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Return to sport matters – longer-term quality of life after ACL reconstruction in people with knee difficulties

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29   surgery, patient reported outcomes, pain, depression

30

ABSTRACT

32   Many individuals experience long-term quality of life (QOL) impairment following anterior

33   cruciate ligament reconstruction (ACLR). Factors contributing to poor QOL and

34   psychological health >5 years after ACLR remain unclear. This study aimed to describe QOL

35   and psychological health outcomes in people with knee difficulties (pain, symptoms or

36   functional limitations) 5-20 years following ACLR and identify factors explaining variability

37   in these outcomes. Participants with knee difficulties 5-20 years following ACLR completed

38   a battery of validated patient-reported outcomes (including the Knee injury and Osteoarthritis

39   Outcome Score (KOOS), ACL-QOL and the Assessment of QOL (AQoL-8D) instrument).

40   Multivariable linear regression was used to identify factors explaining variability in

41   outcomes. 162 participants aged 38±9 (mean±SD) years completed questionnaires 9±4 (range

42   5-20) years following ACLR. 39% of participants returned to competitive sport, 28%

43   returned to a lower level and 32% did not return to sport after ACLR. Not returning to sport

44   after ACLR was associated with worse KOOS-QOL (β=.29, p=0.001 (mean±SD (55±20)),

45   ACL-QOL (β=.48, p<0.001; (57±21)), and AQoL-8D (β=.22, p=0.02 (0.80 ± 0.14)) scores.

46   Increased body mass index (56% were overweight/obese) was related to worse QOL and

47   more depressive symptoms. Subsequent knee surgery and contralateral ACLR were also

48   associated with poorer QOL outcomes in these individuals.

INTRODUCTION

Anterior cruciate ligament (ACL) rupture and subsequent reconstructive surgery can result in persistent knee pain, symptoms, physical activity restrictions and psychological issues (Ardern et al. 2012; Ardern et al. 2014; Lohmander et al. 2004; Wasserstein et al. 2015). Our recent systematic review revealed impaired knee-related quality of life (QOL) in people 5 to 20 years following ACL reconstruction (ACLR) (Filbay et al. 2014). However, few studies have focused on QOL as a primary outcome and consequently, research investigating factors related to longer-term QOL after ACLR is scarce. Furthermore, no studies to date have explored longer-term QOL or psychological health specifically in individuals with knee difficulties after ACLR (Filbay, Ackerman 2014). The impact of living with knee difficulties on the QOL of previously active ACL-reconstructed individuals is poorly understood. Considering ACLR is most prevalent in adolescents and young adults (Granan et al. 2008; Granan et al. 2009; Janssen et al. 2012; Joseph et al. 2013; Lind et al. 2009) persistent knee difficulties could impede on work responsibilities, sporting desires and parenting roles with great potential to impact upon QOL and psychological health.

A recent study found that all individuals undergoing ACLR expected to have normal or almost normal knee function within one year of ACLR, and 91% expected to return to their pre-injury level of sport (Feucht et al. 2014). Despite these high expectations, a large study of 1761 young ACL-reconstructed individuals found that over one in three reported knee difficulties six years following primary ACLR (Wasserstein, Huston 2015). Additionally, a recent meta-analysis found that as many as one in two ACL-reconstructed individuals do not return to non-elite sport (Ardern, Taylor 2014). A mismatch between an individual's desires or expectations and their perceived abilities may impact negatively on their QOL (Carr et al. 2001; Ruta et al. 1994). Investigating factors related to longer-term QOL and psychological health in people with knee difficulties following ACLR could assist in developing strategies to optimise longer-term outcomes after ACLR (Filbay 2015; Filbay, Ackerman 2014). The purpose of this study was to (i) describe QOL and psychological health outcomes and; (ii) identify factors related to variability in QOL and psychological health outcomes, in people with knee difficulties (pain, symptoms or functional limitations) 5 to 20 years following ACLR.

METHODS

Study design

A cross-sectional study design was used. Ethical approval for this study was obtained from
The University of Queensland Medical Research Ethics Committee (approval number
2012001240).

Setting and participant recruitment

All individuals who had undergone a hamstring or patellar tendon autograft ACLR 5 to 20
years previously were identified from the surgical records of four orthopaedic surgeons
(based in Melbourne, Brisbane, Toowomba and Nambour, Australia) and invited by letter to
participate in the study. In total 2391 letters of invitation were sent to archived postal
addresses of potentially eligible patients. Since only eligible individuals were asked to
respond to the invitation and many archived postal addresses were outdated, the exact number
of letters received remains unknown. Participants were also recruited from the general
community through advertisements in public places and online. People having revision or
contralateral ACLR more than 5 years ago, concomitant or subsequent surgery (meniscal,
cartilage or other ligamentous repair) were eligible for the study. Individuals were considered
ineligible if they: (i) reported a comorbidity likely to impact QOL (e.g. chronic back pain,
cancer, acute injury); (ii) were aged under 18 years or over 55 years at the time of
recruitment; (iii) underwent an ACLR (primary or revision) within the past five years; (iv)
were not fluent in written English; (v) were asymptomatic according to predefined Knee
Injury and Osteoarthritis Score (KOOS) cut-off criteria (as outlined below).

Symptomatic cut-off criteria

To ensure all participants experienced a degree of knee difficulties (knee pain, symptoms or
functional limitations) we modified previously published KOOS criteria that were devised to
identify individuals symptomatic enough to seek medical care (Englund et al. 2003). The
published criteria required reporting less than optimal scores on at least 50% of questions for
the KOOS-QOL and two of the additional four KOOS subscales (corresponding to cut-off
values of ≤86.1 (Pain), ≤85.7 (Symptoms), ≤86.8 (ADL), ≤85.0 (Sport/Rec), and

111 ≤87.5 (QOL)). We modified these criteria to include individuals reporting impairment in any

112 two KOOS subscales. The rationale for this modification was to allow for the inclusion of

113 individuals reporting high KOOS-QOL scores despite knee difficulties, since a primary aim

114 of this study was to explore QOL variability in people with knee difficulties after ACLR.

115

Defining knee difficulties

117 For the purpose of this study, knee difficulties were defined as self-reported knee pain,

118 symptoms or functional limitations determined by reporting less than optimal scores on at

119 least 50% of questions on the KOOS Pain, KOOS Symptoms, KOOS Function in daily living

120 (ADL) or KOOS Sport and recreation (Sport/Rec) subscale.

121

Defining quality of life

123 Due to the multiplicity of QOL definitions, it is recommended that researchers be as clear as

124 possible in defining the concept of QOL to enable interpretation and comparisons between

125 studies (Post 2014). Quality of life has been defined by the World Health Organisation as 'an

126 individual's perceptions of their position in life taken in the context of the culture and value

127 systems where they live and in relation to their goals, expectations, standards and concerns'

128 (The World Health Organization Group 1995). One aspect of QOL is the concept of health-

129 related QOL (Barcaccia et al. 2013), which refers to the discordance between an individual's

130 health expectations or desires, and their current health experience (Carr, Gibson 2001). For

131 this research, we have used the term 'knee-related QOL' to refer to the degree that an

132 individual's QOL is impacted by knee-related factors.

133

Procedure

135 All participants completed the KOOS, the Assessment of Quality of Life 8D Utility

136 Instrument (AQoL), the Anterior Cruciate Ligament Quality of Life questionnaire (ACL-

137 QOL), the Workplace Activity Limitations Scale (WALS), the Hospital Anxiety and

138 Depression Scale (HADS) and a questionnaire collecting participant characteristics and

139 additional information (Table 1). Participants elected to complete questionnaires either online

140 or in paper form. Online questionnaires were completed by participants following an email

141 link to a custom built online questionnaire system (Mark-Rite PROMS, University of

142   Queensland, Brisbane). All participants provided informed consent prior to commencing

143   questionnaires. Paper versions of the questionnaire were sent to participants if requested, with

144   a postage paid reply envelope. All participants received a follow-up reminder if the

145   questionnaires were not completed within eight weeks. Questionnaire responses were

146   screened for age, comorbidities, time since surgery and application of the KOOS

147   symptomatic cut-off criteria to confirm participant eligibility.

148

149   **Patient reported outcomes**

150   *Participant demographics and characteristics*

151   Information collected included age, body mass index (BMI), work status, time since most

152   recent ACLR, time from injury to ACLR, mechanism of injury, postoperative symptoms,

153   subsequent surgery (at least one additional knee surgery to an ACL-reconstructed knee (not

154   including revision ACLR or concomitant surgery performed at the time of primary or

155   revision ACLR)), current treatment and OA knowledge. Where there was potential for recall

156   bias, participants were given an 'unsure' option. To evaluate return to sport, participants

157   responded to the following question 'please tick the most appropriate statement regarding

158   your level of sport participation after injuring your ACL' by selecting one of the following

159   three options: 'I returned to competitive sport at the same or higher level than before ACL

160   injury', 'I returned to competitive sport at a lower level than before ACL injury' or 'I did not

161   return to competitive sport after my ACL reconstruction.' Individuals who did not return to

162   the same or higher level of sport were then asked if this was because of their knee ('If you *did*

163   *not* return to competitive sport, or returned to competitive sport at a *lower level* than prior to

164   your ACL reconstruction, was this because of your knee?'). Participants were asked what

165   sports they were participating in at the time of ACL injury, if they were not participating in a

166   competitive sport when they ruptured their ACL, a 'not applicable' response was given to the

167   return to sport question. Participants were also requested to nominate which of the following

168   activities they would prefer to participate in, in the absence of knee pain or impairment:

169   'family duties', 'social activities', 'work-related activities', 'sport' or 'exercise.'

170

171   *Knee-related QOL*

172   Three measures were selected to provide a comprehensive overview of knee-related QOL; the

173   KOOS (the most commonly used measure of knee-related QOL more than five years

174   following ACLR (Filbay, Ackerman 2014; Filbay et al. 2015)) the ACL-QOL (contains items

175   of high importance to ACL-reconstructed individuals compared to other knee-related

176   measures (Tanner et al. 2007)) and a custom QOL question (allows the individual to provide

177   an overall assessment of the impact of their knee on their QOL considering all important and

178   relevant influences).

179

180   The KOOS is a patient reported questionnaire developed to assess an individual's opinion

181   about their knee and associated problems (Roos 2003), it contains five subscales: Pain,

182   Symptoms, ADL, Sport/Rec and QOL. The KOOS-QOL subscale contains four questions

183   addressing knee awareness, knee-related lifestyle modification, knee confidence and knee-

184   related difficulties. The KOOS is valid and reliable for use in ACLR and knee OA

185   populations (Collins et al. 2011; Roos & Lohmander 2003; Salavati et al. 2011). The QOL

186   and Sport/Rec subscales are more valid than other KOOS subscales for use within one year of

187   ACLR (Comins et al. 2008). An individual score for each subscale can be calculated where 0

188   represents no impairment and 100 represents extreme impairment.

189

190   The ACL-QOL is the only patient administered QOL measure specific to an ACL population

191   and is valid, reliable and responsive to change (Mohtadi 1998). The ACL-QOL contains 32-

192   items and five domains (Symptoms/Physical, Work-Related, Sport/Rec, Lifestyle,

193   Social/Emotional). Each ACL-QOL item is measured on a visual analogue scale from 0

194   (severe impairment) to 100 (no impairment). Domain scores are averages of all items in each

195   domain and an overall ACL-QOL score represents the average of all domains.

196

197   We also included a custom 'knee impact question' that allowed individuals to evaluate the

198   impact of their knee on their QOL in line with their expectations, priorities and values.

199   Participants responded to the question: 'do you believe that your knee is impacting on your

200   quality of life?' with one of four responses; 'not at all', 'slightly', 'moderately' and

201   'significantly'.

202

203 *Health-related QOL*

204 The AQoL-8D is a multi-attribute generic (non-disease-specific) measure of health-related

205 QOL and comprises eight dimensions (Independent Living, Happiness, Mental Health,

206 Coping, Relationships, Self-worth, Pain, Senses). The AQoL-8D has demonstrated strong

207 psychometric properties including content validity (Hawthorne & Osborne 2005; Richardson

208 et al. 2014), construct validity and discriminative validity in OA (Whitfield et al. 2006). An

209 AQoL utility value is calculated where 1.00 and 0.00 represent full health and worst possible

210 health, respectively. Summary scores can also be calculated, the 'Physical super-dimension'

211 (covering independent living, pain and senses) and the 'Mental super-dimension' covering

212 mental health, happiness, coping, relationships and self-worth. The minimal important

213 difference in AQoL scores is considered to be 0.06 utility points (Hawthorne & Osborne

214 2005).

215

216 *Psychological health*

217 The HADS is comprised of 14 questions, 7 that evaluate depression, and 7 that evaluate

218 anxiety. Higher scores indicate greater impairment, with a maximum anxiety or depression

219 score of 21. Scores of 0 to 7 indicate no impairment, 8 to 10 a borderline case, and 11 or

220 greater suggest the responder has depression or anxiety (Snaith 2003). HADS has

221 demonstrated strong internal consistency, concurrent validity, sensitivity and specificity in

222 assessing the symptom severity and presence of depression and anxiety disorders in a range

223 of disease-specific patient groups and in the general population (Bjelland et al. 2002).

224

225 *Work Limitations*

226 The WALS is the preferred instrument for measuring productivity in workers with arthritis

227 and is highly responsive to change in work ability over time (Tang et al. 2013). The WALS is

228 comprised of 12 questions, each question addresses activity specific work-related difficulties

229 and responses range from 'no difficulty' to 'not able to do' and higher scores indicate greater

230 impairment.

231

Data and statistical analysis

All variables were normally distributed and independent t-tests were conducted to examine differences in demographic characteristics between participants and ineligible asymptomatic individuals. For the multivariable analyses, to avoid unnecessary adjustment of variables and potential over-adjustment bias (Schisterman et al. 2009) direct acyclic diagrams (featuring hypothesized causal relationships between variables) were used to identify covariates for inclusion in regression analysis (Shrier & Platt 2008). In line with the study aims, we focused on identifying variables that may be assessed at any time after ACLR (such as return to sport and surgical delay) rather than patient reported outcomes measured at the same time as QOL. The reasoning for this was that strong associations between patient reported outcomes assessed concurrently are expected and of limited clinical importance due to overlapping constructs in measures. Justification and selection of potential explanatory variables for use in causal diagrams were based upon current literature findings and clinical reasoning, whereby all variables with a potential to impact on longer-term QOL or psychological health were included. This resulted in the inclusion of theoretically meaningful variables in the absence of statistical significance exploration (Shmueli 2010). Any variables that were not a direct or indirect cause of an exposure, outcome or covariate were excluded from further analyses (Shrier & Platt 2008). This process resulted in the identification of six explanatory variables (years since ACLR, time from ACL injury to ACLR, revision ACLR, contralateral ACLR, return-to-sport) and three demographic variables (BMI, age, sex) with potential to impact upon longer-term QOL outcomes. These variables were assessed for collinearity, multicollinearity, univariate and multivariate outliers. Additionally, the normality, homoscedasticity and linearity of residuals were assessed.

To estimate the proportion of variance in QOL and psychological health scores that were accounted for by the explanatory variables, standard linear multiple regression analysis was performed. A sample size of 162 is greater than the minimal sample size recommended to assume a medium sized effect with 10 explanatory variables in multivariable analysis (Tabachnick & Fidell 2007). We present the unstandardized (B (95% CI)) and standardised coefficients (Beta (β)) for the adjusted analysis (adjusted for age and sex). Our recent systematic review found that the KOOS-Pain subscale was closely related to KOOS-QOL scores 5 to 20 years after ACLR (Filbay, Ackerman 2014). Therefore, we performed a

264   sensitivity analysis adjusting for KOOS-Pain scores (in addition to age and sex). The results

265   of this sensitivity analysis are reported descriptively and presented in Appendix 1.

266

267   # RESULTS

268   **Recruitment**

269   In total, 212 individuals consented to participate and completed questionnaires (Figure 1). Of

270   these, 50 were excluded due to co-morbidities, not completing the KOOS or not meeting the

271   predefined KOOS cut-off criteria (Figure 1). KOOS subscale scores are reported in Figure 2.

272   Asymptomatic individuals did not differ in age, follow-up duration, BMI, or gender from

273   eligible participants ($p > 0.16$ for all analyses). Data were available for analysis from 162

274   eligible participants, of which 83% were recruited from the records of four orthopaedic knee

275   surgeons and 17% recruited through community advertisements.

276

277   **Insert Figure 1 here.**

278

279   **Participant characteristics**

280   Questionnaires were completed on average 9 ± 4 years (range 5 to 20 years) following

281   participants' most recent ACLR. The mean age of participants at the time of questionnaire

282   completion was 38 ± 9 (range 20 to 55) years and 54% were male. The majority of

283   participants were in paid employment (91%) and over half had children (56%). Twenty-three

284   participants (14%) had a revision ACLR more than 5 years ago, and 18 individuals (11%)

285   reported having a previous ACLR on the contralateral knee; these individuals answered

286   questions regarding their most symptomatic knee. One in two participants (48%) had

287   received at least one additional knee surgery (not including revision ACLR or concomitant

288   surgery performed at the time of primary or revision ACLR). Collectively, participants

289   reported playing 26 different sports at the time of ACL rupture, the most common were

290   netball (20%), rugby (11%), Australian rules football (11%), soccer/futsal (16%) basketball

291   (9%), snow/water skiing (8%), and touch football (6%). Only one participant was not taking

292   part in competitive sport at the time of ACL injury. Sixty-three (39%) participants returned to

293   competitive sport after ACLR, 46 (28%) returned at a lower level of competition and 52

294   (32%) did not return to competitive sport following ACLR. One in two participants

295 nominated sport as the activity they would prefer to participate in, in the absence of knee pain

296 or impairment (n=80. 49%). Full participant characteristics are provided in Table 1.

297

298 **Insert Table 1. here.**

299

300 **Patient reported outcomes**

301 *Knee-related QOL*

302 Participants reported a mean KOOS-QOL score of 55 ± 20, indicating impaired knee-related

303 QOL (Figure 2). A mean ACL-QOL score of 57 ± 21 was reported, further indicative of

304 impaired knee-related QOL; the domain with greatest impairment was sport and recreational

305 function (41 ± 28) and the least impaired domain was work-related concerns (78 ± 21)

306 (Figure 3). The knee impact question showed that 17% of participants did not perceive their

307 knee as having an impact on their current QOL, 45% reported a slight impact, 28% a

308 moderate impact and 10% reported that their knee significantly impacted their QOL.

309

310 **Insert Figure 2. here.**

311

312 **Insert Figure 3. here.**

313

314 *Health-related QOL*

315 Participants reported an average AQoL-8D utility score of 0.80 ± 0.14, super dimension

316 mental score of 0.50 ± 0.19 and super dimension physical score of 0.76 ± 0.14 (Figure 4).

317

318 **Insert Figure 4. here.**

319

320 *Psychological health*

321 Participants reported an average HADS anxiety score of 5.5 ± 3.7 and HADS depression

322 score of 2.7 ± 2.6. According to published criteria (Snaith 2003), 93% of participants did not

323 have scores indicative of depression, 10 people (6%) had scores indicating borderline

324 depression, and 2 people (1%) had scores corresponding to symptoms of clinical depression.

325   For items pertaining to anxiety, 73% of participants reported scores reflecting no anxiety,

326   19% reported scores corresponding to borderline anxiety and 4 people (2%) could be

327   considered likely to have anxiety.

328

329   **Explaining variability in quality of life and psychological health outcomes**

330   *Knee-related QOL*

331   Multivariable analysis showed that non-return to sport (compared with returning to sport at

332   the same or higher level), higher BMI and subsequent surgery were independently associated

333   with poorer KOOS-QOL scores. Together, all variables accounted for an estimated 24% of

334   the variability in KOOS-QOL scores (Table 2). Return to sport explained the greatest

335   proportion of variance in KOOS-QOL scores (β =.29, p=0.001) where returning to sport at

336   the same or higher level predicted an estimated 12 points higher KOOS-QOL score,

337   compared to not returning to sport after ACLR. All three variables remained significant

338   explanatory factors after adjusting for KOOS-Pain scores, even though pain explained a large

339   amount of variance in KOOS-QOL scores (Appendix 1).

340

341   Non-return to sport (compared with return to sport at any level), higher BMI, subsequent

342   knee surgery and contralateral ACLR were independently associated with worse ACL-QOL

343   scores. Specifically, all variables in combination accounted for 36% of the variability in

344   ACL-QOL scores (Table 2). Return to sport (at the same or higher level) explained the

345   greatest proportion of variance in ACL-QOL scores (β=.48, p<0.001), where returning to

346   sport predicted an estimated 21 point higher ACL-QOL score, compared to those who did not

347   return to sport. After adjustment for KOOS-Pain scores, BMI no longer explained ACL-QOL

348   scores (β =-0.11, p=0.06), and waiting greater than six months from injury to surgery was

349   found to be significantly associated with worse ACL-QOL scores (β = -.13, p=0.03). Return

350   to sport, subsequent and contralateral injury remained significant explanatory factors after

351   adjustment for KOOS-Pain (Appendix 1). Time since ACLR, revision surgery, age and sex

352   were not significantly associated with knee-related QOL outcomes.

353

354   **Insert Table 2. here.**

355

356 *Health-related quality of life*

357 All explanatory variables in combination explained approximately 19% of the variability in

358 AQoL-8D scores. Return to sport at the same or higher level (compared to not returning to

359 sport at all) and BMI significantly explained the greatest proportion of variance in health-

360 related QOL scores, where returning to sport predicted an estimated .06 higher AQoL-8D

361 scores compared to those who did not return to sport (Table 3). These relationships remained

362 after adjustment for KOOS-Pain (Appendix 1).

363

364 **Insert Table 3. here.**

365

366 *Psychological health*

367 In combination, all variables accounted for 18% of variability in HADS depression scores;

368 specifically, male sex and greater BMI were associated with more depressive symptoms,

369 before and after adjustment for KOOS-Pain scores. There was a trend for return to sport at

370 the same or higher level to be associated with less depressive symptoms (p=0.058). In

371 contrast, none of the included variables significantly explained the variability in HADS

372 anxiety scores (Table 4). KOOS-Pain did not explain a significant proportion of variance in

373 HADS anxiety or depression scores in a multivariable model (Appendix 1).

374

375 **Insert Table 4. here.**

376

377 # DISCUSSION

378 Returning to sport at the same or higher level was related to better knee-related and general

379 health-related QOL in people with knee difficulties 5 to 20 years after ACLR. This

380 relationship remained after adjusting for KOOS-Pain scores despite a clear relationship

381 between knee pain and QOL. Subsequent surgery, increased BMI and contralateral ACLR

382 were also associated with poorer scores on one or more QOL measures. Higher BMI and

383 male sex were associated with more depressive symptoms. Age, gender, time since surgery

384 and revision ACLR were not associated with QOL or psychological health outcomes in

385 individuals with knee difficulties after ACLR.

386

387   KOOS-QOL scores in individuals with knee difficulties more than five years following

388   ACLR were impaired compared with Swedish population norms aged 18 to 54 years

389   (Paradowski et al. 2006), amateur soccer players with minor (14%), severe (23%), or no

390   (63%) history of knee injury (Frobell et al. 2008), and U.S military recruits with no history of

391   knee ligament injury (Cameron et al. 2013). A mean AQOL-8D utility score of 0.80 ± 0.14

392   reported by participants in this study is similar to the mean score reported by Australians who

393   rated their health status as 'good' (mean 0.81 ± 0.19) as opposed to 'excellent' (0.91 ± 0.14),

394   'very good' (0.88 ± 0.14), 'fair' (0.68 ± 0.23), or 'poor' (0.42 ± 0.30) in an earlier population-

395   based study (Hawthorne & Osborne 2005). Unfortunately no physically active reference

396   groups, who are likely to report higher health-related QOL than less active counterparts

397   (Huffman et al. 2008) are available for comparison.

398

399   This is the first study to evaluate the relationship between return to sport and longer-term

400   QOL after ACLR. We did not expect to find such consistent relationships between return to

401   sport and QOL outcomes 5 to 20 years after ACLR in people with knee difficulties. Although

402   return to sport was associated with better QOL, the longer-term impact of returning to sport

403   with knee difficulties on future joint health should be considered (Culvenor & Crossley

404   2015). The high rate of participants reporting a preference to take part in sport in the absence

405   of knee difficulties, over and above other activities including family or occupational duties,

406   suggests that sport participation remains a priority for many individuals. Despite this, one in

407   three participants did not return to any level of competitive sport after ACLR and 79% of

408   individuals reported their knee as the reason for not returning to pre-injury sport. This

409   potential mismatch between sporting desires and outcomes in people with knee difficulties

410   may have contributed to the observed impairment in QOL. A study exploring pre-operative

411   expectations of ACLR found that 91% of participants expected to return to sport one year

412   following surgery with no or slight restrictions (Feucht, Cotic 2014). This contrasts with the

413   actual return to sport rates in our cohort and findings from a recent literature review (Ardern,

414   Taylor 2014). Notably, health-related QOL has been described as 'the gap between our

415   expectations of health and our experience of it' (Carr, Gibson 2001) and discordance between

416   surgical expectations and actual outcomes may have contributed to the identified impairments

417   in QOL. Patients may benefit from pre-operative education to promote realistic expectations

418   prior to ACLR.

419

420   Average HADS depression scores for this sample were less impaired than published

421   population norms (Breeman et al. 2015; Mutrie & Hannah 2007). However, lower rates of

422   depressive symptoms have been associated with increased rates of moderate-to-vigorous

423   physical activity and sports participation (Brunet et al. 2013; Mutrie & Hannah 2007; Pinto

424   Pereira et al. 2014; Sabiston et al. 2013) and ACL-reconstructed individuals may have had

425   less depressive symptoms than the general population prior to injury. We found that people

426   with knee difficulties who returned to the same or higher level of sport after ACLR tended to

427   report less depressive symptoms compared with those who did not return to sport (B (95%

428   CI) -0.94 (-1.9 to 0.0), p=0.06). Furthermore, a large study of similarly aged participants

429   identified physical activity as a key factor contributing to the observed relationship between

430   obesity and increased rates of depression (de Wit et al. 2010). It is possible that for some

431   individuals, ceasing sport resulted in reduced levels of moderate-to-vigorous physical

432   activity, which could be associated with weight gain, depressive symptoms and reduced

433   QOL. Further research is needed to explore these relationships as we did not collect

434   longitudinal data on physical activity levels, dietary intake or pre-injury BMI. Of concern is

435   that over half the study participants were overweight or obese at the time of questionnaire

436   completion and higher BMI was associated with worse QOL. Management strategies aimed

437   at improving QOL following ACLR could include weight maintenance strategies, addressing

438   barriers to returning to sport or facilitating a transition to a healthy lifestyle incorporating

439   regular moderate-to-vigorous physical activity when ceasing sport participation.

440

441   A key strength of this study was the use of patient-reported measures and the inclusion of

442   knee-specific, ACL-specific and generic (non-disease-specific) health-related QOL measures

443   that provided complementary information and enabled a comprehensive picture of QOL to be

444   generated. We also included a custom QOL question that enabled each individual to evaluate

445   the impact of their knee on their QOL in the context of their personal goals, priorities and

446   values. To minimise selection bias, we included recruitment of participants from community

447   advertisements and these participants did not differ in age, gender, BMI or follow-up duration

448   to participants recruited through orthopaedic surgeons' records. Nevertheless, as most

449   participants were recruited through orthopaedic surgeons, a degree of selection bias may

450   exist. These surgeons worked in the private health care system and consequently, these

451   findings may not be generalisable to people undergoing ACLR in public hospital settings.

452   Furthermore, the results of this study are not generalisable to all ACL-reconstructed

453   individuals, as we only included individuals reporting knee pain, symptoms or activity

454   limitations. We also acknowledge the potential for recall bias relating to questions that

455   required participants to answer retrospectively (for example, mechanism of injury, time from

456   injury to surgery). We sought to minimise the likelihood of recall error by including an

457   'unsure' response option for these items. Due to the cross-sectional study design, we were

458   unable to make any causal inferences and due to the nature of recruitment, we could not

459   collect detailed data for all participants on surgical techniques or concomitant surgeries.

460   However, all participants recruited through orthopaedic surgeons underwent a hamstring or

461   patellar tendon autograph ACLR, and no differences in QOL have been reported between

462   these techniques 5 to 20 years following ACLR (Filbay, Ackerman 2014). We also

463   acknowledge that KOOS-QOL and ACL-QOL scores may be negatively biased by sport-

464   related lifestyle modifications or difficulty participating in sport. Due to the nature of

465   questions in these measures, sport-related limitations would result in reduced QOL scores

466   irrespective of the importance that each individual places on sport participation.

467

468   **PERSPECTIVES**

469   Poorer longer-term QOL outcomes were related to not returning to sport, higher BMI,

470   contralateral ACLR and subsequent knee surgery in people with knee difficulties 5-20 years

471   after ACLR, and return to sport explained the greatest variability in QOL. Individuals with

472   knee difficulties who do not return to sport may benefit from targeted strategies to optimise

473   longer-term QOL following ACLR.

474

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586

587 **TABLES**

588

589 **TABLE 1**. Participant characteristics (n=162)

Age at follow-up (years)	38 ± 9

Gender (% female)	n = 75 (46%)
Follow-up duration (years)	9 ± 4
Body mass index	27 ± 6
normal range	n = 71(44%)
Overweight	n = 55 (34%)
Obese	n = 36 (22%)
Percentage with children	n = 90 (56%)
Time from injury to surgery	
< 6 months	n = 117 (72%)
> 6 months	n = 43 (27%)
Unsure	n = 2 (1%)
Revision ACLR	n = 23 (14%)
Left ACLR	n = 68 (42%)
Right ACLR	n = 76 (47%)
Bilateral ACLR	n = 18 (11%)
Subsequent surgery*	n = 77 (48%)
Contact injury	n = 64 (41%)
Return to sport rates	
same or higher level than before ACL injury	n = 63 (39%)
lower level than before ACL injury	n = 46 (28%)
did not return to sport after ACLR	n = 52 (32%)
not applicable	n = 1 (1%)
Return to sport at lower level or not at all due to knee	n = 89 (79%)
Currently receives knee treatment	n = 26 (16%)
Pain/impairment free participation preference (%)	
family duties	n = 22 (14%)
social activities	n = 7 (4%)
Work	n = 3 (2%)
Sport	n = 80 (49%)
Exercise	n = 50 (31%)
Current work status (%)	
full-time	n = 118 (73%)
part-time/casual	n = 29 (18%)

Student		n = 10 (6%)				
stay at home parent/carer		n = 3 (2%)				
Unemployed		n = 2 (1%)				
Work Activity Limitation Scale score		3.9 ± 2.8				

590 ACLR: anterior cruciate ligament reconstruction; Revision ACLR: percent having one or

591 more revision ACLR; Bilateral ACLR: percent having at least one ACLR on each knee; *

592 Subsequent surgery: percent having at least one additional knee surgery to an ACL-

593 reconstructed knee (excluding revision ACLR or concomitant surgery performed at the time

594 of primary or revision ACLR); All results are reported as mean ± standard deviation, or

595 percentage and corresponding number of participants reporting each response.**TABLE 2**.

596 Knee-related quality of life linear regression multivariable analyses

597

Explanatory variables:	KOOS-QOL (n=158)			ACL-QOL (n=157)		
	B (95% CI)	Beta (β)	p value	B (95% CI)	Beta (β)	p value
Years since ACLR	-0.3 (-1.1 to 0.6)	-0.05	0.54	0.0 (-0.8 to 0.9)	0.00	1.00
Injury to ACLR	-4.4 (-11.1 to 2.2)	-0.10	0.19	-6.2 (-12.7 to 0.3)	-0.13	0.06
Revision ACLR	-4.7 (-13.3 to 3.9)	-0.08	0.28	-3.0 (-11.3 to 5.3)	-0.05	0.48
Contralateral ACLR	-7.4 (-16.3 to 1.6)	-0.12	0.11	**-16.3 (-24.9 to -7.8)**	**-0.25**	**<0.001**
Subsequent surgery	**-7.6 (-13.8 to -1.5)**	**-0.19**	**0.02**	**-6.8 (-12.7 to -0.8)**	**-0.16**	**0.03**
RTS same/higher level*	**12.0 (4.8 to 19.1)**	**0.29**	**0.001**	**20.9 (14.0 to 27.8)**	**0.48**	**<0.001**
RTS lower level*	0.3 (-7.3 to 7.8)	0.01	0.94	**7.8 (0.5 to 15.2)**	**0.17**	**0.04**
BMI	**-0.9 (-1.4 to -0.3)**	**-0.24**	**0.002**	**-0.8 (-1.3 to -0.3)**	**-0.21**	**0.003**
Age	0.1 (-0.2 to 0.5)	0.06	0.45	0.1 (-0.2 to 0.5)	0.06	0.45
Sex	4.7 (-1.1 to 10.5)	0.12	0.11	3.4 (-2.3 to 9.0)	0.08	0.24
R^2 (p value)	.24 (p<0.001)			.36 (p<0.001)		

598 B (95% CI): unstandardised coefficient (95% confidence interval); Beta (β): standardised

599 coefficient; Subsequent surgery: at least one additional knee surgery to an ACL-reconstructed

600 knee (excluding revision ACLR or concomitant surgery performed at the time of primary or

601 revision ACLR); RTS: return to sport; BMI: body mass index; ACLR: anterior cruciate

602 ligament reconstruction; KOOS: Knee Injury and Osteoarthritis Outcome score; ACLQOL:

603 Anterior Cruciate Ligament Quality of Life questionnaire; * Did not return to sport =

604 reference category; Sample size does not equal 162 for these analyses due to n=1 not

605 participating in sport at the time of injury, n=2 selected 'unsure' options, and n=1 did not

606 complete the ACL-QOL; injury to ACLR was dichotomised as >6 months (yes/no); All

607 dichotomous variables were coded as no=0, yes=1; Sex was coded as male=0, female=1;

608 Years since surgery, BMI and age were continuous variables.**TABLE 3.** Health-related

609 quality of life linear regression multivariable analyses

610

Explanatory variables:	AQOL-8D (n=157)		
	B (95% CI)	Beta (β)	p value
Years since ACLR	0.00 (-0.0 to 0.0)	-0.05	0.55
Injury to ACLR	-0.03 (-0.1 to 0.0)	-0.09	0.25
Revision ACLR	0.05 (0.0 to 0.1)	0.12	0.13
Contralateral ACLR	0.00 (-0.1 to 0.1)	0.01	0.90
Subsequent surgery	-0.01 (-0.1 to 0.0)	-0.05	0.54
RTS same/higher level*	**0.06 (0.0 to 0.1)**	**0.22**	**0.02**
RTS lower level*	0.00 (-0.1 to 0.1)	0.00	0.96
BMI	**-0.01 (0.0 to 0.0)**	**-0.24**	**0.002**
Age	0.00 (0.0 to 0.0)	-0.11	0.16
Sex	0.01 (0.0 to 0.0)	0.02	0.79
R^2 (p value)	**.19 (p<0.001)**		

611

612 B (95% CI): unstandardised coefficient (95% confidence interval); Beta (β): standardised

613 coefficient; RTS: return to sport; BMI: body mass index; ACLR: anterior cruciate ligament

614 reconstruction; Subsequent surgery: at least one additional knee surgery to an ACL-

615 reconstructed knee (excluding revision ACLR or concomitant surgery performed at the time

616 of primary or revision ACLR); * Did not return to sport = reference category; Sample size

617 does not equal 162 for these analyses due to n=1 was not participating in sport at the time of

618 injury, n=2 selected 'unsure' options, and n=1 did not complete the AQoL-8D; injury to

619 ACLR was dichotomised as >6 months (yes/no); All dichotomous variables were coded as

620 no=0, yes=1; Sex was coded as male=0, female=1; Years since surgery, BMI and age were

621 continuous variables.

622 **TABLE 4.** Psychological health linear regression analyses

623

624

Explanatory variables:	HADS Depression (n=157)			HADS Anxiety (n=157)		
	B (95% CI)	Beta (β)	p value	B (95% CI)	Beta (β)	p value

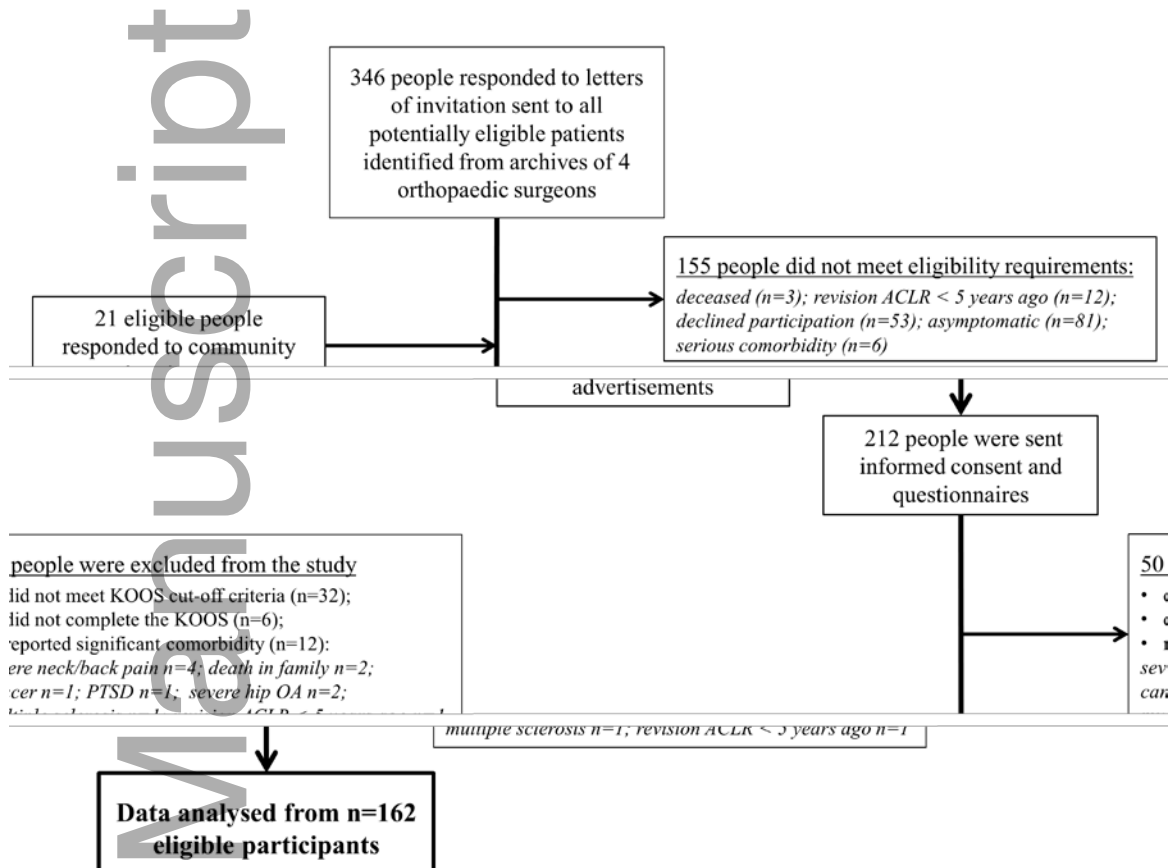|	B (95% CI)	β	p	B (95% CI)	β	p
Years since ACLR	0.07 (-0.1 to 0.2)	0.10	0.24	0.06 (-0.1 to 0.2)	0.06	0.48
Injury to ACLR	0.68 (-0.2 to 1.6)	0.12	0.14	0.29 (-1.1 to 1.6)	0.04	0.68
Revision ACLR	-0.30 (-1.5 to 0.9)	-0.04	0.62	0.36 (-1.4 to 2.2)	0.03	0.69
Contralateral ACLR	0.16 (-1.0 to 1.4)	0.02	0.79	-1.32 (-3.1 to 0.5)	-0.12	0.16
Subsequent surgery	0.34 (-0.5 to 1.2)	0.06	0.43	-0.62 (-1.9 to 0.6)	-0.08	0.33
RTS same/higher level*	-0.94 (-1.9 to 0.0)	-0.18	0.06	-0.65 (-2.1 to 0.8)	-0.09	0.39
RTS lower level*	-0.68 (-1.7 to 0.3)	-0.12	0.19	0.44 (-1.1 to 2.0)	0.05	0.58
BMI	**0.11 (-0.4 to 0.2)**	**0.24**	**0.003**	0.06 (-0.5 to 0.2)	0.09	0.26
Age	0.01 (-0.0 to 0.1)	0.02	0.77	-0.05 (-0.1 to 0.0)	-0.13	0.15
Sex	**-0.94 (-1.7 to -0.2)**	**-0.18**	**0.02**	0.24 (-1.0 to 1.4)	0.03	0.69
R^2 (p value)	**.18 (p=0.001)**			.07 (p=0.39)		

625

626 B (95% CI): unstandardised coefficient (95% confidence interval); Beta (β): standardised

627 coefficient; Subsequent surgery: at least one additional knee surgery to an ACL-reconstructed

628 knee (excluding revision ACLR or concomitant surgery performed at the time of primary or

629 revision ACLR); RTS: return to sport; BMI: body mass index; ACLR: anterior cruciate

630 ligament reconstruction; HADS: Hospital Anxiety and Depression Scale; * Did not return to

631 sport = reference category; Sample size does not equal 162 for these analyses due to n=1 was

632 not participating in sport at the time of injury, n=2 selected 'unsure' options, and n=1 did not

633 complete the HADS; injury to ACLR was dichotomised as >6 months (yes/no); All

634 dichotomous variables were coded as no=0, yes=1; Sex was coded as male=0, female=1;

635 Years since surgery, BMI and age were continuous variables.

636 # FIGURES

637

638

346 people responded to letters of invitation sent to all potentially eligible patients identified from archives of 4 orthopaedic surgeons

21 eligible people responded to community

advertisements

155 people did not meet eligibility requirements:
deceased (n=3); revision ACLR < 5 years ago (n=12); declined participation (n=53); asymptomatic (n=81); serious comorbidity (n=6)

212 people were sent informed consent and questionnaires

people were excluded from the study
lid not meet KOOS cut-off criteria (n=32);
lid not complete the KOOS (n=6);
reported significant comorbidity (n=12):
*ere neck/back pain n=4; death in family n=2;
cer n=1; PTSD n=1; severe hip OA n=2;*

multiple sclerosis n=1; revision ACLR < 5 years ago n=1

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Data analysed from n=162 eligible participants
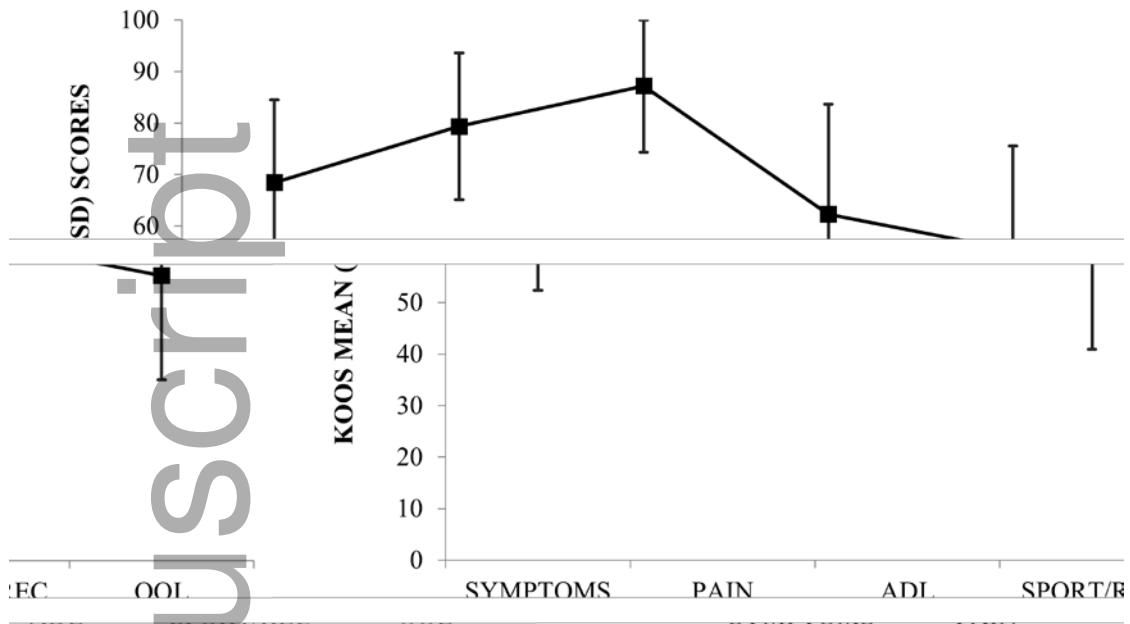
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641 **FIGURE 1.** Recruitment flow chart

642 ACLR: anterior cruciate ligament reconstruction; KOOS: Knee Injury and Osteoarthritis

643 Outcome Score; PTSD: post-traumatic stress disorder; OA: osteoarthritis

644

	87	62	55	Mean	68	79
	(13)	(21)	(20)	(SD)	(16)	(14)

FIGURE 2. Knee injury and Osteoarthritis Outcome Score (KOOS) mean scores (boxes) and SDs (whiskers)

n=162; a lower score indicates poorer outcomes in all subscales; SD: standard deviation; ADL: Activities of Daily Living; Sport/Rec: function in Sport and Recreation; QOL: Quality of Life; KOOS: Knee Injury and Osteoarthritis Outcome Score.
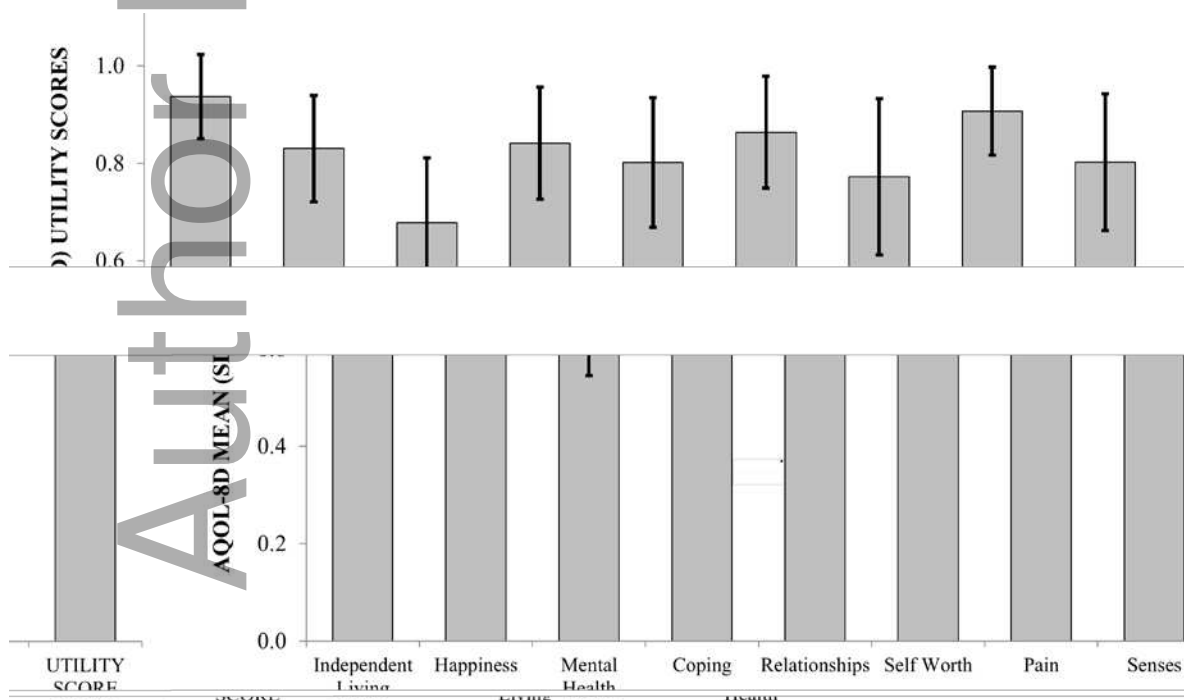
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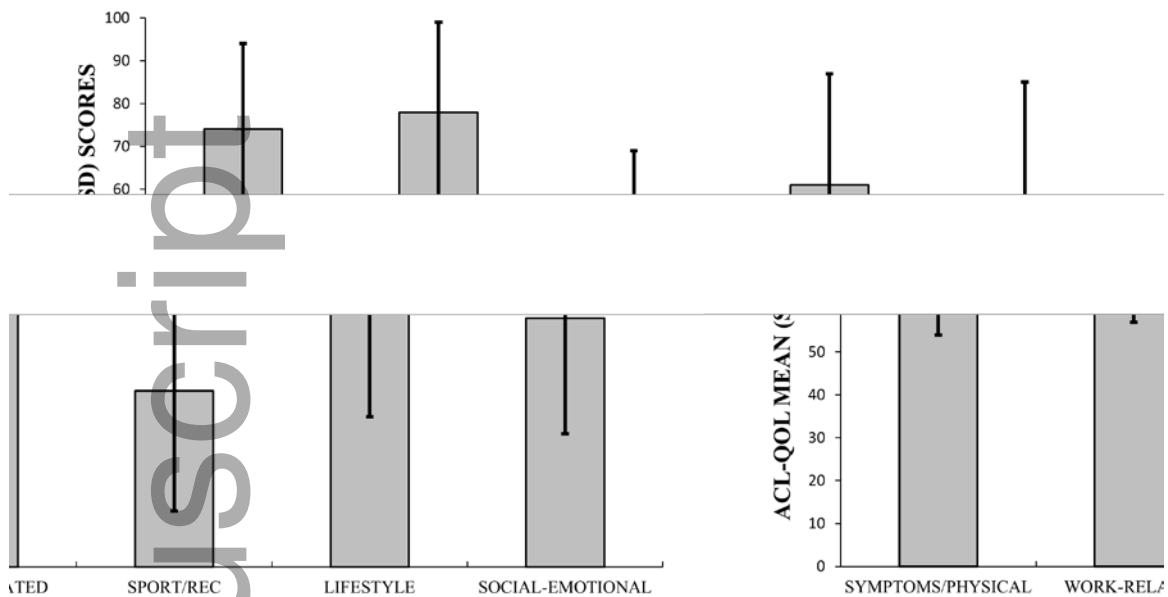
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655 **FIGURE 3.** Anterior Cruciate Ligament Quality of Life questionnaire (ACL-QOL) mean

656 domain scores (bars) and SDs (whiskers)

657 n=161; SD: standard deviation; a lower score indicates poorer outcomes in all domains.

658

659

660   **FIGURE 4.** The Assessment of Quality of Life (AQoL-8D) measure mean dimension scores

661   and utility scores (bars) and SDs (whiskers)

662   n=161; SD: standard deviation; utility scores of 1.0 represent full health and 0.0 worst

663   possible health.

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