

1 **Upper Limb Function in People With Upper and Lower Limb Loss 8 Years**  
2 **Postinjury: The Armed Services Trauma Outcome Study (ADVANCE) Cohort**  
3 **Study**

4  
5 **Running Head:** Upper Limb Disability in People With Limb Loss

6  
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13 **Authors/Affiliations:**

14 Fraje C.E. Watson, PhD<sup>1</sup>; Angela E. Kedgley, PhD<sup>1</sup>; Susie Schofield MSc<sup>2</sup>; Fearghal  
15 P. Behan, PhD<sup>1,3</sup>; Christopher J. Boos, PhD<sup>4</sup>; Nicola, T. Fear, PhD<sup>5</sup>; Alexander N.  
16 Bennett, PhD<sup>1,6</sup>; Anthony M.J. Bull, PhD<sup>1</sup>

17

18 <sup>1</sup> Department of Bioengineering, Imperial College London, London, UK

19 <sup>2</sup> National Heart and Lung Institute, Faculty of Medicine, Imperial College London,  
20 London, UK

21 <sup>3</sup> Discipline of Physiotherapy, School of Medicine, Trinity College Dublin, Dublin,  
22 Ireland

23 <sup>4</sup> Faculty of Health and Social Sciences, Bournemouth University, Poole, UK

24 <sup>5</sup> King's Centre for Military Research, King's College London, London, UK

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33 Physical Therapy Association.

34 <sup>6</sup> Academic Department of Military Rehabilitation, Defence Military Rehabilitation  
35 Centre, Stanford Hall, Loughborough, UK

36

37 **Address all correspondence to Dr Watson at:** [f.watson@imperial.ac.uk](mailto:f.watson@imperial.ac.uk). Follow  
38 the author: @frajewatson.

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42

UNCORRECTED MANUSCRIPT

43 **ABSTRACT**

44 **Objective.** Upper limb (UL) disability in people with UL amputation/s is well reported  
45 in the literature, less so for people with lower limb amputation/s. This study aimed to  
46 compare UL disability in injured (major trauma) and uninjured UK military personnel,  
47 with particular focus on people with upper and lower limb amputation/s.

48 **Methods.** A volunteer sample of injured (n = 579) and uninjured (n = 566) UK  
49 military personnel who served in a combat role in the Afghanistan war were  
50 frequency matched on age, sex, service, rank, regiment, role, and deployment period  
51 and recruited to the Armed Services Trauma Rehabilitation Outcome (ADVANCE)  
52 longitudinal cohort study. Participants completed the Disability of the Arm, Shoulder,  
53 and Hand (DASH) questionnaire, scored from 0 (no disability) to 100 (maximum  
54 disability) 8 years postinjury. Mann-Whitney U and Kruskal Wallis tests were used to  
55 compare DASH scores between groups. An ordinal model was used to assess the  
56 effect of injury and amputation on DASH scores.

57 **Results.** DASH scores were higher in the group with injuries compared to the group  
58 without injuries (3.33 vs 0.00) and higher in people with lower limb loss compared to  
59 the group without injuries (0.83 vs 0.00), although this was not statistically significant.  
60 In the adjusted ordinal model, the odds of having a higher DASH score was 1.70  
61 (95% CI = 1.18-2.47) times higher for people with lower limb loss compared to the  
62 group without injuries. DASH score was not significantly different between people  
63 with major and partial UL loss (15.42 vs 12.92). The odds of having a higher DASH  
64 score was 8.30 (95% CI = 5.07-13.60) times higher for people with UL loss  
65 compared to the uninjured group.

66 **Conclusion.** People with lower limb loss have increased odds of having more UL  
67 disability than the uninjured population 8 years postinjury. People with major and  
68 partial UL loss have similar UL disability. The ADVANCE study will continue to follow  
69 this population for the next 20 years.

70 **Impact.** For the first time, potential for greater upper limb disability has been shown  
71 in people with lower limb loss long-term, likely resulting from daily biomechanical  
72 compensations such as weight-bearing, balance, and power generation. This  
73 population may benefit from prophylactic upper limb rehabilitation, strength, and  
74 technique.

## 77 [H1]Introduction

78 The upper limbs (UL) are integral to performing activities of daily living and provide a  
79 means for communication and self-expression.<sup>1,2</sup> High levels of UL disability in  
80 people with major (proximal to the wrist including wrist disarticulation) and partial  
81 (distal to the wrist) UL loss have been reported in military<sup>3,4</sup> and civilian populations.<sup>5-</sup>  
82 <sup>7</sup> Disability in people with partial UL loss is extremely varied depending on the level  
83 of amputation and thumb involvement.<sup>4,5,8-10</sup> Most research on people with partial UL  
84 loss focuses on outcomes compared to replantation,<sup>8-10</sup> and not compared to people  
85 with major UL loss who may have better access to rehabilitation and prosthetic  
86 devices. Following initial injury, people with major UL loss have increased odds of an  
87 UL overuse musculoskeletal injury in the first year post-amputation<sup>11</sup> and chronic  
88 injury to the contralateral limb,<sup>12</sup> which could further compound initial disability.  
89 Despite the life-long impact of UL amputation coupled with the consequences of

90 biomechanical compensations and aging, a prospective cohort has never been  
91 followed longitudinally beyond medical discharge from hospital care.

92

93 People with lower limb loss have a 2 to 4 times increased risk of UL musculoskeletal  
94 injury 1 year postinjury compared to those with minor lower limb injuries.<sup>13</sup> These  
95 short-term findings mirror long-term UL musculoskeletal injuries reported in  
96 wheelchair and assistive walking device users, resulting from increased forces and  
97 altered biomechanics through the UL joints during propulsion/ambulation and  
98 transfer activities.<sup>14-16</sup> Little is known about the long-term progression and impact of  
99 increased UL musculoskeletal injuries on people with lower limb loss.

100

101 The Armed Services Trauma Rehabilitation Outcome Study (ADVANCE) is a 20 year  
102 cohort study collecting physical and psychosocial outcome data from 1145 male UK  
103 military personnel who deployed to the Afghanistan war between 2003 and 2014.<sup>17</sup>

104 Approximately half of the cohort were severely physically injured requiring  
105 aeromedical evacuation to a UK hospital. The most common mechanism of injury is  
106 blast, so many of this cohort experienced multiple serious injuries including traumatic  
107 amputation. Uninjured personnel were frequency matched on age, service, rank,  
108 regiment, role, and deployment period. Data will be collected at 6 timepoints over 20  
109 years.

110

111 The aims of this study were to test the following hypotheses in the ADVANCE cohort:

112 (1) UL disability in the injured group is greater than the uninjured group; (2) UL

113 disability in people with lower limb loss is greater than the uninjured control group;

114 (3) UL disability in people with major UL loss is greater than in people with partial UL

115 loss; and (4) UL disability in people with major and partial UL loss is greater than the  
116 uninjured control group and remaining injured sub-groups.

117

## 118 **[H1]Materials & Methods**

### 119 [H2]Recruitment & study participants

120 Participants were recruited from Defence Statistics UK lists<sup>17</sup> provided by Defence  
121 Statistics UK. The injured and uninjured cohort were males aged >18 and <50 years.  
122 Exclusion criteria were a diagnosis of cardiac disease, diabetes, renal disease, or  
123 liver disease prior to injury or deployment of interest to ensure long-term outcomes  
124 could be attributed to combat injury instead of potential pre-existing conditions. The  
125 uninjured cohort did not sustain subsequent combat injury requiring aeromedical  
126 evacuation before or after matching. There were very few female UK military combat  
127 casualties such that sufficiently powered or translatable results could not be drawn.

128

129 Ethical approval was granted by the Ministry of Defence Research Ethics Committee  
130 in January 2013 (protocol no: 357/PPE/12).

131

### 132 [H2]Procedure

133 Participants gave informed consent and attended data collection at the Defence  
134 Medical Rehabilitation Centre Headley Court (March 2016 – August 2018) or  
135 Stanford Hall (August 2018 onwards) for comprehensive health tests and  
136 questionnaires.<sup>17</sup>

137

138 [H2]Questionnaire assessment

139 The Disability of the Arm, Shoulder, and Hand (DASH) questionnaire is an  
140 assessment of UL disability<sup>18,19</sup> consisting of a Disability/Symptom module followed  
141 by optional Work and Sport/Music modules, which will not be described here.

142 Responders rate their ability to perform 21 daily activities (eg, wash their hair, use a  
143 knife to cut food) in the last week on a scale from 1 (no difficulty) to 5 (unable),  
144 followed by 9 questions about the impact of any UL challenges.

145

146 The DASH questionnaire is valid when  $\geq 27$  questions have been answered and is  
147 calculated by dividing the sum of scores by the number of scores, subtracting 1 and  
148 multiplying by 25.<sup>20</sup> The final scale is from 0 (no disability) to 100 (greatest disability).

149 The minimum clinically important difference (MCID) is 10.8.<sup>21</sup>

150

151 Handedness was assessed retrospectively for people with major UL loss only.

152 Participants answered 3 questions from the Edinburgh Handedness Inventory<sup>22</sup>

153 about handedness prior to their injury; which hand they used for (i) writing, (ii)

154 throwing, and (iii) holding a knife to cut bread. Responses were 'always right' (2

155 points right), 'always left' (2 points left), 'usually right' (1 point right), 'usually left' (1

156 point left), or 'both equally' (1 point right and left). Results were calculated by dividing

157 scores for right minus left by the sum of right and left, then multiplying by 100 to

158 categorize participants as purely right ( $\geq 60$ ), mixed right ( $\leq 20$  and  $< 60$ ), neutral ( $<$

159  $20$  and  $\leq -20$ ), mixed left ( $< -20$  and  $\geq -60$ ), and purely left ( $< -60$ ).

160

161 [H2]Study Variables

162 Participants were grouped as injured or uninjured, as described above. The injured  
163 cohort were sub-divided into injured – Non-Amputee (Inj-NA), injured – Major Lower  
164 Limb Loss (Inj-LL), injured – Major UL Loss (Inj-ULmajor), and injured – Partial UL  
165 Loss (Inj-ULpartial). Participants with upper and lower limb loss in combination were  
166 grouped as Inj-ULmajor or Inj-ULpartial so that concurrent UL amputations did not  
167 affect conclusions about UL disability in people with lower limb loss.

168

169 The Abbreviated Injury Score (AIS) gives a score of 1 (minor) to 6 (maximal) for the  
170 extent of injury at a single body location.<sup>23</sup> The New Injury Severity Score (NISS) is  
171 the sum of the squares of the 3 highest AISs regardless of body region and has a  
172 maximum score of 75.<sup>24</sup> Socioeconomic status was classified using military rank at  
173 the time of deployment equating to a 3-tier National Statistics Socioeconomic  
174 Classification (NS-SEC); senior ranks are group 1 (eg, Commissioned Officer), mid-  
175 ranks are group 2 (eg, Senior Non-Commissioned Officer), and junior ranks are  
176 group 3 (eg, Junior Non-Commissioned Officer).<sup>25,26</sup> Race was classified as White,  
177 Black, Asian, and Other.

178

179 [H2]Statistical Analysis

180 Thirteen participants were excluded from the analysis, including 11 with invalid  
181 DASH scores (3 uninjured, 8 injured), 1 with a partial UL loss classified as a minor  
182 combat injury, and 1 with non-combat related lower limb loss, both of whom met the  
183 criteria for the uninjured group. Multiple imputation was not used because data loss  
184 was minimal and only in the outcome measure.

185



186 An *a priori* power analysis was conducted according to the study protocol.<sup>17</sup>  
187 Normality of continuous variables were assessed by visual inspection. The Mann  
188 Whitney-U test was used to compare non-parametric continuous variables between  
189 2 groups (eg, injured vs uninjured groups). The Kruskal-Wallis test with Bonferroni  
190 correction was used to compare non-parametric continuous variables between 3 or  
191 more groups with a pre-specified subgroup analysis comparing uninjured versus Inj-  
192 LL, Inj-ULmajor versus Inj-ULpartial, Inj-LL, Inj-NA and uninjured, and Inj-ULpartial  
193 versus Inj-LL, Inj-NA and uninjured groups based on the aforementioned  
194 hypotheses. Additional post hoc comparisons using a Bonferroni correction were  
195 carried out to test the remaining relationships (uninjured vs Inj-NA and Inj-NA vs Inj-  
196 LL). To model the association between exposure and DASH score we fitted a  
197 cumulative probability model (CPM) with a logit link (proportional odds model). The  
198 DASH score is a non-parametric semicontinuous outcome, and the CPM is a flexible  
199 model that can be used for skewed continuous and semicontinuous outcomes.<sup>27</sup>  
200 Age, race, and rank at sampling were included as *a priori* confounding variables and  
201 were controlled for in the model as they are known to affect DASH.<sup>28-30</sup> To relax the  
202 strong assumption of linearity, age was modelled using restricted cubic splines with 4  
203 knots. Odds Ratios and their 95% confident intervals (95% CIs) are reported and can  
204 be interpreted as the odds of having a higher score on DASH for the injured  
205 compared to the uninjured group.<sup>31</sup> For the subgroup model the Inj-ULmajor and Inj-  
206 ULpartial groups were combined due to small numbers and called Inj-UL. Model fit  
207 for ordinal models is often assessed by visually inspecting the Q-Q plot of the  
208 probability scale residuals (PSRs), however, since the outcome DASH is a mixture of  
209 discrete and continuous distributions, the Q-Q plot is not useful to assess the model  
210 fit due to the non-uniformly distributed PSRs. Alternatively, using PSRs in residual-

211 by-predictor plots can detect lack of fit and were visually inspected<sup>25</sup>; plots were  
212 similar for probit and logit links and the loglog link showed poorer fit, therefore a logit  
213 link was used.<sup>27</sup> Statistical tests were undertaken with an alpha level of 0.05, taking  
214 into account Bonferroni correction where post hoc tests were performed. Statistical  
215 analysis was carried out in Stata version 17 (StataCorp LLC; College Station, Texas,  
216 USA) and using the add-on packages PResiduals and rms in R studio version  
217 2023.03.1 (RStudio; Boston, MA, USA).

218

219 [H2]Role of the Funding Source: The funder played no role in the design, conduct, or  
220 reporting of this study.

221

## 222 **[H1]Results**

### 223 [H2]Participant demographics

224 Of the 1132 included participants, 571 (50.4%) were injured. Participants were aged  
225 34.1 (5.4) years at assessment, and the injured group were 8.3 (2.2) years  
226 postinjury. Mean height and weight were 178.9 (6.4) cm and 87.9 (12.3) kg for the  
227 uninjured group and 179.4 (7.1) cm and 90.5 (14.2) kg for the injured group with  
228 adjusted weight values for people with limb loss. Blast injury accounted for 69.2% of  
229 injuries overall, but more than 93% of injuries in people with limb loss.

230

231 contains comprehensive demographic information.

232

233 [H2]Demographics of people with major UL loss

234 Inj-ULmajor participants had shoulder disarticulation (n = 1; 6.2%), transhumeral  
235 amputation (n = 4; 25.0%) and transradial amputation (n = 11; 68.8%). Amputation  
236 combinations are provided in **Error! Reference source not found..**

237

238 Thirteen (81.3%) Inj-ULmajor participants reported using an UL prosthesis for  
239 activities of daily living (n = 8) and/or sport/exercise (n = 8). The participants who  
240 reported not using an UL prosthesis were people with bilateral lower limb and  
241 unilateral UL loss (n = 2) and a person with unilateral UL and ipsilateral-unilateral  
242 lower limb loss (n = 1), all of whom used lower limb prostheses.

243

244 Handedness data were available for 13 (81.3%) patients in the Inj-ULmajor group, of  
245 whom 11 had reported using a prosthesis. Twelve were pure right-handers and 1  
246 was neutral. For the 11 prosthesis users, the dominant UL was amputated for 7  
247 participants, the non-dominant UL was amputated for 3 participants, and 1  
248 participant was neutral.

249

250 UL injuries sustained by the Inj-NA and Inj-LL groups and their DASH scores are  
251 included in the Supplementary Materials.

252

253 [H2]DASH questionnaire

254 *[H3]Uninjured and Injured participants*

255 DASH scores were higher in the injured group compared to the uninjured group  
256 (3.33 vs 0.00;  $P < .001$ ) but did not meet the threshold for MCID ([H3]).

257

258 *[H3]Sub-group analysis*

259 DASH scores were significantly different across sub-groups ( $P < .001$ ) (*[H3]*, **Error!**  
260 **Reference source not found.**). Subgroup analyses showed strong evidence of a  
261 difference between the following subgroups: DASH was higher in both the Inj-  
262 ULmajor and Inj-ULpartial groups compared to the uninjured (15.42 vs 0.00,  $P < .001$   
263 and 12.92 vs 0.00,  $P < .001$ , respectively) and Inj-LL groups (15.42 vs 0.83  $P = .002$   
264 and 12.92 vs 0.83,  $P < .001$ , respectively). All differences met the threshold for  
265 MCID.

266

267 The small non-significant difference in DASH scores between Inj-LL and the  
268 uninjured group (0.83 vs 0.00;  $p = .06$ ) did not meet the threshold for MCID, and  
269 there was no evidence of a difference between Inj-ULmajor and Inj-ULpartial (15.42  
270 vs 12.92;  $P = 1.00$ ).

271

272 Median DASH score for Inj-ULpartial participants with an amputation involving their  
273 thumb ( $n = 8$ ) was 26.67 (range = 0.00 to 56.67) and 11.87 (range = 0.00 to 86.67)  
274 for those without an amputation involving their thumb ( $n = 34$ ) (see Suppl. Materials).

275

276 *[H3]Regression Analysis*

277 After adjustment for confounders, the odds of having a higher DASH score was 2.75  
278 (95% CI: 2.20-3.43) times higher for participants that were injured versus patients  
279 that were uninjured participants (**Error! Reference source not found.**). In the sub-  
280 group analysis and after adjustment for confounders, compared to patients that were  
281 uninjured, the odds of having a higher DASH score was 2.74 (95% CI = 2.15-3.50),  
282 1.70 (95% CI = 1.18-2.47), and 8.30 (95% CI = 5.07-13.60) times higher for Inj-NA

283 participants, Inj-LL participants, and Inj-UL participants, respectively (**Error!**  
284 **Reference source not found.**).

285

## 286 **[H1]Discussion**

287 As expected, people with major and partial UL loss had significantly more UL  
288 disability than injured non-amputees, people with lower limb loss and the uninjured  
289 group. People with partial UL loss reported similar levels of UL disability to people  
290 with major UL loss, suggesting UL disability is linked to full or partial loss of the hand  
291 (and possibly the thumb in particular) regardless of perceived injury severity. Whilst  
292 the difference between people with lower limb loss and the uninjured was very small  
293 and did not meet the MCID, adjusted analysis showed significantly increased odds  
294 (1.70) for a higher DASH score. The ADVANCE study provides a unique opportunity  
295 to monitor this cohort for the next 20 years.

296

297 Research describing UL disability in people with lower limb loss is sparse. A  
298 retrospective study of US military servicemen reported a two- and four-fold increase  
299 in risk of UL musculoskeletal injury in people with traumatic unilateral and bilateral  
300 lower limb loss 1 year post-amputation compared to a minor lower limb injury.<sup>13</sup> Our  
301 study suggests that this increased risk of UL musculoskeletal injury results in  
302 increased odds for more UL disability 8 years post lower limb amputation. It is  
303 important to note that people with lower limb loss in the ADVANCE cohort did  
304 receive UL-specific rehabilitation to mitigate future overuse musculoskeletal injuries  
305 and may have other important characteristics that effect their upper limb function,  
306 such as a non-amputation UL injury (see Suppl. Materials).

307

308 Wheelchair users rely on their ULs for weight-bearing and propulsion and commonly  
309 develop degenerative UL pathologies resulting in disability from about 12 years of  
310 wheelchair use.<sup>14</sup> People with lower limb loss are likely to intermittently use a  
311 wheelchair complementary to their prostheses.<sup>32,33</sup> We expect that the  
312 biomechanical demand on wheelchair user's ULs is higher than in prosthesis users  
313 due to the additional demands of propulsion and performing daily overhead  
314 activities.<sup>14</sup> The current increase in DASH score in small and not clinically significant  
315 but, as in wheelchair users, we expect that people with lower limb loss who use a  
316 prosthesis also deliver increased loads through their ULs and apply altered  
317 biomechanics through weight-bearing, transfer and mobility activities which could  
318 affect their UL disability over time.<sup>13-16</sup> Furthermore, we expect that people with  
319 bilateral lower limb loss will experience UL disability sooner and decline faster than  
320 people with unilateral lower limb loss due to more regular reliance on a wheelchair  
321 and more dependence on their ULs.

322  
323 People with major and partial UL loss had significantly more UL disability than the  
324 uninjured group, and the injured non-amputee and lower limb loss sub-groups. The  
325 combined group had increased odds of having a higher DASH score more than 8  
326 times greater than the uninjured group, although the confidence intervals were wide.  
327 Two recent studies on military personnel with UL loss with a similar follow-up time to  
328 this study both reported much higher mean DASH scores than this study, albeit in  
329 smaller populations.<sup>3,4</sup> We expect participants in both other studies to have had  
330 access to similar levels of rehabilitation as the ADVANCE cohort, as both contain  
331 military personnel (except 2 civilians in 1 paper) injured in recent conflicts. The  
332 DASH questionnaire has been shown to be sensitive to rehabilitation interventions.<sup>5</sup>

333 Sabharwal et al (2022) included only people with transhumeral amputation being  
334 assessed for osseointegration, so higher scores may be expected as a result of high  
335 amputation level and presumed lack of tolerance of standard prosthetics.<sup>3</sup> Pfister et  
336 al (2021) included 2 people with bilateral UL loss, (both with a transradial and partial  
337 upper limb amputation), which could incur more difficulties.<sup>4</sup> Our study included only  
338 people with unilateral UL loss and 5 participants with a transhumeral amputation  
339 whose DASH scores were generally higher than those with a transradial amputation,  
340 but not significantly so, and still much lower than elsewhere<sup>3</sup> (see Suppl. Material).  
341 Lower DASH scores could have been seen in our cohort due to handedness, though  
342 the dominant limb was more often amputated than the non-dominant limb in our  
343 cohort. Other factors such as social support and concomitant injuries (eg, nerve  
344 damage, burns, traumatic brain injury) may also affect DASH score. These studies  
345 both report comparable DASH scores as seen in civilians with major UL loss across  
346 a similar period.<sup>6</sup> Participants with UL loss in the ADVANCE cohort study have  
347 benefitted from high levels of rehabilitation and prosthetic services and report  
348 relatively low UL disability compared to similar military and civilians with UL loss.  
349  
350 Contrary to reports that major UL amputation has a negative effect on mental  
351 health,<sup>34</sup> adjunct mental health research on the ADVANCE cohort has shown a  
352 118% increased relative risk for reporting a large amount of post-traumatic growth  
353 (positive psychological change following trauma) resulting directly from a major  
354 amputation (upper or lower limb), and reported similar mental health outcomes as  
355 the uninjured group.<sup>35</sup> The major UL group in this study contains 12 (75%)  
356 participants who also have bilateral lower limb amputations. Perhaps high levels of  
357 post-traumatic growth in this cohort contributes to better self-reported outcomes.

358

359 UL amputation increases the risk<sup>11</sup> and prevalence<sup>36</sup> of subsequent UL  
360 musculoskeletal injury, reduces shoulder and neck mobility<sup>7</sup> and increases  
361 prevalence of neck and shoulder pain.<sup>37</sup> This is due to altered biomechanics of the  
362 ipsilateral limb,<sup>38</sup> compensatory movements of the contralateral limb and torso<sup>38,39</sup>  
363 and potential for overreliance on the contralateral limb.<sup>40</sup> This could result in an  
364 accelerated increase of disability long-term for people with major and partial UL loss,  
365 compared to the remaining ADVANCE cohort groups.

366

367 Fewer studies report long-term outcomes for people with partial UL loss compared to  
368 major UL loss.<sup>4,5,8-10</sup> A single military study included a sub-set of 2 people with partial  
369 UL loss with mean DASH scores of 45.2 at a mean of 6.5 years postinjury.<sup>4</sup> Short-  
370 term outcomes have been reported in civilian populations reporting DASH scores  
371 between 7 and 47 up to 2 years after injury, depending on the amputation level.<sup>5,8-10</sup>  
372 This study has demonstrated that people with partial and major UL loss have similar  
373 levels of UL disability, thus requiring similar quality and quantity of rehabilitation and  
374 access to advanced prosthetic technology regardless of perceived injury severity.  
375 Though numbers were small, participants with a partial hand amputation involving  
376 the thumb had the highest median DASH score of all people with UL loss (see Suppl.  
377 Materials). Lack of a thumb makes a pinch grip challenging, whereas major UL  
378 prosthesis users are likely to be able to achieve a pinch grip. Details of prosthesis  
379 use in people with partial UL loss was not captured, though anecdotal experience  
380 suggests uptake is low.

381



382 Whilst not an original aim, important results were found for participants who  
383 sustained a combat injury requiring medical evacuation to the UK that did not result  
384 in limb loss. Adjusted regression analysis showed significantly increased odds (2.74  
385 times) of having a higher DASH score than the uninjured group. Basic categorization  
386 of this group's UL injuries is included in the Supplementary Materials, but further  
387 research is required to better understand their injuries to improve preventative  
388 screening, rehabilitation, and education to limit disability progression.

389

## 390 [H2]Limitations

391 The main limitation of this study is the sole use of a patient-reported outcome  
392 measure and inclusion of people with comorbid lower limb loss in the Inj-ULmajor  
393 and Inj-ULpartial groups for statistical robustness means that potential influence of  
394 multiple limb loss on disability cannot be measured. The DASH questionnaire may  
395 not reflect technological advancements such as smartphones and speech-to-text  
396 innovations that are commonplace today and likely aid those with UL loss.

397

398 This young, highly rehabilitated military population with traumatic lower limb loss  
399 does not well reflect the general lower limb loss population, who may be older and  
400 have elective amputations for diabetic or vascular reasons.<sup>41</sup> However, this  
401 population sustained widespread injuries beyond their limb loss status, which could  
402 incur more UL disability than the general lower limb loss population. Detail regarding  
403 musculoskeletal injuries sustained in the period between amputation and data  
404 collection that could have provided a more complete clinical picture.

405

## 406 **[H1]Conclusion**

407 In conclusion, there is some evidence for more UL disability in people with lower limb  
408 loss compared to an uninjured comparison group 8 years postinjury, but it is not  
409 currently clinically significant. People with major and partial UL loss have more UL  
410 disability than other injured sub-groups and the uninjured control group, but this is  
411 low compared to other reported populations, perhaps due to high levels of prosthesis  
412 use, intense rehabilitation, and good mental health. The ADVANCE study will  
413 continue to follow this population for the next 20 years to monitor how UL disability  
414 changes over time, which could impact rehabilitation of people with lower and UL  
415 loss.

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## 427 **Ethics Approval**

428 Ethical approval was granted by the Ministry of Defence Research Ethics Committee  
429 in January 2013 (protocol no: 357/PPE/12).

430

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436 Lottery Community Fund; Blesma, The Limbless Veterans; and the UK Ministry of  
437 Defence.

438

439 **Disclosures and Presentations**

440 The authors completed the ICMJE Form for Disclosure of Potential Conflicts of  
441 Interest and reported no conflicts of interest.

442

443 A portion of this research was presented as an abstract at the International Society  
444 of Biomechanics Conference; August 2023; Fukuoka, Japan.

445

446 **Data statement**

447 Data are available upon reasonable request. Given the sensitive nature of the  
448 participants, the data have not been made widely available. Requests for data will be  
449 considered on a case-by-case basis and subject to UK Ministry of Defence  
450 clearance. The views expressed are those of the authors and not necessarily those  
451 of the NHS, the NIHR or the Department of Health.

452

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UNCORRECTED MANUSCRIPT

566 Table 1: Participant Demographic Information for all Studied Groups<sup>a</sup>

Variable	Uninjured (n = 561)	All Injured (n = 571)	Inj-NA (n = 404)	Inj-LL (n = 109)	Inj-ULmajor (n = 16)	Inj-ULpartial (n = 42)
Age at sampling (y)	26.5 (5.3)	25.8 (5.2)	25.8 (5.4)	25.6 (4.8)	25.1 (4.8)	25.4 (5.1)
Age at assessment (y)	34.3 (5.4)	34.0 (5.4)	34.4 (5.5)	33.2 (4.7)	32.6 (4.3)	32.8 (5.4)
Time between injury and assessment (y)	-	8.3 (2.2)	8.6 (2.2)	7.6 (2.0)	7.5 (1.3)	7.4 (1.8)
Cause of injury						
Blast	-	395 (69.2)	236 (58.4)	103 (94.5)	15 (93.8)	41 (97.6)
Gunshot	-	132 (24.9)	124 (34.1)	6 (5.5)	1 (6.3)	1 (2.4)
Other	-	4 (0.8)	4 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
Height (cm)	178.9 (6.4)	179.4 (7.1)	179.0 (6.7)	180.1 (8.3)	180.4 (5.3)	180.9 (8.2)
Mass <sup>b</sup> (kg)	87.9 (12.3)	90.5 (14.2)	89.7 (13.8)	94.7 (14.6)	91.1 (12.8)	87.6 (15.5)
BMI <sup>b</sup> (kg/m <sup>2</sup> )	27.5 (3.4)	28.1 (3.9)	28.0 (3.7)	29.3 (4.2)	28.4 (4.2)	27.0 (4.5)
Race (White)	490 (87.3)	509 (89.1)	358 (88.6)	99 (90.8)	15 (93.8)	37 (88.1)
NISS (median, 25 <sup>th</sup> -75 <sup>th</sup> percentile)	-	12 (5-22)	9 (4-17)	22 (13-27)	34 (27-41)	29 (17-36)
NS-SEC						
Senior rank	79 (14.1)	59 (10.3)	44 (10.9)	7 (6.4)	1 (6.3)	7 (16.7)
Mid-rank	146 (26.0)	105 (18.4)	82 (20.3)	15 (13.8)	2 (12.5)	6 (14.3)
Junior rank	336 (59.9)	407 (71.3)	278 (68.8)	87 (79.8)	13 (81.3)	29 (69.1)
Still serving in military	463 (82.5)	154 (27.0)	137 (33.9)	8 (7.3)	1 (6.3)	8 (19.1)

567 <sup>a</sup>Groups studied: Uninjured, all injured, Inj-NA (injured – non amputated), Inj-LL (injured –  
568 major lower limb loss), Inj-ULmajor (injured – major upper limb loss), and Inj-ULpartial  
569 (injured – partial upper limb loss). Data are presented as mean (SD), or number (%), unless  
570 otherwise stated. BMI = body mass index; NISS = New Injury Severity Score; NS-SEC =  
571 national statistics - socioeconomic classification.

572 <sup>b</sup>Adjusted for people with limb loss.

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577 Table 2: Details of Number of Participants With Isolated or Combination Upper and Lower  
578 Limb Loss in the Inj-LL, Inj-ULmajor, and Inj-ULpartial Groups<sup>a</sup>

Group	No Lower Limb Loss	Unilateral Lower Limb Loss	Bilateral Lower Limb Loss	Total
Inj-LL	-	70 (64.2%)	39 (35.8%)	109
Inj-ULmajor	3 (18.8%)	1 (6.3%)	12 (75.0%)	16
Inj-ULpartial	11 (26.2%)	6 (14.3%)	25 (59.5%)	42

579 <sup>a</sup>Inj-LL = injured – major lower limb loss; Inj-ULmajor = injured – major upper limb loss; Inj-  
580 ULpartial = injured – partial upper limb loss.

581

582 Table 3: DASH scores for uninjured, Inj-NA, Inj-LL, Inj-ULmajor and Inj-ULpartial Participants  
 583 8 Years Postinjury (or Matched Deployment of Interest)<sup>a</sup>

DASH	Uninjured	Inj-NA	Inj-LL	Inj-ULmajor	Inj-ULpartial
n	561	404	109	16	42
Median	0.00 <sup>bcd</sup>	3.33 <sup>bef</sup>	0.83 <sup>gh</sup>	15.42 <sup>ceg</sup>	12.92 <sup>dth</sup>
Range	0.00–68.33	0.00–70.00	0.00–55.83	0.00–44.17	0.00–86.67

584 <sup>a</sup> DASH = Disability of the Arm, Shoulder, and Hand questionnaire; Inj-LL = injured – major  
 585 lower limb loss; Inj-NA = injured – non amputated; Inj-ULmajor = injured – major upper limb  
 586 loss; Inj-ULpartial = injured – partial upper limb loss.

587 <sup>b-h</sup> Pairs of letters show where  $P < .05$  for all pre-planned and posthoc injured group sub-  
 588 analysis with Bonferroni correction.

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594 Table 4: Odds Ratio From Predictive Odds Ordinal Regression Analysis of DASH Scores for  
 595 Overall Injury Status (Model 1) and Injury Status Subgroups (Model 2)<sup>a</sup>

Predictor Variable	Unadjusted	Adjusted Model 1 <sup>b</sup>		Adjusted Model 2 <sup>c</sup>	
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	P	Odds Ratio (95% CI)	P
<u>Injury status</u>					
Uninjured	1 (ref)	1 (ref)		-	-
Injured	2.72 (2.18–3.39)	2.75 (2.20–3.43)	<.001		
<u>Injury status</u>					
Uninjured	1 (ref)			1 (ref)	
Inj-NA	2.75 (2.16–3.50)	-	-	2.74 (2.15–3.50)	
Inj-LL	1.65 (1.14–2.38)			1.70 (1.18–2.47)	<.001
Inj-UL	8.03 (4.91–13.14)			8.30 (5.07–13.60)	

596 <sup>a</sup>DASH = Disability of the Arm, Shoulder, and Hand questionnaire; Inj-LL = injured – major  
 597 lower limb loss; Inj-NA = injured – non amputated; Inj-UL = injured – upper limb loss; ref =  
 598 reference.

599 <sup>b</sup>Uninjured [n = 561], injured [n = 571].

600 <sup>c</sup>Uninjured [n = 561], Inj-NA [n = 404], Inj-LL [n = 109], and Inj-UL [n = 58].

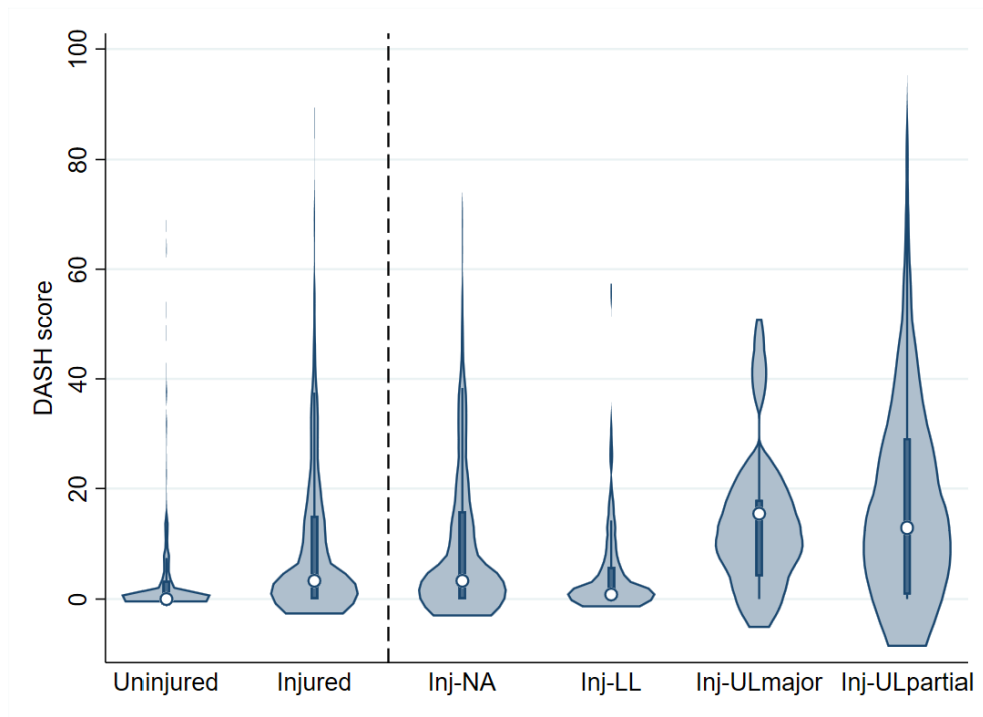
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604 **Figure Legend**



605

606 Figure. Violin plots for DASH scores for the uninjured and injured groups (left of the dashed  
607 line) and the injured sub-groups Inj-NA, Inj-LL, Inj-ULmajor and Inj-ULpartial (right of the  
608 dashed line) 8 years postinjury (or matched deployment of interest). DASH = Disability of the  
609 Arm, Shoulder, and Hand questionnaire; Inj-LL = injured – lower limb loss; Inj-NA = injured –  
610 non amputated; Inj-ULmajor = injured – major upper limb loss; Inj-ULpartial = injured –  
611 partial upper limb loss.

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CRIPPT