QJM: An International Journal of Medicine, 2025, **00(0)**, 1–12
https://doi.org/10.1093/qjmed/hcaf029
Advance Access Publication Date: 24 January 2025
Review

Integrated care management for patients following acute stroke: a systematic review

Ian Eustace [1,2], Benjamin J.R. Buckley [2,3], Isik Kaya[4], Katie L. Hoad [3], Madeleine France-Ratcliffe [3], Andrew M. Hill [5], Gregory Y.H. Lip[2,6], Ian D. Jones [1,2] and Karen Higginbotham [1,2,*]

[1]School of Nursing and Advanced Practice, Liverpool John Moores University, Liverpool, UK
[2]Liverpool Centre for Cardiovascular Science, University of Liverpool, Liverpool John Moores University and Liverpool Heart and Chest Hospital, Liverpool, UK
[3]Cardiovascular Health Sciences, Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, UK
[4]West Hertfordshire Teaching Hospitals NHS Trust, Watford, UK
[5]Mersey and West Lancashire Teaching Hospitals NHS Trust, Liverpool, UK
[6]Danish Center for Health Services Research, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

*Address correspondence to K. Higginbotham, Liverpool John Moores University, School of Nursing and Advanced Practice, Faculty of Health, Innovation, Technology and Science, Rm 2.21, Tithebarn Building, 81 Tithebarn Street, Liverpool, L2 2ER, UK. Email: K.Higginbotham@ljmu.ac.uk

Abstract

Contemporary stroke care is moving towards more holistic and patient-centred integrated approaches, however, there is need to develop high quality evidence for interventions that benefit patients as part of this approach. This study aims to identify the types of integrated care management strategies that exist for people with stroke, to determine whether stroke management pathways impact patient outcomes and to identify elements of integrated stroke care that were effective at improving outcomes. The study is a systematic review with meta-analysis. The review was conducted using Medline, CINAHL, Web of Science and the Cochrane Database of randomized controlled trials from January 2012 to January 2024. Studies that evaluated interventions as part of integrated care against a control or standard treatment group were included. Primary outcomes included mortality, recurrent stroke and major bleeding. Secondary outcomes included quality of life, unplanned readmission, anxiety and depression, lifestyle and cardiovascular risk factors, and adherence to intervention. In total, 99 studies were included and 63 were meta-analysed. Patients receiving integrated stroke care had significant reductions in recurrent stroke (RR 0.79, 95% CI: 0.63–1.00, $P = 0.05$, $I^2 = 39\%$), significant improvements in quality of life (SMD = 0.41, 95% CI: 0.26–0.56, $P < 0.00001$, $I^2 = 91\%$) and reduced incidence of depression (RR 0.95, 95% CI: 0.92–0.99, $P = 0.007$, $I^2 = 22\%$). There were no significant differences in mortality or major bleeding. The findings of this study show that integrated care post-stroke is associated with better quality of life and reduced depression and recurrent stroke.

Introduction

Effective stroke care needs an organizational structure that facilitates best treatments at the right time.[1] Contemporary stroke care commonly involves a multidisciplinary team of healthcare professionals.[2] Integrated care in stroke has been defined as a project network technique involving interdisciplinary interventions to improve communication and co-ordination between disciplines, providing a time frame for patient care, with regular monitoring of patient progression.[3] However, there is no unifying definition or common conceptual understanding of integrated care, and the perspectives that construct the concept can be shaped by views and expectations of various health system stakeholders.[4]

The centralization of stroke services in parts of the UK and the formation of hyperacute stroke units (HASUs) offering continual access to stroke specialists, investigations and interventions[5] can be considered to represent integrated care in acute stroke. The treatment of stroke patients in HASUs has resulted in reductions in mortality and length of hospital stay compared with traditional stroke units.[6,7]

Recently, there has been a move towards a more integrated or holistic management pathway for patients following acute stroke, which might prevent recurrent stroke and could also improve patient functional status, symptoms and comorbidities[2,8] however many challenges remain. These include a lack of consensus on the optimal care pathway for patients,[9,10] high heterogeneity among stroke treatment centres[11] and the continuing need to develop high quality evidence for prevention of secondary vascular events and risk factor management after stroke.[12–14]

With no clear definition of integrated care in stroke and no consensus on optimal patient management in the acute and post-acute settings, some clarification on which integrated care strategies are most beneficial to patients is needed. In this study, we aimed to identify the types of integrated care management strategies that exist for people with stroke, to determine whether stroke management pathways impact patient outcomes and to identify elements of integrated care that improved patient outcomes.

Methods

This systematic review was conducted in accordance with the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).

Received: 02 February 2024. **Revised (in revised form):** 10 January 2025.
© The Author(s) 2025. Published by Oxford University Press on behalf of the Association of Physicians.
This is an Open Access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.

Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025

Inclusion and exclusion criteria

Studies of integrated care in stroke patients were included in the review based on NHS/WHO definitions (Supplementary Material S1). Stroke was defined using the American Heart Association/American Stroke Association (AHA/ASA) guidelines.[12] Patients with any acute stroke or transient ischaemic attack (TIA) of any age, and any pathological type of stroke (ischaemic, venous, intracerebral haemorrhage) were included. All randomized controlled trials (RCTs), uncontrolled comparative trials, observational cohort studies, mixed methods and quantitative case studies were considered for inclusion whereas studies involving patients for which stroke was not the primary event or where a definitive diagnosis of stroke could not be confirmed were excluded.

Search strategy

The search strategy used medical subject headings (MeSH) terms and synonyms for "stroke" and "integrated care". These terms were combined with Boolean operators, truncations and wildcards. Studies with evidence of a multidisciplinary approach to care with or without a patient-centred focus were included. MEDLINE, CINAHL, Web of Science and the Cochrane Central Register of Controlled Trials were searched from 1 January 2012 to 1 January 2024 for relevant studies (Supplementary Material S1).

Data extraction

Data extraction was conducted independently by I.E., K.L.H., M.F-R. and I.K. using a bespoke data extraction tool and included: (a) authors, publication year, country of origin, reference; (b) study design with inclusion/exclusion criteria; (c) aims and objectives; (d) demographic data (including *n*=, age, sex, ethnicity, disease characteristics, co-morbidities); (e) description of intervention and/or comparator; (f) outcomes (effectiveness and safety); (g) results; (h) conclusions and (i) risk of bias assessment.

Risk of bias assessment

Risk of bias was independently assessed in duplicate by I.E. and I.K., K.L.H. or M.F-R. and discrepancies were discussed and resolved with a third reviewer (B.R.J.B). The Cochrane Risk of Bias v.2 (RoB2) tool[15] and the Risk Of Bias In Non-randomized Studies—of Interventions (ROBINS-I)[16] were used for randomized and non-randomized trials, respectively.

Data synthesis

Results of the systematic review were grouped by outcome (primary: mortality, recurrent stroke, major bleeding; secondary: quality of life, unplanned readmission, depression/anxiety, treatment adherence). Meta-analyses were conducted for comparable studies where sufficient data were present. Primary and secondary outcome effect measures with 95% confidence intervals (CI) were pooled using RevMan software version 5.4.[17] Random effects models were used, allowing for between-study variability by weighting studies using a combination of intra- and inter-study variance. Results were presented visually using Forest plots. Heterogeneity was assessed visually and using the I^2 statistic with 25%, 50% and 75% considered moderate, substantial and considerable heterogeneity, respectively.

To measure overall treatment effects, the Der Simonian & Laird method for both binary (e.g. mortality) and continuous (e.g. quality of life) outcomes was used. If continuous data were not homogeneous, an estimate of the standardized mean difference (SMD) with 95% CI was calculated. If quantitative data were too few or too heterogeneous, then a narrative synthesis approach was undertaken.

Analysis of subgroups or subsets

Mortality and other outcomes (where applicable) were analysed according to length of follow-up, via sub-group analyses to stratify for different follow-up time points. Quality of life and depression/anxiety data were grouped and analysed according to type of measurement tool (e.g. VAS, EQ-5D, HADS). Where feasible, SMDs were used to meta-analyse similar scales. Meta-analyses of randomized controlled trials (RCTs) and non-randomized trials (NRCTs) were conducted separately.

Results

An initial search yielded 27 271 records. After removal of duplicates, 330 papers were assessed for eligibility against the inclusion/exclusion criteria. Of these, 99 (30%) were included in the systematic review (Figure 1) and 63 (19%) were included in meta-analysis.

Characteristics of the included studies

The studies included in the review were published between January 2012 and January 2024. Of the 99 studies, the majority (64) were RCTs (Supplementary Material S2). The total number of participants included in the review was 88 435, of which 40 475 received an integrated care intervention or pathway comprising multiple interventions. Mean/median patient age ranged from 53 years[18–21] to 83 years[22] and the proportion of females ranged from 23%[23] to 70%[24].

Of the 64 RCTS, 10 were considered at low risk of bias, 33 were moderate risk and 21 studies were at high risk of bias due to small numbers, study design, confounding factors or missing data. Of 35 NRCTs, 20 were considered at moderate risk of bias and 15 studies were at high risk of bias (Supplementary Material S3).

Of the 99 individual studies, 28 included an exercise intervention, 28 included an educational component, 17 included a psychological intervention and 16 assessed lifestyle and cardiovascular risk factors. Forty-two (42) studies included multiple interventions or complete pathways and 19 studies were considered patient centred. Of the intervention types, exercise, lifestyle and mental health interventions positively impacted on the majority of protocol-specified primary and secondary outcomes across studies however only exercise positively impacted all outcomes.[18,25–36]

Overall, the results of the studies were inconclusive, with 34% showing no significant benefit of the intervention over the control or comparator group and there was substantial heterogeneity between studies.

Meta-analysis

The findings of the meta-analysis are summarized in Table 1.

Primary outcomes

Mortality

A total of 13 ($n = 21\,533$) RCTs compared integrated care with control for mortality (Figure 2A). Integrated care was not associated with reduced mortality (relative risk [RR] 0.79, 95% CI: 0.59–1.06, $I^2 = 74\%$). Sub-group analysis of NRCTs indicated a significant reduction in long-term (>1 year) mortality in favour of integrated

Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025

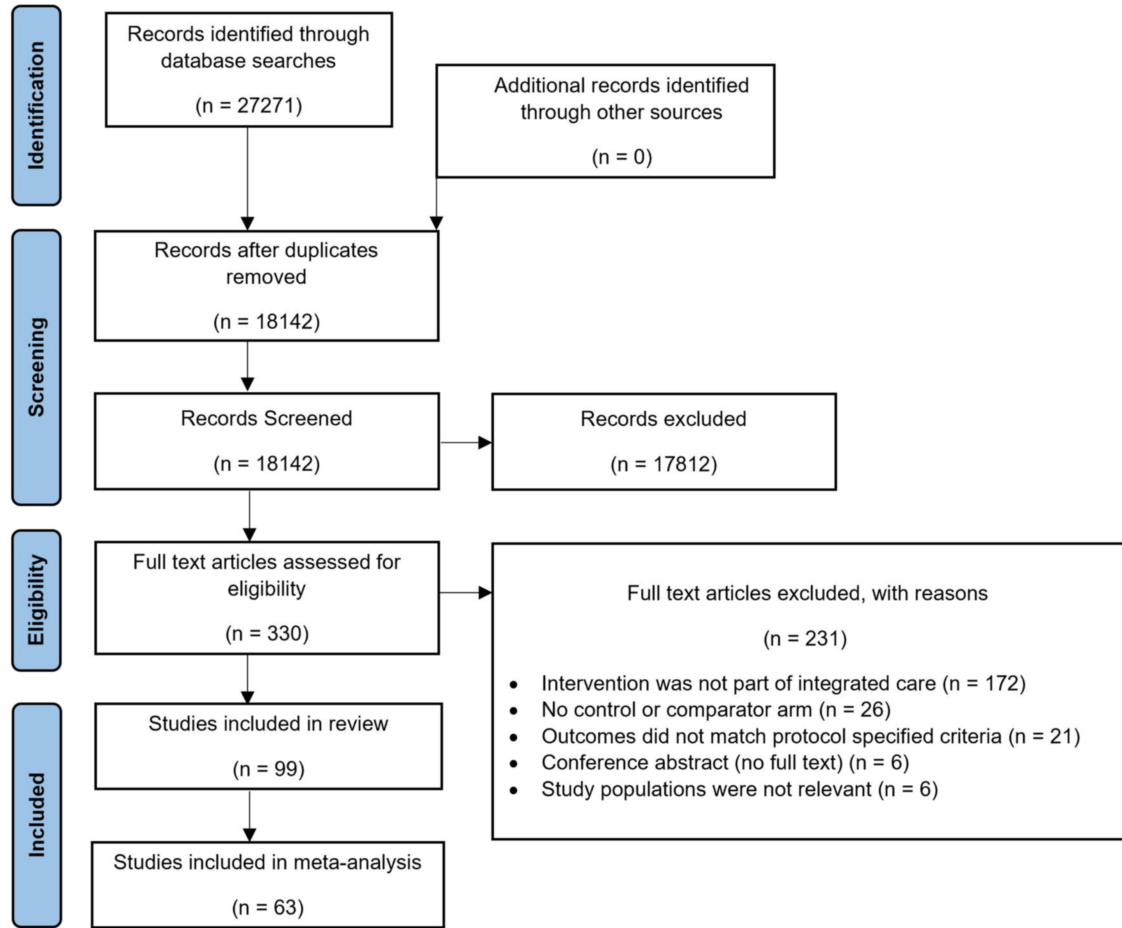


Figure 1. PRISMA chart for systematic review of integrated care in stroke.

care (RR 0.58, 95% CI: 0.43–0.80, $P=0.0007$, $I^2=86\%$) however there were only three studies ($n=9404$) included in this analysis (Figure 2B).

Recurrent stroke

A total of nine ($n=10\,915$) RCTs showed a statistically significant reduction in recurrent stroke in favour of integrated care (RR 0.79, 95% CI: 0.63–1.00, $P=0.05$, $I^2=39\%$, Figure 3A) however there was no difference in recurrent stroke between groups in NRCTs (RR 1.08, 95% CI: 0.64–1.82, $P=0.78$, $I^2=4\%$, Figure 3B).

Major bleeding

A total of four RCTs ($n=8210$) compared integrated care with control for major bleeding (Figure 4). There were more bleeding events associated with integrated care versus control (RR 1.35, 95% CI: 0.56–3.22, $I^2=84\%$), however the difference was not statistically significant ($P=0.50$).

Secondary outcomes

Quality of life

Meta-analysis was conducted on a total of 21 studies ($n=10\,653$) using SMD to combine different quality of life (QoL) scales (Figure 5). Overall, there were significant improvements in QoL in favour of integrated care (SMD = 0.41, 95% CI: 0.26–0.56, $P<0.00001$, $I^2=91\%$). Subgroup meta-analysis showed that the greatest differences in QoL were observed with SF-36 and SSQOL (Supplementary Material S4).

Unplanned readmission

There was no significant difference in unplanned (based on the assumption that the majority of readmissions were due to complications or events such as subsequent stroke or myocardial infarction [MI] that could not be predicted) readmission rates in nine ($n=7236$) RCTs (RR 0.88, 95% CI: 0.73–1.05, $P=0.15$, $I^2=71\%$, Figure 6A) or in five ($n=6370$) NRCTs (RR 0.76, 95% CI: 0.37–1.57, $P=0.46$, $I^2=97\%$, Figure 6B).

Anxiety and depression

Meta-analysis was conducted on seven ($n=36\,044$) RCTs reporting proportions of patients with depression using Yale-Brown, GDS, PROMS, PHQ2 and HADS-D scales (Figure 7). Integrated care was associated with a significant reduction in the proportion of patients with depression (RR 0.95, 95% CI: 0.92–0.99, $P=0.007$, $I^2=22\%$, Figure 7) regardless of follow-up time (up to 6 months or up to 12 months). Meta-analysis also showed that anxiety and depression scores were significantly lower with integrated care regardless of scale or follow-up time (Supplementary Material S4).

Lifestyle and cardiovascular risk factors

Overall, integrated care was associated with a significant improvement in cardiovascular risk (Table 1). Further information can be found in Supplementary Material S4.

Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025

Table 1 Summary of findings table for systematic review of integrated care

Outcomes	Relative effect (95% CI)	Number of participants (studies)	Comments
Primary			
Mortality	RCTs: RR 0.79 (0.59–1.06) NRCTs: RR 0.82 (0.45–1.49)	21 533 (13) 31 223 (9)	There were fewer death events in the integrated care groups compared with control but no significant overall difference in mortality in RCTs or NRCTs. The only significant difference in death events was observed in a subgroup analysis of long-term mortality in NRCTs (>1 year, 9404 patients, three studies, RR = 0.58, $P = 0.0007$)
Recurrent stroke	RCTs: RR 0.79 (0.63–1.00) NRCTs: RR 1.08 (0.64–1.82)	10 915 (9) 1604 (3)	There were significantly fewer recurrent strokes associated with RCTs of integrated care compared with control ($P = 0.05$) however there were no differences in NRCTs
Major bleeding	RR 1.35 (0.56–3.22)	8210 (4)	There were more major bleeding events in the integrated care groups compared with control but the difference was not statistically significant ($P = 0.50$)
Secondary			
Quality of life	SMD: 0.41 (0.26–0.56)	10 653 (21)	Integrated care interventions significantly improved quality of life ($P < 0.00001$), with the greatest difference in QoL scoring observed with the SF-36 general health questionnaire and the SSQOL scoring tools
Unplanned readmission	RCTs: RR 0.88 (0.73–1.05) NRCTs: RR 0.76 (0.37–1.57)	7236 (9) 6370 (5)	There were fewer unplanned readmission events associated with integrated care interventions however the differences were not significant in either RCTs ($P = 0.15$) or NRCTs ($P = 0.46$)
Anxiety and depression	Depression: RR 0.95 (0.92–0.99) Anxiety (HADS-A): RR 0.75 (0.57–0.99)	36 044 (7) 606 (3)	The proportion of patients with depression was significantly lower with integrated care compared with control ($P = 0.007$). An analysis of anxiety using the HADS-A assessment tool showed that the proportion of patients with anxiety was significantly lower with integrated care ($P = 0.04$)
Lifestyle and cardiovascular risk factors	SMD −0.17 (−0.25 to −0.09)	4538 (9)	Overall, integrated care was associated in a significant improvement in cardiovascular risk factors ($P < 0.0001$), with significant reductions in SBP and LDL-cholesterol (both $P \leq 0.03$) however there were no differences between groups for total cholesterol, BMI or the proportion of patients stopping smoking
Adherence to intervention	RR 1.31 (0.77–2.23)	3646 (4)	Integrated care was associated with higher rates of adherence compared with control however the difference was not statistically significant ($P = 0.32$)
Exploratory			
Favourable outcome (mRS ≤ 2)	RR 1.02 (0.98–1.07)	4751 (4)	There was no difference in the proportion of patients with favourable outcome between integrated care and control ($P = 0.35$)
Recurrent risk of cardiovascular disease: Myocardial infarction Vascular death	RR 0.60 (0.34–1.05) RR 0.58 (0.21–1.60)	7733 (3) 4221 (2)	There were fewer events of myocardial infarction and vascular death associated with integrated care however these differences were not statistically significant (MI, $P = 0.07$; vascular death, $P = 0.30$)

Patient or population: people with stroke.
Setting: during and after care.
Intervention: Integrated care.
Comparison: Control; end of intervention.
BMI, body mass index; CI, confidence interval; HADS-A, hospital anxiety and depression scale-anxiety component; LDL, low density lipoprotein; MI, myocardial infarction; mRS, modified Rankin Scale; NRCT, nonrandomized controlled trial; RCT, randomized controlled trial, RR, risk ratio; SBP, systolic blood pressure; SMD, standardized mean difference.

Adherence to intervention

Overall, adherence rates were higher with integrated care but the difference was not statistically significant ($P = 0.32$, Table 1). Further information can be found in Supplementary Material S4.

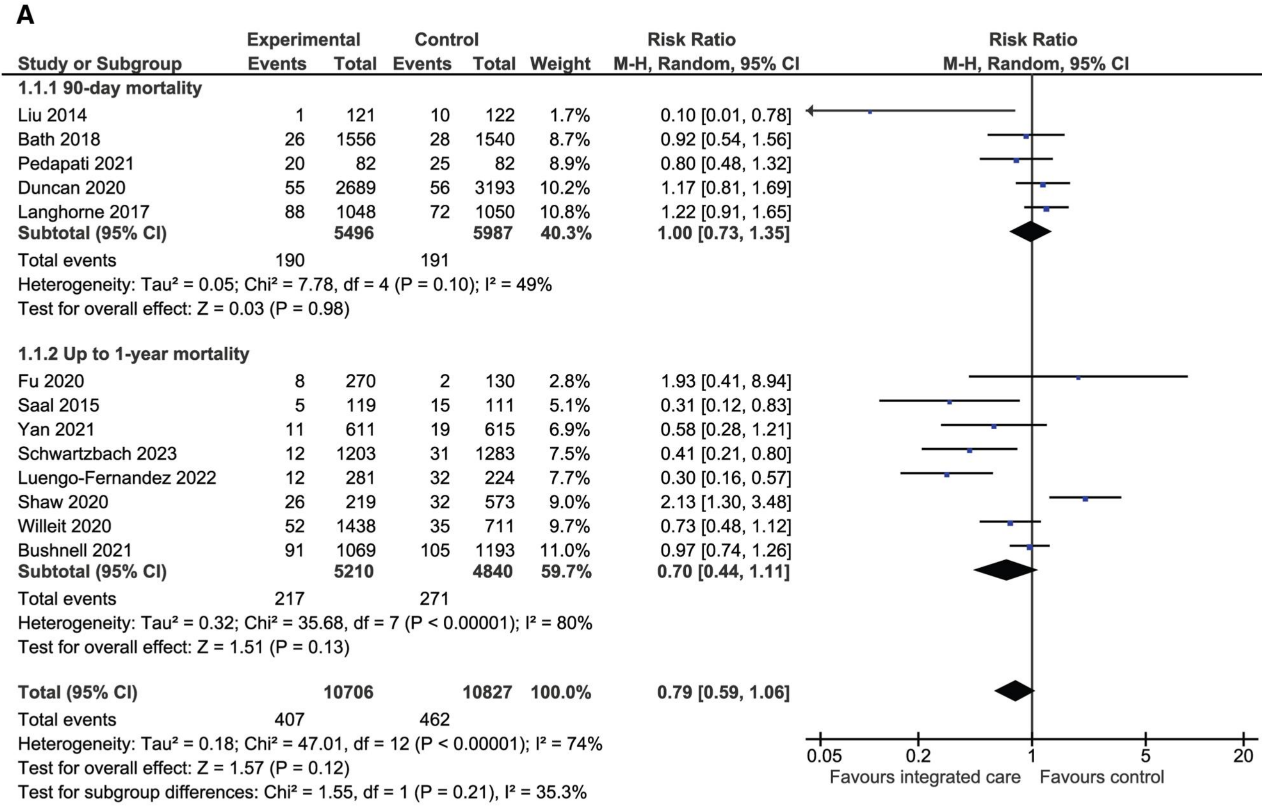
Exploratory analysis: functional status

An exploratory meta-analysis was conducted on four RCTs ($n = 4751$) that included data on functional status according to the modified Rankin Scale (mRS). This analysis showed no significant difference in favourable outcome (defined as mRS ≤ 2) between integrated care and control (RR 1.02, 95% CI: 0.98–1.07, $P = 0.35$, $I^2 = 77\%$, Figure 8).

Exploratory analysis: recurrent risk of cardiovascular disease

Meta-analysis was conducted for MI (three studies, $n = 7733$) and vascular death events (two studies, $n = 4221$). Although there were fewer events associated with integrated care, these differences were not statistically significant (Table 1). Further information can be found in Supplementary Material S4.

Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025



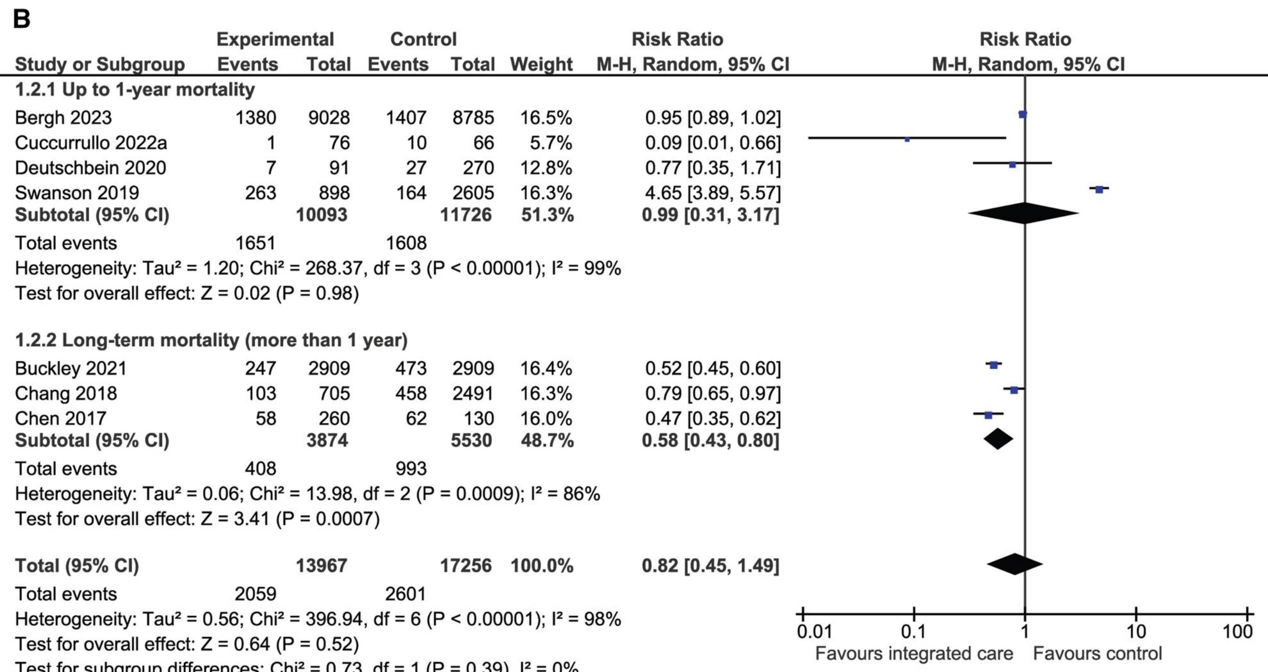


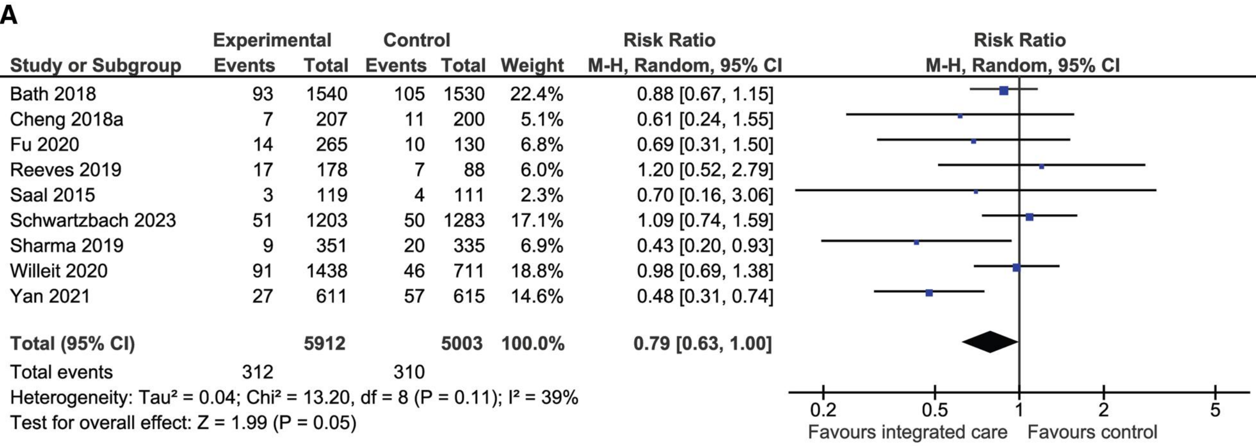
Figure 2. Comparison of integrated care with control for mortality (A, randomized controlled trials; B, nonrandomized trials).

Discussion

To our knowledge, this is the first comprehensive systematic review with meta-analyses of integrated care in stroke showing that integrated care was associated with improvements in QoL, reductions in recurrent stroke, anxiety and depression and positive benefits on some cardiovascular risk factors but did not impact mortality, major bleeding or readmission rates. Other systematic reviews have evaluated interventions such as organized inpatient stroke care,[37] exercise,[38–41] early supported discharge[42–44] and interventions for cognitive rehabilitation,[45] depression[46] and anxiety[47] however none of these reviews were conducted in the setting of integrated care.

Whilst some studies demonstrated a benefit in outcomes with integrated care interventions, other studies using similar

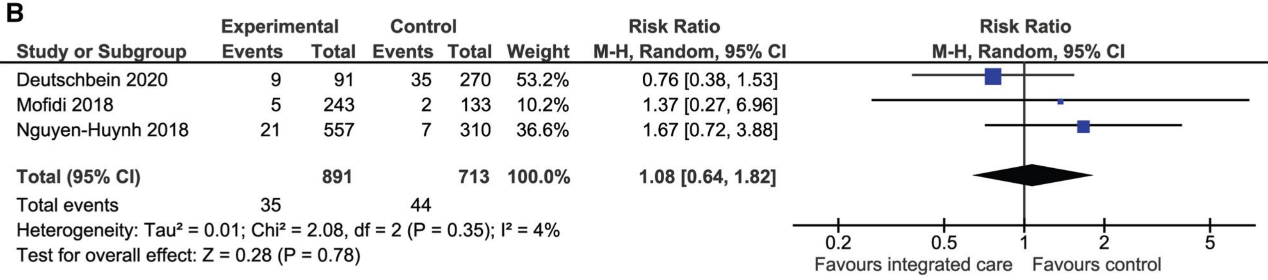
Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025



A

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Bath 2018	93	1540	105	1530	22.4%	0.88 [0.67, 1.15]
Cheng 2018a	7	207	11	200	5.1%	0.61 [0.24, 1.55]
Fu 2020	14	265	10	130	6.8%	0.69 [0.31, 1.50]
Reeves 2019	17	178	7	88	6.0%	1.20 [0.52, 2.79]
Saal 2015	3	119	4	111	2.3%	0.70 [0.16, 3.06]
Schwartzbach 2023	51	1203	50	1283	17.1%	1.09 [0.74, 1.59]
Sharma 2019	9	351	20	335	6.9%	0.43 [0.20, 0.93]
Willeit 2020	91	1438	46	711	18.8%	0.98 [0.69, 1.38]
Yan 2021	27	611	57	615	14.6%	0.48 [0.31, 0.74]
Total (95% CI)		**5912**		**5003**	**100.0%**	**0.79 [0.63, 1.00]**
Total events	312		310			

Heterogeneity: Tau² = 0.04; Chi² = 13.20, df = 8 (P = 0.11); I² = 39%
Test for overall effect: Z = 1.99 (P = 0.05)



B

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Deutschbein 2020	9	91	35	270	53.2%	0.76 [0.38, 1.53]
Mofidi 2018	5	243	2	133	10.2%	1.37 [0.27, 6.96]
Nguyen-Huynh 2018	21	557	7	310	36.6%	1.67 [0.72, 3.88]
Total (95% CI)		**891**		**713**	**100.0%**	**1.08 [0.64, 1.82]**
Total events	35		44			

Heterogeneity: Tau² = 0.01; Chi² = 2.08, df = 2 (P = 0.35); I² = 4%
Test for overall effect: Z = 0.28 (P = 0.78)

Figure 3. Comparison of integrated care with control for recurrent stroke (A, randomized controlled trials; B, nonrandomized controlled trials).

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Bath 2018	31	1541	14	1531	25.7%	2.20 [1.18, 4.12]
Schwartzbach 2023	31	1151	8	1152	24.1%	3.88 [1.79, 8.40]
Sharma 2019	12	351	19	335	24.8%	0.60 [0.30, 1.22]
Willeit 2020	20	1438	15	711	25.3%	0.66 [0.34, 1.28]
Total (95% CI)		**4481**		**3729**	**100.0%**	**1.35 [0.56, 3.22]**
Total events	94		56			

Heterogeneity: Tau² = 0.66; Chi² = 19.11, df = 3 (P = 0.0003); I² = 84%
Test for overall effect: Z = 0.67 (P = 0.50)

Risk Ratio M-H, Random, 95% CI: 0.1 0.2 0.5 1 2 5 10 — Favours Integrated care / Favours control

Figure 4. Comparison of integrated care with control for major bleeding (randomized controlled trials).

interventions did not. These observations highlight a lack of consensus over which components should form part of an integrated stroke pathway and how they should be implemented. Indeed, individual studies demonstrated that interventions such as exercise, rehabilitation, risk factor management and mental health initiatives were most effective at improving outcomes in people with stroke. These included studies of cardiovascular exercise and high-intensity rehabilitation that were associated with significantly lower mortality rates.[25,35,48] The EXPRESS study of rapid assessment and treatment initiation with high-dose aspirin or clopidogrel and intensive and regular follow-up demonstrated a reduction in stroke risk and disability (mRS ≥ 2) even after 10 years.[49] Similarly, the COMPASS study of combined anticoagulant and antiplatelet therapy significantly reduced the risk of ischaemic/unknown stroke in 1032 patients with prior stroke (HR, 0.33, 95% CI: 0.14–0.77, $P = 0.01$).[50] The STROKE-CARD study, a comprehensive disease management program delivered by a multidisciplinary team that included risk factor management and patient education, reported reduced cardiovascular risk and improved QoL.[51] Studies employing interventions such as early supported discharge, regular community follow-up, education, cognitive and motivational training, and goal setting reported significant reductions in the proportions of participants with depression or anxiety and improvements in QoL,[30,36,52–57] with individualized care pathways and mhealth technology providing substantial improvements in these outcomes.[20,55,58–60]

Conversely, there are large and well-designed randomized trials of comprehensive integrated care interventions that did not demonstrate any substantial benefit over standard care. The structured ambulatory post-stroke care program (SANO) study, a 1-year patient-centred integrated care intervention including regular follow-up, lifestyle advice, goal setting and motivational interviewing, demonstrated positive benefits in controlling CV risk factors such as blood pressure and LDL cholesterol, but did not reduce the rate of major cardiovascular events.[61] In the Triple Antiplatelets for Reducing Dependency after Ischaemic

Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025

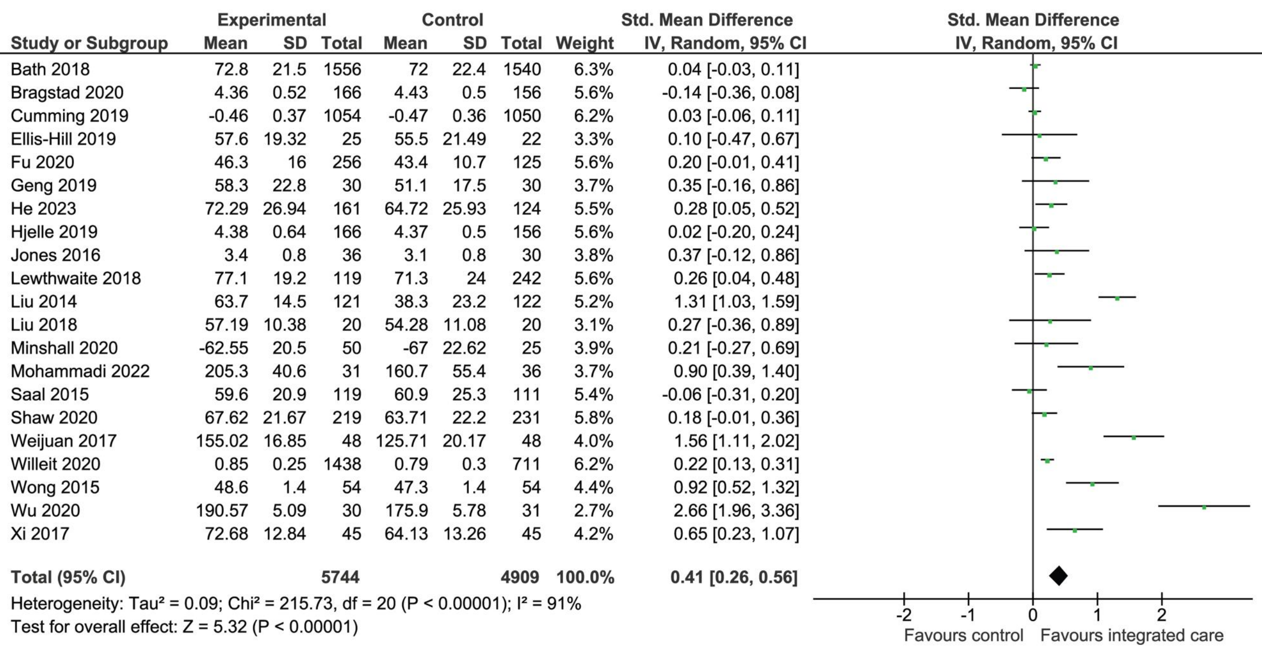
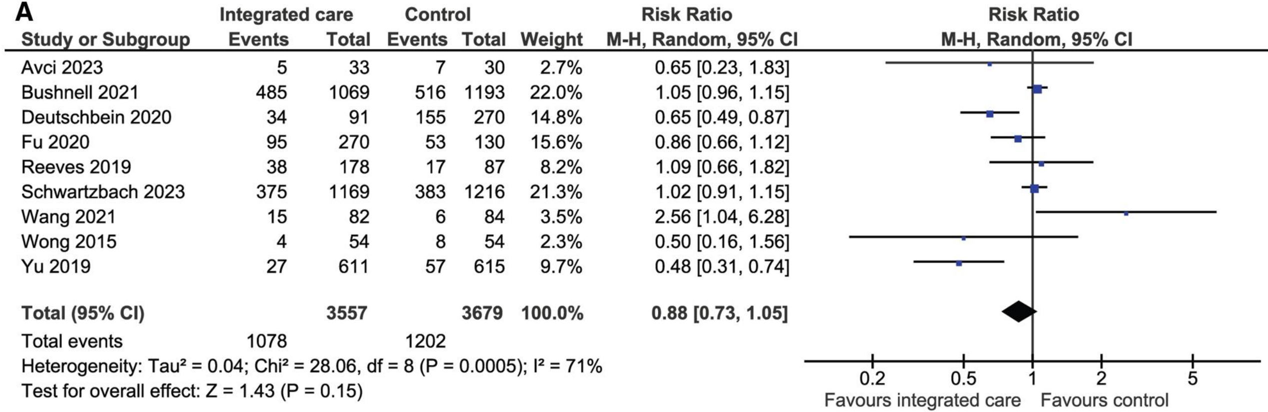


Figure 5. Comparison of integrated care with control for quality of life (randomized controlled trials).



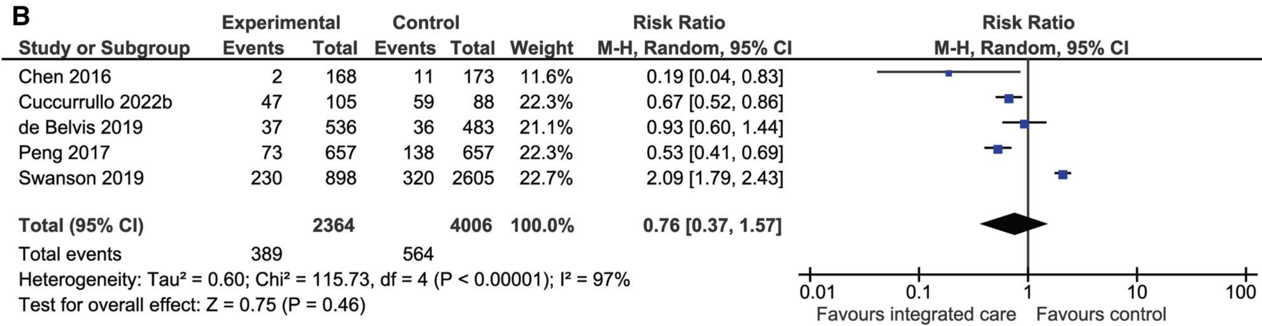


Figure 6. Comparison of integrated care with control for unplanned readmission (A, randomized controlled trials; B, nonrandomized controlled trials).

Stroke (TARDIS) study, significantly more bleeding events were reported overall in the TARDIS group (19.8%) compared with the control group (9.1%, $P < 0.001$), prompting the study to be stopped early.[62] The Very Early Rehabilitation Trial for stroke study (AVERT) showed significantly fewer participants in the AVERT group had favourable outcome and there was no difference in mortality or QoL.[63–65]

Overall, the results of this systematic review are inconsistent, with 34% of reviewed studies showing no benefit over comparator treatment and substantial heterogeneity between studies.

The centralization of stroke services and the creation of HASUs has improved outcomes for patients compared with traditional stroke units, reflected in reduced mortality rates and hospital length of stay[6,7] however there is currently no standard

Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025

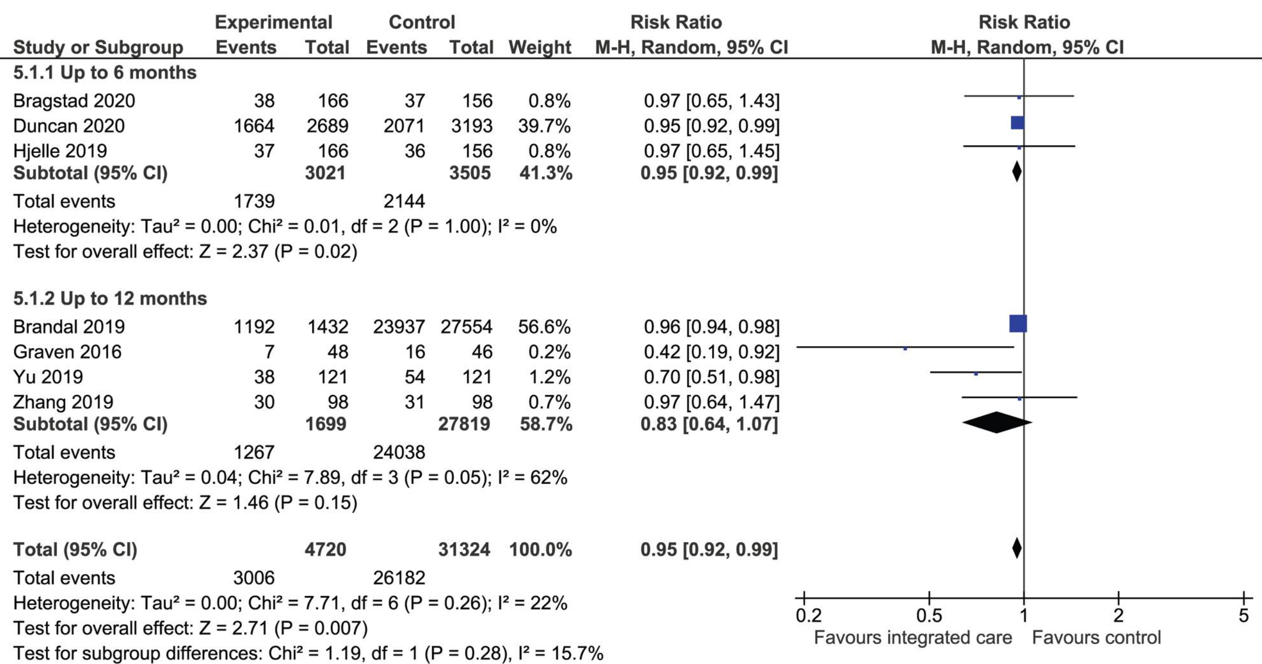


Figure 7. Comparison of integrated care with control for proportion of patients with depression by follow-up time.

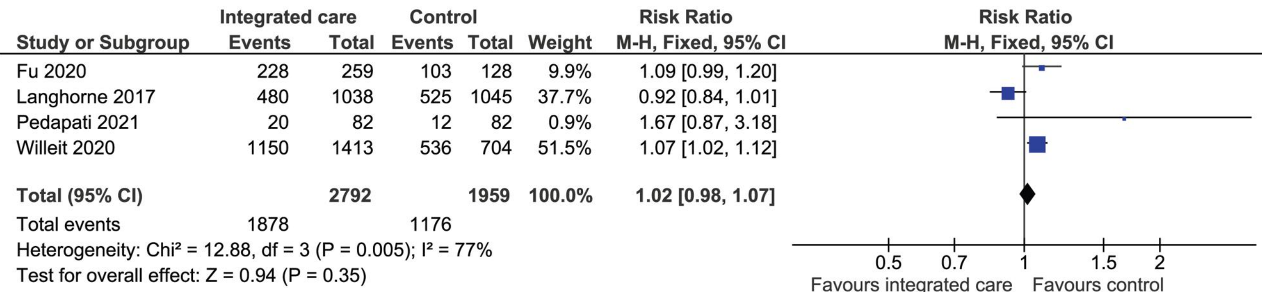


Figure 8. Comparison of integrated care with control for proportion of patients with favourable outcome (mRS $\leq$ 2).

HASU care pathway and outcomes vary widely as a result.[66,67] Much of the published data on stroke care management is in the acute setting,[68] where integrated care plans such as early supported discharge[43,44,53,69,70] are often clearly defined however less is known about patient care following discharge back into the community and studies show that care from this point onwards is often discontinuous,[71–73] which can result in unmet needs and increased potential for hospitalization and institutionalization.[72] A recent Sentinel Stroke National Audit Programme (SSNAP) annual report identified a decline in the proportion of patients receiving a 6-month review and highlighted the need for an adequately resourced multidisciplinary team of healthcare professionals required to deliver the recommended amount of rehabilitation of patients according to their need, especially in the community setting.[74]

Primary outcomes

Meta-analysis showed no difference overall in mortality between integrated care and control or standard care. Although subgroup analysis showed a significant reduction in long-term mortality in favour of integrated care, there were only three studies in this subgroup and the findings must be interpreted with caution. The overall findings are consistent with the published literature with systematic reviews of early supported discharge and exercise showing no significant differences in mortality rates compared with standard care.[43,44,75]

A statistically significant reduction in recurrent stroke in favour of integrated care was observed with RCTs but not with NRCTs. Few systematic reviews have directly assessed the impact of interventions on recurrent stroke as an outcome however the interventions in this analysis that were associated with reductions in recurrent stroke (lifestyle and cardiovascular risk factor management) have also been shown to reduce recurrent stroke rates in meta-analyses.[76–78]

Integrated care was associated with more major bleeding events compared with standard care however the difference was not statistically significant ($P = 0.50$). There are numerous meta-analyses comparing oral anticoagulants for stroke prevention in patients with atrial fibrillation (AF) and in general direct oral anticoagulants (DOAC) have a lower bleeding risk than Vitamin K agonists (VKA).[79–82] Combination treatment with anticoagulant and antiplatelets is associated with increases in the risk of major bleeding in cardiovascular disease (CVD).[83,84] In this review, the TARDIS and COMPASS studies reported increased major bleeding events with triple therapy and reduced events with low-dose rivaroxaban and aspirin treatment, respectively.[50,62] Meta-analyses of major

Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025

bleeding risk in stroke survivors are currently lacking in the published literature.

Secondary outcomes

Overall, integrated care was associated with improvements in QoL and the magnitude of improvement was greatest with the SF-36 and SSQOL assessment tools however these findings must be interpreted in the presence of substantial (>75%) heterogeneity between studies. Meta-analysis also showed that integrated care was associated with statistically significant reductions in the proportion of patients with anxiety and depression, with a statistically significant benefit for the cardiovascular risk factors of systolic blood pressure (SBP) and LDL cholesterol.

Improvements in QoL are documented in the literature with interventions such as organized stroke care[37] and exercise[75,85,86] however the degree of improvement in QoL is difficult to define due to lack of information.[75]

Limitations

There is currently no standard or unifying definition of integrated care and delivery is likely to be influenced by views and expectations of various stakeholders in the health system,[4] an observation that has been confirmed in studies of hyperacute stroke care where different outcomes were reported due to differences in care models and priorities.[66,67] For example, centralization of stroke services in London resulted in a significant reduction in mortality rates since almost all London patients were treated in a HASU and were more likely to receive evidence-based care whereas stroke patients in Manchester were far less likely to be treated in a HASU and receive evidence-based care, resulting in unchanged mortality rates.[66] The WHO reports large variations in the definition of integrated care and for the purposes of this review, we used a definition of integrated care developed by the NHS and WHO (Supplementary Material S1) and included studies where there was evidence of an integrated care approach according to this definition however some studies could have been missed during the literature searches if they were not considered to be integrated care per definition. Due to the volume of published studies in stroke, the search was restricted to 12 years however it is possible that some important studies could have been missed if they fell outside of the search window. Most of the integrated care trials in this review included multiple interventions or comprised complete pathways and the effect of individual interventions could not be assessed.

Meta-analysis of outcomes indicates high heterogeneity between studies, in particular those evaluating QoL, which confounds interpretation of the findings. Due to the majority of studies having small patient numbers and the paucity of data available for some outcomes, the systematic review did not exclude studies considered to be at moderate or high risk of bias and these studies may have influenced the results of the meta-analyses.

Conclusions

The findings of this systematic review demonstrate that integrated care improves quality of life, reduces recurrent stroke, anxiety and depression and is associated with a positive benefit on some cardiovascular risk factors but does not impact mortality or readmission rates. Further research is necessary to fully determine which elements of integrated care provide the most benefit to people with stroke.

Acknowledgements

We are grateful to Isik Kaya for his contribution to the systematic review screening, data extraction and risk of bias assessments, and to Katie L. Hoad and Madeleine France-Ratcliffe for their assistance with data extraction and risk of bias assessments.

Author contributions

Ian Eustace (Conceptualization [equal], Data curation [lead], Formal analysis [lead], Investigation [lead], Methodology [lead], Project administration [lead]), Benjamin Buckley (Conceptualization [equal], Data curation [supporting], Formal analysis [supporting], Investigation [supporting], Methodology [supporting], Project administration [supporting], Supervision [equal]), Isik Kaya (Data curation [supporting], Formal analysis [supporting]), Katie Hoad (Formal analysis [supporting]), Madeleine France-Ratcliffe (Formal analysis [supporting]), Andrew M. Hill (Investigation [supporting]), Ian Jones (Conceptualization [equal], Methodology [supporting], Supervision [equal]), Karen Higginbotham (Conceptualization [equal], Methodology [supporting], Supervision [equal]), and Gregory Lip (Conceptualization [equal], Investigation [supporting], Methodology [supporting], Supervision [equal])

Supplementary material

Supplementary material is available at *QJMED* online.

Conflict of interest: G.Y.H.L. is a consultant and speaker for BMS/Pfizer, Boehringer Ingelheim, Daiichi-Sankyo, Anthos. No fees are received personally. He is a National Institute for Health and Care Research (NIHR) Senior Investigator and co-principal investigator of the AFFIRMO project on multimorbidity in AF, which has received funding from the European Union's Horizon 2020 research and innovation programme under grant Agreement No. 899871. B.J.R.B. has received research grants from BMS/Pfizer. I.D.J. has received investigator-initiated funds from Bristol Myers Squibb and Astra Zeneca. No fees are received personally. A.M.H., K.H., I.E., I.K., K.L.H. and M.F-R. have no conflicts of interest to declare.

Funding

No special funding was provided for this study.

References

1. Intercollegiate Stroke Working Party. National Clinical Guideline for Stroke for the UK and Ireland. 2023. https://www.strokeguideline.org/
2. Lip GYH, Ntaios G. "Novel clinical concepts in thrombosis": integrated care for stroke management-easy as ABC. *Thromb Haemost* 2022; **122**:316–9.
3. Sulch D, Kalra L. Integrated care pathways in stroke management. *Age Ageing* 2000; **29**:349–52.
4. Satylganova A, Tello J, Barbazza E. Integrated care models: an overview. World Health Organization [Internet]. 2016. https://www.researchgate.net/publication/315493946_Integrated_care_models_an_overview_Copenhagen_WHO_Regional_Office_for_Europe_2016
5. Liu SD, Rudd A, Davie C. Hyper acute stroke unit services. *Clin Med (Lond)* 2011; **11**:213–4.

Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025

6. Hunter RM, Davie C, Rudd A, Thompson A, Walker H, Thomson N, *et al.* Impact on clinical and cost outcomes of a centralized approach to acute stroke care in London: a comparative effectiveness before and after model. *PLoS One* 2013; **8**:e70420.
7. Morris S, Hunter RM, Ramsay AI, Boaden R, McKevitt C, Perry C, *et al.* Impact of centralising acute stroke services in English metropolitan areas on mortality and length of hospital stay: difference-in-differences analysis. *BMJ* 2014; **349**:g4757.
8. Lip GYH, Lane DA, Lenarczyk R, Boriani G, Doehner W, Benjamin LA, *et al.* Integrated care for optimizing the management of stroke and associated heart disease: a position paper of the European Society of Cardiology Council on Stroke. *Eur Heart J* 2022; **43**:2442–60.
9. McMahon NE, Bangee M, Benedetto V, Bray EP, Georgiou RF, Gibson JME, *et al.* Etiologic workup in cases of cryptogenic. *Stroke* 2020; **51**:1419–27.
10. Norrving B, Barrick J, Davalos A, Dichgans M, Cordonnier C, Guekht A, *et al.* Action plan for stroke in Europe 2018–2030. *Eur Stroke J* 2018; **3**:309–36.
11. Ali M, Salehnejad R, Mansur M. Hospital heterogeneity: what drives the quality of health care. *Eur J Health Econ* 2018; **19**:385–408.
12. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, *et al.* 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/ American Stroke Association. *Stroke* 2021; **52**:e364–467.
13. Mackay-Lyons M, Thornton M, Ruggles T, Che M. Non-pharmacological interventions for preventing secondary vascular events after stroke or transient ischemic attack. *Cochrane Database Syst Rev* 2013; Mar 28(3):CD008656.
14. Stinear CM, Lang CE, Zeiler S, Byblow WD. Advances and challenges in stroke rehabilitation. *Lancet Neurol* 2020; **19**:348–60.
15. Sterne JAC, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, *et al.* RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019; **366**:l4898.
16. Sterne JA, Hernan MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, *et al.* ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016; **355**:i4919.
17. The Cochrane Collaboration. Review Manager (RevMAN) [Computer program]. Version 5.4, 2020.
18. Lee A-Y, Park S-A, Park H-G, Son K-C. Determining the effects of a horticultural therapy program for improving the upper limb function and balance ability of stroke patients. *Horts* 2018; **53**:110–9.
19. Pedapati R, Bhatia R, Shakywar M, Gupta A, Vishnubhatla S, Srivastava MVP, *et al.* Educating caregivers to reduce complications and improve outcomes of stroke patients (ECCOS) – a cluster-randomized trial. *J Stroke Cerebrovasc Dis* 2021; **30**:105966.
20. Xi W, Duan Y, Wang A. Influence of continuing nursing outside hospital on rehabilitation effect and quality of life in patients with stroke. *Chin Nurs Res* 2017; **31**:3760–2.
21. Chen L, Sit JW-H, Shen X. Quasi-experimental evaluation of a home care model for patients with stroke in China. *Disabil Rehabil* 2016; **38**:2271–6.
22. Swanson JO, Moger TA. Comparisons of readmissions and mortality based on post-discharge ambulatory follow-up services received by stroke patients discharged home: a register-based study. *BMC Health Serv Res* 2019; **19**:4.
23. Long W, Zhang J. Patient caregiver comprehensive rehabilitation nursing training joint continued nursing care for ischemic stroke patients at home impact on quality of life and activities of daily living. *Chin Nurs Res* 2017; **31**:2456–61.
24. Vluggen TPMM, van Haastregt JCM, Tan FE, Verbunt JA, van Heugten CM, Schols JMGA. Effectiveness of an integrated multidisciplinary geriatric rehabilitation programme for older persons with stroke: a multicentre randomised controlled trial. *BMC Geriatr* 2021; **21**:134.
25. Buckley BJR, Harrison SL, Fazio-Eynullayeva E, Underhill P, Lane DA, Thijssen DHJ, *et al.* Exercise-based cardiac rehabilitation associates with lower major adverse cardiovascular events in people with stroke. *Cerebrovasc Dis* 2022; **51**:488–92.
26. Chen CM, Yang YH, Chang CH, Chen PC. Effects of transferring to the rehabilitation ward on long-term mortality rate of first-time stroke survivors: a population-based study. *Arch Phys Med Rehabil* 2017; **98**:2399–407.
27. Yang GY, Min HS. The effects of an integrated management program on physical function, cognitive function, and depression in patients with subacute stroke. *J Korean Crit Care Nurs* 2021; **14**:50–62.
28. Wong FKY, Wang SL, Ng SSM, Lee PH, Wong AKC, Li H, *et al.* Effects of a transitional home-based care program for stroke survivors in Harbin, China: a randomized controlled trial. *Age Ageing* 2022; **51**:afac027.
29. Khramov W, Kogaeva KP, Arkhipova LU, Alekseeva VO, Lukyanova MI. Effectiveness of post-stroke social rehabilitation in patients with moderate impairments. *BRSMU* 2021; **2**:62–8.
30. Lewthwaite R, Winstein CJ, Lane CJ, Blanton S, Wagenheim BR, Nelsen MA, *et al.* Accelerating stroke recovery: body structures and functions, activities, participation, and quality of life outcomes from a large rehabilitation trial. *Neurorehabil Neural Repair* 2018; **32**:150–65.
31. Lin RC, Chiang SL, Heitkemper MM, Weng SM, Lin CF, Yang FC, *et al.* Effectiveness of early rehabilitation combined with virtual reality training on muscle strength, mood state, and functional status in patients with acute stroke: a randomized controlled trial. *Worldviews Evid Based Nurs* 2020; **17**:158–67.
32. Peng LN, Lu WH, Liang CK, Chou MY, Chung CP, Tsai SL, *et al.*, Taiwan Stroke Postacute Care (PAC) Study Group. Functional outcomes, subsequent healthcare utilization, and mortality of stroke postacute care patients in Taiwan: a nationwide propensity score-matched study. *J Am Med Dir Assoc* 2017; **18**: 990.e7–12.
33. Teuschl Y, Matz K, Firlinger B, Dachenhausen A, Tuomilehto J, Brainin M, ASPIS Study Group. Preventive effects of multiple domain interventions on lifestyle and risk factor changes in stroke survivors: evidence from a two-year randomized trial. *Int J Stroke* 2017; **12**:976–84.
34. Cuccurullo SJ, Fleming TK, Kostis JB, Greiss C, Eckert A, Ray AR, *et al.* Impact of modified cardiac rehabilitation within a stroke recovery program on all-cause hospital readmissions. *Am J Phys Med Rehabil* 2022; **101**:40–7.
35. Cuccurullo SJ, Fleming TK, Zinonos S, Cosgrove NM, Cabrera J, Kostis JB, *et al.* Stroke recovery program with modified cardiac rehabilitation improves mortality, functional & cardiovascular performance. *J Stroke Cerebrovasc Dis* 2022; **31**:106322.
36. Rasmussen RS, Østergaard A, Kjær P, Skerris A, Skou C, Christoffersen J, *et al.* Stroke rehabilitation at home before and after discharge reduced disability and improved quality of life: a randomised controlled trial. *Clin Rehabil* 2016; **30**:225–36.
37. Langhorne P, Ramachandra S, Stroke Unit Trialists C. Organised inpatient (stroke unit) care for stroke: network meta-analysis. *Cochrane Database Syst Rev* 2020; **4**:CD000197.

Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025

38. Mehrholz J, Kugler J, Pohl M. Water-based exercises for improving activities of daily living after stroke. *Cochrane Database Syst Rev* 2011; **2011**:CD008186.
39. Mehrholz J, Thomas S, Elsner B. Treadmill training and body weight support for walking after stroke. *Cochrane Database Syst Rev* 2017; **8**:CD002840.
40. Pollock A, Baer G, Campbell P, Choo PL, Forster A, Morris J, *et al.* Physical rehabilitation approaches for the recovery of function and mobility following stroke. *Cochrane Database Syst Rev* 2014; **2014**:CD001920.
41. Saunders DH, Sanderson M, Hayes S, Johnson L, Kramer S, Carter D, *et al.* Physical fitness training for patients with stroke. *Stroke* 2020; **51**:E299–300.
42. Goncalves-Bradley DC, Iliffe S, Doll HA, Broad J, Gladman J, Langhorne P, *et al.* Early discharge hospital at home. *Cochrane Database Syst Rev* 2017; **6**:CD000356.
43. Jee S, Jeong M, Paik NJ, Kim WS, Shin YI, Ko SH, *et al.* Early supported discharge and transitional care management after stroke: a systematic review and meta-analysis. *Front Neurol* 2022; **13**:755316.
44. Williams S, Morrissey AM, Steed F, Leahy A, Shanahan E, Peters C, *et al.* Early supported discharge for older adults admitted to hospital with medical complaints: a systematic review and meta-analysis. *BMC Geriatr* 2022; **22**:302.
45. das Nair R, Cogger H, Worthington E, Lincoln NB. Cognitive rehabilitation for memory deficits after stroke. *Cochrane Database Syst Rev* 2016; **9**:Cd002293.
46. Allida S, Cox KL, Hsieh C-F, Lang H, House A, Hackett ML, Cochrane Stroke Group. Pharmacological, psychological, and non-invasive brain stimulation interventions for treating depression after stroke. *Cochrane Database Syst Rev* 2020; **1**:CD003437.
47. Knapp P, Campbell Burton CA, Holmes J, Murray J, Gillespie D, Lightbody CE, *et al.*, Cochrane Stroke Group. Interventions for treating anxiety after stroke. *Cochrane Database Syst Rev* 2017; **5**:CD008860.
48. Chang K-V, Chen K-H, Chen Y-H, Lien W-C, Chang W-H, Lai C-L, *et al.* A multicenter study to compare the effectiveness of the inpatient post acute care program versus traditional rehabilitation for stroke survivors. *Sci Rep* 2022; **12**:12811.
49. Luengo-Fernandez R, Li L, Silver L, Gutnikov S, Beddows NC, Rothwell PM. Long-term impact of urgent secondary prevention after transient ischemic attack and minor stroke: ten-year follow-up of the EXPRESS study. *Stroke* 2022; **53**:488–96.
50. Sharma M, Hart RG, Connolly SJ, Bosch J, Shestakovska O, Ng KKH, *et al.* Stroke outcomes in the COMPASS trial. *Circulation* 2019; **139**:1134–45.
51. Willeit P, Toell T, Boehme C, Krebs S, Mayer L, Lang C, *et al.*, STROKE-CARD study group. STROKE-CARD care to prevent cardiovascular events and improve quality of life after acute ischaemic stroke or TIA: a randomised clinical trial. *EClinicalMedicine* 2020; **25**:100476.
52. Bragstad LK, Hjelle EG, Zucknick M, Sveen U, Thommessen B, Bronken BA, *et al.* The effects of a dialogue-based intervention to promote psychosocial well-being after stroke: a randomized controlled trial. *Clin Rehabil* 2020; **34**:1056–71.
53. Brandal A, Eriksson M, Glader EL, Wester P. Effect of early supported discharge after stroke on patient reported outcome based on the Swedish Riksstroke registry. *BMC Neurol* 2019; **19**:40.
54. Hjelle EG, Bragstad LK, Kirkevold M, Zucknick M, Bronken BA, Martinsen R, *et al.* Effect of a dialogue-based intervention on psychosocial well-being 6 months after stroke in Norway: a randomized controlled trial. *J Rehabil Med* 2019; **51**:557–65.
55. Yu HL, Cao DX, Liu J. Effect of a novel designed intensive patient care program on cognitive impairment, anxiety, depression as well as relapse free survival in acute ischemic stroke patients: a randomized controlled study. *Neurol Res* 2019; **41**:857–66.
56. Zhang L, Zhang T, Sun Y. A newly designed intensive caregiver education program reduces cognitive impairment, anxiety, and depression in patients with acute ischemic stroke. *Braz J Med Biol Res* 2019; **52**:e8533.
57. Graven C, Brock K, Hill KD, Cotton S, Joubert L. First year after stroke: an integrated approach focusing on participation goals aiming to reduce depressive symptoms. *Stroke* 2016; **47**:2820–7.
58. Wu Z, Xu J, Yue C, Li Y, Liang Y. Collaborative care model based telerehabilitation exercise training program for acute stroke patients in China: a randomized controlled trial. *J Stroke Cerebrovasc Dis* 2020; **29**:105328.
59. Yan LL, Gong E, Gu W, Turner EL, Gallis JA, Zhou Y, *et al.* Effectiveness of a primary care-based integrated mobile health intervention for stroke management in rural China (SINEMA): a cluster-randomized controlled trial. *PLoS Med* 2021; **18**:e1003582.
60. Mohammadi E, Hassandoost F, Mozhdehipanah H. Evaluation of the “partnership care model” on quality of life and activity of daily living in stroke patients: a randomized clinical trial. *Jpn J Nurs Sci* 2022; **19**:e12448.
61. Schwarzbach CJ, Eichner FA, Rücker V, Hofmann AL, Keller M, Audebert HJ, *et al.*, SANO study group. The structured ambulatory post-stroke care program for outpatient aftercare in patients with ischaemic stroke in Germany (SANO): an open-label, cluster-randomised controlled trial. *Lancet Neurol* 2023; **22**:787–99.
62. Bath PM, Woodhouse LJ, Appleton JP, Beridze M, Christensen H, Dineen RA, *et al.* Triple versus guideline antiplatelet therapy to prevent recurrence after acute ischaemic stroke or transient ischaemic attack: the TARDIS RCT. *Health Technol Assess* 2018; **22**:1–76.
63. Cumming TB, Churilov L, Collier J, Donnan G, Ellery F, Dewey H, *et al.*, AVERT Trial Collaboration group. Early mobilization and quality of life after stroke: findings from AVERT. *Neurology* 2019; **93**:e717–28.
64. Langhorne P, Wu O, Rodgers H, Ashburn A, Bernhardt J. A very early rehabilitation trial after stroke (AVERT): a phase III, multicentre, randomised controlled trial. *Health Technol Assess* 2017; **21**:1–120.
65. Bernhardt J, Langhorne P, Lindley RI, Thrift AG, Ellery F, Collier J, *et al.* Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): a randomised controlled trial. *Lancet* 2015; **386**:46–55.
66. Fulop NJ, Ramsay AI, Perry C, Boaden RJ, McKevitt C, Rudd AG, *et al.* Explaining outcomes in major system change: a qualitative study of implementing centralised acute stroke services in two large metropolitan regions in England. *Implement Sci* 2016; **11**:80.
67. Ramsay AI, Morris S, Hoffman A, Hunter RM, Boaden R, McKevitt C, *et al.* Effects of centralizing acute stroke services on stroke care provision in two large metropolitan areas in England. *Stroke* 2015; **46**:2244–51.
68. Gilham SC, Clark L. Psychological care after stroke: improving stroke services for people with cognitive and mood disorders. NHS Improvement—Stroke. 2021. NHS Improvement, Leicester, UK.
69. Langhorne P, Jepsen BG, Larsen T. Early home-supported discharge after stroke. *Int J Rehabil Res* 2014; **37**:192–4.
70. Rafsten L, Danielsson A, Nordin A, Björkdahl A, Lundgren-Nilsson A, Larsson M, *et al.* Gothenburg very early supported discharge study (GOTVED): a randomised controlled trial

Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025

investigating anxiety and overall disability in the first year after stroke. *BMC Neurol* 2019; **19**:277.

71. de Mooij MJ, Ahayoun I, Leferink J, Kooij MJ, Karapinar-Çarkit F, Van den Berg-Vos RM. Transition of care in stroke patients discharged home: a single-center prospective cohort study. *BMC Health Serv Res* 2021; **21**:1350.
72. Chen L, Xiao LD, Chamberlain D. An integrative review: challenges and opportunities for stroke survivors and caregivers in hospital to home transition care. *J Adv Nurs* 2020; **76**:2253–65.
73. NHS England. RightCare Pathway: Stroke. 2017. https://www.england.nhs.uk/rightcare/wp-content/uploads/sites/40/2017/09/stroke-pathway.pdf
74. Sentinel Stroke National Audit Programme (SSNAP). The Road to Recovery: The Ninth SSNAP Annual Report. 2022. https://www.strokeaudit.org/Documents/National/Clinical/Apr2021Mar2022/Apr2021Mar2022-AnnualReport.aspx
75. Saunders DH, Sanderson M, Hayes S, Johnson L, Kramer S, Carter DD, *et al.* Physical fitness training for stroke patients. *Cochrane Database Syst Rev* 2020; **3**:CD003316.
76. Lambert CM, Olulana O, Bailey-Davis L, Abedi V, Zand R. “Lessons learned” preventing recurrent ischemic strokes through secondary prevention programs: a systematic review. *J Clin Med* 2021; **10**:4209.
77. Yin Y, Zhang L, Marshall I, Wolfe C, Wang Y. Statin therapy for preventing recurrent stroke in patients with ischemic stroke: a systematic review and meta-analysis of randomized controlled trials and observational cohort studies. *Neuroepidemiology* 2022; **56**:240–9.
78. Kitagawa K, Yamamoto Y, Arima H, Maeda T, Sunami N, Kanzawa T, *et al.*, Recurrent Stroke Prevention Clinical Outcome (RESPECT) Study Group. Effect of standard vs intensive blood pressure control on the risk of recurrent stroke: a randomized clinical trial and meta-analysis. *JAMA Neurol* 2019; **76**:1309–18.
79. Cameron C, Coyle D, Richter T, Kelly S, Gauthier K, Steiner S, et al Systematic review and network meta-analysis comparing antithrombotic agents for the prevention of stroke and major bleeding in patients with atrial fibrillation. *BMJ Open* 2014; **4**:e004301.
80. Cohen AT, Hill NR, Luo X, Masseria C, Abariga SA, Ashaye AO. A systematic review of network meta-analyses among patients with nonvalvular atrial fibrillation: a comparison of efficacy and safety following treatment with direct oral anticoagulants. *Int J Cardiol* 2018; **269**:174–81.
81. Lei H, Yu L-T, Wang W-N, Zhang S-G. Warfarin and the risk of death, stroke, and major bleeding in patients with atrial fibrillation receiving hemodialysis: a systematic review and meta-analysis. *Front Pharmacol* 2018; **9**:1218.
82. Tawfik A, Bielecki JM, Krahn M, Dorian P, Hoch JS, Boon H, *et al.* Systematic review and network meta-analysis of stroke prevention treatments in patients with atrial fibrillation. *Clin Pharmacol* 2016; **8**:93–107.
83. Barnes GD. Combining antiplatelet and anticoagulant therapy in cardiovascular disease. *Hematology Am Soc Hematol Educ Program* 2020; **2020**:642–8.
84. Szapáry L, Tornyos D, Kupó P, Lukács R, El Alaoui El Abdallaoui O, Komócsi A. Combination of antiplatelet and anticoagulant therapy, component network meta-analysis of randomized controlled trials. *Front Cardiovasc Med* 2022; **9**:1036609.
85. Ali A, Tabassum D, Baig SS, Moyle B, Redgrave J, Nichols S, *et al.* Effect of exercise interventions on health-related quality of life after stroke and transient ischemic attack: a systematic review and meta-analysis. *Stroke* 2021; **52**:2445–55.
86. Chen MD, Rimmer JH. Effects of exercise on quality of life in stroke survivors: a meta-analysis. *Stroke* 2011; **42**:832–7.

Downloaded from https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaf029/7978926 by Sarah Dakin user on 01 April 2025

© The Author(s) 2025. Published by Oxford University Press on behalf of the Association of Physicians.
This is an Open Access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.
QJM: An International Journal of Medicine, 2025, 00, 1–12
https://doi.org/10.1093/qjmed/hcaf029
Review