Exploring autistic-like traits relating to empathic attitude and psychological distress in hospital pharmacists

Authors:

Yuji Higuchi ¹, Yosuke Uchitomi ², Maiko Fujimori ³, Toshihiro Koyama ⁴, Hitomi Kataoka ⁵, Yoshihisa Kitamura ⁴, Toshiaki Sendo ⁴, Masatoshi Inagaki ⁶

Authors' affiliations:

¹Department of Neuropsychiatry, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

²Innovation Center for Supportive, Palliative and Psychosocial Care, National Cancer

Center Hospital, Tsukiji, Chuo-ku, Tokyo, Japan

³Center for Suicide Prevention, National Institute of Mental Health, National Center for Neurology and Psychiatry, Kodaira, Tokyo, Japan

⁴Department of Clinical Pharmacy, Okayama University Graduate School of Medicine,

Dentistry and Pharmaceutical Sciences, Okayama, Japan

⁵Department of Primary Care and Medical Education, Okayama University Graduate

School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

⁶Department of Neuropsychiatry, Okayama University Hospital, Okayama, Japan

the number of words of

the article (3486), of the abstract (339), and of the references (1191).

Ethical considerations

This study was approved by the Ethics Committee of the Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences on December 25, 2013 (receipt number 776).

Acknowledgements

The authors thank the Okayama Society of Hospital Pharmacists, Shoko Yoshimoto,

Yifei Tang and Kyoko Hageshita.

Funding

The Research for Promotion of Cancer Control Programmes (H26-Gan

Seisaku-ippan-002 and H25-Seishin-ippan-001) Health and Labour Sciences Research

Grants from the Ministry of Health, Labour and Welfare, Japan.

1 Introduction

2 Pharmacists have traditionally played a leading role in cancer care teams in establishing 3 central services for compounding cytotoxic drugs and offering therapeutic drug monitoring for critical substances [1]. However, the Cancer Control Act, enforced in 4 2007 in Japan, has made pharmacists essential members of palliative care teams. Cancer 5 6 care involves dealing with patient emotions and empathizing with psychological distress. 7 Unsurprisingly, cancer imposes a heavy psychological burden on the patient during the 8 process of diagnosis and treatment. Treatments such as cancer chemotherapy are 9 accompanied by both the communication of bad news (e.g., end-of-life treatment 10 recommendations) and painful physical symptoms [2]. Healthcare providers' empathic 11 attitude toward patients is thought to be associated with good outcomes, such as 12 successful doctor-patient relationships and patient satisfaction [3]. In support of this, we demonstrated that a Communication Skills Training (CST) 13 14 intervention to improve oncologists' empathic communication, effective behaviours, and confidence in their ability to communicate with patients decreased depression 15 symptoms among cancer patients [4]. Additionally, we conducted a review of cancer 16 patient preferences regarding the communication of bad news [5]. This confirmed that 17 18 empathy is considered the most critical factor in cancer medicine, particularly in Japan. 19 While the empathic attitude of healthcare providers involved in cancer care is important, 20 the contribution of psychological health also needs attention. Our research has revealed 21 that although the CST improved the confidence of Japanese oncologists to communicate 22 with patients, their emotional exhaustion also increased [6]. These findings are not just relevant to cancer care, but apply more widely to the general practice of hospital 23 24 pharmacists.

The World Health Organization has defined pharmaceutical care as "a philosophy of 25 practice in which the patient is the primary beneficiary of the pharmacist's actions" [7]. 26 27 In 1993, the American Society of Health-System Pharmacists stated that "pharmaceutical care is the direct, responsible provision of medication-related care for 28 the purpose of achieving definite outcomes that improve a patient's quality of life, and 29 in the provision of pharmaceutical care, professional communication is essential" [8]. 30 Some researchers have emphasized the importance of pharmacists having empathy and 31 communication skills. For example, Wallman et al. state that "the role of the pharmacist 32 as a communicator of information and advice between patients, other healthcare 33 34 practitioners, and the community is recognized as a vital component of a practicing pharmacist" [9], and Berger suggests that "pharmaceutical care requires the formation 35 of a therapeutic alliance, and pharmacists will be able to treat patients more effectively 36 by their basic understanding and true desire to care for the patient" [10]. One study 37 reported that pharmacists who provided direct patient care scored higher on a measure 38 of caring ability than those who did not [11]. Another study concluded that the interplay 39 of empathic development and social learning in pharmacists appears to facilitate 40 empathic responding to patients who are experiencing physical or emotional distress 41 [12]. Recently, the need for education in empathy has been recognized. One recent 42 43 randomized prospective study was carried out to examine the effects of an empathy intervention on pharmaceutical students; although the intervention increased empathy 44 45 levels, these effects were not sustained [13]. 46 In 2009, the Japan Pharmaceutical Association published guidelines regarding the professional standard required of pharmacists. In these guidelines, the importance of

47

pharmacists' role in providing empathy, communication, and spiritual care to terminally 48

ill patients is mentioned. Though these requirements are quite recent, in current practice
in Japan, hospital pharmacists must directly communicate with cancer patients and are
expected to support patients, showing empathic concern and engaging in patient
counselling through drug guidance.

53 In the current study, we focused on autistic-like traits (ALTs) as a characteristic related to both empathy and psychological distress in hospital pharmacists. ALTs restrict 54 55 intuitive social interaction, communication, and flexibility of interests and behaviours [14]. Though autism spectrum disorder (ASD) and ALTs differ in severity, ALTs are 56 not a characteristic of ASD but could be seen as a milder form of ASD; that is, within 57 58 the spectrum of "normality" [15]. People with ASD display a classic triad comprising 59 impairments of social communication, social relationships, and imagination. Empathy includes cognitive skills, which allow an understanding of the thoughts and feelings of 60 others, and emotional aspects, allowing the sharing of others' feelings [16]. The relation 61 62 between ASD and empathy has been widely discussed. Recent evidence indicates that people with ASD have difficulties with cognitive empathy, whereas the deficit in 63 affective empathy is specific for negative emotion [17]. However, Baron-Cohen claims 64 that people with ASD have difficulties with cognitive empathy, but not with emotional 65 empathy, and are able to care about others [18]. Perhaps ALTs also involve problems 66 67 with empathy. Furthermore, people with ALTs are also vulnerable to psychiatric problems, such as depression [14]. To the best of our knowledge, the existence of ALTs 68 in healthcare providers has never been investigated. 69

70

71 Aim of the study

72 In this study, we aimed at examining the relationship in hospital pharmacists between ALTs and empathy in a medical context, and between ALTs and psychological distress. 73 We tested two main hypotheses. First, we hypothesized that ALTs would inversely 74 influence empathic attitude in a medical context. Second, we predicted that ALTs would 75 76 inversely influence pharmacists' psychological health. Additionally, we predicted that this association would be mediated mainly by various factors related to empathy, such 77 as perspective taking, empathic concern, and personal distress, and secondarily by other 78 79 ALT-related aspects, such as poor imagination or exceptional attention to detail. 80 **Ethical approval** 81 82 This study was approved by the Ethics Committee of the Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences on December 25, 2013 83 (receipt number 776). 84 85

86 Method

87 Participants

88 Eligibility criteria for inclusion were certified pharmacists working at hospitals for

89 patient care who provided informed consent for participation in this study. We

90 confirmed their consent by returning their answers. We contacted the pharmacy

91 representative of 154 hospitals to invite all pharmacists working at hospitals for patient

92 care and belonging to the Okayama Society of Hospital Pharmacists (officially reported

- figure of 823, with a median of 11 years' experience after qualification as a pharmacist,
- though n = 10 did not share this information) to participate in the study. We posted
- self-administered questionnaires to participants and informed them in writing of the aim,

96 methods, risks, and benefits of the study. Participants were asked to complete the

97 questionnaires anonymously. With the approval of the Ethics Committee, we assumed

- 98 that the return of questionnaires constituted informed consent. We asked participants to
- 99 confirm that they engaged in direct patient care.
- 100 The Okayama Society of Hospital Pharmacists covers all areas of Okayama Prefecture,

101 which is located approximately 500 km west of Tokyo.

102

103 Procedures

104 Materials

105 Demographics

106 Participants initially completed questions about their demographic and professional

107 background, providing information about (a) age; (b) gender; (c) number of beds in the

108 hospital in which they worked; and (d) number of years since qualification as a

109 pharmacist.

110 The Autism-Spectrum Quotient (AQ)

111 People with ASD scored highly on the AQ compared with the control group [19]. The

AQ is composed of 50 items on a four-point Likert scale ranging from 1 (not at all) to 4

113 (very well) with a dichotomous scoring method (0-0-1-1) and a maximum score of 50.

114 There are five subitems including attention-switching, social skills, communication

skills, imagination, and local details [19]. The Japanese version of the AQ shows

remarkably similar results to those of the original among both the general population

and clinical groups. For the Japanese version of the scale, the cut-off point for ASD is

above 33 [20].

119 The Jefferson Scale of Empathy (JSE)

The JSE was developed by Hojat (2001) to measure empathy in the context of medical 120 education and patient care [21, 22]. Hojat suggests that perspective taking and empathic 121 122 concern, but not personal distress, are important in establishing an empathic attitude in a 123 medical context [23, 24]. Evidence in support of the JSE's construct validity [21, 23, 124 25], internal consistency reliability [21, 22, 25], and test-retest reliability [25] has been reported for physicians. Two reports showed significant associations between JSE 125 scores and patient outcomes in diabetic patients (haemoglobin A1c, low-density 126 lipoprotein cholesterol, and acute metabolic complications) [26, 27]. The JSE includes 127 128 20 items on a seven-point Likert scale ranging from 1 (strongly disagree) to 7 (strongly 129 agree). Three versions of the JSE are available, with a version for physicians and other 130 health professionals (HP-Version), medical students (S-Version), and students in health professions other than medicine (HPS-Version). These versions share similar contexts 131 and differ mainly in their subjects, such as "I" in the HP-Version, "Physicians" in the 132 S-Version, and "Healthcare providers" in the HPS-Version. Only the S-Version has 133 been validated for Japanese samples. The Japanese JSE (S-Version) has a similar factor 134 structure to that of the original and a Cronbach alpha coefficient of 0.80 [28]. In this 135 136 study, we amended "Physicians" to "Pharmacists" in each of the Japanese S-Version questions. For example, "Pharmacists should try to stand in their patients' shoes when 137 providing care to them." 138

139 The General Health Questionnaire-12 (GHQ-12)

140 The General Health Questionnaire (GHQ) is a self-administered screening instrument

141 aimed at detecting individuals with a diagnosable psychiatric disorder [29]. The 12-item

142 General Health Questionnaire (GHQ-12) produced results comparable to longer

143 versions of the GHQ in a World Health Organization study of psychological disorders

in general healthcare [30]. In the present study, we used a four-point Likert scale

ranging from 0 (not at all) to 3 (very well) for correlation and mediation analyses,

146 because this scoring method produces a wider and smoother score distribution and

147 enough screening validity, with an area under the receiver-operating-characteristic curve

148 of 0.85, sensitivity of 78.9%, and specificity of 77.4% [30].

149 The Interpersonal Reactivity Index (IRI)

150 We used this scale to examine whether perspective taking, empathic concern, or personal distress mediated the associations of the AQ with the JSE and GHQ-12. The 151 152 IRI was developed by Davis (1980) to separate the multiple dimensions of empathy into 153 four components. These are IRI-PT (Perspective Taking, the ability to adopt the 154 perspective of others), IRI-EC (Empathic Concern, the tendency to experience feelings of compassion and sympathy for others' misfortune), IRI-PD (Personal Distress, the 155 tendency to feel uncomfortable about the distress of others), and IRI-FS (Fantasy Scale, 156 measuring the proclivity to identify with fictitious characters). The latter subscale was 157 not used in this study because it is not directly related to medical competency [31]. The 158 IRI-EC and IRI-PD are considered two independent measures of emotional empathy 159 160 focusing on self- and other-oriented sets of feelings, while the IRI-PT measures 161 cognitive aspects of empathy. Each subscale has seven items on a four-point Likert scale ranging from 1 (not at all) to 4 (very well) [31]. The Japanese version was 162 163 evaluated with university students. The correlation coefficients between the subscales 164 and α coefficients were similar to those for the original, and this version correlates with the Japanese version of the Questionnaire Measure of Emotional Empathy [32], 165 166 showing good reliability and validity. Following the methodology of previous research studies, we did not sum the three subscale scores but treated them as independent scales. 167

168 The Emotional Contagion Scale (ECS)

We evaluated emotional empathy using the ECS, in addition to the IRI. We used the 169 170 ECS as an ancillary scale because, as previously mentioned, the association between ALTs and emotional empathy is currently a topic of debate. The ECS evaluates the 171 likelihood of emotional contagion of five specific emotions in a particular scene (love, 172 happiness, anger, fear, and sadness) [33]. It comprises 15 items on a four-point Likert 173 scale ranging from 1 (not at all) to 4 (very well). The process of translating and 174 175 validating the scale resulted in a four-point response scale rather than the original 176 five-point scale [34]. 177 Statistical analysis 178 All analyses were performed using IBM SPSS, version 22 (IBM Japan, Tokyo). Alpha levels were set at p < 0.05 (two-tailed). The data were not normally distributed. 179 Correlations between variables were analysed using Spearman's coefficient for discrete 180 181 variables. A subanalysis examined whether pharmacists with AQ scores above the cut-off point 182 scored lower on the JSE. To examine the association between AQ and psychiatric 183 184 morbidity, AQ was entered as an independent variable into a logistic regression analysis. Cross-sectional research indicates that women show consistently more empathy than 185 186 men, and middle-aged adults show higher empathy than young adults [35]. Therefore, 187 our subgroup analysis included stratification analyses accounting for gender and median of years after qualification. We used years after qualification instead of age because age 188 data for some participants were missing. Number of years after qualification was 189 strongly correlated with age. 190

191	We investigated the mediation effect of the IRI subscales on the relationship between
192	AQ and JSE/GHQ-12 to eliminate the possibility that the other characteristics of ALTs
193	(e.g., poor imagination or attention to local detail, which are evaluated by the AQ)
194	would strongly influence JSE scores. The sizes of the indirect effects of AQ on
195	JSE/GHQ-12 through IRI subscales were estimated using a bias-corrected bootstrapping
196	method [36] with 1000 replications. Bootstrap 95% confidence intervals (CIs) were
197	obtained. The outcome variable was JSE or GHQ, the independent variable was AQ
198	total score, and the mediators were IRI subscales (IRI-PT/EC for JSE, IRI-PD for
199	GHQ-12; see Figure 1). [INSERT FIGURE 1 HERE] We further controlled for gender
200	and years after qualification.
201	The present study was reported in accordance with guidelines outlined in the
202	STrengthening the Reporting of OBservational studies in Epidemiology (STROBE)
203	statement.
204	
205	Results

All participants were certified pharmacists in Japan and were currently working in 206 207 hospitals for patient care (Figure 2). [INSERT FIGURE 2 HERE] Ninety-two hospitals responded positively to our survey request and questionnaires were subsequently posted 208 to 437 pharmacists. Complete responses were obtained from 379 pharmacists, yielding a 209 210 response rate of 46%. A demographic summary of respondents is shown in Table 1 [INSERT TABLE 1 HERE]. There were 151 males (39.8%), with a mean age of 37.7 \pm 211 212 10.8 years (missing data, n = 13) and a median of 11 years after qualification as a pharmacist. Other data and descriptive statistics for questionnaire responses are shown 213 in Table 1. 214

215	Table 2 shows the results of the correlation analyses. AQ showed a significant inverse
216	correlation with JSE ($r = -0.22$, $p < 0.001$) and a significant positive correlation with
217	GHQ-12 ($r = 0.40$, $p < 0.001$). [INSERT TABLE 2 HERE] AQ had a significant but
218	weak inverse correlation with ECS ($r = -0.121$, $p = 0.019$). Pharmacists with AQ scores
219	higher than the cut-off point ($n = 13$) scored significantly lower on the JSE (98.15 vs.
220	109.23, Mann–Whitney U test, $p = 0.026$). AQ was significantly associated with
221	psychological distress (odds ratio 1.107, 95% confidence intervals 1.071–1.144, $p <$
222	0.001). Results stratified by the median of gender or median of years after qualification
223	were similar to those that were not stratified (data not shown).
224	Table 3 shows the results of the mediation analyses. In the models without mediation,
225	AQ showed a significant inverse path coefficient on JSE (= c, $p < 0.001$) and a
226	significant positive path coefficient on GHQ (= C, $p < 0.001$). In the models with
227	mediation, the bootstrap 95% CI of a*b, d*e, and A*B did not include zero, which
228	indicated that all the indirect effects in the model were significant. There were also
229	direct effects, with significant effects of AQ on JSE (= c', $p < 0.05$) and on GHQ (= C',
230	p < 0.02). [INSERT TABLE 3 HERE]
231	For confirmation, we performed the same analyses excluding 40 participants who
1 2 1	answered "no" to the question of interpersonal work to obtain similar results (data not

answered "no" to the question of interpersonal work to obtain similar results (data notshown).

234

235 **Discussion**

236 This study shows significant relationships between pharmacists' empathic attitude in a

237 medical context and their ALT scores. Pharmacists with AQ scores higher than the

cut-off point displayed less empathic attitudes. Additionally, AQ was significantly

associated with psychological distress. Thus, pharmacists with high ALTs showed 239 240 decreased empathy and impaired psychological health. As expected, in our mediation 241 model, the ratios of path coefficients showed that 52.1% of the relation between AQ and 242 JSE was mediated by empathy subscales (perspective taking and empathic concern), and 24.8% of the relation between AQ and GHQ was mediated by empathy (personal 243 distress). This indicates that the associations revealed here are partly a result of factors 244 245 relating to empathy. 246 Our results indicated that overall emotional empathy (ECS), including items similar to 247 items in the IRI-EC and IRI-PD, had a significant but weak inverse correlation with AQ. 248 Consistent with previous research, this indicates that those with high ALTs may have intact emotional empathy when IRI-EC and IRI-PD are not discriminated [37]. 249 Pharmacists with high ALTs have biased empathy (low perspective taking, low 250 empathic concern, and high personal distress). Thus, they display weak cognitive 251 252 empathy but almost intact emotional empathy. However, the latter is biased to personal 253 distress. This biased empathy could cause two undesirable results: lower empathic attitude in a medical context and higher risk of psychological problems. 254 255 We found an inverse correlation between AQ and JSE. This result is consistent with previous research showing that people with ASD are unlikely to display empathic 256 behaviour [37]. Previous work suggests that individuals with ASD need to emotionally 257 258 regulate themselves to overcome strong personal distress, but often have weak emotion regulation abilities [38]. This leads to a failure of appropriate empathic behaviour and to 259 psychological distress when they are forced to act prosocially. This finding is consistent 260 with our results, which indicate a positive correlation between AQ and GHQ-12. 261

262 It has been suggested that the key skills necessary for oncologists engaged in patient-centred medical care, such as exploring patients' perspectives and responding to 263 264 emotion with empathy, can be learned through interventions like CST [39]. Additional 265 interventions exist that can improve physicians' empathic behaviour. For example, 266 emotion regulation skill training can improve empathic behaviour when personal distress causes negative emotions [40]. On a different note, some research shows that 267 reading literary fiction improves the skill of understanding the mental states of others 268 [41]. There have been attempts to introduce literature to medical education programs to 269 270 promote empathy among physicians [42]. Such interventions for improving deficits in 271 understanding patients' perspectives may also be helpful for those with high ALT 272 levels.

Our results indicate a need to develop specialized interventions for medical staff with 273 high ALT levels to reduce their psychological distress. One survey of primary care 274 275 physicians reported improvement in empathic attitude and psychological health 276 following an educational program for mindfulness [43]. Similarly, a controlled study demonstrated that adult patients with ASD suffering from anxiety and depression 277 278 symptoms benefit from mindfulness-based therapy, although the targeted population 279 was not medical staff [44]. Another study examined the effectiveness of a cognitive 280 behavioural intervention program for ALTs characterized by psychological distress 281 deriving from social deficits [45]. Thus, we believe that CST and mindfulness training would increase JSE scores and that mindfulness training and CBT would decrease GHQ 282 283 scores.

Compared with scores in previous studies [19-22], the mean AQ and JSE scores in thisstudy were within normal range, suggesting that no intervention is necessary for these

participants. Nevertheless, we believe that effective patient care requires a more 286 287 empathic attitude. However, the findings of one RCT that a CST targeting residents and 288 nurses with little experience resulted in a slight increase in patients' depressive symptoms [46] suggests that the success of interventions to increase empathy may 289 290 depend on the type of subjects (and on the presence of ALTs, as the present findings indicate). Thus, we need to determine appropriate targets of effective interventions. 291 292 Our study has some limitations. First, this was a cross-sectional study. Therefore, the 293 causality between variables cannot be definitely determined. Second, the response rate 294 was less than 50%, perhaps because the 118-item questionnaire was too large; as such, 295 there may have been selection bias. However, given that the received responses were 296 anonymous, the possibility of reporting bias may be considered low. Third, the JSE is a self-administered questionnaire and although it is used worldwide to examine the 297 empathic attitude of various medical professionals, future observational research of 298 299 pharmacist behaviour and patient outcomes is needed. Fourth, a single question was 300 perhaps insufficient to confirm that hospital pharmacists really engaged in direct patient care, and this question might have been difficult for respondents to interpret. Finally, 301 302 the generalizability of the present study to the rest of the world may be limited because our participants were drawn from a specific area in Japan. Additionally, this study was 303 performed to reflect mainly the oncology care situation in Japan; thus, the external 304 305 validity of our findings for other countries may be limited.

306

307 Conclusion

For pharmacists required to engage in empathic behaviour in a medical context, ALTs
may affect empathic attitude, which in turn may affect patient outcome. ALTs may also

- affect pharmacists' own psychological health. While interventions such as CST can
- 311 improve empathic attitude, our results suggest caution when using these with people
- 312 with high ALT levels. We should consider whether these interventions improve
- 313 empathic attitude in those with high ALT levels, and whether enhancement of empathic
- behaviour increases psychological distress, especially in this group. The development of
- 315 more specific interventions may be helpful for some individuals.

510	Texilo wreagements
317	The authors thank the Okayama Society of Hospital Pharmacists for study participation,
318	and all the participants. The authors thank Akio Wakabayashi for permission to use the
319	Japanese AQ. The authors express their gratitude for the enormous help of Shoko
320	Yoshimoto for fund management and Yifei Tang and Kyoko Hageshita for excellent
321	data management.
322	
323	Funding
324	This study was supported by the Research for Promotion of Cancer Control
325	Programmes (H26-Gan Seisaku-ippan-002 and H25-Seishin-ippan-001) Health and
326	Labour Sciences Research Grants from the Ministry of Health, Labour and Welfare,
327	Japan.
328	
329	Conflict of interests
330	The authors declare that they have no conflicts of interest.

331

316 Acknowledgements

332 **References**

- 333 1. Liekweg A, Westfeld M, Jaehde U. From oncology pharmacy to pharmaceutical care: new
- 334 contributions to multidisciplinary cancer care. Support Care Cancer 2004;12:73-9.
- 2. Pollak KI, Arnold RM, Jeffreys AS, Alexander SC, Olsen MK, Abernethy AP, et al.
- 336 Oncologist communication about emotion during visits with patients with advanced
- **337** cancer. J Clin Oncol 2007;25:5748-52.
- 338 3. Larson EB, Yao X. Clinical empathy as emotional labor in the patient-physician
 339 relationship. Jama-J Am Med Assoc 2005;293:1100-6.
- 340 4. Fujimori M, Shirai Y, Asai M, Kubota K, Katsumata N, Uchitomi Y. Effect of
- 341 Communication Skills Training Program for Oncologists Based on Patient Preferences
- 342 for Communication When Receiving Bad News: A Randomized Controlled Trial. J Clin
- **343** Oncol 2014;32:2166-72.
- 344 5. Fujimori M, Uchitomi Y. Preferences of Cancer Patients Regarding Communication of
- Bad News: A Systematic Literature Review. Jpn J Clin Oncol 2009;39:201-16.
- 346 6. Fujimori M, Oba A, Koike M, Okamura M, Akizuki N, Kamiya M, et al. Communication
- 347 skills training for Japanese oncologists on how to break bad news. J Cancer Educ
- **348** 2003;18:194-201.
- 349 7. World-Health-Organization. The Role of the Pharmacist in the Health Care System.
- 350 1994 <u>http://apps.who.int/medicinedocs/en/d/Jh2995e/2.2.html</u>. Accessed 21 Jun 2015.
- 351 8. American-Society-of-Health-System-Pharmacists. ASHP Statement on Pharmaceutical
 352 Care. Am J Hosp Pharm 1993;50:1720-3.
- 353 9. Wallman A, Vaudan C, Sporrong SK. Communications training in pharmacy education,
- 354 1995-2010. Am J Pharm Educ 2013;77:36.
- 355 10. Berger BA. Building an effective therapeutic alliance: competence, trustworthiness, and
- 356 caring. Am J Hosp Pharm 1993;50:2399-403.
- 357 11. Fjortoft N, Zgarrick D. An assessment of pharmacists' caring ability. Journal of the
- 358 American Pharmacists Association : JAPhA 2003;43:483-7.

12. Lonie JM. From counting and pouring to caring: the empathic developmental process of
community pharmacists. Research in social & administrative pharmacy : RSAP

361 2006;2:439-57.

- 362 13. Lor KB, Truong JT, Ip EJ, Barnett MJ. A randomized prospective study on outcomes of
- an empathy intervention among second-year student pharmacists. Am J Pharm Educ
 2015;79:18.
- 365 14. Lundstrom S, Chang Z, Kerekes N, Gumpert CH, Rastam M, Gillberg C, et al.

366 Autistic-like traits and their association with mental health problems in two nationwide

twin cohorts of children and adults. Psychological Medicine 2011;41:2423-33.

- 368 15. Lundstrom S, Chang Z, Rastam M, Gillberg C, Larsson H, Anckarsater H, et al. Autism
- 369 Spectrum Disorders and Autisticlike Traits Similar Etiology in the Extreme End and the
- 370 Normal Variation. Archives of General Psychiatry 2012;69:46-52.
- 371 16. Zaki J, Ochsner K. The neuroscience of empathy: progress, pitfalls and promise. Nat
 372 Neurosci 2012;15:675-80.
- 373 17. Mazza M, Pino MC, Mariano M, Tempesta D, Ferrara M, De Berardis D, et al. Affective
- and cognitive empathy in adolescents with autism spectrum disorder. Front Hum
- **375** Neurosci 2014;8:791.
- 376 18. Baron-Cohen S. Zero Degrees of Empathy: A new theory of human cruelty: Penguin
 377 Books Limited; 2011.
- 378 19. Baron-Cohen S, Wheelwright S, Skinner R, Martin J, Clubley E. The Autism-Spectrum
- 379 Quotient (AQ): Evidence from Asperger syndrome/high-functioning autism, males and
- females, scientists and mathematicians. J Autism Dev Disord 2001;31:5-17.
- 381 20. Wakabayashi A, Baron-Cohen S, Wheelwright S, Tojo Y. The Autism-Spectrum Quotient
- 382 (AQ) in Japan: A cross-cultural comparison. J Autism Dev Disord 2006;36:263-70.
- 383 21. Hojat M, Mangione S, Nasca TJ, Cohen MJM, Gonnella JS, Erdmann JB, et al. The
- 384 Jefferson Scale of Physician Empathy: Development and preliminary psychometric data.
- 385 Educ Psychol Meas 2001;61:349-65.

- 386 22. Hojat M, Gonnella JS, Mangione S, Nasca TJ, Veloski JJ, Erdmann JB, et al. Empathy
- in medical students as related to academic performance, clinical competence and gender.
 Med Educ 2002;36:522-7.
- 389 23. Hojat M. Empathy in Patient Care: Antecedents, Development, Measurement, and
- **390** Outcomes: Springer; 2007.
- 391 24. Hojat M, Mangione S, Kane GC, Gonnella JS. Relationships between scores of the
- Jefferson scale of physician empathy (JSPE) and the interpersonal reactivity index (IRI).
 Med Teach 2005;27:625-8.
- 394 25. Hojat M, Gonnella JS, Nasca TJ, Mangione S, Vergare M, Magee M. Physician empathy:
- 395 Definition, components, measurement, and relationship to gender and specialty.
- American Journal of Psychiatry 2002;159:1563-9.
- 26. Hojat M, Louis DZ, Markham FW, Wender R, Rabinowitz C, Gonnella JS. Physicians'
 empathy and clinical outcomes for diabetic patients. Acad Med 2011;86:359-64.
- 399 27. Del Canale S, Louis DZ, Maio V, Wang XH, Rossi G, Hojat M, et al. The Relationship
- 400 Between Physician Empathy and Disease Complications: An Empirical Study of Primary
- 401 Care Physicians and Their Diabetic Patients in Parma, Italy. Acad Med 2012;87:1243-9.
- 402 28. Kataoka HU, Koide N, Ochi K, Hojat M, Gonnella JS. Measurement of Empathy Among
- 403 Japanese Medical Students: Psychometrics and Score Differences by Gender and Level of
- 404 Medical Education. Acad Med 2009;84:1192-7.
- 405 29. Goldberg DP, Hillier VF. A scaled version of the General Health Questionnaire. Psychol
 406 Med 1979;9:139-45.
- 407 30. Goldberg DP, Gater R, Sartorius N, Ustun TB, Piccinelli M, Gureje O, et al. The validity
- 408 of two versions of the GHQ in the WHO study of mental illness in general health care.
- 409 Psychological Medicine 1997;27:191-7.
- 410 31. Davis MH. Measuring individual differences in empathy : Evidence for a
- 411 multidimensional approach. Journal of Personality and Social Psychology
- **412** 1983;44:113-26.

- 413 32. Aketa Y. Structure and measurement of empathy: Japanese version of Davis's
- 414 Interpersonal Reactivity Index (IRI-J). The Psychological report of Sophia University
 415 1999;23:19-31.
- 416 33. Doherty RW. The emotional contagion scale: A measure of individual differences. J
- 417 Nonverbal Behav 1997;21:131-54.
- 418 34. Kimura M, Yogo M, Daibo I. Development of a Japanese version of the Emotional
- 419 Contagion Scale. Japanese Journal of Interpersonal and Social Psychology 2007;7:31-9.
- 420 35. O'Brien E, Konrath SH, Gruhn D, Hagen AL. Empathic Concern and Perspective
- 421 Taking: Linear and Quadratic Effects of Age Across the Adult Life Span. J Gerontol
- 422 B-Psychol 2013;68:168-75.
- 423 36. Preacher KJ, Hayes AF. Asymptotic and resampling strategies for assessing and
- 424 comparing indirect effects in multiple mediator models. Behav Res Methods
 425 2008;40:879-91.
- 426 37. Hadjikhani N, Zurcher NR, Rogier O, Hippolyte L, Lemonnier E, Ruest T, et al.
- 427 Emotional contagion for pain is intact in autism spectrum disorders. Transl Psychiatry
 428 2014;4:e343.
- 429 38. Mazefsky CA, Herrington J, Siegel M, Scarpa A, Maddox BB, Scahill L, et al. The Role of
- 430 Emotion Regulation in Autism Spectrum Disorder. Journal of the American Academy of
- 431 Child and Adolescent Psychiatry 2013;52:679-88.
- 432 39. Epner DE, Baile WF. Difficult Conversations: Teaching Medical Oncology Trainees
 433 Communication Skills One Hour at a Time. Acad Med 2014;89:578-84.
- 434 40. Buruck G, Wendsche J, Melzer M, Strobel A, Dorfel D. Acute psychosocial stress and
- emotion regulation skills modulate empathic reactions to pain in others. Front Psychol2014;5:517.
- 437 41. Kidd DC, Castano E. Reading Literary Fiction Improves Theory of Mind. Science
 438 2013;342:377-80.
- 439 42. McLellan MF, Jones AH. Why literature and medicine? Lancet 1996;348:109-11.

440	43. Krasner MS, Epstein RM, Beckman H, Suchman AL, Chapman B, Mooney CJ, et al.
441	Association of an Educational Program in Mindful Communication With Burnout,
442	Empathy, and Attitudes Among Primary Care Physicians. Jama-J Am Med Assoc
443	2009;302:1284-93.
444	44. Spek AA, van Ham NC, Nyklicek I. Mindfulness-based therapy in adults with an autism
445	spectrum disorder: a randomized controlled trial. Research in developmental disabilities

446 2013;34:246-53.

447 45. White SW, Albano AM, Johnson CR, Kasari C, Ollendick T, Klin A, et al. Development of

448 a cognitive-behavioral intervention program to treat anxiety and social deficits in teens

449 with high-functioning autism. Clinical child and family psychology review 2010;13:77-90.

450 46. Curtis JR, Back AL, Ford DW, Downey L, Shannon SE, Doorenbos AZ, et al. Effect of

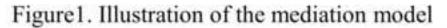
451 communication skills training for residents and nurse practitioners on quality of

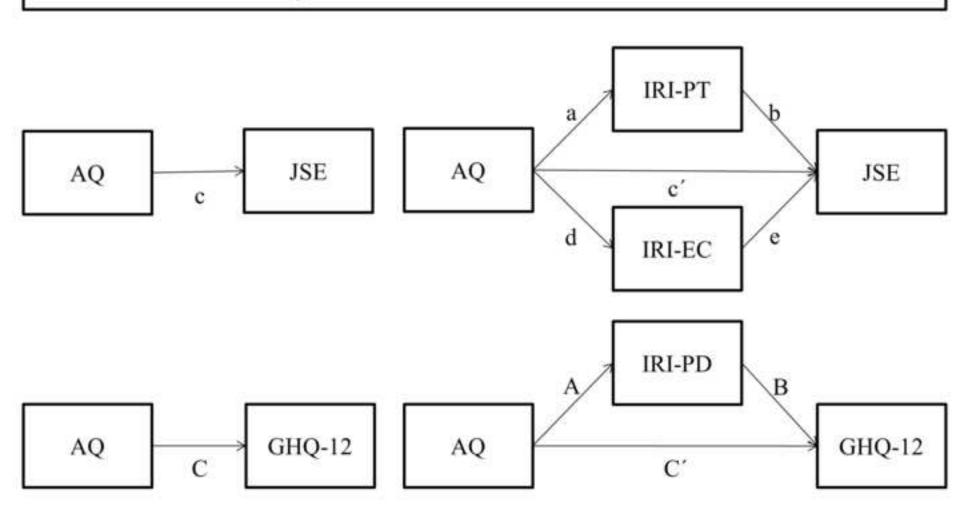
452 communication with patients with serious illness: a randomized trial. Jama

453 2013;310:2271-81.

454

455





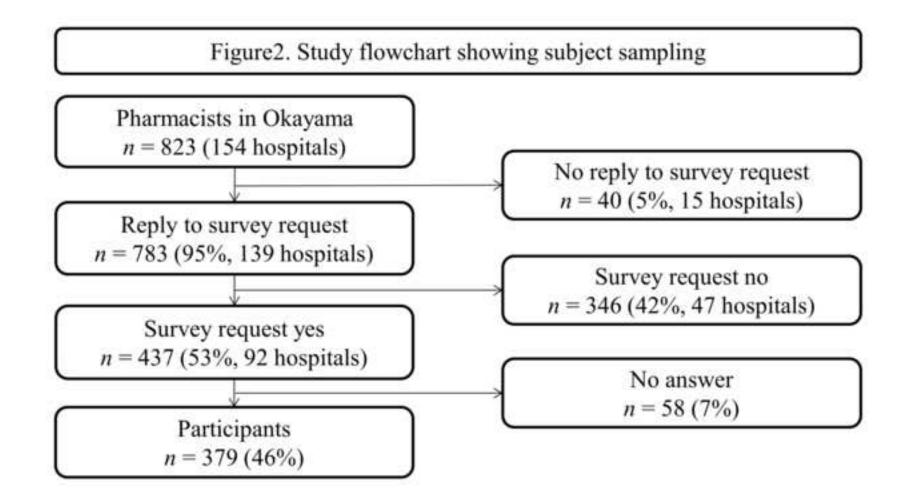
AQ: The Autism-Spectrum Quotient; JSE: The Jefferson Scale of Empathy GHQ-12: The General Health Questionnaire-12 IRI: The Interpersonal Reactivity Index PT: Perspective Taking; EC: Empathic Concern; PD: Personal Distress

Figure.1

Title: Illustration of the mediation model

Legend: The model hypothesizes that the Autism-Spectrum Quotient exerts an indirect effect on the Jefferson Scale of Empathy and the 12-item General Health Questionnaire through Interpersonal Reactivity Index subscales (Interpersonal Reactivity Index-Perspective Taking/Empathic Concern/Personal Distress). Path c represents the effect of the Autism-Spectrum Quotient on the Jefferson Scale of Empathy without indirect path. Path a represents the effect of the Autism-Spectrum Quotient on Interpersonal Reactivity Index-Perspective Taking. Path b represents the effect of Interpersonal Reactivity Index-Perspective Taking on the Jefferson Scale of Empathy partialling out the effect of the Autism-Spectrum Quotient. Path c' (= c-a*b-d*e) is the direct effect of the Autism-Spectrum Quotient on the Jefferson Scale of Empathy. The indirect effect of the Autism-Spectrum Quotient on the Jefferson Scale of Empathy. The indirect effect of the Autism-Spectrum Quotient on the Jefferson Scale of Empathy through Interpersonal Reactivity Index-Perspective Taking/Empathic Concern is a*b and d*e, which is tested with the bootstrap confidence interval obtained through the bootstrapping method.

Path C represents the effect of the Autism-Spectrum Quotient on the 12-item General Health Questionnaire without indirect path. Path A represents the effect of the Autism-Spectrum Quotient on Interpersonal Reactivity Index-Personal Distress. Path B represents the effect of Interpersonal Reactivity Index-Personal Distress on the 12-item General Health Questionnaire partialling out the effect of the Autism-Spectrum Quotient. Path C[′] (C-A*B) is the direct effect of the Autism-Spectrum Quotient on the 12-item General Health Questionnaire. The indirect effect of the Autism-Spectrum Quotient on the 12-item General Health Questionnaire through Interpersonal Reactivity Index-Personal Distress is A*B, which is also tested with the bootstrap confidence interval.



1 Figure 2

- 2 Title: Study flowchart showing subject sampling
- 3 Legend: (none)

4

	Particip	oants (n = 37				
Gender	n	%				
Men	151	39.8				
Women	228	60.2				
	Mean	Median	SD	Range		
Age ^a (years)	37.3	34	10.8	[24-66]		
Years after qualification	13.6	11	11.3	[0-44]		
Years after qualification ^b	14.1	11	12.2	[0-50]		
Hospital beds						
<100	33	8.7				
100–500	184	48.5				
>500	162	42.7				
Questionnaire results					Full rang	
ÂQ	19.7	19	7.3	[5-41]	[0-50]	
JSE	108.9	109	12.5	[58–140]	[20-140]	
GHQ-12 (Likert score)	14.8	14	4.8	[2-32]	[0-36]	
IRI-Perspective Taking	20.2	20	3.1	[9–28]	[7–28]	
IRI-Empathic Concern	19.9	20	2.9	[8–28]	[7–28]	
IRI-Personal Distress	16.3	16	2.5	[10-24]	[7–28]	
ECS	40.1	40	5.4	[23-60]	[1-60]	
AQ: The Autism-Spectrum						
Quotient						
JSE: The Jefferson Scale of E	Empathy				1	
GHQ-12: The 12-item General Health Questionnaire						
IRI: The Interpersonal Reacti	vity Index	ζ.				
ECS: The Emotional Contagi	on Scale					

Table 2. Results of	correlation	analyses					
	1	2	3	4	5	6	7
1:AQ	1						
2:JSE	-0.221**	1					
3:GHQ-12	0.419**	-0.123*	1				
4:IRI-Perspective Taking	-0.305**	0.309**	-0.053	1			
5:IRI-Empathic Concern	-0.298**	0.309**	-0.103	0.352**	1		
6:IRI-Personal Distress	0.462**	-0.076	0.436**	-0.174**	0.037	1	
7:ECS	-0.121*	0.255**	0.016	0.183**	0.338* *	0.186**	1
AQ: The Autism-Sp	ectrum Quot	ient					
JSE: The Jefferson S							
GHQ12: The 12-item		-	ionnaire				
IRI: The Interperson							
ECS: The Emotional		Scale					
$p^{**} > 0.001, p^{*} < 0.001$	5						

Table 3. F	Regression co	oefficients betwee	en variables ir	n the media	tion models
Associatio	n Between A	AQ and JSE			
	с	c´	a	b	a*b,
		(= c - a * b - d * e)			[Bootstrap 95% CI]
AQ on	-0.4378*	-0.2096*	-0.135**	0.7258**	-0.0980,
JSE	*				[-0.1739 to
					-0.0464]
			d	e	d*e,
					[Bootstrap 95% CI]
			-0.1229**	1.0587**	-0.1301,
					[-0.2323 to
					-0.0617]
Associatio	n Between A	AQ and GHQ-12			
	С	C	А	В	A*B,
		(= C-A*B)			[Bootstrap 95% CI]
AQ on	0.2696**	0.2027**	0.1506**	0.4443**	0.0669,
GHQ-12					[0.0332 to 0.1031]
AQ: The A	Autism-Spect	rum Quotient			
JSE: The J	efferson Sca	le of Empathy			
		General Health Qu	uestionnaire		
$p^{**} > 0.00$	$1, p^* < 0.05$				
Indirect ef	fects of recei	ving AQ on JSE a	nd GHQ-12 th	nrough IRI s	ubscales were
estimated,	controlling f	or sex and years a	fter qualificati	ion; bootstra	p 95% CIs were
obtained th	nrough the bo	ootstrapping metho	od evaluating	these indirec	et effects.
Regression	n coefficients	(a, b, c, c´, d, e, A	A, B, C, C') are	e illustrated	in Figure 2.