# Translation and cross-cultural adaptation with preliminary validation of GCOS-24 for use in Spain

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**ABSTRACT**

The aim in this study was to translate and cross-culturally adapt the Genetic Counseling Outcome Scale (GCOS-24) for use in Spain and to carry out a preliminary psychometric validation in a sample of Spanish patients. With oversight by an expert panel, forward and backward translations were conducted to create the draft Spanish GCOS-24. Fourteen patients were recruited from a clinical genetics service in Madrid, Spain to participate in cognitive interviews designed to explore readability and interpretability of the draft. Following qualitative analysis of interview transcripts, a final version of the Spanish GCOS-24 was agreed with the expert panel. No significant cross-cultural differences were identified. The Spanish GCOS-24 was then completed prior to and 2-4 weeks after genetic counseling by 59 patients attending the service, and data were analysed using analysis of variance. Preliminary psychometric validation of the Spanish GCOS-24 showed significantly higher GCOS-24 scores after genetic counseling ($p<0.0001$), with good internal consistency ($\alpha=0.84$) and sensitivity to change over time, with a medium-to-large size effect (Cohen´s $d=0.70$). This compares well with the original English language GCOS-24. Findings demonstrate that the Spanish GCOS-24 has potential for use in evaluating clinical genetics services in Spain, but would benefit from assessment of test-retest reliability as well as structural and construct validity.

**Keywords:** Empowerment, genetic counseling, evaluation, patient-reported outcome measure, clinical genetics services, translation, cultural adaptation.

**Running Head:** Translation and cross-cultural adaptation of GCOS-24 for use in Spain.

## INTRODUCTION

Genetic counseling is a process of communication that can help patients, their partners and other family members to understand and adapt to the medical, psychological, familial and reproductive implications of having a genetic condition in the family (Resta et al. 2006). However, there is little agreement about the best way to evaluate genetic counseling interventions in terms of patient benefits delivered since it has been difficult to identify what are the outcomes that patients most value (Payne et al. 2008; Wang et al. 2004).

It is becoming increasingly important that clinical services can demonstrate that they provide benefits to the patients they serve. There are global moves to link healthcare funding to delivery of these benefits (Devlin and Appleby 2010; Snyder et al. 2012). One important way in which patient benefits are measured is using patient-reported outcome measures (PROMs). These are short questionnaires that capture patients' subjective outcomes from using healthcare, e.g. health gain. In England, all patients undergoing hip replacement, knee replacement, varicose vein and groin hernia surgery are asked to complete a set of PROMs before and after surgery, and these are used to assess effectiveness of the care delivered (Black 2013).

At present, collection of PROMs data is not routinely done for clinical genetics services, but this may change in the future. A recently developed PROM, the Genetic Counseling Outcome Scale (GCOS-24), has potential to be useful for assessing patient-reported outcomes (benefits) from genetic counseling interventions (McAllister and Dearing 2015; McAllister et al. 2011a). GCOS-24 captures a construct labelled "empowerment", defined as "set of beliefs that enable a person from a family affected by a genetic condition to feel that they have some control over and hope for the future" (McAllister et al. 2011b, p. 125). The "empowerment" construct was developed with significant patient involvement, and is grounded in extensive qualitative research with patients of clinical genetics services, representatives from patient support groups for genetic conditions, and genetics health professionals (McAllister et al. 2011b). The

"empowerment" construct summarises subjective outcomes from using clinical genetics services that are valued by those stakeholders and includes the following dimensions, captured by GCOS-24:

- Cognitive control: having a good explanation for what has happened in the family, and a good understanding of the risks for self and other family members, and of healthcare and other resources available.
- Decisional control: having clear options for managing the genetic disorder and its risks, and feeling able to make decisions between the options available.
- Behavioural control: being able to use health and social care resources effectively to reduce harm and improve the lives of self and other family members.
- Hope: having hope for a fulfilling family life for oneself, other family members and future descendants.
- Emotional regulation: feeling able to manage the emotional challenges of having a genetic condition in the family.

GCOS-24 is a PROM designed to capture empowerment and comprises 24 questions, each with seven Likert-style response categories, with scores ranging from 24 (lowest empowerment score) to 168 (highest empowerment score). GCOS-24 was subject to robust psychometric validation in large samples of patients and members of families affected by genetic conditions in the UK. This work demonstrated that GCOS-24 is valid, reliable and sensitive to change over time, with a medium-to-large effect size (McAllister et al. 2011a). GCOS-24 enables measurement of empowerment before and after genetic counseling, with significant positive change in GCOS-24 scores reflecting positive patient-reported outcomes. Evaluation of a psychiatric genetic counseling service in Canada identified significant improvement in GCOS-24 scores with a large effect size (Inglis et al. 2014). GCOS-24 has recently been used in a quality improvement initiative by a clinical genetics team in the UK, who found patients' GCOS-24 responses useful for providing insight into patients' needs, identifying where these needs were

being met or unmet, evidencing the benefits of the services provided and, importantly, for prompting consideration of areas of practice that required attention, thereby encouraging professional and service development (Costal Tirado et al., 2017).

The Spanish National Health System (*Sistema Nacional de Salud*) has a similar organisational structure to the British National Health Service (NHS). Health services in Spain are currently available to all residents, including access to clinical genetics services located in tertiary referral hospitals. It is noteworthy that the specialty of Clinical Genetics has only recently been recognised in Spain (Real Decreto 639/2014, Boletin Oficial del Estado, Julio 2014), so it is timely to have a tool to assess and evaluate genetic counseling in order to assist in the planning of how genetics services are provided in Spain. This is even more important with the implementation of increasingly complex molecular techniques, such as next generation sequencing (NGS) (van El et al. 2013). To date, no Spanish language version of GCOS-24 with appropriate cross-cultural adaptation is available for use in Spain. The term cross-cultural adaptation is used to describe a process that examines both language (translation) and cultural adaptation issues in the process of preparing a questionnaire for use in another setting (Beaton et al. 2000).

The aims in the present study were to use international guidelines for the translation and cross-cultural adaptation of health-related quality of life instruments to: (i) translate GCOS-24 into Spanish, (ii) examine any cross-cultural issues to ensure that the Spanish language version is appropriate for use in Spain, and (iii) carry out a preliminary assessment of the psychometric properties of the Spanish language GCOS-24 in a sample of patients referred to a genetics clinic in Madrid, Spain.

## MATERIAL AND METHODS

### Setting

La Paz University Hospital was opened in 1961, as part of the Spanish National Health System hospital network. It is the referral hospital for an area with a population of 820,000 inhabitants and provides a full range of medical services. It also serves as teaching hospital for the Autonomous University of Madrid. La Paz University Hospital has around 1,300 beds in four buildings: General Hospital, Rehabilitation and Traumatology Hospital, Maternity, and the Children's Hospital. There are about 50,000 admissions annually, more than 200,000 patients are treated by the emergency services, and more than 1,300,000 outpatients are seen.

The Institute of Medical and Molecular Genetics (INGEMM) at La Paz Hospital opened in August 2011 as an expansion of the Medical Genetics Unit to house the outpatient clinics, cytogenetics laboratory and both service and research molecular laboratories, all in one building. The outpatient clinics include the prenatal diagnosis clinic (staffed by two clinical geneticists with a special interest in fetal medicine), and the (general) clinical genetics clinic (staffed by two clinical geneticists with a special interest in dysmorphology and a genetic counsellor). About two thirds of the patients seen in the latter are pediatric patients and one third adult patients with a wide range of genetic conditions (neurological disorders, cardiovascular, hearing loss, carriers of monogenic disorders such as cystic fibrosis, etc). Patients are usually referred by hospital specialists or by general practitioners for diagnosis, genetic testing and/or genetic counseling. Although patients with a family history of cancer are initially assessed at the Familial Cancer Clinic, organised by the Oncology Department, family members with a demonstrable pathogenic variant in a cancer predisposing gene are referred to the genetics clinic for counseling. At the time of making an appointment at the clinic, all patients receive a leaflet explaining what the consultation entails.

**STUDY 1: GCOS-24 translation and adaptation to the Spanish language**

The aim in Study 1 was to translate the English language GCOS-24 into Spanish and conduct a cross-cultural validation study to ensure the Spanish language GCOS-24 is appropriate for use in Spain. The design of this study was informed by international guidance on translation and cross-cultural adaptation of health questionnaires and PROMs (Beaton et al. 2000; Wild et al. 2005), and by published standards for the methodological quality of studies on the measurement properties of health measurement instruments (Mokkink et al. 2010; Terwee et al. 2012; Mokkink et al. 2009). The developer of GCOS-24 (MM) was involved in the process from the outset. Figure 1 shows a graphic representing the stages of the adaptation process. The study was approved by the Hospital Ethics Committee. Informed consent was obtained from all individuals participants included in the study in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Stage 1: Initial translation**

A forward translation into Spanish was performed by a clinical geneticist (SGM) whose mother tongue is Spanish, and who has a good command of the English language and previous experience in health services research. In this initial translation several potentially controversial terms were identified.

**Stage 2: Back translation**

Two independent professional translators, whose mother tongue is English and with no medical background, translated the questionnaire back into English (BT1, BT2). Both translators were naïve to the concepts explored and totally blind to the original version of the questionnaire. This helped to identify unclear wording in the translation.

**Stage 3: Expert committee review**

An expert committee comprising the developer of GCOS-24 (MM), who is also a genetic counsellor, one of the translators (AS), two additional UK genetic counsellors, a Spanish clinical

geneticist (SGM) and a Spanish genetic counsellor (PMC) was convened to review each step of the process. The translators were provided with the original English language questionnaire to comment on the translations, after the two back-translations had been completed. A meeting was held by video-conference to review the discrepancies between the translations and discuss potential cross-cultural issues. For some items no consensus could be reached at this stage, and these were flagged to be discussed in the cognitive interviews and reviewed afterwards accordingly. A pre-final version for testing with a patient sample was generated.

**Stage 4: Cognitive interviews**

The aim of this stage was to check the understanding and interpretation of the translated items in a sample of Spanish patients attending the genetics clinic in Madrid, in order to assess the conceptual equivalence between the English and the Spanish versions of GCOS-24.

Cognitive interviews were conducted with a sample of patients from the target setting. Families with similar genetic conditions who were booked for a review appointment over a one-month period (November 2013), who had already received genetic counseling and were familiar with the process, were selected by the clinicians prior to the appointment and were invited to participate at the end of the consultation. Cognitive interviews were carried out in a structured way, according to international guidelines, with an interview guide (Online Resource 1) and using a "think-aloud" method (Drennan 2003; Irwin et al. 2009). Each subject read the questionnaire in the presence of the genetic counsellor (PMC). After reading each item, they were asked if they had understood the question, and if not, they were asked to suggest how would they change the words to make it more clear, and whether they thought the item was difficult to answer. They were encouraged to make comments. Both the meaning of the items and the responses were explored to ensure the adapted version retained its equivalence in the target setting. Special attention was paid to items highlighted as controversial by the expert committee and for which no consensus had been reached. Alternative wording was offered by participants for certain items. Participants were also asked

if the instructions were clear and if the rating scale was easy to use. Responses were analysed by genetic counsellor PMC using qualitative methods (content analysis) and descriptive statistics.

**Stage 5: Expert committee review**

A further meeting was held by the expert committee to discuss the findings from the cognitive interviews. A few additional minor changes were made and a final version of the Spanish language GCOS-24 was agreed upon.

**STUDY 2: Preliminary test of the GCOS-24 adaptation to the Spanish language**

The aim in Study 2 was to test internal consistency and responsiveness (sensitivity to change) of the Spanish Language GCOS-24 in a sample of Spanish patients attending a clinical genetics service. For this study, pediatric and adult patients referred for the first time to the (general) clinical genetics clinic at the INGEMM were selected over a period of ten months (May 2014 to February 2015), with conditions representative of the range of referrals seen in clinic: learning disability with/without associated anomalies and/or dysmorphic features, chromosomal anomalies, hereditary neurological disorders, cardiovascular disease, non-syndromic hearing loss, predictive testing for hereditary cancer, and a range of different monogenic conditions. Patients with non-specific intellectual disability or essential autism were excluded, as it was considered that the likelihood of identifiying a specific underlying cause in the majority of these cases is very low and the situation of these families, in terms of genetic counseling, might differ from those with a specified genetic condition or cause. Immigrants whose mother tongue was not Spanish were excluded. Immigrants from Latin America were also excluded because of cross-cultural differences, despite the same language, and the likelihood of not being fully familiar with the Spanish National Health System and the resources available.

Elegible individuals were identified and selected on a weekly basis at the Monday morning department meeting, when patients to be seen in clinic during the week are discussed and distributed among the clinical geneticists (SGM, FSS) and the genetic counsellor (PMC).

When the selected patients arrived at the reception desk on the day of the appointment they were given an information leaflet explaining the aims of the study, which also stated clearly that participation was voluntary. Those who agreed to participate let the secretary know, and were then approached by the genetic counsellor (PMC) who led them to a consultation room. They were asked to sign the informed consent form and proceeded to answer the questionnaire prior to genetic counseling (T0). If both parents or both members of the couple agreed to participate, only one of them was asked to complete the questionnaire. Once the questionnaire was completed, a date to complete the questionnaire after genetic counseling (T1) was arranged and a fresh blank copy of the questionnaire was provided to take home with them. Patients went on to attend the appointment with one of the clinical geneticists (SGM, FSS), who was unaware of whether they had accepted or not to participate in the study. A follow-up telephone call was held between 2-4 weeks later and patients were asked to complete the blank copy of the questionnaire provided and provide their responses to the genetic consellor (PMC).

Statistical analysis was performed with the IBM SPSS Statistics v.22 software for Windows with the assistance of two lecturers from the Sociology Department at Universidad Complutense de Madrid (MEEV, LFF). Paired samples t-test analysis was used to assess whether there was a significant difference between the group Spanish language GCOS-24 scores before (T0) and after (T1) genetic counseling. Cohen´s d statistic was used to measure the effect size. Internal consistency of the Spanish language GCOS-24 was assessed using Cronbach´s alpha.

**RESULTS**

**STUDY 1: GCOS-24 translation and adaptation to the Spanish language**

**Translation and adaptation process (stages 1 to 3)**

During the first expert committee meeting several discrepancies were identified between the translation and the original items. Scale response option 4 ("neither agree nor disagree"), initially translated as *indiferente* ("indifferent"), was replaced by its literal equivalent: *ni de acuerdo ni en desacuerdo*. In 10 of the 24 items (5, 7, 12, 13, 14, 15, 17, 19, 20, 24) the backward translation arrived at almost or exactly the same wording as in the original English language version and was therefore considered non-controversial. In 5 items (4, 8, 9, 10, 11), minor discrepancies were observed between the two backward translations and the original, due to a change of words that did not alter the semantic equivalence, and were therefore considered by the expert committee to be non-controversial:

| **Item** | **Original English wording** | **Spanish equivalent** |
|---|---|---|
| 4 | I get upset | *Me altera* |
| 8 | I feel positive | *Me siento optimista* |
| 9 | I am able to cope | *Puedo afrontar* |
| 10 | What could be gained | *Qué se puede conseguir* |
| 11 | It makes me anxious | *Me causa ansiedad* |

In the remaining 9 items (1, 2, 3, 6, 16, 18, 21, 22, 23) discrepancies involved more significant grammatical changes, either in the structure of the question or the choice of words, to achieve semantic equivalence:

1) Item 1: "I am clear in my own mind", the only idiomatic difference in the questionnaire, was translated as *Tengo claro*.

2) Clinical genetics "service" was translated in the forward translation to *consulta* and then back to "consultation". The expert committee consensus was to accept *consulta*, as this term in Spanish applies both to the premises and to the

appointment; the Spanish equivalent to "service" (*servicio*) was considered too broad and general.

3) The word "condition", which features in 15 of the 24 questions, was translated as *trastorno genético* ("genetic disorder"). The same word in Spanish (*condición*) is largely confined to the field of demography or sociology and seldom applied to health issues. *Trastorno genético* is also the term commonly used by the professionals in consultation, letters and medical reports. The developer of GCOS-24 (MM) intially expressed her objection to the use of "genetic" (disorder), because the intention when developing GCOS-24 was for it to be useful for evaluating the service for patients who do not get a diagnosis of a genetic condition or who are reassured after their use of the service. However, adding the term "genetic" to "disorder" makes it more specific and easier to understand in Spanish, as the use of *trastorno* by itself is more commonly used in the context of mental health issues and equivalent to "derangement" (e.g. "mental derangement").

4) Item 2 ("what the condition means") was translated as *las implicaciones* ("the implications"). This word was considered by some British members of the expert committee not to be of common usage in the UK, but it was argued by both the translator and the Spanish specialists that the Spanish word is in more common usage than the same word in English. This also applied to other words such as *repercusión* ("repercussion", instead of "impact", item 3) and *transmitir* ("to transmit", instead of "to pass on", item 21).

5) Item 6 (" I can see that good things have come from having this condition in my family") was considered somewhat challenging and difficult to comprehend in

Spanish. A negative form of the same question ("I can´t see that good things…") was preferred instead.

6) Item 18 (… who in my family "might be at risk") was translated as *podría afectarles* ("could be affected")

7) Item 22 ("I am powerless to do anything about this condition in my family") was translated as *No hay nada que pueda hacer en relación con este trastorno genético en mi familia* ("There is nothing I can do about…"), as it was considered it reflects better the meaning of "powerless".

8) "Guilty" (item 21) was translated as *responsable* ("responsible", "accountable"). The literal equivalent in Spanish (*culpable*) was considered too strong.

9) "Concerns" (item 22) was translated as *problema* ("problem") or *circunstancias* ("circumstances"). The same word in Spanish (*preocupaciones*) was considered too light, and *problema* more equivalent to "concerns" in the context of the question asked.

The use of these terms was to be explored and clarified in the cognitive interviews.

**Cognitive interview (stage 4)**

Sixteen out of 47 families were selected. Two declined to participate because of time constraints. Fourteen patients agreed to participate, reviewed the prefinal adaptation, explained their understanding of items, specifically those identified as potentially controversial or unclear, and made suggestions.

Instructions for completion of the Spanish language GCOS-24 were considered to be clear and easy to understand by all participants. Nine out of 14 participants considered that seven Likert-style response categories were excessive and there was no great difference between categories "agreeing" and "strongly agreeing"; likewise for "disagreeing" and "strongly

disagreeing". The expert committee, however, decided to keep the seven categories in order to be methodologically consistent with the original and to ensure comparability of results.

Table I shows the nine items for which consensus could not be reached by the expert committee, participant´s understanding of the items, the revised items and reasons for revision where applicable. The expert committee decided that it would be easier to understand item 6 ("I can see that good things have come from having this condition in my family") if it were phrased in the negative tense ("I can´t see that good things have come from having this condition in my family" – *No veo el lado positivo de tener este trastorno genético en la familia*). Indeed, 9 out of the 14 participants found the original wording of item 6 somewhat puzzling and difficult to comprehend:

- "Nobody gains anything from having a genetic condition in the family".
- "It sounds better" [in a negative form].

However, a significant proportion of participants found it more difficult to comprehend questions in a negative form: 5/14 for item 5 ("I don´t know where to go to get the medical help I/my family need(s)"), 3/14 for items 10 ("I don´t know what could be gained from each of the options available to me") and 12 ("I don´t know if this condition could affect my other relatives…"), and 5/14 for items 13 ("…nothing I decide will change the future for my children…") and 17 ("I don´t know who else in my family might be at risk…").

All participants considered the term *consulta* was the right term for the appointment at the clinical genetics service. Eleven out of the 14 participants indicated their preference for the term *trastorno genético,* instead of *condición:*

- "The term condition sounds to me as if the genetic disorder conditioned my life".

Alteración ("alteration") was suggested by two respondents.

Words considered to be in more common usage in Spanish than the same word in English, such as *implicaciones* ("implications", item 2) and *repercusiones* ("repercussion", item 3), were understood unambiguously by most (11/14) participants. *Consecuencias* ("consequences") was

suggested as an alternative term to repercussions. A few, however, were unclear about these questions:

- "It is difficult to know the implications before having been informed about the condition".
- "Repercussions? Do you mean physical, psychological, what repercussions?"

All participants understood unambiguously *podría afectarles* ("might be at risk") in item 18. In item 21 ("I feel guilty because I might have passed on this condition on to my children"), 10 out of 14 participants considered the word guilty (*culpable*) too strong and the term *responsable* ("responsible", "accountable") more appropriate. In the same question, all understood unambiguously the word *transmitir* ("to transmit") and preferred it to *pasar* ("to pass on").

Ten out of 14 participants were unclear about the meaning of *incapaz* ("powerless") in item 22 ("I am powerless to do anything about this condition in my family"). All participants understood unambiguously the alternative wording (*No hay nada que pueda hacer en relación con este trastorno genético en mi familia).*

In item 23 ("I understand what concerns brought me to the clinical genetics service"), the term "concerns" was replaced by Spanish equivalents *problema* ("problem") and *circunstancias* ("circumstances"). Both terms were understood, but over half of the participants preferred *circunstancias* and fewer of them *problemas*.

Interestingly, some participants found it difficult to understand the meaning of apparently common words in the context of the question: what was meant by "options" in item 10 ("I don´t know what could be gained from each of the options available to me"), and what was meant by "control" in item 7 ("I can control how this condition affects my family"):

- "Reproductive options? What was discussed in clinic? Social benefits?"
- "Control seems to imply that you are in full control when, in fact, in these situations, many things get out of control".

**Final adaptation**

Following further review and discussion by the expert committee based on the results of the cognitive interviews, a consensus was reached and a final adaptation was generated (figure 2). Table II shows the COSMIN score for cross-cultural validity.

**STUDY 2: Preliminary test of the GCOS-24 adaptation to the Spanish language**

**Sample characteristics**

Of the 114 patients elegible to participate in the study, six failed to attend the appointment. Twenty eight of the 108 (26%) declined and 80 (74%) agreed to participate. Of these, 59 (73.7%) completed both questionnaires (T0 + T1) within the study period. Twenty one patients failed to complete the second questionnaire because they could not be contacted in time.

All the items in the Spanish language GCOS-24 were answered by all participants and there were no missing data. It should be noted that, although the genetic counsellor was present and available to clarify any questions that should arise while the patients completed the questionnaire, there were no significant difficulties understanding the questions, in contrast with the experience during the cognitive interviews. In 20 instances (33.9%) it was the patient him/herself who answered the questionnaire, in 34 (57.6%) it was the father or mother, and in five (8.5%) a different family member (sibling, uncle, foster parent). The mean age of respondents was 38.6 years (age range: 17-64). Over half of respondents (32, 54.2%) were women. Thirteen (22%) described themselves as affected by the condition, 29 (49.1%) as parent of an affected child, 2 (3.4%) as concerned that they may be at risk for developing the genetic condition themselves, and 43 (76.3%) as concerned that they may be at risk for having an affected child. There were overlaps between these four groups. Table III shows the sample characteristics and the genetic condition in the family.

**Preliminary psychometric validation of the Spanish language GCOS-24**

The internal consistency of the Spanish Language GCOS-24 in our sample was good (Cronbach's $\alpha$ = 0.84). Empowerment scores after clinic attendance (mean score post-clinic =

123.49, standard deviation = 15.43) were significantly higher than before clinic attendance (mean score before-clinic = 113.08, standard deviation = 14.09), ($t(58)= 6.322$, $p<0.0001$), with a medium-to-large effect size (Cohen's d = 0.70). This suggests that the Spanish Language GCOS-24 is responsive to change in empowerment levels following attendance at a clinical genetics service.

## DISCUSSION

### Strengths of the study

This is the first study to report the translation, cross-cultural adaptation and preliminary psychometric validation of a patient-reported outcome measure suitable for use with Spanish patients of clinical genetics services, following international guidelines for cross-cultural adaptation of health measurement scales. It is the second study to report on successful translation and implementation of GCOS-24 in a non-English speaking clinical genetics context. A Danish translation has also been developed using a similar methodology, which demonstrated good internal consistency (Cronbach's $\alpha = 0.79$), although responsiveness (sensitivity to change) of the Danish GCOS-24 has not yet been assessed (Diness et al. 2017).

Few difficulties were reported by clinical genetics patients with understanding or interpretation of the GCOS-24 items when translated into Spanish, indicating that the Spanish language GCOS-24 retains the conceptual meaning of the original English language items. Most of the changes made concerned semantic differences. No significant cross-cultural differences were identified.

Cognitive interviewing is a useful method in the development and adaptation of questionnaires. It allows assessment of understanding and interpretation of the questionnaire items from the respondent´s perspective. However, it has also been criticized for being subjective and artificial (Drennan 2003). Both in the cognitive interview and in the preliminary

test, the majority of questions were well understood. Participants in the cognitive interview were more inquisitive about the actual meaning of some of the items, and this helped the team to adapt the wording to be more clear.

There was a high response rate in the preliminary validation test. A total of 74% of patients approached completed matched pre-clinic and post-clinic questionnaires. This response rate is significantly higher than in other studies using the English language GCOS-24: the Canadian study reported a response rate of 55% (Inglis et al. 2014) and the British study reported a response rate of 32.8% (McAllister et al. 2011a). In the former, participants were asked to complete the questionnaire at the beginning of the appointment in the clinic. In the latter, patients were contacted by letter prior to their first appointment, and those who returned a pre-clinic questionnaire were then sent a post-clinic questionnaire pack. In the current study patients were approached and invited to participate as they turned up on the day of the appointment, and the questionnaire was completed in the presence of the genetic counsellor. This might explain the higher response rate, but it also prevented selection bias in favour of more motivated patients being the only ones to reply to an invitation letter sent by post. However, the presence of the genetic counsellor may have influenced how participants responded to the questionnaire items. Whilst we acknowledge that this may have posed a threat to validity, it was emphasised to all participants that their responses would not be reported to the clinician who would see them in clinic, and that their responses would remain confidential.

**Study limitations**

The content validity of the Spanish language GCOS-24 was not assessed in this study as this was assured in the original development work for the English language GCOS-24 (McAllister et al. 2011a; McAllister et al. 2011b), which was developed following extensive qualitative research that identified the patient benefits from using clinical genetics services. The preliminary test of the Spanish language GCOS-24 in a sample of 59 patients attending the

genetics clinic showed statistically significantly higher empowerment scores after clinic attendance, with good internal consistency (Cronbach's α=0.84) and sensitivity to change over time with a medium-to-large effect size (Cohen´s d=0.70). This compares well with the original English language GCOS-24, which demonstrated very similar internal consistency (Cronbach's α = 0.87) and sensitivity to change over time with the same medium-to-large effect size (Cohen's d = 0.70). Internal consistency is considered good if values of Cronbach's alpha are between 0.70 and 0.95. However, Terwee et al. (2007) recommend a sample size greater than or equal to 100 for assessment of internal consistency, so the sample size in the present study was rather small. Although an effect size of 0.70 is considered medium-to-large, interpretability of the statistical effect size would benefit from assessment of how much change in GCOS-24 scores is meaningful and useful to patients. To this end, it will be important to establish the Minimum Clinically Important Difference (MCID) for GCOS-24, in English, Danish and Spanish, as this will contribute to interpretability of patient change scores following attendance at a clinical genetics service (King 2011).

Neither test-retest reliability, structural validity nor construct validity of the Spanish language GCOS-24 was assessed in the current study. For assessment of test-retest reliability, a follow-up study is planned with a sample of 100 patients from the same setting who will be asked to complete the questionnaire 2-4 weeks apart with no intervention in between, as both responsiveness and test re-test reliability are key properties of any measure intended for use as a PROM (McAllister and Dearing 2015). It would also be of interest to assess structural validity of the Spanish language GCOS-24 by exploring the dimensional structure using factor analysis, although this would require a larger sample size, with recommendations suggesting a sample size of seven times the number of items (n= 7 x 24 = 168) for GCOS-24 (Mokkink et al. 2010; Terwee et al. 2012; Mokkink et al. 2009). Construct validity assessment would require testing hypotheses regarding how GCOS-24 respondent scores correlate with respondent scores on other measures capturing theoretically related and unrelated constructs. The English

language GCOS-24 was validated against measures of health locus of control, perceived personal control (PPC), anxiety, depression, satisfaction with life and authenticity (McAllister et al. 2011a). Equivalent measures of PPC and authenticity are not available in Spanish, but there are Spanish language measures of satisfaction with life, anxiety, depression and health locus of control (Vázquez et al. 2013; Novy et al. 1995; Ruggero et al. 2004; Tomás-Sábado and Montes-Hidalgo 2016), so it would be possible to assess construct validity of the Spanish GCOS-24 in this way. However, completion of a large battery of questionnaires, containing up to 100 items, would be burdensome for patients.

For both the cognitive interviews and the preliminary psychometric assessment, families were selected who were attending the clinical genetics service for the first time, and who were therefore unlikely to have been previously exposed to genetic counseling. We excluded a small proportion of patients with non-specific intellectual disability and essential autism and their parents because in most of these cases no genetic cause is identified, recurrence risks remain uncertain, and there are limited reproductive options. This approach could be argued, but we do not think it represents a threat to the validity of the study. The same applies to the significant proportion of pediatric cases, a true reflection of the patients seen in our clinic. Regarding a possible “intervention” bias (i.e. clinical geneticists providing a better service for those patients who agreed to participate in the study), this is unlikely since they were blind to whether patients had agreed or declined to participate, and often they had already forgotten which patients had been selected as potential participants in the study.

Empowerment may be influenced by culture (McAllister et al. 2008; McAllister et al. 2011b). Findings in this study, and in the Danish study (Diness et al. 2017) support validation of empowerment as a suitable patient-reported outcome for clinical genetics services in non-English speaking European countries, and validation of GCOS-24 as an appropriate measure of this. Because of possible cross-cultural differences, further adaptation may be needed for use of the Spanish language GCOS-24 in Spanish-speaking Latin American countries. Indeed, we are

aware that there are significant differences in the pragmatic use of the Spanish language, not only between Spain and Latin American countries, but also between different Latin American countries. Therefore, we would caution against the use of our Spanish version with Latin American populations without further adaptation to the Spanish language as used in the specific country.

**Practice implications**

This study describes the translation, cross-cultural adaptation and preliminary psychometric validation of GCOS-24 for use in Spain. The methodology employed ensures that the Spanish language GCOS-24 is semantically and conceptually equivalent to the original English language GCOS-24. Further psychometric validation, in particular test re-test reliability assessment as well as structural and construct validity, and establishment of the MCID are needed to ensure that the Spanish language GCOS-24 will be useful to evaluate clinical genetics services in Spain, and could also be useful for identifying areas where services could focus on quality improvement (Costal Tirado et al., 2017). In Spain, where clinical genetics services are in their infancy, the Spanish language GCOS-24 may also be useful to demonstrate the positive effects of genetic counseling and to highlight the contribution that genetic counselors make to delivering positive patient outcomes in clinical genetics services. Because of possible cross-cultural differences, further adaptation may be needed for use of the Spanish language GCOS-24 in Spanish-speaking Latin-American countries.

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**Compliance with Ethical Standards**

**Conflicts of Interest:** Patricia Muñoz-Cabello, Sixto García-Miñaúr, Manuel Eliecer Espinel-Vallejo, Lorenzo Fernández-Franco, Alexandra Stephens, Fernando Santos-Simarro, Pablo Lapunzina-Badía and Marion McAllister declare that they have no conflicts of interest

**Human Studies and Informed Consent:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individuals participants included in the study.

**Animal Studies:** No animal studies were carried out by the authors for this article.

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**FIGURES AND TABLES**

Figure 1. Graphic representation of the stages of the adaptation process.

Figure 2. Final adaptation of GCOS-24 to Spanish language.

Table I. Items for which consensus could not be reached by the expert committee, participant´s understanding of the items, the revised items and reasons for revision where applicable.

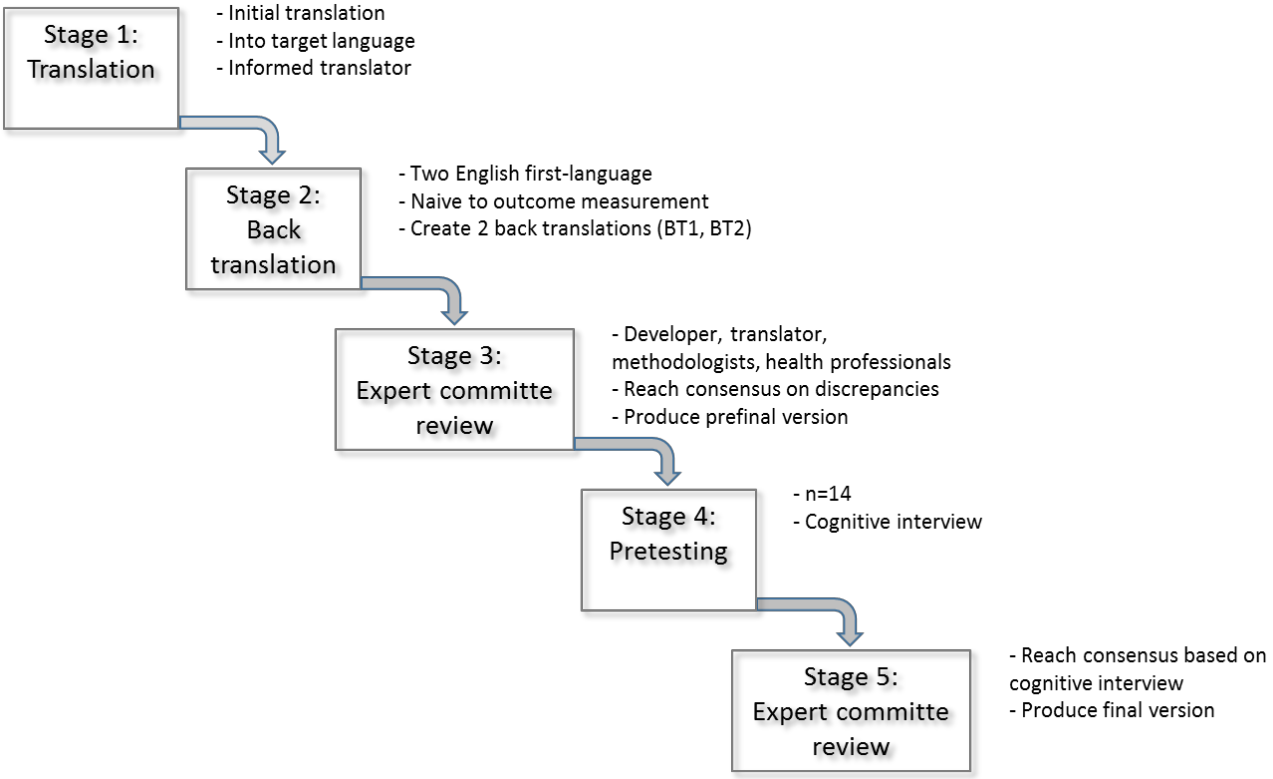
Table II. Cross-cultural validity COSMIN score.

Table III. Sample characteristics of participants in Study 2 (Preliminary test of the GCOS-24 adaptation to the Spanish language.

**Supplementary material**

Online resource 1 (ESM_1.pdf): Interview guide used for the cognitive interviews.

Figure 1. Graphic representation of the stages of the adaptation process (adapted from Beaton et al. 2003).



Figure

Click here to download Figure Munoz-Cabello P et al. Translation GCOS-24 ES_Figure 2.docx

# Escala de resultado del asesoramiento genético (GCOS-24)

Utilizando la escala que se muestra a continuación, **rodee con un círculo su grado de conformidad con cada una de las afirmaciones**. Por favor, **rellene todas las casillas**. Elija la opción 4 ("Ni de acuerdo ni en desacuerdo") si considera que la afirmación no se aplica a su caso.

**Escala de respuestas:**
**1 = Totalmente en desacuerdo**
**2 = En desacuerdo**
**3 = Algo en desacuerdo**
**4 = Ni de acuerdo ni en desacuerdo**
**5 = Algo de acuerdo**
**6 = De acuerdo**
**7 = Totalmente de acuerdo**

| | | Totalmente en descuerdo | En desacuerdo | Algo en desacuerdo | Ni de acuerdo ni en desacuerdo | Algo de acuerdo | De acuerdo | Totalmente de acuerdo |
|---|---|---|---|---|---|---|---|---|
| 1 | Tengo claro por qué acudo a una consulta de genética clínica | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 2 | Puedo explicar las implicaciones que tiene este trastorno genético a aquellos miembros de mi familia que necesiten saberlo | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 3 | Entiendo las repercusiones que este trastorno genético puede tener para mis hijos | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 4 | Me altera pensar en el trastorno genético que afecta a mi familia | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 5 | No sé dónde acudir para obtener la ayuda médica que mi familia o yo necesitamos | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 6 | No veo el lado positivo de tener este trastorno genético en la familia | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 7 | Tengo la sensación de que puedo controlar el modo en que este trastorno genético afecta a mi familia | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 8 | Me siento optimista con respecto al futuro | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 9 | Puedo afrontar la situación de que este trastorno genético se dé en mi familia | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 10 | No sé qué se puede conseguir con cada una de las opciones que me han ofrecido | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 11 | Me causa ansiedad tener este trastorno genético en mi familia | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 12 | No sé si este trastorno genético podría afectar a otros familiares (hermanos/as, tíos/as, primos/as) | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 13 | En relación con este trastorno genético, nada de lo que yo decida podrá cambiar el futuro de mis hijos o de los hijos que pueda tener | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 14 | Entiendo los motivos por los que mi médico me derivó a la consulta de genética clínica | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 15 | Sé cómo conseguir ayudas no médicas (educativas, económicas, de asistencia social, etc.) para mí o para mi familia | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 16 | Puedo explicar las implicaciones que tiene este trastorno genético a personas ajenas a mi familia que necesiten saberlo (profesores, asistentes sociales, etc.) | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 17 | No sé qué puedo hacer para cambiar el modo en el que este trastorno genético me afecta a mí o a mis hijos | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 18 | No sé a qué otros miembros de mi familia podría afectarles este trastorno | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 19 | Tengo la esperanza de que mis hijos puedan aspirar a tener una vida familiar gratificante | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 20 | Soy capaz de hacer planes de futuro | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 21 | Me siento responsable de haber transmitido, o de poder haber transmitido, este trastorno genético a mis hijos | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 22 | No hay nada que pueda hacer en relación con este trastorno genético en mi familia | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 23 | Entiendo las circunstancias que me han traído a la consulta de genética | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 24 | Puedo tomar decisiones sobre este trastorno genético que puedan cambiar el futuro de mis hijos o de los hijos que pueda tener | 1 | 2 | 3 | 4 | 5 | 6 | 7 |

Table I. Items for which consensus could not be reached by the expert committee, participant´s understanding of the items, the revised items and reasons for revision where applicable.

| **Original GCOS-24 item** | **Controversial terms in first Spanish version reached by expert committee (Literal English equivalent)** | **Revised version after Cognitive Interview** | **Reason for revision** |
|---|---|---|---|
| Clinical Genetics Service | *Consulta* (Consultation) | *Consulta* | All participants understood the word unambiguously and considered that it was the right term to use. |
| Condition | *Trastorno genético/Condición* (Genetic disorder/Condition) | *Trastorno genético* | Eleven out of 14 participants understood the wording and preferred it to *condición* (condition), considered ambiguous. Two participants suggested the term *alteración* (alteration). |
| …what the condition means | *Las implicaciones* (The implications) | *Las implicaciones* | Eleven out of 14 participants understood the wording unambiguously. Two participants considered difficult to know the full implications of a given condition without having been previously informed. |
| …the impact of the condition | *Las repercusiones* (The repercussions) | Las repercusiones | Eleven out of 14 participants understood the wording unambiguously. One participant was unclear about whether it referred to the physical or psychological impact. Two participants suggested the term *consecuencias* (consequences). |
| Might be at risk | *Podría afectarles* (Could be affected) | *Podría afectarles* | Understood by all participants |
| I feel guilty | *Me siento culpable/responsable* (I feel guilty / responsible) | *Me siento responsable* | Ten out of 14 participants considered the term *responsable* more appropriate |
| I might have passed | *Transmitir/Pasar* (To transmit/to pass on) | *Transmitir* | Understood by all participants |
| I am powerless | *No hay nada que pueda hacer* (There is nothing I could do) | *No hay nada que pueda hacer* | Understood by all participants |
| The concerns | *Los problemas /Las circunstancias* (The problems/circumstances) | *Las circunstancias* | Seven out of 14 participants preferred the term *circunstancias* and five *problemas* |

Table II. Cross-cultural validity COSMIN score.

| | Excellent | Good | Fair | Poor |
|---|---|---|---|---|
| **Design requirements**<br>1. Was the percentage of missing items given? | No missing items | | | |
| 2. Was there a description of how missing items were handled? | Not applicable | | | |
| 3. Was the sample size included in the analysis adequate? | | | | CTT (14)<br><120 |
| 4. Were both the original language in which the HR-PRO instrument was developed, and the language in which the HR-PRO instrument was translated described? | √ | | | |
| 5. Was the expertise of the people involved in the translation process adequately described? e.g. expertise in the disease(s) involved, expertise in the construct to be measured, expertise in both languages? | √ | | | |
| 6. Did the translators work independently from each other? | √ | | | |
| 7. Were items translated forward and backward? | | 1 forward, 2 backward | | |
| 8. Was there an adequate description of how differences between the original and translated versions were resolved? | √ | | | |
| 9. Was the translation reviewed by a committee (e.g. original developers)? | √ | | | |
| 10. Was the HR-PRO instrument pre-tested (e.g. cognitive interviews) to check interpretation, cultural relevance of the translation, and ease of comprehension? | √ | | | |
| 11. Was the sample used in the pre-test adequately described? | √ | | | |

| | | | | |
|---|---|---|---|---|
| 12. Were the samples similar for all characteristics except language and/or cultural background? | √ | | | |
| 13. Were there any important flaws in the design or methods of the study? | None identified | | | |
| **Statistical methods**<br><br>14. (for CTT): Was confirmatory factor analysis performed? | | | | Not performed |

(HR-PRO: Health-Related Patient-Reported Outcome; CTT: Classic Test Theory)

Table III. Sample characteristics of participants in Study 2 (Preliminary test of the GCOS-24 adaptation to the Spanish language)

| | **Number of participants (%)** |
|---|---|
| **Gender** | |
| Female | 32 (54.2%) |
| Male | 27 (45.8%) |
| **Age** | |
| Age range: 17-64 years | |
| Mean age: 38.6 years | |
| **Respondent** | |
| Patient himself | 20 (33.9%) |
| Mother or father | 34 (57.6%) |
| Other family member | 5 (8.5%) |
| **Described themselves as** | |
| Affected by the condition | 13 (22%) |
| Parent of an affected child | 29 (41%) |
| Concerned that they may be at risk for developing the genetic condition themselves | 2 (3.4%) |
| Concerned that they may be at risk for having and affected child | 43 (76.3%) |
| **Genetic condition** | |
| Learning disability with dysmorphic features | 17 (28.8%) |
| Neuromuscular | 8 (13.6%) |
| Cardiovascular | 6 (10.2%) |
| Chromosomal anomalies | 6 (10.2%) |
| Hearing loss (non-syndromic) | 4 (0.07%) |
| Cancer predisposition | 3 (0.05%) |
| Renal | 3 (0.05%) |
| Skeletal dysplasia | 3 (0.05%) |
| Other (cystic fibrosis, septo-optic dysplasia, cleft lip and palate, HHT, Hirschsprung´s disease, consanguinity, OTC, connective tissue disorder) | 9 (15.2%) |