

1 **Prevalence, Trajectory and Predictors of Post Stroke Pain: Retrospective Analysis of Pooled Clinical**  
2 **Trial Datasets**

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20 **Short title:** Prevalence, and Predictors of Post Stroke Pain

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30 **Abstract**

31 **Background:** Post-stroke pain remains under-diagnosed and inadequately managed. To inform the  
32 optimum time to initiate interventions, we examined prevalence, trajectory and participant factors  
33 associated with post-stroke pain.

34 **Methods:** Eligible studies from the Virtual International Stroke Trials Archives (VISTA) included an  
35 assessment of pain. Analyses of individual participant data (IPD) examined demography, pain,  
36 mobility, independence, language, anxiety/depression and vitality. Pain assessments were  
37 standardised to the European Quality of Life Scale [EQ-5D-3L] pain-domain, describing no, moderate  
38 or extreme pain. We described pain prevalence, and associations between participant characteristics  
39 and pain using multivariable models.

40 **Results:** From 94 studies (n>48,000 individual participant data [IPD]) in VISTA, 10 (n=10,002 IPD)  
41 included a pain assessment. Median age was 70.0 years (IQR [59.0,77.1]), 5,560 (55.6%) were male,  
42 baseline stroke-severity was NIHSS 10 (IQR [7,15]). Reports of extreme pain ranged between 3%-9.5%  
43 and was highest beyond 2 years post-stroke (31/328 [9.5%]); pain trajectory varied by study. Poorer  
44 independence was significantly associated with presence of moderate or extreme pain (5weeks-  
45 3months OR=1.5, 95%CI [1.4, 1.6]; 4-6months OR=1.7 95%CI [1.3, 2.1]; >6months OR=1.5, 95%CI [1.2,  
46 2.0]), and increased severity of pain (5weeks-3months: OR=1.2, 95%CI [1.1,1.2]; 4-6months OR=1.1;  
47 95%CI [1.1, 1.2]; >6months, OR=1.2, 95%CI [1.1, 1.2]), after adjusting for covariates.  
48 Anxiety/depression and lower vitality were each associated with pain severity.

49 **Conclusions:** Between 3%-9.5% of participants reported extreme post-stroke pain; presence and  
50 severity of pain were independently associated with dependence at each time point. Future studies  
51 could determine whether and when interventions may reduce prevalence and severity of post-stroke  
52 pain.

53 Non-standard Abbreviations and Acronyms

<b>Abbreviation</b>	<b>Description</b>
VISTA	Virtual International Stroke Trials Archives
IPD	Individual Participant Data
EQ-5D-3L	European Quality of Life Scale 3 -Level
IQR	Interquartile Range
NIHSS	National Institutes of Health Stroke Scale
CPSP	Central Post-Stroke Pain
ADL	Activities of Daily Living
QoL	Quality of Life
SF-36	RAND 36 Item Health Survey 1.0
NPRS	Numeric Pain Rating Scale
EQ-5D-5L	European Quality of Life Scale 5 -Level

54

## 55 Introduction

56 Post-stroke pain is common<sup>1</sup> with prevalence between 10%<sup>2</sup> and 70%<sup>3-5</sup>, and is poorly  
57 understood<sup>6</sup>. Pain has been reported by 48% of stroke survivors at 1 year<sup>7</sup>, and persistent shoulder  
58 pain has been reported by 20% of people at 4 years<sup>8</sup>. Aetiology can be mixed but includes central post-  
59 stroke pain (CPSP)<sup>9</sup>, headaches, and musculoskeletal issues often arising from post-stroke  
60 impairments,<sup>2,9</sup> commonly affecting the shoulder<sup>1,10</sup>. With increasing numbers surviving stroke with  
61 long-term impairments, the number of people with post-stroke pain will also increase<sup>11</sup>, impacting on  
62 rehabilitation needs.

63 Pain is associated with poor outcomes including restricted mobility<sup>12</sup> and activities of daily  
64 living (ADL)<sup>13</sup>, poorer participation in rehabilitation<sup>14,15</sup>, decreased quality of life (QoL)<sup>16</sup>, presence of  
65 depression<sup>17</sup> and fatigue<sup>18</sup>. QoL and recovery were each rated poorer in those who experienced  
66 frequent post-stroke pain, compared to those who experienced less frequent pain<sup>19</sup>.

67 Despite the impact on everyday life, pain is under-diagnosed and inadequately managed<sup>12</sup>,  
68 with other interventions prioritised<sup>20</sup>. A 5-year follow up study reported that a quarter of participants  
69 had unmet pain management needs<sup>19</sup>, while up to two thirds of those who identified central pain  
70 following stroke reported inadequate intervention for their pain<sup>16</sup>. Management is further hindered  
71 by the different aetiologies of post-stroke pain, and a paucity of available treatment guidelines<sup>21</sup>.  
72 Nevertheless, the causes and factors associated with frequent occurrence of pain can be managed<sup>19</sup>,  
73 and good pain management has been linked with functional improvement and better QoL<sup>22</sup>,  
74 highlighting the importance of monitoring and developing interventions for post-stroke pain<sup>19</sup>.

75 Monitoring post-stroke pain is complex as pain may coexist with complications such as fatigue  
76 or depression<sup>22</sup>. Additionally, stroke-related communication, cognition, perceptual, visual or upper  
77 limb impairments can hinder a person's ability to express pain or participate in a self-rated  
78 assessment<sup>2,10</sup>. Further, pain may be exacerbated by post-stroke consequences such as impaired  
79 motor function, and problems with gait, balance and posture<sup>23</sup>, or influenced by pre-existing age-  
80 related pain such as arthritis. Information on pain symptoms is also not commonly volunteered,

81 particularly in elderly populations<sup>24</sup>, thereby necessitating active enquiries about pain by clinicians.  
82 Post-stroke pain can therefore be overlooked by healthcare professionals<sup>12</sup>.

83 Examination of data across the stroke recovery continuum and different recruitment settings  
84 would increase the generalisability of findings to the wider population. Further, to inform treatments  
85 for pain, we need a better understanding of assessment and epidemiology. Future pain intervention  
86 studies would benefit from estimates of post-stroke pain prevalence across the recovery continuum,  
87 information on patient characteristics associated with pain, and prognostic models of the natural  
88 history of pain progression.

## 89 **Aims**

90 We sought to describe the prevalence of, populations affected by, trajectory of and  
91 participant-related factors associated with post-stroke pain.

## 92 **Methods**

93 **Data Availability:** Data are available upon request to the Virtual Trials Archive  
94 [vista.coordinator@glasgow.ac.uk](mailto:vista.coordinator@glasgow.ac.uk). R scripts for data processing and analysis are available at  
95 [https://github.com/hollytibble/Stroke\\_Pain](https://github.com/hollytibble/Stroke_Pain).

96

## 97 **Data**

98 We conducted retrospective analyses of pooled, anonymised individual participant data (IPD)  
99 from the Virtual International Stroke Trials Archive (VISTA)<sup>25</sup>. IPD were included where participants  
100 had at least one assessment of pain reported during the study, using the pain domain of the European  
101 Quality of Life Scale (EQ-5D) 3 Level/ 5 Level scale, the pain domain of the RAND 36 Item Health Survey  
102 1.0 item 21 (SF-36)<sup>26</sup> or the 0-10 Numeric Pain Rating Scale (NPRS). Data on demography, mobility  
103 using the Barthel Index (BI), independence using the modified Rankin scale (mRS), presence of a

104 language impairment (aphasia), stroke severity, medical history, fatigue, anxiety or depression  
105 (anxiety/depression) were extracted.

106 We defined language impairment as a score of  $\geq 1$  on the Best Language domain of the  
107 National Institutes of Health Stroke Scale (NIHSS) at baseline. Anxiety or depression was defined as a  
108 score of 2 or 3 on the anxiety/depression scale of the EQ-5D-3L and a score of 2 to 5 on the EQ-5D-5L  
109 scale. Fatigue was described according to a composite of items 23,27,29 and 31 of the SF-36 scale, as  
110 per scoring guidelines. An acute setting was defined as enrolment within 24 hours of stroke onset, a  
111 non-acute setting was described as enrolment  $>1$  month from stroke onset, while mixed settings  
112 included enrolment within 7 days to 1-month post-stroke. Time since stroke onset was categorised *a*  
113 *priori* as 0 to 4 weeks, 5 weeks to 3 months, 4 to 6 months and  $>6$  months. Where more detailed  
114 analyses of later time points were required, we described time points as 6 to 12 months,  $>1$  to 2 years,  
115 and  $>2$  years post-stroke.

116 Pain was defined pragmatically to consider the range of scoring conventions. “Some” pain was  
117 defined as a score above the scale minimum (minimum scoring =no pain on all assessment tools), and  
118 “extreme” pain as a maximum score on each of the assessment tools. Mobility using the BI mobility  
119 domain was transformed into a linear score to account for different scoring methods within studies,  
120 and combining wheelchair independence and independence, such that scores from studies reporting  
121 mobility on a 0-3 scale were multiplied by 5 to form a 0-15 score. We then allocated scores of 0- $>1$ ,  
122 10- $>2$ , and both 5 and 15 became 3. Thus, mobility was described on a linear 1-3 scale.

### 123 ***Pain Data Transformation***

124 To facilitate analyses and interpretation of data on a single, clinically meaningful pain scale,  
125 we used a transformation algorithm previously adapted from the Early Breast Cancer Trialists  
126 Collaboration for use in a post-stroke aphasia population<sup>27,28,29</sup>. Briefly, we identified the most  
127 commonly used assessment tool and designated this as an “anchor measure,” to which all other pain  
128 measures were transformed (matching value ranges for the anchor measure but preserving the

129 original scores' distributions). Therefore, all usable pain data were pooled and presented using a  
130 clinically relevant assessment scale as a reference point.

131 Data from the SF-36, EQ-5D-5L, and 0-10 NPRS were transformed to fit the range of the EQ-  
132 5D-3L pain domain (anchor measure). Patients in whom the 0-10 NPRS was assessed also had pain  
133 assessments available using the EQ-5D-3L and 5L, which enabled us explore this transformation in the  
134 context of a post-stroke pain population.

## 135 ***Analyses***

### 136 Transformation Validation

137 Where pain assessments using different tools were present for the same participant, the  
138 transformed pain values were compared to the anchor measure values recorded on the same day.  
139 Spearman correlation coefficients were calculated between the transformed pain values and the  
140 anchor measure score, and between the original pain assessment value and the anchor measure  
141 score.

### 142 Population Description

143 We described the demography of the participants in our dataset using summary statistics. We  
144 compared participant characteristics for those with no or moderate pain (EQ-5D-3L=1 or 2) and those  
145 with extreme pain (EQ-5D-3L=3) using Mann-Whitney and  $\chi^2$  tests, as appropriate.

### 146 Prevalence and Trajectory of Pain

147 We described the number of participants with "some" pain, and with extreme pain (both  
148 stratified by assessment tool), in each time period. Trajectories of pain were described for participants  
149 with multiple measurements of pain within the first year since the onset of stroke.

### 150 Factors Associated with Post-Stroke Pain

151 We used logistic regression to investigate the factors associated with presence of moderate  
152 or extreme pain, and extreme pain alone, stratified by time period, and recruitment setting. Factors  
153 included participants' age, sex, initial stroke severity, mobility problems, diabetes, baseline aphasia,



154 and independence (median value by time period). If coefficients over 1000 or under 0.001 were  
155 observed due to small numbers, the variable was removed to improve model fit.

156 We used linear regression to investigate associations between participant factors and the  
157 reported pain severity. Where a participant had multiple pain measurements in the same time period,  
158 the median pain value was used. The linearity of the association with pain was tested for the  
159 continuous features (age, initial stroke severity, and independence) for each time-period and if the  
160 assumption was not held then they were converted to categorical variables. The variance of pain  
161 across the range of each continuous feature was assessed to confirm homoscedasticity.

#### 162 Pain, Anxiety/Depression and Fatigue

163 Linear regression models examined associations between pain severity (1=no pain,  
164 2=moderate pain, 3=extreme pain) and anxiety/depression on the EQ-5D. Where a participant had  
165 multiple measurements in the same time period, the median values were used. Finally, we examined  
166 associations between fatigue and pain using the Spearman correlation coefficient.

### 167 **Results**

168 From 94 studies comprising >48,000 IPD in VISTA, 10 studies included an assessment of pain  
169 (figure S1); 2 studies used a pain-specific assessment, and 8 captured pain in multidomain  
170 assessments.

#### 171 ***Pain Measurement Transformations in the Post-Stroke Pain Population***

172 One study used both EQ-5D-3L and the 0-10 NPRS. The values of the 0-10 NPRS (n=1064)  
173 transformed to fit the range of the EQ-5D-3L were compared to the originally recorded EQ-5D-3L  
174 values. The median difference between the observed EQ-5D-3L pain score and the transformed 0-10  
175 NPRS was 0 (interquartile range -0.4 to 0.2), meaning that there was no substantial systematic change  
176 in value after the transformation algorithm was applied. The Spearman correlation coefficient  
177 between the transformed 0-10 NPRS value and the observed EQ-5D-3L pain score was 0.49. This was  
178 only slightly lower than the correlation between the EQ-5D-3L pain score and the untransformed 0-10

179 NPRS, at 0.50, demonstrating that the strength of the relationship between the pain measures was  
180 unchanged by transformation, which provided further reassurance that the transformation was valid  
181 in this population.

182 A second study used the EQ-5D-5L and the 0-10 NPRS. The transformed values from both EQ-  
183 5D-5L and pain as measured by the 0-10 NPRS, were compared when measured on the same day,  
184 (n=1956). The median difference between the original EQ-5D-5L and the 0-10 NPRS transformed to fit  
185 the range of the EQ-5D-5L was 0, with an interquartile range of -1 to 0, and a Spearman correlation  
186 coefficient of 0.31. The correlation coefficient between the untransformed values of both measures  
187 was also 0.31.

### 188 ***Participant Characteristics***

189 In our sample, 10,002 participants had at least one pain assessment after stroke. The median age was  
190 70 (interquartile range: IQR [59, 77.1], Table 1), 5,560 (55.6%) were male, a majority had a confirmed  
191 ischaemic stroke (5,421; 54.2%) and the median time since stroke was 1.4 days (IQR [1,7]). Upper-limb  
192 pain was assessed for 1,102 participants; 8 studies used the EQ-5D or the SF36, with no indication of  
193 pain localisation; further, pre-stroke pain was available for only 330 participants, of whom, 306/330  
194 (92.8%) reported no pre-stroke pain.

### 195 ***Pain Assessments***

196 For the EQ-5D-3L, 5,167/10,834 measurements were reported by the participants themselves,  
197 and the remaining by proxy. The median pain score (across all time points) when reported by the  
198 participant was 1 (IQR 1-2) compared to a median of 2 when reported by proxy (IQR 1-2). There was  
199 a significant difference between proxy and participant reported pain values ( $p < 0.001$ ). Table S1  
200 describes the availability of pain measurements across different time points.

### 201 ***Prevalence and Trajectory of Post-Stroke Pain***

202 Figure 1 describes the transformed pain scores compared to scores from each assessment tool  
203 (up to 2 years post-stroke). Reported pain generally appeared to peak in the first 100 days after stroke.

204 Table 2 describes the number of participants with at least one measurement of pain greater than each  
205 scale's minimum at each timepoint, defined as "some" pain. For those in whom assessment of pain  
206 was available, between 51.3% reported presence of "some" pain between 5 weeks and 3 months post-  
207 onset of stroke. For the three time periods between 4 months and 2 years post-stroke, between 62.5-  
208 67.3% of participants reported presence of "some" pain. In participants with data more than 2 years  
209 after stroke, 89.0% reported having "some" pain on at least one measurement timepoint.

210 Table 2 also describes the proportion of participants who had extreme pain at each time point.  
211 For those in whom assessment of pain was reported, between 3.0-5.4% reported extreme pain  
212 between onset and up to 3 months after stroke. Where assessed, between 6.1%-9.4% reported  
213 extreme pain between 4 months and 2 years after stroke. In participants with data more than 2 years  
214 after stroke, 9.5% reported having extreme pain at least once.

215 There were 1156 participants across four studies who had multiple pain measurements within  
216 the first year of stroke onset, however the trajectory of pain for these participants varied between  
217 studies (Figure 2). Study participant characteristics, recruitment setting, and eligibility criteria  
218 appeared to play a role in the trajectory of pain.

### 219 ***Participants Characteristics with and without Pain***

220 Participants with extreme pain between 5 weeks and 3 months had worse initial stroke  
221 severity (baseline NIHSS= 15[IQR10,19] compared with 11 [8,15]; Table 3) and participants with  
222 extreme pain beyond 5 weeks post-stroke had consistently poorer independence (at the respective  
223 time points) compared to those with no or moderate pain.

### 224 ***Factors Associated with Pain***

225 In studies that took place in an acute setting, poorer independence (at the respective time  
226 point) was consistently associated with presence of moderate or extreme pain at each time point  
227 (Table S2). We observed fewer reports of moderate or extreme pain in people with aphasia in the  
228 acute setting after accounting for initial stroke severity ( $p<0.001$ ; OR=0.77, 95% CI [0.67,0.88]), and

229 greater reports of pain in this population after 6 months post-stroke ( $p=0.029$ ; OR=2.02 95% CI  
230 [1.08,3.8]).

231 Poorer independence was only significantly associated with presence of extreme pain in the  
232 time period of 5 weeks to 3 months ( $p<0.001$ ; OR=1.8; 95%CI [0.43,0.8]; Table 4).

233 In our adjusted linear regression examining reported pain severity (Table S3), poorer  
234 independence was associated with an increased pain severity across all time points in studies taking  
235 place in an acute setting; analysis of non-acute studies did not show significant relationships.

### 236 ***Associations between Pain, Anxiety/Depression and Vitality***

237 Table S4 shows the adjusted linear regressions examining associations between pain and the  
238 anxiety/depression domain of the EQ-5D-3L and 5L at all available time points. Higher anxiety/  
239 depression domain scores were significantly associated with more severe pain for both scales across  
240 all available time points.

241 For 621 participants, concurrent measurement of pain and vitality were available as measured  
242 by the SF-36 at a single timepoint of 90 days. Vitality scores were generated using SF-36 scoring  
243 guidelines for the domain Energy/Fatigue (vitality) and involved transposing scores to fit a scale of 0-  
244 100, where a low score indicates lower vitality<sup>30</sup>. Those with lower vitality reported more severe pain  
245 (Spearman Correlation coefficient=-0.32,  $p<0.001$ , Figure S2).

### 246 **Discussion**

247 We observed that targeted measurement of pain was uncommon in stroke studies, where the  
248 aims seldom related to pain outcome assessment. Only 10 from 94 identified studies included an  
249 assessment of pain, and of these, 8 were multidomain scores that included a pain item. By 2 years  
250 post-stroke, almost 10% of participants reported extreme pain; participants with extreme pain had  
251 poorer independence at each follow up time point compared to those with no or moderate pain.  
252 Presence of anxiety/depression and lower vitality were associated with more severe pain. We  
253 observed peaks of extreme pain between 4 to 6 months and beyond 2 years post-stroke. This is

254 consistent with previous reports of development of CPSP by 6 months of stroke onset<sup>31</sup>. Other reports  
255 suggest that almost a third of people have moderate to severe pain at 4 months post-stroke and this  
256 decreases to 21% by 16 months<sup>32</sup>.

257 Our study expands on previous work by using a much larger sample size (n=5,094 pain  
258 assessments by 3 months, n=4,776 pain assessments between 6-12 months, n=773 with pain  
259 assessments between 1-2 years, compared to n=318 at 4 months and n=300 at 16 months in previous  
260 work<sup>32</sup>). Our observations are much more conservative, estimating extreme pain to affect a maximum  
261 of 9.5% beyond 2 years post-stroke. However, when using a measure of “some” pain, we observed  
262 ranges between 47.4% (at 0-4 weeks) to 89% (beyond 2 years post-stroke). We were also able to  
263 describe reporting of pain in the aphasia population, which is typically under-represented in clinical  
264 research. We observed that in the acute phase, there were fewer reports of moderate or extreme  
265 pain in those with aphasia and this was independent of initial stroke severity. By 6 months post stroke,  
266 people with aphasia reported increased prevalence of moderate or extreme pain, compared to those  
267 without aphasia.

268 Our findings are congruent with previous studies that reported associations between  
269 dependence, limitations in mobility, presence of depression<sup>33</sup> and pain<sup>19</sup>, establishing the  
270 relationships between pain, dependency, vitality and anxiety/depression in a much larger sample size,  
271 and including both acute and non-acute recruitment settings, thereby increasing generalisability of  
272 results. While some previous studies have found a link between age and initial stroke severity with  
273 pain<sup>34</sup>, others reported no association with age, sex, type of stroke or comorbidities<sup>12</sup>. Our study did  
274 not demonstrate a consistent trend of association across all time periods under investigation.  
275 Similarly, we observed inconsistent associations between sex and presence and amount of pain,  
276 whereas previous studies reported associations between female sex and risk of development of post-  
277 stroke pain<sup>1</sup>. However, previous observations could be due to use of single time points for assessment  
278 across those studies.

279 Half of stroke survivors report fatigue as a central issue after their strokes, affecting  
280 rehabilitation and ability to regain independence<sup>35</sup>. We reported a moderate association between  
281 vitality and pain, consistent with previous reports of an independent association between pain,  
282 fatigue<sup>18</sup> and depression<sup>17</sup>.

283 Our study has several strengths. Data were derived from studies across a range of settings,  
284 allowing for examination of stroke in acute as well as non-acute settings and across a range of time  
285 points. Follow up of participants in stroke research for more than 2 years is uncommon yet our study  
286 included participants who were more than 2 years post-stroke. We also had data available on our  
287 anchor measure (EQ-5D-3L) in conjunction with a specific pain assessment tool (0-10 NPRS), which  
288 allowed us to explore the transformation algorithm in the context of post-stroke pain. This  
289 transformation also allowed us to make use of all available data, regardless of the assessment tool  
290 that was used in each study, thereby increasing our sample size and aggregating data across time  
291 points and settings.

292 Localisation of pain was available for 1,102 participants (11%); data were not available on the  
293 initiation or contents of rehabilitation in response to observed pain. Previous literature has estimated  
294 the prevalence of new post-stroke pain to be between 10%<sup>36</sup> to 21.8%<sup>37</sup>, and post-stroke pain is more  
295 common in those with pre-stroke pain<sup>38</sup>. Data were only available on pre-stroke pain for 330  
296 participants. We were therefore unable to identify whether our observed pain values were new or  
297 due to pre-existing pain. However, from the small sample in whom pre-stroke pain was assessed, more  
298 than 92% had no pre-stroke pain.

299 Post-stroke pain commonly comprises two main types: peripheral pain such as headaches,  
300 spasticity-related pain, or musculoskeletal pain; or CPSP<sup>39</sup>, with CPSP being a commonly reported  
301 complication of strokes affecting the thalamus<sup>40</sup>, medulla<sup>41</sup> and affecting 41% between 1 month and  
302 1-year post-stroke, decreasing to 5% beyond 1-year post-stroke<sup>42</sup>. CPSP is associated with younger

303 age, smoking history, poorer initial stroke severity, and a history of depression<sup>36</sup>. We observed similar  
304 associations between poorer initial stroke severity, depression and presence of pain in our sample.

305 Our study did not differentiate by the types of pain experienced, though 4 studies included  
306 presence of limb impairment or weakness as an eligibility criterion. We were therefore unable to  
307 account for the types of pain that emerged at different time periods. We were also limited by the  
308 types of pain assessment that were used across studies in VISTA. However, it provided an indication  
309 of the types of pain assessment captured in typical stroke studies.

### 310 **Conclusion**

311 Our findings are congruent with previous recommendations in the context of CPSP<sup>42</sup>, that  
312 clinicians should continue to check for presence of post-stroke pain up to 12 months post-stroke. Our  
313 findings also highlight the complexity of the relationships between different participant factors and  
314 pain, over different time periods. Future investigation could determine whether and when  
315 interventions may reduce the occurrence and severity of post-stroke pain, while documenting the  
316 presence of pre-stroke pain, stroke location, and type of pain.

### 317 **\*Appendix:**

#### 318 **VISTA-Acute Steering Committee**

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329

330 **VISTA-ICH Steering Committee**

331 DF Hanley (Chair), K Butcher, S Davis, B Gregson, KR Lees, P Lyden, S Mayer, K Muir, and T Steiner.

332

333 **Conflicts of interest:** AP has no personal disclosures, is employed by Bournemouth University and sits  
334 on the Board for: Wessex AHSN, ARC Wessex and Wessex Health Partners. MCB and the NMAHP  
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339

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342

343 **Supplemental Material**

344 Figure S1: STROBE Flowchart

345 Figure S2: Boxplots of SF-36 Vitality Score by SF-36 Pain Score

346 Table S1: Availability of pain measurements by time period and scale

347 Table S2: Adjusted Logistic Regression: Presence of moderate or extreme pain, stratified by timepoints

348 Table S3: Adjusted Linear Regression: Severity of pain, stratified by timepoints

349 Table S4: Linear Regression for associations between severity of pain (on EQ5D 3-level and 5-level)  
350 adjusted for EQ-5D domains

351



352 **Figure Titles:**

353

354 Figure 1: Smoothed estimates of standardised pain scores compared to each pain assessment tool  
355 score (up to 2 years post-stroke)

356 Figure 2: Loess smoothed estimates of pain over time in studies with multiple measurements per  
357 person

358

359 **References**

- 360 1. Harrison RA, Field TS. Post Stroke Pain: Identification,  
361 Assessment, and Therapy. *Cerebrovascular Diseases*.  
362 2015;39:190–201.
- 363 2. Treister AK, Hatch MN, Cramer SC, Chang EY. Demystifying  
364 Poststroke Pain: From Etiology to Treatment. *PM&R*.  
365 2017;9:63–75.
- 366 3. Hamzat TK, Osundiya OC. Musculoskeletal pain and its  
367 impact on motor performance among stroke survivors. *Hong  
368 Kong Physiotherapy Journal*. 2010;28:11–15.
- 369 4. Lindgren I, Jönsson A–C, Norrving B, Lindgren A. Shoulder  
370 Pain After Stroke. *Stroke*. 2007;38:343–348.
- 371 5. Klit H, Finnerup NB, Andersen G, Jensen TS. Central  
372 poststroke pain: A population–based study. *Pain*.  
373 2011;152:818–824.
- 374 6. Merskey N. Classification of chronic pain; Description of  
375 chronic pain syndromes and definitions of pain Terms. Task  
376 force on taxonomy of the international association for the  
377 study of pain. . Task force on taxonomy of the international  
378 association for the study of pain. 1994;41–43.
- 379 7. Naess H, Lunde L, Brogger J. The Triad of Pain, Fatigue and  
380 Depression in Ischemic Stroke Patients: The Bergen Stroke  
381 Study. *Cerebrovascular Diseases*. 2012;33:461–465.

- 382  
383  
384  
385  
386  
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413  
414  
415  
416  
417
8. G. BROEKS , J., LANKHORST , G. J., RUMPING , K., PREVO AJH. The long-term outcome of arm function after stroke: results of a follow-up study. *Disabil Rehabil.* 1999;21:357-364.
  9. Leijon G, Boivie J, Johansson I. Central post-stroke pain — neurological symptoms and pain characteristics. *Pain.* 1989;36:13-25.
  10. Edwards SA, Ioannou A, Carin-Levy G, Cowey E, Brady M, Morton S, Sande TA, Mead G, Quinn TJ. Properties of Pain Assessment Tools for Use in People Living With Stroke: Systematic Review. *Front Neurol.* 2020;11.
  11. Maaijwee NA, Rutten-Jacobs LC, Schaapsmeeders P, van Dijk EJ, de Leeuw FE. Ischaemic stroke in young adults: risk factors and long-term consequences. . *Nat Rev Neurol.* 2014;10:315-325.
  12. Appelros P. Prevalence and predictors of pain and fatigue after stroke: a population-based study. *International Journal of Rehabilitation Research.* 2006;29:329-333.
  13. de Vries NJ (Carolien), Sloot PH, Achterberg WP. Pain and pain assessment in stroke patients with aphasia: a systematic review. *Aphasiology.* 2017;31:703-719.
  14. Langhorne P, DJ S, Robertson L, MacDonald J, Jones L, McAlpine C, Dick F, GS T, Murray G. Medical complications after stroke: A multicentre study. *Stroke* [Internet]. 2000;31:1223-1229. Available from: <http://stroke.ahajournals.org/cgi/content/abstract/31/6/1223>
  15. Yang S, Grabois M, Bruel B. Post-stroke Pain. *Pract Pain Manag.* 2009;9.
  16. Widar M, Samuelsson L, Karlsson-Tivenius S, Ahlström G. Long-term pain conditions after a stroke. *J Rehabil Med.* 2002;34:165-170.
  17. Lundström E, Smits A, Terént A, Borg J. Risk factors for stroke-related pain 1 year after first-ever stroke. *Eur J Neurol.* 2009;16:188-193.
  18. Lan Nguyen Hoang C, Salle J-Y, Mandigout S, Hamonet J, Macian-Montoro F, Daviet J-C. Physical Factors Associated

- 418 With Fatigue After Stroke: An Exploratory Study. *Top Stroke*  
419 *Rehabil.* 2012;19:369–376.
- 420 19. Westerlind E, Singh R, Persson HC, Sunnerhagen KS.  
421 Experienced pain after stroke: a cross-sectional 5-year  
422 follow-up study. *BMC Neurol.* 2020;20:4.
- 423 20. McArthur KS, Quinn TJ, Higgins P, Langhorne P. Post-acute  
424 care and secondary prevention after ischaemic stroke. *BMJ.*  
425 2011;342:d2083–d2083.
- 426 21. Kim JS. Pharmacological Management of Central Post-Stroke  
427 Pain: A Practical Guide. *CNS Drugs.* 2014;28:787–797.
- 428 22. Katz N. The Impact of Pain Management on Quality of Life. *J*  
429 *Pain Symptom Manage.* 2002;24:S38–S47.
- 430 23. de Haart M, Geurts AC, Huidekoper SC, Fasotti L, van Limbeek  
431 J. Recovery of standing balance in postacute stroke patients:  
432 a rehabilitation cohort study<sup>1</sup> No commercial party having a  
433 direct financial interest in the results of the research  
434 supporting this article has or will confer a benefit upon the  
435 authors(s) or upon any organization with which the author(s)  
436 is/are associated. *Arch Phys Med Rehabil.* 2004;85:886–895.
- 437 24. Catananti C, Gambassi G. Pain assessment in the elderly. *Surg*  
438 *Oncol.* 2010;19:140–148.
- 439 25. Ali M, Bath P, Brady M, Davis S, H-C D, Donnan G, Fisher M,  
440 Hacke W, DF H, Luby M, et al. Development, Expansion and  
441 Use of a Stroke Clinical Trials Resource for Novel Exploratory  
442 Analyses. *International Journal of Stroke.* 2012;7:133–138.
- 443 26. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form  
444 health survey (SF-36). I. Conceptual framework and item  
445 selection. *Med Care.* 1992;30:473–483.
- 446 27. The RELEASE Collaborators. RELEASE: An individual  
447 participant data meta-analysis, incorporating systematic  
448 review and network meta-analysis, of complex speech-  
449 language therapy interventions for stroke-related aphasia. .  
450 *National Institutes of Health Research: Health Services and*  
451 *Delivery Research.* 2022;2022.
- 452 28. Ali M, VandenBerg K, Williams LJ, Williams LR, Abo M, Becker  
453 F, Bowen A, Brandenburg C, Breitenstein C, Bruehl S, et al.

- 454 Predictors of Poststroke Aphasia Recovery. *Stroke*.  
455 2021;52:1778–1787.
- 456 29. Brady MC, Ali M, VandenBerg K, Williams LJ, Williams LR, Abo  
457 M, Becker F, Bowen A, Brandenburg C, Breitenstein C, et al.  
458 Dosage, Intensity, and Frequency of Language Therapy for  
459 Aphasia: A Systematic Review–Based, Individual Participant  
460 Data Network Meta–Analysis. *Stroke*. 2022;53:956–967.
- 461 30. Mead GE, Graham C, Dorman P, Bruins SK, Lewis SC, Dennis  
462 MS, Sandercock PAG. Fatigue after Stroke: Baseline Predictors  
463 and Influence on Survival. Analysis of Data from UK Patients  
464 Recruited in the International Stroke Trial. *PLoS One*.  
465 2011;6:e16988.
- 466 31. Canavero S, Bonicalzi V. Central Pain of Brain Origin:  
467 Epidemiology and Clinical Features. Cambridge University  
468 Press; 2007.
- 469 32. Jonsson A–C, Lindgren I, Hallstrom B, Norrving B, Lindgren A.  
470 Prevalence and intensity of pain after stroke: a population  
471 based study focusing on patients’ perspectives. *J Neurol*  
472 *Neurosurg Psychiatry*. 2006;77:590–595.
- 473 33. Delpont B, Blanc C, Osseby GV, Hervieu–Bègue M, Giroud M,  
474 Béjot Y. Pain after stroke: A review. *Rev Neurol (Paris)*.  
475 2018;174:671–674.
- 476 34. O’Donnell MJ, Diener H–C, Sacco RL, Panju AA, Vinisko R,  
477 Yusuf S. Chronic Pain Syndromes After Ischemic Stroke.  
478 *Stroke*. 2013;44:1238–1243.
- 479 35. The Stroke Association. Fatigue after Stroke. 2012.
- 480 36. O’Donnell MJ, Diener H–C, Sacco RL, Panju AA, Vinisko R,  
481 Yusuf S. Chronic Pain Syndromes After Ischemic Stroke.  
482 *Stroke*. 2013;44:1238–1243.
- 483 37. Bovim MR, Indredavik B, Hokstad A, Lydersen S, Askim T.  
484 New–onset pain in the early phase and three months  
485 following stroke &ndash; data from a multicenter study. *J*  
486 *Pain Res*. 2018;Volume 11:1869–1876.
- 487 38. Hansen AP, Marcussen NS, Klit H, Andersen G, Finnerup NB,  
488 Jensen TS. Pain following stroke: A prospective study.  
489 *European Journal of Pain*. 2012;16:1128–1136.

- 490  
491  
492  
493  
494  
495  
496  
497  
498  
499  
500  
501  
502  
503  
504  
505  
506  
507  
508
39. Seifert CL, Mallar Chakravarty M, Sprenger T. The complexities of pain after stroke--a review with a focus on central post-stroke pain. *Panminerva Med.* 2013;55:1-10.
  40. Krause T, Brunecker P, Pittl S, Taskin B, Laubisch D, Winter B, Lentza ME, Malzahn U, Villringer K, Villringer A, et al. Thalamic sensory strokes with and without pain: differences in lesion patterns in the ventral posterior thalamus. *J Neurol Neurosurg Psychiatry.* 2012;83:776-784.
  41. MacGowan DJL, Janal MN, Clark WC, Wharton RN, Lazar RM, Sacco RL, Mohr JP. Central poststroke pain and Wallenberg's lateral medullary infarction: Frequency, character, and determinants in 63 patients. *Neurology.* 1997;49:120-125.
  42. Liampas A, Velidakis N, Georgiou T, Vadalouca A, Varrassi G, Hadjigeorgiou GM, Tsivgoulis G, Zis P. Prevalence and Management Challenges in Central Post-Stroke Neuropathic Pain: A Systematic Review and Meta-analysis. *Adv Ther.* 2020;37:3278-3291.

## Tables

**Table 1: Baseline characteristics**

Variable	Value (N=10,002)
Age (median [IQR] years)	70.0 (59.0 – 77.1)
Sex (n male; %)	5560 (55.6%)
Time since stroke; days (median [IQR])	1.4 (1 – 7)
Stroke Type	
Missing	3912 (39.1%)
Assumed Ischaemic	30 (0.3%)
Intracerebral Haemorrhage (ICH)	625 (6.2%)
Ischaemic & ICH	4 (<0.1%)
Confirmed Ischaemic	5421 (54.2%)
Subarachnoid Haemorrhage (SAH)	10 (0.1%)
Baseline National Institutes of Health Stroke Scale Score (NIHSS; median [IQR])	10 (7 – 15)
Immobility at any time point (n yes; %)	1707 (17.1%)
Diabetes (n yes; %)	1355 (20.5%)
Aphasia at Baseline (n yes; %)	2269 (37.4%)

Notes: NIHSS n available=5587, diabetes n=6621, and aphasia n=6066.

**Table 2: Proportion of participants with some and extreme pain at each time point**

	Timepoint	EQ5D-3L	EQ5D-5L	0-10 Numeric Pain scale	SF-36	Transformed Pain Scale
		n with 1+ measurement of pain > scale minimum / N with 1+ measurement of pain [Binomial Proportion 95% Cis]				
Some Pain	0-4 WEEKS	26/68 (38.2%) [26.7 – 50.8%]	32/64 (50.0%) [37.2 – 62.8%]	13/63 (20.6%) [11.5 – 32.7%]	NA	63/132 (47.7%) [39.0 – 56.6%]
	5 WEEKS – 3 MONTHS	2181/4375 (49.9%) [48.4 – 51.3%]	67/96 (69.8%) [59.6 – 78.7%]	97/142 (68.3%) [60.0 – 75.9%]	354/623 (56.8%) [52.8 – 60.8%]	2615/5094 (51.3%) [50.0 – 52.7%]
	4-6 MONTHS	316/560 (56.4%) [52.2 – 60.6%]	222/292 (76.0%) [70.7 – 80.8%]	284/391 (72.6%) [67.9 – 77.0%]	NA	582/865 (67.3%) [64.0% – 70.4%]
	6 – 12 MONTHS	2597/4311 (60.2%) [58.8 – 61.7%]	329/441 (74.6%) [70.3 – 78.6%]	358/566 (63.3%) [59.1 – 67.2%]	NA	2984/4776 (62.5%) [61.1 – 63.9%]
	1 – 2 YEARS	249/461 (54.0%) [49.3 – 58.6%]	210/281 (74.7%) [69.2 – 79.7%]	220/411 (53.5%) [48.6 – 58.4%]	NA	495/773 (64.0%) [60.5 – 67.4%]
	>2 YEARS	117/141 (83.0%) [75.7 – 88.8%]	154/184 (83.7%) [77.5 – 88.7%]	198/327 (60.6%) [55.0 – 65.9%]	NA	292/328 (89.0%) [85.1 – 92.2%]
Extreme Pain	0-4 WEEKS	2/68 (2.9%) [0.4 – 10.2%]	0/64 (0%) [0.0 – 5.6%]	2/63 (3.2%) [0.4 – 11.0%]	NA	4/132 (3.0%) [0.8 – 7.6%]
	5 WEEKS – 3 MONTHS	257/4375 (5.9%) [5.2 – 6.6%]	1/96 (1.0%) [0.0 – 5.7%]	8/142 (5.6%) [2.5 – 10.8%]	11/623 (1.8%) [0.9- 3.1%]	274/5094 (5.4%) [4.8 – 6.0%]
	4-6 MONTHS	52/560 (9.3%) [7.0 – 12.0%]	5/292 (1.7%) [0.6 – 4.0%]	28/391 (7.2%) [4.8 – 10.2%]	NA	81/865 (9.4%) [7.5 – 11.5%]

	6 – 12 MONTHS	260/4311 (6.0%) [5.3 – 6.8%]	8/441 (1.8%) [0.8 - 3.5%]	31/566 (5.5%) [3.8 - 7.7%]	NA	292/4776 (6.1%) [5.5 – 6.8%]
	1 – 2 YEARS	31/461 (6.7%) [4.6 -9.4%]	11/281 (3.9%) [2.0 - 6.9%]	13/411 (3.2%) [1.7- 5.3%]	NA	53/773 (6.9%) [5.2 – 8.9%]
	>2 YEARS	19/141 (13.5%) [8.3- 20.2%]	6/184 (3.3%) [1.2 – 7.0%]	9/327 (2.8%) [1.3 -5.2%]	NA	31/328 (9.5%) [6.5 -13.1%]



**Table 3: Unadjusted associations between the presence of extreme pain and participant characteristics**

Time Period	Variable	Extreme Pain	No, or moderate, Pain	Mann Whitney / $\chi^2$ p-value: Pain vs. No Pain
		Median / N (IQR / %)		
0-4 weeks (n=132, studies=2)	Age	66 (58 – 73)	69 (55 – 80)	0.868
	Male Sex	1 (25.0%)	75 (58.6%)	0.409
	Initial Stroke Severity	Insufficient data		
	Presence of Baseline Severe-Global Aphasia	0	10 (8.6%)	1.000
	Diabetes	No data		
	Independence	3.5 (3.25- 3.75)	4 (4 – 5)	0.200
	Mobility	2.5 (1.75 – 3)	1.5 (1 – 2)	0.220
5 weeks – 3 months (n=5094, Studies=7)	Age	69 (58 - 77)	68 (58 - 76)	0.396
	<b>Male Sex</b>	<b>124 (45.3%)</b>	<b>2719 (56.4%)</b>	<b>&lt;0.001</b>
	<b>Initial Stroke Severity</b>	<b>15 (10 – 19)</b>	<b>11 (8 – 15)</b>	<b>&lt;0.001</b>
	Presence of Baseline Severe-Global Aphasia	100 (37.2%)	1895 (39.5%)	0.483
	Diabetes	53 (23.0%)	920 (21.5%)	0.632
	<b>Independence</b>	<b>4 (3 – 5)</b>	<b>2 (1 – 4)</b>	<b>&lt;0.001</b>
	<b>Mobility</b>	<b>2 (1 – 3)</b>	<b>3 (2 – 3)</b>	<b>&lt;0.001</b>
4 months – 6 months (n=865, studies=7)	Age	64 (51- 72)	62 (52- 71)	0.593
	Male Sex	44 (54.3%)	473 (60.3%)	0.352
	Initial Stroke Severity	6 (4 – 20.5)	8 (4 – 18)	0.899
	Presence of Baseline Severe-Global Aphasia	23 (35.9%)	281 (40.5%)	0.563
	Diabetes	6 (18.2%)	10 (9.7%)	0.315
	<b>Independence</b>	<b>4 (3 – 5)</b>	<b>3 (2 – 4)</b>	<b>0.013</b>
	Mobility	3 (1 – 3)	3 (2 – 3)	0.156
> 6 months (n=5229, studies=6)	Age	68 (60- 78)	70 (59 – 78)	0.205
	Male Sex	196 (54.7%)	2709 (55.6%)	0.792
	Initial Stroke Severity	6 (3 – 13)	6 (4 – 11)	0.979
	Presence of Baseline Severe-Global Aphasia	48 (36.6%)	433 (34.8%)	0.742
	Diabetes	25 (16.4%)	354 (18.2%)	0.656
	<b>Independence</b>	<b>4 (3 – 5)</b>	<b>3 (2 – 4)</b>	<b>&lt;0.001</b>
	<b>Mobility</b>	<b>3 (1.13 – 3)</b>	<b>3 (3 – 3)</b>	<b>&lt;0.001</b>

**Table 4: Adjusted Logistic Regression: Presence of “extreme” pain, stratified by timepoints**

Time Period	Covariate	Value	Acute Studies			Non-Acute Studies		
			Adjusted Odds Ratio Estimates					
			Point Estimate	95% Confidence Limits	Wald P-value	Point Estimate	95% Confidence Limits	Wald P-value
5 weeks -3 months (4 Acute studies: n=4803, 3 chronic/mixed studies: n = 134)	Age		0.983	(0.972, 0.994)	0.003	0.993	(0.929, 1.061)	0.836
	Male Sex		0.671	(0.513, 0.878)	0.004	2.797	(0.280, 27.900)	0.381
	Higher Initial Stroke Severity		1.033	(1.007, 1.060)	0.013	1.141	(0.964, 1.350)	0.125
	Mobility Problems		1.175	(0.802, 1.722)	0.408	0.559	(0.075, 4.163)	0.570
	Diabetes	No	{ref}			Omitted: 82% missing		
		Yes	0.983	(0.706, 1.368)	0.917			
		Missing	0.492	(0.297, 0.816)	0.006			
	Presence of Aphasia at Baseline		0.583	(0.425, 0.800)	0.001	0.983	(0.092, 10.503)	0.989
	Poorer Independence		1.823	(1.559, 2.132)	<0.001	Omitted: 80% missing		
4 months – 6 months (1 Acute study: n=343, 6 chronic/mixed studies: n = 271)	Age		0.917	(0.868, 0.968)	0.002	0.938	(0.953, 1.013)	0.263
	Male Sex		0.597	(0.198, 1.799)	0.359	0.804	(0.333, 1.944)	0.628
	Higher Initial Stroke Severity		1.039	(0.980, 1.102)	0.195	0.989	(0.843, 1.160)	0.893
	Mobility Problems		1.630	(0.331, 8.023)	0.548	1.052	(0.405, 2.734)	0.917
	Diabetes		Omitted as 100% missing			Omitted: 72% missing		
	Presence of Aphasia at Baseline		1.459	(0.244, 8.735)	0.679	0.811	(0.214, 3.078)	0.758
	Poorer Independence		1.390	(0.708, 2.731)	0.339	Omitted: 84% missing		
> 6 months (1 Acute study: n=338, 5 chronic/mixed studies: n = 660)	Age		0.958	(0.919, 0.999)	0.044	0.984	(0.963, 1.006)	0.163
	Male Sex		1.267	(0.539, 2.981)	0.587	1.165	(0.625, 2.173)	0.631
	Higher Initial Stroke Severity		0.967	(0.919, 1.016)	0.183	0.921	(0.812, 1.045)	0.203
	Mobility Problems		1.187	(0.334, 4.219)	0.791	2.774	(1.441, 5.341)	0.002
	Diabetes		Omitted as 100% missing			Omitted: 82% missing		
	Presence of Aphasia at Baseline		1.172	(0.389, 3.531)	0.779	1.531	(0.725, 3.232)	0.264
	Poorer Independence		1.720	(0.996, 2.971)	0.052	Omitted: 80% missing		