1. General information

<table>
<thead>
<tr>
<th>Section</th>
<th>Institute</th>
<th>Postal address</th>
<th>Zipcode + city</th>
<th>Telephone</th>
<th>E-mail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coordinating investigator 1</td>
<td>Prof. dr. J. van der Palen</td>
<td>PO Box 217</td>
<td>7500 AE Enschede</td>
<td>06-31762463</td>
<td><a href="mailto:j.vanderpalen@mst.nl">j.vanderpalen@mst.nl</a></td>
</tr>
<tr>
<td>Institute</td>
<td>University of Twente</td>
<td></td>
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<tr>
<td>Section</td>
<td>Department of Research Methodology, Measurement and Data Analysis, Faculty of Behavioral Sciences</td>
<td></td>
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</tr>
<tr>
<td>Coordinating investigator 2</td>
<td>Dr. P.D.L.P.M. van der Valk</td>
<td>PO Box 50000</td>
<td>7500 KA Enschede</td>
<td>053-4872610</td>
<td><a href="mailto:p.vandervalk@mst.nl">p.vandervalk@mst.nl</a></td>
</tr>
<tr>
<td>Institute</td>
<td>Medisch Spectrum Twente</td>
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<tr>
<td>Section</td>
<td>Department of Pulmonary Medicine</td>
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<tr>
<td>Coordinating investigator 3</td>
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<td>Section</td>
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1.2 Financial administr.

<table>
<thead>
<tr>
<th>Institute</th>
<th>Wim Smit</th>
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<th>Zipcode + city</th>
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<tbody>
<tr>
<td>Institute</td>
<td>University of Twente</td>
<td>PO Box 217</td>
<td>7500 AE Enschede</td>
<td>053 – 489 5436</td>
<td><a href="mailto:w.smit@utwente.nl">w.smit@utwente.nl</a></td>
</tr>
<tr>
<td>Position</td>
<td>Financial projectadministrator</td>
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</table>

Lees s.v.p. zorgvuldig de handleiding.
Klik bovenaan de 1e pagina in de cel ‘Coordinating investigator 1’. Gebruik de tab-toets om binnen pagina 1 naar een ander veld te gaan. Klik bovenaan de volgende pagina weer in de 1e cel (vraag 1.3) om verder te gaan. Gebruik daarna weer de tab-toets.
### 1.3 Title of project:

<table>
<thead>
<tr>
<th>Language</th>
<th>Description</th>
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<tbody>
<tr>
<td>English</td>
<td>Development and evaluation of a Computerized Adaptive Test for measuring Quality of Life in patients with COPD</td>
</tr>
<tr>
<td>Dutch</td>
<td>Ontwikkeling en evaluatie van het meten van Kwaliteit van Leven via Computerized Adaptive Testing in patiënten met COPD</td>
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### 1.4 Time schedule:

<table>
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<th>Time</th>
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<tr>
<td>Start of project</td>
<td>01-08-2012 (dd-mm-yyyy)</td>
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<tr>
<td>Duration of project</td>
<td>41 (months)</td>
</tr>
<tr>
<td>Period of funding</td>
<td>from 01-08-2012 (dd-mm-yyyy) till 31-07-2015 (dd-mm-yyyy)</td>
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</tbody>
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### 1.5 Grant

| € 250.000 |

### 1.6 Short description of the project for public information (in Dutch, see guidelines) (max. 250 words):

Kwaliteit van leven kan worden onderverdeeld in een aantal domeinen die betrekking hebben op fysiek, sociaal en psychisch functioneren. Kwaliteit van leven wordt vaak gemeten met papieren vragenlijsten, die de patiënt zelf invult. Deze vragenlijsten zijn onder te verdelen in 'generieke' en 'ziekte-specifieke' vragenlijsten. Generieke vragenlijsten kunnen gebruikt worden bij patiënten met verschillende aandoeningen, terwijl ziekte-specifieke lijsten alleen kunnen worden gebruikt bij patiënten met een specifieke aandoening. Vaak worden in de praktijk zowel generieke als ziekte-specifieke lijsten gebruikt. Het doel van dit onderzoek was een nieuw, op de individuele patiënt toegesneden, meetinstrument te ontwikkelen om kwaliteit van leven bij COPD patiënten te meten. Dit type test heet een Computer Adaptieve Test (CAT); de vraag die wordt gesteld wordt uitgekozen op basis van het antwoord op de vorige vraag. De test kan er dus anders uitzien voor verschillende patiënten. In de test die we hebben ontwikkeld, verenigen we de voordelen van generieke, ziekte-specifieke en adaptieve tests. Op basis van interviews met COPD patiënten en health professionals hebben we de meest relevante domeinen uitgekozen voor het generieke deel van onze test: fysiek functioneren, sociale rollen en activiteiten, en vermoeidheid. Daarnaast hebben we op basis van bestaande vragenlijsten en interviews met patiënten vragen ontworpen voor het ziekte-specifieke onderdeel van de test. Deze vragen hebben betrekking op COPD-specifieke klachten, en hoe patiënten omgaan met de gevolgen van COPD. De ingevulde vragen worden automatisch omgezet in totaalscores, en deze worden weergegeven in een makkelijk te interpreteren grafiek om communicatie tussen arts en patiënt te vergemakkelijken.

### 2. Report

#### 2.1 Summary:

<table>
<thead>
<tr>
<th>Title</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Title of report</td>
<td>A report on the development of a multidimensional computerized adaptive test to measure quality of life in patients with COPD</td>
</tr>
<tr>
<td>Authors</td>
<td>Muirne Paap, Job van der Palen, Karel Kroeze, Cees Glas, Bernard Veldkamp</td>
</tr>
<tr>
<td>Dept./Institute(s)</td>
<td>Department of Research Methodology, Measurement, and Data-Analysis, Behavioral Sciences, University of Twente, Enschede, The Netherlands</td>
</tr>
<tr>
<td>Keywords (max. 6)</td>
<td>Item response theory; IRT; patient perspective; item bank; Chronic Obstructive Pulmonary Disease; CAT</td>
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</table>
### Abstract (max. 250 words):

We propose a new approach to measuring quality of life (QoL) in patients with Chronic Obstructive Pulmonary Disease (COPD): using a multidimensional Computerized Adaptive Test (CAT) based on generic as well as COPD-specific items. In addition to providing a very broad picture of QoL, it would ensure comparability with other patient groups and at the same time provide sensitivity for measuring change. Using a multidimensional CAT allows us to take into account the correlation among the different domains to increase efficiency and measurement precision. Items from three generic domains were selected from the framework of the Patient Reported Outcome Measurement Information System (PROMIS), using input from both patients and healthcare professionals. We developed disease-specific items based on a review of the literature, existing measures, and interviews with patients. The final item bank consisted of 148 PROMIS items and 46 COPD-specific items, and was calibrated using the multidimensional Graded Response Model using data from 795 Dutch COPD patients. Our results showed that multidimensional CAT resulted in more accurate and less biased QoL estimates than separate unidimensional CATs. An operational CAT was developed using an R package developed by our team, in conjunction with an interface developed by a specialized programmer. An automatic score report is generated based on the answers given by the test-taker, which includes a graphic representation of the estimated domain scores to facilitate patient-doctor communication as well as more detailed information designed for the HCP using this tool.

### 2.2 Description of original question/aim (max. 150 words):

The aim of this project was to develop and evaluate an item bank and a fully functional, clinically relevant and psychometrically robust multidimensional CAT for measuring HRQoL in patients with COPD, avoiding ceiling effects. The CAT can also be used to monitor a patient’s HRQoL over time, and detect changes in HRQoL as a result of treatment or interventions.

### 2.3 Results (max. 2500 words, please submit a maximum of 4 figures and diagrams separately):

The goal of this study was to develop a working computerized adaptive test (CAT) to measure health-related quality of life (HRQoL) in patients with Chronic Obstructive Pulmonary Disease (COPD). In the Appendix accompanying our first paper (Paap et al., 2014), we outlined which steps had to be followed to achieve this goal, namely:

1. Defining target domains and subdomains based on interviews with COPD patients and clinicians, a literature review, and existing frameworks;
2. Composing new items based on cognitive interviews and/or selecting individual items for each (sub)domain from existing generic and COPD-specific measures;
3. Constructing an item pool for each identified (sub)domain with special focus on content validity (whether the entire breadth of the (sub)domains is covered by the items);
4. Determining psychometric properties of the item bank using a representative sample of COPD patients resulting in a calibrated item bank ready for use;
5. Develop a working multi-dimensional CAT (MCAT).

These five steps have now all been successfully completed; the results of each step will be discussed in more detail below.

**Step 1: Defining target domains and subdomains**

We conducted two rounds of interviews in the first step: one round with COPD-patients (n=21) and one round with healthcare professionals (HCPs; n=13). We used a funnel-shaped interviewing strategy, starting with an open-ended question followed by the use of cues. The open-ended question focused on what aspects of HRQoL are important to COPD patients. In the second part of the interview, respondents were presented with cards on
which the name of a domain was printed and were asked to choose the domains which were most relevant to them (COPD patients). We used domains from the Patient Reported Outcomes Measurement Information System (PROMIS): an initiative originating from the US (funded by the NIH) with a focus on developing item banks covering physical, mental and social health. At the time of our study, 17 of these item banks were available in Dutch (Terwee et al., 2014). The interviews were transcribed verbatim, and analysed using open and axial coding. In addition, the number of times domains had been selected was counted. The results from the patient interviews and HCP interviews are presented in two separate papers. For feasibility reasons, we decided to not select more than 4 domains to be included in the MCAT. Taking the findings of two aforementioned papers together (Paap et al., 2014; Paap, Bode, Lenferink, Terwee, & van der Palen, 2015), we decided to include 3 PROMIS domains (Fatigue, Physical function, and Ability to participate in social roles and activities) and develop a new, COPD-specific item bank.

Step 2 and 3: Developing a multi-dimensional item bank
The PROMIS item banks Fatigue and Physical function are quite long and contain several item “sets” that are highly similar in content (and probably follow a Guttman scale (e.g., Fayers & Machin, 2007; Hays & Revicki, 2005)) as well as items that can be expected to be uninformative for COPD patients (based on expert judgement). Therefore, subsets of the Fatigue (50 items) and Physical Function (60 items) item banks were selected for inclusion in our CAT. The selection was done by a Dutch COPD expert, and reviewed by an expert from Canada. The Ability to participate in social roles and activities item bank consists of 35 items and was included in its entirety.

A review of the literature and the results of the patient interviews in the first step clearly indicated that there were themes important to COPD patients that were not covered by the PROMIS domains used as cues. Therefore, we decided to develop items for a COPD-specific domain. We used – with written permission of Prof. Paul Jones – items from a well-known legacy instrument as our starting-point: the SGRQ-C (Meguro, Barley, Spencer, & Jones, 2007). We evaluated candidate items both psychometrically and qualitatively (based on a new round of patient interviews; n=20) (Paap, Brouwer, et al., 2015; Paap, Lange, van der Palen, & Bode, 2015). Based on these evaluations, we selected a subset of SGRQ-C items and made adjustments to phrasing based on patient feedback. Next, we identified which themes had yet to be covered and identified items from other existing measures tapping into these themes. Subsequently, we wrote new items to cover remaining gaps. These two groups of items were subsequently evaluated in cognitive interviews (n=16) and rephrased based on patient input. Finally, the psychometric quality of the items in the COPD-specific bank was evaluated using a unidimensional Item Response Theory (IRT) model. Based on this analysis, a final selection of 46 COPD-specific items was made.

Step 4: Determining the psychometric properties of the multidimensional item bank
In order for an MCAT to work, an item bank is needed that is calibrated using a multidimensional IRT model. In this study, we used the multidimensional extension of the Graded Response Model (GRM); a model that is able to handle polytomous (Likert-scale) data. Two types of parameters were estimated for each item: a discrimination parameter (similar in interpretation to a factor loading) and threshold parameters. Theoretically, it is possible for items to load on (be related to) more than one content domain. This type of model is much harder to interpret, however. We chose to apply “simple structure”, meaning that each item loaded onto one content domain only; in other words, only one discrimination parameter (and not four) was estimated per item. The other three were constrained to 0. In a multidimensional model, only one set of threshold parameters can be estimated. They link the items to a position in the multidimensional space. The number of thresholds estimated per item equals the number of response categories minus one; just like in the unidimensional case. In addition to the item parameters, a covariance matrix is estimated which indicates the strength and direction of the relationships among the content domains. This information is used in the MCAT to enhance measurement efficiency and precision. We estimated the multidimensional GRM using data from 795
Dutch COPD patients. The estimated correlations between the domains were high: 0.76-0.86. The added value of using MCAT over unidimensional CAT (UCAT) is expected to be considerable in case of high correlations among domains.

**Step 5: Develop a working multi-dimensional CAT (MCAT)**

This step consisted of three parts:

1. Developing an R-package to generate MCATs (also referred to as the CAT “engine”)
2. Evaluating the performance of MCAT using simulation studies; and
3. Designing and developing a working CAT ready for implementation in clinical practice.

We used both real and simulated data for simulating CATs. We compared MCAT to UCAT, as well as a number of start and stopping rules. We compared fixed-length to variable-length conditions, and also evaluated whether starting with 3 items per domain would result in better estimates than using 1 start item per domain. The outcome variables used in the CAT simulation studies included bias and accuracy of the theta-estimates (estimates of content domain scores), as well as content balancing (number of items chosen per domain). The results of the simulation studies supported our choice for MCAT (instead of developing four unidimensional CATs: 1 per content domain). MCAT clearly outperformed UCAT with respect to bias and accuracy; this was especially true for short tests with fixed length (10 items). For variable-length tests, the gains of MCAT were highest for more extreme scores. Fixed-length tests resulted in better content balancing. By and large, using either 1 or 3 start items did not have substantial consequences for bias and accuracy.

The final product was built using several building blocks: CAT software (engine) especially developed for this project in an open source environment (R), a set of rules used as input for the CAT (these were based on the simulation study), a front-end which functions as a link between the person responding to questions and the CAT engine, and a design for a report that is automatically generated based on the responses entered by the respondent. The front end was developed by a specialized programmer familiar with establishing links between R packages and a front-end user interface (as well as databases in which the data can be stored). The MCAT is available as a so-called image, meaning that it can be installed on any PC or system and run locally. We will gladly demonstrate the MCAT at your convenience. In addition, we have been collaborating with the Dutch-Flemish PROMIS group so that our MCAT can be implemented within the framework they are developing together with VitalHealth as well.

**References:**


2.4 Did the study solve the original question? yes/no (explain) (max. 250 words):

Yes, the aim we set ourselves was met. We developed:

- A multidimensional item bank consisting of both generic COPD-relevant as well as COPD-specific items (providing both breadth and sensitivity to pick up change) that are of high psychometric quality;
- An MCAT engine in the open-source software R; and
- A multidimensional CAT that is ready for use (fully functional), tapping into domains that are deemed relevant by both patients and healthcare professionals (clinically relevant).

Our results showed that:

- Our item bank does not have a floor or ceiling effect; and
- Multidimensional CAT results in better QoL estimates compared to separate unidimensional CATs.

3 Papers (see instructions)

3.1 All publications (published or submitted peer-reviewed manuscripts):


Questionnaire for COPD patients (SGRQ-C). *Quality of Life Research*, Advance online publication. doi:10.1007/s11136-015-1192-3


3.2 All publications (not peer-reviewed like abstracts, newspapers, websites, etc.):

Published abstracts conference presentations:


Conference reports published on the Longfonds website:


4. **Implementation (see instructions):**

The developed Multidimensional CAT allows the accurate measurement of health-related quality of life in patients with COPD. It can be done online, with relatively few questions, and it assesses domains identified as most relevant to patients with COPD. The results are presented both graphically as well as numerically. These results can be used in a clinical setting as well as in a research setting.

**In a clinical setting:** The Multidimensional CAT can be used as a stand-alone instrument, providing clinicians with an assessment of health-related quality of life of their patients. An automatic report is generated, bypassing the necessity for manual scoring. A graphical representation is provided to the clinician, facilitating patient-doctor communication. Because of the fast and accurate assessment, it can be repeated often, with little burden for the patients and healthcare professionals. The hope is that in the future treatment can
(also) be adjusted, based on health-related quality of life, and not only on e.g. lung function tests. We are collaborating with the Dutch-Flemish PROMIS group so that our Multidimensional CAT can be implemented within the framework they are developing together with VitalHealth. VitalHealth develops assessment tools for general practitioners and they are interested to add our CAT to their arsenal. Also, VUMC is working on a repository of CAT’s to be offered to the medical community and they are very interested to add the Multidimensional COPD CAT as well.

For research: The Multidimensional CAT can be used in research settings as well. Health-related quality of life is nowadays one of the most important outcomes in many studies in COPD, both behavioural intervention studies as well as pharmaceutical studies. The Multidimensional CAT can measure health-related quality of life both accurately and with a high precision, in four relevant domains, and with relatively little burden to the patients. An advantage is that patients will only have to answer questions that are relevant to them, and they will be asked different questions each time they are asked to complete the online questionnaire. This will keep them motivated and will prevent choosing the same answers over and over again.

The Multidimensional CAT is operational, and can already be used by researchers and clinicians without restrictions. It is available as an image, meaning that it can be installed on any PC or system and run locally.

Follow-up research: In 2015 we applied for a Horizon2020 grant, where the development of a Multidimensional CAT for children with asthma was included. Unfortunately, the grant was not awarded. We are still looking for other opportunities to obtain funding to develop this. We are at present developing an item bank of relevant questions for children with asthma, again with the Dutch-Flemish PROMIS group. In the near future we will also try to calibrate this item bank.

**Ondertekening**

**Datum:** 28-4-2016

**Handtekening aanvrager:**

[Signature]