medications;
- vii) assessments for post-acute rehabilitation;
- viii) referral patterns within the acute setting or to downstream services.

### Secondary outcomes

Where reported we will consider summarising information on the following.

1. Patient outcomes, including mortality, morbidity, disability levels, medical complications, quality of life, or health benefit

measures used in economic analyses such as quality-adjusted life years.

2. Utilisation, coverage or access outcomes, for example, length of stay.
3. Resource use or economic outcomes.
  - i) Direct medical costs.
  - ii) Non-direct medical costs, such as out-of-pocket expenses.
  - iii) Indirect costs, such as productivity impacts from inability to work.
  - iv) Incremental cost-effectiveness, cost-utility, or cost-benefit impacts of an intervention versus the comparator.
4. Health professional knowledge.
  - i) Attitudes toward, or intentions to use evidence-informed recommendations.
  - ii) Change in the knowledge or attitudes of acute stroke unit professionals regarding recommended acute stroke management.

We will include studies with measures of these secondary outcomes in this review. However, we will exclude studies that only report these outcomes with no objective measure of professional behaviour.

## Search methods for identification of studies

### Electronic searches

We will identify primary studies using the following bibliographic databases, sources, and methods. We will identify related systematic reviews by searching the Cochrane Database of Systematic Reviews, and the databases listed below.

### Databases

- Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, Wiley (current issue)
- MEDLINE and MEDLINE In-Process and other non-indexed citations, OvidSP (1950 onwards)
- Embase OvidSP (1947 onwards)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature), EbscoHost (1980 onwards)
- The Joanna Briggs Institute EBP Database, OVID SP (1998 onwards)
- ProQuest Dissertations & Theses Full Text (all dates)

The OVID MEDLINE search strategy provided in [Appendix 1](#) is a draft developed by one author in consultation with a research librarian at the University of South Australia. We will present the finalised strategy in the review. We will adapt the MEDLINE strategy for other databases using appropriate syntax and vocabulary for those databases. We will not limit the search by date or language.

## Searching other resources

### Grey literature

We will conduct a grey literature search to identify studies not indexed in the databases listed above. Sources will include the sites listed below. We will document additional sources, if any, in the review.

- Open Grey ([www.greynet.org/opengreyrepository.html](http://www.greynet.org/opengreyrepository.html)).
- Grey Literature Report (New York Academy of Medicine) ([www.greylit.org](http://www.greylit.org)).
- Agency for Healthcare Research and Quality (AHRQ) ([www.ahrq.gov](http://www.ahrq.gov)).
- National Institute for Health and Clinical Excellence (NICE) ([www.nice.org.uk](http://www.nice.org.uk)).
- Stroke associations/foundations websites.

### Trial Registries

We will search the following registries for ongoing and completed trials.

- International Clinical Trials Registry Platform (ICTRP), World Health Organization (WHO) ([www.who.int/ictrp/en](http://www.who.int/ictrp/en)).
- ClinicalTrials.gov, US National Institutes of Health (NIH) ([clinicaltrials.gov](http://clinicaltrials.gov)).

We will also:

- review reference lists of all included studies, relevant systematic reviews and primary studies;
- contact corresponding authors of relevant studies or reviews to assist with identification of unpublished or ongoing studies; and
- conduct forward citation searching of included studies.

## Data collection and analysis

### Selection of studies

To ensure consistent application of inclusion criteria, we will conduct a pilot, whereby all review authors will independently screen a randomly selected subset of five studies using a predetermined form and guidance instructions. All review authors will discuss any discrepancies and, if required, we will revise the form and guidance to optimise consistency of screening decisions.

Two review authors will independently screen the titles and abstracts to identify potentially relevant papers, including those where the description of the intervention, study design, setting, participants, or outcomes is insufficient to make a decision about inclusion. We will obtain the full text of all potentially relevant studies, and two review authors will independently assess these

for inclusion in the review according to the eligibility criteria described previously. We will resolve disagreements through discussion until reaching consensus, and by arbitration from a third review author or all authors if required. Review authors who are also authors of included studies, will not be involved in appraising their study for inclusion. We will refer unresolved disagreements to the EPOC contact editor. We will provide reasons for excluding full text studies that we had initially considered to be potentially relevant. We will document the study selection process in a PRISMA chart (Moher 2009).

### Contacting corresponding authors

Where insufficient published data are available, one review author will contact the study's corresponding author (for example, to determine details of the types of settings, the components and complexity of the implementation intervention, or to request further information or access to unpublished results).

### Data extraction and management

At least two review authors working independently will undertake data extraction from each included study using a modified and piloted version of the Cochrane EPOC Group Data Collection Checklist (EPOC 2013a), including: characteristics of the study (design, methods of randomisation), participants, interventions and outcomes (types of outcome measures, adverse events). We will resolve any data extraction discrepancies through discussion between the two data extractors, with a third review author acting as arbiter if required. We will then check for errors before entering the data into Review Manager 5 software (RevMan 2014). Review authors who are also authors of included studies, will not be involved in appraising their study for data extraction.

### Scope of the implementation intervention

We will extract data to describe the scope of the intervention, specifically whether the intervention was targeted at a single acute stroke unit at one study site or at single acute stroke units at multiple study sites with an interorganisation intervention component (such as a regional stroke management improvement collaborative).

### Organisational context framing the intervention

We will extract descriptions of the healthcare setting(s), including information to decide the type of acute stroke unit as per the Stroke Unit Trialists' Collaboration 2013 categories (acute intensive, acute semi-intensive, comprehensive or integrated traditional Chinese medicine stroke units). In our analysis, we will include type of acute stroke unit as a potential effect modifier (Stroke Unit Trialists' Collaboration 2013). Other descriptive data extracted



will include size of unit (number of patients with stroke admitted per year, number of beds allocated to stroke), urban or rural setting, public/private health insurance funding, and level of advantage or disadvantage (e.g. socioeconomic characteristics of the setting).

### **Components and complexity of the implementation intervention**

We will extract data on the intervention components using a framework based on the Cochrane EPOC taxonomy to guide data extraction (EPOC 2016a). Data will include specific tools or processes used in the implementation, categorised as either delivery arrangements, financial arrangements, governance arrangements or implementation strategies.

We will extract descriptions of the intervention(s) and implementation methods used to improve health professionals' performance (planned and actual), and classify studies as single intervention strategies or multifaceted intervention strategies (two or more interventions). This is because we are interested in contributing to building the understanding of whether there is a differential effect between single and multifaceted interventions (Squires 2014).

We will also extract data on the intervention duration, the number and composition of participating acute stroke professionals including professional disciplines, cost of the implementation intervention (where reported), and details of the implementation intervention including content, personnel delivering the intervention, delivery method and duration.

### **Complexity of the targeted professional performance change**

For each study, we will report on the stated purpose of the targeted change (e.g. appropriate performance based on evidence-informed clinical practice guidelines, cost containment) and the nature of the desired change (e.g. reduction, increase, cessation). Two review authors will independently categorise the complexity of the targeted change in a subjective manner as high, moderate or low using the method proposed by Brennan 2009. We will resolve disagreements by discussion among all review authors. The categories will be based on the:

- number of changes required;
- extent to which complex judgements or skills are necessary;
- number of staff and professions involved in the change; and
- number of facilities or departments involved in the change.

### **Assessment of risk of bias in included studies**

Two review authors will independently assess the risk of bias for each included study, using the Cochrane 'Risk of bias' tool (Higgins 2011), plus additional criteria developed by the Cochrane EPOC Group (EPOC 2016b). We will resolve any disagreements through discussion involving a third review author.

Review authors who are also authors of included studies, will not be involved in appraising their study for risk of bias. We will consider risk of bias in the analysis (see [Data synthesis](#) and [Sensitivity analysis](#)) and fully describe it in the 'Characteristics of included studies' table.

For randomised trials and cluster-randomised trials, we will assess the risk of bias associated with the following six domains from the 'Risk of bias' tool: sequence generation; allocation concealment; blinding of participants, personnel, and outcome assessors; incomplete outcome data; selective outcome reporting; and other potential threats to validity (Higgins 2011). We will include three additional domains that assess design-specific threats to validity covered by the Cochrane EPOC group: imbalance of outcome measures at baseline, comparability of intervention and control group characteristics at baseline, and protection against contamination (EPOC 2016b).

Finally, for clustered study designs, we will assess the risk of bias associated with an additional domain: selective recruitment of participants. That is, in studies eligible for inclusion in this review, the term 'participant' may refer to acute stroke unit teams, team members or patients. Selective recruitment can occur at any of these levels when those responsible for recruitment have knowledge of the group allocation. We will use the criteria for assessing selective recruitment in clustered designs developed in Brennan 2009 and based on guidance in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

We will assess risk of bias in controlled before-after studies using the same domains and criteria applied to randomised trials (EPOC 2016b). For interrupted time series studies, we will assess risk of bias associated with the following seven domains: intervention independent of other changes; shape of intervention effect prespecified; intervention unlikely to affect data collection; blinding of outcome assessors to intervention allocation; incomplete outcome data; selective outcome reporting; and other sources of bias (EPOC 2016b). We will use the criteria specified in the *Cochrane Handbook for Systematic Reviews of Interventions* and Cochrane EPOC Group guidance to judge whether a study is at low, high, or unclear risk of bias for each domain.

For each included study, we will report our assessment of risk of bias for each domain together with a descriptive summary of the information that influenced our judgment. We will judge the overall risk of bias for each study according to the criteria described under [Data synthesis](#).

In relation to reporting on secondary outcomes related to costs or the incremental cost-effectiveness of interventions against a comparator group, we will refer to the Consensus on Health Economic Criteria list for assessing methodological quality of economic evaluations (Evers 2005). This includes noting whether: the economic study design was appropriate to the stated objective; the chosen time horizon was appropriate for including all relevant costs and outcomes; costs and outcomes beyond 12 months were discounted appropriately; costs and outcomes were measured and valued ap-

appropriately; and important variables with uncertain values were appropriately subjected to sensitivity analysis.

## Measures of treatment effect

### Outcomes

Outcome categories may include dichotomous or continuous measures of health professional performance; health professionals' knowledge, attitudes or intentions; or patient or system outcomes. For each category, we will include the primary outcome as identified by the trial authors. Where possible for randomised trials, we will verify that the primary outcomes reported in the publications are consistent with those specified in the trial protocols or published trial registration information. When trial authors do not specify primary outcomes, we will use the one specified in the sample size calculation. If there are no primary outcomes specified and no sample size calculations, or if there are multiple primary outcomes reported, we will rank the intervention effect estimates as reported in the publication, selecting the outcome that provides the median value for the effect estimate. When there is an even number of outcomes, we will include the outcome whose effect estimate is ranked  $n/2$ , where  $n$  is the number of outcomes. In the results tables, we will report whether we have used the authors' nominated primary outcome or the outcome providing the median effect estimate.

We will collect and report all outcomes described by trial authors in results tables, along with how they were measured (for example self-report, chart audit).

### Measures of treatment effect for randomised trials, cluster-randomised trials, non-randomised trials and controlled before-after studies

We will extract the intervention effect estimate for included outcomes reported in the publications along with its P value and confidence interval (CI) or interquartile range, as appropriate, and the statistical analysis method used to calculate these measures. If trial authors used an inappropriate statistical method, we will not present the P value or confidence interval except if we are able to re-analyse the data. In this circumstance, the P value will be annotated with the word 're-analysed' in the results tables.

To make comparisons between studies, where possible, we will calculate the effect estimates. For binary outcomes, our primary effect estimate will be the risk ratio (RR), and for continuous outcomes our primary effect estimate will be the standardised mean difference (SMD). We will calculate P values for these effect estimates, adjusting appropriately for the design, where possible. We will standardise the effect estimates so that ratios greater than one, and differences between the intervention and comparator groups greater than zero, represent benefit for the intervention group (Brennan 2009).

If we cannot summarise results as above, we will report them as part of a narrative of 'other data', and we will not include them in a meta-analysis (Deeks 2011).

### Measures of treatment effect for interrupted time series studies

For interrupted time series studies, we plan to report the following estimates and their P values from regression analyses that adjust for autocorrelation: change in level of the outcome at the first point after the introduction of the intervention (immediate effect of the intervention); and the postintervention slope minus the pre-intervention slope (long-term effect of the intervention).

## Unit of analysis issues

### Clustering

For studies where clusters of individuals are randomised (cluster-randomised trials, controlled clinical trials) or allocated (controlled before-after trials) to intervention groups, but where inference is intended at the level of the individual, the analysis will need to account for correlation of observations within clusters (Brennan 2009). The use of standard statistical methods assumes independence of observations and in clustered studies can result in artificially small P values and overly narrow CIs for the effect estimates (Ukoumunne 1999). We will seek assistance from a statistician where trial authors have used inappropriate statistical methods to assist us with re-analysis of the data. If re-analysis is not possible, we will report the effect estimate and annotate the phrase 'unit of analysis error'.

### Interrupted time series studies

We will consult a statistician to assist in re-analysis of results from interrupted time series studies whose authors used incorrect statistical methods that did not account for the autocorrelation of data points (Ramsay 2003). We will obtain data from graphs or tables within the publication, or from the trial authors, where possible. We will use either regression analysis with time trends before and after the intervention, adjusted for autocorrelation and any periodic changes, or autoregressive integrated moving average (ARIMA) analysis. We will present the results for the outcomes as changes along two dimensions: change in level and change in slope. Change in level is the immediate effect of the intervention and is measured as the difference between the fitted value for the first post-intervention data point (e.g. one month after the intervention) minus the predicted outcome one month after the intervention based on the pre-intervention slope only. Change in slope is the change in the trend from pre- to postintervention, reflecting the 'long-term' effect of the intervention (EPOC 2013b; Ramsay 2003).

### Dealing with missing data

We will attempt to contact authors of the primary studies to obtain relevant missing data. Where the study has involved mixed settings, we will contact trial authors to request separate data for acute stroke units. Where trials reported that patients with stroke did not spend all their admission in the acute stroke unit, we will note this and report it descriptively. We will also seek clarification when necessary for descriptions of interventions (i.e. mode of delivery, format, duration), trial conduct (i.e. method of random sequence generation, method of allocating participants to treatment groups, blinding of trial personnel), and availability of unpublished outcome data. We will consider intention-to-treat analysis as part of the 'Risk of bias' assessment and will record the details of losses to follow-up.

We will consult a statistician to assist in dealing with remaining missing data. We will make explicit the assumptions of any methods used to account for missing data: e.g. that the data are assumed missing at random, or that missing values were assumed to have a particular value such as a poor outcome. We will perform sensitivity analyses (see [Sensitivity analysis](#)) to assess how sensitive results are to reasonable changes in the assumptions that are made and address the potential impact of missing data on the findings of the review in the Discussion section ([Higgins 2011](#)).

### Assessment of heterogeneity

We will decide whether to pool RRs measuring the effectiveness of the implementation interventions versus no intervention on healthcare professional performance based on the similarity of the interventions in the included trials. In any meta-analyses undertaken, we will assess statistical heterogeneity by visually inspecting the scatter of effect estimates on the forest plots and by means of the  $I^2$  statistic ([Higgins 2011](#)).

We will use the following as a guide for interpretation of the  $I^2$  statistic: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; and 75% to 100% may represent considerable heterogeneity ([Higgins 2011](#)). In cases of substantial to considerable heterogeneity (defined as  $I^2 > 50\%$ ), we will explore the data further by comparing the characteristics of individual studies and any subgroup analyses and report any differences when interpreting the results.

### Assessment of reporting biases

Included in our search strategy is a comprehensive search of the International Clinical Trials Registry Platform, the Australia New Zealand Clinical Trials Registry and the US National Institutes of Health (NIH) Clinical Trials register. We will contact investigators of these trials for further information, including the identification of any unpublished results.

We will explore the potential for small-study effects in the main outcomes of the review if we include at least 10 studies in a meta-

analysis. We will do this by using funnel plots and formal statistical tests for funnel plot asymmetry ([Egger 1997](#)). As considerable heterogeneity is anticipated, we will consult a statistician to assist in any required asymmetrical funnel plot analysis ([Higgins 2011](#)).

### Data synthesis

We expect to find considerable heterogeneity in this review, including variability in settings, the changes being implemented, implementation interventions used, types of studies and outcomes. For this reason the review may largely be a narrative synthesis of results, in particular for our secondary outcomes, whereby conducting a meta-analysis is problematic due to systematic variation between centres and over time.

Where studies are sufficiently homogenous in terms of setting, design and intervention, we will carry out meta-analysis using [RevMan 2014](#). We will use random-effects models for all meta-analyses. Where studies show unacceptable heterogeneity, we will present the results of studies in tabular form and provide a narrative summary of study results.

We will report tables of summary statistics for each comparison in each of the included studies (randomised trials, cluster-randomised trials, controlled before-after studies). The tables will include study design, baseline and follow-up summary statistics, effect estimates and statistical significance, and information on effect modifiers. Outcomes reported in these tables will include health professionals' performance (e.g. adherence to recommended practice or process of care) and where available, patient outcomes (e.g. mortality, morbidity, disability levels, medical complications, quality of life); utilisation, coverage or access outcomes; resource use or economic outcomes; and health professional knowledge of, attitudes toward, or intentions to use evidence-informed recommendations. We will make comparisons as outlined in the 'Subgroup analysis and investigation of heterogeneity' section below.

We will summarise the effect estimates for the dichotomous health professionals' performance outcome within comparison, type of implementation intervention and study design. This will include the presentation of the median effect estimate, interquartile range and range. We will display these data graphically using graphs, such as box plots, where appropriate.

We plan to use meta-analytical methods if possible, to pool RRs measuring the effects of the following three comparisons on health professionals' performance.

1. Single implementation interventions versus no intervention.
2. Multifactorial implementation interventions versus no intervention.
3. Multifactorial implementation interventions versus single interventions.

We will only include randomised trials or cluster-randomised trials that we judge as being at low risk of bias in these analyses. We will make an assessment of the clinical and methodological diversity before deciding whether to undertake meta-analyses (see

[Assessment of heterogeneity](#)). We will use a random-effects meta-analysis to pool intervention effects because of anticipated clinical and methodological diversity.

### **'Summary of findings' table and assessing the certainty of the evidence**

We will use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to make judgements on the certainty of the available evidence (high-certainty, moderate-certainty, low-certainty, and very low-certainty) for each main outcome ([Guyatt 2011](#)). Two review authors will independently carry out this assessment, resolving discrepancies by discussion, or with a third review author as arbiter if required. We will present the information in a 'Summary of findings' table along with key information on the findings for each outcome including RR, comparative risks and the number of participants ([Higgins 2011](#)). We will justify all decisions to down- or upgrade the certainty of the evidence in relation to each outcome within footnotes.

We will use the GRADE software to generate the 'Summary of findings' table and the EPOC worksheets ([EPOC 2013c](#); [GRADEpro GDT 2014](#)). The 'Summary of findings' table will display evidence for the primary outcome domain (quality of care) and four secondary outcome domains (patient outcomes; utilisation, coverage or access outcomes; resource use or economic outcomes; and health professionals' knowledge and attitudes.) If during the review process, we become aware of an important outcome that we failed to list in our planned 'Summary of findings' table(s), we will include the relevant outcome and explain the reasons for this in the section 'Differences between protocol and review'. As we cannot anticipate which specific outcomes our included studies will use, we will attempt to include at least one outcome from each of these four domains. As well as presenting the findings by outcome, we will also present the findings by study design in the 'Summary of findings' table.

We will consider whether there is any additional outcome information that was not able to be incorporated into meta-analyses and note this in the comments and state if it supports or contradicts the information from the meta-analyses. If it is not possible to meta-analyse the data we will summarise the results in the text.

### **Subgroup analysis and investigation of heterogeneity**

For each of the three planned comparisons, we plan to investigate if the effect is modified by:

- the type of implementation intervention (i.e. delivery arrangements, financial arrangements, governance arrangements or implementation strategies as per [EPOC 2016a](#)); and
- the type of setting (i.e. acute stroke units with intensive, semi-intensive, or non-intensive models of care; and comprehensive stroke units; [Stroke Unit Trialists' Collaboration 2013](#)).

We will investigate this visually (for example, using box plots and bubble plots) and formally through subgroup analyses, and if there are enough trials, we will use random-effects metaregression. If sufficient data are available, we will perform subgroup analyses to establish effectiveness relative to: study population characteristics - including professional disciplines, level of experience; intervention characteristics - including intended practice change, intervention content, personnel delivering intervention, delivery method, duration; study design - including randomised trials, cluster-randomised trials; and risk of bias - including random sequence generation, allocation concealment, blinding of outcomes, incomplete outcome data and selective outcome reporting.

### **Sensitivity analysis**

For the primary meta-analyses comparing the effectiveness of single implementation interventions to multiple interventions or no interventions on professionals' performance, we will undertake a sensitivity analysis to investigate how the inclusion of studies at an unclear or high risk of bias affects the pooled intervention effect. Where there are missing data, we will assess how sensitive results are to reasonable changes in the assumptions that are made to account for this, as part of our [Data synthesis](#) methods.

## **ACKNOWLEDGEMENTS**

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\* Indicates the major publication for the study

## APPENDICES

### Appendix I. Draft MEDLINE search strategy

MEDLINE (OVID) Search String		
1	cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp cerebrovascular trauma/ or exp intracranial arterial diseases/ or exp intracranial arteriovenous malformations/ or exp intracranial embolism/ or exp intracranial thrombosis/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ or vasospasm, intracranial/ or vertebral artery dissection/	
2	(stroke or cerebrovasc\$ or brain vas\$ or cerebral vas\$ or cva\$ or apoplex\$).mp	
3	((brain\$ or cerebr\$ or cerebell\$ or vertebrbasilar or hemispher\$ or intracran\$ or intracerebral or infratentorial or supratentorial or MCA or anterior circulation or posterior circulation or basal ganglia) adj5 (isch?emi\$ or infarct\$ or thrombo\$ or emboli\$)).mp	
4	((brain\$ or cerebr\$ or cerebell\$ or intracerebral or intracran\$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli\$) adj5 (haemorrhage\$ or hemorrhage\$ or haematoma\$ or hematoma\$ or bleed\$)).mp	
5	1 OR 2 OR 3 OR 4	Stroke
6	Hospital units/ or Patient care team/	
7	(stroke adj3 (unit\$ or ward\$ or hospital\$ or centre\$ or team\$)).mp	
8	((organi?ed or structured) adj3 care).mp.	
9	(rehabilitation adj3 (unit\$ or ward\$ or hospital\$ or centre\$ or team\$)). mp	
10	(multidisciplinary adj3 (unit\$ or ward\$ or hospital\$ or centre\$ or team\$)). mp	



(Continued)

11	((dedicated or discrete or comprehensive) adj5 (unit\$ or ward\$ or hospital\$ or centre\$ or team\$)). mp	
12	((specialist or speciali?ed) adj5 (nurs\$ or staff\$ or care or unit\$ or ward\$)).mp	
13	(organi?ed adj3 (unit\$ or ward\$)).mp.	
14	OR/ 6-13	
15	5 AND 14	Stroke unit
16	health educators/ or infection control practitioners/ or medical staff/ or nurses/ or nursing staff/ or medical staff, hospital/ or nursing staff, hospital/ or pharmacists/ or physicians/	
17	occupational therapy/ or physical therapy specialty/ or speech-language pathology/ or technology, radiologic/ or pharmacy/ or podiatry/ or licensed practical nurses/ or medical secretaries/ or nurses' aides/ or nutritionists/ or operating room technicians/ or pharmacists' aides/ or physical therapist assistants/ or physical therapists/ or physician assistants/ or audiology/ or social work/	
18	(nurs\$ or physiotherapy\$ or physical therap\$ or or or occupational therap\$ or pharmac\$ or speech therap\$ or speech pathology\$ or speech\$ language path\$ or doctor\$ or physician\$ or neurologist\$ or nutritionist\$ or dietician\$ or dietetic\$ or social worker\$).mp	
19	OR/ 16-18	Professional staff
20	15 AND 19	Stroke unit professional staff
21	practice guidelines/ or practice guidelines as a topic/ or clinical protocols/	
22	education, continuing/ or nurse education research/ or education, professional/	
23	inservice training/ or competency-based education/	

(Continued)

24	(educat\$ or Inform\$) adj2 (program\$ or intervene\$ or meet\$ or session\$ or strateg\$ or workshop\$ or visit\$).mp	
25	teaching materials /	
26	(leaflet? or booklet? or poster? Or writ\$ or print\$) adj3 (inform\$ Or educat\$).mp	
27	OR/ 21- 26	Educational materials, educational meetings, outreach visits
28	mentors/	
29	leadership/	
30	((opinion or educat\$ or influen\$) adj1 leader\$).mp.	
31	OR/ 28- 30	Opinion leaders
32	patient-centred care/	
33	((patient\$ or client\$ or survivor\$) adj2 (mediat\$ or direct\$)).mp	
34	OR/ 32-33	Patient mediated interventions
35	Clinical audit/ or Medical audit/ or Nursing audit/	
36	Benchmarking/	
37	Guideline adherence/ or quality indicators, healthcare/	
38	Process assessment health care/	
39	Physician practice patterns/ or Nurses practice patterns/	
40	((Audit\$ or process assess\$ or benchmark\$) adj3 feedback)	
41	OR/ 35- 40	Audit & feedback - 'instrumental knowledge use'
42	Reminder systems/	

(Continued)

43	(remind\$ or Prompt\$).mp.	
44	OR/ 42-43	Reminders
45	Total quality management/	
46	Quality improvement/	
47	Evidence based practice/	
48	Quality of healthcare/	
49	Communication barriers/	
50	(barrier\$ or facilitat\$) adj3 (best or recom- mend\$ or evidence).mp	
51	(individual\$ or tailor\$) adj3 (best or recom- mend\$ or evidence or implement\$).mp	
52	OR/ 45- 51	Tailored interventions
53	Mass media/	
54	Telecommunications/	
55	Marketing/	
56	Information dissemination/	
57	Audio-visual aides/	
58	OR/53-57	Mass media
59	Health services research/	
60	((action or participat\$) adj1 research\$).mp.	
61	OR/ 59-60	Action research
62	Health knowledge, attitudes or practices/	
63	Attitude of Health Personnel/	
64	((attitude\$ or knowledge) adj3 (staff or clinic\$ or profession\$ or nurs\$ or physiotherapy\$ or physical therap\$ or ot or occupational therap\$ or pharmac\$ or speech therap\$ or speech	

(Continued)

	pathology\$ or speech\$language path\$ or doctor\$ or physician\$ or neurologist\$ or nutritionist\$ or dietician\$ or dietetic\$ or social worker\$)).mp	
65	OR/ 62- 64	Other outcomes - “conceptual use of knowledge”
66	27 or 31 or 34 or 41 or 44 or 52 or 58 or 61 or 65	All EPOC professional interventions
67	Health Services Administration/ or “Organization and Administration”/ or Hospital administration/ or health facility administration/	
68	Centralized hospital services/ or hospital restructuring/ or hospital shared services/	
69	health planning organizations/ or health care coalitions/ or health planning councils/ or “state health planning and development agencies”/	
70	Health policy/ or Health care reform/	
71	clinical governance/ or “constitution and by-laws”/ or decision making, organizational/ or efficiency, organizational/	
72	governing board/ or trustees/ or institutional management teams/	
73	management audit/ or benchmarking/ or models, organizational/	
74	organizational culture/ or organizational innovation/ or organizational objectives/	
75	Capacity building/ or Program development/	
76	“Diffusion of Innovation”/ or Knowledge Management/	
77	Technology Transfer/ or Translational Research/	
78	“organization & administration”.fs.	

(Continued)

79	organi?ational.ti,ab.	
80	organi?ation\$.hw.	
81	(organi?ation? adj3 (change or changes or changing or collaborat\$ or development or impact or influenc\$ or infrastructure? or interprofession\$ or inter-profession\$ or intervention? or multicomponent or multi-component or multidisciplin\$ or multi-disciplin\$ or multifacet\$ or multi-facet\$ or multimodal\$ or multi-modal\$ or policy or policies or strategy or strategies or strategic or structur\$ or support\$ or system?)).ti,ab	
82	policy.hw.	
83	(policy or policies or (nurse adj4 managed) or (quality adj2 improvment) or (QI adj2 (initiative? or program\$ or hospital\$))).ti,ab	
84	(decentral\$ or empower\$ or governance or jurisdiction? or roster\$ or stewardship? or structural or team\$ or ((change? or changing) adj2 (direct\$ or initiat\$ or role or roles))).ti,ab	
85	(administrative or administrator?).ti.	
86	((administrative or administrator?) adj4 (change or changes or changing or collaborat\$ or development or impact or influenc\$ or infrastructure? or interprofession\$ or inter-profession\$ or intervention? or multi-component or multi-component or multidisciplin\$ or multi-disciplin\$ or multifacet\$ or multi-facet\$ or multimodal\$ or multi-modal\$ or policy or policies or strategy or strategies or strategic or structur\$ or support\$ or system?) ).ab	
87	(governance or jurisdiction? or roster\$ or team\$ or structural or organizational or self-direct\$ or (nurse adj2 (direct\$ or initiat\$))).ti, ab	
88	(stewardship or decentral\$ or reform? or reforming).ti,ab.	

(Continued)

89	OR 67-88	Organisational/Admin Terms
90	career mobility/ or employee incentive plans/ or job description/ or personnel administration, hospital/ or personnel delegation/ or "personnel staffing and scheduling"/ or staff development/ or workload/ or workplace/	
91	Professional Autonomy/ or Professional role/	
92	((professional\$ or clinician\$) adj2 (autonomy or independence or self-reliance)).ti,ab	
93	(professional adj2 development).ti,ab.	
94	(advance\$ or scope) adj3 (practice\$).ti,ab.	
95	OR/ 90-94 [Personnel Management-organisational terms]	Personnel Management - organisational terms
96	66 OR 89 OR 95	EPOC professional or organisational interventions]
97	20 AND 96	
	Limit to humans	
	Limit to RCTs, CRCTs, non-randomised controlled trials, controlled before-after studies, interrupted time series, repeat measures studies	

## CONTRIBUTIONS OF AUTHORS

JL is leading the project and will be involved in the selection of studies, quality assessment of studies, data abstraction, data entry and analysis.

DC, JB, SM, IG, EL, TT and LC contributed to the development of the protocol, and they will assist with the selection of studies, quality assessment of studies, data abstraction and analysis.

## DECLARATIONS OF INTEREST

Julie Luker: research affiliate with the NHMRC's Centre of Research Excellence in Stroke Rehabilitation and Brain Recovery has received travel costs and expenses to present at the Stroke Society of Australasia Annual Scientific Meeting.

Julie Bernhardt: none known.

Ian Graham: none known.

Sandy Middleton: lead author of a trial that may be included in this review (if that is the case, Sandy Middleton will not be involved in data extraction or analysis of such a trial). Co-Chair of Acute Stroke Nursing Education Network part funded by an AUD 20,000 unrestricted educational grant from Boehringer Ingelheim: no funds received by myself or my institution.

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