

ORIGINAL CONTRIBUTION



Recovery of Visuospatial Neglect With Standard Treatment: A Systematic Review and Meta-Analysis

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BACKGROUND: Visuospatial neglect is a common consequence of stroke and is characterized by impaired attention to contralesional space. Currently, the extent and time course of recovery from neglect are not clearly established. This systematic review and meta-analysis aimed to determine the recovery trajectory of poststroke neglect with standard treatment.

METHODS: PsycInfo, Embase, and MEDLINE were searched for articles reporting recovery rates of neglect after stroke. Time since stroke was categorized into early (0–3 months), mid (3–6 months), and late (>6 months) recovery phases. Random-effects models for pooled prevalence were generated for each phase, and potential sources of heterogeneity were explored with metaregressions. Methodological quality of each study was assessed using the Joanna Briggs Institute checklist, with low-quality studies excluded in sensitivity analyses.

RESULTS: The search captured 4130 articles including duplicates, and 111 full-text reviews were undertaken. A total of 27 studies reporting data from 839 stroke survivors with neglect were included for review. Meta-analyses indicated a recovery rate of 42% in the early phase, which increased to 53% in the mid-recovery phase. Additional recovery in the late phase was minimal, with an estimated 56% recovery rate. Heterogeneity of studies was high ($I^2 > 75\%$) in all 3 phases of recovery. Estimates were robust to sensitivity analyses. Metaregressions showed significantly greater recovery in studies that included patients with left-hemisphere lesions ($\beta = 0.275$, $P < 0.05$, $I^2 = 84\%$).

CONCLUSIONS: Most recovery from neglect occurs in the first 3 months, although additional gains can be expected up to 6 months poststroke. While a large proportion of patients recover from neglect, over 40% show persistent symptoms. Further research is needed on effective rehabilitation interventions, particularly focusing on patients most at risk of chronic visuospatial neglect.

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Key Words: cognition ■ cognitive dysfunction ■ neuropsychology ■ systematic review ■ stroke ■ stroke rehabilitation

Visuospatial neglect is a common poststroke syndrome characterized by inattention to stimuli in contralesional space, which cannot be attributed to primary sensory or motor deficits.¹ Neglect is a heterogeneous disorder, encompassing various subtypes that can occur in isolation or in conjunction.² Among others,

neglect can affect distinct spatial regions (eg, personal, peripersonal, or extrapersonal space) and manifest as person-centered (egocentric) or stimulus-centered (allocentric) spatial attention deficits.³ Recent estimates indicate that $\approx 30\%$ of patients with stroke present with neglect acutely poststroke, with prevalence rates

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Nonstandard Abbreviations and Acronyms

BIT Behavioural Inattention Test

typically being higher after right- than left-hemisphere lesions.⁴ Neglect negatively impacts a wide range of outcomes, including discharge destination and independence in daily activities,^{5–7} rehabilitation efficacy,⁸ and quality of life.^{9,10} An improved understanding of the persistence of neglect over time is, therefore, of high clinical relevance. However, there is currently no consensus regarding either the extent or time course of recovery from neglect. Natural or spontaneous recovery refers to the improvement of function determined by the progression of time.¹¹ The degree of natural recovery after stroke varies substantially across domains and has been most extensively studied in the context of motor impairment, although several overarching principles have been identified. First, significant recovery typically occurs within 3 months poststroke.¹² Second, recovery tends to be proportional to the severity of acute deficits.¹³ Patients with more severe impairments are expected to make significant improvements over time but may be less likely to reach formal recovery thresholds compared with those with milder deficits. Third, functional gains beyond the first 3 months are more common for cognitive difficulties than motor impairments,¹² with residual improvements observed years after stroke for language, working memory, and global cognition.^{14–16} The specific trajectory of visuospatial neglect recovery, however, remains under-defined. Therefore, the primary aim of this systematic review is to identify the longitudinal pattern of recovery from visuospatial neglect after stroke. It should be noted that stroke survivors typically receive standardized therapeutic support within a neurorehabilitation context. In this review, we will, therefore, use the term recovery with standard treatment rather than natural recovery to highlight the possible contribution of conventional rehabilitation therapy. Importantly, stroke survivors who do not meet criteria for full recovery may still demonstrate clinically significant gains in function over time. Accordingly, the secondary aim is to examine improvement of neglect over time. Finally, previous research suggests certain patient and study characteristics can impact on the observed recovery of neglect. Specifically, lesion side, severity of stroke and neglect, and time of the first assessment may influence reported recovery rates.^{17–19} We hypothesize that (1) left-hemisphere lesions are associated with higher recovery rates than right-hemisphere stroke,^{19,20} (2) greater severity of stroke or neglect at baseline is associated with reduced likelihood of recovery,¹⁰ and (3) studies that conducted initial assessments of neglect in the acute stroke phase (first week poststroke⁴) will report higher levels of recovery

than those recruiting patients at a later time, as acute neglect can resolve within days after stroke.^{19,20}

METHODS

The protocol for this systematic review was registered with PROSPERO (International Prospective Register of Systematic Reviews). The review was reported according to the PRISMA guidelines ([Preferred Reporting Items for Systematic Reviews and Meta-Analysis]; [Supplemental Material](#)).²¹

Search Strategy

The Ovid platform was used to search PsycInfo, Embase, and MEDLINE databases from inception to December 13, 2022. The search strategy was developed in consultation with a librarian and a neuropsychologist specializing in stroke. Title, abstract, and relevant topic terms were searched with boolean operators using the keywords “stroke,” “neglect,” and “neuropsychological assessment” (see [Supplemental Material](#) for the detailed search strategy). References in the selected journals were reviewed to identify additional relevant studies.

Eligibility Criteria

Study inclusion criteria were as follows: (1) peer-reviewed observational studies, (2) published in English language, (3) included patients who developed visuospatial neglect following stroke, (4) assessed neglect with a standardized test, and (5) included ≥ 2 different time points. Case studies, commentaries, review articles, and conference abstracts were not considered. Articles that included patients below the age of 18 years, patients with dementia, or patients who had neglect before a stroke diagnosis were excluded. Studies were also excluded if they involved a neglect-specific intervention beyond standard treatment protocols or if only tests for global cognition were used.

Screening and Data Extraction

Following the removal of duplicates, screening of titles, abstracts, and full texts was conducted by E.B. The resulting list of studies was reviewed by a second author (M.J.O.), with any disagreements regarding study eligibility being reconciled in consultation with a third reviewer (N.D.). Data from each eligible report were independently extracted by 2 authors (E.B. and M.J.O.) using a predefined extraction template, with any discrepancies resolved through discussion with all authors. Data extracted included authors, publication year, sample size, number of patients with neglect, country, study setting, age, sex, stroke etiology, stroke severity as measured with the National Institutes of Health Stroke Scale,²² thrombolysis or thrombectomy treatment, standard rehabilitation procedures, neuropsychological assessments used, average performance on neglect assessments, and time of assessment.

Outcomes

The primary outcome of interest was the proportion of stroke survivors with neglect at each time point. For every study, only patients who were diagnosed with neglect at baseline and completed follow-up were included in analyses. It was not possible to stratify studies based on neglect characteristics (eg,

egocentric versus allocentric) due to limited reporting of neglect subtypes. Where studies reported recovery rates for different neglect subtypes but did not specify which patients presented with co-occurring symptoms, we selected the subtype with the largest sample size for analyses. Recovery percentage was calculated at every assessment: (patients recovered from neglect/total number of patients)×100. Across all studies, scores on the Behavioural Inattention Test (BIT)²³ were most frequently reported. The conventional BIT consists of 6 subtests, including line crossing, letter cancellation, star cancellation, figure and shape copying, line bisection, and representational drawing tasks. The maximum total score on the BIT is 146, with scores below 129 being indicative of visuospatial neglect.²⁴ To assess improvement of neglect severity over time as a secondary outcome, average scores on the BIT were extracted from each study where available.

Quality Assessment

The methodological quality of included articles was assessed using the Joanna Briggs Institute critical appraisal checklist for studies reporting prevalence data.²⁵ Study quality was determined by the number of items with a “yes” response (maximum, 9), with the total score converted into a percentage. Studies scoring <50% were categorized as low quality, 50% to 69% as moderate quality, and ≥70% as high quality.²⁶ All studies were rated independently by 2 authors (E.B. and M.J.O.), with any differences in ratings resolved through discussion with all authors.

Statistical Analysis

All analyses were performed using R software (version 4.1.2). For each study, time since stroke was categorized into early (0–3 months; ie, acute and subacute phases of neglect recovery), mid (3–6 months), and late (>6 months) recovery phases in line with categories used by Esposito et al.⁴ Meta-analyses of the key outcomes of interest were stratified by recovery phase. Where patients were assessed multiple times within the same phase, the time point with the largest sample size was used for meta-analyses. Pooled estimates were generated with random-effects meta-analyses using the meta package. To estimate overall proportion of neglect recovery, the metaprop function was applied using the inverse variance method with a Freeman-Tukey double arcsine transformation. The level of heterogeneity was estimated using the restricted maximum likelihood method, with significance indicated by the Cochran Q test $P<0.05$. Heterogeneity between studies was quantified by the resulting I^2 statistic and interpreted as low (<25%), medium (50%–75%), or high (>75%).²⁷ All results are presented as forest plots and associated 95% CIs. In sensitivity analyses, studies rated as low quality on the Joanna Briggs Institute were excluded to evaluate the robustness of results. Where sufficient data were available, metaregressions were performed to explore variability in recovery outcomes using the metareg function with meta objects created by the main meta-analyses. Key predictors of interest were lesion side, stroke and neglect severity, and time of first assessment (≤7 versus >7 days poststroke).

Data Availability

The full R code and extracted data can be freely accessed through <https://osf.io/zwkty/>.

RESULTS

Study Selection

The initial search identified a total of 4130 records. Following removal of duplicates, the titles and abstracts of 2321 publications were screened. The full texts of 131 articles were reviewed, with 36 studies meeting the inclusion criteria. Nine papers did not clearly identify which patients with neglect versus nonneglect at baseline completed follow-up assessments and were, therefore, excluded, resulting in a total of 27 publications. The study selection process is displayed in Figure 1.

Population and Study Characteristics

Table 1 provides a summary of the characteristics of all studies included in the meta-analyses. The 27 included studies reported data from a total of 839 stroke survivors with neglect at baseline. Sample sizes ranged from 6 to 142 patients (median, 23 patients). Stroke survivors were predominantly recruited from hospital sites including rehabilitation centers (n=22), while 1 study recruited from a regional stroke register and 4 studies did not explicitly report recruitment setting. Studies were conducted in Europe (n=21), Australia (n=2), Asia (n=2), and North America (n=2). The average age of stroke survivors with neglect was reported in 19 studies and ranged from 54.7 to 80.1 years. Ischemic stroke was most common (n=331 [39.5%] patients), followed by hemorrhagic stroke (n=20 [2.4%] patients). Etiology was unreported or unknown for 488 (58.2%) patients. Twenty studies only included patients with a right-hemisphere lesion. Overall, 600 (71.5%) patients had a right-hemisphere stroke, 56 (6.7%) patients had a left-hemisphere stroke, 9 (1.1%) patients had a diffuse or bilateral stroke, and lesion side was unknown for 174 (20.7%) patients. Baseline assessment ranged from 2.5 to 48.9 days poststroke, and total follow-up time ranged from 8.6 to 491 days poststroke. A diagnosis of visuospatial neglect was most often based on BIT scores (n=13), with the presence of neglect being determined by total scores <129 and performance below cutoff scores for ≥2 of 6 subtasks. The remaining studies used (a combination of) cancellation tasks (n=11), figure copying (n=4), text reading (n=4), line bisection (n=2), writing (n=2), the Catherine Bergego Scale⁵³ (n=2), face matching tasks (n=1), Raven colored progressive matrices⁵⁴ (n=1), or a full neglect test battery (n=1). Stroke severity as measured with the National Institutes of Health Stroke Scale was reported in 7 studies, with average scores ranging from 3 to 12.3 (ie, mild to moderately severe²²).

Quality Assessment

Thirteen studies were rated as high quality,²⁵ 8 studies as moderate quality, and 6 studies as low quality. All

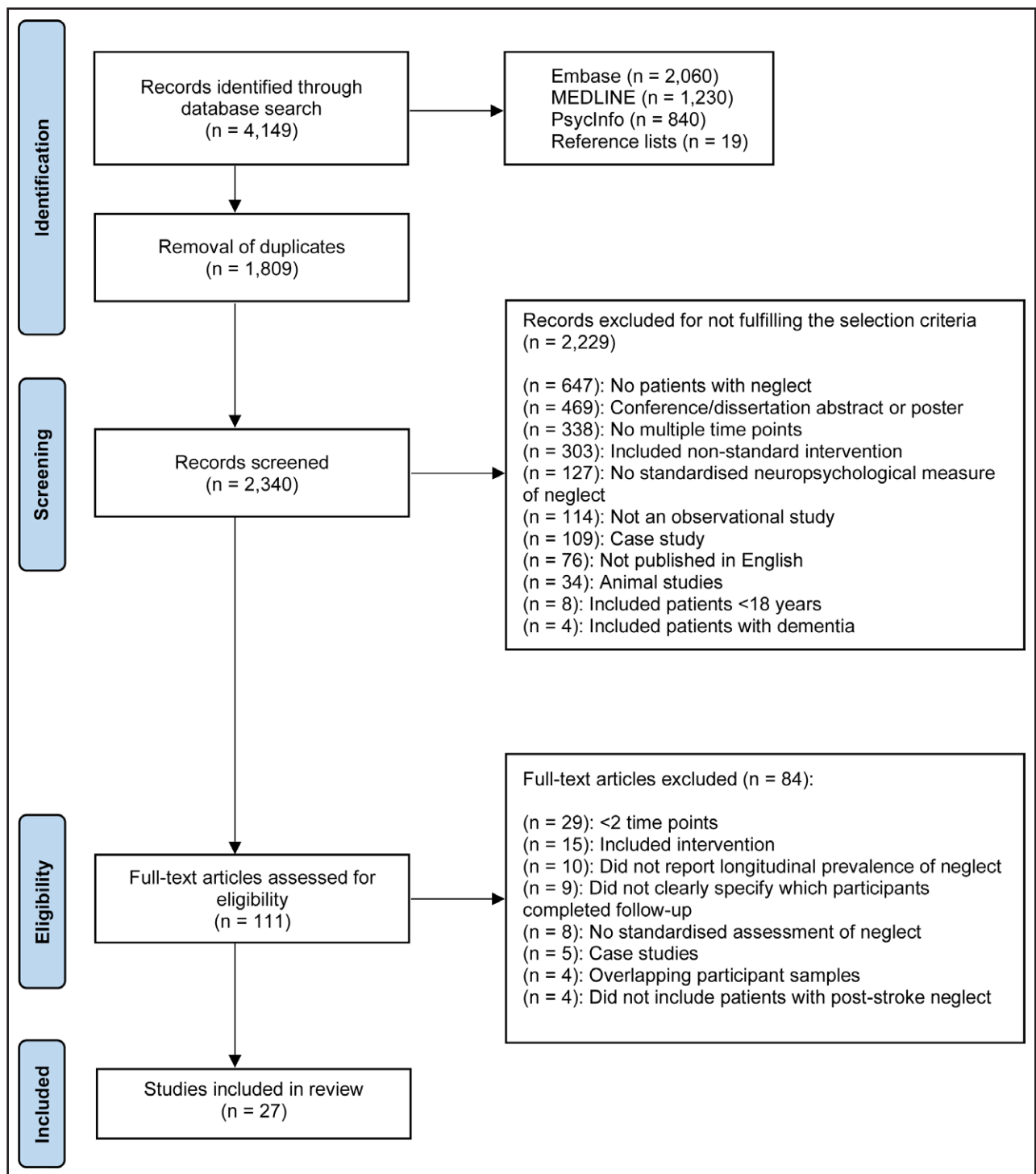


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis flowchart of study selection.

studies measured neglect with standard and reliable methods, and all but 1 study used validated measures for the identification of neglect. Only 4 studies had a sufficient sample size, highlighting the need for large-scale studies of visuospatial neglect. Additionally, sample frame proved to be a problematic item with only 6 studies representing the target population. The main reason for

failing this criterion was the exclusion of patients with a left-hemisphere stroke. Visuospatial neglect has consistently been observed after left-hemisphere lesions,⁵⁵ and exclusion of left-hemisphere patients with stroke was, therefore, treated as nonrepresentative of the entire target population.⁵⁶ An item-by-item overview of the quality assessment for all studies is presented in Table 2.

Table 1. Summary of Study and Patient Characteristics

Study details								Participant characteristics				
First author (y)	Country	Recruitment site	Nr patients at baseline (neglect/total)	Inclusion criteria	Diagnostic task	Time		Average age, y	Sex (%female)	Stroke etiology	Lesion side	Stroke severity (average NIHSS score)
						First assessment	Final follow-up					
Appellos ²⁸ (2004)	Sweden	Acute and rehabilitation wards	36/37*	Diagnosis of left-sided neglect First-ever stroke MMSE score ≥17	BIT	2–4 wk	12 mo	74.0†	59.5%†	Infarct, 89.2%; hemorrhage, 10.8% ^b	Right, 100%	11.0
Cassidy ²⁹ (1998)	United Kingdom	General medical and geriatric medicine wards	27/27	Diagnosis of neglect First-ever right-hemisphere stroke	BIT	3 d	3 mo	73.0	48.0%	Infarct, 48.1%; hemorrhage, 7.4%; NR, 44.4%	Right, 100%	NR
Demeyere ² (2019)	United Kingdom	Acute stroke units	94/366	<3 wk poststroke Able to concentrate for 15 min Able to give written or witnessed informed consent	Broken hearts task	6 dt	6 mo	73.0†	47.5%†	Ischemia, 53.3%; hemorrhage, 9.3%; NR, 37.7%†	Right, 49.5%; left, 40.4%; bilateral, 6.6%; NR, 3.6%†	NR
Farnè ³⁰ (2004)	Italy	Inpatient and outpatient stroke services	23/33	<6 wk poststroke No previous neurological or DSM-IV axis I disorders	BIT	21.6 d	>3 mo	68.0	52.2%	NR	Right, 100%	NR
Jehkonen ³¹ (2007)	Finland	Not reported	21/56	First-ever right-hemisphere infarct No previous neurological disorders No severe primary visual impairment Right handed Aged <75 y	BIT	6 d	12 mo	63.2	42.9%	Infarct, 100%	Right, 100%	NR
Johannsen ³² (2004)	Germany	Not reported	25/25	Diagnosis of severe neglect Right-hemisphere stroke	Letter cancellation Bells cancellation	35 d#	491 d	71.0#	10%#	Infarct, 90%; hemorrhage, 10%#	Right, 100%	NR
Kamakura ³³ (2017)	Japan	Neurology and rehabilitation departments	18/18	Diagnosis of left-sided neglect Right-hemisphere ischemic lesion Sufficient level of consciousness as assessed with the Glasgow Coma Scale No history of cerebrovascular disease or other neurological disorders Able to maintain a sitting position Right handed Able to understand Japanese	BIT	5.2 d	18.2 d	70.0	55.6%	Ischemia, 100%	Right, 100%	12.3
Karnath ³⁴ (2011)	Germany	Neurology center	24/54	Right-hemisphere stroke No brain tumors	Letter cancellation Bells cancellation Copy task	12.4 dt	490.8 dt	64.9	72.7%	Infarct, 91.7%; hemorrhage, 8.3%	Right, 100%	NR
Kettunen ³⁵ (2012)	Finland	Hospital	10/37	First-ever stroke No neurological or psychiatric history >80 y Right handed	BIT	4.4 d	186.3 d	65.0	30.0%	Ischemia, 100%	Right, 100%	6.5

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Table 1. Continued

Study details							Participant characteristics					
First author (y)	Country	Recruitment site	Nr patients at baseline (neglect/total)	Inclusion criteria	Diagnostic task	Time		Average age, y	Sex (%female)	Stroke etiology	Lesion side	Stroke severity (average NIHSS score)
						First assessment	Final follow-up					
Klinke ³⁶ (2018)	Iceland	Neurological or neurosurgical wards	23/23	First-ever right-hemisphere stroke No psychiatric or neurological pathologies Right handed Aged 35–85 y Living in own home before stroke Medically stable	BIT Catherine Bergego Scale	10.3 d	141.5 d	67.5	69.9%	Ischemia, 91.3%; hemorrhage, 8.7%	Right, 100%	12.3
Levine ³⁷ (1986)	The United States	Stroke rehabilitation unit	12/29	Right cerebral infarction No history or radiological evidence of prior stroke, dementia, or other neurological illness Right handed	Rey-Osterrieth complex figure copy Line cancellation Line bisection Paragraph reading Sentence writing	2–4 wk	10–20 wk	62.6	58.3%	Infarct, 100%	Right, 100%	NR
Lundervold ³⁸ (2005)	Norway	Neurology department	13/13	Diagnosis of neglect Right-hemisphere stroke	BIT	1–4 wk	11.2 wk	62.2	38.5%	Infarct, 100%	Right, 100%	NR
Lunven ³⁹ (2015)	France	Neurology unit	27/45	First-ever right-hemisphere stroke No history of neurological disease No impaired vigilance, general mental degeneration, or psychiatric disorders	BEN	30.8 d	457.1 d	54.7	55.6%	NR	Right, 100%	NR
Marsh ⁴⁰ (1993)	New Zealand	Stroke rehabilitation unit	13/27	No significant prestroke physical or mental disorder No other illness precluding rehabilitation Aged ≥60 y No blindness One functional hand	Line crossing Star cancellation Indented paragraph task Line bisection	15–20 d	90 d	75.4†	38.5%	Infarct, 100%	Right, 76.9%; left, 7.7%; diffuse, 15.4%	NR
Mattingley ⁴¹ (1994)	Australia	Not reported	13/13	Diagnosis of neglect Unilateral right-hemisphere lesion	Line cancellation Circle cancellation Star cancellation Face matching task Chimeric faces task	48.9 d	427.6 d	64.4	38.5%	NR	Right, 100%	NR
Moore ¹⁰ (2021)	United Kingdom	Acute stroke units	142/400	Complete data on broken hearts task and Stroke Impact Scale	Broken hearts task	9.4 d	6 mo	72.1	47.9%	Ischemia, 62.7%; hemorrhage, 9.9%; NR, 27.5%	Right, 40.8%; left, 29.6%; bilateral, 4.2%; NR, 25.3%	3.0

(Continued)

Table 1. Continued

Study details								Participant characteristics				
First author (y)	Country	Recruitment site	Nr patients at baseline (neglect/total)	Inclusion criteria	Diagnostic task	Time		Average age, y	Sex (%female)	Stroke etiology	Lesion side	Stroke severity (average NIHSS score)
						First assessment	Final follow-up					
Nijboer ⁴² (2013)	The Netherlands	Hospital	51/101	First-ever ischemic stroke of the medial or anterior cerebral artery No complicating medical history, such as cardiac, pulmonary, or orthopedic disorders No severe communication or memory deficits MMSE score >24 Written or verbal informed consent and sufficient motivation to participate Inability to walk at the first assessment Aged 30–80 y	Letter cancellation task	8 d	12 mo	66.6	49.0%	Ischemia, 100%	Right, 82.4%; left, 17.6%	NR
Nurmi ⁴³ (2018)	Finland	Hospital	18/65	First-ever right-hemisphere infarct No neurological or psychiatric diagnosis No significant cerebral atrophy No significant loss of consciousness, primary vision, or hearing No substance abuse Finnish as native language Aged 30–85 y Able to live independently before infarct	BIT	12 d	376 d	72.0	50.0%	Infarct, 100%	Right, 100%	9.0
Saj ⁴⁴ (2012)	Switzerland	Not reported	31/69	First-ever right-hemisphere stroke	Bell cancellation Letter cancellation Copy of scene Line bisection (5 and 20 cm) Clock drawing Text reading Writing	7.5 d	357.7 d	65.0†	NR	NR	Right, 100%	NR
Samuelsson ⁴⁵ (1996)	Sweden	Stroke unit	18/60	Right-hemisphere stroke Right handed Age <78 y No history of alcoholism No mental retardation No hospitalization for psychiatric treatment	BIT	1–8 wk	6–7 mo	62.1	55.6%	NR	Right, 100%	NR
Small ⁴⁶ (1994)	United Kingdom	Hospital	10/10	Diagnosis of neglect Presence of anosognosia	BIT	<9 d	31.1 wk	80.1	50.0%	Infarct, 60%; NR, 40%	Right, 50%; bilateral, 10%; NR, 40%	NR

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Table 1. Continued

Study details						Participant characteristics						
First author (y)	Country	Recruitment site	Nr patients at baseline (neglect/total)	Inclusion criteria	Diagnostic task	Time		Average age, y	Sex (%female)	Stroke etiology	Lesion side	Stroke severity (average NIHSS score)
						First assessment	Final follow-up					
Sunderland ⁴⁷ (1987)	United Kingdom	Stroke register	15/197	No history of stroke Unilateral weakness or sensory loss	Raven colored progressive matrices	3 wk	12 mo	70.2 ^b	NR	NR	Right, 73.3%; left, 26.7%	NR
Takamura ⁴⁸	Japan	Hospital	79/174	Right-hemisphere stroke No bilateral lesions No history of a major psychiatric or neurological disorder No pure hemianopia	BIT	57.8 d	139.5 d	70.1	42.9%	NR	Right, 100%	NR
Timbeck ⁴⁹ (2013)	Canada	Hospital	6/16	First-ever right-hemisphere stroke as diagnosed with CT scan No other disabling pathologies No language or cognitive impairments Aged ≥18 y English as first language	BIT	35.9 d	74.1 d	77.0	50%	NR	Right, 100%	NR
Umarova ⁵⁰ (2016)	Germany	Neurology department	24/50	First-ever territorial ischemic stroke in the right middle cerebral artery Absence of hemianopia and severe sight defects Absence of other neurological or psychiatric conditions Absence of occlusion or severe stenosis of the carotid or middle cerebral arteries Sufficient consciousness or arousal level Aged ≤80 y Right handed No MRI contraindications	Line cancellation Letter cancellation Star cancellation Text reading Picture copying	2.5 d	8.6 d	67.3	NR	Ischemia, 100%	Right, 100%	8.9
Vanbellingen ⁵¹ (2017)	Switzerland	Neurorehabilitation center	51/82	First-ever right-hemisphere stroke Not 100% bedridden No additional degenerative or psychiatric diseases	Catherine Bergego Scale	11.3 d	44.5 d	67.9 [†]	42.7% [†]	Ischemia, 74.4% [†] ; hemorrhage, 25.6% [†]	Right, 100%	NR
Wade ⁵² (1988)	United Kingdom	Hospital	15/62	NR	Cancellation task	<14 d	13 wk	67.7 [†]	54.8% [†]	NR	NR	NR

BEN indicates Batterie d'Evaluation de la Négligence; BIT, Behavioural Inattention Test; CT, computed tomography; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders; MMSE, Mini-Mental State Examination; MRI, magnetic resonance imaging; NIHSS, National Institutes of Health Stroke Scale; and NR, not reported.

*Patients with extrapersonal neglect/patients with all types of neglect.

†Reported for full cohort including stroke survivors without neglect.

‡Reported for subset, only patients with chronic neglect (n=10).

Recovery of Neglect With Standard Treatment

Figure 2 displays the reported recovery of neglect over time with standard treatment for all 27 studies. Meta-analyses

were stratified by recovery phase (Figure 3). In the early recovery phase (0–3 months), pooled data from 12 studies including 262 patients indicated an estimated recovery rate of 42% (CI, 20%–64%; I²=91%). The proportion of

Table 2. Quality Assessment of Included Studies

Study	Q1 Sample frame	Q2 Sampling method	Q3 Sample size	Q4 Study description	Q5 Sample coverage	Q6 Validity of assessment	Q7 Standardized measurement	Q8 Statistical analysis	Q9 Response rate	Total score	Quality rating
Appelros ²⁸	N	Y	N	Y	Y	Y	Y	Y	U	6	Moderate
Cassidy ²⁹	U	Y	N	Y	Y	Y	Y	Y	Y	7	High
Demeyere ²	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	High
Farné ^{30,31}	Y	U	N	Y	U	Y	Y	Y	U	5	Moderate
Jehkonen ³¹	N	Y	N	Y	N	Y	Y	Y	U	5	Moderate
Johannsen ³²	U	Y	N	N	N	Y	Y	Y	Y	5	Moderate
Kamakura ³³	N	Y	N	Y	Y	Y	Y	Y	N	6	Moderate
Karnath ³⁴	N	Y	N	Y	Y	Y	Y	Y	Y	7	High
Kettunen ³⁵	N	Y	N	Y	Y	Y	Y	Y	Y	7	High
Klinke ³⁶	N	Y	N	Y	Y	Y	Y	Y	Y	7	High
Levine ³⁷	N	U	N	Y	Y	Y	Y	Y	N	5	Moderate
Lundervold ³⁸	U	Y	N	N	U	Y	Y	Y	N	4	Low
Lunven ³⁹	N	Y	N	Y	Y	Y	Y	Y	Y	7	High
Marsh ⁴⁰	Y	Y	N	Y	Y	Y	Y	Y	Y	8	High
Mattingley ⁴¹	U	U	N	Y	Y	Y	Y	Y	U	5	Moderate
Moore ¹⁰	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	High
Nijboer ⁴²	Y	U	Y	Y	Y	Y	Y	Y	Y	8	High
Nurmi ⁴³	N	Y	N	Y	Y	Y	Y	Y	Y	7	High
Saj ⁴⁴	N	U	N	N	U	Y	Y	Y	Y	4	Low
Samuelsson ⁴⁵	N	Y	N	Y	Y	Y	Y	Y	Y	7	High
Small ⁴⁶	N	U	N	N	N	Y	Y	U	N	2	Low
Sunderland ⁴⁷	Y	Y	N	N	N	N	Y	Y	Y	5	Moderate
Takamura ⁴⁸	N	U	N	Y	N	Y	Y	Y	U	4	Low
Timbeck ⁴⁹	N	Y	N	Y	Y	Y	Y	Y	Y	7	High
Umarova ⁵⁰	U	U	N	N	Y	Y	Y	Y	U	4	Low
Vanbellingen ⁵¹	N	Y	Y	Y	Y	Y	Y	Y	Y	8	High
Wade ⁵²	U	Y	N	N	U	Y	Y	U	N	3	Low

N indicates no; U, unclear; and Y, yes.

patients who recovered from neglect increased further in the mid-recovery phase (3–6 months) to 53% (CI, 35%–70%; $I^2=89\%$) based on 11 studies with a total of 426 patients. There was minimal further recovery in the late phase (>6 months), with an estimated recovery prevalence of 56% (CI, 41%–70%; $I^2=77\%$) across 12 studies with 257 patients. Results from sensitivity analyses, which excluded low-quality studies, were similar to the main meta-analyses with estimated recovery rates of 38% (early), 53% (mid), and 56% (late) phases (Figure S1).

Sources of Heterogeneity

Heterogeneity of studies was high ($I^2>75\%$) in all 3 phases of recovery. Using metaregressions, we explored factors that were hypothesized to contribute to variable outcomes across studies. First, we assessed the impact of inclusion versus exclusion of patients with left-hemisphere lesions. We found that studies that included patients with left-hemisphere stroke reported greater recovery rates

compared with studies that only included right-hemisphere lesions ($\beta=0.275$, $P<0.05$, $I^2=84\%$; Table S1). We also examined whether timing of baseline assessment, which varied substantially between studies (Figure 2), affected recovery rates. Results showed no evidence that time of first assessment (≤ 7 versus >7 days poststroke) moderated reported rates of recovery ($\beta=-0.211$, $P=0.101$, $I^2=86\%$; Table S1). Due to limited reporting of the National Institutes of Health Stroke Scale scores and neglect severity, it was not possible to formally investigate the influence of stroke and neglect severity on recovery.

Improvement of Neglect

To determine improvement of neglect symptoms over time, changes in scores on the BIT²³ were examined. A total of 8 studies with 128 patients reported average or individual BIT scores at multiple time points (Figure 4). Due to the limited number of studies per phase, it was not possible to carry out meta-analyses using BIT scores.

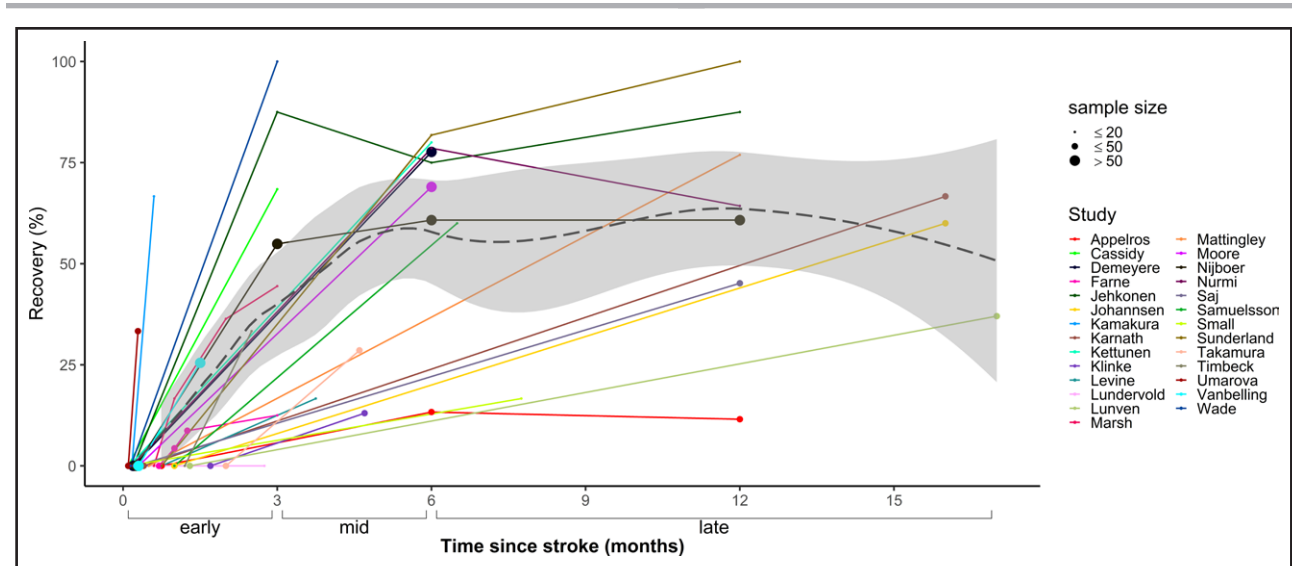


Figure 2. Recovery of visuospatial neglect with standard treatment in the early, mid, and late phases after stroke.

Individual lines indicate the proportion of recovered patients at each assessment point for every study, with dot size reflecting the sample size. The Locally Estimates Scatterplot Smoothing (LOESS) line (dashed) shows the estimated smooth fit of the regression model of recovery rates predicted by time across all studies, with the 95% CI shaded in gray. Most recovery occurred in the early phase (0–3 months), with smaller increases observed in the mid-recovery phase (3–6 months). No additional recovery was observed in the late recovery phase (>6 months).

Therefore, a descriptive overview of the BIT data is provided. At baseline, patients across studies had a mean score of 87.3 (mean range, 56.3–121.7). In the early recovery phase, there was a substantial improvement in scores with an average performance of 122.1 (mean range, 96.2–136.8). Scores increased further in the mid-recovery phase to a mean of 138.1 (mean range, 114.1–139.9) but remained stable in the late recovery phase (mean = 138.0; mean range, 137.9–138.2).

DISCUSSION

This systematic review and meta-analysis of 27 studies showed that 42% of stroke survivors with neglect recover within the first 3 months after stroke. The pooled prevalence of neglect recovery increased further between 3 to 6 months poststroke, with an average of 53% of patients meeting recovery criteria. There was no evidence of clinically significant additional recovery with standard treatment beyond this period, with an estimated recovery rate of 56% between 6 and 17 months after stroke. To gain a more detailed understanding of changes in neglect severity over time, scores on a standardized assessment of neglect were investigated. In a subset of 8 studies, mean BIT scores were just below the cutoff for normal performance at 3 months poststroke. This showed that although not all stroke survivors met the formal threshold of recovery, patients on average showed material improvements of neglect symptoms in the early recovery phase. In line with the main meta-analyses, additional but less extensive improvements were observed up to 6 months poststroke, with minimal changes in longer term follow-up assessments. Collectively, these findings

are consistent with the literature on motor and cognitive impairments poststroke, which indicates that most natural recovery occurs within the first 3 months.^{12,57} However, our results demonstrate that patients with visuospatial neglect can expect smaller but clinically significant gains up to 6 months poststroke.

Variability in Neglect Recovery Rates

There was substantial heterogeneity across studies, with some reporting complete recovery while others observed chronic neglect in all stroke survivors. There are likely several factors contributing to this variability in patient outcomes. First, as highlighted in our study quality assessment, sample sizes tended to be relatively small. Fourteen studies involved fewer than 20 participants, and only 4 studies had a sample size of ≥ 50 patients with neglect at baseline. Notably, 3 studies that had fewer than 10 participants at follow-up reported either minimal^{38,46} or complete recovery.⁴⁷ Such extreme outcomes can likely be attributed, at least in part, to insufficient sample sizes. Additionally, the quality assessment indicated that most studies excluded patients with left-hemisphere lesions. Although neglect is more prevalent after right-hemisphere damage,⁵⁸ a recent review showed that 20% of all stroke survivors with left-hemisphere lesions are also affected by neglect.⁴ Moreover, the impact of neglect on rehabilitation outcomes is similar for left- and right-hemisphere stroke survivors.^{4,58} It is, therefore, important to understand the recovery of neglect following lesions within either hemisphere. Most studies claim neglect is more persistent after right- than left-hemisphere stroke.^{19,20,59} This review supports this notion as we observed greater recovery in studies that

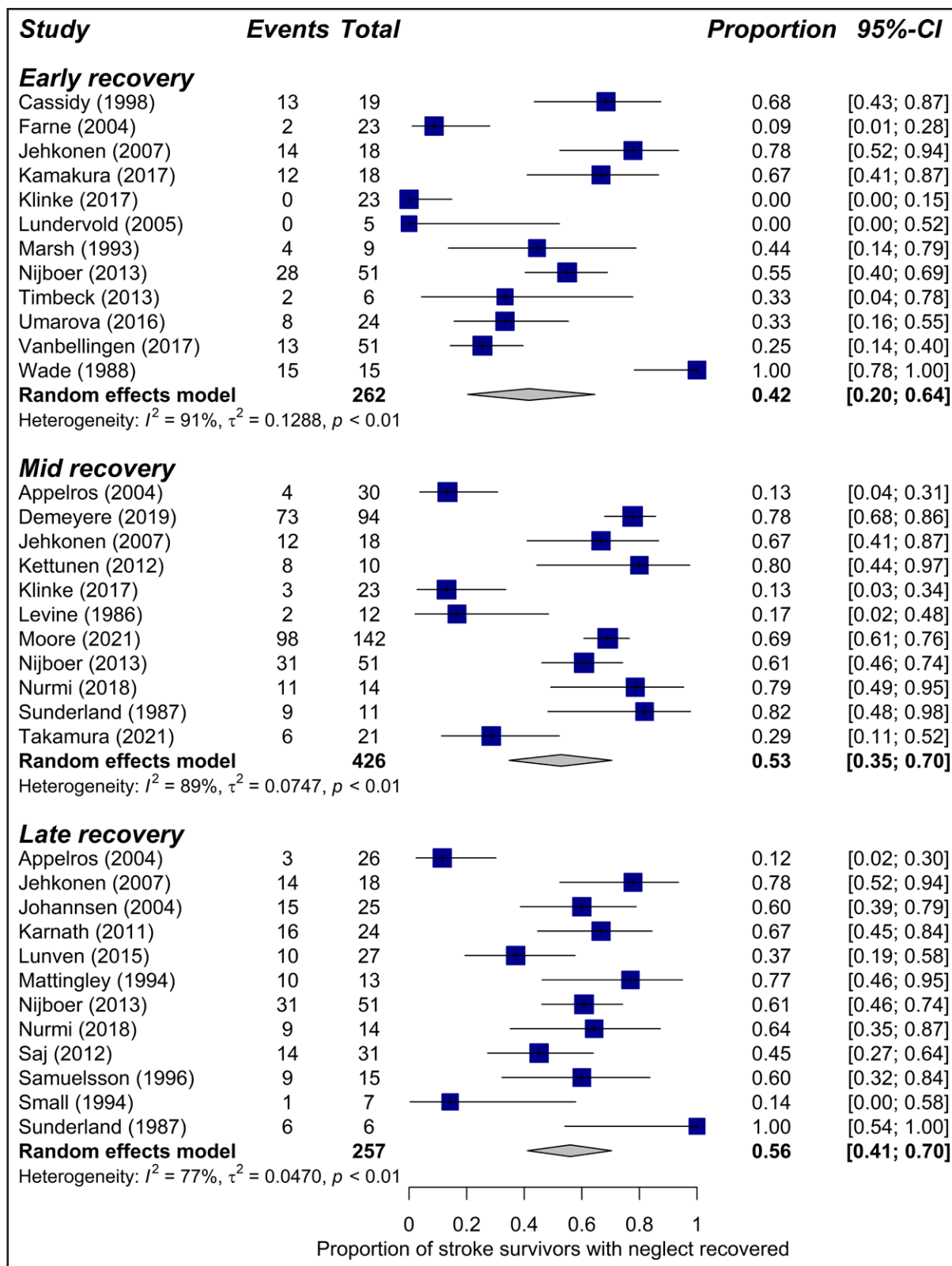


Figure 3. Forest plots of random-effects models for neglect recovery stratified by phase.

included patients with left-hemisphere stroke. However, as few studies reported recovery outcomes separately for patients with left- and right-hemisphere stroke, it was not

possible to directly contrast recovery patterns between these 2 groups. We also hypothesized that studies that conducted the baseline assessment of neglect within

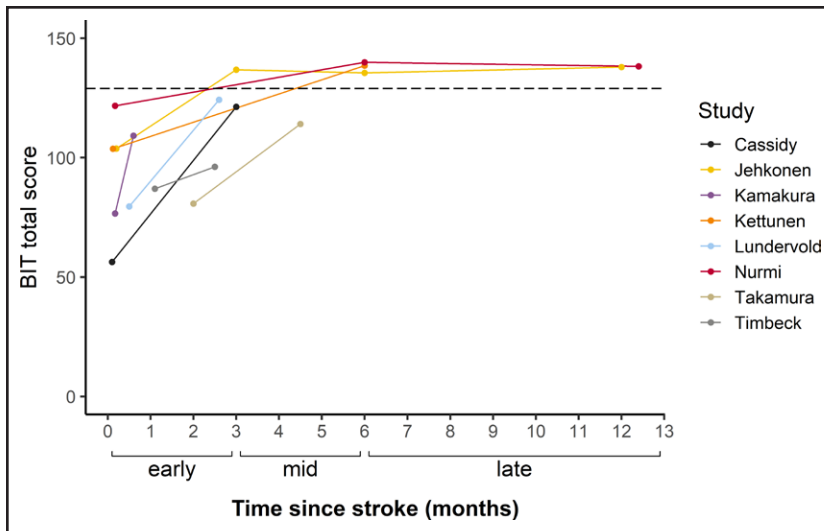


Figure 4. Changes in average scores over time for studies reporting Behavioural Inattention Test (BIT) performance.

Individual lines indicate mean scores reported by each study. The dashed line represents the cutoff score for a diagnosis of neglect.

the first week after stroke would observe higher levels of recovery relative to studies that recruited patients at a later time. Contrary to our expectations, metaregressions showed no evidence that the time at which the first assessment was completed influenced reported recovery rates. However, only 6 studies examined patients within the first week after stroke, with 2 studies completing neuropsychological examinations in the first 3 days. Given the limited amount of information on these initial days poststroke, it is possible that this review underestimates potential rapid recovery from hyperacute neglect. Finally, greater stroke severity is associated with higher risk of neglect,⁵ and the severity of both the lesion itself and symptoms of neglect have previously been shown to predict poorer recovery.^{18,60} Accumulating evidence suggests that neglect follows principles of proportional recovery,^{10,61,62} such that patients with severe symptoms show quantitatively greater improvements over time but are less likely to meet formal recovery criteria. Due to limited information on either the severity of stroke or neglect across studies, we could not formally evaluate this possibility. Of the studies reporting high stroke or neglect severity rates, 2 observed below-average recovery rates (<15%),^{28,36} whereas 1 study found a 75% recovery rate.³³ Additionally, 2 studies showed that baseline symptoms were more severe in patients with chronic neglect compared with patients who recovered.^{34,39} These findings suggest that acute severity could predict recovery rates. However, there is emerging evidence that the impact of severity on neglect recovery is complex and may vary depending on different factors, such as age⁶² and neglect subtype.¹⁰ Future studies exploring predictors of recovery should, therefore, consider potential interactions of severity and patient characteristics.

Strengths and Limitations

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines

to produce a methodologically robust synthesis of the literature on visuospatial neglect recovery. High levels of heterogeneity were observed across studies, limiting the precision of estimated recovery rates. We addressed this by carrying out sensitivity analyses that excluded low-quality studies, with resulting recovery rates being similar to the main meta-analyses. We also examined the contribution of patient and study characteristics to variability in metaregressions. However, we acknowledge that our exploration of sources of heterogeneity was limited by the availability of primary data and could, therefore, not evaluate the impact of variables such as stroke severity. In addition, there were insufficient data to determine the influence of medical treatments or standard rehabilitation procedures on neglect recovery. Only 5 studies reported details on standard rehabilitation protocols for stroke survivors, such as provision of physiotherapy and occupational therapy. In addition, while thrombolysis and thrombectomy are known to improve outcomes after stroke,^{63,64} there were insufficient studies ($n=3$) reporting administration rates to analyze the impact of these treatments on neglect recovery. However, as there were few studies that assessed patients in the hyperacute phase (ie, the period in which this treatment takes place), this is unlikely to have affected the main results. The present review focused on spatial deficits that are central to the neglect syndrome. However, it is important to note that nonspatial impairments may exacerbate difficulties experienced by patients with neglect.⁶⁵ As the majority of studies did not use nonspatial measures of cognition, it remains unclear whether the presence of nonspatial cognitive impairments contributes to differences in recovery outcomes. In addition, assessments typically focused on the visual domain and did not measure neglect across sensory modalities, although it has been shown that multiple sensory domains are frequently affected in neglect.⁶⁶ It is currently unclear whether

recovery varies across modalities or differs between multimodal and unimodal impairments. Finally, included studies used a wide range of instruments for diagnosing neglect, which could lead to differences in sensitivity to neglect symptoms. We aimed to address this by evaluating changes in scores on the BIT, a well-validated and standardized assessment for neglect. Although the limited number of studies reporting BIT scores precluded formal analyses of this outcome, descriptive data showed a pattern of recovery, which was highly comparable to the main results. Previously, it has also been proposed that recovery may differ for specific subtypes of neglect. Specifically, research suggests that egocentric neglect (ie, neglect with a self-centered reference frame) tends to show proportional recovery, such that more severe cases demonstrate the greatest improvements over time. In contrast, recovery of allocentric neglect (ie, neglect with an object-centered reference frame) was not related to initial symptom severity.¹⁰ This finding indicates that stroke survivors with particular types of neglect, such as allocentric neglect, may have a worse prognosis. However, as few studies distinguished between different subtypes of neglect, it was not possible to investigate this possibility in the present review.

Clinical Implications

Meta-analyses findings indicate that a large proportion of patients with neglect recover within the first 6 months after stroke. These findings provide useful information for both stroke survivors and clinicians, who benefit from having a clearer understanding of the prognosis for neglect and associated support needs. Additionally, estimates of neglect recovery can be applied to inform policy and care services as to the predicted needs of stroke survivors over time. It is important to emphasize that, while the present results suggest most stroke survivors will recover from neglect, $\approx 40\%$ with neglect are expected to have persistent impairments. Given that neglect is associated with poor functional outcomes and reduced rehabilitation efficacy, it is critical that clinicians are aware that patients with neglect may need continued support to cope with their symptoms. While neglect severity appears to be a potential factor,¹⁰ further research is needed to converge on predictors of chronic neglect and to devise appropriate support and interventions for these patients.

Conclusions

This systematic review and meta-analysis shows that 53% of stroke survivors with neglect recover within the first 6 months, with most recovery with standard treatment taking place within 3 months poststroke. However, heterogeneity within the existent literature is high; further large-scale studies are needed to confirm the factors that influence neglect recovery, most likely lesion

site and severity. Future studies on visuospatial neglect should prioritize the identification of predictors for chronic symptoms, improving our understanding of which subgroups of stroke survivors with neglect may benefit most from additional therapies, and the development of support and interventions for stroke survivors with persistent neglect.

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Disclosures

None.

Supplemental Material

Search Strategy

Sensitivity Analyses

Figure S1

Table S1

PRISMA 2020 Checklist



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Stroke