

# The prevalence of fatigue after stroke: A systematic review and meta-analysis

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## Abstract

**Background:** Fatigue is a common and debilitating symptom after stroke. The last decade has seen rapid expansion of the research literature on post-stroke fatigue, but prevalence remains unclear.

**Aims:** To estimate post-stroke fatigue prevalence and to identify the contributing factors to fatigue, by conducting a systematic review and meta-analysis.

**Summary of review:** We included all studies of adult stroke survivors that used a recognized assessment scale for fatigue (search date September 2014). Two reviewers independently reviewed all full texts for inclusion. Data were extracted by one reviewer and independently cross-checked by a second. Risk of bias was evaluated using a critical appraisal tool. From an overall yield of 921 studies, 101 full text papers were screened, and 49 of these met inclusion criteria. The most widely used measure of fatigue was the Fatigue Severity Scale ( $n = 24$  studies). Prevalence estimates at a cut-off score of  $>$  or  $\geq 4$  were available for 22 of these 24 studies (total  $n = 3491$ ), and ranged from 25 to 85%. In random effects meta-analysis, the pooled prevalence estimate was 50% (95% CI 43–57%), with substantial heterogeneity ( $I^2 = 94\%$ ). Neither depression status nor time point post-stroke explained the heterogeneity between studies. In post-hoc analysis, fatigue prevalence was found to be lower in the four Asian studies (35%; 95% CI 20–50;  $I^2 = 96\%$ ).

**Conclusions:** Our results confirm that fatigue is a widespread issue for stroke survivors, although it may be less prevalent in Asia. Further research is needed to explain the wide variability in prevalence estimates between studies.

## Keywords

Stroke, fatigue, prevalence, depression, systematic review, meta-analysis

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## Introduction

Post-stroke fatigue is common. In large studies across the first two years following stroke, fatigue is reported by more than 50% of stroke survivors.<sup>1,2</sup> Even in cohorts of people with mild stroke and little disability, the majority report fatigue.<sup>3</sup> Prevalence of fatigue in stroke survivors is more than three times that of age-matched controls.<sup>4</sup> The definition and assessment of fatigue after stroke borrows heavily from previous work in other medical conditions, such as multiple sclerosis. Fatigue can be defined as “*a subjective lack of physical or mental energy (or both) that is perceived by the individual to interfere with usual or desired activities.*”<sup>5</sup> Given that fatigue is a subjective experience, its measurement typically includes a phenomenological dimension. Self-report fatigue scales that have been used in stroke populations include the Fatigue Severity Scale (FSS),<sup>6</sup> the Fatigue Assessment Scale<sup>7</sup> and the Multidimensional Fatigue Inventory (MFI).<sup>8</sup>

While it is generally accepted that fatigue is widespread after stroke, there is large variability between studies in reported prevalence.

The reason for this variability remains unclear. It is not just an artifact of small samples. In studies both featuring  $>200$  participants, fatigue prevalence of 68% in the Netherlands<sup>9</sup> dwarfed that of 25% in Hong Kong.<sup>10</sup> Methodological differences, such as assessment technique and diagnostic cut-off used, undoubtedly contribute to variability in fatigue prevalence estimates. Yet this is not the full explanation; in the above

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comparison, both studies used the same assessment tool with the same fatigue cut-off. The presence of depression is important, as it is strongly associated with fatigue after stroke.<sup>11</sup> Studies in stroke populations with low levels of depression—or studies where depression is an exclusion criterion, as in the previously cited Hong Kong study<sup>10</sup>—are likely to have lower estimates of fatigue prevalence. Another potential explanation relates to the timing of assessment after stroke. The onset of fatigue typically occurs early, within the first two weeks of stroke,<sup>1,12</sup> and longitudinal studies indicate that fatigue rates are more likely to decline than to increase across time.<sup>13</sup> This suggests that cohorts of participants assessed earlier after stroke may yield higher fatigue prevalence estimates.

It is important to understand the scope of the problem, and the contributing factors, as fatigue can have debilitating effects on stroke survivors. Post-stroke fatigue is significantly related to poor quality of life, even after adjusting for depression, disability and age.<sup>14</sup> It is very meaningful for patients: 40% report fatigue as their worst or one of their worst symptoms.<sup>15</sup> Post-stroke fatigue limits participation in everyday life, with detrimental effects on social participation, return to work, driving, reading, and sleeping.<sup>16</sup> It increases dependence in activities of daily living and institutionalization<sup>17</sup> and has been linked to increased mortality.<sup>17,18</sup>

The objective of this systematic review was to synthesize the available data on post-stroke fatigue prevalence. Given the wide variability in reported prevalence of post-stroke fatigue, we sought to not only establish a pooled prevalence estimate but also to identify study-specific factors that influence variability in fatigue prevalence. We predicted greater fatigue prevalence in studies that: (i) included samples with higher rates of depression and (ii) assessed fatigue earlier after stroke.

## Methods

This review was registered with Prospero, the International Prospective Registry of Systematic Reviews (Registration Number CRD42015016096).

### *Search strategy and selection criteria*

A comprehensive literature search was performed in September 2014. Databases searched included the Cochrane Stroke Group Trials Register (inception to September 2014), Medline (1948 to September 2014), EMBASE (1980 to September 2014), Cumulative Index to Nursing and Allied Health Literature (1982 to September 2014), The Allied and Complementary Medicine Database (1985 to September 2014), PsycINFO (1967 to September 2014), and Physiotherapy Evidence Database (PEDro) (inception to September 2014). Search

terms included words related to stroke, fatigue, and rehabilitation (see online supplementary Appendix I for full Medline search strategy). The search was supplemented by hand-searching reference lists of major review articles. Gray literature was not included; we restricted the search to peer-reviewed publications to maintain rigor. Studies were eligible, if they measured fatigue using a dedicated fatigue scale at any time post-stroke and were published in English in a peer-reviewed journal. Intervention studies were included if baseline (pre-intervention) fatigue data were available. Studies were excluded if they were not in stroke (e.g. transient ischemic attack, traumatic brain injury), if they specified presence of fatigue or depression as an inclusion criterion, if they tested only exertional fatigue, or if fatigue was assessed using a single question (e.g. “Do you feel fatigued?”). In cases where more than one study reported data from the same participant cohort, we included only the study that contained the largest sample size.

### *Procedure*

One researcher (MP) performed the search, scrutinizing all titles and abstracts for eligibility against the inclusion and exclusion criteria. Irrelevant references and duplicates were eliminated, and full text versions were obtained for potentially relevant studies. MP and a second researcher (CM) independently reviewed all full texts for eligibility. Disagreements between these researchers on eligibility were resolved by consensus, with the involvement of a third researcher (CE) where necessary. Methodological quality of included articles was assessed using a modified version of the Scottish Intercollegiate Guidelines Network Methodology for case-control studies.<sup>19</sup> This tool was designed specifically for case-control observational studies and has been through a process of robust development.<sup>20</sup> The tool was modified to allow different types of quantitative research designs to be analyzed, and the major areas of potential bias to be emphasized. The four quality criteria were: (1) eligibility criteria clearly stated, (2) consecutive recruitment strategy used, (3) time point post-stroke clearly defined, and (4) confounding variables considered. Adaptations were made in accordance with the Cochrane Collaboration guidelines for assessing risk of bias.<sup>21</sup> The critical appraisal was performed independently by two researchers (MP and TC). Disagreements between researchers were resolved by consensus, with the involvement of a third researcher (CE) where necessary.

### *Data extraction*

Descriptive data were extracted from each of the included articles. This included study design,

recruitment procedure, inclusion, and exclusion criteria, whether prevalence of fatigue was the primary outcome, fatigue assessment and cut-off score used, language the assessment was administered in, total number of participants, number and percentage of fatigued participants, age of participants, time since stroke, and country of study. In studies with multiple fatigue assessments, prevalence data were extracted for the earliest fatigue measurement. In cases where further information regarding fatigue prevalence or cut-off score was required, study authors were contacted and asked to provide the information. Data on depression were extracted if they were reported.

### Statistical analysis

Studies that used the same fatigue assessment scale and cut-off point were pooled together, and meta-analysis was conducted using Review Manager 5.3 software. Prevalence values from individual studies were recorded, and standard errors were computed using the prevalence value and the sample size from each study. Random effects meta-analyses using the generic inverse variance method were performed to determine fatigue prevalence and heterogeneity between studies for each outcome measure. Random effects models were used, rather than fixed effect models, as it was implausible to assume an identical effect size across our studies.<sup>22</sup> Using the same method, planned subgroup analyses were conducted to compare fatigue prevalence across studies according to (i) depression status and (ii) time point of fatigue assessment. Post-hoc subgroup analyses were used to assess the influence of other study-specific factors, including whether study recruitment was consecutive or not and geographic location.

### Results

The initial search yielded 921 studies; following exclusion of duplicates and clearly ineligible studies, 101 studies remained for which full text versions were sought; 49 studies ( $n=7475$ ) were included in the review (see PRISMA flowchart in Figure 1). All but 2 of these 49 studies (96%) were published since 2005.

### Fatigue scale used

The different fatigue scales used included: the FSS ( $n=23$ ), the MFI ( $n=7$ ), the SF-36 vitality scale ( $n=6$ ), the Fatigue Assessment Scale ( $n=4$ ), the Checklist of Individual Strength ( $n=2$ ), the Fatigue Impact Scale ( $n=1$ , modified FIS  $n=2$ ), the Fatigue Assessment Instrument ( $n=1$ ), the Brief Fatigue Inventory ( $n=1$ ), the Chalder Fatigue Scale ( $n=1$ ), the Fatigue Self-Observation List ( $n=1$ ), the

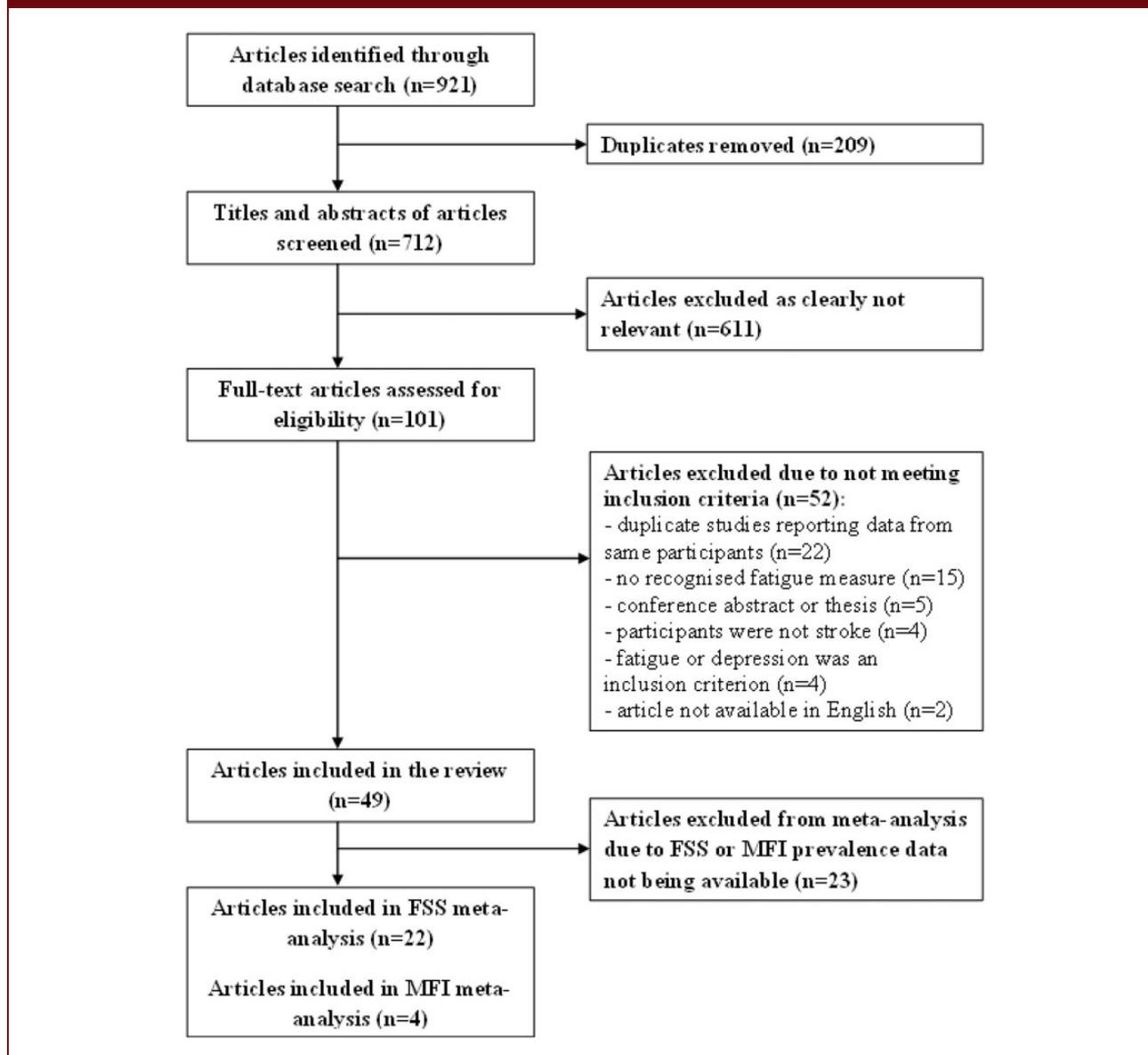
Functional Assessment of Chronic Illness Therapy fatigue subscale ( $n=1$ ), the Self-Assessment of Mental Fatigue ( $n=1$ ), the Neuropsychological Assessment Schedule fatigue subscale ( $n=1$ ), the Neurological Fatigue Index ( $n=1$ ), the Medical Outcomes Study energy/fatigue scale ( $n=1$ ), the Profile of Mood States fatigue component ( $n=1$ ). Several studies employed more than 1 fatigue scale.

### FSS

A total of 24 studies contained FSS data, including one that employed the 11-item version and one that administered the full Fatigue Assessment Instrument, of which the FSS is a part. Characteristics of these 24 studies are outlined in Table 1, with references listed in Supplementary Appendix II. Results from the critical appraisal (see online supplementary Table I) showed that 20/24 studies satisfied at least three of the four quality criteria; the most commonly failed criterion was consecutive recruitment (10/24). Of the 24 studies, 15 reported fatigue prevalence using a cut off of  $\geq 4$  and 3 reported fatigue prevalence at a cut-off of  $> 4$ . These cut-offs were deemed similar enough to be pooled together. We contacted the authors of the other six papers requesting additional data. Prevalence data were clarified or obtained for four of these studies.<sup>1,25,38,39</sup> Data were therefore pooled for 22 studies ( $n=3491$ ) in the meta-analysis. The pooled estimate of fatigue prevalence was 50% (95% CI 43–57%), with substantial heterogeneity between studies ( $I^2=94\%$ ) (see Figure 2).

Data on depression that could be extracted from the studies are outlined in online supplementary Table II. Studies that specified depression or psychiatric history as an exclusion criterion reported slightly lower rates of fatigue ( $n=8$ , 47% fatigued, 95% CI 33–60%,  $I^2=95\%$ ) than those that did not exclude on the basis of depression ( $n=14$ , 53% fatigued, 95% CI 45–60%,  $I^2=92\%$ ), but the difference was not significant ( $\chi^2=0.5$ ,  $df=1$ ,  $p=0.46$ ). Deriving subgroups based on current depression levels was more difficult, given the wide variability in assessment tools used and cut-offs applied (see online supplementary Table II). The 11 studies with data on both fatigue and depression prevalence were median split into low depression (prevalence range 6–16%) and high depression (prevalence range 24–55%) groups. Studies with low prevalence of depression had very similar rates of fatigue ( $n=5$ , 50% fatigued, 95% CI 32–67%,  $I^2=96\%$ ) to studies with high prevalence of depression ( $n=6$ , 48% fatigued, 95% CI 41–55%,  $I^2=62\%$ ). Fatigue prevalence was relatively stable across time points after stroke: within one month of stroke ( $n=3$  studies, 55% fatigued, 95% CI 25–85%,  $I^2=97\%$ ), one

Figure 1. Modified PRISMA flow diagram.



month to six months ( $n = 7$  studies, 46% fatigued, 95% CI 31–62%,  $I^2 = 97\%$ ), beyond six months ( $n = 12$  studies, 53% fatigued, 95% CI 48–58%,  $I^2 = 75\%$ ).

Additional post-hoc comparisons were made to further interrogate the heterogeneity between studies. Studies that used consecutive recruitment reported slightly lower prevalence ( $n = 13$ , 49% fatigued, 95% CI 39–59%,  $I^2 = 96\%$ ) than those without consecutive recruitment ( $n = 9$ , 54% fatigued, 95% CI 49–59%,  $I^2 = 65\%$ ), but this was not significant ( $\chi^2 = 0.8$ ,  $df = 1$ ,  $p = 0.37$ ). Studies conducted in Asia reported lower fatigue prevalence ( $n = 4$ , 35% fatigued, 95% CI 20–50%,  $I^2 = 96\%$ ) than those conducted in Europe ( $n = 13$ , 55% fatigued, 95% CI 50–61%,

$I^2 = 84\%$ ) or the US ( $n = 3$ , 52% fatigued, 95% CI 37–67%,  $I^2 = 80\%$ ). The difference between Asian and non-Asian ( $n = 18$ , 54% fatigued, 95% CI 49–59%,  $I^2 = 82\%$ ) studies was significant ( $\chi^2 = 5.8$ ,  $df = 1$ ,  $p = 0.02$ ), but heterogeneity remained high.

### MFI

A total of seven studies ( $n = 462$ ) used the MFI to assess fatigue. Characteristics of these studies are outlined in Table 2, with references listed in online supplementary Appendix III. Four of the seven studies reported prevalence of fatigue at a “General” subscale cut-off of  $> \text{or} \geq 12$ . One did not administer the

**Table 1.** Characteristics of the 24 included studies that employed the FSS (reference citations in Supplementary Appendix II)

Study	N	Time after stroke	Fatigue %	Male %	Age <sup>†</sup>	Country
Badaru (2013)	65	0 to > 4 y	46	57	Range 58–80	Nigeria
Chestnut (2010)	13	Mean 8 d	85	24	Range 60–80	UK
Choi-Kwon (2005)	220	Mean 15 m (range 3–27)	57	73	60.4 ± 9.0	S Korea
Crosby (2012)	64	Mean 4.9 m ± 4.6	48	33	Range 37–94	UK
Ghotbi (2013)	83	Mean 30.9 m ± 33.2	46	55	Range 30–85	Iran
Harbison (2009)	69	1 to 6 m	51	49	69 ± 11.3	Ireland
Hoang (2012)	32	Mean 40 m ± 42.2	66	66	64.6 ± 11.2	France
Lerdal (2011)	115	Mean 4.6 d ± 3.2	57	59	68.3 ± 13.3	Norway
Michael (2007)	79	Mean 10 m (range 6–120)	42	53	65 (range 45–84)	USA
Miller (2013)	77	>6 m	66	75	Range 48–89	USA
Mills (2012)	282	Mean 17.2 m ± 11.4	62	62	67.3 ± 13.4	UK
Naess (2005)	192	Mean 6.0 y (range 1.4–12.3)	51	57	47.8	Norway
Naess (2012)	333	Mean 382 d (range 185–756)	60	62	67.9	Norway
Park (2009)	40	Mean 32.7 m ± 27.4	30	65	59.9 ± 11.8	S Korea
Radman (2012)	109	6 m	30	66	51.1 ± 13.8	Switzerland
Robinson (2011)	50	Mean 85.0 m ± 89.9	48	54	65.0 ± 8.4	USA
Suh (2014)	282	Mean 6.7 d ± 1.9	26	59	62.3 ± 12.8	S Korea
Tang (2013)	500	3 m	25	61	65.0 ± 10.8	Hong Kong
Tseng (2010) <sup>a</sup>	21	Mean 4.1 y ± 3.5	NR	57	59.5 ± 10.3	USA
Valko (2008)	235	Mean 1.2 y ± 0.6	49	69	63.0 ± 14.0	Switzerland
van de Port et al. (2007)	223	6 m	68	60	57.3 ± 11.1	Netherlands
van de Port (2012)	250	3 m	57	65	57.0 ± 10.0	Netherlands
Vuletic (2011)	35	3 m	45	57	61.8 ± 14.2	Croatia
Yang (2013) <sup>a</sup>	122	Inpatient rehabilitation	NR	59	58.2 ± 10.5	Singapore

NR: not reported.

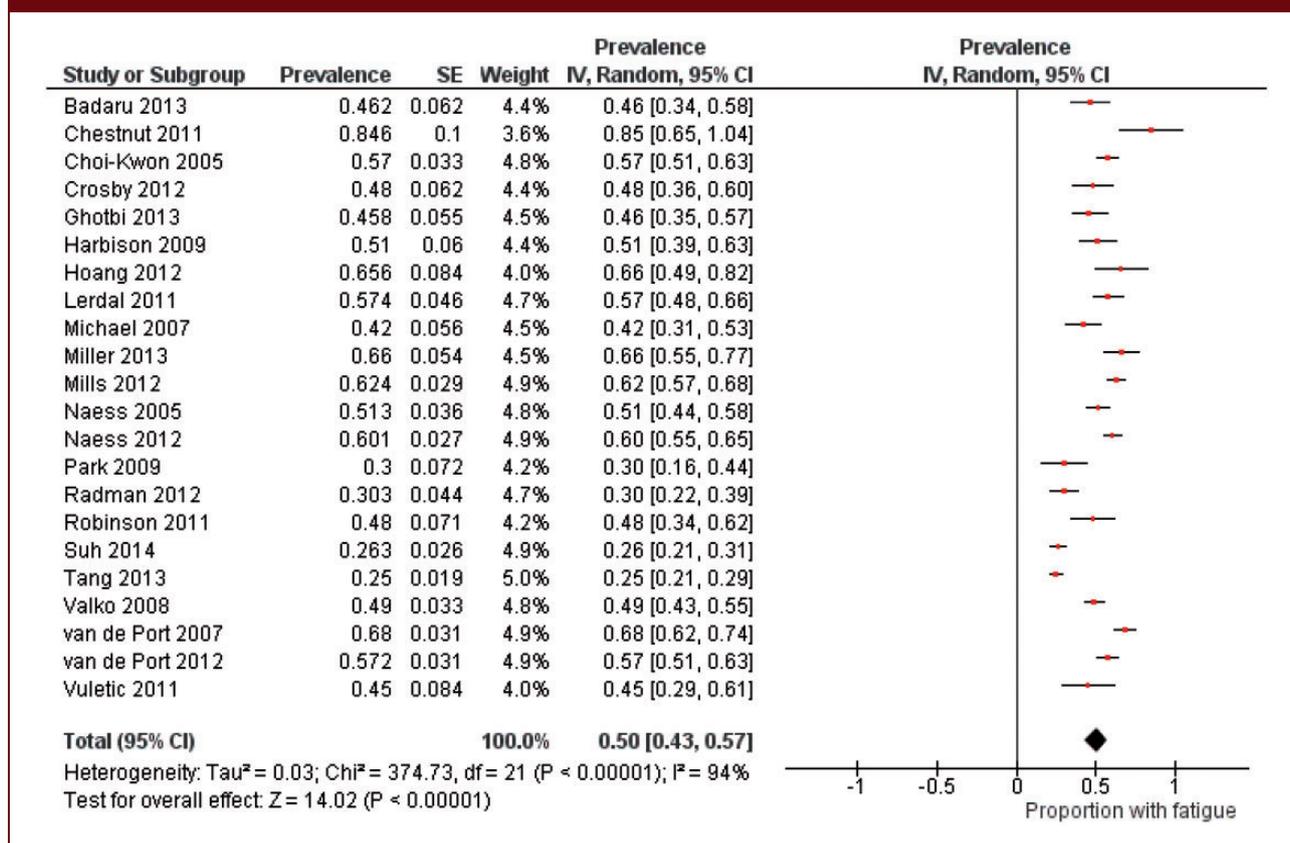
<sup>a</sup>Study not included in meta-analysis; <sup>†</sup>Mean ± standard deviation unless otherwise specified.

“General” subscale and authors of the other two studies were contacted for additional data but did not respond. Across the four studies ( $n = 345$ ) included in meta-analysis, fatigue prevalence was 56% (95% CI 51–62%), and there was little heterogeneity between studies ( $I^2 = 0\%$ ) (see Figure 3).

### Other fatigue scales

No other scales yielded sufficient prevalence data for meta-analysis. Both the SF-36 vitality scale (6 studies,  $n = 2534$ ) and the Fatigue Assessment Scale (4 studies,  $n = 201$ ) were used in multiple studies, but both scales

**Figure 2.** Random effects meta-analysis of fatigue prevalence at FSS > or ≥ 4 cut-off (reference citations in Supplementary Appendix II).



**Table 2.** Characteristics of the seven included studies that employed the MFI (reference citations in Supplementary Appendix III)

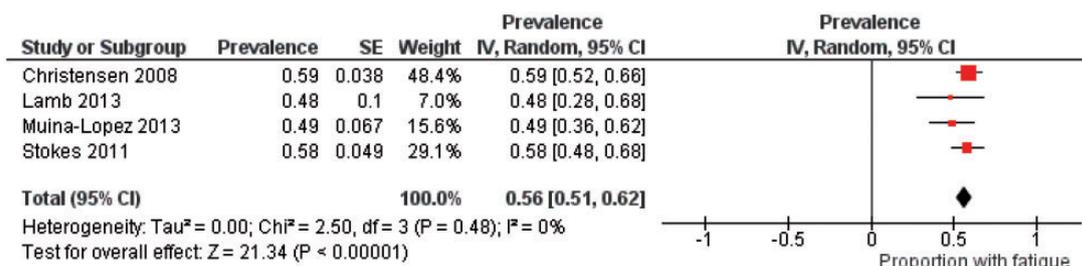
Study	N	Time after stroke	Fatigue %	Male %	Age <sup>a</sup>	Country
Christensen (2008)	165	10 d	59	56	Median 64.5 (IQR 55.8–72.5)	Denmark
Lamb (2013)	25	Mean 6.6 m ± 1.3	48	64	67 ± 10	Australia
Lord (2006) <sup>b</sup>	27	Mean 45.8 m ± 34.2	NR	74	61.0 ± 11.6	NZ
Lynch (2007) <sup>b</sup>	55	Median 23 d (40 inpatients), 137 d (15 community)	NR	56	Median 73 (IQR 66–81)	UK
Muina-Lopez (2013)	55	Median 5.5 y (27 fatigue), 3.3 y (28 no fatigue)	49	64	67.0 ± 9.2 (fatigue), 70.8 ± 10.2 (no fatigue)	Ireland
Stokes (2011)	100	Mean 16 m (range 1–36)	58	55	72.4 ± 9.0	Ireland
Vuletic (2011) <sup>b</sup>	35	3 months	NR	57	61.8 ± 14.2	Croatia

NR: not reported.

<sup>a</sup>Mean ± standard deviation unless otherwise specified.

<sup>b</sup>Study not included in meta-analysis.

**Figure 3.** Random effects meta-analysis of fatigue prevalence at MFI “General” subscale  $\geq$  12 cut-off (reference citations in Supplementary Appendix II).



lack a recognized cut-off for fatigue. Only one of these studies reported fatigue prevalence: 30% at a cut-off of  $\leq 47$  (calculated as 1 standard deviation below the national norm) on the SF-36 vitality scale.<sup>23</sup>

## Discussion

Clinicians have known for some time that fatigue is a major issue for many of the stroke survivors in their care. The yield of this systematic review demonstrates that fatigue is, somewhat belatedly, being acknowledged by researchers as a consequence of stroke worthy of investigation. We identified 49 studies that met our inclusion criteria, and 47 of these were published in the last decade. Many different scales have been employed to assess post-stroke fatigue, but the FSS stood out as the most widely used. In meta-analysis of the 22 studies with available FSS data, the pooled prevalence of fatigue was 50% (95% CI 43–57%). This estimate should be treated with caution as there was high heterogeneity between studies ( $I^2 = 94\%$ ). Yet, even if we conservatively accept the lower bound of the confidence interval as our prevalence estimate, 43% is still a very high proportion of stroke survivors. The only other scale with sufficient data for meta-analysis was the MFI: pooled prevalence across the four studies was 56% (95% CI 51–62%), with little heterogeneity ( $I^2 = 0\%$ ).

One of the central findings of this review was the marked between-study variability in estimates of fatigue prevalence. This could not be attributed to differences in assessment methodology; in the 22 studies featured in Figure 2, all used the FSS with either  $>$  or  $\geq 4$  as the cut-off for fatigue. Simple demographics did not seem to explain the variability either, with the age and sex profile of the stroke populations being broadly similar (note some exceptions: younger age (24, 25), fewer males (26, 27)). Any study that excludes participants with a history of depression was expected to yield a lower estimate of fatigue, given the

strong relationship between these two factors.<sup>11</sup> Our results did not bear this out; fatigue was common even in studies using depressive history as an exclusion criterion (47%). While current depression rates were hard to ascertain, with many different tools and cut-offs used, a crude comparison of low-depression and high-depression studies revealed no difference in fatigue levels. This surprising finding adds weight to the conclusion that heterogeneity in fatigue prevalence is not explained by depression. Our second hypothesis was also unsupported. Time since stroke did not account for the variability in prevalence; the majority of people with acute stroke reported fatigue (55%) as well as the majority of people later after stroke (53%). While a review of nine longitudinal studies reported fatigue decline in seven studies and increase in only two,<sup>13</sup> our results give support to the idea that fatigue is persistent across time after stroke.

The most important aspect of study quality in this setting is whether or not recruitment was consecutive, as this has a direct impact on selection bias. It is possible that non-consecutive sampling might lead to an over-representation of people with less severe strokes (“healthy volunteer” effect), and thus be associated with lower rates of fatigue. Our results did not reflect this: there was no difference in fatigue prevalence between studies with non-consecutive (54%) and consecutive (49%) recruitment. It should be noted that other forms of selection bias were also present at the individual study level. For example, many studies excluded patients with impairments in cognition or communication, limiting the generalizability of their findings. Although this limitation of external validity is common to many stroke studies, its importance should not be overlooked. Our fatigue prevalence estimates may not be an accurate reflection of fatigue prevalence in stroke survivors with severe stroke or cognitive impairments or aphasia.

The other study-specific factor that we considered in subgroup analysis was geographical region. Compared

to other regions, we identified significantly lower fatigue prevalence in Asian populations (35% vs. 54%). It should be noted that the four Asian studies were all from East Asia (three South Korea, one Hong Kong). There are different epidemiological patterns of stroke in Asia, including younger age and greater likelihood of hemorrhagic stroke,<sup>28,29</sup> but there is little evidence that these factors are strongly related to fatigue. In stroke samples, younger age has been related to lower likelihood of fatigue,<sup>18</sup> but also to greater likelihood of fatigue,<sup>30</sup> with other studies finding no significant association.<sup>1,15,24</sup> Hemorrhagic stroke does not necessarily lead to greater fatigue than ischemic stroke.<sup>2</sup> An alternative explanation for the lower prevalence is that it may reflect a more generalized cultural difference in the psychosocial factors that contribute to fatigue. A 14-country comparative epidemiological study of fatigue syndromes found lower prevalence in Asian regions (e.g. Bangalore, Shanghai).<sup>31</sup> Low fatigue prevalence has also been reported in Asian people living in multi-ethnic communities in the United States.<sup>32,33</sup>

While dividing studies into subgroups revealed several interesting differences, caution should be taken in interpreting post-hoc comparisons. Heterogeneity in prevalence between studies was not adequately explained by any of the factors we looked at, with the value of  $I^2$  remaining above 65% for all subgroups. The variability may be partly attributable to lack of reliability of the FSS itself. A Rasch analysis of the FSS in a large group of stroke survivors indicated that items 1 and 2 did not have acceptable goodness-of-fit, and removing these items enhanced the psychometric properties of the scale.<sup>34</sup> Furthermore, the FSS was considered to have insufficient face validity to be included in a comparison of scales used to assess post-stroke fatigue.<sup>35</sup> Given these concerns, it is unclear why the FSS continues to be such a popular choice in the stroke research community. Heterogeneity in fatigue prevalence was much lower in the meta-analysis of four studies that used the MFI “General” subscale. This is probably attributable to the fact that the “General” subscale includes only four broadly similar items (“I feel fit”, “I feel tired”, “I am rested”, “I tire easily”). While this assessment may lead to more homogeneous estimates of prevalence across studies, it lacks the more comprehensive assessment of fatigue contained in other measures such as the Fatigue Assessment Scale.

A limitation of the current review was our inability to compare the studies on many of the characteristics that might contribute to post-stroke fatigue. There were insufficient data available at the study level to be able to drill down into factors that we know are associated with greater fatigue, including female sex,<sup>2</sup> physical disability,<sup>1</sup> cognitive impairment,<sup>25</sup> mood disorder<sup>11</sup> and pre-stroke fatigue.<sup>36</sup> Answering these questions would

require meta-analysis of individual patient data. An individual patient data meta-analysis would also allow the full spectrum of fatigue severity to be examined via raw scale scores, thus overcoming the need to dichotomize fatigue data. Another limitation was the wide post-stroke time points specified in many of the chronic studies. It was not uncommon for studies to include participants who were a mean of 2–4 years and standard deviation of 2–4 years post-stroke. These large ranges may obscure important differences in fatigue prevalence across time within their samples. It should be noted that our search was conducted in late 2014 and therefore does not contain more recent papers; we know of at least one that could have been included in the meta-analysis.<sup>37</sup>

## Conclusions

This is the first systematic review to report pooled prevalence estimates for post-stroke fatigue. Our results confirm that fatigue is a widespread issue for stroke survivors, although it may be less commonly reported in Asian populations. We identified substantial between-study variability in fatigue prevalence that was not easily explained by differences in either methodology or participant characteristics. Further work is needed to understand this condition, to identify the factors contributing to it and to develop effective intervention strategies that can be applied in stroke care settings.

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## Authors' contribution

TBC conceived the study, helped with critical appraisal, analyzed the data and led the writing of the paper. MP built the search strategy, conducted the search, identified eligible studies, extracted the data and wrote the initial draft of the manuscript. SK contributed to data analysis, presentation of results and drafting of the paper. CE was involved in the conception and development of the study, helped to design the search strategy, contributed to selection and critical appraisal of studies, and helped draft the paper.

## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## References

1. Choi-Kwon S, Han SW, Kwon SU and Kim JS. Poststroke fatigue: characteristics and related factors. *Cerebrovasc Dis* 2005; 19: 84–90.
2. Schepers VP, Visser-Meily AM, Ketelaar M and Lindeman E. Poststroke fatigue: course and its relation to personal and stroke-related factors. *Arch Phys Med Rehabil* 2006; 87: 184–188.
3. Winward C, Sackley C, Metha Z and Rothwell PM. A population-based study of the prevalence of fatigue after transient ischemic attack and minor stroke. *Stroke* 2009; 40: 757–761.
4. van der Werf SP, van den Broek HL, Anten HW and Bleijenberg G. Experience of severe fatigue long after stroke and its relation to depressive symptoms and disease characteristics. *Eur Neurol* 2001; 45: 28–33.
5. Guidelines MSCfCP *Fatigue and multiple sclerosis: evidence-based management strategies for fatigue in multiple sclerosis*. Washington, DC: Paralyzed Veterans of America, 1998.
6. Krupp LB, LaRocca NG, Muir-Nash J and Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol* 1989; 46: 1121–1123.
7. Michielsen HJ, De Vries J and Van Heck GL. Psychometric qualities of a brief self-rated fatigue measure: The Fatigue Assessment Scale. *J Psychosom Res* 2003; 54: 345–352.
8. Smets EM, Garssen B, Bonke B and De Haes JC. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *J Psychosom Res* 1995; 39: 315–325.
9. van de Port IG, Kwakkel G, Schepers VP, Heinemans CT and Lindeman E. Is fatigue an independent factor associated with activities of daily living, instrumental activities of daily living and health-related quality of life in chronic stroke? *Cerebrovasc Dis* 2007; 23: 40–45.
10. Tang WK, Liang HJ, Chen YK, et al. Poststroke fatigue is associated with caudate infarcts. *J Neurol Sci* 2013; 324: 131–135.
11. Wu S, Barugh A, Macleod M and Mead G. Psychological associations of poststroke fatigue: a systematic review and meta-analysis. *Stroke* 2014; 45: 1778–1783.
12. Christensen D, Johnsen SP, Watt T, Harder I, Kirkevold M and Andersen G. Dimensions of post-stroke fatigue: a two-year follow-up study. *Cerebrovasc Dis* 2008; 26: 134–141.
13. Duncan F, Wu S and Mead GE. Frequency and natural history of fatigue after stroke: a systematic review of longitudinal studies. [Review]. *J Psychosom Res* 2012; 73: 18–27.
14. Naess H, Waje-Andreassen U, Thomassen L, Nyland H and Myhr KM. Health-related quality of life among young adults with ischemic stroke on long-term follow-up. *Stroke* 2006; 37: 1232–1236.
15. Ingles JL, Eskes GA and Phillips SJ. Fatigue after stroke. *Arch Phys Med Rehabil* 1999; 80: 173–178.
16. White JH, Gray KR, Magin P, et al. Exploring the experience of post-stroke fatigue in community dwelling stroke survivors: a prospective qualitative study. *Disabil Rehabil* 2012; 34: 1376–1384.
17. Glader EL, Stegmayr B and Asplund K. Poststroke fatigue: a 2-year follow-up study of stroke patients in Sweden. *Stroke* 2002; 33: 1327–1333.
18. Mead GE, Graham C, Dorman P, et al. Fatigue after stroke: baseline predictors and influence on survival. Analysis of data from UK patients recruited in the International Stroke Trial. *PLoS ONE* 2011; 6: e16988.
19. Scottish-Intercollegiate-Guidelines-Network. Methodology Checklist 4: case-control studies, www.sign.ac.uk/methodology/checklists.html (accessed 21 May 2015).
20. Sanderson S, Tatt I and Higgins J. Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography. *Int J Epidemiol* 2007; 36: 666–676.
21. Higgins J and Green S (eds). *Cochrane handbook for systematic reviews of interventions*. Hoboken, NJ: Wiley-Blackwell, 2009.
22. Borenstein M, Hedges LV, Higgins JPT and Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synthesis Meth* 2010; 1: 97–111.
23. Feigin VL, Barker-Collo S, Parag V, et al. Prevalence and predictors of 6-month fatigue in patients with ischemic stroke: a population-based stroke incidence study in Auckland, New Zealand, 2002–2003. *Stroke* 2012; 43: 2604–2609.
24. Naess H, Nyland HI, Thomassen L, Aarseth J and Myhr KM. Fatigue at long-term follow-up in young adults with cerebral infarction. *Cerebrovasc Dis* 2005; 20: 245–250.
25. Radman N, Staub F, Aboulaflia-Brakha T, Berney A, Bogousslavsky J and Annoni J-M. Poststroke fatigue following minor infarcts: a prospective study. *Neurology* 2012; 79: 1422–1427.
26. Chestnut TJ. Fatigue in stroke rehabilitation patients: a pilot study. *Physiotherapy Res Int* 2011; 16: 151–158.
27. Crosby GA, Munshi S, Karat AS, Worthington E and Lincoln NB. Fatigue after stroke: frequency and effect on daily life. *Disabil Rehabil* 2012; 34: 633–637.
28. Krishnamurthi RV, Feigin VL, Forouzanfar MH, et al. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. *Lancet Global Health* 2013; 1: e259–e281.
29. van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A and Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. *Lancet Neurol* 2010; 9: 167–176.
30. Snaphaan L, van der Werf S and de Leeuw FE. Time course and risk factors of post-stroke fatigue: a prospective cohort study. *Eur J Neurol* 2011; 18: 611–617.
31. Skapinakis P, Lewis G and Mavreas V. Cross-cultural differences in the epidemiology of unexplained fatigue syndromes in primary care. *Br J Psychiatry* 2003; 182: 205–209.

32. Steele L, Dobbins JG, Fukuda K, et al. The epidemiology of chronic fatigue in San Francisco. *Am J Med* 1998; 105: 83S–90S.
33. Zheng YP, Lin KM, Takeuchi D, Kurasaki KS, Wang Y and Cheung F. An epidemiological study of neurasthenia in Chinese-Americans in Los Angeles. *Compr Psychiatry* 1997; 38: 249–259.
34. Lerdal A and Kottorp A. Psychometric properties of the Fatigue Severity Scale-Rasch analyses of individual responses in a Norwegian stroke cohort. *Int J Nurs Stud* 2011; 48: 1258–1265.
35. Mead G, Lynch J, Greig C, Young A, Lewis S and Sharpe M. Evaluation of fatigue scales in stroke patients. *Stroke* 2007; 38: 2090–2095.
36. Lerdal A, Bakken LN, Rasmussen EF, et al. Physical impairment, depressive symptoms and pre-stroke fatigue are related to fatigue in the acute phase after stroke. *Disabil Rehabil* 2011; 33: 334–342.
37. Egerton T, Hokstad A, Askim T, Bernhardt J and Indredavik B. Prevalence of fatigue in patients 3 months after stroke and association with early motor activity: a prospective study comparing stroke patients with a matched general population cohort. *BMC Neurol* 2015; 15: 181.
38. Mills R, Pallant J, et al. Validation of the Neurological Fatigue Index for stroke (NFI-Stroke). *Health Qual Life Outcomes* 2012; 10: 51.
39. Naess H, Lunde L, Brogger J and Waje-Andreassen U. Fatigue among stroke patients on long-term follow-up. The Bergen Stroke Study. *J Neurol Sci* 2012; 312: 138–141.