



PRE-STROKE PHYSICAL ACTIVITY IN RELATION TO POST-STROKE OUTCOMES LINKED TO THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH: A SCOPING REVIEW

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Objective: This scoping review aims to identify how pre-stroke physical activity has been studied in relation to outcomes after stroke using the International Classification of Functioning, Disability and Health (ICF) framework.

Methods: MEDLINE, CINAHL, Scopus, and grey literature databases were systematically searched from inception to 15 March 2021, with no language restrictions. Risk of bias was evaluated for all included studies. Identified outcome measures were linked to ICF components using linking rules, and the main findings were summarized.

Results: Of 3,664 records screened, 35 studies were included. The risk of bias was graded as moderate to critical for all studies. A total of 60 unique outcome measures were identified, covering the hyperacute to chronic phases of stroke recovery. Outcome measures linked to body functions were most common ($n=19$), followed by activities and participation ($n=14$), body structures ($n=7$), environmental factors ($n=4$) and personal factors ($n=2$). The majority of studies collected data on pre-stroke physical activity retrospectively, and no study used objective methods to measure physical activity. Only one study analysed haemorrhagic cases separately.

Conclusion: Pre-stroke physical activity has been studied in relation to a variety of outcome measures linked to ICF after stroke. However, this review highlights the high risk of bias, and limited quality of the current literature.

Key words: exercise; outcomes research; risk factor; systematic review; stroke recovery.

Accepted Nov 24, 2021; Epub ahead of print

J Rehabil Med 2021; 53: jrm002XX

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The consequences of stroke vary greatly among individuals, and throughout the stages of recovery (1). Stroke research has traditionally focused on physical disability; however, many stroke survivors experience long-lasting sequelae involving emotional, cognitive, social, and financial domains of health (2). The International Classification of Functioning, Disability

LAY ABSTRACT

We used the International Classification of Functioning, Disability and Health (ICF) to categorise the outcome measures of 35 studies. The ICF includes the following domains of health: body functions, body structures, activities, participation, and environmental factors. We identified 60 outcome measures, covering all domains of the ICF. Most common were measures related to body functions such as stroke symptoms, cognition or respiratory function, and activities or participation, such as functional recovery and walking ability. Few studies evaluated personal and environmental factors. Most studies collected information on physical activity before the stroke after the stroke had occurred, and all studies used self-reported information which is problematic from a scientific point of view and can lead to erroneous results. Future studies are needed to determine the true impact of physical activity on outcomes after stroke.

and Health (ICF) was developed by the World Health Organization (WHO) and provides a standardized framework for health and health-related states (3). The biopsychosocial approach in ICF suggests comprehensive evaluations of health, and covers a wide range of outcomes, from the basic functions required for life to complex abilities needed for behavioural adaptation (4).

Modifiable risk factors for stroke, and post-stroke recovery are receiving increasing interest. One emerging topic is the potentially neuroprotective effect of pre-morbid physical activity (PA) (5). The health benefits of PA are well-established, and the WHO recommends that every adult perform 150–300 min of moderate-intensity PA or 75–150 min of vigorous-intensity PA each week (6). These recommendations also apply to older adults, and adults with non-communicable diseases. Regular PA has a strong inverse relationship with cardiovascular morbidity and all-cause mortality (7). Moreover, PA independently reduces the risk of stroke, and may counteract several other cerebrovascular risk factors including hypertension, diabetes, obesity, and psychosocial stress (6, 8). It is not known whether pre-stroke PA has a significant effect on post-stroke outcomes.

To date, a wide range of outcome measures, recorded at different time-points after stroke, have been studied in relation to pre-morbid PA. Prior systematic reviews have evaluated the impact of pre-stroke PA on acute

stroke severity (9), and post-stroke disability (10). Moving forward, there is a need to systematically identify the available evidence, address knowledge gaps, and inform future research. The primary aim of this scoping review is to classify all post-stroke outcome measures that have been studied in relation to pre-stroke PA, using the ICF framework. Secondary aims are to summarize methods used for assessment of pre-stroke PA, and to grade the quality of evidence in the existing body of literature.

METHODS

This study follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) statement (11), and a prespecified study protocol was published online in the Open Science Framework (12). A glossary is provided in Table I.

The condition being studied is stroke, defined according to the WHO criteria as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 h or leading to death, with no apparent cause other than that of vascular origin” (13). The exposure being studied is pre-stroke PA, defined as “any bodily movement produced by the contraction of skeletal muscles that results in energy expenditure” (14). Examples of the exposure include objective measures of energy expenditure, and self-perceived or observed measures of aerobic exercise, occupational PA, or leisure-time activities. No study was excluded based on the assessment-method of PA. Both prospective and retrospective assessments of pre-stroke PA were included.

Search strategy

A systematic literature search was performed on 9 June 2020, and an updated search on 15 March 2021 in MEDLINE, CINAHL, and Scopus, with no language or time restrictions. The search was all-inclusive, with terms relating to PA and stroke (Appendix S1). In addition, the same terms were applied in a systematic search for grey literature using Grey Literature Report (GreyLit.org) and Google Advance search engines. The

Grey Literature Report comprises grey literature publications in health services research and selected urban health topics between 1999 and 2016. Google Advance was used to find grey literature published between 1 January 2017 and 15 March 2021.

Eligibility criteria

Studies that met the following criteria were included: a study population of adults with a clinically or radiologically verified stroke; a quantifiable measurement of pre-stroke PA; any type of outcome measure recorded after stroke, analysed in relation to pre-stroke PA. Exclusion criteria were: study populations including participants with conditions beyond stroke, without relevant subgrouping; not enough information to interpret the analyses regarding pre-stroke PA; qualitative studies, review studies, case reports, and animal studies.

Inclusion process

Pilot testing of the study selection, data extraction and risk of bias assessment were conducted to ensure consistency among authors. Two authors (AV and MR) independently screened and selected articles that fulfilled the inclusion criteria, based on title and abstract. If eligibility was unclear at this stage, the full text was checked. In addition, all reference lists of selected articles were reviewed to ensure literature saturation. Four authors (AV, MR, AD and AP) reviewed the full text of all selected articles, in pairs. Data extraction and risk of bias assessments were performed by 2 authors independently for each article. Discrepancies were resolved by the most senior author (KSS). Four studies with no full text published in English were identified, for which a native speaker with experience within the stroke research field was solicited for translation (Polish, Chinese, Turkish and Spanish). Fig. 1 details the selection process. Reasons for exclusion in the full-text review are stated.

Data extraction and analysis

The data extraction was standardized among authors by using a specified form. Information was collected on study characteristics and methodology, pre-stroke PA assessments, outcome measures analysed in relation to pre-stroke PA, and important study findings. The PA assessments were evaluated in terms of assessment tool, assessment time-point, and what period before

Table I. Glossary

ACS	acute coronary syndrome	mRS	modified Rankin Scale
ADL	activities of daily living	MWS	maximal walking speed
AFT	Animal Fluency Test	NIHSS	National Institutes of Health Stroke Scale
BBS	Berg Balance Scale	OHS	Oxford Handicap Scale
BDNF	brain-derived neurotrophic factor	OUES	oxygen uptake efficiency slope
BMI	body mass index	PA	physical activity
CVD	cardiovascular disease	PASE	Physical Activity Scale for the Elderly
DVT	deep vein thrombosis	PSD	post-stroke dementia
ETT	exercise tolerance test	RPE	rating of perceived exertion
FEV1	forced expiratory volume in 1 s	SDMT	Symbol Digit Modalities Test
FIM	Functional Independence Measure	SGPALS	Saltin-Grimby Physical Activity Level Scale
FSS	Fatigue Severity Scale	SIS	Six-Item Screener
FVC	forced vital capacity	SOEE	Short Outcome Expectations for Exercise
G-CSF	granulocyte colony stimulating factor	SSEE	Short Self-Efficacy for Exercise scale
GOS	Glasgow Outcome Scale	SSS	Scandinavian Stroke Scale
HADS	Hospital Anxiety and Depression Scale	TIA	transient ischaemic attack
IADL	Instrumental Activities of Daily Living	UGI	upper gastrointestinal
ICF	International Classification of Functioning, Disability and Health	VEGF	vascular endothelial growth factor
ICU	intensive care unit	WHO	World Health Organization
IGF-I	insulin-like growth factor I	WLD	Word List Delayed Global
MET	metabolic equivalent of task	WLL	Word List Learning
MMSE	Mini-Mental State Examination	Vmax	maximal work load (Watt)

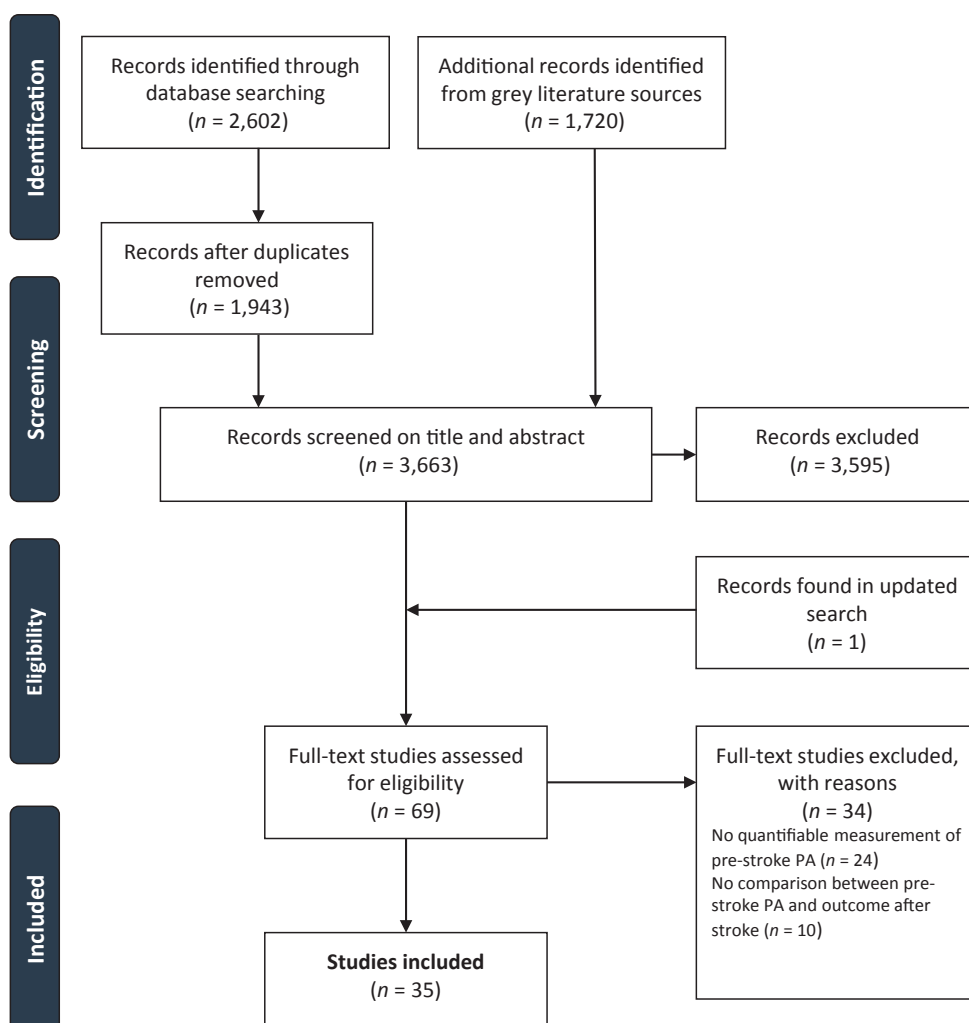


Fig. 1. Inclusion process: Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flowchart. PA: physical activity.

stroke the assessment referred to. Studies with data from the same patient cohort were pooled for descriptive statistics.

Outcome measures were mapped according to the main ICF components: body structures, body functions, activities and participation, environmental factors and personal factors. ICF linking rules were used to connect the content of each outcome measure to the ICF framework (15). For each outcome, all meaningful concepts were identified and linked to the most precise alphanumeric ICF category code. For outcome measures linked to category codes from more than one of the main ICF components, the number of meaningful concepts linked to each component determined where it was placed in the ICF model. However, there are no category codes for personal factors in the ICF framework. Therefore, outcome measures strongly related to personal factors, which could not be linked to the other ICF components, were placed directly in the ICF model under personal factors. Outcome measures not covered by the ICF framework (i.e. mortality, morbidity and complications) were placed outside the model. The time-points for registration of outcome measures were classified in accordance with the consensus definition of phases in stroke recovery: hyperacute (0–24 h), acute (1–7 days), early subacute (7 days to 3 months), late subacute (3 to 6 months) and chronic (>6 months) (1). Studies that did not detail an exact time-point for collection of outcomes were arbitrarily classified.

Risk of bias

The risk of bias was evaluated using the Risk Of Bias In Non-randomised Studies of Exposures (ROBINS-E) tool (16). The ROBINS-E is provided by the University of Bristol, Bristol, UK, and contains 7 domains: confounding, selection of participants, classification of exposures, departures from intended exposures, missing data, measurement of outcomes, and selection of reported results. Inadequate confounding adjustment was considered for studies controlling for no or a limited number of covariates, post-exposure covariates, or large numbers of unnecessary covariates. Each domain can be rated as low, medium, serious or critical risk of bias. The highest risk of bias recorded in a domain determines the overall judgement. MR and AP authored one included article, and KSS 2 included articles, for which AV and AD performed the risk of bias assessments.

RESULTS

Of 3,664 records screened, 35 studies with data from 33 cohorts were included in this scoping review. The risk of bias was assessed as moderate to critical in all studies, with most studies being at a serious risk of bias (Fig.

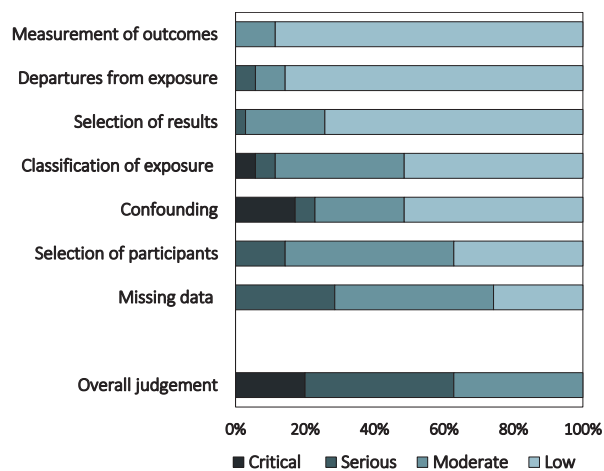


Fig. 2. Risk of bias: frequency of assessments in each domain of the Risk Of Bias In Non-randomised Studies of Exposures (ROBINS-E) tool.

2). Missing data, exclusion of cases with missing data, and inadequate adjustment for confounding factors were the major reasons behind the serious and critical risk of

bias assessments. Characteristics of included studies are summarized in Table II. Three studies did not report any subclassification of stroke diagnoses, and 2 studies included either only men or women. There were 13,569 unique cases with ischaemic stroke. In addition, there were 16,405 cases of ischaemic stroke and transient ischaemic attack (TIA) intermixed. Similarly, there were a total of 8,162 cases with haemorrhagic stroke. Five studies included cases with subarachnoid haemorrhage (17–21). The majority of cases of haemorrhagic stroke (86%) were from one study, in which cases of intracerebral haemorrhage and subarachnoid haemorrhage were not reported separately. Only one study analysed the relationship between pre-stroke PA and outcome measures separately for haemorrhagic stroke cases (22). Four studies used data from randomized controlled trials, in which participants were allocated to remote ischaemic preconditioning (23), treatment with citalopram (24), repeated encouragement of PA in addition to standard post-stroke follow-up (25), or intensive cardiovascular risk factor interventions (26).

Table II. Characteristics of included studies

Reference	Year	Language	Design	PA assessment	Stroke cases (n)	Stroke type (n)		Sex (n)	
						Ischaemic	Haemorrhagic	Men	Women
Aberg et al. (27)	2020	English	OS, LO	Retro	380	380	–	241	139
Baert et al. (17)	2012	English	OS, LO	Retro	33	26	7	23	10
Bell et al. (18)	2013	English	OS, LO	Pros	3,173 ^d	2,255	540	–	3,173
Blauenfeldt et al. (23)	2017	English	RCT, LO	Retro	102	102	–	62	40
Boden-Albala et al. (28)	2005	English	OS, LO	Retro	655	655	–	295	360
Bovim et al. (29)	2019	English	OS, LO	Retro	205	181	24	110	95
Damsbo et al. (24)	2020	English	RCT, LO	Retro	625	625	–	410	215
Decourcelle et al. (30)	2015	English	OS, LO	Retro	519	519	–	256	263
Deplanque et al.a (31)	2006	English	OS, CS	Retro	291	291	–	167 ^c	195 ^c
Deplanque et al.a (32)	2012	English	OS, CS	Retro	291	291	–	167 ^c	195 ^c
García-Bouyssou et al. (33)	2018	Spanish	OS, CC	Retro	93	93	–	44	49
Gezer et al. (34)	2017	Turkish	OS, CS	Retro	42	42	–	27	15
Krarp et al. (25)	2008	English	RCT, LO	Retro	265	265	–	148	117
Lacroix et al.(35)	2016	English	OS, CS	Retro	88	63	25	52	36
Levine et al. (36)	2018	English	OS, LO	Pros	694 ^d	637	55	344	350
Li et al. (37)	2005	Chinese	OS, LO	Retro	189	?	?	115	74
Lopez-Cancio et al.b (38)	2017	English	OS, LO	Retro	83	83	–	48	35
Ricciardi et al.b (39)	2014	English	OS, LO	Retro	159	159	–	98	61
Mahendran et al. (40)	2020	English	OS, LO	Retro	36	?	?	25	11
Mediano et al. (21)	2021	English	OS, LO	Pros	881	807	111	420	461
Morovatdar et al.(19)	2020	English	OS, LO	Retro	395	339	48	197	198
Olsson et al. (41)	2017	English	OS, LO	Retro	77	66	11	46	31
Persson et al. (42)	2020	English	OS, LO	Retro	215	203	?	110	105
Redfors et al. (43)	2016	English	OS, LO	Retro	600	600	–	385	215
Reinholdsson et al. (44)	2018	English	OS, CS	Retro	925 ^d	868	54	507	418
Rist et al. (45)	2017	English	OS, LO	Pros	1,853	?	?	800	1,053
Rist et al. (22)	2011	English	OS, LO	Pros	1,378 ^d	1,146	221	1,378	–
Shaughnessy et al. (46)	2006	English	OS, CS	Retro	304	?	?	127	177
Stroud et al. (47)	2009	English	OS, LO	Retro	673	673	–	381	292
Urbanek et al. (48)	2018	English	OS, LO	Retro	1,370	1370	–	693	677
Ursin et al. (26)	2015	English	RCT, LO	Retro	152	135	17	95 ^c	88 ^c
Wang et al. (49)	2014	English	OS, CS	Retro	265	265	–	151	114
Wen et al. (20)	2017	English	OS, LO	Retro	39,835 ^d	16,405 ^{c,e}	6,979	23,867 ^c	15,968 ^c
Wong et al. (50)	2016	English	OS, LO	Retro	872 ^d	709	72	564 ^c	449 ^c
Yamaguchi et al. (51)	2018	English	OS, LO	Retro	130	95	35	86	44

PA: physical activity; OS: observational study; RCT: randomized controlled trial; LO: longitudinal design; CS: cross-sectional design; CC: case-control design; Retro: retrospectively collected; Pros: prospectively collected. ^{a,b}Data from the same study cohort; ^cIschaemic stroke and TIA are not separately reported; ^dIncluding strokes of unknown type; ^enumber was revised after contact with authors. ?: Not reported; -: Not included.

Table III. Time-points for registration of outcome measures in relation to the phases of stroke recovery

Phase	Time-point	Outcome measures
Hyperacute	< 24 h	VEGF, G-CSF, BDNF, recanalization
	24 h	infarct growth, NIHSS
Acute	4 days	IGF-I
	7 days	NIHSS, mRS, Barthel Index, MWS, BBS, VEGF, G-CSF, BDNF
Early Subacute	8 days	mRS, Barthel Index, NIHSS
	10 days	SSS, mRS, NIHSS, in-hospital mortality, ICU, nasogastric tube, Foley catheter, rehabilitation, haemorrhagic infarct, pneumonia, DVT, UTI, depression, seizure, ACS, UGI bleeding, pulmonary oedema, pressure sore
	2 weeks	FSS
	1 month	Infarct volume, SDMT, mRS, Barthel Index, GOS, OHS, NIHSS
	2 months	PA time, FIM, ETT, VO ₂ max, Wmax, RPE, FEV1, FVC, FEV1/FVC
Late Subacute	3 months	IGF-I, VO ₂ peak, OUES, HADS, mRS, Mortality, IPAQ, VEGF, G-CSF, BDNF, walking volume
	6 months	VO ₂ peak, OUES, SDMT, MMSE, mRS, SGPALS, PSD
Chronic	1 year	VO ₂ peak, OUES, mortality, stroke reoccurrence, mRS, Barthel Index, SGPALS, NIHSS, MWS, BBS
	2 years	mRS
	3 years	ADL, IADL, Mortality, CVD, stroke reoccurrence
	≥ 5 years	mortality, adverse events, SIS, AFT, WLL, WLD, mRS, Barthel Index, stroke reoccurrence, SSEE, SOEE

Phases in stroke recovery: hyper acute (0 to 24 hours), acute (1 to 7 days), early subacute (7 days to 3 months), late subacute (3 to 6 months) and chronic (> 6 months) (1). (See Table I for abbreviations.).

All identified studies used self-reported assessment methods for pre-stroke PA, and all but 5 studies collected the data retrospectively. Table SI details PA assessments in included studies. Nine different questionnaires were used for assessment of pre-stroke PA in 19 studies. For statistical analyses, 26 of the studies divided the study population into groups based on PA levels.

Outcome measures and linking to the ICF

Pre-stroke PA has been studied in relation to outcome measures recorded in all phases of stroke recovery (Table III). In total, 60 unique outcome measures were

identified, of which 46 could be linked to 64 category codes in the ICF framework (Table SII). Fig. 3 portrays all outcome measures classified in the ICF model. Outcomes linked to body functions were highest in number (19 outcome measures), followed by activities and participation (14 outcome measures), body structures, (7 outcome measures) environmental factors (4 outcome measures) and personal factors (2 outcome measures). Post-stroke mortality, morbidity and complications could not be linked to the ICF framework, and are thus placed outside of the model. Being physically active was not related to adverse outcomes in any study.

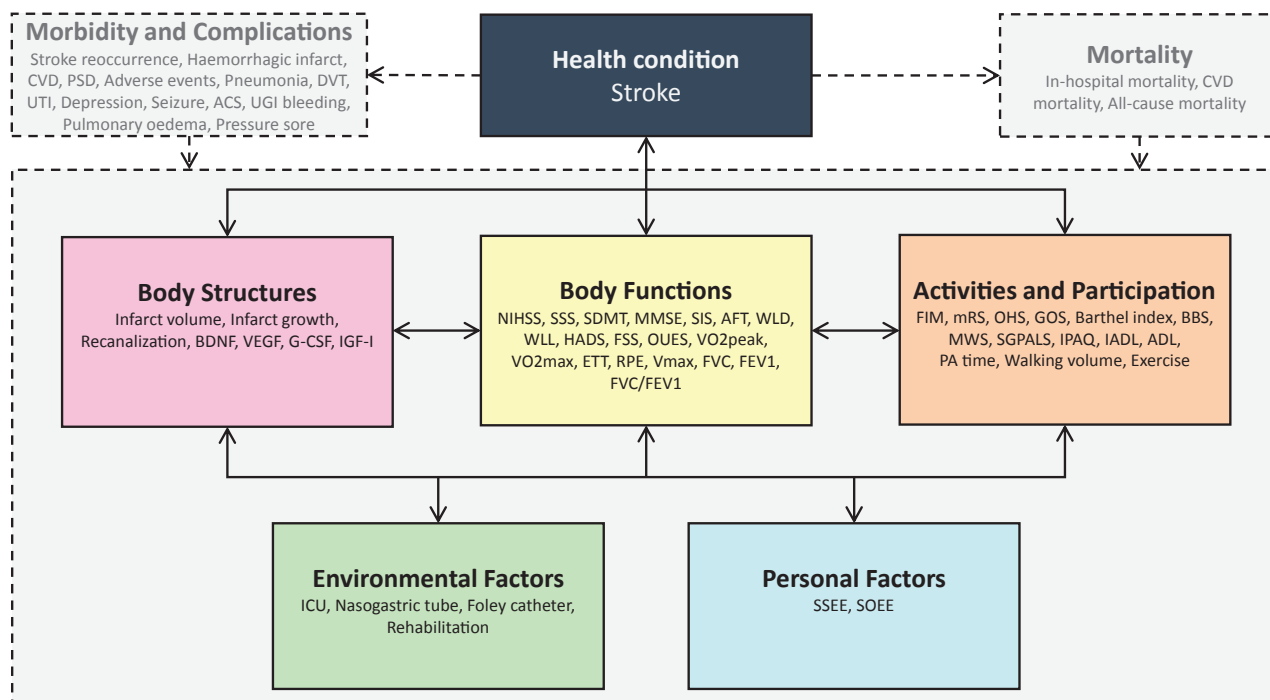


Fig. 3. Outcome measures classified using the International Classification of Function, Disability, and Health (ICF) model. (See Table I for abbreviations.)

Body structures

In the hyperacute phase of ischaemic stroke, a higher level of pre-stroke PA was significantly associated with complete arterial recanalization (39), and decreased 24-h infarct growth (23). These studies also reported smaller infarct volumes among those previously active (23, 39), although there was no association between pre-stroke PA and infarct volume at the same time-point in another, larger, population (47). Serum levels of neurotrophic factors (vascular endothelial growth factor (VEGF), granulocyte colony stimulating factor (G-CSF), brain-derived neurotrophic factor (BDNF) and insulin-like growth factor I (IGF-I)) have been studied in relation to pre-stroke PA in 2 ischaemic stroke populations (27, 38). Pre-stroke PA was associated with higher levels of VEGF one week and 3 months post-stroke, with a significantly higher increment in VEGF measured on the seventh day (38). However, there were no associations between pre-stroke PA and post-stroke serum levels of G-CSF or BDNF. In the acute phase, higher pre-stroke PA predicted higher levels of IGF-I in models adjusted for age, sex, history of previous stroke, and myocardial infarction. This relationship did not exist when further adjusting for diabetes, hypertension, smoking and initial stroke severity (27). There was also a dose-response relationship between higher pre-stroke PA and decreased IGF-I levels at 3 months, which remained significant after adjustment.

Body functions

Stroke severity has been studied in relation to pre-stroke PA using the National Institutes of Health Stroke Scale (NIHSS) in 7 studies with data from 6 cohorts, and the Scandinavian Stroke Scale (SSS) in one study. Six studies reported less severe strokes for those with higher pre-stroke PA (20, 25, 31, 32, 39, 44), whereas 2 studies found no association after adjustment (26, 47). One study found that pre-stroke PA predicted better global cognition (Mini-Mental State Examination; MMSE) measured at 6 months post-stroke (50). In another study, higher pre-stroke PA predicted better cognitive processing speed (Symbol Digit Modalities Test; SDMT) 1- and 6-months post-stroke, but was not associated with MMSE at 6 months (24). No associations have been found between pre-stroke PA and executive function (Animal Fluency Test; AFT), verbal memory (Word List Delayed Global; WLD), new learning (Word List Learning; WLL), or global cognition (Six-Item Screener; SIS) in the chronic phase of stroke recovery (36). Symptoms of depression measured with the Hospital Anxiety and Depression Scale (HADS) during late subacute phase of stroke recovery

was associated with pre-stroke inactivity (29). Also, moderate to strenuous exercise before stroke was found to reduce the likelihood of post-stroke fatigue (Fatigue Severity Scale; FSS) (49). There were no associations between pre-stroke PA and outcome measures related to cardiorespiratory fitness (oxygen uptake efficiency slope (OUES), $\text{VO}_{2\text{peak}}$, $\text{VO}_{2\text{max}}$, exercise tolerance test (ETT), \dot{V}_{max} , forced vital capacity (FVC), forced expiratory volume in one s (FEV1), and FVC/FEV1) or perceived exertion (rating of perceived exertion; RPE) in 2 small stroke populations (17, 34).

Activities and participation

Seven studies have found associations between higher pre-stroke PA and less post-stroke disability evaluated using modified Rankin Scale (mRS) (20, 25, 26, 31, 39, 48), and Oxford Handicap Scale (OHS) (47). However, 4 studies found no associations with mRS (19, 22, 24, 30), or the Glasgow Outcome Scale (GOS) (47), in analyses adjusted for covariates. Being pre-morbidly active predicted independence in activities of daily living (ADL) (Barthel Index) upon hospital admission (26, 31, 47), at 3 months (47), and one year after stroke (26). Higher pre-stroke PA also predicted independence in 5 ADL and Instrumental Activities of Daily Living (IADL) tasks, evaluated 3 years after stroke (45). In addition, higher pre-stroke PA predicted gait independence after in-hospital stroke rehabilitation using Functional Independence Measure (FIM) (51), and post-stroke balance using Berg Balance Scale (BBS) in the acute, and chronic phase of stroke recovery (26). Associations between high pre- and post-stroke PA have been reported using the Saltin-Grimby Physical Activity Level Scale (SGPALS) at 6 months (42), and one year after stroke (41). Furthermore, 3 studies reported bivariate correlations between pre- and post-stroke PA during hospitalization (35), at 3 months (33), and 5 years after stroke (46). Higher pre-stroke PA measured using total scores in Physical Activity Scale for the Elderly (PASE) predicted increased walking volume (number of steps) 3 months post-stroke (40). Frequent walking before stroke predicted a faster maximal walking speed (MWS) in the acute and chronic phase of stroke recovery (26).

Environmental factors

Regular pre-stroke PA predicted reduced usage of nasogastric tubes, and decreased in-hospital rehabilitation, but had higher odds for treatment in the intensive care unit (ICU) (20). There was no association between pre-stroke PA and usage of Foley catheters after covariate adjustment (20).

Personal factors

Evaluated a mean of 5 years after stroke, pre-stroke PA was not significantly correlated with self-efficacy (Short Self-Efficacy for Exercise scale; SSEE) or expectations of exercise (Short Outcome Expectations for Exercise; SOEE) among stroke survivors (46).

Mortality, morbidity and complications

Being physically active before stroke has been associated with reduced risk of in-hospital mortality (20), cardiovascular mortality (21), and all-cause mortality evaluated up to 8 years after stroke (18, 19, 21, 37). Conversely, 2 studies found no relationship between pre-stroke PA and post-stroke mortality in adjusted analyses (30, 43). Pre-stroke PA has also been associated with fewer adverse events (myocardial infarction, stroke recurrence, or death) 5 years after stroke (28). Premorbid stretching and toning exercises were associated with a reduced risk of dementia 6 months after stroke (50). Stroke recurrence has been evaluated in relation to pre-stroke PA in 2 studies, but there were no significant associations (19, 21). Moreover, one study found no association between pre-stroke PA and post-stroke cardiovascular disease (21). Higher pre-stroke PA has also been associated with lower odds of in-hospital pressure sores, seizures, urinary tract infections, depression, haemorrhagic transformation of ischaemic strokes, and upper gastrointestinal bleedings, but not with in-hospital deep vein thrombosis, pneumonia, pulmonary oedema, or acute coronary syndrome (20).

DISCUSSION

This scoping review classifies outcome measures studied in relation to pre-stroke PA using the ICF framework, and details the quality of the current evidence. Successful recovery is imperative for reducing the individual and societal burden of stroke (1). The ICF provides a comprehensive view on how various modifiable aspects of health can influence stroke recovery, and a commonly recognized international language to describe post-stroke functioning (3). The linking between ICF code categories and outcome measures can serve as a rationale for researchers studying the role of pre-stroke PA henceforth. Homogenous use of outcome measures may also enable across-study comparisons. However, it is important to ensure that the selected outcome measures are meaningful to all stakeholders (i.e. stroke survivors, clinicians, and researchers). To that end, the ICF framework constitutes a well-studied foundation for future post-stroke research.

This study demonstrates that pre-stroke PA has been studied in relation to outcome measures covering all ICF domains, and beyond the ICF framework in studies investigating post-stroke mortality, morbidity and in-hospital complications. The majority of studies evaluated pre-stroke PA in relation to post-stroke body functions, body structures, activities and participation. Most of the identified outcome measures are validated and commonly used in stroke populations (52). Through classification by the main ICF components, it is apparent that knowledge regarding personal and environmental factors is lacking. Contextual factors could hinder stroke survivors from taking part in rehabilitative efforts, and a person's mindset can be either a barrier or a facilitator to functional recovery (3). Future research on pre-stroke PA should address this, along with applying validated outcome measures across the whole ICF framework.

Knowledge regarding modifiable predictors of stroke outcomes may improve public health strategies targeted to decrease the burden of stroke. PA is a cost-effective and easily accessible way to promote public health, with a well-documented effect (6, 7). Summarizing the results of 35 studies, pre-stroke PA was not associated with adverse outcomes in any study. However, all studies except one exclusively reported the results from analyses with a majority of ischaemic stroke cases, and the current knowledge on how pre-stroke PA affects post-stroke outcomes cannot be extrapolated to persons with haemorrhagic stroke. Pre-stroke PA likely affects the mechanisms involved in stroke-related brain injury differently for ischaemic and haemorrhagic cases (53). Moving forward, clinical studies should aim to include enough haemorrhagic stroke cases to enable separate analyses.

The most common methodology in included studies was a retrospective, longitudinal data collection. The majority of studies utilized information on pre-stroke PA collected during the hospital stay. The retrospective design is cheaper and less time consuming than the prospective counterpart, but introduces recall and selection bias. In the retrospective assessments of pre-stroke PA, several studies failed to adequately report the intensity, duration and frequency of PA. Furthermore, the majority of included studies exclusively evaluated one domain of leisure-time, work or sports-related PA. This could lead to misclassification, as there may be large intra-individual differences in the level of PA performed within each domain (54). Five of the included studies did, however, perform prospective data collections and should be considered more reliable in this regard (18, 21, 22, 36, 45). A prospective study design also allows for quantification of PA through objective measurements

with accelerometers, pedometers, or global positioning systems, but such methods were not applied in any of the included studies. An important limitation of the current literature is the lack of objective measurements for pre-stroke PA. The inherent limitations of self-reported data decrease the reliability of PA assessments used in this scoping review, in particular since having a stroke may decrease a person's ability to give correct estimates of previous activity (55). Although some studies have taken efforts to reduce the risk of recall bias via confirmatory questions to relatives and care givers, objective measures of pre-stroke PA should be included in future studies. In addition, there has been substantial heterogeneity in covariate adjustment between studies. Future studies should carefully adjust for potential confounders to the effect that pre-stroke PA may yield for post-stroke outcomes.

The risk of bias is significant in all included studies. Due to the retrospective data collection, lack of objective measurements for pre-stroke PA, inadequate adjustment of confounding factors, large proportions of missing data, and exclusion of cases with missing data, causal inference is not possible. Tumaszczyk et al. conducted the first systematic review on this topic, investigating how pre-stroke PA affects functional status beyond the acute phase of stroke (10). At that time, the authors could only include 3 studies (22, 25, 47) 2 of which reported no significant associations. Notwithstanding, both prior, and more recent studies that were not included by Tumaszczyk et al. have investigated functional outcomes after stroke in relation to premorbid PA. A recent systematic review by Hung et al. investigated the association between pre-stroke PA and admission stroke severity (9). The authors overall interpretation of the 7 studies included was that PA may reduce the acute symptoms of stroke, but that future studies are needed to confirm the potentially neuroprotective effect (20, 30–32, 38, 39, 44). To this date, no meta-analyses have been conducted due to the heterogeneity in pre-stroke PA assessments.

The current review was conducted without time and language restrictions, and includes studies written in English, Chinese, Spanish and Turkish. Thus, we have been able to comprise a wider selection of studies than any prior review. In this comprehensive overview of the research field, we provide a foundation for future studies that is essential to counteract the current methodological heterogeneity and knowledge gaps. Limitations to the scoping review approach are the lack of in-depth analysis and inclusion of studies despite high risk of bias. A scoping review, in comparison with the traditional systematic review, does not provide a summary answer to a specific research question, and information needed to correctly interpret the strength

of associations, such as confounding factors, treatment groups and interventions, is not accounted for. When interpreting the results, readers must be careful to consider the difference in quality between studies, made evident in the risk of bias assessments and study characteristics. There is no universally accepted standard instrument for assessing the risk of bias in non-randomized studies of exposures. ROBINS-I is the preferred tool in Cochrane reviews for non-randomized studies of interventions; however, it is not applicable for studies of exposures. The ROBINS-E was presented a modified version of ROBINS-I in 2017, and has since been used in several systematic reviews (16). ROBINS-E has been criticised for underestimating the risk of bias, and for being time consuming (56). However, the majority of studies included in this scoping review were determined as being of high risk of bias, which contradicts that the ROBINS-E instrument underestimated the true risk of bias.

Conclusion

This scoping review identified 60 post-stroke outcome measures, studied in relation to pre-stroke PA. Included outcome measures cover all components in the ICF framework. The majority of studies collected information on pre-stroke PA retrospectively, and all studies used self-reported assessments of pre-stroke PA. No study evaluated pre-stroke PA objectively through quantifiable methods. Evidently, there are significant limitations in research design and methodology within the current literature. Due to high risk of bias, causal inference is not possible for any of the studied outcomes. Furthermore, studies evaluating the impact of premorbid PA on environmental and personal factors are limited in numbers, and there is insufficient information on how pre-stroke PA impact outcomes following haemorrhagic stroke. Future studies should focus on validating the associations between pre-stroke PA and post-stroke outcomes using prospective designs and objective measurements.

ACKNOWLEDGEMENTS

The authors thank Helen Sjöblom and Linda Hammarbäck at Gothenburg University Biomedical Library for their assistance in the systematic literature search. We thank Izabella Miernik Zetterqvist for assistance in Polish translation, Dongni Buvarp for assistance in Chinese translation, Maria Munoz for assistance in Spanish translation, and Pelin Atalan for assistance in Turkish translation.

Funding. This study was funded by the Swedish Research Council (VR2017-00946), the Swedish Heart and Lung Foundation, the Swedish Brain Foundation, the Swedish Stroke Association, Promobilia, and the Swedish state under an agreement between the Swedish government and the county councils: the ALF agreement (ALFGBG-71980).

The authors have no conflicts of interest to declare.

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