Health utilities and costs for neuromyelitis optica spectrum disorder

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15

16   **Declarations**

17   *Ethics approval and consent to participate:*

18   Ethical approval that was granted by the London - Hampstead NHS Research Ethics Committee

19   (reference 15/LO/1433).

20   *Consent for publication:*

21   All the authors provide final approval of the version to be published, and agree to be

22   accountable for all aspects of the work in ensuring that questions related to the accuracy or

23   integrity of any part of the work are appropriately investigated and resolved.

24   *Availability of data and material:*

25   Study participants did not consent explicitly for their responses to be shared publicly.

26   *Competing interests:*

27   DAH is recipient of a Health and Care Research Wales Senior Research Leader award. DAH and

28   AJ received funding from Alexion Pharmaceuticals Inc. (currently Alexion, Astra Zeneca Rare

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32   KM have no interests to declare.

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36   *Authors' contributions:*

37   Conception and design of the work (DAH, SB, AJ); acquisition, analysis or interpretation of data

38   (DAH, SB, AJ, RB, SH, KM, AJ); drafting the work (DAH, SB); revising the work critically for

39   important intellectual content (AJ, RB, SH, KM, AJ).

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44   **Abstract**

45   Background: Neuromyelitis optica spectrum disorder (NMOSD) is a rare, neurological disease

46   that places a significant burden on patients, their carers, and healthcare systems.

47   Objectives: To estimate patient and carer health utilities and costs of NMOSD within the UK

48   setting.

49   Methods: Patients with NMOSD and their carers, recruited via a regional specialist treatment

50   centre, completed a postal questionnaire that included a resource use measure, the EuroQoL

51   (EQ)-5D-5L, EQ-5D-VAS, Vision and Quality of Life Index (VisQoL), Carer Experience Survey

52   (CES) and the Expanded Disability Status Scale (EDSS). The questionnaire asked about

53   respondents' use of health and community care services, non-medical costs, informal care and

54   work capacity. Data were analysed descriptively. Uncertainties in costs and utilities were

55   assessed using bootstrap analysis.

56   Results: 117 patients and 74 informal carers responded to the survey. Patients' mean EQ-5D-

57   5L and VisQoL health utilities (95% central range) were 0.54 (-0.29, 1.00) and 0.79 (0.11, 0.99),

58   respectively. EQ-5D-5L utility decreased with increasing EDSS score bandings, from 0.80 (0.75,

59   0.85) for EDSS ≤ 4.0, to 0.20 (-0.29, 0.56) for EDSS 8.0 to 9.5. Mean, 3-month total costs were

60   £5,623 (£2,096, £12,156), but ranged from £562 (£381, £812) to £32,717 (£2,888, £98,568)

61   for these EDSS bandings. Carer-reported EQ-5D-5L utility and CES index scores were 0.85

62   (0.82, 0.89) and 57.67 (52.69, 62.66). Mean, 3-month costs of informal care were £13,150 to

63   £24,560.

64   Conclusions: NMOSD has significant impacts on health utilities and NHS and carer costs. These

65   data can be used as inputs to cost-effectiveness analyses of new medicines for NMOSD.

66

67   **Keywords:** Neuromyelitis optica spectrum disorder; carers; cost of illness; EQ-5D; utility.

Introduction

68

69 Neuromyelitis optica spectrum disorder (NMOSD) is a rare (1-2 people per 100,000)

70 neurological, autoimmune disease typically characterised by episodes of optic neuritis,

71 transverse myelitis, together with one or more other diagnostic criteria including the presence

72 of serum aquaporin-4 antibodies [1]. Patients experience optic neuritis as pain which is rapidly

73 followed by loss of acuity. Individuals affected by myelitis typically experience pain in the spine

74 or limbs, mild to severe paralysis of the lower limbs, and loss of bowel and bladder control.

75 Recurrent relapses of optic neuritis and/or myelitis, from which recovery is often incomplete,

76 results in residual and accumulating impairment (such as blindness and paraplegia).

77 Conventionally managed with corticosteroids, azathioprine, mycophenolate mofetil and

78 rituximab, new immunosuppressive treatments – including eculizumab, satralizumab, and

79 inebilizumab – are changing the therapeutic landscape for NMOSD [2]. These treatments have

80 different targets within the immune pathogenic process and while they are not curative, they

81 reduce relapse rate and neurological deficit. However, they are very expensive. The annual

82 cost of eculizumab is approximately £327,600 in the UK, based on four 300 mg vials every 2

83 weeks and a National Health Service (NHS) indicative price of £3,150 per vial [3]. The costs of

84 satralizumab and inebilizumab in the USA are $219,231 and $393,000 for the first year,

85 respectively, and $190,000 and $262,000 per year thereafter [2].

86 In the UK, treatments for NMOSD are commissioned via NHS specialised services; and

87 consequently, they compete with other specialised services for funding, and must therefore

88 demonstrate value for money to gain routine adoption. Economic evaluations assess value for

89 money by estimating the incremental cost associated with achieving additional quality-

90 adjusted life years (QALYs). Within the technology appraisal programme of the National

91 Institute for Health and Care Excellence (NICE), a cost per QALY below £20,000 to £30,000 is

92   deemed to be cost-effective [4]. However, for Highly Specialised Technologies, the threshold

93   increases to £100,000 (and exceptionally, up to £300,000) per QALY [4].

94   Highly effective treatments that prevent hospital admissions, reduce caregiver costs and

95   improve health-related quality of life may conceivably achieve cost-effectiveness, even at

96   these high prices. However, there is very limited evidence on the direct and indirect costs of

97   care for patients with NMOSD, and considerable uncertainty surrounding the cost-

98   effectiveness of treatments. NICE was unable to make a recommendation on eculizumab as

99   the sponsor did not provide an evidence submission [5].

100 Improved accuracy and precision in the estimates of costs and health outcomes will result in

101 more reliable inputs to economic models concerning treatments of NMOSD. This should

102 provide decision makers greater confidence in the results of cost-effectiveness analyses. The

103 aim of this research, therefore, was to estimate the costs associated with NMOSD, and

104 measure health-related quality of life weights, expressed in terms of utilities, that would allow

105 for the calculation of QALYs, given that a QALY is the time integral of utility.

106 **Methods**

107 A sample of patients with NMOSD and their carers were recruited and consented to complete

108 a postal survey which included a resource use questionnaire, the EuroQol (EQ)-5D-5L and

109 visual analogue scale (VAS), the Carer Experience Scale, the Vision and Quality of Life Index

110 (VisQoL) and the Expanded Disability Status Scale (EDSS) measures. The survey was

111 undertaken between January 2016 and July 2018, following ethical approval that was granted

112 by the London - Hampstead NHS Research Ethics Committee (reference 15/LO/1433).

113 Patient questionnaire

114   Patient questionnaires were in three parts: (i) demographics (age and sex); (ii) resources used

115   or lost; and (iii) health outcomes, in terms of health-related quality of life, health utilities and

116   disease severity. Clinical characteristics were obtained from patients' medical records, and

117   included the duration since onset of NMOSD symptoms, length of time for referral to the

118   treatment centre, and whether and how many relapses were experienced in the past year.

119   *Resource use*

120   The Database of Instruments for Resource Use Measurement [6] was searched for a

121   neurological-based questionnaire which was suitable for adaptation for NMOSD. We selected

122   a comprehensive questionnaire originally developed for epilepsy [7,8], but modified for

123   amyotrophic lateral sclerosis [9] and multiple sclerosis [10]. Additional items were included to

124   account for ophthalmology services. The resource use questionnaire included items on

125   hospital admission (emergency department, outpatient and inpatient visits), primary care

126   services (general practitioner, nurse), tests and investigations, medicines (prescribed, and

127   over-the-counter purchases), personal social services, mobility and any required adaptations,

128   non-medical costs (such as in relation to transport), and indirect costs (based on productivity

129   losses). Patients were asked to provide information on costs which were related and unrelated

130   to NMOSD, in order to ensure that the analysis considered insofar as was possible, those costs

131   which were associated with NMOSD.

132   An important consideration for self-reported data for resource use was the recall period as

133   this can lead to bias if respondents do not recall some aspects of care when asked. Generally,

134   it is accepted that the longer the recall period the higher the risk of reduced accuracy of the

135   data [11]. As there is no optimal length of recall period, a three-month recall period was used

136   [12], with the exception of adaptations or any equipment purchased, where a timeframe of

137   the preceding year was given to reflect the infrequency by which patients would receive these

138   high-cost items; and prescribed medicines for which a one-month recall period was specified.

139   *Health outcomes*

140   Health utilities were based on the EQ-5D-5L questionnaire [13], which is a generic, multi-

141   attribute instrument consisting of five dimensions: mobility, self-care, usual activities,

142   pain/discomfort, and anxiety/depression. A total of 3125 possible health states are defined in

143   the EQ-5D-5L, each associated with a corresponding utility score which is anchored at 0

144   (death) and 1 (perfect health). Negative utility scores indicate states perceived to be worse

145   than death. The EQ-5D-5L value set for England was used, based on a study which followed

146   the EuroQol Group's international protocol for valuing EQ-5D-5L health states [14].

147   Subsequent to our study protocol being approved, NICE recommended the use of the EQ-5D-

148   3L mapping function proposed by van Hout et al. (2012) [15], and later a mapping function by

149   Hernández Alava et al. (2017) [16]. Given also the ongoing research to develop a new UK value

150   set for the EQ-5D-5L [17], we decided to continue with the approach recommended by the

151   EuroQol group, as originally planned. The second part of the EQ-5D-5L consisted of a vertical

152   visual analogue scale (VAS), where 0 represents the worst and 100 represents the best

153   possible health state imaginable. Respondents marked a point on the scale to reflect their

154   overall health on the day of completion.

155   A recognised limitation of the EQ-5D-5L is that it lacks sensitivity to changes in visual

156   impairment that affects NMOSD patients [18]. The VisQoL was therefore included as a multi-

157   attribute, vision-related utility measure which disaggregates vision into six items [19]. These

158   include: vision related injury, vision and the demands in their life, vision effect on friendship,

159   organising assistance, vision impact on fulfilment of roles and confidence to join everyday

160   activities. The VisQoL value set was derived from a face-to-face time trade-off study which

161 involved 374 participants, with utility anchored at 0 to represent death and 1 representing full

162 health [20]. Missing values in the VisQoL were replaced with the mean of the other items,

163 rounded to the nearest integer [21].

164 Self-assessed disease severity was assessed using banded scores of the Kurtzke Expanded

165 Disability Status Scale (EDSS) [22], with 0.0 ≤ EDSS ≤ 4.0 representing an ability to walk for at

166 least 500 meters without using a stick, splint or other support, or resting; 4.5 ≤ EDSS ≤ 6.5

167 representing an ability to walk between 20-499 meters, using aids such as stick or splint if

168 needed; 7.0 ≤ EDSS ≤ 7.5 corresponding to not being able to walk for more than 5 meters,

169 even with aid (such as frame); and 8.0 ≤ EDSS ≤ 9.5 indicating a need for a wheelchair all the

170 time. Patients' medical records were reviewed by a neurologist from the NMOSD diagnostic

171 and advisory service to ensure that patient-reported scores were in keeping with their

172 recorded disability and visual acuity. Where there were discrepancies, checks were made for

173 data entry errors and confirmation with the patient.

174 <u>Informal carers' questionnaire</u>

175 Data collection for patients' informal carers related to: (i) their relation to the patient and their

176 caring activities, including the types of activities and the number of hours spent completing

177 these activities (daily or weekly); (ii) work and employment, their economic status and income,

178 any days of work missed due to caring activities; and (iii) their health-related quality of life and

179 wellbeing.

180 Carer health utility was measured using the EQ-5D-5L. Carer wellbeing was gauged using the

181 Carer Experience Scale [23], which contains six attributes, including activities, support,

182 assistance, fulfilment, control and relationships, with three levels for each (most, some and

183   few). Attribute level index values enabled the caring experience to be measured and valued

184   through the use of a simple profile measure.

185   <u>Recruitment and survey administration</u>

186   Patients and their carers were recruited via the Walton Centre NHS Foundation Trust, which

187   is one of two specialist centres for NMOSD serving patients from the north of England,

188   Scotland and North Wales. About 200 NMOSD patients are seen by the NMOSD diagnostic and

189   treatment service at the Walton Centre, accounting for approximately a quarter of the total

190   estimated adult NMOSD population in the UK [24].

191   Patients eligible for enrolment had clinically or laboratory-supported NMOSD diagnosis

192   according to the 2006 criteria of Wingerchuk et al. [25], were at least 18 years of age and

193   spoke English. Informed consent was obtained prior to their participation.

194   All data were collected via a postal questionnaire, with reminders to complete the forms given

195   at clinic visits. Follow-up questionnaires were scheduled for 6, 9, 12 and 15 months following

196   baseline administration.

197   <u>Unit costs</u>

198   Inpatient and outpatient appointment costs were calculated using gross costing techniques,

199   assuming national averages for nurse support for outpatient procedures in neurology, and

200   consultant-led neurological procedures (Table 1). Ophthalmology appointments related to

201   NMOSD were costed as the weighted mean of face-to-face consultant-led procedures in

202   ophthalmologist and medical ophthalmologist services, and based on the national reference

203   costs [26]. NMOSD inpatient bed-days were costed as a weighted mean of the elective and

204   non-elective admissions for multiple sclerosis patients. The unit costs of appointments with

205   other NHS professionals, such as a psychologist, social worker and physiotherapist, and for

206 personal social services, were obtained from the compendium of Unit Costs of Health and

207 Social Care [27]. The unit costs of medicines were taken from the British National Formulary

208 [3]. Test costs, including computerized tomography scan, ultrasound, X-ray (Direct Access

209 Plain Film), Dual-energy X-ray absorptiometry (DEXA), lumbar puncture (Diagnostic Spinal

210 Puncture – neurology only) were retrieved from the national reference costs [26]. Urine and

211 blood test costs were obtained from the National Clinical Guideline Centre [28]. The costs of

212 adaptations and travel were estimated from patients' self-reported data. The analysis was

213 based on 2016/17 costs.

214 Two methods were used to estimate the cost of carer activities, the proxy method and the

215 opportunity cost method [30]. For the proxy cost method, informal care costs were matched

216 with those from formal services as follows: personal care, physical help and giving medicines

217 were valued at the time of a formal carer; help dealing with care services or financial matters

218 was assigned a value corresponding to that of a social worker; and other practical help and

219 social activities were estimated at the minimum wage rate (Table 1). The opportunity cost

220 method used the national average hourly wage, stratified by age and sex to estimate the daily

221 cost of caring. To avoid double counting activities that a caregiver may be preforming during

222 the course of the day, a sensitivity analysis was undertaken for the cost of social caring

223 activities. This considered the cost of a hospital sitter (proxy cost), the minimum payment of

224 carers benefit, and the maximum payment of carers benefit (opportunity cost method).

225 For both carers and patients currently in employment, productivity loss was assessed through

226 the analysis of the rate of sick leave. The productivity of a person was valued at the average

227 market price in terms of age and gender. For short-term sick leave the labour costs were

228 adjusted to the respondents' reported missing working hours.

229 Statistical analysis

230 Data from questionnaire responses were analysed descriptively as frequencies, means,

231 standard deviations and ranges. Non-parametric bootstrap analyses (bias-corrected and

232 accelerated) with 10,000 replications were used to estimate the 95% central range (CR) in

233 total costs and utilities, acknowledging the skewness in the distribution of these variables.

234 Data management and statistical analyses were performed using Stata version 13

235 (StataCorp LP, TX).

236 **Results**

237 <u>Patient characteristics</u>

238 Questionnaire packs were sent to 190 patients, of which 117 (62%) returned at least one

239 completed pack. Fifty-three returned a second questionnaire, 20 a third, 8 a fourth and one

240 patient returned a fifth questionnaire. Participants were predominantly female, with a mean

241 age of 53 years, and had waited 6 years for referral to the specialist NMOSD service (Table 2).

242 The mean length of time since the onset of symptoms was 12 years; and participants reported

243 an average of 3 relapses after their first attack since diagnosis. The majority (56; 50%) of the

244 111 patients who completed the EDSS questionnaire reported moderate disability (4.5 ≤ EDSS

245 ≤ 6.5).

246 *Health utilities*

247 Baseline responses to the EQ-5D-5L indicated that 106 (93% of completed questionnaires)

248 patients reported problems in one or more of the dimensions. Thirty-three (29%) reported

249 severe or extreme pain or discomfort, and 14 (12%) were unable to walk (Table 3). For usual

250 activities, 101 (88%) reported difficulty undertaking work, study, housework, family, or leisure

251 activities. Mean utility at baseline was 0.54 (95% CR 0.49, 0.60; n=113). The mean EQ-5D VAS

252 score was 52.8 (95% CR 48.60, 56.93; n=113). Longitudinally, EQ-5D-5L utility scores remained

253 consistent with means of 0.56, 0.56 and 0.59 for the second, third and fourth survey.

254 Ninety-seven (83%) participants completed the VisQoL questionnaire at baseline. Most

255 reported difficulty in one or more dimensions, with the greatest difficulties being in vision

256 making it difficult for people to cope with the demands in their lives, affecting confidence to

257 join in everyday activities, and making it difficult to fulfil the roles they would like to fulfil in

258 life (Table 3). Respondents were least affected by the effect of their vision on the potential for

259 injury or ability to have friendships. The mean VisQoL utility score at baseline was 0.79 (95%

260 CR 0.74, 0.84).

261 Significant reductions in utility were observed between disease states, ranging from 0.80 for

262 patients who reported EDSS ≤ 4.0, to 0.20 for those with scores 8.0 ≤ EDSS ≤ 9.5 (Table 4).

263 Monotonically decreasing EQ-5D VAS scores and VisQoL utilities were not as apparent with

264 increasing EDSS scores.

265 *Healthcare resource use and costs*

266 Costs were based on responses to baseline questionnaires. Hospitalisation was not common

267 in the patient cohort, with only 10 (9%) of patients reporting that they had been hospitalised

268 in the preceding 3 months. However, patients who had undergone an inpatient stay reported

269 a considerable length of stay, with a mean duration of hospitalisation of 12.5 days (median:

270 1.5, range: 1 to 90). Lengths of stay varied by disease severity, ranging from 5 days with EDSS

271 ≤ 4.0, to 90 days with 8.0 ≤ EDSS ≤ 9.5. The mean cost of hospitalisation was £3,954 (95% CR

272 £509, £9,221).

273 Table 5 presents the costs by category and EDSS score. Mean total costs increased with

274 disability, from £562 (95% CR £381, £812) in patients with EDSS ≤ 4.0, to £32,717 (95% CR

275   £2,888, £98,568) with 8.0 ≤ EDSS ≤ 9.5. Inpatient hospitalisations accounted for the majority

276   of these costs.

277   *Out-of-pocket and productivity losses*

278   Seventeen (15%) patients reported that they had purchased items in the previous year for

279   home adaptations, wheelchairs and mobility scooters, public liability insurance, medication

280   and private prescriptions. The average cost of adaptations was £4,843 (95% CR £3,273,

281   £6,412). Additional travel expenses were reported by 44 (38%) patients, at a mean cost of £80

282   (95% CR £ 41, £119) over a 3-month period.

283   Forty-seven patients had left the workforce including 16 due to their long-term illness and

284   retirement. Seven patients stated that their employment situation had been affected due to

285   NMOSD. Only 13 of all patients responded that they were in paid employment, of which 7

286   reported taking an average of 30 days off in the previous 3 months because of sickness.

287   <u>Carer survey</u>

288   A total of 123 survey responses was received from 74 informal carers (Table 6). The mean age

289   of carers was 55 (range 22 to 79), with 75% of carers being 50 years old or more. Most carers

290   were male (61%) and retired (26%), and most were married to the patient (74%) or were the

291   patient's son or daughter (11%). A higher proportion of male carers (96%) lived with the

292   person they cared for compared to females (72%) and were the spouse/partner of the patient

293   (86%). 55% of female carers cared for their spouse or partner and 30% were looking after

294   other family relatives. Of the carers who responded, only females were caring for non-

295   relatives.

296   Twenty-five (34%) carers reported being affected by their carer roles (Table 6). Carer-reported

297   EQ-5D-5L utility for baseline responses was 0.85 (95% CR 0.82, 0.89; range 0.3 to 1.0), and was

298 comparable between males and females. Mean EQ-5D VAS scores were 77 (95% CR 72, 81;

299 range 20 to 100), and CES index scores were 57.67 (95% CR 52.69, 62.66; range 0 to 100). The

300 most frequent response to each CES item indicated that most had little support from family,

301 friends, organisations or the government (Table 7). Carers mostly found fulfilment from caring

302 and were able to undertake most desired tasks outside of carer responsibilities.

303 *Carer burden*

304 Of those who responded, 19 (26%) spent between 35 and 49 hours per week caring for

305 patients, spending most of this time on social aspects of caring, physical help and other

306 practical help. Other activities included travel assistance, keeping an eye on patients, help with

307 social activities, physical help, help with administration tasks or financial matters, personal

308 care, and giving medicines.

309 Twenty-eight (38%) carers reported that their carer commitments affected their employment,

310 although 17 of these did not elaborate on how their employment had changed. Those who

311 reported that they had reduced the number of hours worked, took up new employment, or

312 lost a paying job.

313 *Carer costs*

314 The mean daily cost of informal care was estimated to be £144 (95% CR £18, £240) using the

315 proxy good method, and £269 (95% CR £255, £283) using the opportunity cost method (Table

316 8). With the exception of the costs of social caring activities, the proxy method estimates a

317 higher average cost per task completed.

318 **Discussion**

319 *Principal findings*

320   This is the first study to quantify the economic burden of NMOSD on patients and their

321   informal caregivers in the UK. It reveals the high costs of health and social care and private

322   expenditures that are associated with increasing disease severity, as well as the economic

323   impacts on care-giving family members. The mean, total costs of the whole cohort were

324   estimated as £5,623 per quarter (equivalent to £22,492 over 1-year), but were higher for

325   patients with 8.0 ≤ EDSS ≤ 9.5, at £32,717 (equivalent to £130,868 over 1-year) mainly due to

326   increased hospitalisation. The association between healthcare costs and EDSS disability scores

327   has been documented previously for patients with multiple sclerosis [31].

328   Patients with NMOSD report low utility scores on the EQ-5D-5L. Their mean score of 0.54

329   compares with 0.57 for patients with amyotrophic lateral sclerosis [9] and 0.64 for patients

330   with multiple sclerosis [32]. As the EQ-5D is unresponsive to different levels of visual acuity,

331   our use of the VisQoL aimed to better characterise utilities associated with vision impairment.

332   Our respondents' mean score of 0.79 is similar to utility scores reported for patients with age-

333   related macular degeneration, diabetic retinopathy or macular oedema [33]. However, a

334   direct comparison of VisQoL and EQ-5D utilities is not possible given their different constructs.

335   Carer-reported EQ-5D-5L utility was 0.85 which is higher than reported for carers for people

336   with dementia (0.78), but carers for NMOSD are younger by around a decade [34]. However,

337   the burden on carers is significant, with over 22% of carers spending more than 100 hours per

338   week caring for NMOSD patients, and 40% reporting impact on their employment. On average,

339   patients were provided about 15 hours per day each day of the year, which we estimate costs

340   between £144 and £269 per day, depending on the method of analysis. This corresponds to

341   between £13,150 and £24,560 over 3-months (or £52,600 to £98,240 over 1-year).

342   *Comparison with other research*

343 A previous study conducted in a small sample of 21 patients with NMOSD in the USA and which

344 utilised the EQ-5D-5L, yielded higher utility of 0.74 [35], but this analysis applied the EQ-5D-

345 3L crosswalk [15] making the values incomparable. A cost study based on US claims database,

346 found that patients with highly active NMOSD had approximately a 10-times higher hospital

347 inpatient admission rate compared with patients without NMOSD [36]. Annual mean costs of

348 inpatient hospitalisation for NMOSD patients was US$29,054 (approximately £22,800 at 2019

349 prices), which compares to £15,816 in the present analysis. A further US study estimated the

350 mean, annualised all-cause healthcare expenditure among patients with NMOSD was $60,599

351 (approximately £45,400) [37]. However, making comparisons across health systems, has little

352 validity given the significant differences in prices, pathways of care and how healthcare is

353 financed.

354 *Strengths and limitations*

355 Our study has strengths in having recruited a significant proportion of UK patients with

356 NMOSD. The findings are therefore likely to be generalisable to the whole of the UK.

357 Examining informal carer costs and health impacts adds value to the analysis given the

358 significance of the spillover effects in the context of chronic neurological diseases such as

359 NMOSD.

360 There are some limitations with this study. Firstly, the questionnaire was for self-completion

361 and this reliance on patients can lead to problems including recall and social desirability bias.

362 Patients who may be more engaged with the service, and carers who are less burdened may

363 be more likely to report, although we have no evidence for this. Secondly, completion rates of

364 follow-up questionnaires was low, meaning that a robust longitudinal analysis was not

365 possible. Costs and health-related quality of life are likely to change over time, particularly

366 during episodes of relapses. In relation to costs, we focused on resources that patients

367   reported to be related explicitly to NMOSD. While this approach has the advantage of being

368   conservative, it also represents a lower bound, as costs of NMOSD are amplified by

369   comorbidities [38]. Also, indirect costs were limited to productivity losses; other costs, such

370   as due to premature mortality or retirement were not collected. With regards to outcomes,

371   the study utilised the 2006 criteria for NMOSD as it was well validated, although broader

372   criteria were introduced in 2015 [39]. Patients were also asked to self-assess their level of

373   disability based on bandings of EDSS scores, presented in terms of their ability to walk. The

374   EDSS measure is limited by not being disease specific nor does it include any reference to optic

375   neuritis or other disabilities that affect patients with NMOSD [40]. Finally, the VisQol has

376   limited generalisability in that the value set is based on mapping onto AQoL-7D utilities, which

377   are in turn derived from Australian patients with impaired vision. Alternative instruments such

378   as the bolt-on vision dimension for the EQ-5D may have been more appropriate [41].

379   **Conclusions**

380   This research represents a significant contribution to documenting and quantifying the

381   resource use, costs and health outcomes of patients with NMOSD in the UK. The study also

382   shows the substantial amount of informal care provided by family members and impacts on

383   their health. The inclusion of carer health-related quality of life in economic evaluations is

384   relatively uncommon but has implications for calculating the cost-effectiveness of treatments.

385   NICE specifies that economic evaluations should include direct health effects for carers where

386   relevant. A recent review of technology appraisals [42] highlighted the significant impact of

387   the inclusion of carer EQ-5D utility scores on estimates of the incremental cost-effectiveness

388   ratios. Economic evaluations of treatments for NMOSD that consider the broader implications

389   of treatments on carer wellbeing and costs are more likely to demonstrate cost-effectiveness.

390　The study findings have value for decision-makers who may want to highlight the burden of a

391　disease beyond measures of disease incidence, prevalence, morbidity and mortality. The data

392　are also compatible for future health economic analyses of interventions for NMOSD, as they

393　report health state costs and utilities relevant to UK populations.

394　**References**

395　1.　Huda S, Whittam D, Bhojak M, Chamberlain J, Noonan C, Jacob A. Neuromyelitis optica

396　　spectrum disorders. Clin Med (Lond). 2019;19(2):169-176.

397　2.　Levy M, Fujihara K, Palace J. New therapies for neuromyelitis optica spectrum disorder.

398　　Lancet Neurol. 2021;20(1):60-67.

399　3.　Joint Formulary Committee. British National Formulary 79. London: BMJ Publishing and

400　　the Royal Pharmaceutical Society. 2020. https://bnf.nice.org.uk/ Accessed 1 September

401　　2021.

402　4.　National Institute for Health and Care Excellence. NICE health technology evaluations:

403　　The manual. 2022. https://www.nice.org.uk/process/pmg36 Accessed 7 March 2022.

404　5.　National Institute for Health and Care Excellence. Eculizumab for treating relapsing

405　　neuromyelitis optica. 2020. https://www.nice.org.uk/guidance/TA647 Accessed 1

406　　September 2021.

407　6.　Database of Instruments for Resource Use Measurement. Bangor: Bangor University.

408　　2020. https://www.dirum.org/ Accessed 1 September 2021.

409　7.　Marson AG, Al-Kharusi AM, Alwaidh M, Appleton R, Baker GA, Chadwick DW, Cramp C,

410　　Cockerell OC, Cooper PN, Doughty J, Eaton B, Gamble C, Goulding PJ, Howell SJ, Hughes

411　　A, Jackson M, Jacoby A, Kellett M, Lawson GR, Leach JP, Nicolaides P, Roberts R, Shackley

412　　P, Shen J, Smith DF, Smith PE, Smith CT, Vanoli A, Williamson PR; SANAD Study group.

413　　The SANAD study of effectiveness of carbamazepine, gabapentin, lamotrigine,

414   oxcarbazepine, or topiramate for treatment of partial epilepsy: an unblinded randomised

415   controlled trial. Lancet. 2007;369(9566):1000-15.

416   8. Marson A, Burnside G, Appleton R, Smith D, Leach JP, Sills G, Tudur-Smith C, Plumpton C,

417   Hughes DA, Williamson P, Baker GA, Balabanova S, Taylor C, Brown R, Hindley D, Howell

418   S, Maguire M, Mohanraj R, Smith PE; SANAD II collaborators. The SANAD II study of the

419   effectiveness and cost-effectiveness of valproate versus levetiracetam for newly

420   diagnosed generalised and unclassifiable epilepsy: an open-label, non-inferiority,

421   multicentre, phase 4, randomised controlled trial. Lancet. 2021;397(10282):1375-1386.

422   9. Moore A, Young CA, Hughes DA. Health Utilities and Costs for Motor Neurone Disease.

423   Value Health. 2019;22(11):1257-1265.

424   10. Trajectories of Outcome in Neurological Conditions (TONiC).

425   https://tonic.thewaltoncentre.nhs.uk/tonic-ms Accessed 1 September 2021.

426   11. Bhandari A, Wagner T. Self-reported utilization of health care services: improving

427   measurement and accuracy. Med Care Res Rev. 2006;63(2):217-35.

428   12. Short ME, Goetzel RZ, Pei X, Tabrizi MJ, Ozminkowski RJ, Gibson TB, Dejoy DM, Wilson

429   MG. How accurate are self-reports? Analysis of self-reported health care utilization and

430   absence when compared with administrative data. J Occup Environ Med.

431   2009;51(7):786-96.

432   13. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, Bonsel G, Badia X.

433   Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L).

434   Qual Life Res. 2011;20(10):1727-36.

435   14. Devlin NJ, Shah KK, Feng Y, Mulhern B, van Hout B. Valuing health-related quality of life:

436   An EQ-5D-5L value set for England. Health Econ. 2018;27(1):7-22.

437   15. van Hout B, Janssen MF, Feng YS, Kohlmann T, Busschbach J, Golicki D, Lloyd A, Scalone L,

438   Kind P, Pickard AS. Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L

439   value sets. Value Health. 2012;15(5):708-15.

440   16. Hernández-Alava M, Pudney S. Econometric modelling of multiple self-reports of health

441   states: The switch from EQ-5D-3L to EQ-5D-5L in evaluating drug therapies for

442   rheumatoid arthritis. J Health Econ. 2017;55:139-152.

443   17. EuroQol. Study team appointed for the new UK EQ-5D-5L valuation study. 2020.

444   https://euroqol.org/blog/full-study-team-appointed/ Accessed 7 March 2022.

445   18. Tosh J, Brazier J, Evans P, Longworth L. A review of generic preference-based measures

446   of health-related quality of life in visual disorders. Value Health. 2012;15(1):118-27.

447   19. Peacock S, Misajon R, Iezzi A, Richardson J, Hawthorne G, Keeffe J. Vision and quality of

448   life: development of methods for the VisQoL vision-related utility instrument.

449   Ophthalmic Epidemiol. 2008;15(4):218-23.

450   20. Chen G, Finger RP, Holloway EE, Iezzi A, Richardson J. Estimating Utility Weights for the

451   Vision Related Quality of Life Index. Optom Vis Sci. 2016;93(12):1495-1501.

452   21. Misajon R, Hawthorne G, Richardson J, Barton J, Peacock S, Iezzi A, Keeffe J. Vision and

453   quality of life: the development of a utility measure. Invest Ophthalmol Vis Sci.

454   2005;46(11):4007-15.

455   22. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability

456   status scale (EDSS). Neurology. 1983;33(11):1444-52.

457   23. Al-Janabi H, Flynn TN, Coast J. Estimation of a preference-based carer experience scale.

458   Med Decis Making. 2011;31(3):458-68.

459   24. Papp V, Magyari M, Aktas O, Berger T, Broadley SA, Cabre P, Jacob A, Kira JI, Leite MI,

460   Marignier R, Miyamoto K, Palace J, Saiz A, Sepulveda M, Sveinsson O, Illes Z. Worldwide

461   Incidence and Prevalence of Neuromyelitis Optica: A Systematic Review. Neurology.

462   2021;96(2):59-77.

463   25. Wingerchuk DM, Lennon VA, Pittock SJ, Lucchinetti CF, Weinshenker BG. Revised

464   diagnostic criteria for neuromyelitis optica. Neurology. 2006;66(10):1485-9.

465   26. National Health Service Improvement. Reference costs 2016/17.

466   https://improvement.nhs.uk/documents/6467/201617_ReferenceCostData.zip Accessed

467   1 September 2021.

468   27. Curtis L, Burns A. Unit Costs of Health and Social Care 2017. Personal Social Services

469   Research Unit. Canterbury: University of Kent.

470   https://doi.org/10.22024/UniKent/01.02/65559 Accessed 1 September 2021.

471   28. National Institute for Health and Care Excellence. Routine preoperative tests for elective

472   surgery, 2016: Routine preoperative tests for elective surgery. BJU Int. 2018;121(1):12-

473   16.

474   29. Office for National Statistics. Annual Survey of Hours and Earnings: 2017 provisional and

475   2016 revised results.

476   https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworki

477   nghours/bulletins/annualsurveyofhoursandearnings/2017provisionaland2016revisedresu

478   lts#earnings-by-age-group Accessed 1 September 2021.

479   30. Koopmanschap MA, van Exel JN, van den Berg B, Brouwer WB. An overview of methods

480   and applications to value informal care in economic evaluations of healthcare.

481   Pharmacoeconomics. 2008;26(4):269-80.

482   31. Chataway J, Murphy N, Khurana V, Schofield H, Findlay J, Adlard N. Secondary

483   progressive multiple sclerosis: a systematic review of costs and health state utilities. Curr

484   Med Res Opin. 2021;37(6):995-1004.

485   32. Mulhern B, Feng Y, Shah K, Janssen MF, Herdman M, van Hout B, Devlin N. Comparing

486   the UK EQ-5D-3L and English EQ-5D-5L Value Sets. Pharmacoeconomics. 2018;36(6):699-

487   713.

488   33. Finger RP, Fenwick E, Hirneiss CW, Hsueh A, Guymer RH, Lamoureux EL, Keeffe JE. Visual

489   impairment as a function of visual acuity in both eyes and its impact on patient reported

490   preferences. PLoS One. 2013;8(12):e81042.

491   34. Longo F, Faria R, Parker G, Gridley K, Aspinal F, Van den Berg B, Weatherly H.

492   Investigating the economic case of a service to support carers of people with dementia:

493   A cross-sectional survey-based feasibility study in England. Health Soc Care Community.

494   2019;27(5):e734-e743.

495   35. Mealy MA, Boscoe A, Caro J, Levy M. Assessment of Patients with Neuromyelitis Optica

496   Spectrum Disorder Using the EQ-5D. Int J MS Care. 2019;21(3):129-134.

497   36. Exuzides A, Sheinson D, Sidiropoulos P, Gholizadeh S, Magrini F, Surinach A, Cook L,

498   Meyer CS, Yeaman MR. The costs of care from a US claims database in patients with

499   neuromyelitis optica spectrum disorder. J Neurol Sci. 2021;427:117553.

500   37. Royston M, Kielhorn A, Weycker D, Shaff M, Houde L, Tanvir I, Bhattacharyya S, Levy M.

501   Neuromyelitis Optica Spectrum Disorder: Clinical Burden and Cost of Relapses and

502   Disease-Related Care in US Clinical Practice. Neurol Ther. 2021;10(2):767-783.

503   38. Exuzides A, Sheinson D, Sidiropoulos P, Magrini F, Gholizadeh S, Surinach A, Cook L,

504   Meyer CS, Yeaman M. Burden and cost of comorbidities in patients with neuromyelitis

505   optica spectrum disorder. J Neurol Sci. 2021;427:117530.

506   39. Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, Chitnis T, de Seze J, Fujihara

507   K, Greenberg B, Jacob A, Jarius S, Lana-Peixoto M, Levy M, Simon JH, Tenembaum S,

508   Traboulsee AL, Waters P, Wellik KE, Weinshenker BG; International Panel for NMO

509   Diagnosis. International consensus diagnostic criteria for neuromyelitis optica spectrum

510   disorders. Neurology. 2015;85(2):177-89.

511   40. Jacob A. Endpoints in a treatment trial in NMO: Clinician's view EMA, 2014. London EMA.

512   https://www.ema.europa.eu/documents/presentation/presentation-endpoints-

513   treatment-trial-neuromyelitis-optica-clinicians-view-anu-jacob_en.pdf Accessed 1

514   September 2021.

515   41. Yang Y, Rowen D, Brazier J, Tsuchiya A, Young T, Longworth L. An exploratory study to

516   test the impact on three "bolt-on" items to the EQ-5D. Value Health. 2015 Jan;18(1):52-

517   60.

518   42. Pennington BM. Inclusion of Carer Health-Related Quality of Life in National Institute for

519   Health and Care Excellence Appraisals. Value Health. 2020;23(10):1349-1357.

520

521 **Table 1.** Unit costs

NHS Services	Unit cost (£)		Reference
Emergency department	149.78		26
Admitted to hospital as an inpatient	484.38		26
Inlier bed days	484.37		26
Excess bed days	346.00		26
Doctor hospital outpatient	346.03		27
GP doctor appointment	36.88		27
GP practice nurse	32.40		27
Nurse at home	26.65		27
Nurse hospital	90.81		26
Ophthalmologist hospital	95.22		26
Podiatrist	47.37		27
Specialist Doctor	173.01		26
Specialist nurse	90.81		26
Tests			
Urine	3.85		28
Blood	6.00		28
CT	101.57		26
Ultrasound	53.25		26
MRI	144.26		26
X-Ray	29.78		26
DEXA scan	81.15		26
Lumbar puncture	230.77		26
Carer costs - proxy method	**Cost (£) per hour**		
Personal care /physical care /giving medicines	24.00		27
Dealing with care services /benefits /financial matters	30.00		27
Other practical help	7.90		Minimum wage
Social activities	7.90		Minimum wage
Carer costs - opportunity cost method	**Male**	**Female**	
22-29 years	15.34	14.40	29
30-39 years	19.94	18.24	29
40-49 years	22.28	17.62	29
50-59 years	21.62	16.54	29
60+ years	18.60	14.35	29

522

523   **Table 2.** Patient demographic and clinical characteristics

Characteristic	Mean (SD, range) or (%)
Total number of patients, N	117
Gender, female N (%)	91 (78%)
Age at baseline, years (SD, range)	53 (15, 18-86)
Age at first onset of symptoms, years (SD, range)	44 (15, 14-85)
Length of time until referral to the Walton centre, years (SD, range)	6 (7, 0-36)
Duration since first attack, years (SD, range)	12 (8, 1-45)
Number of relapses per patient, mean (range)	3 (0-10)
Mild disability (EDSS ≤ 4.0) N (%)	29 (26%)
Moderate disability (4.5 ≤ EDSS ≤ 6.5) N (%)	56 (50%)
Moderate to severe disability (7.0 ≤ EDSS ≤ 7.5) N (%)	14 (13%)
Severe disability (8.0 ≤ EDSS ≤ 9.5) N (%)	12 (11%)

524

525 **Table 3.** Baseline patient responses to the EQ-5D-5L and VisQoL, N(%)

EQ-5D-5L					
Levels / Attributes	Mobility	Self-care	Usual Activities	Pain or discomfort	Anxiety or depression
1	21 (18.2%)	46 (40.4%)	14 (12.2%)	8 (7.0%)	34 (29.6%)
2	22 (19.1%)	26 (22.8%)	32 (27.8%)	29 (25.4%)	46 (40.0%)
3	39 (33.9%)	27 (23.7%)	38 (33.0%)	44 (38.6%)	22 (19.1%)
4	19 (16.5%)	10 (8.8%)	20 (17.4%)	21 (18.4%)	7 (6.1%)
5	14 (12.2%)	5 (4.4%)	11 (9.6%)	12 (10.5%)	6 (5.2%)

VisQoL						
Levels / Attributes	Injury	Demands of Life	Friendships	Assistance	Roles	Confidence
1	48 (49%)	30 (31%)	6 (6%)	40 (41%)	42 (43%)	6 (6%)
2	35 (36%)	18(19%)	77 (79%)	26 (27%)	17 (18%)	48 (49%)
3	10 (10%)	28 (29%)	6 (6%)	8 (8%)	17 (18%)	26 (26%)
4	0 (0%)	11 (11%)	4 (4%)	6 (6%)	9 (9%)	9 (9%)
5	4 (4%)	9 (9%)	2 (2%)	2 (2%)	10 (10%)	6 (6%)
6	-	1 (1%)	1 (1%)	15 (15%)	2 (2%)	2 (2%)
7	-	-	1 (1%)	-	-	-

526

527   **Table 4.** Estimates of patient EQ-5D-5L utilities, EQ-5D VAS and VisQoL utilities, by EDSS
528   scores.

EDSS scores (number per banding)	EQ-5D-5L (95% CR, range)	EQ-5D VAS (95% CR, range)	VisQoL (95% CR, range)
EDSS ≤ 4.0 (n=29)	0.80 (0.75-0.85, 0.44-1.00)	49.41 (43.50-55.32, 10-95)	0.85 (0.77-0.94, 0.23-0.99)
4.5 ≤ EDSS ≤ 6.5 (n=56)	0.54 (0.48-0.60, -0.01 to 0.87)	67.37 (59.71-75.03, 30-100)	0.78 (0.70-0.85, 0.1-0.99)
7.0 ≤ EDSS ≤ 7.5 (n=14)	0.31 (0.12-0.50, -0.22 to 0.78)	41.79 (30.77-52.80, 10-75)	0.83 (0.71-0.95, 0.37-0.99)
8.0 ≤ EDSS ≤ 9.5 (n=12)	0.20 (0.02-0.38, -0.29 to 0.56)	51.81 (39.41-64.23, 25-80)	0.60 (0.34-0.85, 0.23-0.99)
All patients (n=111)	0.54 (0.49-0.60, -0.29 to 1.00)	52.77 (48.60-56.93, 10-100)	0.79 (0.74-0.84, 0.11-0.99)

529

530

531 **Table 5.** Patient costs over the 3 months preceding the first questionnaire completed – totals

532 and by EDSS score

	Total costs Mean (95% CR)	EDSS ≤ 4.0 Mean (95% CR)	4.5 ≤ EDSS ≤ 6.5 Mean (95% CR)	7.0 ≤ EDSS ≤ 7.5 Mean (95% CR)	8.0 ≤ EDSS ≤ 9.5 Mean (95% CR)
Travel	£69 (£49-£89)	£43 (£14-£84)	£68 (£13-102)	£56 (£3-£110)	£157 (£89-218)
Patient Costs	£704 (£217-£1,511)	-	£366 (£33-£1,113)	£162 (£2-£324)	£4,898 (£1,030-£12,984)
GP Practice	£154 (£124-£197)	£93 (£49-£143)	£151 (£110-£199	£225 (£111-£437)	£259 (£153-£419)
Other contacts	£55 (£33-£98)	£12 (£4-£23)	£36 (£19-£67)	£33 (£0-£75)	£269 (£89-539)
Tests	£78 (£61-£104)	£70 (£31-£120)	£78 (£55-£113)	£102 (£29-£189)	£241 (£124-£372)
Medications	£607 (£208-£1459)	£89 (£44-£180)	£1,135 (£289-£3,422)	£216 (£96-£412)	£408 (£112-£917)
A&E attendances	£70 (£44-122)	£23 (£0-£67)	£70 (£35-£117)	£160 (£0-£366)	£116 (£15-291)
Hospital out-patients	£318 (£245-£420)	£212 (£125-£323)	£322 (£201-£426)	£482 (£270-£957)	£428 (£179-921)
Hospital in-patient stay	£3,954 (£509-£9,221)	£23 (£0-£90)	£1,436 (£22-£3,778)	£4,670 (£0-£13,829)	£25,951 (£0-£71,746)
Total cost	£5,623 (£2,096-£12,156)	£562 (£381-£812)	£3,674 (£1,813-£6,347)	£6,106 (£923-£20,562)	£32,717 (£2,888-£98,568)

533

534 Notes: *Patient costs* are self-reported by patients, and include private medication, house

535 adjustments; *GP Practice* includes out-of-hours services, practice nurse and GP home visits;

536 *Other contacts* include physiotherapy, occupational health, social work, counselling and

537 psychotherapy.

538

539   **Table 6.** Carer demographics

Characteristic	Mean
Number	74
Mean age (range)	55 (22-79)
Male (%)	45 (61%)
Carers age profile (years)	
20-29	3 (4%)
30-39	5 (7%)
40-49	8 (11%)
50-59	31 (44%)
60-69	17 (24%)
70-79	6 (9%)
Relationship to the NMOSD patient	
Spouse/partner (%)	55 (74%)
Son/daughter (%)	8 (11%)
Parent/guardian (%)	5 (7%)
Sibling (%)	2 (3%)
Other non-relative (%)	4 (5%)
Living Arrangements	
Patient lives with carer	64 (86%)
Patient lives in own home	9 (12%)
Patient lives in Care Home	1 (1%)
Carer Employment Status	
In full time employment	27 (36%)
In part-time employment	8 (11%)
Unemployed and not looking for work	4 (5%)
Unable to work due to caring commitments	15 (20%)
On a government employment or training scheme	1 (1%)
Retired	19 (26%)
Carer commitments affecting career	
Yes	25 (34%)
No	46 (62%)
Other	3 (4%)
Reasons for caring commitments affecting work	
Lost a paid job and still have not got another one	2 (8%)
Changed the type of job/tasks done	1 (4%)
Lost a paid job but have since got another one	1 (4%)
Changed my place of work	2 (8%)
Changed the number of hours worked	8 (31%)
Unemployed for the last three months	2 (8%)
Unemployed then got a paid job	2 (8%)
Opted to take early retirement due to caring commitments	8 (31%)
Carers' weekly earnings	

None	18 (29%)
Less than £99	9 (14%)
£100-£199	9 (14%)
£200-£299	8 (13%)
£300-£399	5 (8%)
£400-£499	8 (13%)
£500-£599	1 (2%)
£600-£699	2 (3%)
£700-£799	2 (3%)
More than £800	1 (2%)

540

541   **Table 7.** Responses to the Carer Experience Scale

Attribute (levels)	N (%)
Activities Outside Caring	
Can do most of the things they want to do	32 (46%)
Can do some of the things they want to do	22 (31%)
Can do a few of the things they want to do	16 (23%)
Support from family and friends	
A lot	17 (24%)
Some	23 (33%)
A little	30 (43%)
Assistance from organisations and the government	
A lot	3 (5%)
Some	6 (9%)
A little	55 (86%)
Finding fulfilment from caring	
Mostly	31 (46%)
Sometimes	27 (40%)
Rarely	9 (13%)
Level of control over aspects of caring	
Mostly	28 (41%)
Some	29 (43%)
A few	11 (16%)
Getting on with the person you care for	
Mostly	62 (90%)
Sometimes	7 (10%)
Rarely	0 (0%)

542

543

544   **Table 1.** Daily costs of informal care

	Time (minutes per day)	Cost (proxy method) Mean (95% CR)	Cost (opportunity cost method) Mean (95% CR)
Personal care	60	£22 (£20.12-£23.51)	£16.36 (£15.04-£17.67)
Physical help	81	£26 (£23.56-£27.25)	£19.09 (£17.78-£20.40)
Helping to deal with care services	23	£6.00 (£5.57-£6.75)	£3.98 (£3.60-£4.35)
Help dealing with paperwork and financial services	36	£13.00 (£12.16-£14.66)	£8.15 (£7.47-£8.83)
Other practical help	82	£12 (£11.47-£13.05)	£30.32 (£28.64-£32.01)
Giving medicines	25	£13 (£11.55-£14.79)	£10.45 (£9.19-£11.69)
Social caring activities	600	£75 (£71-£80)	£189.99 (£179.90-£201.08)
Total	907	£144.25 (£18-£240)	£269.07 (£255.31-£282.85)

545