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1 **Evaluating Empowerment in Genetic Counseling Using Patient Reported**  
2 **Outcomes**

3 Running head: Evaluating empowerment arising from cancer genetic counseling  
4  
5

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41

42 **Conflict of Interests**

43 All authors have no conflicts of interest to declare.

44

45 **Data Availability**

46 The data that support the findings of this study are available from the corresponding  
47 author upon reasonable request.

48

## ABSTRACT

49 Data about patient-reported outcomes from cancer genetics services (CGS) are  
50 lacking but are essential to guide service evaluation and improvements. We measured  
51 improvement in empowerment, following genetic counseling in Singapore using a  
52 culturally-adapted version of the Genetic Counseling Outcome Scale (GCOS-24); and  
53 sought to identify factors associated with change in empowerment. The GCOS-24 was  
54 administered to 155 patients of the CGS, at pre- and post-counseling or testing  
55 timepoints. Of which, 110 patients underwent genetic testing. Individual pre- and post-  
56 counseling responses were subjected to Rasch analysis; the scale was subsequently  
57 split into Cognitive Control (CC) and Emotional Control (EC) domains. Associations of  
58 baseline characteristics with changes in pre- and post-CC and EC scores were  
59 assessed using multiple regression analysis. Both CC and EC scores showed  
60 significant improvement following genetic counseling and testing. While all items in the  
61 CC domain of being showed increases at follow-up, aspects of EC related to alleviating  
62 negative emotions ( $p = 0.88$ ) and hopelessness ( $p = 0.2$ ) did not demonstrate  
63 significant improvement. Our study revealed significant improvement in patient  
64 empowerment in patients who have received cancer genetic counselling, while  
65 revealing a need to cultivate hope and facilitate the alleviation of negative emotions in  
66 patients during genetic counselling.

67

68 Word count: 200

69

70 **Keywords:** Genetic Counseling, Genetic Testing, Genetic Services, Rasch Analysis,  
71 Regression Analysis, Hope

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73

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75

76 **INTRODUCTION**

77

78 Genetic counseling is a communication process which aims to help individuals and  
79 families understand and adapt to the medical, psychological, familial and reproductive  
80 implications of a heritable genetic condition.<sup>1,2</sup> Though the practice of clinical genetics  
81 was established in the 1970s,<sup>3</sup> evaluation of its impact on patient-reported outcomes  
82 has been lacking, due to the paucity in the availability of robust outcomes.<sup>4,5</sup>

83 In Singapore, there is a growing demand for cancer genetic services<sup>6,7</sup> and, as such,  
84 it is a priority to evaluate patient-reported outcomes from genetic counseling and  
85 testing. The lack of such information impedes progress in the field, as evidence-based  
86 improvements cannot be made.

87 The Genetic Counseling Outcome Scale (GCOS-24) (**Supplementary Materials 1**)  
88 is a validated genetics-specific Patient Reported Outcome Measure (PROM) and  
89 assesses patient-reported outcomes from genetic counseling and testing.<sup>8</sup> It captures  
90 a construct coined '*empowerment*', defined as '*a set of beliefs that enable a person*  
91 *from a family affected by a genetic condition to feel that they have some control over*  
92 *and hope for the future*'.<sup>9</sup> It encompasses components of decisional control, cognitive  
93 control, behavioural control, emotional regulation and hope. Furthermore, the GCOS-  
94 24 has demonstrated utility in service evaluation<sup>10</sup> and quality improvement<sup>11</sup> in  
95 genetic counseling services.

96 It has been used in a study of 42 patients from a cardiology setting in USA by Ishon et  
97 al<sup>12</sup>, which demonstrated significant improvement in empowerment scores, which  
98 consequentially led to a greater awareness for surveillance recommendations in  
99 patients following genetic counseling. In the psychiatric context, a recent publication  
100 which used the GCOS-24 on a larger sample size showed an increase in  
101 empowerment following genetic counseling.<sup>13</sup> Similar increases in empowerment were  
102 observed in Danish<sup>14</sup>, Dutch<sup>15</sup> and Spanish<sup>11</sup> validations of the GCOS-24.

103 However, one limitation of the GCOS-24 is that psychometric evaluation of GCOS-24  
104 has largely involved classical test theory to date. Rasch analysis, a form of item  
105 response theory, provides significant insight into the psychometric properties of a  
106 scale,<sup>16,17</sup> including: appropriate use of response categories; measurement precision;  
107 how well items 'fit' the underlying trait; how well the items measure a specific construct

108 (unidimensionality); targeting of item difficulty to participants' ability; and differential  
109 item functioning (DIF; item bias). Rasch analysis has used by Grant et al<sup>18</sup> to develop  
110 a short-form of the GCOS-24, to create a less burdensome scale for respondents that  
111 is similarly capable of capturing genetic counseling and testing-derived empowerment.  
112

113 The aims of this study were threefold. Firstly, we aimed to measure the improvement  
114 in patient empowerment, if any, following cancer genetic counseling using the GCOS-  
115 24; with the secondary intention to identify and understand the factors associated with  
116 change in empowerment. Finally, we aimed to evaluate the psychometric properties  
117 of the GCOS-24 using Rasch analysis.  
118

## 119 **MATERIALS AND METHODS**

### 121 **Study Design**

122 This was a single arm, pre-post counseling (intervention) study conducted between  
123 May 2016 and May 2017 at the Cancer Genetics Service (CGS) at the National Cancer  
124 Centre Singapore (NCCS). We represent a specialized cancer genetics service with  
125 master's level trained genetic counsellors working under a model of care adapted from  
126 the United States.<sup>19</sup> The CGS sees predominantly Singaporean Chinese, Malay, and  
127 Indian patients with a personal and/or family history of cancer referred from general,  
128 surgical, oncologic and gynecological specialties. The GCOS-24 was offered to  
129 English-speaking, adult ( $\geq 21$  years old) participants attending the CGS for the first  
130 time. Individuals with significant hearing impairment (questionnaire administration  
131 could take place over the telephone), cognitive impairment or any physical disability  
132 that prevented them from participating in the study were excluded. Written informed  
133 consent was obtained from all participants prior to the study and the study protocol  
134 was approved by the SingHealth Centralised Institutional Review Board (CIRB number  
135 2016/2367).  
136

### 137 **Study procedure**

138 Participants were recruited face-to-face at the clinic, and after informed consent was  
139 obtained, they were asked to complete the pre-counseling GCOS-24 prior to their first  
140 genetic counseling session. The recruitment process was conducted by a research  
141 coordinator (HS). The pre-test genetic counseling session was led by a genetic

142 counsellor (STL, EC, or YC) or a clinical cancer geneticist (JN). It typically included a  
143 verbal discussion, with the use of visual aids, to provide information on the suspected  
144 genetic condition and cancer risk assessment based on personal and family history.  
145 Counselling skills are applied to facilitate coping and adaptation to the knowledge of a  
146 possible hereditary condition that runs in the family. The goal of the session is to reach  
147 a shared decision for genetic testing between the participant and their families, that is  
148 aligned with clinical recommendations. These sessions generally lasted between 30  
149 to 45 minutes. Participants had the option of completing the post-counseling GCOS-  
150 24 via telephone, mail (written) or online methods (via Google survey), which was  
151 facilitated by a research coordinator (HS).

152  
153 During the counselling session, patients who met clinical testing criteria<sup>20</sup> were offered  
154 genetic testing to understand if they carried a pathogenic variant that predisposes  
155 them to cancer. There were also asymptomatic patients who came for genetic  
156 counseling as they were considering predictive testing for a familial condition. For  
157 patients who declined genetic testing, the post-counseling GCOS-24 was conducted  
158 2 weeks after their most recent counseling session. They were subsequently given an  
159 open date appointment. For patients who elected to undergo genetic testing, an in-  
160 person result disclosure appointment (with STL, EC, YC or JN) was scheduled 2 to 6  
161 weeks after, dependent on turnaround time for testing ordered. These appointments  
162 typically last for 15 to 45 minutes, dependent on the type of result that was returned.  
163 The post-counseling GCOS-24 was administered 2 weeks after results disclosure (i.e.  
164 4 to 8 weeks after they completed the pre-counseling GCOS-24).

165  
166 Participants also completed a sociodemographic questionnaire which captured  
167 information about their gender, age, ethnicity, education status, genetic testing subsidy  
168 eligibility (eligible <SGD\$1,800 monthly household income per person) and personal  
169 and family history of cancer. All data collected were anonymized.

170

#### 171 **Cultural Adaptation of GCOS-24**

172 The GCOS-24 scale comprises 24 items across five domains (decisional control: three  
173 items, cognitive control: six items, behavioral control: eight items, emotional regulation:  
174 three items and hope: four items) which are rated on a seven-point Likert-type  
175 response scale ranging from 'strongly agree' to 'strongly disagree'.<sup>21</sup> Scores are

176 summed to provide an overall ‘empowerment’ and domain scores, where higher  
177 scores equal higher levels of empowerment.

178

179 Because the GCOS-24 was developed in the UK, we first conducted some cognitive  
180 interviews with patients to assess the clarity and cross-cultural applicability of the  
181 GCOS-24 items for eliciting the required information.<sup>22</sup> English-speaking patients aged  
182 21 and above, who had previously received genetic counseling at the CGS (n=12),  
183 were interviewed by trained interviewers. Interviews were audio-recorded and noted  
184 on standardized interview forms (**Supplementary Materials 2**). Responses were  
185 reviewed iteratively by the study team (JY, EF, MM & JN), and were used to guide  
186 edits to the GCOS-24 to improve clarity and comprehensibility of the items  
187 (**Supplementary Materials 1**). There were no edits that changed the original meaning  
188 of items made (**Supplementary Materials 1**). Item 6 was modified to ‘*I can see that*  
189 *good things (e.g. early detection & personalized screening) have come from having*  
190 *this condition in my family.*’, where the examples of ‘*early detection & personalized*  
191 *screening*’ were added for better comprehension of what ‘*good things*’ might refer to.  
192 Item 10 was edited to ‘*I don’t know what could be gained from each of the options (e.g.*  
193 *genetic testing) available to me.*’, where the example of ‘*genetic testing*’ was included  
194 to explain what ‘*options*’ might refer to.

195

#### 196 **Other Modifications of the GCOS-24**

197 The response scale was modified to include a ‘*not applicable*’ option for items relating  
198 to children (items 3, 13, 19, 21, 24) to provide an appropriate response for those  
199 participants who did not have and were not considering children in the future. This was  
200 an outcome of participant feedback we received from the cognitive interview exercise.  
201 While the addition of a ‘*not applicable*’ option response may influence the  
202 psychometric properties of the instrument as it creates the potential for missing data.  
203 Unlike in classical test theory, where missing data is a problem, Rasch analysis does  
204 not require complete data in order to generate person measure estimates. Therefore,  
205 the addition of a ‘*not applicable*’ option instead has improved the psychometric  
206 properties of the GCOS-24 as participants are not forced to answer items irrelevant to  
207 them, and any ensuing missing data will not affect the score provided by Rasch  
208 analysis.

209



## 210 **Psychometric Assessment of the GCOS-24**

211 Rasch analysis was used to assess the psychometric properties of the adapted  
212 GCOS-24 using the Andrich rating scale model<sup>23</sup> with Winsteps software (version  
213 3.92.1), Chicago, Illinois, USA.<sup>24</sup> Rasch analysis transformed the ordinal ratings of the  
214 questionnaire into estimates of interval measures (expressed in log of the odds units,  
215 or logits) to allow for parametric testing.<sup>25</sup> Item bias, thereby DIF was assessed for  
216 gender, age, educational status and presence of strong cancer family history to  
217 establish possible associations between baseline patient characteristics with  
218 magnitude of change in empowerment. To ensure that differences between the pre-  
219 post counseling GCOS-24 scores were valid indicators of changes over time, pre-  
220 counseling and post-counseling GCOS-24 data were stacked and DIF for time points  
221 was assessed. Absence of DIF was considered evidence of invariance over time.

222

223 The adapted GCOS-24 displayed good precision (person separation index (PSI) > 2.0)  
224 and targeting (difference between person and item means <1.0) and no DIF for age,  
225 gender or time (**Table 1**). However, there was evidence of multidimensionality within  
226 the scale, with the eigenvalue for the first contrast >2.0, the variance explained by the  
227 first factor <50% and 3 mis-fitting items. Moreover, inspection of the standardized  
228 residual loadings for items indicated that 6 items were all relating to cognitive,  
229 behavioral or decisional control, loaded together. Therefore, based on this and the  
230 domain structure posited in the paper by Tirado et al,<sup>11</sup> this supported the splitting of  
231 GCOS-24 into two discrete scales which were analyzed separately: 1) 'Cognitive  
232 control' [CC] (items 1-3, 5, 7, 10, 12-18, 23 and 24), which encompassed making  
233 informed decisions about the future, forward planning, decision-making, the utilization  
234 of socioeconomic and health-related resources and systems and the integration and  
235 contextualization into one's own healthcare blueprint; and 2) 'Emotional control' [EC]  
236 (items 4, 6, 8, 9, 11, 19-22), which encompassed hope and emotional regulation.

237

238 The CC scale initially displayed disordered thresholds (meaning that some of the  
239 response categories were not being used as intended) and multidimensionality with a  
240 high eigenvalue, low variance explained for the first contrast and two mis-fitting items  
241 (**Table 1**). However, upon iterative removal of items 13, 12, 18 and 5, measurement  
242 precision increased and the disordered thresholds and multidimensionality were  
243 largely resolved. The emotional domain had suboptimal precision (PSI <2.0) and

244 possible evidence of multidimensionality (eigenvalue of first contrast >2.0) (**Table 1**).  
245 However, only three items (4, 11 and 21) loaded together, which was not enough to  
246 form a separate scale; therefore, no further splitting was applied.

247

### 248 **Statistical Analysis**

249 Responses of participants who failed to complete the post-counseling GCOS-24 were  
250 excluded from analysis. The patient sample was characterized using mean (standard  
251 deviation [SD]) and median (interquartile range [IQR]) for description of normally and  
252 non-normally distributed data respectively.

253

254 Wilcoxon signed-rank test was used to determine significant differences in the CC and  
255 EC domains post-intervention. We also present an item-by-item analysis as well as for  
256 the overall score. Additionally, effect sizes (ES; calculated as the difference in the  
257 mean scores between the baseline and follow-up examinations divided by the  
258 standard deviation (SD) of the scores for the baseline group) were utilized to determine  
259 clinically significant pre-post changes.<sup>26</sup> An ES of 0.20-0.49 was considered small,  
260 0.50-0.79 as moderate and  $\geq 0.80$  as large.<sup>27</sup>

261

262 The association of baseline characteristics with pre-post counseling changes in  
263 cognitive and emotional control domains were assessed by multiple regression models  
264 fit using the baseline characteristics as independent variables, with changes in CC  
265 and EC scores between baseline and post-counseling scores as dependent variables,  
266 respectively. For each model, variable selection was conducted via best subsets  
267 selection using the Akaike Information Criterion (AIC), leading to a final reduced  
268 model. All analyses were performed using Stata 15.0 (Statacorp LP, College Station,  
269 TX, USA), and statistical significance was defined as  $p < 0.05$ .

270

## 271 RESULTS

### 272 Baseline Characteristics

273 Of the 208 participants who were invited to participate in this study, 155 completed the  
274 GCOS-24 at both time-points and were included in the analysis (response rate:  
275 74.5%). Most were female (n=136, 87.7%), median age was 46 (18-71) years old, and  
276 majority were Chinese (n=111, 71.6%) (**Table 2**). Most patients (n=84, 54.2%) had a  
277 personal history of breast and/or ovarian cancer. Most patients had a personal (n=115,  
278 74.2%) and/or family history of cancer (n=109; 70.3%). The majority (n=110, 71.0%)  
279 of participants opted to proceed with genetic testing after counseling, where most  
280 consented to a multi-gene diagnostic test (n=96; 61.9%), while the remainder  
281 consented to a predictive test for a known familial pathogenic variant (n=14; 9.0%).  
282 Majority of our participants (n=79; 50.0%) received a negative or a variant of uncertain  
283 significance (VUS) genetic test result, others (n=21; 20.0%) received a positive genetic  
284 test result, while a minority (n=45; 29.0%) of participants declined genetic testing.

285

286

### 287 GCOS-24 Scores Pre- and Post-Intervention

288

289 Scores in both domains (CC and EC) (**Supplementary Materials 3**) increased  
290 following genetic counseling (**Table 3**). Overall post-intervention CC score [median  
291 1.23, IQR (-0.33 - 6.16)] was significantly higher ( $p < 0.001$ ) than the pre-intervention  
292 score [median 0.46, IQR (-1.10 - 3.55)]. A similar significant trend was noted for overall  
293 post-intervention EC scores [median 0.99, IQR (-1.14 - 6.41)] versus pre-intervention  
294 scores [median 0.61, IQR (-1.14 - 3.90)].

295

296 In our item by item analysis for CC, several items showed substantial increases post-  
297 intervention. For example, item 1 “I am clear ... why I am attending the clinical genetics  
298 service” [pre-intervention: median 0.56, IQR (-2.33 - 3.55); post-intervention: median  
299 2.74, IQR (-1.01 - 6.16);  $p < 0.001$ ], item 7 “I can control how this condition affects my  
300 family”, item 10 “I don’t know what could be gained of the options (e.g. genetic testing)  
301 available to me”, [pre-intervention: median 0.36, IQR (-2.74 - 4.11); post-intervention:  
302 median 1.93, IQR (-2.74 - 6.16);  $p < 0.001$ ], and item 17 “I don’t know what I can do to  
303 change how to condition affects me / my children”, [pre-intervention: median 0.55, IQR  
304 (-2.55 - 4.30); post-intervention: median 2.12, IQR (-0.77 - 6.16);  $p < 0.001$ ] (**Table 3**)  
305 demonstrated the largest effect sizes.

306  
307 The overall increase in scores for the EC domain was largely attributed to feeling more  
308 capable of coping with the condition post-counseling (item 9) [pre-intervention: median  
309 0.98, IQR (-2.04 - 3.90); post-intervention: median 0.98, IQR (-2.04 - 6.41),  $p=0.046$ ],  
310 being more positive about the future (item 20) [pre-intervention: median 0.90, IQR (-  
311 2.12 - 3.90); post-intervention: median 0.90, IQR (-2.12 – 6.41);  $p=0.024$ ], and learning  
312 the positive aspects of having such a diagnosis (item 6) [pre-intervention: median 0.69,  
313 IQR (-2.33 – 3.90); post-intervention: median 0.69, IQR (-2.33 – 6.41);  $p=0.014$ ].  
314 However, it was notable that genetic counseling had little to no impact on participants'  
315 feelings of being upset (item 4) and hopefulness for their children to have a rewarding  
316 family life (item 9).

317

### 318 **Baseline factors associated with change in CC and EC scores**

319 Compared to those without a family history of cancer, participants with a family history  
320 of cancer ~~was~~were significantly associated with a smaller increment in CC scores ( $\beta$ :  
321 0, -0.56; CI: -0.99, -0.03;  $p$  value = 0.036) (**Table 4**). Females was significantly  
322 associated with a greater increment in EC scores than males ( $\beta$ : 0, -0.61; CI: -1-17, -  
323 0.05;  $p$  value =0.033) (**Table 5**). Compared to participants who did not proceed with  
324 genetic testing, those who received a negative or VUS result were significantly  
325 associated with a greater increment in CC scores ( $\beta$ : 0, 0.76; CI: 0.28, 1.24;  $p$  value  
326 =0.002) (**Table 4**) and EC scores ( $\beta$ : 0, 0.78; CI: 0.35, 1.21;  $p$  value <0.001) (**Table**  
327 **5**). Similarly, participants who received a positive result were associated with greater  
328 increments in CC scores ( $\beta$ : 0, 0.81; CI: 0.21, 1.42;  $p$  value =0.009) (**Table 4**) and EC  
329 scores ( $\beta$ : 0, 0.64; CI: 0.10, 1.19;  $p$  value = 0.02) (**Table 5**) than participants who did  
330 not proceed with genetic testing. Of those who underwent genetic testing, the extent  
331 to which CC scores (**Table 4**) and EC scores (**Table 5**) increased were largely similar  
332 between participants who received positive results and those who received negative  
333 or VUS results.

334

335 **DISCUSSION**

336 Our study explored the impact of cancer genetic counseling provided by the NCCS  
337 CGS on patient empowerment using the culturally-adapted GCOS-24 instrument. We  
338 found a statistically significant increase in EC and CC scores following genetic  
339 counseling and testing (in patients who underwent genetic testing). These findings  
340 provide empirical evidence that genetic counseling provided by the CGS improves  
341 patient empowerment, thus highlighting its value in the delivery of genetics services in  
342 Singapore. Secondly, our psychometric analysis of the adapted GCOS-24 found that  
343 while the instrument as a whole was multidimensional, two key domains, namely CC  
344 and EC, were valid measures to assess the extent of patient empowerment arising  
345 from genetic counseling and testing.

346  
347 Our study found that CC and EC were significantly improved post-genetic counseling  
348 and testing, and with the magnitude of improvement greater for the CC domain. These  
349 findings are concordant with recent systematic reviews of clinical genetics outcome  
350 research which have concluded that patients benefit from genetic counseling and  
351 testing, particularly in the areas of knowledge, '*perceived personal control*' (PPC),  
352 improved risk perception accuracy, and reduced anxiety.<sup>28,29</sup> Our findings were largely  
353 concordant with that of Tirado et al,<sup>11</sup> who found that the overall GCOS-24 score  
354 improved post-counseling and testing, specifically the cognitive domain. This is  
355 consistent with our findings that patients were in a better position to establish control  
356 over their conditions, namely by managing how it affects their families. We also found  
357 that patients felt better equipped to navigate educational, financial and social  
358 resources available to consequentially make better autonomous decisions that are  
359 potentially life-altering for them and their descendants. Genetic counseling and testing  
360 was also observed to improve patients' knowledge of what they could do to change  
361 the impact of the condition.

362 With a growing demand for cancer genetic services in Singapore<sup>6</sup> and as the inclusion  
363 of genetic counsellors in patient care is increasingly found to be cost-effective,<sup>30</sup> our  
364 study demonstrates that this model of care is beneficial for patients in the Asian  
365 context, where patients benefit from increased empowerment following genetic  
366 counseling and testing. Genetic counseling has been found to provide patients with a  
367 better knowledge of surveillance and risk-reducing options,<sup>31</sup> which was subsequently

368 reported to empower patients in their decision-making regarding genetic testing by  
369 Augestad et al.<sup>32</sup>

370 Notably, there were items pertaining to feelings of sadness and hopelessness in the  
371 EC domain in which no statistically significant improvement was reflected. This is  
372 similar to Tirado et al<sup>11</sup> who highlighted a lack of significant improvement in the  
373 emotional regulation domain of the GCOS-24 (items 4, 11, and 21), which overlaps  
374 with the EC category defined here. These findings suggest a place for hope-based  
375 interventions, warranting research to understand how hope can be appropriately  
376 introduced during genetic counseling. Hope-based interventions, in the form of group  
377 therapy sessions where psychological questionnaires were administered, were found  
378 to be effective in allaying anxiety of patients with a predisposition to psychological  
379 conditions who were undergoing genetic testing.<sup>33</sup> Hope-based interventions, focuses  
380 on prioritizing hope in patients and encourages *goal-directed thinking*,<sup>34</sup> which enable  
381 recipients to achieve a higher dispositional hope. When achieved, patients benefit from  
382 greater psychological well-being, improved health knowledge, adoption of preventive  
383 health behaviors and adaptation to chronic illnesses. In the same vein, the reciprocal  
384 engagement model (REM) for genetic counseling provides a useful framework for the  
385 design of counseling strategies for the delivery of genetic results. These strategies  
386 have been proven to personalize the result communication and risk counseling  
387 process,<sup>35</sup> which could be a way to improve emotional control in patients receiving  
388 genetic results. The incorporation of such interventions in genetic counseling practice  
389 may promote the delivery of holistic care, whilst presenting a systematic approach to  
390 instilling and improving emotional regulation in patients. Our findings highlight the  
391 growing importance of addressing emotional issues in genetic counseling. This is  
392 consistent with a review of genetic risk communication measures, which found  
393 emotional counseling elements to confer more benefit than informational elements.<sup>36</sup>  
394 In our study, higher empowerment levels were observed in patients who elected to  
395 proceed with genetic testing over patients who declined testing, suggesting that  
396 patients who underwent testing possessed a better understanding of their condition,  
397 as well as medical and non-medical resources available. Furthermore, they were also  
398 the group identified with higher emotional control levels, which meant they could cope  
399 better with new information that genetic testing provides them with. A better

400 understanding of the motivations and deterrents for genetic testing in at-risk patients  
401 is also warranted.

402

403 Rasch analysis was used to optimize the psychometric properties of the GCOS-24,  
404 which found that the scale was multidimensional in its overall form. Multidimensionality  
405 is problematic as patients respond differently to subsets of items and, if an overall  
406 score is used, true changes in sub-domains may be masked or neutralized, thus  
407 affecting the study conclusions. Therefore, we recommend that an overall score be  
408 avoided for the GCOS-24 and that separate CC and EC domain scores should be  
409 reported instead. Our findings demonstrate the importance of using Rasch analysis to  
410 verify and optimize the psychometric properties of PROMs in clinical research and our  
411 application of Rasch analysis to the GCOS-24 represents a useful contribution to  
412 clinicians and researchers hoping to measure patient-reported outcomes such as  
413 patient empowerment following genetic counseling. However, given our relatively  
414 small sample size in a culturally-diverse Asian population, further studies of similar  
415 design are required to confirm our findings. Recently, another PROM has been  
416 developed for the measurement of outcomes research related to risk communication  
417 in genetic counseling as part of the FOCUS-GC (Framework for Outcomes of Clinical  
418 Communication Services in Genetic Counseling).<sup>37</sup> Further psychometric evaluation  
419 would be useful to determine if it is a useful PROM for measuring clinically significant  
420 changes in empowerment.

421

422 Strengths of our study include a cross-cultural adaptation of the GCOS-24 in an Asian  
423 population and our use of Rasch analysis to optimize the psychometric properties of  
424 the scale and enhance measurement precision and improve the robustness of our  
425 results; a well-characterized cohort with an equal distribution in age and a variety of  
426 cancers with suspicions for hereditary conditions, such as breast, ovarian, and  
427 colorectal cancers; inclusion of unaffected patients allowed us to measure genetic  
428 counseling-derived empowerment in individuals with a family history suggestive of a  
429 genetic condition.

430

431 There are several limitations to this study. Firstly, patient empowerment as  
432 operationalized in the GCOS-24 may not capture certain important patient reported  
433 outcomes that result from genetic counseling. This is complicated by the lack of  
434 consensus on tools reliable for such an assessment and what constitutes genetic

435 counseling-derived benefits.<sup>4</sup> The study conducted in U.K. utilized the EQ-5D scale  
436 and an internal audit survey tool for comparison, while our study was limited to the  
437 GCOS-24. Without EQ-5D, the calculation of Quality Adjusted Life Years (QALY)  
438 delivered to patients seen by the CGS was unattainable, which demonstrates the  
439 limitation of the GCOS-24 for use in economic evaluation of a service. However, in a  
440 study comparing EQ-5D against the GCOS-24,<sup>11</sup> EQ-5D was found to have  
441 problematic ceiling effects, with no detectable pre-post changes in scores, as it fails to  
442 capture patient outcomes of clinical genetics. Second, the post- GCOS-24 was  
443 administered relatively quickly after their genetic counseling session, which denied a  
444 longitudinal follow up of the patient's emotional status (including that of hope), which  
445 might prove more effective in capturing patients with a reduced ability for emotional  
446 regulation. It would be meaningful to clarify if poor emotional control is attributed to  
447 pre-existing conditions or in fact exacerbated by genetic counseling. Studies have  
448 identified several risk factors that predispose patients to long-term post-testing  
449 distress, namely a pre-existing history of anxiety, depression, or psychiatric  
450 conditions,<sup>38-44</sup> as well as pre-existing heightened cancer worry, elevated cancer risk  
451 perception, poor support networks, and an unfavorable test result. Voorwinden,  
452 Jaspers<sup>45</sup> Screening for patients who demonstrate these prognostic variables for  
453 increased psychological distress from genetic testing, would allow for the  
454 personalization of a counseling program for them, thereby facilitating better  
455 psychological adaptation to their condition.

456 Third, neither the CC or EC domains achieved perfect fit to the Rasch model, both  
457 demonstrating some evidence of multidimensionality, while the EC domain  
458 demonstrated suboptimal precision. Therefore, the results should be interpreted with  
459 caution and future studies with larger sample sizes are required to confirm our domain  
460 structure.

461

## 462 **CONCLUSION**

463 In conclusion, our study revealed that patients who received cancer genetic counseling  
464 by trained genetics clinicians experienced a significant improvement in empowerment.  
465 However, more emphasis must be placed on cultivating hope and alleviating emotions  
466 of distress in patients during genetic counseling. Finally, our study demonstrated the  
467 utility of Rasch analysis in revealing multidimensionality of the GCOS-24, for which



468 scores for cognitive control and emotional regulation should be reported separately.

469 **Authorship Contributions**

470 JY was responsible for design, acquisition, analysis and interpretation of data, as  
471 well as drafting of the manuscript for publication.

472

473 SYL was involved in the analysis and interpretation of the data as well as drafting of  
474 the manuscript for publication.

475

476 EC was involved in the analysis and interpretation of the data, and critically reviewed  
477 the manuscript for publication.

478

479 JL was involved in the analysis of the data and critically reviewed the manuscript for  
480 publication.

481

482 HS was involved in the acquisition of the data and critically reviewed the manuscript  
483 for publication.

484

485 STL was involved in the acquisition of the data and critically reviewed the manuscript  
486 for publication.

487

488 YC was involved in the acquisition of the data and critically reviewed the manuscript  
489 for publication.

490

491 MM was involved in the conception and design of the study, and critically reviewed  
492 the manuscript for publication.

493

494 EKF was involved in the design and data analysis of the study, and critically  
495 reviewed the manuscript for publication.

496

497 JN was responsible for the conception, design and progress of the study, critically  
498 reviewed the study at the stages of data acquisition, interpretation and manuscript  
499 drafting.

500

501

502

503 **Ethics Approval**

504

505 All procedures followed were in accordance with the ethical standards of the  
506 responsible committee on human experimentation (institutional and national) and with  
507 the Helsinki Declaration of 1975, as revised in 2000 (5). This study was approved by  
508 the SingHealth Centralised Institutional Review Board (CIRB number 2016/2367).

509

510 **Patient Consent and Confidentiality**

511 Informed consent was obtained from all patients included in the study.

512

513

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