Current, future and avoidable costs of stroke in the UK

Economic case for wider implementation of interventions that work

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1. Introduction

There are over 113,000 strokes every year in the UK (Rothwell et al., 2004)* and over 950,000 stroke survivors among those aged 45 years and over (Geddes et al., 1996).* Many of these stroke survivors experience significant and long-term physical and psychological consequences, repeat strokes, transient ischaemic attacks (TIAs) and/or death within a year of stroke (Stroke Association, 2017).

Preventing, treating and managing the resulting illness or death from stroke all carry economic consequences, not just for healthcare services but also more widely across society (Saka et al., 2009; National Audit Office, 2010). For example, given that a quarter of all strokes in the UK happen among people of working age (Stroke Association, 2017), stroke can reduce employment prospects and productivity for society. It can also affect family and friends who are often involved with a stroke survivor’s care and are unpaid in this caring role. This is even more concerning given current and likely ongoing financial pressures on health and social care services, families and other unpaid carers.

Despite significant progress in prevention, treatment and rehabilitation, there is still great capacity for further improvements, which in turn could reduce these large economic burdens. Tackling a public health issue such as stroke requires a broad set of measures working together. For example, ensuring current services and support is configured optimally in all areas. Also, wider roll out of interventions that are not yet fully implemented (despite evidence of effectiveness and/or cost-effectiveness).

We aim to examine evidence for existing interventions that have potential for broader implementation and their associated gains. Where appropriate, we build on the evidence base to produce new estimates that serve as illustrations of such gains.

2. Methods

We aim to conduct a series of focused literature reviews related to interventions spanning three overarching areas of the stroke care pathway: rehabilitation/long-term care, acute care and prevention. As the purpose here is to illustrate the evidence that already exists and potential gains from implementation (rather than to conduct a thorough review of evidence of stroke interventions), these reviews are pragmatic rather than systematic. They focus on identifying interventions with evidence of potential economic gains, as well as evidence of effectiveness. Wherever available, we prioritise evidence from systematic reviews over that from individual studies, and to draw out information that would enable us to highlight or estimate potential economic gains. Our methodological approaches vary across each intervention, led by the nature and strength of evidence.

* Estimates of the number of strokes and stroke survivors can vary across different studies depending on many factors, including the population sample and data sources that are used. While we have used alternative estimates in our other publications (e.g. Stroke Association, 2017), we use averages from a range of estimates for the purpose of this work.
3. Key findings

Rehabilitation/long-term care

- A significant body of evidence related to various types of physical rehabilitation indicates its effectiveness for recovery of function and mobility after stroke (Pollock et al., 2014). In comparison, the evidence base for occupational therapy interventions is smaller but suggests improved outcomes from interventions focussing on activities of daily living (Legg et al., 2007). Evidence for rehabilitation therapy in the longer-term is limited (Aziz et al., 2009).

- A fifth of people with stroke are likely to suffer from dysphagia and a fifth of these are likely to develop pneumonia (Arnold et al., 2016). This means that around 4,700 people annually experience pneumonia following a stroke in the UK, incurring an annual treatment cost of approximately £2.5 million.

- NHS England estimates for extending provision of early supported discharge schemes following a stroke suggest that 170 lives could potentially be saved in England, generating a saving of £15,100 per 100,000 (NHS England, 2014).

- It is thus difficult to draw robust conclusions on effectiveness or cost-effectiveness of psychological support for stroke patients because evidence is limited in extent, quality and nature. Also, screening for psychological state after stroke remains hampered by clinician uncertainty about which screening tools to use.

Acute care

- Major acute system reconfiguration to increase delivery of effective urgent care has been successful in London and Greater Manchester (Morris et al., 2015). In London, a significantly higher proportion of patients received care compliant with care processes, and the new model delivered a 5% relative reduction in mortality at 90 days. Both areas saw reductions in length of hospital stay. The West Midlands is another major urban region with a population size broadly equivalent to Greater Manchester’s, so could potentially achieve similar gains to the Greater Manchester reconfiguration i.e. ~18,000 hospital days/£5 million saving over 2 years.

- Delivering thrombolysis within three hours of stroke is effective in reducing death or dependency (Wardlaw et al., 2014). We estimate that for the 2,000 eligible patients who do not receive the drug each year the NHS incurs £8.2 million in avoidable costs over 5 years.

- Thrombectomy is highly cost-effective, with an incremental cost per QALY gained of £7,061 (over 20 year horizon) – significantly lower than many other NHS interventions (Ganesalingam et al., 2015). Guijarro et al. (2017) suggest that on average one extra patient receiving thrombectomy would save the NHS £47,000 over 5 years, thus representing potential annual savings of millions. The benefits of thrombectomy are substantial: for every 100 patients treated, 38 have a less disabled outcome than with best medical management, and 20 more achieve functional independence (mRS 0–2) (Goyal et al., 2016). Thus higher treatment costs in the short-term can be offset in the longer term (Lobotesis et al., 2016).

Prevention

- We estimate that an atrial fibrillation screening programme could avoid 500 new strokes each year. This corresponds to £10.7 million of savings to NHS and social care, or £28.4 million of savings in broader societal costs. Accounting for longer-term post-stroke survival rates, potential cost savings to society (excluding costs of implementing the intervention) over a 5 year period amount to £233 million, £147 million of which relates to the opportunity cost of unpaid care and lost employment opportunities.

- Appropriate anticoagulant management of atrial fibrillation in all eligible patients could avert an estimated 4,551 strokes each year. This translates to £97 million savings in NHS and social care costs or £259 million savings in societal costs in the first year. Over 5 years, corresponding savings would be 22,755 fewer new strokes, 8,727 fewer prevalent cases of stroke and societal savings of £2 billion, including £691 million savings to NHS and social care.
Increasing time spent within the therapeutic range for warfarin from 60% to 70% can potentially result in societal cost savings of £908 million within 5 years of implementation.

A successful strategy to increase the proportion of diagnosed hypertension cases by 15% could potentially avoid 10,790 new cases and 4,138 prevalent cases of stroke over 5 years, yielding potential cost savings of £772 million to society, £284 million of which is attributed to NHS and social care.

A strategy to increase the proportion of patients on treatment for hypertension who achieve blood pressure <140/90 mm Hg from 63% to 78% would allow an additional 1.3 million patients to benefit from a reduced risk of stroke. Improved blood pressure control can avoid an estimated 2,000 new stroke cases each year.

Increasing the proportion of individuals with diagnosed hypertension who achieve blood pressure <140/90 mm Hg by 15% could potentially save £36.1 million in NHS and social care for first-time stroke each year. A further £51.8 million of informal care and £2.9 million of lost employment costs could be avoided. Over 5 years, 9,995 new cases and 3,833 prevalent cases of stroke could be avoided, yielding potential cost savings of £715 million to society, £263 million of which is attributed to NHS and social care.
4. Findings: rehabilitation/long-term care

4.1 Early mobilisation

The AVERT programme assessed very early mobilisation (VEM), delivered within 24 hours of stroke onset, against usual care (Langhorne et al., 2017). They defined early mobilisation as the commencement of sitting, standing and walking using a clinical protocol tailored to the severity of the stroke. It was delivered by a team of nurses and physiotherapists. Phase III of AVERT randomised 2,104 patients (610 in the UK; Langhorne et al., 2017). The primary outcome was survival without major disability using the modified Rankin scale (a score of 0–2; Howard et al., 2012) at 3 months after stroke. Secondary outcomes included the proportion of patients achieving unassisted walking (50m) by 3 months and health-related quality of life assessed at 12 months.

The trial found that fewer patients in the VEM group survived without major disability (OR 0.73, 95% CI 0.59 to 0.90). There were no significant differences in walking ability at 3 months (VEM 75% vs UC 76%; OR 0.83, 95% CI 0.64 to 1.07) or health-related quality of life at 12 months. These results were largely replicated when the analysis was restricted to UK participants only. Among UK participants, the difference between groups on the primary outcome was not statistically significant.

As part of this study, the authors conducted a systematic review of similar randomised controlled trials. They identified eight such studies (including their own) which included 2,618 participants overall. The median time to starting mobilisation after stroke across these studies was 18.5 hours. This was compared to 33.3 hours for the participants in the control arms of these studies, described as ‘delayed mobilisation’. The meta-analysis of these data found that at 3 months after stroke (n=2,542), early mobilisation showed a non-significant increase in the odds of death or dependency (OR 1.10, 95% CI 0.94 to 1.29). The authors conclude:

“...our high-dose frequent mobilisation protocol within 24 hours of stroke onset was less effective than usual care and should not be routinely applied. However, because the usual care protocol is also complex in nature, and increasingly featured a shift to early onset mobilisation, then it is over-simplistic to simply advise usual care. When mobilisations are attempted early after stroke, short, frequent mobilisations are associated with better outcomes. Further exploration of this data set is essential... we propose further dose-response analyses to explore the effect of dose rehabilitation on clinical and safety outcomes.”

The conclusion that early mobilisation cannot be assumed to be without benefit is, in part, justified by the authors by having observed significant positive benefit of early mobilisation in a Phase II randomised controlled trial of the same intervention. Based on 71 stroke patients recruited between 2004 and 2006, AVERT found that early mobilisation was significantly associated with returning to independent walking sooner, and better Barthel Index scores at 3 months than standard care (Cummings et al., 2011).
4.2 Occupational therapy

A systematic review of randomised trials of occupational therapy for patients following stroke was published by Legg et al. (2007). The authors searched for randomised controlled trials in which occupational therapy focussing on activities of daily living was compared to non-routine inputs. The occupational therapy had to be delivered by, or under the supervision of, an occupational therapist.

The review found nine relevant studies encompassing 1,258 participants. The participants were mostly drawn from hospital outreach and community settings. One study was set in a community nursing home. Eight of the nine studies were set in the UK and their publication spanned from 1995 to 2006. The median time to follow-up was six months and ranged from 3 to 12 months.

Scores for personal activities of daily living were available for eight of the trials – six of which used the Barthel Index. A standardised mean difference favouring occupational therapy was observed across these eight studies (SMD 0.18, 95% CI 0.04 to 0.32) which the authors observe as “equivalent to a one point (5%) difference on the 20 point Barthel Index, assuming a population (standard deviation) of six points.” No significant difference was observed on the secondary outcomes of mood or distress scores for participants and carers. The authors judged the studies to be of a good quality, though acknowledged that, “the exact nature of the interventions in each study differed according to the type of patient, the expertise of the therapist and the resources available”.

Another review focussed on the effectiveness of occupational therapy for improving cognitive impairment in stroke patients (Hoffman et al., 2010). It included randomised controlled trials, quasi-randomised studies and cross-over trials; and interventions carried out, or supervised, by an occupational therapist. The primary outcome measure was assessment of activities of daily living. Only one trial met the inclusion criteria and this was a US-based study published in 1983. It included 33 people who received rehabilitation in hospital following a stroke. The 16 participants in the intervention group received cognitive skills remediation training on an individual basis for 30 to 40 minutes three times per week, for an average of three to four weeks. There was no statistically significant difference in Barthel Index score compared with rehabilitation as usual.

Sackley et al. (2016) recently published results from a randomised controlled trial of occupational therapy for care home residents with stroke-related disabilities. This study was set in England and Wales encompassing 228 care homes. Participants had to have a history of stroke or transient ischaemic attack. The intervention was a personalised, three-month course of occupational therapy by qualified therapists and the control consisted of usual care for residents.

The primary outcome measure was the Barthel Index of activities of daily living score at three months. Secondary outcomes included the Barthel Index at 6 and 12 months, the Geriatric Depression Scale-15 and European Quality of Life-5 Dimensions. Data were collected from 1,042 individuals between 2010 and 2012. The non-significant adjusted mean difference in the Barthel Index score was 0.19 points higher in the intervention arm (95% CI -0.33 to 0.70). In addition, no significant differences on the secondary outcome measures were observed at any of the follow-up time points.

The mean cost of the intervention (including training, contact and non-contact time, travel and equipment) per participant was £399 (2010/11 prices). The mean incremental cost in the cost-utility analysis, accounting for intervention and other NHS and PSS (personal social services) costs, was £439 (95% CI £361 to £1,238; 2010/11 prices) per participant. Inflated to 2015/16 prices, using the hospital and community health services index (Curtis and Burns 2016), the mean intervention cost and incremental cost are £428 and £471 (95% CI £387 to £1,329) respectively. Thus, scaled up, the cost of the intervention would be £428,000 per 1,000 service users with an overall incremental cost (including intervention and service use) of £471,000 per 1,000 service users.
4.3 Physiotherapy

A recent review of randomised controlled trials of physical rehabilitation interventions, delivered by physiotherapists and aimed at promoting recovering balance, lower limb function or general functional ability, was conducted by Pollock et al. (2014). The primary outcomes of the review were measures of disability, including the Barthel and Katz indices and motor function scales, including the Motor Assessment Scale and Rivermead Motor Assessment. Eight of the studies were set in the UK. Eight of the included studies were published in 2010 or later.

The review identified 96 trials encompassing data from 10,401 participants. As would be expected, this number of studies included a vast range of active interventions – 122 in total. The most common intervention category was functional task training, included as a treatment component in 101 of the interventions. The control group was either no treatment (55 studies), usual care (19 studies) or another active intervention (23 studies).

Different subsets of studies were used across comparisons conducted in the review. Physical rehabilitation was found to have a positive effect on activities of daily living scales (standard mean difference 0.78, 95% CI 0.58 to 0.97) using data from 27 studies (3,423 participants). Data from nine studies were used to determine that this difference persisted beyond the length of the intervention. Pooled data from 12 studies (887 participants) found physical rehabilitation to be more effective than usual care in improving motor function (SMD 0.37, 95% CI 0.20 to 0.55). Physical rehabilitation was also more effective in improving balance (five studies including 246 participants and gait velocity (14 studies including 1,126 participants)). The authors conclude that, “physical rehabilitation, comprising a selection of components from different approaches, is effective for recovery of function and mobility after stroke. Evidence related to dose of physical therapy is limited by substantial heterogeneity and does not support robust conclusions”.


4.4 Physiotherapy and/or occupational therapy

An earlier review by Aziz et al. (2009) looked at the impact of rehabilitation therapy delivered by a physiotherapist or occupational therapist in randomised controlled trials of stroke patients resident in the community more than one year after stroke onset. The control groups were to include routine or usual care received by patients, including any therapy provided in outpatient departments or day hospitals. The primary outcome measures were death or poor outcome – the latter defined as death, deterioration in ability to perform activities of daily living, being dependent (based on an activities of daily living scale) or requiring new institutional care placement; and performance of activities of daily living at follow-up.

The review identified five trials for synthesis of data for 487 participants. Two of the included studies were also included in the review by Pollock et al. (2014). Three of the studies were set in the UK but the latest was published in 2006. Two of the studies focussed on physiotherapy, one on occupational therapy and two used a multi-disciplinary rehabilitation intervention where a combination of physiotherapy and occupational therapy in an outpatient setting was used.

As in the Pollock et al. (2014) review, subsets of studies were analysed depending on the comparison and availability of data. Only one study reported poor outcome at the end of six-month follow-up. This was a UK residential care home study with an occupational therapy intervention (Sackley et al., 2006). In this study there was a significant difference in favour of rehabilitation, as compared to control on the prevalence of a poor outcome (51% versus 76%, 95% CI 3% to 48%). The pooled data from two of the trials were available to assess differences across the treatment arms on Barthel Index scores (Green et al., 2002; Wade et al., 1992). Both randomised controlled trials were set in the UK and assessed a physiotherapy intervention. There was no significant difference in this outcome between the groups (SMD -0.06, 95% CI -0.32 to 0.20).

A randomised control trial of an intervention by UK NHS physiotherapists and occupational therapists found that an outdoor mobility intervention was neither clinically effective nor cost-effective (Logan et al., 2014). This study included 568 stroke patients living at home. The intervention was a targeted outdoor mobility rehabilitation programme of up to 12 sessions over four months. The primary outcome was participant health-related quality of life, measured on the Short Form questionnaire-36 items, at six months after randomisation into the study. The median duration of the intervention sessions was 369 minutes (inter-quartile range 170 to 692 minutes). The mean, per-participant, incremental (NHS and PSS) cost of the intervention was £475 (2010/11 prices). Accounting for both intervention costs and other NHS and PSS costs, the difference in costs between groups was £3,414 (95% CI £448 to £7,121; 2010/11 prices). Inflated to 2015/16 prices, using the hospital and community health services index (Curtis and Burns, 2016), the difference in intervention costs would be £510 and the difference in total costs would be £3,664 (95% CI -£481 to £7,643). Thus, scaled up, the cost of the intervention would be £510,000 per 1,000 service users with an incremental cost of £3,664,000 (including intervention and service use) per 1,000 service users.
4.5 Speech and language therapy

**Aphasia**

A one-year prospective, population-based study in Switzerland estimated that, annually, 43 of 100,000 inhabitants had aphasia resulting from first ischaemic stroke (Engelter et al., 2006). In the UK, it has been estimated that of people affected by a stroke each year in the UK, about one third have aphasia (Stroke Association, 2017), which may be associated with a range of psychosocial health problems that are inadequately addressed by healthcare services (Northcott et al., 2018). Applying this proportion to prevalence extrapolations to 2025, when we expect annual stroke prevalence in the UK to be 1,424,149 (Patel et al., forthcoming), the number affected could rise from approximately 316,000 in 2015 to nearly 475,000 by 2025.

However, cost-effective interventions are still lacking. In a large trial of enhanced communication therapy after stroke for aphasia and dysarthria in the first four months after stroke compared with an attention control (unstructured social contact), the intervention provided no added benefit or savings (Bowen et al., 2012).

**Dysphagia**

In a prospective registry-based study in Switzerland, Arnold et al. (2016) found that dysphagia affected more than a fifth of patients with ischaemic stroke and persisted in half of these at hospital discharge. Importantly, severe dysphagia strongly predicted mortality (8.5-fold higher risk of death) at 3 months. Furthermore, it was independently associated with:

- in-hospital pneumonia: occurred in 22.9% of patients with dysphagia versus 1.1% without dysphagia (p<0.001);
- discharge destination: higher chance of transfer to a rehabilitation clinic (78.0% vs. 35.4%, p=0.001) and a lower chance of being discharged home (19.5% vs. 63.7%, p=0.001) compared to those without dysphagia; and
- institutionalisation: at 3 months, those with dysphagia were less likely to live at home (38.8% vs. 76.5%, p<0.001).

However, it should be noted that there are wide discrepancies in reported frequencies of dysphagia, often due to differences in screening techniques and tests (Martino et al., 2005). Screening for dysphagia before first oral intake of fluids or food after stroke can reduce aspiration/pneumonia and is recommended regardless of initial stroke severity (Bray et al., 2017; Palli et al., 2017).

A registry-based study in a national cohort (England and Wales) of unselected stroke patients suggests that patients with the longest delays in dysphagia screening and speech and language therapy (SALT) dysphagia assessment had a higher risk of stroke associated pneumonia, with an absolute increase of pneumonia incidence of 1% per day of delay (Bray et al., 2017). The study also suggests that “30-day mortality was 13.2% overall, 10.2% in patients screened for dysphagia, 14.7% in patients referred for SALT assessment and 34.6% in patients in whom a dysphagia screen was not carried out” (Bray et al., 2017).

After adjusting for patient characteristics, there remained a modest association between screening delays in dysphagia and incidence of stroke associated pneumonia, and strong association between delays in comprehensive dysphagia assessment and incidence of stroke associated pneumonia (+3% over the first 24 hours). Delays beyond 24 hours were associated with an additional 4% absolute increase in incidence of stroke associated pneumonia which is an approximate threefold increase in relative incidence (Bray et al., 2017).

Bray et al. (2017) conclude that “since stroke associated pneumonia is one of the main causes of mortality after acute stroke, early dysphagia assessment may contribute to preventing deaths from acute stroke and could be implemented even in settings without access to high-technology specialist stroke care”.

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New calculations

Assuming 117,600* new strokes per year in the UK, of which 99,960 (85%) will be ischaemic stroke, using incidence figures from Arnold et al. (2016), 20,692 (20.7%) are likely to suffer from dysphagia, and 4,738 (22.9%) of these are likely to develop pneumonia. Associated treatment costs for pneumonia could be approximately £2.5m (based on a unit cost of £532 for treating pneumonia; NHS reference cost 2015-16; currency code DZ23M for non-elective short stays).

*Calculation in Patel et al. (forthcoming) based on mid-point incidence from three studies (Rothwell et al., 2004; Stewart et al., 1999; Wolfe et al., 2002), adjusted for population size and age composition in England in 2016.
4.6 Early supported discharge

The 2016 SSNAP Acute Organisational Audit (RCP, 2016) found that 81% of hospitals had specialist early supported discharge (ESD) services available to them compared to 74% in 2014. The proportion of people discharged with stroke specialist ESD increased from 25% in 2013/14 to 33% in 2015/2016.

A recent systematic review of early supported discharge services for people with acute stroke (Langhorne et al., 2017) summarised evidence from randomised controlled trials (RCTs) which recruited stroke patients in hospital “to receive either conventional care or any service intervention that has provided rehabilitation and support in a community setting with an aim of reducing the duration of hospital care”. The review findings relate to 17 trials which recruited 2,422 participants with outcomes data. The participants tended to be a selected elderly group of stroke survivors with moderate disability. It should be noted that only 5 of the studies included in the review are post-2007, and only 4 are UK-based studies of which none are post-2007.

The review showed positive findings for appropriately resourced ESD services with co-ordinated multidisciplinary team input provided for a selected group of stroke patients, but inconclusive results for services without co-ordinated multidisciplinary team input. The review found that for the ESD group, initial hospital stay was reduced by approximately five days. Also, at an average of six months after stroke, those who received ESD were more likely to be living at home (“an extra five patients living at home for every 100 receiving ESD services; moderate-quality evidence”). They were also more likely to be independent (“an extra six patients independent for every 100 receiving ESD services; moderate-quality evidence”). No risks were identified in terms of readmission risk or patient/carer mood or quality of life. Trials based around a co-ordinated ESD team seemed to suggest the greatest disability reductions. ESD costs ranged from lower to modestly higher than usual care. The authors therefore supported appropriately resourced and co-ordinated ESD as a useful component of a comprehensive stroke service.

Fisher et al. (2015) conducted a cohort study of 293 stroke survivors recruited from two acute stroke units in Nottinghamshire (‘ESD’ n=135 and ‘Non ESD’ n=158) and 84 caregivers. The ‘Non ESD’ group experienced standard practices for discharge and onward referral. Outcomes (primary: Barthel) were assessed at baseline, 6 weeks, 6 months and 12 months. It found that the ESD group had significantly shorter length of hospital stay (P=0.029) and higher levels of satisfaction with services (P<0.001). In an analysis adjusting for baseline age differences, the ESD group had a greater chance of being in the ⩾90 Barthel Index category at 6 weeks (OR = 1.557, 95% CI 2.579 to 8.733), 6 months (OR = 1.541, 95% CI 2.617 to 8.340) and 12 months (OR 0.837, 95% CI 1.306 to 4.087) compared with baseline. Carers in the ESD group also showed improved mental health (P<0.01).
In terms of cost-effectiveness, a modelling study compared stroke unit care followed by ESD with stroke unit care without ESD, and with general medical ward care without ESD (Saka et al., 2009). They used data for incident ischaemic stroke cases (N=844), observed between 2001 and 2006, from stroke units in the coverage area of the South London Stroke Register. Main outcome measures were societal costs (health and social care, plus lost income due to morbidity and mortality) and quality-adjusted life-years gained (QALYs). QALYs were estimated from death status and Barthel scores, and 1-year outcomes were extrapolated to a 10 year period, assuming no stroke recurrence. They found that stroke unit care followed by ESD offered the best value for money, with a cost per QALY gain over 10 years of £10,661 compared with the general medical ward without ESD care, and £17,721 compared with the stroke unit care without ESD. Thus the additional quality of life benefits derived from ESD are associated with additional costs, but within the acceptable threshold of £20,000 per QALY gain. It is unclear from the paper what the cost-effectiveness ratios would be without the inclusion of lost income costs.

NHS England estimates for extending provision of Early Supported Discharge (ESD) schemes following a stroke - from 20% of patients to 40% of patients - suggest a potential 170 lives could be saved in England and a cost saving of £15,100 per 100,000 (NHS England, 2014). In turn, they cite National Audit Office modelling which suggests that “increasing the availability of early supported discharge from its current level to all stroke units providing early supported discharge would be cost-effective over a ten-year timeframe, costing about £5,800 per QALY gained” (National Audit Office, 2010).
4.7 Psychological support

Treatment interventions

Few randomised controlled trials and even fewer reviews have assessed the effectiveness of psychological support for stroke patients. Those that have been researched include studies of psychotherapy, yoga and mindfulness. A number of interventions which potentially could provide psychological support for stroke patients have, as yet, been assessed for their feasibility only. For example, Simblett et al. (2017) report on the feasibility and acceptability of computerised cognitive behavioural therapy to treat depression and anxiety in stroke patients; Ali et al. (2014) report the feasibility of art therapy, facilitated by an art psychotherapist, delivered to stroke patients receiving inpatient hospital rehabilitation; and Chan et al. (2012) report on the feasibility of yoga and exercise for improving symptoms of depression and anxiety in individuals with post stroke disability in a small pilot study. Similarly, feasibility studies of interventions to improve the psychological wellbeing of carers of individuals who have had a stroke have been reported in the literature (Woodford et al., 2014).

A recent review of interventions to treat anxiety after stroke identified three trials, including 196 participants (Knapp et al., 2017). They described the quality of the evidence as low. The first trial included was a pilot study of 21 stroke patients and the third considered pharmacological intervention only. The second trial (Wang et al., 2005), set in China, randomised 81 participants, subsequent to a first stroke, with co-morbid anxiety and depression. The intervention group received a pharmacological intervention plus psychotherapy (30 to 60 minutes once per week administered by a psychiatrist for six weeks) and the control group received standard care. The improvement in anxiety at the end of the six week follow-up period, as measured on the HAM-A anxiety scale, was significantly greater for the intervention group as compared to the control. The generalisability of the findings to England are unclear but we estimate the cost of this intervention in the UK NHS would be £948 (2015/2016 prices) per patient, based on a per attendance unit cost of psychotherapy of £158 (NHS Reference Costs, 2016).

A review of the benefits of yoga in reducing anxiety and depression in stroke patients (Thayabaranathan et al., 2017) found five papers based on four randomised controlled trials, none of which had sample sizes of over 50 participants. Although the authors found evidence that yoga was beneficial in reducing anxiety and depression, they described the quality of the included trials as low to moderate and concluded that large well-designed randomised controlled trials are needed to confirm their findings.

A relatively recent review assessed the benefit of mindfulness-based interventions following transient ischaemic attack or stroke (Lawrence et al., 2013). Statistical meta-analysis was not performed in this review, however, because the authors deemed the included studies to be too heterogeneous. Of four included studies, only one was a randomised controlled trial, including only 12 participants. None of the studies were set in the UK.

Psychological assessment

Despite guideline recommendations to routinely screen stroke survivors for the presence of mood disorders, screening rates remain suboptimal. Burton and Tyson (2014) suggest that clinician uncertainty about which tool to use is one practical barrier and thus review a range of available tools. They identified a number of valid and clinically feasible tools: “the GDS-15 can detect any depressive disorder and the PHQ-9 can detect severe depression whereas the SADQ-H can be used with stroke survivors who are unable to self-report. The HADS (both the total scale and the anxiety subscale) can effectively identify anxiety post-stroke but clinical utility is limited by the costs involved.” However, they were unable to identify the optimal cut-off scores for these tools (and the other tools they identified) due to the heterogeneity of studies they reviewed, thus some uncertainty surrounding screening tool choice still remains.

Forster et al. (2014) reported on a randomised controlled trial of a protocol for identifying stroke patients and their carers in need of psychological support (among other needs). The trial, set in the UK, randomised stroke patients and carers to receive either a system of care which included a structured assessment, care plan, checklist, manual containing reference guide and service information...
delivered by a stroke care co-ordinator, or usual care, described as current community-based care as determined by local policy and practices. The primary outcome measure was the General Health Questionnaire – 12 item (GHQ-12) assessed at 6 months after recruitment. Analysis of data from 610 patients found no significant difference on GHQ-12 scores between treatment arms at 6 months. The difference for carers (n=162) on the GHQ-12 approached statistical significance (P=0.061). There was also no evidence of cost-effectiveness of the intervention. The mean cost of the intervention in stroke care co-ordinator inputs was £277 (2010/2011 prices) and £239 for the control group. Updated to 2015/16 prices, using the hospital and community health services index (Curtis and Burns, 2016), these costs are £297 and £257 for the intervention and control groups, respectively. Thus the mean cost of the intervention, scaled up, would be £40,000 per 1,000 service users. The authors conclude that, “… successfully addressing the needs of a heterogeneous post-stroke population remains problematic. Future work could explore stratifying patients and targeting services towards patients (and carers) with specific needs, leading to a more specialised bespoke service”.
5. Findings: acute care

5.1 Acute system reconfiguration

Evidence from other countries suggests that centralised specialist stroke care can improve use of evidence-based care in the first few hours after a stroke. For London, a modelling study by Hunter et al. (2013) estimated the 90-day saving to the NHS at around £800 per patient and the 10-year saving at around £3,900 per patient, and that such savings would offset reconfiguration implementation costs (estimated at around £10 million) within two years (Hunter et al., 2013).

Morris et al. (2014) examined the impact of major acute system reconfiguration in London and Greater Manchester using routine data for all patients in England who had a stroke during a 51 month period. They conducted a difference in differences analysis, comparing (a) changes over time in London versus changes over time in rest of England and (b) changes over time in Manchester versus changes over time in rest of England.

In London, the reconfiguration resulted in 8 hyperacute stroke units (HASUs) operating 24/7 with capacity for immediate imaging and thrombolysis, and 24 stroke units designated to provide acute rehabilitation (8 of these attached to a HASU). Five hospitals previously providing acute stroke care were no longer to do so. In Manchester, there were concerns such as transporting patients over greater distances that resulted in patients presenting only within four hours of developing stroke symptoms (the time limit for antiplatelet treatment) being taken directly to a comprehensive stroke centre or primary stroke centre, while other patients were taken to one of 10 district stroke centres. In contrast to London, no hospitals stopped providing stroke services entirely.

A significantly higher proportion of patients received care compliant with care processes (Ramsay et al., 2015) and, consistent with evidence of better compliance being negatively correlated with mortality, the new model delivered a 5% relative reduction in mortality at 90 days in London. Although the Manchester model was not implemented as intended, both areas saw reductions in length of hospital stay: by 9% in Greater Manchester and by 7% in London, implying 17,685 fewer hospital days in Greater Manchester and 22,341 fewer in London (Morris et al., 2014).

New calculations

Although these findings may not be generalisable to less urban areas, they are likely to be relevant for other urban areas. Another major urban region in England, the West Midlands, has a population size (2.83 million in 2015) broadly equivalent to Greater Manchester’s (2.76 million in 2015; ONS, 2016). Thus, we estimate that service reconfiguration just in the West Midlands alone could potentially achieve similar gains to the Greater Manchester reconfiguration i.e. ~18,000 hospital days/£5 million over 2 years (assuming a cost of £283 per day; Department of Health, 2015).
5.2. Thrombolysis

Approximately 20% of stroke patients are eligible to receive thrombolysis treatment and virtually all sites can now offer this at all times, through various models of implementation ranging from on-site delivery to a telemedicine service with remote advice from a stroke consultant (Royal College of Physicians, 2016).

Outcomes are better the earlier it is administered (Royal College of Physicians, 2016). A Cochrane review of 27 trials (all using a placebo control) involving 10,187 patients, found that “thrombolytic therapy, mostly administered up to six hours after stroke, significantly reduced the proportion of participants who were dead or dependent (modified Rankin 3 to 6) at three to six months after stroke (odds ratio (OR) 0.85, 95% confidence interval (CI) 0.78 to 0.93” (Wardlaw et al., 2014). While thrombolytic therapy was associated with increased risks of various negative outcomes (e.g. symptomatic intracranial haemorrhage, early death (generally attributable to intracranial haemorrhage) and death by three to six months after stroke), treatment within three hours of stroke was more effective in reducing death or dependency (OR 0.66, 95% CI 0.56 to 0.79) without any increase in death (OR 0.99, 95% CI 0.82 to 1.21; 11 trials, 2187 participants).

Various modelling studies have attempted to examine the potential gains from wider implementation of thrombolysis. Most recently, NCGC/SSNAP (2016) estimated cost savings and QALY gains for each extra person thrombolysed. Their findings suggest that after 5 years, it can be expected that each extra patient thrombolysed saves £4,100 in NHS costs, £6900 in social care costs, and generates an extra 0.26 QALYs. Thus, we estimate that the 2,000 eligible patients who do not receive the drug each year incur £8.2 million in avoidable costs to the NHS over 5 years.

Using a decision tree model from an NHS and social care perspective, Penaloza-Ramos et al. (2014) attempted to establish the cost-effectiveness of increasing thrombolysis rates through a series of theoretical change strategies (drawn from the literature) designed to optimise the acute care pathway for stroke. The model’s base case consisted of data for 488 consecutive stroke events following the acute stroke pathway in participating hospitals, with data on effectiveness of treatment and costs from published sources. A total of 33 patients (9%) received thrombolysis. They report that current practice resulted in 2,251 QALYs per 100,000 population at a cost of £14.2 million (2010/11 prices) and that all proposed change strategies reduced costs and increased QALYs (Penaloza-Ramos et al., 2014). A strategy of computed tomography (CT) scanning immediately on arrival suggested the largest cost saving (£51,000, 5.4 additional QALYs) (Penaloza-Ramos et al., 2014).

In a discrete–event simulation modelling exercise using five year retrospective data, Barton et al. (2012) suggested that the total overall cost of treating 50% of eligible patients in Northern Ireland with thrombolysis, instead of standard therapy, could decrease from £6,355 to £6,243 per appropriate patient. While increasing thrombolysis rates from 10% to 50% is associated with an additional £300 per person, there are savings elsewhere: £149 in acute care, £22 for long–stay care, £5 for rehabilitation and £213 for cost of discharge to institutional care. There would also be corresponding improvements in quality of life: the average number of QALYs per potentially clinically appropriate patient could increase from 5.442 to 5.475 - a gain of 0.033 which equates to 12 days of life in full health. Within a Northern Ireland context, the study estimates an annual gain of approximately 13 QALYs should the provision of thrombolysis be increased from 10% to 50% of patients that are clinically appropriate. Barton et al. (2012) therefore concluded that thrombolysis would produce moderate overall improvement to the service costs and outcomes assuming current levels of funding.

A further modelling study by Sandercock et al. (2004) showed that compared with standard care, treating eligible patients with recombinant tissue plasminogen activator (rt-PA) up to 6 hours after stroke is associated with a 78% probability of a gain in quality-adjusted survival during the first year, at a cost of £13,581 per QALY gained. However, they acknowledged variations in conclusions depending on the assumptions made.
5.3 Mechanical thrombectomy

Around 40% of strokes are caused by a large artery occlusion (LAO), and mechanical thrombectomy is gradually being used more for the treatment of large-vessel ischaemic stroke in patients arriving at the hospital outside of the 3-hour time window for thrombolysis. It is effective at preventing severe disability and increasing independence (Jovin et al., 2015) and is highly cost-effective at an incremental cost per QALY gained of £7,061 over 20 years (significantly lower than many other NHS interventions) and a 100% likelihood of being cost-effective in the UK (Ganesalingam et al., 2015). In estimating the budget impact to the NHS, Guijarro et al. (2017) suggest that on average one patient would save the NHS £47,000 over 5 years, thus representing potential annual savings of millions.

In a pooled analysis of patient-level data from five trials (1,287 patients), Goyal et al. (2016) showed that modern endovascular thrombectomy led to significantly reduced disability at 90 days compared with control (adjusted cOR 2·49, 95% CI 1·76–3·53; p<0·0001). Findings held in a range of subgroups, including in patients 80 years or over, patients not eligible for intravenous alteplase, and patients randomised more than 300 minutes from symptom onset. They reported that “the degree of benefit conferred by endovascular thrombectomy is substantial: for every 100 patients treated, 38 will have a less disabled outcome than with best medical management, and 20 more will achieve functional independence (mRS 0–2) as a result of treatment” (Goyal et al., 2016).

A review by Ferri et al. (2016), which included the same five trials plus three earlier ones that showed no benefit, concluded that “patient inclusion criteria and the type of device used, as well as the timing of endovascular treatment were important aspects that might have influenced the positive results of these recent trials.” They also note that a further 13 randomised controlled trials are ongoing.

After implementing the endovascular treatment (thrombectomy) pathway at University Hospitals of North Midlands NHS Trust, “94% of patients with severe strokes due to large vessel occlusion were discharged to their own homes rather than to a nursing home; 23% were discharged home within 1 week. Before implementing the treatment pathway, when only intravenous tissue alteplase was used, 70% of patients were discharged to inpatient rehabilitation, with significant annual costs” (Royal Stoke University Hospital, University Hospitals of North Midlands NHS Trust, 2016). Savings amounted to £0.8 million related to reductions in length of hospital stay and £1.6 million from reductions in social care costs. Costs to commissioners (who were paying for the procedure) were estimated at £0.5 million per annum and were expected to reduce as the procedure becomes established within national tariff.

In a modelling based cost-effectiveness study, Lobotesis et al. (2016) reported that higher treatment costs were offset by long-term cost savings due to improved patient health status, resulting in overall cost savings of £33,190 per patient and a net benefit of £79,402. It was also estimated that “costs saved due to improvement by one mRS [modified Rankin Scale] varied from £5,248 (moving from mRS 2 to mRS 1) and £111,209 (moving from mRS 3 to mRS 2). The cost savings associated with stent retriever + IV t-PA [intravenous tissue-type plasminogen activator] were greatest in patients with higher functional dependence (mRS 3 +)” (Lobotesis et al., 2016).

A health technology assessment by Health Quality Ontario (2016) stated that “experts have stated that since the technology has demonstrated a beneficial effect in the RCTs examined in this report, the number of eligible patients has increased, and that as many as 10% of all acute ischaemic stroke patients may have intracranial artery occlusion that could be considered for endovascular treatment”. Over 8,000 people a year in England could be eligible for thrombectomy but currently only 10% of eligible patients receive it. There is also huge geographic variation in access, with 37% of sites in England having no access to the procedure locally or by referral (Royal College of Physicians, 2016).
New calculations

Given the under-implementation of thrombectomy despite promises of large economic gains, we estimate cost savings and health gains associated with increased implementation over the next three years. We assume the following accumulation in the number of eligible patients treated:

- By 2018/19, 1,750 eligible patients are treated with thrombectomy
- By 2019/20, 2,500 eligible patients are treated with thrombectomy
- By 2020/21, 3,250 eligible patients are treated with thrombectomy

We previously estimated average care costs associated with different stroke severities (Patel et al., forthcoming). We estimated that those with moderate/severe stroke or severe stroke (NIHSS scores 16–42; referred to as NIHSS score groups 4–5 in our report) incurred NHS costs of £18,012 in their first year after stroke, and that those with minor stroke (NIHSS scores 1–4; referred to as NIHSS score groups 1–2 in our report) incurred NHS costs of £9,261. This represents a cost differential of £8,751 between those with NIHSS scores of 1–4 and those with NIHSS scores of 16–42.

Goyal et al. (2016) reported that for every 100 people treated with thrombectomy, 20 more will achieve functional independence (mRS 0–2). Assuming that the severity difference, as categorised by NIHSS scores, in the two groups described above is broadly equivalent to moving from mRS scores of 4–5 down to mRS scores of 0–2, the cost differential of £8,751 could indicate the potential NHS cost saving associated with each additional person gaining functional independence. On this basis, the overall NHS savings per 100 people treated with mechanical thrombectomy could be £175,020.

Using this approach, Table 1 sets out the estimated NHS, social care and combined savings (£3.9 million in 2018/19 and £7.2 million in 2020/21) associated with the aforementioned annual increases in numbers of people receiving thrombectomy. (For ease of calculation, all costs relate to 2015 prices).

<table>
<thead>
<tr>
<th>Year</th>
<th>Number Treated</th>
<th>Cost savings (£, 2015, ’000)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>NHS (20% of number treated, saving average of £8,751 each)</td>
</tr>
<tr>
<td>2018/19</td>
<td>1,750</td>
<td>3,063</td>
</tr>
<tr>
<td>2019/20</td>
<td>2,500</td>
<td>4,375</td>
</tr>
<tr>
<td>2020/21</td>
<td>3,250</td>
<td>5,688</td>
</tr>
</tbody>
</table>

Note: numbers within table may not sum exactly due to rounding
We also estimate QALY gains and associated monetary benefits. Assuming that mean QALY gain with thrombectomy plus intravenous thrombolysis is 0.12 at one year follow-up compared to intravenous thrombolysis only (Achit et al., 2017), we estimate QALY gains for the increased number treated. The associated monetary benefit is assumed to be £20,000 per QALY gain (i.e. the approximate willingness to pay threshold used by the National Institute for Health and Care Excellence (NICE)). Treating 1,750 patients could provide a QALY gain of 210/monetary benefit of £4.2 million (Table 2). Increasing coverage to 3,250 by 2020/21 raises these gains to 390 QALYs/monetary benefit of £7.8 million.

Table 2: Estimated QALY gains and net monetary benefits, for different targets for thrombectomy to 2020/21

<table>
<thead>
<tr>
<th>Year</th>
<th>Number Treated</th>
<th>QALY gain</th>
<th>Associated monetary gain (£) = QALY * £20,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018/19</td>
<td>1,750</td>
<td>210</td>
<td>4,200,000</td>
</tr>
<tr>
<td>2019/20</td>
<td>2,500</td>
<td>300</td>
<td>6,000,000</td>
</tr>
<tr>
<td>2020/21</td>
<td>3,250</td>
<td>390</td>
<td>7,800,000</td>
</tr>
</tbody>
</table>
6. Findings: stroke prevention

Avoiding new strokes, and thus reducing the number of people living with its effects, may offer the greatest scope for savings. We examine interventions for better diagnosis and management of two specific health conditions which are risk factors for stroke, atrial fibrillation (AF) and hypertension.

6.1 Atrial fibrillation

There is significant scope for reduction in stroke related morbidity through timely diagnosis and management of AF, which is associated with a 5-fold increase in the risk of stroke (Wolf et al., 1991). Using anticoagulant medication has been shown to reduce the risk of stroke by 61% compared to no treatment (Aguilar & Hart, 2005) and 32% compared to antiplatelets alone (Aguilar et al., 2007) based on evidence from two Cochrane systematic reviews.

New estimates

Stroke in the presence of AF results in worse outcomes for patients, including coma, paralysis and 30 day mortality (Lin et al., 1996; Lamassa et al., 2001). This is explained by higher mean age of patients suffering AF-related stroke and higher severity of stroke on average, with a median National Institute of Health Stroke Score (NIHSS) of 3 in AF-related cases, compared to 2 in the general stroke population (Lopes et al., 2011). Based on the current costs of stroke estimated in Patel et al. (forthcoming), we estimate the mean cost of stroke with NIHSS score 3 (moderate stroke) to be £21,343 from the perspective of NHS and personal social services (PSS). It was also assumed that AF-related strokes lead to moderate disability on average (score of 10-14 on the Barthel scale) and incur an additional £33,545 in terms informal care and £1,959 in terms of lost employment. In subsequent years post-stroke, patients with AF are expected to incur £8,547 in NHS and PSS costs, £20,207 in informal care costs and £2,014 in lost productivity. The total societal cost of AF-related stroke is thus £56,847 in the first year and £30,768 in subsequent years conditional on survival.

We estimate, in turn, the potential economic gains associated with three implementation scenarios for AF:

- By 2020/21, reduce the number of people with undetected AF by 50%
- By 2020/21, increase proportion of known AF on anticoagulation to 89% preventing 5,000 strokes
- By 2021/22, improvement in warfarin time in therapeutic range

By 2020/21, reduce the number of people with undetected AF by 50%
The Department of Health reports that 18% of AF cases remain undiagnosed, with many cases identified only upon investigation following an adverse event or complication (Department of Health, 2013). An estimated 8.1% of patients admitted for stroke have previously undiagnosed AF (Friberg et al., 2014). Prevalence of previously diagnosed AF is 1.76% based on data from 1,857 general practices in England (Cowan et al., 2013). This corresponds to 1.16 million cases based on Office for National Statistics population figures for 2016 (ONS, 2016). Given that 18% of all AF cases are undiagnosed, an estimated 254,000 people are living with undiagnosed AF in the UK.

If the number of cases of undiagnosed AF through opportunistic or targeted screening is reduced by 50%, and 89% of these receive anticoagulant therapy (all those eligible for whom it is not contraindicated), 113,000 patients can benefit from a reduced risk of stroke. If we assume that these patients were not undergoing antiplatelet therapy and their risk of stroke is reduced by 61% using anticoagulant medication, an AF screening programme could avoid an estimated 500 stroke cases each year. This corresponds to £28.4 million in savings from a societal perspective, which includes £10.7 million of savings to NHS and social care. Stroke often leads to dependence on formal and informal care in future years of life, meaning that the longer-term cost savings are likely to be far higher. We modelled post-stroke survival rates for medium and severe stroke using data from SSNAP (Royal College of Physicians, 2017). The proportion of patients alive was 63% after 1 year, 52% after 2 years, 43% after 3 years and 34% after 4 years. The potential cost savings (excluding the cost of implementing the intervention) to society over a 5 year period amounts to £233 million, £137 million of which relates to informal care (Table 3).

The cost of implementing a strategy of opportunistic or targeted screening at the national level is unknown. One randomised controlled trial estimated the cost of screening with a 12-lead electrocardiogram (ECG) interpreted by a consultant to be £16.25 per patient and the cost of a routine pulse reading to be £1.83 per patient (Hobbs et al., 2005). These costs would need to be combined with the total number of patients who undergo screening to estimate the aggregate cost of carrying out the strategy from the NHS perspective. Additional costs, including administration and promotion of the strategy would also need to be considered.
By 2020/21, increase proportion of known AF on anticoagulation to 89%

An estimated 117,600* new stroke cases per year occur in the UK. Given that one in five patients admitted for stroke in England, Wales and Northern Ireland have previously diagnosed AF (Royal College of Physicians, 2017), the estimated number of AF-related stroke cases is 23,520. Based on SSNAP data, 35% of AF cases are not treated with anticoagulants, excluding patients in whom therapy was contra-indicated due to a high risk of bleeds or another reason (Royal College of Physicians, 2017). Therefore an estimated 8,232 strokes are potentially avoidable through appropriate management of AF.

*Calculation in Patel et al. (forthcoming) based on mid-point incidence from three studies (Rothwell et al., 2004; Stewart et al., 1999; Wolfe et al., 2002), adjusted for population size and age composition in England in 2016.

Patients with AF do not receive anticoagulant therapy for a number of reasons. As noted above, in a small proportion of patients anticoagulant therapy is contra-indicated due to a high risk of bleeding. Patients who are not given anticoagulants for one reason or another are often given antiplatelets, which is less effective at preventing stroke. The protective effect of anticoagulant therapy is higher in trials which use placebo as the control treatment compared to antiplatelets.

To gauge the number of strokes which could be avoided through appropriate anticoagulant therapy of all eligible stroke patients with AF, we estimate the proportion of patients admitted for stroke with a prior diagnosis of AF who were treated with anticoagulants and antiplatelets using SSNAP data (Royal College of Physicians, 2017).

We assume that all patients with a contra-indication for anticoagulant medication are treated with antiplatelets (626, 10.9% of all patients with AF). This is subtracted from the number of patients who took anticoagulants only (1,022) to derive the number of stroke patients who are eligible for anticoagulants, but are given an antiplatelet instead (396). We then apply the odds ratio estimates from relevant systematic reviews (Aguilar & Hart, 2005; Aguilar et al., 2007) to work out the number of averted strokes per year.

The final figure represents the estimated number of strokes which could be prevented if (a) all patients eligible for anticoagulation who are currently on antiplatelets only are switched to an anticoagulant and (b) all patients eligible for anticoagulation who are currently not medicated are given an anticoagulant. The calculations are summarised in Tables 4 and 5.

### Table 4: Estimated proportion of patients not on anticoagulant therapy who were on antiplatelets

<table>
<thead>
<tr>
<th>Patient category</th>
<th>Number of patients in SSNAP</th>
<th>% of total</th>
<th>% of eligible but not taking anticoagulant</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stroke cases</td>
<td>5,739</td>
<td>100.00</td>
<td></td>
</tr>
<tr>
<td>Taking anticoagulant</td>
<td>3,099</td>
<td>54.0</td>
<td></td>
</tr>
<tr>
<td>Ineligible for anticoagulant</td>
<td>626</td>
<td>10.9</td>
<td></td>
</tr>
<tr>
<td>Eligible but not taking anticoagulant</td>
<td>2,014</td>
<td>35.1</td>
<td>100.0</td>
</tr>
<tr>
<td>Taking antiplatelets†</td>
<td>396</td>
<td>6.9</td>
<td>19.7</td>
</tr>
<tr>
<td>Not taking antiplatelets</td>
<td>1,618</td>
<td>28.2</td>
<td>80.3</td>
</tr>
</tbody>
</table>

† It is assumed that all patients with diagnosed AF ineligible for anticoagulant therapy are treated with antiplatelets.
Appropriate anticoagulant management of AF in all eligible patients could avert an estimated 4,551 strokes each year. This translates to £97 million savings in NHS and PSS costs through avoiding the need for acute stroke treatment each year. Estimated societal cost savings are £259 million in the first year after achieving the target. Potential cost savings over a 5-year period, which incorporate savings arising from reduced burden on informal carers in subsequent years post-stroke, are summarised in Table 6. Over a 5 year period, appropriate management of all previously diagnosed AF cases eligible for anticoagulant medication could lead to 22,755 fewer new strokes, 8,727 fewer prevalent cases of stroke by year 5 and produce societal savings of £2 billion, including £691 million in savings to NHS and PSS. These estimates do not include the additional cost of medication and administration associated with the strategy.

Table 5: Estimated number of strokes avoidable through anticoagulant therapy

<table>
<thead>
<tr>
<th>Patient category</th>
<th>Number of strokes per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of AF-related strokes not treated with anticoagulants</td>
<td>8,232</td>
</tr>
<tr>
<td>Taking antiplatelets (19.7%)</td>
<td>1,622</td>
</tr>
<tr>
<td>Number of strokes avoided (OR 0.68)</td>
<td>519</td>
</tr>
<tr>
<td>Not taking antiplatelets (80.3%)</td>
<td>6,610</td>
</tr>
<tr>
<td>Number of strokes avoided (OR 0.39)</td>
<td>4,032</td>
</tr>
<tr>
<td><strong>Total number of avoided strokes</strong></td>
<td><strong>4,551</strong></td>
</tr>
</tbody>
</table>

Table 6: Estimated cost savings over 5 years (2015 prices) of appropriate anticoagulant management of all AF patients

<table>
<thead>
<tr>
<th>Year</th>
<th>Incident</th>
<th>Prevalent</th>
<th>NHS and PSS</th>
<th>Informal care</th>
<th>Lost Productivity</th>
<th>Total societal cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4,551</td>
<td>0</td>
<td>£97,132</td>
<td>£152,663</td>
<td>£8,915</td>
<td>£258,711</td>
</tr>
<tr>
<td>2</td>
<td>4,551</td>
<td>2,867</td>
<td>£121,636</td>
<td>£210,597</td>
<td>£14,690</td>
<td>£346,922</td>
</tr>
<tr>
<td>3</td>
<td>4,551</td>
<td>5,247</td>
<td>£141,978</td>
<td>£258,689</td>
<td>£19,483</td>
<td>£420,150</td>
</tr>
<tr>
<td>4</td>
<td>4,551</td>
<td>7,191</td>
<td>£158,593</td>
<td>£297,972</td>
<td>£23,398</td>
<td>£479,963</td>
</tr>
<tr>
<td>5</td>
<td>4,551</td>
<td>8,727</td>
<td>£171,722</td>
<td>£329,010</td>
<td>£26,492</td>
<td>£527,223</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>22,755</strong></td>
<td></td>
<td><strong>£691,061</strong></td>
<td><strong>£1,248,931</strong></td>
<td><strong>£92,977</strong></td>
<td><strong>£2,032,970</strong></td>
</tr>
</tbody>
</table>

By 2021/22, improvement in warfarin time in therapeutic range

The effectiveness of warfarin is dependent on the quality of anticoagulation, whilst balancing the risk of haemorrhage. Optimal risk reduction occurs when the International Normalised Ratio (INR) is between 2 and 3. The proportion of time spent within this therapeutic range (TTR) during warfarin therapy is an indicator of quality of therapy and a predictor of stroke and mortality. However, evidence from large randomised controlled trials of
Anticoagulant medications suggest that only 60% of patients on warfarin achieve the TTR for warfarin (ACTIVE Writing Group of the ACTIVE Investigators et al., 2006; Miura et al., 2009; The SPAF III Writing Committee for the Stroke Prevention in Atrial Fibrillation Investigators, 1998).

A TTR of ≥70% is associated with a four-fifth reduction in the risk of stroke (RR 0.21, C.I. 0.18-0.25) compared to patients with a TTR of 30% or less, based on data from UK general practices (Gallagher et al., 2011). Another study used pooled data from three major randomised controlled trials of anticoagulant therapy in AF to demonstrate a statistically significant effect of TTR for warfarin therapy on the rate of stroke. They reported that for every 10% increase in TTR, stroke event rates decreased by 0.32% per year. Specifically, the rate of stroke at 60% TTR was 1.25, 1.04 for 70% TTR, 0.83 for 80% TTR and 0.62 for 90% TTR. In case of haemorrhagic stroke, the rate was 0.44 for 60% TTR, 0.37 for 70% TTR, 0.29 for 80% TTR and 0.22 TTR for 90%. Varying TTR did not have a significant effect on the rate of major bleeding (Amin et al., 2014).

Based on these findings, we can assume that increasing TTR for warfarin from 60% to 70%, 80% and 90% would reduce the rate of stroke by an estimated 16%, 34% and 50%, respectively. Assuming that 20% of 117,600 patients admitted for stroke each year have a prior diagnosis of AF, 54% of whom are treated with anticoagulants, 12,701 stroke cases each year could be avoided by improving TTR during warfarin therapy. If we assume a modest increase in mean TTR from 60% to 70%, 16% of the above incident cases could potentially be prevented (2,032 per year). This corresponds to 10,160 incident cases and 3,897 prevalent cases of stroke prevented at 5 years after implementation. If we apply the same broad logic as for the two previous scenarios to estimate potential cost savings from different cost perspectives, increasing TTR of warfarin from 60% to 70% can potentially result in societal cost savings of £908 million within 5 years of implementation (Table 7).

This estimate is subject to certain assumptions. The distribution of TTR across the population of patients with AF is unknown; the calculation assumes that the distribution is sufficiently narrow so that improvement in anticoagulant treatment across the board results in the mean TTR value moving from 60% to 70% and a proportional effect on the risk of stroke. In reality the risk of stroke is most likely non-linear, e.g. moving from 60% to 70% represents a larger reduction than moving from 70% to 80%.

### Table 7: Estimated cost savings (2015 prices) at 5 years after achieving target, if time spent within therapeutic range of warfarin is increased from a reference base case of 60% to 70%.

<table>
<thead>
<tr>
<th>Number of cases avoided</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident</td>
<td>10,160</td>
</tr>
<tr>
<td>Prevalent</td>
<td>3,897</td>
</tr>
<tr>
<td><strong>Cost (£m)</strong></td>
<td></td>
</tr>
<tr>
<td>NHS and PSS</td>
<td>£308.6</td>
</tr>
<tr>
<td>Informal care</td>
<td>£557.7</td>
</tr>
<tr>
<td>Lost productivity</td>
<td>£41.5</td>
</tr>
<tr>
<td><strong>Total societal cost</strong></td>
<td>£907.7</td>
</tr>
</tbody>
</table>
6.2 Hypertension

Hypertension is a major modifiable risk factor for stroke. Stroke sufferers were 2.79 times more likely to have pre-existing hypertension compared to non-stroke controls in high-income countries, according to a large case-control study carried out in 22 countries (INTERSTROKE study; O’Donnell et al., 2010). Hypertension is highly prevalent in the UK population, with an estimated 13.8% of people in England with a diagnosis of high blood pressure according to data collected in the Quality and Outcomes Framework (QOF) in 2015–16 (NHS Digital, 2016). Furthermore, a large number of people in England live with high blood pressure which has not been formally diagnosed. Public Health England (PHE) estimated that a further 5.6 million people in England (9.8% of the population) lived with undiagnosed hypertension in 2014, by modelling data from Health Survey for England (Public Health England, 2016).

New calculations

A new strategy to increase the proportion of diagnosed and appropriately treated hypertension could reduce the number of new stroke cases, yield significant savings from avoided treatment costs and yield gains in quality of life and reduced stroke-related mortality. Here, we estimate such potential gains associated with two scenarios:

- **By 2021/22, 15% increase in proportion of adults with blood pressure controlled to 140/90**
- **By 2021/22, 15% increase in hypertension diagnosis**

The two scenarios are not assumed to be mutually exclusive and their economic impact would be additive to some extent if both were to be implemented. Literature-based estimates of the potential reduction in the number of new stroke cases in the UK are combined with our estimates of the mean cost of incident and prevalent stroke (Patel et al., forthcoming). In the first year post-stroke, average per-person costs were £18,081, £25,897 and £1,431 for NHS and PSS, informal care and lost productivity respectively; in subsequent years post-stroke, equivalent costs were £7,759, £15,354 and £1,666 respectively. Total societal cost of stroke was thus £45,409 in the first year and £24,778 in subsequent years conditional on survival.

**Public Health England (PHE) estimates:**

In 2014 PHE commissioned Optimity Matrix to produce a report on the cost-effectiveness of selected interventions in the prevention and management of hypertension (Optimity Matrix, 2014; Public Health England, 2014). They undertook an extensive literature review and a modelling study to estimate potential cost savings, life-year gains and QALY gains from improved management and detection of hypertension. Incremental cost-effectiveness ratios (ICERs) were computed for specific interventions. Economic benefits were presented for a range of time horizons: 1, 5, 10 years and lifetime. The main findings relevant to our scenarios are as follows:

- **a 15% increase (from 59% to 74%) in the proportion of adults who have their high blood pressure diagnosed translates to 1.94 million people diagnosed, of whom 1.13 million will control their blood pressure. This translates to £33.3 million in NHS and PSS cost savings and 3,317 QALYs gained at 5 years; and**

- **a 15% increase (from 58% to 73%) in the proportion of adults treated for hypertension controlling their blood pressure to 140/90 mm Hg or lower is equivalent to 1.14 million people controlling their blood pressure. This translates to a saving of £33.7 million in NHS and PSS cost savings and 3,356 additional QALYs.**

These benefits and savings estimates were based on reduced risk of four conditions associated with hypertension: coronary heart disease, stroke, vascular dementia and chronic kidney disease. To isolate the economic benefits of reducing the risk of stroke, we combine the estimates from the Optimity Matrix model relating to stroke risk reduction with our own estimates of the cost of stroke to the NHS and PSS and society (in the 2015/16 cost year).
The distribution of hypertension is assumed to be the same as in the Optimity Matrix model: 31% normotensive (systolic blood pressure <120 mm Hg), 39% pre-hypertensive (≥120 and <140), 18% with stage 1 hypertension (≥140 and <160), 12% with stage 2 hypertension (≥160). The distribution of the risk of stroke across hypertension groups is taken from the INTERSTROKE study (O'Donnell et al., 2010). It reported the population attributable risk (PAR) of 0.346 and 0.518 for patients with blood pressure ≥140/90 mm Hg and ≥160/90 mm Hg, respectively. This corresponds to a relative risk of 2.2 and 3, respectively, compared to <140/90 mm Hg (O’Donnell et al., 2010). Thus the weighted annual risk of stroke is 0.001 in individuals with blood pressure below 140/90 mm Hg and 0.0025 for ≥140/90 mm Hg, given a crude incidence rate of 1.45 per 1,000 based in the OXVASC study (Rothwell et al., 2004) (details of calculation are in Table 8).

Table 8: Annual risk of stroke in different hypertension categories

<table>
<thead>
<tr>
<th>Category (mm Hg systolic)</th>
<th>Distribution</th>
<th>Relative risk of stroke</th>
<th>Annual risk of stroke, weighted by relative risk of stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sub-categories</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normotensive (&lt;120)</td>
<td>0.31</td>
<td>1</td>
<td>0.0000996</td>
</tr>
<tr>
<td>Pre-hypertensive (120-139)</td>
<td>0.39</td>
<td>1</td>
<td>0.0000996</td>
</tr>
<tr>
<td>Stage 1 HT (140-159)</td>
<td>0.18</td>
<td>2.2</td>
<td>0.002191</td>
</tr>
<tr>
<td>Stage 2+ HT (≥160)</td>
<td>0.12</td>
<td>3</td>
<td>0.002988</td>
</tr>
<tr>
<td><strong>Grouped categories</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;140 mm Hg</td>
<td>0.7</td>
<td>1</td>
<td>0.0000996</td>
</tr>
<tr>
<td>≥140 mm Hg</td>
<td>0.3</td>
<td>2.52</td>
<td>0.00251</td>
</tr>
<tr>
<td>Whole population</td>
<td>1</td>
<td>1.456</td>
<td>0.00145</td>
</tr>
</tbody>
</table>

Estimated cost savings associated with a 15% increase in the proportion of adults who have had their high blood pressure diagnosed (from 59% to 74%): The benefits of increasing the proportion of patients with a blood pressure diagnosis are estimated in terms of reduced risk of stroke associated with moving from high blood pressure (≥140/90 mm Hg) to normotensive (<140/90 mm Hg). It is assumed that 13.8% of the UK population (8.8 million) have a prior diagnosis of hypertension, which represents 58% of the total population of hypertensive adults, based on data from the Quality and Outcomes Framework (NHS Digital, 2016). An absolute increase of 15% would increase the total number of hypertensive individuals eligible for treatment by 2.3 million. Given that the proportion of individuals with a prior diagnosis and on treatment for hypertension who achieve BP <140/90 mm Hg is 63% (according to Public Health England data; Public Health England, 2014), the extra number who will achieve this target is 1.4 million. By applying the difference in the annual risk of stroke computed earlier, we estimate that 2,158 strokes may be avoided each year (details of the calculation are included in Table 9).
The estimated number of averted stroke cases is combined with mean costs of care for incident and prevalent stroke to gauge the total cost to the NHS and PSS and society over a 5 year period (Table 10). Increasing the proportion of hypertensive individuals with a diagnosis by 15% could potentially save £39 million in NHS and PSS costs for first-time stroke each year (excluding the cost of implementing the intervention). A further £55.9 million of informal care and £3.1 million of lost productivity could be avoided. Over a 5 year period, 10,790 new cases and 4,138 prevalent cases of stroke could be avoided, yielding potential cost savings of £772 million to society, £284 million of which is attributed to NHS and PSS.

### Table 9: Estimated number of stroke cases avoided through improved diagnosis of hypertension

<table>
<thead>
<tr>
<th>Category</th>
<th>N</th>
<th>Sources/notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid-2016 England population</td>
<td>63,818,387</td>
<td>ONS, 2016</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>15,082,984</td>
<td>Sum of diagnosed and undiagnosed</td>
</tr>
<tr>
<td>Prior diagnosis of hypertension (58%)</td>
<td>8,802,823</td>
<td>≈13.8% of population in QOF (NHS Digital, 2016)</td>
</tr>
<tr>
<td>Undiagnosed = (42%)</td>
<td>6,280,161</td>
<td>≈12% of those aged ≥16 (Public Health England, 2016)</td>
</tr>
<tr>
<td>Total eligible for treatment if proportion of diagnosed increased by 15%</td>
<td>2,262,448</td>
<td>Based on figures reported above</td>
</tr>
<tr>
<td>Proportion of above expected to achieve BP &lt;140/90 mm Hg</td>
<td>1,425,342</td>
<td>63% (Public Health England, 2014)</td>
</tr>
<tr>
<td>Expected no. of strokes in this category, without treatment</td>
<td>3,578</td>
<td>Assuming annual rate 2.51 per 1000 from Table 1</td>
</tr>
<tr>
<td>Expected no. of strokes in this category, with treatment</td>
<td>1,420</td>
<td>Assuming annual rate 0.996 per 1000 from Table 1</td>
</tr>
<tr>
<td>Potential no. of averted stroke cases</td>
<td>2,158</td>
<td></td>
</tr>
</tbody>
</table>

### Table 10: Estimated cost savings over 5 years (2015 prices) from a 15% increase (from 59% to 74%) in the proportion of adults who have their high blood pressure diagnosed

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of cases</th>
<th>Potential cost savings (£ '000)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incident</td>
<td>Prevalent</td>
</tr>
<tr>
<td>1</td>
<td>2,158</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>2,158</td>
<td>1,359</td>
</tr>
<tr>
<td>3</td>
<td>2,158</td>
<td>2,488</td>
</tr>
<tr>
<td>4</td>
<td>2,158</td>
<td>3,410</td>
</tr>
<tr>
<td>5</td>
<td>2,158</td>
<td>4,138</td>
</tr>
<tr>
<td>Total</td>
<td>10,790</td>
<td></td>
</tr>
</tbody>
</table>
**Estimated cost savings associated with a 15% increase in the proportion of adults treated for hypertension controlling their blood pressure to 140/90 mm Hg or lower (from 63% to 78%):**

The benefits of increasing the proportion of patients treated for hypertension who control their blood pressure is estimated in terms of reduced risk of stroke associated with moving from high blood pressure (≥140/90 mm Hg) to normotensive (<140/90 mm Hg). Based on QOF data, 13.8% of the population in England have a diagnosis of hypertension (8.8 million) (NHS Digital, 2016). Given that the proportion of individuals with a prior diagnosis and on treatment for hypertension who achieve BP <140/90 mm Hg is 63% (according to Public Health England data; Public Health England, 2014), currently 5.5 million people with hypertension control their blood pressure. If this proportion were to be increased by 15% to 78%, an additional 1.3 million people would benefit from a reduced risk of stroke. This translates to around 2,000 avoided stroke cases annually, by applying the annual risk estimates reported in Table 11.

**Table 11: Estimated number of stroke cases avoided through improvement in control of blood pressure below 140/90 mm Hg**

<table>
<thead>
<tr>
<th>Category</th>
<th>N</th>
<th>Sources/notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid-2016 England population</td>
<td>63,818,387</td>
<td>ONS, 2016</td>
</tr>
<tr>
<td>Prior diagnosis of hypertension</td>
<td>8,802,823</td>
<td>≈13.8% of population in QOF (NHS Digital, 2016)</td>
</tr>
<tr>
<td>No. treated for hypertension expected to achieve BP &lt;140/90 mm Hg</td>
<td>5,545,779</td>
<td>63% (Public Health England, 2014)</td>
</tr>
<tr>
<td>Additional no. to achieve BP &lt;140/90 mm Hg if proportion increased by 15%</td>
<td>1,320,424</td>
<td>Based on figures reported above</td>
</tr>
<tr>
<td>Expected no. of strokes in additional 15%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current (not achieving &lt;140/90 mm Hg)</td>
<td>3,314</td>
<td>Assuming annual rate 2.51 per 1000 from Table 1</td>
</tr>
<tr>
<td>Future (achieving &lt;140/90 mm Hg)</td>
<td>1,315</td>
<td>Assuming annual rate 0.996 per 1000 from Table 1</td>
</tr>
<tr>
<td>Potential no. of avoided stroke cases</td>
<td>1,999</td>
<td>Difference between future and present no. of strokes</td>
</tr>
</tbody>
</table>
The estimated number of averted stroke cases is combined with mean costs for incident and prevalent stroke to gauge the total cost to the NHS and PSS and society over a 5 year period (Table 12). Increasing the proportion of individuals with diagnosed hypertension who achieve BP <140/90 mm Hg by 15% could potentially save £36.1 million in NHS and PSS care for first-time stroke each year. A further £51.8 million in informal care costs and £2.9 million in lost productivity costs could be avoided. Over a 5 year period, 9,995 new cases and 3,833 prevalent cases of stroke could be avoided, yielding potential cost savings of £715 million to society, £263 million of which is attributed to NHS and PSS (Table 12).

Table 12: Estimated cost savings over 5 years (2015 prices) from a 15% increase (from 63% to 78%) in the proportion of adults treated for hypertension controlling their blood pressure to 140/90 mm Hg or lower

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of cases</th>
<th>Potential cost savings (£ ‘000)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incident</td>
<td>Prevalent</td>
</tr>
<tr>
<td>1</td>
<td>1,999</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1,999</td>
<td>1,259</td>
</tr>
<tr>
<td>3</td>
<td>1,999</td>
<td>2,305</td>
</tr>
<tr>
<td>4</td>
<td>1,999</td>
<td>3,159</td>
</tr>
<tr>
<td>5</td>
<td>1,999</td>
<td>3,833</td>
</tr>
<tr>
<td>Total</td>
<td>9,995</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions

We have examined evidence for various existing interventions related to stroke rehabilitation and long-term care, acute care and prevention: early mobilisation, physiotherapy, occupational therapy, speech and language therapy, psychological assessment and support, early supported discharge, centralisation of acute care services, thrombolysis, thrombectomy, management of atrial fibrillation and management of hypertension.

In the broad area of rehabilitation and long-term care, we find savings-potential from extending early supported discharge provision and preventing post-stroke pneumonia through better management of dysphagia. Economic evidence for effective interventions related to physiotherapy, occupational therapy and psychological support, especially in the longer term, is sparse.

In acute care, centralising services to increase the delivery of effective urgent care offers opportunities to decrease mortality and reduce hospital stay and there is much scope to reduce costs by increasing the proportion of eligible people who receive thrombolysis and thrombectomy.

Better stroke prevention, in the form of greater diagnosis and treatment of atrial fibrillation and hypertension, offers significant scope for cost savings.

Inevitably, current resources, system pressures and practical hurdles create challenges for achieving such measures. Increased investments and a more co-ordinated approach could alleviate the future burden of stroke, improve outcomes and reduce variations in stroke care.


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Email: info@stroke.org.uk  
From a textphone: 18001 0303 3033 100

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