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Master's thesis

Statistical challenges in measuring hindrance in activities and participation of clients with acquired brain injury

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Thesis presented in fulfillment of the requirements for the degree of Master of Statistics

Transnational University Limburg is a unique collaboration of two universities in two countries: the University of Hasselt and Maastricht University.

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Statistical challenges in measuring hindrance in activities and participation of patients with acquired brain injury

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Abstract

Worldwide, many people incur an acquired brain injury which involves different function limitations in activities and participation. The encompassing objective of this study contains in finding statistical ways to analyze the hindrance in activities and participation of patients with acquired brain injury. Data as a result of the FINAH digital measuring instrument were available from 22 patients and their caregivers. A total of 53 ICF-items across different themes related to activities and participation, were used to measure the amount of hindrance caused by the brain injury. Factor analysis and latent class analysis were considered based on simulated data, to measure associations between items and to find underlying constructs. As a manner of illustration, both methods provided some different results, but items within a theme did not always correlate more often compared to items between themes. Generalized estimating equations (GEE) and generalized linear mixed models (GLMMs) were used to measure the effect of covariates on the experience of hindrance and the assessment quality of the professional caregiver. In 67% of the evaluations of the professional caregivers, the hindrance assessment was done properly. Theme had an effect on hindrance experience and assessment quality, with the largest amount of hindrance and smallest probability of correct assessment in mobility activities and the smallest amount of hindrance and best assessment for items related to interpersonal interactions and relationships. Setting was found to be a borderline case, with larger probability of hindrance experience for patients in the chronic setting compared to the ambulatory setting. Based on the results of the GLMM, patients indicated the smallest amount of hindrance, whereas professional caregivers reported the largest amount of hindrance. Moreover, using the GLMM, setting had an effect on the assessment quality with a better performance of the caregivers from the ambulatory setting and more overestimation of hindrance by caregivers from the chronic care setting.

Keywords: *Acquired brain injury, Hindrance, Factor analysis, Latent class analysis, GEE, GLMM*

1 Introduction

Yearly, over 10 million people incur an acquired brain injury across the globe (Bragge *et al.*, 2012). Acquired brain injury has many possible causes and can result in a large number of potential consequences for the individual, the partner, family members and people in the immediate social living environment. The World Health Organization defines acquired brain injury as an injury to the brain which is not hereditary, congenital or degenerative (Stables, 2010). The brain can be injured as a result of an accident, a stroke, alcohol or drug abuse, tumors, poisoning, infection and disease, near drowning, haemorrhage, AIDS, and a number of progressive neurological disorders such as Parkinson's disease, Multiple Sclerosis, and Alzheimer's disease (Synapse, 2013). Turner-Stokes et al. (2011) also mention diffuse acquired brain injury and other causes such as neurosurgical operations, radiotherapy, cerebral abscess, bacterial meningitis, and gunshot wounds. Traumatic brain injury is the most common cause of acquired brain injury and refers to an external injury to the brain which can be classified into two subgroups: closed head injury and penetrating head injury. A closed head injury occurs when an object suddenly and forcefully comes into contact with the head of an individual, while a penetrating head injury occurs when an object enters the individual's brain tissue. Most often a traumatic brain injury is a result of falls, motor vehicle accidents, being struck by an object, sports accidents, or physical assaults. The second major cause of acquired brain injury results from internal injury to the brain. A cerebrovascular accident or stroke, is the most common type of internal brain injury in which blood supply to the brain is disrupted. This loss of access to blood can cause brain cells to die, leading to brain injury. Because cerebrovascular accident can impact a variety of areas of the brain, the resulting damage and deficits vary across individuals (Rispoli *et al.*, 2014). While traumatic brain injury tends to have the highest incidence in people between the ages of 15 and 24, cerebrovascular accident is most likely to affect people over the age of 65 years (NINDS, 2002). The complications and difficulties that arise are varied and may include a range of hidden cognitive disabilities such as short-term memory loss, through to physical difficulties such as fatigue, paralysis and visual or hearing impairment (Synapse, 2013). These deficits can negatively impact the individual's social relationships, educational gains, employability, and community life (Ross *et al.*, 2011). They present to rehabilitation with various combinations of physical, communicative, cognitive, behavioural, psychosocial, and environmental problems. This means that each individual has a unique set of needs. Different individuals need different programmes of rehabilitation and, moreover, the same individual will need different programmes of rehabilitation at different stages in their recovery (Turner-Stokes *et al.*, 2011). Treatment goals for persons with acquired brain injury may be restorative or compensatory in nature by restoring or improving the individual's functioning and assisting the person in adapting their skill loss in order to interact with the environment (Rispoli *et al.*, 2014).

Worldwide, the statistics about brain injury are bald (Stables, 2010). Individual plans taking each person's skills and abilities into account can be developed but due to the complexity it is not straightforward. The ERNAH project, started in 2012, is a collaboration between five partners (hogeschool PXL, vzw Mané, stichting Adelante (NL), UC Leuven-Limburg and SEN vzw) and includes three subprojects, formulated from a diagnostic, a therapeutic, and advisory and sensitizing point of view. The project has the goal to improve the care for patients with acquired brain injury. The digital meter called FINAH is the end result of the diagnostic part with which the discomfort experienced as a result of a function limitation caused by acquired brain injury, is mapped. Starting point of FINAH is the international classification of functioning, disability and health (ICF) model (Houben, 2015). The ICF is a classification of health and health-related domains developed by the World Health Organization and provides a framework for measuring health and disability at both individual and population levels (World Health Organization, 2001).

The main goal of this study contains in finding statistical ways to analyze the hindrance in activities and participation of patients with acquired brain injury, based on the reported results of the FINAH digital measuring instrument. More specifically, it is of interest to explore the items and themes which are less or most frequently indicated as problematic by the patient or corresponding informal caregiver. Furthermore, one wants to know if the experience of hindrance differs for patients in the ambulatory and chronic setting of care and is influenced by possible other covariates. Another purpose is to investigate whether the formal caregivers estimate the restrictions as a result of acquired brain injury and associated hindrance, in an unambiguous and correct way. Again, it is of interest to study the effect of setting and other covariates on the quality of hindrance assessment by the professional caregiver. A last objective is to determine possible correlations between the answers on the different ICF-items and to investigate items which are given the same answers routinely by the patient or caregivers.

In sections 2 and 3 the data and methodology are described and explained. The main analyse proposals with emphasis on factor analysis, latent class analysis, generalized estimating equations and generalized linear mixed models are discussed and motivated in section 3. The results and associated interpretations are provided in section 4. Finally, in section 5 main conclusions and a brief discussion on the considered models and other possible analyze techniques are cited.

2 Data description

Data were available from 22 patients with acquired brain injury, 11 from Jessa hospital (ambulatory setting) and 11 from Mané (chronic setting), as well as from their corresponding caregivers. The digital FINAH instrument had been used and contains about 10 domains with corresponding items. The themes and items were built on the basis of activities and participation within ICF. Only the items from ICF that apply to the acquired brain injury were included in the screening tool. The following themes were used to measure possible hindrance: learning and applying knowledge, general tasks and demands, communication, mobility, self-care, domestic life, interpersonal interactions and relationships, major life areas, community, social and civic life, and emotion and behaviour. A total of 53 items across the different domains were considered in the FINAH instrument (see Table A1). The patient, his or her informal caregiver, and the professional caregiver indicated for each item whether they experienced discomfort. The following five possible categories were used: there is no problem, problem but no hindrance, hindrance for the patient, hindrance for the informal caregiver, or hindrance for both patient and informal caregiver. Only one answer could be given for each item. Besides, they indicated whether there is a need to work on the problem when there is a feeling of discomfort. In every case, the three corresponding individuals answered the questionnaire independently from each other. In addition to these items, also the acquired brain injury type (traumatic, internal or progressive neurological brain injury), the relation between the informal caregiver and the patient (parent of patient, partner of patient, other connection), and the age category of the patient and the informal caregiver, were collected.

3 Methodology

3.1 Hindrance dichotomization

In order to indicate whether a subject experienced hindrance, a dichotomization of all 53 variables was considered. If someone had no problem or a problem but no hindrance for a particular item, then he or she did not experience discomfort. In that case the binary hindrance response got value "0". For the other three nominal categories, where there was hindrance for at least one person, the binary hindrance response got value "1". Although some information was lost after this recoding process, information about the main interest, namely hindrance, was captured and in addition possible statistical techniques could be enhanced due to the elimination of the nominal nature of the data.

3.2 Exploratory data analysis

As a first attempt to gain insight in the data, an overview of the patients and informal caregivers who experienced hindrance is presented by item, theme, acquired brain injury type, the relation of patient and informal caregiver, and the setting. In addition, the items which were most indicated as problematic and those where there was no hindrance, are briefly discussed. Furthermore, differences in hindrance for both settings were explored via descriptive statistics.

Next, in order to explore whether the professional caregiver estimated the hindrance in a correct way compared to the answers of the particular patient and informal caregiver, an overview of the assessment quality is provided. For each item, the number of professional caregivers who assessed correctly, and who underestimated or overestimated the hindrance, are mentioned. In addition, the percentage of correct, overrated and underrated items were explored, stratified by theme, acquired brain injury type, the relation of patient and informal caregiver, and the setting. Also an overall percentage of professional caregivers who assessed the hindrance correctly, is shown.

3.3 Factor analysis

As a possible method to measure association between answers on the different ICF-items, factor analysis was considered. Factor analysis is a multivariate statistical approach with main purpose to study and describe the relationship among variables in terms of a few underlying, but unobservable factors (Bhuyan, 2005; Johnson and Wichern, 2007). From a practical view, it is clear that factor analysis can be seen as a data reduction technique, since it aims is to reduce the original number of variables in a smaller set of new variables, called factors. Factor analysis was performed by analyzing the correlation structure of the data. The group of variables that are highly correlated represents a particular underlying construct, or factor, that is responsible for these observed correlations (Johnson and Wichern, 2007). Familiar factor analysis procedures, such as common factor analysis, maximum likelihood factor analysis, and principal components analysis, produce meaningful results only if the data are truly continuous and multivariate normal. However, for dichotomous items, these requirements are often not met (Bernstein and Teng, 1989). In addition, some problems associated with factor analysis of items have been commented (De Bruin, 2004). When the variables are under consideration dichotomous, tetrachoric in stead of Pearson correlations are preferred. A tetrachoric correlation is a specific case of polychoric correlations where both ordinal variables are binary. Using these correlations is under the assumption that the observed pairs of dichotomous items respresent underlying variables which have a bivariate normal distribution. Primary concerns related to the use of tetrachoric correlations are the normality assumption, inflated sample size requirements and increased computing costs (Gorsuch, 1983; Pearson and Mundform, 2010). In addition, checking multivariate normality is conceptually not as straightforward as assessing univariate normality. Moreover, due to the small sample size, violations of the normality assumption are very likely to happen. However, development of the latent constructs does not require a multivariate normal assumption when no further inferences are made (Johnson and Wichern, 2007).

The general factor model as described by Johnson and Wichern (2007) assumes that the observable random vector of items X is linearly dependent upon a few unobservable random variables F_1, F_2, ..., F_m, called common factors, and p additional sources of variation ε_1, ε_2, ..., ε_p , called errors. The following common factor model based on all 53 items was fitted:

$$
\begin{aligned}
X_1 - \mu_1 &= \gamma_{11}F_1 + \gamma_{12}F_2 + \ldots + \gamma_{1m}F_m + \varepsilon_1 \qquad (1) \\
X_2 - \mu_2 &= \gamma_{21}F_1 + \gamma_{22}F_2 + \ldots + \gamma_{2m}F_m + \varepsilon_2 \\
&\vdots \\
X_{53} - \mu_{53} &= \gamma_{(53)1}F_1 + \gamma_{(53)2}F_2 + \ldots + \gamma_{(53)m}F_m + \varepsilon_{53}
\end{aligned}
$$

The coefficient γ_{ij} is the loading of the i^{th} variable on the j^{th} factor. Next, the i^{th} specific factor ε_i is associated only with the i^{th} response X_i. The factor loadings represent the correlation of the variables and the factor. As a rule of thumb, if $|\gamma_{ij}| \geq 0.4$ then the j^{th} factor is good to explain the variation of the i^{th} item. The final communality for the i^{th} item is computed by taking the sum of all squared loadings for that item and indicates the amount of variance of that item that is accounted for (Bhuyan, 2005).

Concerning the sample size, there are different opinions and several rules of thumbs in practice. Tabachnick and Fidell (2007) suggest at least 300 observations for factor analysis, whereas Hair et al. (2009) propose having at least 10 observations per variable. However, dichotomization requires a larger sample size and has the greatest impact on necessary sample size when communalities are low, the ratio of variables to factors is low or the number of factors is high (Pearson and Mundform, 2010). In addition, dichotomization results in increased sampling error in correlation estimates and attenuated correlation coefficients, which in turn results in decreased communalities. Since the total number of variables is 53 and the total sample size 66 where separated analysis were needed for patients and the caregivers, factor analysis based on the true data was not reliable and caused many problems. Therefore, data were simulated with same characteristics as the true data in order to perform factor analysis. A total of 3000 observations per variable were simulated, with same univariate probability of hindrance and approximately same correlated multivariate binary variables by thresholding a normal distribution (Leisch *et al.*, 1998). Although bivariate correlations and univariate probabilities of the real data were taken into account in the simulation process, the results might not give reliable or true insights concerning the real data. In addition, no distinction was made between data of patients, informal and formal caregivers. However, it is interpreted and explained as an example when more data is available, despite its restrictions. In addition, Kaiser-Meyer-Olkin measure of sampling adequacy and the Bartlett's test of sphericity were considered as possible tests to check the suitability of the simulated data. Kaiser-Meyer-Olkin measure of sampling adequacy is a statistic that indicates the proportion of variance in your variables that might be caused by underlying factors, where a value less than 0.5 indicates that the results of the factor analysis might not be useful. The Bartlett's test of sphericity tests the hypothesis that the correlation matrix is the identity matrix, which means that the variables are unrelated, therefore implying that factor analysis is not appropriate for the data in hand (IBM Corp., 2013).

It is possible for a tetrachoric correlation matrix, which becomes more an issue as the number of items increases, not to be positive definite. According to Knol and Berger (1991), a maximum likelihood factor analysis and generalized (weighted) least-squares estimation require a nonsingular correlation matrix which is invertible and are often not appropriate when tetrachoric correlations are considered. An unweighted least-squares (ULS) estimation or iterated principal factor (PRINIT) analysis is preferable when tetrachoric correlations are used to estimate the factor model and they do not assume multivariate normally distributed data. Both methods were considered and give most often same results, since they are similar in nature. The PRINIT method is dependent on the quality of starting estimates of communalities. The squared multiple correlations of each variable with all the other variables are mostly used as the prior communality estimates. However, when the correlation matrix is singular, the prior communality estimate for each variable should be set to its maximum absolute correlation with any other variable. The ULS method minimizes item uniquenesses (residuals) and maximizes factor loading values, which is recommended when tetrachoric correlation coefficients are used. In addition, ULS is preferable in order to avoid possible Heywood cases, meaning a communality estimate becomes 1.0 or greater (Knol and Berger, 1991). There are several criteria to help extracting the optimal number of factors, with the latent root criterion as most popular one (Hair *et al.*, 2009). Therefore, factors with eigenvalues greater than one were retained. In order to simplify the interpretation of the factors, VARIMAX orthogonal rotation was applied. The VARIMAX rotation makes certain that a factor has high factor loads on some items and low on other items, where the factors remain uncorrelated. Orthogonal rotation was chosen since no knowledge about possible factors was available and therefore the assumption of theoretically independent factors was deemed to be reasonable.

3.4 Latent class analysis

As another way to measure assocation between answers on the 53 different ICF-items, latent class analysis was considered. Latent class models are often referred to as finite mixture models, which can be used to identify underlying subgroups in a population (McLachlan and Peel, 2000). Different from factor analysis, latent class analysis provides a framework for measuring categorical, in stead of continuous, latent variables and is more concerned with the structure of cases (i.e. the latent taxonomic structure). However, both factor analysis and latent class analysis are useful for data reduction and latent classes are also unobserved constructs. Similar to cluster analysis, latent class analysis is used to discover groups or types of cases based on observed data. However, cluster analysis is not based on a statistical model.

Equation 2, as defined by Collins and Lanza (2010), expresses how the probability of observing a particular vector of responses is a function of the probabilities of membership in each latent class (γ's) and the probabilities of observing each response conditional on latent class membership (ρ's):

$$P(Y = y) = \sum_{c=1}^{C} \gamma_c \prod_{j=1}^{J} \prod_{r_j=1}^{R_j} \rho_{j,r_j|c}^{I(y_j=r_j)} \tag{2}$$

with in this case $j = 1, ..., 53$ observed items ($J = 53$), $r_j = 1, 2$ response categories ($R_j = 2$), C latent classes, and indicator function $I(y_j = r_j)$ which equals to 1 when the response to variable $j = r_j$, and equals to 0 if otherwise. In order to do the latent class analysis, the data was recoded with $r_j = 1$, indicating no experience of hindrance (original value 0) and $r_j = 2$, meaning experience of hindrance (original value 1). Both γ's and ρ's are the parameters and express together how well individuals can be classified into latent classes given the set of observed variables. The item-response probability $\rho_{j,r_j|c}$ is the probability of response r_j to observed variable j, conditional on the membership in latent class C. Latent classes are mutually exclusive and exhaustive, indicating that each individual is a member of one and only one latent class. In addition, because each individual provided one and only one response alternative to item j, the vector of item-response probabilities for a particular item conditional on a particular latent class, always sums to one. Further, the assumption of local independence holds, which specifies that conditional on the latent variable, the observed variables are independent. In contrast to factor analysis, no distributional assumptions such as multivariate normality need to be made (Collins and Lanza, 2010).

The parameters in the latent class model were estimated in an iterative way by the expectation-maximization with Newton-Raphson incorporated, which search for maximum likelihood parameter estimates or to put another way, attempt to maximize the likelihood function. To find the optimal number of classes, the fit of the statistical model were evaluated. There are a few ways to select a best model depending on the chosen criteria. Calculating Pearson's χ^2 goodness of fit and likelihood ratio chi-square G^2 statistics for the observed versus predicted cell counts, are one method to help determine how well a particular model fits the data (Goodman, 1970). However, due to the complexity of the data with a large amount of variables, these statistics were not reliable and therefore not used for model selection. In complex latent class models, sparseness can arise and causes issues for the Pearson and likelihood ratio statistics (Collins and Lanza, 2010). More advanced approaches such as parametric bootstrap and Bayesian procedure called posterior predictive checks, are possible solutions for model selection (Collins and Lanza, 2010; Dziak *et al.*, 2014; McLachlan and Peel, 2000). As an alternative way to select the final model with a specific number of classes, Akaike information criterion (AIC) and the Bayesian information criterion (BIC) were used for comparing models in terms of balance between fit and parsimony. Smaller AIC or BIC values correspond to more parsimonious models. The BIC will usually be more appropriate for basic latent class models because of their relative simplicity and was therefore considered as main criterion for model selection (Linzer and Lewis, 2011). Finally, the meaning of the latent classes is interpreted, based on the estimated item-response probabilities.

Again, due to the small sample size of 66 subjects and the large amount of items, latent class analysis was performed on the same simulated data as used for conducting factor analysis, with 3000 observations per item. Although bivariate correlations and univariate probabilities of the real data were taken into account in the simulation process, the results might not give reliable or true insights concerning the real data. In addition, no distinction was made between data of patients, informal and formal caregivers. Still, these analysis are meaningful when more data is available and can be used to compare with the results produced by factor analysis. In addition, the latent class model can be extended to multiple-group analysis where for instances both the class membership and item-response probabilities can vary across patients and their caregivers. Furthermore, covariates such as setting or acquired brain injury type can be included in the model as well, leading to latent class regression models (Lanza *et al.*, 2007). However, in this project only a basic latent class model without distinction of groups and inclusion of covariates, was fitted.

3.5 Generalized estimating equations

The effect of covariates on the experience of hindrance and the quality of hindrance assessment was investigated by fitting two marginal models with generalized estimating equations (GEE) techniques. Another way to do this is by fitting individual logit regression models for each of the items. However, due to the small sample size of 66 subjects and the presence of clusters, overall binary responses for hindrance and assessment were considered. This implied a sample size of about 53 times larger, had additional practical advantages and was also able to deal with the prespecified objectives. The considered new binary outcome indicating hindrance, was the same as in the individual item-cases but combined over all items. For the construction of the binary response reflecting the quality of assessment of the professional caregiver, following decisions were made. The professional caregiver estimated the situation correctly if he and both the patient and informal caregiver experienced no hindrance, or if he indicated hindrance and the patient or informal caregiver expressed this too. In all other cases, the quality of hindrance assessment was considered as bad.

Since the nature of the data were clustered in cases of patients of the same size, appropriate analyze techniques called GEE were used to estimate the parameters of a population-averaged generalized linear model in order to investigate the mentioned questions of interest. GEE only require the correct specification of the univariate marginal distributions provided one is willing to adopt working assumptions about the association structure. It is worth noting that GEE have the net benefit of yielding asymptotically and consistent estimates, even under wrong working correlation assumption (Fitzmaurice *et al.*, 2009). For both considered models with different responses, a positive association between the answers within a cluster is expected. More specifically, the answers between the patient and corresponding caregivers were assumed to be correlated. In addition, if a specific professional caregiver could assess hindrance situations properly, it might be more likely that he will have better result in the assessment of the hindrance experiences. The independence and exchangeable working correlation structures were considered in the GEE estimation. To define the most appropriate working assumption for the data, the model-based and empirical standard errors were compared under both structures. The working assumption leading to in general the smallest discrepancies between model-based and robust standard errors, was considered as being more plausible (Molenberghs and Verbeke, 2005). The QIC statistic proposed by Pan (2001) was also used in addition in order to define the best working correlation structure, preferring the assumption leading to the smallest QIC value. The empirical estimators were used for interpretation since they are more robust to misspecification of the correlation structure (Molenberghs and Verbeke, 2005).

Taking the clustered nature of the data into account, the following marginal model for the probability of hindrance experience $P(Y_{ij} = 1)$ was fitted:

$$\begin{aligned}\text{logit}[P(Y_{ij}=1)] = \beta_0 &+ \beta_1 Setting_i + \beta_2 Patient_{ij} + \beta_3 InfCareg_{ij} + \beta_4 Trauma_i + \beta_5 Internal_i \\ &+ \beta_6 Parent_i + \beta_7 Partner_i + \beta_8 ThemeA_{ij} + \beta_9 ThemeB_{ij} + \beta_{10} ThemeC_{ij} + \beta_{11} ThemeD_{ij} \\ &+ \beta_{12} ThemeE_{ij} + \beta_{13} ThemeF_{ij} + \beta_{14} ThemeG_{ij} + \beta_{15} ThemeH_{ij} + \beta_{16} ThemeI_{ij}\end{aligned} \tag{3}$$

where Y_{ij} is the hindrance indicator for patient i at answer/observation j. All covariates were treated as dummy variables since they indicate to which category of the specific covariate the observation belongs. $Setting_i$ is equal to 1 if patient i comes from the Mané setting and 0 if from Jessa hospital. $Patient_{ij}$ and $InfCareg_{ij}$ are dummies indicating whether observation j of patient i is coming from the patient ($Patient_{ij} = 1$), informal caregiver ($InfCareg_{ij} = 1$) or professional caregiver (as reference category). $Trauma_i$ and $Internal_i$ are dummies indicating whether patient i has a traumatic ($Trauma_i = 1$), internal ($Internal_i = 1$) or progressive (reference category) brain injury. Further, $Parent_i$ and $Partner_i$ are dummies about the relation of the patient and his of her informal caregiver, indicating whether patient i his or her caregiver is a parent ($Parent_i = 1$), partner ($Partner_i = 1$) or someone with another connection (reference category). The last covariate "theme" with 10 categories was included as 9 dummy variables with the J^{th} theme as reference category.

The second marginal model fitted by GEE estimation for the probability of correct assessment of the professional caregiver $P(Y_{ij} = 1)$ is:

$$\begin{aligned} \text{logit}[P(Y_{ij} = 1)] = \beta_0 + \beta_1 Setting_i + \beta_2 Trauma_i + \beta_3 Internal_i + \beta_4 Parent_i + \beta_5 Partner_i \\ +\beta_6 ThemeA_{ij} + \beta_7 ThemeB_{ij} + \beta_8 ThemeC_{ij} + \beta_9 ThemeD_{ij} + \beta_{10} ThemeE_{ij} \\ +\beta_{11} ThemeF_{ij} + \beta_{12} ThemeG_{ij} + \beta_{13} ThemeH_{ij} + \beta_{14} ThemeI_{ij} \end{aligned} \tag{4}$$

where Y_{ij} is the indicator of correct assessment of hindrance by the formal caregiver of item j about corresponding patient i. Again the same covariates as dummy variables were included in the model, with the same notations and reference groups. However, no dummy variables for the assessor of hindrance were included since they were collapsed to create the response about assessment quality. In both models 3 and 4, interactions between setting and the other covariates were found to be insignificant and therefore removed from the final models. To test the significance of the regression parameters, no likelihood ratio test could be used, since no likelihood is formulated in GEE models (Fitzmaurice *et al.*, 2009). However, a generalization of the score test designed for GEE models, was used to test the significance of the covariates at 5% significance level.

3.6 Generalized linear mixed model

Another considered way to analyze the binary outcomes with same purposes as in the GEE estimation, was to fit two random effects models. The effect of covariates on the experience of hindrance and the assessment quality by the professional caregiver was investigated by fitting two generalized linear mixed models (GLMMs). Same binary responses were used as in the GEE analysis.

GLMM can be seen as a straightforward extension of generalized linear models by adding random effects. In contrast to marginal models, random effects models allow one to study the evolution of each patient separately and also predict the patient-specific evolution (Molenberghs and Verbeke, 2005). In GLMM, the marginal likelihood is used as the basis for inferences about fixed parameters. In general, evaluation and maximization of the marginal likelihood for GLMMs requires integration over the distribution of the random effects. Since no closed form for the integral exists for non-Gaussian response, different numerical approximations have been proposed: approximation of integrand (e.g Laplace approximation), approximation of data (e.g penalized quasi-likelihood and marginal quasi-likelihood), and approximation of the integral (e.g adaptive and non-adaptive Gaussian quadrature). Due to the fact that the data is discrete, the Laplace and quasi-likelihood approaches yield quite biased estimators of the variance components, which leads to biased estimators of the fixed effect parameters and were therefore not considered. Adaptive Gaussian quadrature, with numerical integration centered around empirical Bayes estimates of the random effects, allows maximization of the marginal likelihood with any desired degree of accuracy (Fitzmaurice *et al.*, 2009). Taking all this into account, adaptive Gaussian quadrature was used to fit the random effects models.

The following GLMM by adding random intercepts was fitted for the probability of hindrance experience $P(Y_{ij} = 1)$:

$$\begin{aligned}\text{logit}[P(Y_{ij} = 1)] = (\beta_0 + b_{0i}) + \beta_1 Setting_i + \beta_2 Patient_{ij} + \beta_3 InfCareg_{ij} + \beta_4 Trauma_i + \beta_5 Internal_i \\ + \beta_6 Parent_i + \beta_7 Partner_i + \beta_8 ThemeA_{ij} + \beta_9 ThemeB_{ij} + \beta_{10} ThemeC_{ij} + \beta_{11} ThemeD_{ij} \\ + \beta_{12} ThemeE_{ij} + \beta_{13} ThemeF_{ij} + \beta_{14} ThemeG_{ij} + \beta_{15} ThemeH_{ij} + \beta_{16} ThemeI_{ij}\end{aligned} \tag{5}$$

where Y_{ij} is the hindrance indicator for patient i at answer/observation j. All covariates were treated as dummy variables with same notations and reference categories as in the marginal models 3 and 4 in GEE section. For random intercept b_{0i} a normal distribution with mean 0 and variance d was assumed.

The next GLMM with random intercept was fitted for the probability of correct assessment by the professional caregiver $P(Y_{ij} = 1)$:

$$\begin{aligned}\text{logit}[P(Y_{ij} = 1)] = (\beta_0 + b_{0i}) + \beta_1 Setting_i + \beta_2 Trauma_i + \beta_3 Internal_i + \beta_4 Parent_i + \beta_5 Partner_i \\ + \beta_6 ThemeA_{ij} + \beta_7 ThemeB_{ij} + \beta_8 ThemeC_{ij} + \beta_9 ThemeD_{ij} + \beta_{10} ThemeE_{ij} \\ + \beta_{11} ThemeF_{ij} + \beta_{12} ThemeG_{ij} + \beta_{13} ThemeH_{ij} + \beta_{14} ThemeI_{ij}\end{aligned} \tag{6}$$

where Y_{ij} is the indicator of correct assessment of hindrance by the formal caregiver of item j about corresponding patient i. Again, the covariates were treated as dummy variables with same notations and reference categories as in the marginal models 3 and 4 in GEE section. The random intercept b_{0i} for patient i was assumed to be normally distributed with mean 0 and variance d. In both GLMMs 5 and 6, interactions between setting and the other covariates were not included based on insignificance, simplification and interpretation of the model. Type 3 tests for fixed effects were conducted to test the significance of the covariates at 5% significance level (Fitzmaurice *et al.*, 2009).

3.7 Software

`SAS software version 9.4` together with `R version 3.2.0` were used for statistical analysis. Latent class analysis, performed in SAS by the procedure PROC LCA, was not written or distributed by the SAS institute Inc. This procedure could be used thanks to the Pennsylvania State University (Lanza *et al.*, 2015) and was available from methodology.psu.edu. The most relevant SAS and R software codes are included in Appendix A6.

4 Results

4.1 Exploratory data analysis

A total of 66 subjects divided into 22 clusters, each including a patient with acquired brain injury together with an informal and formal caregiver, were involved in the study. All subjects were in between 20 and 80 years old and no missing data was found. Data were equally available from both the chronic (Mané) and ambulatory (Jessa) care setting. Of all patients, nine were classified having a traumatic brain injury, 12 having an internal brain injury and only one with a progressive disorder. In nine cases the patient with acquired brain injury was a child of the informal caregiver. Half of the patients was a partner of the informal caregiver and only two patients had another relation with their caregiver.

In Table 1 the number of patients and informal caregivers who experienced hindrance per item with increasing hindrance experience for patients, is provided. Since only 22 patients and informal caregivers were involved in the study, conclusions and percentages should be regarded with caution. All patients experienced no hindrance for six items coming from different themes. Only items C5 "producing nonverbal messages" and I3 "religion and spirituality" were indicated as no feeling of discomfort by all patients and all informal caregivers. Item J8 "faster and more often tired" was found to be most problematic with 15 patients and 13 informal caregivers reporting the experience of hindrance. According to the informal caregivers, most hindrance for patients or themselves was found for item D2 "lifting and carrying objects" with 16 caregivers indicating the experience of hindrance. In general, hindrance was more often reported by informal caregivers compared to patients. The number of patients and informal caregivers who experienced hindrance on average per item is tabulated by theme (see Table 2) and by acquired brain injury type, the relation of the patient and the informal caregiver, and setting (see Table 3). Theme G "interpersonal interactions and relationships" with on average one patient per item feeling discomfort, was found to be the least problematic. In contrast, theme D "mobility" was experienced as problematic since more than 11 patients and caregivers per item indicated that there is hindrance. The patient with progressive brain injury experienced less hindrance compared to the averages in the two other groups. However, due to the small sample sizes, these results are not reliable. The least amount of hindrance was experienced by patients who were child of the informal caregiver. However, again caution should be mentioned due to small sample sizes. Finally, a small difference between Jessa hospital and Mané was observed with on average 23.5% of the patients from Jessa hospital and 18.7% of the patients from Mané reporting hindrance per item. From all 22 patients, on average 4.6 (21.1%) patients indicated the presence of hindrance concerning a particular item. On the basis of the results of the informal caregivers, on average 5.2 (23.4%) caregivers indicated some hindrance per item.

Table 1: Number of patients and informal caregivers who experienced hindrance by item

	Hindrance frequency (%)			Hindrance frequency (%)	
Item	**Patient**	**Informal caregiver**	**Item**	**Patient**	**Informal caregiver**
C5; I3	0 (0.0%)	0 (0.0%)	E3; F1	4 (18.2%)	5 (22.7%)
G5	0 (0.0%)	1 (4.5%)	F3	4 (18.2%)	6 (27.3%)
B1	0 (0.0%)	3 (13.6%)	I2	5 (22.7%)	3 (13.6%)
E6; E7	0 (0.0%)	4 (18.2%)	A1; A3; E1; E4	5 (22.7%)	6 (27.3%)
C2	1 (4.5%)	0 (0.0%)	A6 ; F2	5 (22.7%)	7 (31.8%)
A7; G4	1 (4.5%)	1 (4.5%)	J2	5 (22.7%)	9 (40.9%)
G1	1 (4.5%)	2 (9.1%)	C7	6 (27.3%)	3 (13.6%)
G2	1 (4.5%)	3 (13.6%)	D4	7 (31.8%)	3 (13.6%)
H1	1 (4.5%)	4 (18.2%)	A2; B3	7 (31.8%)	8 (36.4%)
E5	1 (4.5%)	6 (27.3%)	J4	8 (36.4%)	5 (22.7%)
C1; G3	2 (9.1%)	0 (0.0%)	J1	8 (36.4%)	12 (54.5%)
C3; J6	2 (9.1%)	2 (9.1%)	B4	9 (40.9%)	8 (36.4%)
B2	2 (9.1%)	4 (18.2%)	C4	10 (45.5%)	5 (22.7%)
C8	2 (9.1%)	5 (22.7%)	J5	11 (50.0%)	8 (36.4%)
A5 ; J7	3 (13.6%)	2 (9.1%)	D1	11 (50.0%)	10 (45.5%)
I1	3 (13.6%)	3 (13.6%)	C6	12 (54.5%)	7 (31.8%)
E2 ; H3	3 (13.6%)	5 (22.7%)	D3	12 (54.5%)	15 (68.2%)
H2	3 (13.6%)	7 (31.8%)	D2	12 (54.5%)	16 (72.7%)
A4	4 (18.2%)	3 (13.6%)	D5	14 (63.6%)	13 (59.1%)
J3	4 (18.2%)	4 (18.2%)	J8	15 (68.2%)	13 (59.1%)

Table 2: Number of patients and informal caregivers who experienced hindrance on average per item by theme

	Hindrance frequency per item (%)			Hindrance frequency per item (%)	
Theme	**Patient**	**Informal caregiver**	**Theme**	**Patient**	**Informal caregiver**
A	4.3 (19.5%)	4.7 (21.4%)	F	4.3 (19.5%)	6.0 (27.3%)
B	4.5 (20.5%)	5.8 (26.4%)	G	1.0 (4.5%)	1.4 (6.4%)
C	4.4 (20.0%)	2.8 (12.7%)	H	2.3 (10.5%)	5.3 (24.1%)
D	11.2 (50.1%)	11.4 (51.8%)	I	2.7 (12.3%)	2.0 (9.1%)
E	2.6 (11.8%)	5.1 (23.2%)	J	7.0 (31.8%)	6.9 (31.4%)

Table 3: Number of patients and informal caregivers who experienced hindrance on average per item by acquired brain injury type, relation patient and informal caregiver, and setting

		Hindrance frequency per item (%)	
Variable	**Category**	**Patient**	**Informal caregiver**
Acquired brain injury type	Traumatic (n=9)	1.9 (21.6%)	2.1 (22.9%)
	Internal (n=12)	2.6 (21.4%)	3.0 (24.7%)
	Progressive (n=1)	0.1 (13.2%)	0.1 (13.2%)
Relation patient and informal caregiver	Parent and child (n=9)	1.7 (18.4%)	1.4 (15.1%)
	Partner (n=11)	2.6 (23.3%)	3.1 (28.1%)
	Other (n=2)	0.4 (20.8%)	0.7 (34.9%)
Setting	Jessa hospital (n=11)	2.6 (23.5%)	2.6 (23.8%)
	Mané (n=11)	2.1 (18.7%)	2.5 (23.0%)
Total (n=22)		4.6 (21.1%)	5.2 (23.4%)

In order to get more insight in the quality of the hindrance assessment of the professional caregiver, a comparison between the answers of the patient and informal caregiver with those from the professional caregiver was made. The professional caregiver estimated the situation correctly if he and both the patient and informal caregiver indicated no hindrance, or if he mentioned presence of hindrance and the patient or informal caregiver indicated this as well. The professional caregiver underestimated the problem if he reported no hindrance, but the patient or informal caregiver experienced hindrance. There was overestimation of the problem, when the professional caregiver reported hindrance while both the patient and informal caregiver did not experience hindrance.

In Table 4 a hindrance assessment comparison is presented for each item with decreasing percentage of correct estimation. Hindrance perception of item C5 "producing nonverbal messages" was in 95% of the cases assessed in a correct way by the professional caregiver. As mentioned before, no patients and informal caregivers indicated this item as problematic in terms of discomfort. Only one formal caregiver indicated hindrance for this item, which was a case of overestimation of the problem. The assessment of hindrance by the professional caregivers of item D5 "driving" was not done well with only five correct estimations. In general, underestimation happened more often (21%) than overestimation (12%). However, most of the items were assessed reasonable good, with on average 67% correct evaluations. The quality of assessment by the professional caregiver was found to be best for theme G "interpersonal interactions and relationships", where 85% of the items was properly evaluated (see Table 5). Only 52% of the items of theme D "mobility" and 57% of the items of theme J "emotion and behaviour" was reported correctly in terms of hindrance. Further, it is striking that hindrance of 40% of the items was underestimated in theme D, and 29% in theme J. With regard to the acquired brain injury type, the relation of patient with the informal caregiver, and the setting, some observations can be made (see Table 6). For the particular patient with progressive acquired brain injury, the assessment of the professional caregiver was well with 81% correct evaluations. For the two other types, the percentage of correct evaluations were close to each other. With respect to the relation between the patient and informal caregiver, the results were very similar with 67% correct evaluations in each group of patients. However, a small difference was observed between the assessment of discomfort for patients in the chronic and ambulatory setting. The correct assessment of professional caregivers was found to be slightly higher for patients coming from the Jessa hospital (71%) compared to the Mané setting of care (62%). In Mané, the overestimation of hindrance was larger (19%) in comparison with Jessa (6%).

Table 4: Hindrance assessment comparison of professional caregiver by item

	Assessment professional caregiver				Assessment professional caregiver		
Item	**Correct (%)**	**Overrated**	**Underrated**	**Item**	**Correct (%)**	**Overrated**	**Underrated**
C5	21 (95%)	1	0	E5; F3	14 (64%)	3	5
C2; G4	20 (91%)	1	1	C7	14 (64%)	2	6
I3	19 (86%)	3	0	A3; J4	14 (64%)	1	7
G5	19 (86%)	2	1	D2	14 (64%)	0	8
E3; E7; G3	19 (86%)	1	2	J2	13 (59%)	2	7
C1; E6; G1	18 (82%)	2	2	C4	13 (59%)	1	8
C3	17 (77%)	3	2	A4	12 (55%)	6	4
G2; H1	17 (77%)	2	3	E4	12 (55%)	4	6
A5	16 (73%)	5	1	D4	12 (55%)	3	7
A2; A7	16 (73%)	4	2	B4	12 (55%)	2	8
H2; J6	16 (73%)	3	3	J8	12 (55%)	1	9
F1; I1	16 (73%)	2	4	J3	11 (50%)	7	4
I2	16 (73%)	1	5	E1	11 (50%)	4	7
B3; J7	15 (68%)	4	3	J5	11 (50%)	3	8
A6	15 (68%)	3	4	D1	11 (50%)	2	9
H3	15 (68%)	2	5	F2	10 (45%)	5	7
D3	15 (68%)	0	7	J1	9 (41%)	3	10
B1	14 (64%)	6	2	C6	8 (36%)	2	12
B2	14 (64%)	5	3	D5	5 (23%)	4	13
A1; C8; E2	14 (64%)	4	4	**Total**	780 (67%)	143 (12%)	243 (21%)

Table 5: Hindrance assessment comparison of professional caregiver by theme (percentage items)

	Assessment professional caregiver (% items)				Assessment professional caregiver (% items)		
Theme	**Correct**	**Overrated**	**Underrated**	**Theme**	**Correct**	**Overrated**	**Underrated**
A	67%	17%	16%	F	61%	15%	24%
B	63%	19%	18%	G	85%	7%	8%
C	71%	9%	20%	H	73%	10%	17%
D	52%	8%	40%	I	77%	9%	14%
E	70%	12%	18%	J	57%	14%	29%

Table 6: Hindrance assessment comparison of professional caregiver by acquired brain injury type, relation patient and informal caregiver, and setting (percentage items)

		Assessment professional caregiver (% items)		
Variable	**Category**	**Correct**	**Overrated**	**Underrated**
Acquired brain injury type	Traumatic (n=9)	65%	15%	20%
	Internal (n=12)	67%	11%	21%
	Progressive (n=1)	81%	0%	19%
Relation patient and informal caregiver	Parent and child (n=9)	67%	15%	18%
	Partner (n=11)	67%	10%	23%
	Other (n=2)	67%	8%	25%
Setting	Jessa hospital (n=11)	71%	6%	23%
	Mané (n=11)	62%	19%	19%
Total (n=22)		67%	12%	21%

4.2 Factor analysis

One way to summarize the data was by looking to possible underlying constructs which explain correlations among the different items. Due to small sample sizes and large number of variables, factor analysis was applied on the simulated data with 3000 observations and no missingness. The following results and conclusions might not be appropriate for the real data but can be used as a guide in order to perform factor analysis on the same items with more patients involved. As a first way to check whether the data was appropriate for factor analysis, Kaiser-Meyer-Olkin measure of sampling adequacy and Bartlett's test of sphericity were performed. The overall measure of sampling adequacy was found to be 0.79 (> 0.5) indicating that there is enough variance that might be caused by underlying factors. The Bartlett's test of sphericity was found to be highly significant ($\chi_{1378} = 33719.77$; p-value < 0.0001), meaning that the variables were not uncorrelated. It can therefore be concluded that the simulated data were deemed appropriate for factor analysis.

Since the items were dichotomous indicating the presence of hindrance, tetrachoric correlations were used as the basis for factor analysis. In Table A2 a reduced, since the full matrix contained 1378 correlations, version of the tetrachoric correlation matrix of the simulated data is presented. It can be observed that there were some strong correlations between items (e.g. $\rho_{A1;A3} = 0.4453$). Moreover, positive as well as negative correlations between the items can be observed. The full tetrachoric correlation matrix was used as input for the factor analysis. However, the matrix was found not to be positive definite, implying nonsingularity. As a consequence, maximum likelihood method could not be used and unweighted least-squares (ULS) and iterated principal factor analysis (PRINIT) with prior communality estimate for each item set to its maximum absolute correlation with any other item, were considered. The latent root criterion to extract an optimal number of factors and VARIMAX orthogonal rotation was specified in both cases. As expected, both ULS and PRINIT method gave the same results.

The scree plot shown in Figure 1 graphs the eigenvalue (variance of factor) against the factor number before rotation. From this plot it can be observed that no clear inflection point to indicate the optimal number of factors can be noticed. Next, a number of factors with negative variances can be noticed since the correlation matrix was not of full rank. Although it is strange to have a negative variance, this happened because factor analysis is only analyzing the common variance, which is less than the total variance. By using the latent root criterion, 11 factors were retained with eigenvalues greater than one. In Table 7 the variance explained by each factor before and after rotation, is shown. It can be noticed that the individual variances changed after rotation, but the total variance explained, remained the same.

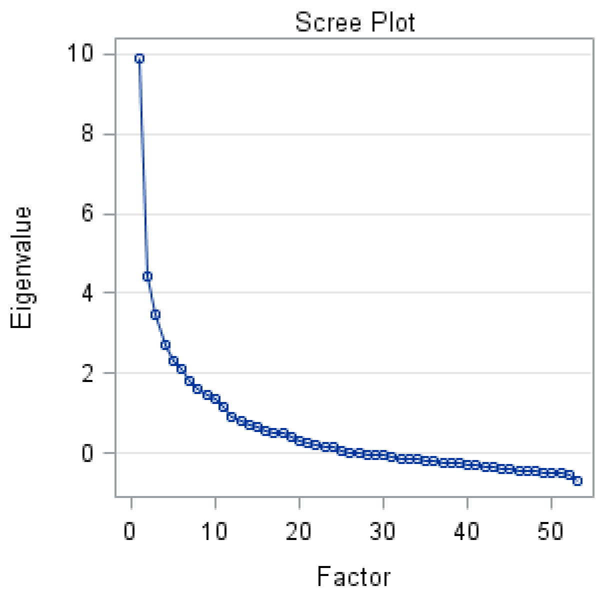

Figure 1: Scree plot of eigenvalues based on the simulated data

Table 7: Variance explained by each factor before and after rotation based on the simulated data

	Variance explained	
Factor	Before	After
1	9.9555	4.3086
2	4.4979	3.9136
3	3.5089	3.5268
4	2.7900	3.3127
5	2.3570	3.2296
6	2.1796	2.9894
7	1.8855	2.8009
8	1.6814	2.5583
9	1.5259	2.4176
10	1.4136	2.0313
11	1.2349	1.9413

In order to simplify the interpretation of the factors, orthogonal rotation was considered. In Table A3 the orthogonal transformation matrix is provided, which was multiplied with the unrotated factor matrix to get the rotated factor matrix. The final rotated factor pattern is presented in Table A4. This pattern contains the rotated factor loadings of each variable on each factor. As a rule of thumb, if the absolute value of a factor loading was greater than or equal to 0.4, then the variable contributed enough to the underlying construct. For each rotated factor, the variables with absolute value of factor loadings greater than or equal to 0.4 were selected and shown in Table 8. From this table, some interpretations can be derived. Since these loadings were found using simulated data, following results and interpretations might not hold for the true data in hand. It can be noticed that items B4, C2, C6, D4, D5, J2 and J6 did not contribute enough to one particular factor. After consulting the final communalities, it can be noticed that the communalities of all these items, except item D4, were less than 0.5, indicating that the proportion of those items variance explained by the factors after rotation, was small. Item D4 has a larger communality since not all individual factor loadings were found to be small (see Table A4). In contrast, item G5 has for example a communality of 0.9310 and contributed to three factors. As mentioned before, from the tetrachoric correlation matrix (see Table A2) there were some strong correlations such as between items A1 and A3 with $\rho_{A1;A3} = 0.4453$. This was confirmed by the fact that both items contributed to factor 8.

Table 8: Rotated factor loadings ($|\gamma_{ij}| \geq 0.4$) of items on the 11 extracted factors based on simulated data

Factor	**Variables with factor loadings**							
1	C8	E1	E2	E4	G2	I2		
	0.6579	0.7265	0.7953	0.7339	0.4463	0.4177		
2	E7	G1	G2	G4	G5	I3	J5	J7
	0.7088	0.5601	0.6451	0.6038	0.4767	0.6287	0.4876	0.5945
3	A4	B1	B2	C5	E5	E6		
	0.4499	0.7207	0.4593	0.4170	0.7705	0.8014		
4	F3	H2	I1	I2				
	0.5215	0.7888	0.7380	0.5978				
5	A6	B2	B3	F1	F2	H3		
	0.5329	0.4460	0.5647	0.6732	0.7222	0.4298		
6	C1	C3	C4	C5	C7	G3		
	0.6482	0.5984	0.4681	0.4017	0.6513	0.5492		
7	J1	J4	J5	J8				
	0.5745	0.7919	0.4604	0.5690				
8	A1	A3	A7	C5				
	0.6200	0.7058	0.5771	0.4337				
9	D2	D3						
	0.8894	0.8256						
10	A5	E3	G5	H1				
	0.4384	0.4581	0.4608	0.8179				
11	A2	D1	G5	J3				
	0.5213	-0.4425	0.4201	0.4167				

Using the information provided in Table 8, underlying factors with respect to hindrance can be explored and interpreted. Six major contributions of items are observed concerning the first factor, with three items from theme E "self-care" having the greatest loadings, namely "washing onself", "caring for body parts" and "dressing". The other three items are "using communication devices", "intimate relationships" and "recreation and leisure". It is difficult to discover an underlying construct. A possible factor might be "skillfulness" or maybe "age", with older people that have difficulties with these tasks. The second factor is highly correlated with four items of theme G "interpersonal interactions and relationships" and two items of theme J "emotion and behavior". The other two items are "looking after one's health" and "religion and spirituality". A possible factor might be "problems with imposed rules and social norms and behaviors". The third factor might be tasks related to drinking and eating, since it was highly correlated to items "drinking", "eating", "carrying out daily routine (such as breakfast)", and "undertaking a single task (such as setting the table)". The fourth factor might be called "engagement hindrance" since items "engaging in all aspects of community social life" and "work and employment" loaded high on it. The fifth factor could include "meal-related tasks and capabilities", with for instance items "acquisition of goods and services", "preparing meals" and "underlying tasks such as make message list for shopping, set the table and cooking" loading high on it. The sixth factor is highly related to five items of theme C "communication" and item "family relationships" and can therefore be considered as the factor of "communication difficulties". Factor 7 is highly correlated with four items of theme J "emotion and behavior" and can therefore be seen as a factor of "emotion and behavior". The eighth factor could be called "confrontation and interaction of something new" according to the items of which three from theme A "learning and applying knowledge". Next, the ninth factor only has two items with high loadings both coming from theme D "mobility", with "lifting and carrying objects" and "fine hand use". Although only two variables loaded, but very high, on this factor, a possible interpretation might be "task-specific problems and functional arm and hand movements". Although interpretation is not easy for factor 10, a possible meaning of the factor could be "dealing with unfamiliar surroundings and formal relationships". Same to factor 11 which is not easy to interpret, some comments can be made. Item D1 "changing basis body position" was negatively correlated with the factor while all other items were positively correlated to this factor. It can be said that if more hindrance was experienced for "focusing attention", "formal relationships" and "unrealistic expectations", then less hindrance was expected for "changing basis body position". The underlying construct on the basis of this, could be many things.

4.3 Latent class analysis

Another way to get more insight in patterns of answers among the items was by conducting latent class analysis. The following results were based on simulated data with 3000 observations and no missingness. When enough data is available, one can do latent class analysis with group specification for patient, informal and professional caregiver. In addition, covariates can be included. In this report only a basic latent class model was considered and fitted without group and covariate inclusion. Models were fitted with one up to 15 classes. The maximum absolute deviation between the parameter estimates in two successive iterations of the estimation procedure was used as stopping rule to get convergence. From all fitted models, the latent class model with 9 classes was found to have the smallest BIC with maximum log-likelihood of -69587.83. Models with more classes had smaller AIC values but due to the increase in complexity of models by adding more classes, BIC values became larger when more than 9 classes were included. By adding one class, 54 extra parameters (53 item-response probabilities and 1 class membership probability) have to be estimated. A total of 485 parameters were estimated by the final class model consisting of 9 classes.

In Table 9 the parameter estimates of the latent class membership probabilities are displayed. These probabilities indicate how likely a person belongs to a particular latent class. The estimated latent class membership probabilities vary from 5.61% to 18.80% and sum op to 100%. After interpretation of the different classes, it might be interesting to predict and identify to which class an individual is most likely to belong, depending on his or her answers on the items. This prediction and classification is not done here, but can be included in the analysis as well.

Table 9: Parameter estimates of latent class membership probabilities based on the simulated data

Class	Parameter	Estimate
1	γ_1	0.1725
2	γ_2	0.1224
3	γ_3	0.1010
4	γ_4	0.1880
5	γ_5	0.0561
6	γ_6	0.1025
7	γ_7	0.0754
8	γ_8	0.0722
9	γ_9	0.1100
Sum	$\sum_{c=1}^{9} \gamma_c$	1.0000

The other set of estimated parameters, the item-response probabilities, are provided in Table A5. These are the probabilities of experience of hindrance on a particular item, given the latent class to which the individual belongs. Only the item-response probabilities with $r_j = 2$ are displayed, indicating hindrance experience, since this was of interest. To facilitate interpretation of these 9 classes, only the item-response probabilities larger than 0.5 were retained (see Table 10). Before looking to the individual classes, it can be observed that some items such as J8 "faster and more often tired" had large item-response probabilities of hindrance in many classes. This was expected since item J8 was found to have the largest hindrance experience with 15 patients indicating to have a feeling of discomfort. The univariate probabilities of hindrance per item were taken into account in the simulation process. In contrast, for instance item C5 "producing nonverbal messages" had very small conditional item-response probabilities of hindrance. Also this was expected, since in the real dataset no patient or informal caregiver indicated an experience of hindrance for this activity (see Table 1).

Table 10: Estimated item-response probabilities ($\rho_{j,r_j|c} \geq 0.50$) of hindrance with 9 classes based on simulated data

Class	**Variables with conditional item-response probabilities of hindrance**									
1										
2	A1	A2	A3	A6	B3	B4	D3	J1	J2	J3
	0.5707	0.5844	0.5542	0.7447	0.6064	0.5820	0.5162	0.6684	0.5176	0.6528
	J5	J8								
	0.6752	0.7856								
3	D1	D5	H2	J1	J5	J8				
	0.5734	0.7396	0.5459	0.6495	0.5874	0.7500				
4	D2	D3	J8							
	0.9459	0.8876	0.5842							
5	A2	A3	A6	B3	B4	D1	D2	D3	D4	D5
	0.7217	0.5165	0.6802	0.7062	0.7325	0.6797	0.6090	0.6811	0.6583	0.7875
	E1	E2	E3	E4	F1	F2	F3	G2	H1	H2
	0.5779	0.6015	0.6652	0.7346	0.5482	0.6195	0.6833	0.5240	0.5203	0.6109
	I1	I2	J1	J2	J3	J4	J5	J7	J8	
	0.5314	0.6083	0.6449	0.5426	0.5623	0.5459	0.8032	0.5028	0.9080	
6	B4	C6	D1	D2	D3	D5	E1	E2	E4	J8
	0.5492	0.5642	0.6939	0.8832	0.8756	0.7468	0.7400	0.6809	0.8096	0.8594
7	A2	A4	B1	B2	B3	B4	C6	C8	D1	D2
	0.5002	0.5082	0.6815	0.6371	0.6790	0.7272	0.7269	0.5566	0.5215	0.6778
	D3	D5	E1	E2	E4	E5	E6	F2	F3	J8
	0.7070	0.6790	0.7879	0.7669	0.8848	0.7517	0.5917	0.5024	0.5004	0.6749
8	B3	D2	D3	D5	F1	F2	F3	H2	J1	J2
	0.6672	0.5251	0.5220	0.7374	0.6774	0.6720	0.6300	0.5365	0.5295	0.5141
9	A2	A4	A5							
	0.5243	0.5554	0.5445							

In the first class, no items with conditional item-response probabilities of hindrance of at least 0.5 are observed. In general, in this class the probability to experience hindrance is small. Individuals in this class have a small chance to experience hindrance on activities and participation, such that the class can be labeled as "no hindrance". In class 4 only three items have a item-response probability of at least 0.5. A possible interpretation for this class might be "problems related to task-specific and functional arm and hand movements" since two items come from theme D "mobility", namely "lifting and carrying objects" and "fine hand use". In class 9, three items from theme A "learning and applying knowledge" had high item-response probabilities of hindrance. Although it is difficult to find the meaning of this class, a possible label could be "concentration problems", with having more difficulties with some activities that requires specific concentration. Next, class 3 has six items with item-response probabilities of at least 0.5. It might be the case that this class has to do with specific parts of mobility, related with emotional discomfort. The other five classes contain many items with experience of hindrance. For instance class 2 can be labeled as "mental task problems" since most items came from theme A "learing and applying knowledge" and theme B "general tasks and demands". Again, there is a related emotional and behavioral discomfort. Class 6 contains many items from theme D "mobility" and theme E "self-care" with specific emphasis on the tasks which involve body movements, hand coordination, etc. Therefore, a possible label for this class can be "locomotion hindrance". The eighth class can be interpret as "hindrance related to household tasks" with almost all items related to a specific household task such as acquisition of goods and services, preparing meals, and doing housework. Class 5 and 7 contain the largest number of items with high item-response probabilities and are therefore very difficult to interpret. However, it can be noticed that class 5 can stand for "hindrance in almost all activities and participation" as a kind of counterpart of latent class 1. The probability for an individual to belong to classes 5 or 7 with a lot of hindrance experience, is small as noticed in Table 9. There is a larger probability to belong to class 1 with almost no hindrance or class 4 with problems related to task-specific and functional arm and hand movements.

4.4 Generalized estimating equations

A marginal model (3) was fitted with independence and exchangeable working correlation structure for the probability of overall experience of hindrance. GEE was used to estimate the parameters of the model, taking the clustered nature of the data into account. In Table 11 the parameter estimates together with the model-based and empirical standard errors under independence and exchangeable working correlation assumption, are presented. It can be noticed that the parameter estimates and empirical standard errors are pretty close under both assumptions. In addition, the intraclass correlation under exchangeable structure was found to be 0.04, which is not large. In other words, a patient had different experiences of hindrance, depending on the particular item. Under independence structure, the QIC was equal to 3635.69, while under the exchangeable assumption the QIC was found to be 3653.56. The discrepancies between the model-based and empirical estimates for both cases were not particularly favoring an assumption. Since the choice of an correlation assumption does not harm the parameter estimates and based on the QIC values, the independence structure was preferred.

Table 11: GEE parameter estimates of model 3 under different working assumptions

		Independence		**Exchangeable**	
Effect	**Parameter**	**Estimate**	**Standard Error***	**Estimate**	**Standard Error***
Intercept	β_0	-2.5104	(0.4146; 0.5562)	-1.7714	(0.9542; 0.5978)
Setting	β_1	0.7586	(0.1426; 0.2016)	0.4367	(0.3411; 0.1931)
Patient	β_2	-0.2720	(0.1025; 0.3268)	-0.2702	(0.1001; 0.3219)
InfCareg	β_3	-0.1266	(0.1007; 0.2843)	-0.1258	(0.0982; 0.2807)
Trauma	β_4	1.2129	(0.2943; 0.2043)	1.1908	(0.6732; 0.2199)
Internal	β_5	1.3188	(0.3155; 0.1964)	1.1151	(0.7298; 0.2195)
Parent	β_6	-0.0978	(0.1891; 0.4794)	-0.5091	(0.4679; 0.5068)
Partner	β_7	0.5538	(0.1994; 0.5029)	0.0090	(0.4871; 0.5259)
Theme A	β_8	-0.2867	(0.1437; 0.2045)	-0.2849	(0.1402; 0.2024)
Theme B	β_9	-0.1297	(0.1675; 0.2338)	-0.1289	(0.1633; 0.2314)
Theme C	β_{10}	-0.9354	(0.1541; 0.2612)	-0.9291	(0.1522; 0.2581)
Theme D	β_{11}	0.6426	(0.1474; 0.2346)	0.6388	(0.1440; 0.2336)
Theme E	β_{12}	-0.6556	(0.1521; 0.3077)	-0.6513	(0.1490; 0.3047)
Theme F	β_{13}	-0.3416	(0.1920; 0.2844)	-0.3394	(0.1872; 0.2814)
Theme G	β_{14}	-1.8445	(0.2371; 0.3442)	-1.8305	(0.2416; 0.3479)
Theme H	β_{15}	-0.7081	(0.2073; 0.1749)	-0.7034	(0.2026; 0.1750)
Theme I	β_{16}	-1.2763	(0.2428; 0.3337)	-1.2673	(0.2395; 0.3324)
Correlation	ρ	-		0.04	

$*$ *(Model-based standard error; Empirically corrected standard error)*

Under the independence correlation assumption, both the setting (p-value = 0.0349) and theme (p-value = 0.0323) were found to be significant. However under exchangeable structure, setting was insignificant (p-value = 0.0722) and can therefore be seen as a borderline situation. For patients from the chronic setting, a higher probability of feeling discomfort is observed compared to patients from the ambulatory setting. It is important to mention that this difference between the settings was caused by the professional caregivers, with caregivers from the chronic setting indicating more hindrance for the patient or informal caregiver compared to the professional caregivers of the ambulatory setting. This was already noticed in Table 6 with more overestimation of hindrance in the Mané setting. In addition, theme D "mobility" was found to have the highest probability of hindrance experiences, whereas theme G "interpersonal interactions and relationships" was found to have the smallest amount of hindrance. Further, it can be noticed that the assessor groups did not differ in terms of the probability of hindrance experience. However, this has nothing to do with the quality of assessment. The acquired brain injury type and the relation between the patient and informal caregiver had no significant effect on the probability of hindrance experience.

Next, a marginal model (4) was fitted with independence and exchangeable working correlation structure for the probability of hindrance assessment of the professional caregivers per item. The professional caregiver estimated the situation correctly if he and both the patient and informal caregiver experienced no hindrance, or if he indicated hindrance and the patient or informal caregiver expressed this too. Again, GEE was used to estimate the parameters and to correct for the possible associations within patients/professional caregivers. The parameter estimates together with the model-based and empirical standard errors under both working correlation assumptions are displayed in Table 12. As in the previous GEE estimation, similar estimates and empirical standard errors under different assumptions can be observed with same exchangeable working correlation of 0.04. The QIC values were very close with 1458.02 under independence and 1459.29 under exchangeable working assumption. Also, based on the differences between the model-based and empirical estimates no specific assumption can be favored. However, in both cases same conclusions can be made in terms of significance.

Table 12: GEE parameter estimates of model 4 under different working assumptions

		Independence		**Exchangeable**	
Effect	**Parameter**	**Estimate**	**Standard Error***	**Estimate**	**Standard Error***
Intercept	β_0	2.9950	(0.5869; 0.8979)	2.7373	(0.9590; 0.9034)
Setting	β_1	-1.1654	(0.2245; 0.3833)	-1.0691	(0.3738; 0.3847)
Trauma	β_2	-0.9791	(0.3734; 0.1852)	-0.9076	(0.6145; 0.1920)
Internal	β_3	-1.5398	(0.4134; 0.4359)	-1.4027	(0.6828; 0.4483)
Parent	β_4	-0.7638	(0.2976; 0.5572)	-0.6779	(0.5016; 0.5658)
Partner	β_5	-1.0969	(0.3165; 0.5409)	-0.9838	(0.5314; 0.5397)
Theme A	β_6	0.4191	(0.2331; 0.2885)	0.4176	(0.2280; 0.2863)
Theme B	β_7	0.2207	(0.2724; 0.3681)	0.2199	(0.2664; 0.3655)
Theme C	β_8	0.6186	(0.2292; 0.3369)	0.6165	(0.2242; 0.3343)
Theme D	β_9	-0.2331	(0.2487; 0.3407)	-0.2322	(0.2434; 0.3387)
Theme E	β_{10}	0.5426	(0.2359; 0.3611)	0.5407	(0.2308; 0.3584)
Theme F	β_{11}	0.1379	(0.2996; 0.4361)	0.1374	(0.2930; 0.4332)
Theme G	β_{12}	1.4408	(0.3084; 0.3558)	1.4363	(0.3028; 0.3531)
Theme H	β_{13}	0.7054	(0.3204; 0.3208)	0.7030	(0.3134; 0.3186)
Theme I	β_{14}	0.9548	(0.3355; 0.3717)	0.9517	(0.3283; 0.3689)
Correlation	ρ	-		0.04	

$*$ *(Model-based standard error; Empirically corrected standard error)*

Among all included covariates, only theme was found to be significant (p-value = 0.0447) as a borderline situation. The assessment of hindrance experience by the formal caregiver related to interpersonal interactions and relations (theme G) was found to be the best among all other themes. In contrast, the probability of correct assessment by the professional caregiver was the smallest for items of theme D "mobility". This was also explored in Table 5 with hindrance underestimation of 40% of the items by the professional caregivers. The setting had no effect on the probability of correct assessment. Although there was more overestimation of hindrance by the professional caregivers from the Mané setting, the difference in probability of correct assessment in both settings was not found to be significant. Furthermore, the acquired brain injury type and the relation between the patient and informal caregiver had no significant effect on the assessment quality of hindrance experience reported by the formal caregiver.

4.5 Generalized linear mixed model

A GLMM was also fitted for both the experience of hindrance and the assessment quality of the professional caregivers. In Table 13 the parameter estimates and standard errors are provided of the GLMM for the probability of overall experience of hindrance. Compared to marginal model 3 using GEE and the independence working correlation structure, the parameter estimates are similar and have the same directions of effect (see Table 11). In addition, the estimated variance of the random intercepts was found to be 0.2778, indicating a small size of deviation from the mean intercept as a source of within-patient variability.

Theme was found to be highly significant (p-value < 0.0001) with theme D "mobility" having the largest and theme G "interpersonal interactions and relationships" the smallest probability of hindrance experience. Although in the marginal model with GEE the assessors did not differ in terms of the probability of hindrance experience, it was significant in the GLMM (p-value = 0.0252). Based on the GLMM, patients indicated the smallest amount of hindrance, whereas the professional caregivers reported the largest amount of hindrance. The setting was not significant (p-value = 0.0689) as a borderline case. Although it was not significant, the probability of hindrance experience was larger for patients in the chronic setting, compared to those from the ambulatory setting. The acquired brain injury type and the relation between the patient and informal caregiver had no significant effect on the probability of hindrance experience.

Table 13: GLMM parameter estimates of model 5 by adaptive Gaussian quadrature

Effect	**Parameter**	**Estimate**	**Standard Error**
Intercept	β_0	-2.4494	1.0141
Setting	β_1	0.7092	0.3897
Patient	β_2	-0.2848	0.1050
InfCareg	β_3	-0.1327	0.1031
Trauma	β_4	1.2056	0.6388
Internal	β_5	1.2550	0.7158
Parent	β_6	-0.1208	0.5567
Partner	β_7	0.4942	0.5777
Theme A	β_8	-0.3017	0.1475
Theme B	β_9	-0.1366	0.1719
Theme C	β_{10}	-0.9776	0.1576
Theme D	β_{11}	0.6813	0.1519
Theme E	β_{12}	-0.6872	0.1558
Theme F	β_{13}	-0.3593	0.1967
Theme G	β_{14}	-1.9093	0.2402
Theme H	β_{15}	-0.7418	0.2118
Theme I	β_{16}	-1.3289	0.2467
var(b_{0i})	d	0.2778	0.0996

In Table 14 the results of the parameter estimation of GLMM (6) for the probability of correct assessment of the formal caregiver, are shown. As mentioned before, correct assessment was obtained if hindrance was reported, while the patient or informal caregiver also indicated hindrance. The assessment of no hindrance for all three subjects, was also considered as a correct assessment of the professional caregiver. Again, similar parameter estimates with same direction of effects were noticed in the GLMM compared to those from the marginal model obtained by the GEE estimation (see Table 12). The estimated variance of the random intercepts was equal to 0.2778 with standard error of 0.0996, which was close to the ones estimated in previous GLMM.

Table 14: GLMM parameter estimates of model 6 by adaptive Gaussian quadrature

Effect	Parameter	Estimate	Standard Error
Intercept	β_0	2.9281	0.9966
Setting	β_1	-1.1269	0.3870
Trauma	β_2	-0.9958	0.6197
Internal	β_3	-1.4994	0.6957
Parent	β_4	-0.7266	0.5442
Partner	β_5	-1.0465	0.5694
Theme A	β_6	0.4382	0.2384
Theme B	β_7	0.2308	0.2786
Theme C	β_8	0.6466	0.2345
Theme D	β_9	-0.2438	0.2543
Theme E	β_{10}	0.5672	0.2413
Theme F	β_{11}	0.1442	0.3064
Theme G	β_{12}	1.5013	0.3147
Theme H	β_{13}	0.7374	0.3276
Theme I	β_{14}	0.9966	0.3427
var(b_{0i})	d	0.2097	0.0966

Based on the type 3 test for fixed effects, theme was found to be highly significant (p-value < 0.0001) with smallest probability of correct assessment for items of theme D "mobility" and largest amount of assessment quality for items of theme G "interpersonal interactions and relationships". Moreover, setting had an effect on the probability of correct assessment (p-value = 0.0037) with a better performance of the professional caregivers from the ambulatory setting (Jessa hospital) in hindrance assessment. This is not surprising since more overestimation of hindrance by the professional caregivers was observed in the chronic setting (Mané), as shown in Table 6. Finally, the acquired brain injury type and the relation between the patient and informal caregiver had no significant effect on the quality of hindrance estimation.

5 Discussion and conclusions

The main objective of this study contains in finding statistical ways to analyze the hindrance in activities and participation of patients with acquired brain injury. The ERNAH project, started in 2012 and managed by five partners, had developed a screening tool called FINAH and contains 53 ICF-items to measure hindrance in activities and partication of patients with acquired brain injury. Data were available from 22 patients with acquired brain injury and their caregivers, coming from different care settings. As a way to increase the possible statistical techniques, dichotomization of the hindrance response was considered to eliminate the nominal nature of the data. In addition, no missing observations were found.

Based on the exploratory data analysis, following observations were made. Two items were found without any experience of hindrance for both the patient and informal caregiver, namely the production of nonverbal messages and religion and spirituality. On the basis of the results of patients, faster and more often tired was indicated as most problematic. According to the informal caregivers, lifting and carrying objects gave most of the problems. On average 21.1% of the patients and 23.4% of the informal caregivers indicated the presence of hindrance concerning a particular item. Based on the specified rules of correct assessment of the professional caregiver, 67% of the evaluations were done properly. The assessment of hindrance concerning the production of nonverbal messages was found to be the best with 95% correct evaluations. In contrast, only 23% correct assessments were made of problems about driving. Items related to mobility were not properly evaluated with only 52% correct assessments and 40% of the items where the hindrance is underestimated by the professional caregiver.

Factor analysis and latent class analysis were considered to measure the assocation between answers on the different ICF-items and to investigate items which were given the same answers routinely by the patient or caregiver. Both methods are different in nature and make different assumptions, but can be applied on the data. Different from factor analysis, latent class analysis provides a framework for measuring categorical, in stead of continuous, latent variables and is more concerned with the structure of cases (McLachlan and Peel, 2000). However, due to small sample sizes and a large amount of variables, more data was needed. Therefore, data was generated via simulation. As a result, the conclusions were not reliable for the real data but can be used as an example when more data is available. By using factor analysis 11 factors were retained, while in latent class analysis 9 classes were selected. Based on subjective method of interpretation, following names were given to the factors: skillfulness or age problems, hindrance with regard to imposed rules and social norms or behaviors, drinking and eating problems, hindrance concerning engagement, meal-related tasks and capabilities, communication problems, emotion and behavior discomfort, confrontation and problems with interaction of something new, task-specific and functional arm and hand movement problems, and dealing with unfamiliar surroundings and formal relationships. In latent class analysis, the classes were labelled as follows: no hindrance, problems related to task-specific and functional arm and hand movements, concentration problems, problems concerning mobility activities, mental task problems, locomotion hindrance, hindrance related to household tasks, and hindrance in almost all activities and participation. In both methods it was observed that answers on some items within a specific theme were related. However, the themes did not explain all association between items and high correlations between items from different themes were observed as well. For instance, washing oneself and caring for body parts were highly associated as items coming from theme called self-care, while work and employment and engaging in all aspects of community social life were correlated in terms of hindrance experience, though both partipation items came from different themes. These findings and interpretations should be regarded with caution since it is based on subjective decisions and simulated data.

Generalized estimating equations (GEE) and generalized linear mixed models (GLMMs) were considered to measure the effect of covariates on the experience of hindrance and the assessment quality of the professional caregiver, taking the clustering effect of patients into account. While the marginal model with GEE techniques has a population-averaged focus, the random effects model has the benefit to draw inferences on the level of the specific patient (Verbeke and Molenberghs, 2000). Although the parameter estimates for the marginal model and random effects model cannot be compared, similar directions of effects were noticed. Based on the results of both GEE and GLMM, theme had a significant effect on hindrance experience and assessment quality, with the largest amount of hindrance and smallest probability of correct assessment in mobility activities and the smallest amount of hindrance and best assessment for items related to interpersonal interactions and relationships. Setting was found to be a borderline situation, with larger probability of hindrance experience for patients in the chronic setting compared to the ambulatory setting. However, 23.5% of the patients from the ambulatory setting and 18.7% of the patients from the chronic setting of care, reporting hindrance per item. This is the result of worse quality of hindrance assessment by professional caregivers in the chronic setting with a larger amount of overestimation of the problems. This was confirmed by the GLMM, where the care setting was found to have an effect on the assessment quality with a better performance of the caregivers from the ambulatory setting and more overestimation of hindrance by caregivers from the chronic care setting. In addition, based on the results of the GLMM, patients indicated the smallest amount of hindrance, whereas professional caregivers reported the largest amount of hindrance. The acquired brain injury type and the relation between the patient and informal caregiver did not have an effect on the hindrance experience and on the quality of hindrance assessment by the professional caregiver.

This study has some limitations and concerns. Firstly, there was no need to deal with missing data in the analysis. However, when missing observations are present, additional requirements might be needed depending on the mechanism. When the mechanism is missing at random (MAR), but not completely at random (MCAR), multiple imputation with replacement of missing data with imputed values can be considered in the process of factor analysis or latent class analysis (Schafer, 1997). Likelihood-based methods such as GLMM are still valid under MAR, whereas GEE estimation can provide biased estimates. Possible solutions could be to perform a weighted GEE or GEE with multiple imputation techniques (Fitzmaurice *et al.*, 2004). Under the mechanism of missing not at random (MNAR) missingness cannot be ignored and more advanced techniques are required. Sensitivity analysis could be considered as a way to carefully check the assumptions of missing mechanism to be plausible (Ibrahim and Molenberghs, 2009). Secondly, information was lost due to the dichotomization of the response. However, keeping the nominal nature of the data involves limitations in the analysis options and can give many problems (Pearson and Mundform, 2010). Other recode possibilities could also be considered. In third place, both factor analysis and latent class analysis were performed on simulated data since the sample size was found to be small and the number of variables large. Due to this, the results can not be trust. Moreover, an interesting extention of the latent class analysis model by including covariates and varying the probabilities across patients and their caregivers, was not applied. In addition, no specific required sample size for factor analysis and latent class analysis was specified. Besides, the use of tetrachoric correlations in factor analysis can be problematic in terms of normality assumption and inflated sample size requirements (Gorsuch, 1983; Pearson and Mundform, 2010). However, since the analysis were conducted on the level of exploration, the multivariate normality assumption was not required (Johnson and Wichern, 2007). Fourthly, no inferences were done on the individual items. GEE and GLMM were applied on the answers of all items combined as a practical consideration. Individual (exact) logit regression models for each of the item could be fitted, but leads to a number of 53 models for each method. When one is only interested in differences between the chronic and ambulatory care setting in terms of hindrance assessment and quality of assessment per item, Fisher's exact test used in the analysis of contingency tables, can be conducted. However, many tests need to be conducted and an appropriate multiple test correction such as false discovery rate, should be applied (Benjamini and Hochberg, 1995). At last, multitrait-multimethod (MTMM) analysis could also be considered as a way to measure the association between the answers of the patient and caregivers. MTMM designs have frequently been applied to investigate convergent and disciminant validity of several traits assessed by multiple informants (Campbell and Fiske, 1959). Due to complexities, confirmatory factor analysis has become a valuable tool to evaluate multiple informant reports (Kuppens *et al.*, 2009).

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Appendix

Table A1: Overview of selected ICF themes and items for FINAH instrument

Theme A: Learning and applying knowledge
Item 1: Acquiring skills
Item 2: Focusing attention
Item 3: Thinking
Item 4: Reading
Item 5: Calculating
Item 6: Solving problems
Item 7: Making decisions

Theme B: General tasks and demands
Item 1: Carrying out daily routine
Item 2: Undertaking a single task
Item 3: Undertaking multiple tasks
Item 4: Handling stress situations

Theme C: Communication
Item 1: Communicating with spoken messages
Item 2: Communicating with nonverbal messages
Item 3: Communicating with written messages
Item 4: Speaking
Item 5: Producing nonverbal messages
Item 6: Writing messages
Item 7: Conversation
Item 8: Using communication devices/techniques

Theme D: Mobility
Item 1: Changing basic body position
Item 2: Lifting and carrying objects
Item 3: Fine hand use
Item 4: Using transportation
Item 5: Driving

Theme E: Self-care
Item 1: Washing oneself
Item 2: Caring for body parts
Item 3: Toileting
Item 4: Dressing
Item 5: Eating
Item 6: Drinking
Item 7: Looking after one's health

Theme F: Domestic life
Item 1: Acquisition of goods and services
Item 2: Preparing meals
Item 3: Doing housework

Theme G: Interpersonal interactions and relationships
Item 1: Basic interpersonal interactions
Item 2: Intimate relationships
Item 3: Family relationships
Item 4: Informal social relationships
Item 5: Formal relationships

Theme H: Major life areas
Item 1: Education or training
Item 2: Work and employment
Item 3: Economic life

Theme I: Community, social and civic life
Item 1: Engaging in all aspects of community social life
Item 2: Recreation and leisure
Item 3: Religion and spirituality

Theme J: Emotion and behaviour
Item 1: Gloomy, dejected and depressed
Item 2: Anxiousness
Item 3: Unrealistic expectations
Item 4: Faster emotionally
Item 5: More irritable and snappish
Item 6: Indifference
Item 7: Disinhibition and problems in controlling behavior
Item 8: Faster and more often tired

Table A2: Reduced tetrachoric correlation matrix of the 53 items based on the simulated data

Variable	A1	A2	A3	A4	...	J5	J6	J7	J8
A1	1.0000	0.2783	0.4453	0.1164	...	-0.0165	0.1609	0.1503	0.0470
A2		1.0000	0.1154	0.0994	...	0.0558	0.3079	0.2186	0.2413
A3			1.0000	0.0373	...	0.2606	0.0624	0.1804	0.4028
A4				1.0000	...	0.0550	-0.0947	-0.0810	-0.3361
$\vdots$					$\ddots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
J5						1.0000	0.2748	0.4497	0.1729
J6							1.0000	0.3694	0.2017
J7								1.0000	0.2084
J8									1.0000

Table A3: Orthogonal transformation matrix based on the simulated data

	Orthogonal transformation matrix										
	1	2	3	4	5	6	7	8	9	10	11
1	0.4874	0.4060	0.3164	0.3408	0.4119	0.2572	0.2070	0.1850	0.0921	0.2244	0.0982
2	0.3419	-0.4675	0.5527	-0.3749	-0.0670	0.2517	-0.2361	0.1520	0.1474	-0.1845	-0.1270
3	-0.4207	0.2002	0.1989	-0.3345	0.0842	0.3007	-0.0370	0.3791	-0.5373	0.0890	0.3038
4	-0.0822	-0.1624	-0.0328	-0.2159	0.1275	-0.2884	0.7068	0.4504	0.2569	-0.2158	0.0687
5	0.1802	-0.1433	-0.4597	0.0634	-0.4083	0.6922	0.2573	0.1059	0.0263	0.0021	0.0878
6	-0.2607	-0.5569	0.1492	0.2605	0.4108	0.2232	0.3047	-0.4144	-0.2004	0.0853	0.0351
7	0.0065	0.0678	0.2558	0.3316	-0.3417	-0.0675	0.2430	0.1463	-0.4685	-0.1845	-0.6039
8	-0.1983	-0.3471	0.0976	0.5239	-0.2087	-0.1427	-0.2514	0.4946	0.1643	0.3365	0.2104
9	-0.5483	0.2765	0.2137	0.1558	0.0009	0.3559	-0.0492	-0.0358	0.5345	-0.3209	-0.1843
10	-0.1101	-0.0653	-0.2645	-0.2310	0.3107	0.1171	-0.0825	0.2263	0.1038	0.5082	-0.6504
11	-0.0966	0.1171	0.3602	-0.2255	-0.4584	-0.0520	0.3316	-0.3077	0.1768	0.5877	0.0482

Table A4: Rotated factor loadings of each variable on the 11 extracted factors

	Rotated factor pattern (γ_{ij})										
Var	1	2	3	4	5	6	7	8	9	10	11
A1	0.0636	0.0863	0.0370	-0.0707	0.0056	-0.0102	-0.1152	0.6200	-0.0019	0.0617	0.2459
A2	0.1340	-0.0490	-0.0132	0.0557	0.0374	0.1101	0.2103	0.2144	-0.0285	0.1672	0.5213
A3	0.0956	0.1372	0.0703	-0.0152	0.0427	0.1157	0.3113	0.7058	0.0918	0.0779	-0.1818
A4	-0.0391	-0.0126	0.4499	0.0125	0.1344	0.3519	-0.2802	0.1184	-0.1604	0.2099	-0.0591
A5	-0.0237	-0.1063	0.3098	-0.0067	0.1980	0.5062	-0.0010	-0.0151	-0.2004	0.4384	0.2064
A6	-0.0470	0.1375	0.1247	-0.1009	0.5329	0.1200	0.3532	0.3015	0.0893	0.1027	0.1838
A7	0.0468	0.0770	0.2235	0.0607	0.1571	0.2000	0.2188	0.5771	-0.1987	-0.0393	0.0113

B1	0.2279	0.1177	0.7207	0.1771	0.1951	0.0033	-0.0574	0.1323	0.0560	0.0977	0.1751
B2	0.1025	0.0128	0.4593	-0.0855	0.4460	0.2724	0.1451	0.1692	-0.0571	-0.1688	0.0993
B3	0.1037	0.1151	0.1599	0.0639	0.5647	-0.0006	-0.0081	0.2953	0.1099	0.0293	0.1274
B4	0.3160	0.1153	0.1827	-0.0961	0.2134	0.2020	0.1911	0.1814	0.0488	-0.0481	0.1372
C1	0.1059	0.0709	0.0313	-0.0387	-0.0663	0.6482	-0.0137	0.2282	-0.1251	0.1252	0.1683
C2	0.3863	0.2284	-0.1577	0.2550	0.0769	0.2556	-0.0843	0.1480	-0.0777	-0.0780	0.1872
C3	0.2613	0.0920	0.3485	-0.0910	0.0184	0.5984	-0.2941	0.0952	-0.1264	0.0560	-0.1411
C4	0.1595	-0.1727	-0.0668	-0.1245	0.0321	0.4681	0.2455	-0.1700	0.3567	-0.1007	-0.1666
C5	0.1529	-0.1763	0.4170	-0.1103	-0.0219	0.4017	-0.2318	0.4337	0.1428	0.0273	0.0319
C6	0.3917	-0.0154	0.1550	0.0319	0.1997	0.2917	-0.0340	-0.0139	0.1172	-0.0352	-0.2307
C7	0.0150	0.0004	-0.0306	0.0964	0.1255	0.6513	0.2239	0.1233	0.0145	-0.0061	0.1736
C8	0.6579	-0.0540	0.1694	0.1300	0.1623	-0.0125	-0.1424	0.3409	0.0167	-0.0974	0.1880
D1	0.1868	0.0602	0.0725	0.1858	0.0591	-0.0830	0.2553	0.1822	0.2700	0.0467	-0.4425
D2	0.1606	-0.0956	0.0249	0.1104	0.0002	-0.1023	-0.1026	0.0077	0.8894	-0.0046	-0.0329
D3	0.1680	-0.0234	0.0561	0.0461	0.1278	-0.0272	0.0393	-0.0136	0.8256	-0.0577	-0.0473
D4	0.2805	0.0466	-0.2458	0.3052	0.3325	0.1866	0.2062	-0.0162	-0.1202	0.2968	0.0330
D5	0.2693	0.0965	-0.0510	0.3662	0.1314	0.0391	0.1385	-0.2131	0.0464	-0.0084	0.0584
E1	0.7265	0.0806	0.2300	0.1452	-0.0227	0.2270	0.0571	-0.0935	0.2484	0.0938	0.0132
E2	0.7953	0.0627	0.2707	0.1649	0.1807	0.0118	0.1571	0.0926	0.1506	0.0508	-0.0438
E3	0.3993	0.2902	0.1591	-0.1454	0.2590	0.0607	0.0896	0.2305	0.1329	0.4581	-0.1863
E4	0.7339	0.0204	0.3184	0.2363	0.1234	0.1556	0.1141	-0.0111	0.1918	0.1804	0.0171
E5	0.1872	0.1060	0.7705	0.0918	0.1159	0.0539	0.0194	0.0302	0.0465	-0.0232	-0.0397
E6	0.2731	-0.0920	0.8014	-0.0886	-0.0017	0.0102	0.0936	0.0622	0.0300	-0.0161	-0.1462
E7	0.2309	0.7088	0.0820	-0.0203	0.2820	-0.1013	-0.0981	0.0981	-0.0647	0.1724	-0.0927
F1	0.1140	0.1129	0.1820	0.3959	0.6732	0.1037	0.0731	-0.2128	-0.0719	0.0767	-0.3065
F2	0.1566	0.1123	0.0402	0.1790	0.7222	-0.0679	0.0215	0.0082	0.0688	0.0202	-0.0050
F3	0.2202	0.1260	0.1739	0.5215	0.3878	0.0113	0.2012	-0.0795	-0.0164	0.0893	-0.0995
G1	-0.1196	0.5601	0.0038	0.3483	0.0501	0.0566	-0.0497	0.0354	0.1369	0.2377	0.2521
G2	0.4463	0.6451	0.0917	0.0575	0.2186	-0.0708	0.0558	0.0779	-0.1570	0.1475	-0.0792
G3	0.1573	0.2686	0.0429	0.2681	-0.0843	0.5492	0.0187	-0.1658	0.0405	-0.0696	-0.0638
G4	-0.0207	0.6038	-0.0444	0.0964	-0.0729	0.3612	-0.0998	-0.0153	-0.1599	-0.0398	-0.1597
G5	-0.0351	0.4767	-0.0214	0.3684	0.3344	0.1903	-0.0101	-0.1308	0.1110	0.4608	0.4201
H1	0.0517	0.2273	-0.0146	0.3255	0.0098	0.0062	0.0483	0.1065	-0.0741	0.8179	0.0799
H2	0.0478	-0.0165	0.2512	0.7888	0.0221	-0.0395	0.1660	0.0148	-0.0429	0.1532	0.0029
H3	0.2068	0.2879	0.0724	-0.1251	0.4298	0.0570	0.1731	-0.2488	0.0969	0.2669	0.3099
I1	0.1663	0.2016	-0.1260	0.7380	0.2124	0.1115	-0.0377	-0.0205	0.2975	0.0376	0.0901
I2	0.4177	0.3765	-0.1474	0.5978	-0.1851	0.0317	0.1000	0.1452	0.0755	0.0657	-0.1875
I3	0.2902	0.6287	0.1827	0.1738	0.3372	0.0531	-0.0615	-0.0983	-0.0252	0.2173	0.1930
J1	-0.1139	0.0029	-0.0330	0.2595	0.2303	-0.0108	0.5745	0.1147	-0.0547	0.1277	0.1052
J2	-0.3457	0.2412	-0.1145	0.2894	0.1752	-0.0958	0.2107	0.2472	-0.1203	0.1767	-0.1138
J3	-0.0253	0.3279	0.3140	-0.0489	0.1590	-0.0030	0.1708	0.2729	0.1176	-0.2423	0.4167
J4	0.1255	-0.0072	0.0764	0.1193	0.0740	0.0486	0.7919	-0.0418	-0.1146	-0.0545	0.0344
J5	-0.1261	0.4876	0.1734	0.1296	-0.0426	-0.0083	0.4604	0.0780	0.0269	-0.1150	-0.0009
J6	0.1839	0.3553	-0.0853	0.1523	0.1112	0.0840	0.2597	0.0550	-0.1814	-0.0070	0.3846
J7	-0.1376	0.5945	-0.0994	0.0412	0.0417	0.0180	0.2777	0.1896	0.0230	-0.0312	0.0876
J8	0.3085	0.0762	-0.1931	-0.0548	-0.0164	0.0395	0.5690	0.1603	0.2885	0.1674	0.0173

Table A5: Estimated item-response probabilities of hindrance, conditional on latent class with $C = 1, ..., 9$ and $r_j = 2$

	Conditional item-response probabilities of hindrance ($\rho_{\mathbf{j},\mathbf{r_j}|\mathbf{c}}$)								
Var	1	2	3	4	5	6	7	8	9
A1	0.2057	0.5707	0.1284	0.2400	0.4453	0.2370	0.4164	0.2705	0.3762
A2	0.3038	0.5844	0.4611	0.3039	0.7217	0.4540	0.5002	0.3368	0.5243
A3	0.0874	0.5542	0.2109	0.1282	0.5165	0.2549	0.4248	0.1235	0.1786
A4	0.1342	0.1606	0.0510	0.1087	0.2509	0.0739	0.5082	0.3769	0.5554
A5	0.0979	0.2092	0.1360	0.0388	0.3724	0.0803	0.4384	0.2780	0.5445
A6	0.0981	0.7447	0.2131	0.1052	0.6802	0.3110	0.4688	0.4393	0.2352
A7	0.0136	0.2708	0.0595	0.0131	0.2422	0.0409	0.2150	0.0725	0.1043
B1	0.0000	0.1416	0.0157	0.0446	0.3267	0.1228	0.6815	0.2277	0.1813
B2	0.0393	0.3951	0.0484	0.0647	0.3406	0.1447	0.6371	0.2171	0.3376
B3	0.1635	0.6064	0.2187	0.2756	0.7062	0.4540	0.6790	0.6672	0.3985
B4	0.1658	0.5820	0.3160	0.2285	0.7325	0.5492	0.7272	0.2033	0.4461
C1	0.0172	0.0669	0.0573	0.0146	0.1468	0.0143	0.1171	0.0187	0.1889
C2	0.0125	0.0207	0.0434	0.0065	0.1415	0.0309	0.0759	0.0158	0.0279
C3	0.0456	0.0750	0.0345	0.0445	0.1573	0.0926	0.4308	0.0971	0.3602
C4	0.0824	0.2555	0.3301	0.3463	0.2626	0.4395	0.3787	0.0135	0.3282
C5	0.0009	0.0094	0.0000	0.0055	0.0000	0.0000	0.1008	0.0000	0.0430
C6	0.1377	0.2723	0.2482	0.2821	0.4890	0.5642	0.7269	0.3169	0.4173
C7	0.0356	0.3051	0.2705	0.0845	0.4020	0.1556	0.2953	0.1116	0.3074
C8	0.0222	0.1647	0.0287	0.1053	0.3872	0.3735	0.5566	0.0983	0.1993
D1	0.2125	0.4440	0.5734	0.4123	0.6797	0.6939	0.5215	0.3794	0.2454
D2	0.1856	0.4314	0.4891	0.9459	0.6090	0.8832	0.6778	0.5251	0.3180
D3	0.1058	0.5162	0.4466	0.8876	0.6811	0.8756	0.7070	0.5220	0.3154
D4	0.0771	0.1648	0.4433	0.0528	0.6583	0.3156	0.2673	0.3815	0.1505
D5	0.3863	0.4433	0.7396	0.4432	0.7875	0.7468	0.6790	0.7374	0.3907
E1	0.0207	0.0850	0.1251	0.1516	0.5779	0.7400	0.7879	0.1309	0.2284
E2	0.0068	0.0801	0.0462	0.0317	0.6015	0.6809	0.7669	0.0966	0.0975
E3	0.0429	0.2488	0.0497	0.0728	0.6652	0.3673	0.4923	0.2487	0.1915
E4	0.0051	0.0602	0.0928	0.0763	0.7346	0.8096	0.8848	0.1872	0.2300
E5	0.0134	0.1609	0.0263	0.0985	0.2619	0.1527	0.7517	0.2431	0.3294
E6	0.0115	0.0883	0.0172	0.0670	0.0781	0.1387	0.5917	0.0631	0.2462
E7	0.0542	0.1449	0.0431	0.0171	0.4345	0.0759	0.1905	0.3316	0.0173
F1	0.0482	0.1253	0.2256	0.0652	0.5482	0.3152	0.4494	0.6774	0.1377
F2	0.1062	0.3637	0.1699	0.1620	0.6195	0.4055	0.5024	0.6720	0.1745
F3	0.0314	0.1244	0.3557	0.0654	0.6833	0.4305	0.5004	0.6300	0.1016
G1	0.0256	0.0850	0.1495	0.0495	0.3924	0.0174	0.0674	0.3308	0.0338
G2	0.0371	0.0949	0.0635	0.0000	0.5240	0.1135	0.2564	0.2754	0.0274
G3	0.0165	0.0227	0.0634	0.0102	0.1094	0.0613	0.1143	0.0711	0.0627
G4	0.0605	0.0610	0.0744	0.0023	0.1505	0.0161	0.0678	0.0892	0.0652
G5	0.0039	0.0202	0.0280	0.0017	0.3312	0.0054	0.0237	0.2050	0.0000
H1	0.0480	0.0864	0.2103	0.0385	0.5203	0.1344	0.1174	0.3326	0.1079
H2	0.0997	0.1340	0.5459	0.0999	0.6109	0.3282	0.4137	0.5365	0.1518
H3	0.0593	0.2289	0.1052	0.0813	0.4937	0.1679	0.3194	0.3132	0.1024

I1	0.0095	0.0131	0.3219	0.0397	0.5314	0.2200	0.1890	0.3404	0.0057
I2	0.0317	0.0629	0.4021	0.0882	0.6083	0.3389	0.2415	0.2760	0.0274
I3	0.0037	0.0223	0.0000	0.0000	0.3493	0.0265	0.1037	0.1825	0.0000
J1	0.2651	0.6684	0.6495	0.1696	0.6449	0.4327	0.4119	0.5295	0.2017
J2	0.3446	0.5176	0.4887	0.1386	0.5426	0.1766	0.1769	0.5141	0.1287
J3	0.1084	0.6528	0.1717	0.2166	0.5623	0.1845	0.4644	0.3572	0.2522
J4	0.1215	0.3961	0.4739	0.0659	0.5459	0.4095	0.2674	0.1216	0.1707
J5	0.3581	0.6752	0.5874	0.2742	0.8032	0.3400	0.4703	0.4989	0.2457
J6	0.0583	0.1911	0.1695	0.0147	0.4675	0.0765	0.1061	0.1518	0.0575
J7	0.1354	0.4091	0.2240	0.0563	0.5028	0.0576	0.1051	0.2020	0.0614
J8	0.3424	0.7856	0.7500	0.5842	0.9080	0.8594	0.6749	0.3111	0.3352

A6: Most relevant SAS and R codes used for analysis

1. **Simulation of data (R code)**

```
## Real data with 66 observations for each item ##
items<-data[,c("A1b",..., "J8b")]

## Pearson correlation matrix ##
sigma<-cor(items, method="pearson")

## Marginal probabilities of hindrance per item ##
margprob=c(0.30303030, ..., 0.57575758)

## Correlated multivariate binary random variables with 3000 observations ##
set.seed(103)
simdata<-rmvbin(3000,margprob,sigma=sigma)
```

2. **Factor analysis (R and SAS code)**

```
## Kaiser-Meyer-Olkin measure and Bartlett's test of sphericity ##
KMO(simdata[,c(1:53)])
cortest.bartlett(cor(simdata[,c(1:53)]),n=3000)

/* Tetrachoric correlation matrix */
proc freq data = simdata;
  tables (A1b ... J8b) / NOPRINT plcorr;
  ods output measures=mycorr (where=(statistic="Tetrachoric Correlation" or
  statistic="Polychoric Correlation") keep = statistic table value); run;

data mycorrt;
  set mycorr;
  group = floor((_n_ - 1)/53);
  x = scan(table, 2, " *");
  y = scan(table, 3, " *");
  keep group value table x y; run;

proc transpose data = mycorrt out=mymatrix (drop = _name_ group);
  id x;
  by group;
  var value; run;

Data fa(type=corr);
  set mymatrix(type=corr);
  _type_ = 'corr';

/* Factor Analysis with methods "prinit" and "ULS" */
Proc Factor data=fa nobs=3000 plots=scree method=prinit priors=max mineigen=1
  rotate=varimax; var A1b ... J8b; run;

Proc Factor data=fa nobs=3000 scree method=ULS priors=max mineigen=1
  rotate=varimax; var A1b ... J8b; run;
```

3. **Latent class analysis (R and SAS code)**

```
## LCA and final model in R ##
items <- simdata[,1:53]
items1 <- items+1
formula1 <- cbind(A1b, ..., J8b) ~ 1
LCAmodel <- poLCA(formula1,items1,nclass=9,maxiter=10000, nrep=5)

/* LCA and final model in SAS */
data lca;
  set simdata;
  if A1=0 then A1b=1; if A1 =1 then A1b=2;
  ...
  if J8=0 then J8b=1; if J8 =1 then J8b=2; drop A1 ... J8; run;

Proc lca data=lca outparam=par;
  title 'class analysis'; nclass 9; items A1b ... J8b; categories 2 ... 2;
  seed 200; nstarts 50; run;
```

4. **Generalized estimating equations (SAS code)**

```
/* GEE with binary response: probability of hindrance experience */
proc genmod data=hinder desc;
  class cluster_id setting (ref='0') theme (ref='J')  subject (ref='3')
  CM_relation (ref='2') NAH_type (ref='2')/param=ref;
  model hinder = setting subject NAH_type CM_relation theme /dist=bin type3;
  repeated subject=cluster_id / type=ind/exch modelse; run;

/* GEE with binary response: probability of correct assessment */
proc genmod data=assessment desc;
  class cluster_id setting (ref='0') theme (ref='J') CM_relation (ref='2')
  NAH_type (ref='2')/param=ref;
  model assessment = setting NAH_type CM_relation theme/dist=bin type3;
  repeated subject=cluster_id / type=ind/exch modelse; run;
```

5. **Generalized linear mixed model (SAS code)**

```
/* GLMM with binary response: probability of hindrance experience */
proc glimmix data=hinder method=QUAD(QPOINTS=50);
  class cluster_id setting (ref='0') subject (ref='3') NAH_type (ref='2')
  CM_relation (ref='2') theme (ref='J');
  model hinder = setting subject NAH_type CM_relation theme/dist=bin solution;
  random intercept / subject=cluster_id type=un; run;

/* GLMM with binary response: probability of correct assessment */
proc glimmix data=assessment method=QUAD(QPOINTS=50);
  class cluster_id setting (ref='0') NAH_type (ref='2') CM_relation (ref='2')
  theme (ref='J');
  model assessment = setting  NAH_type CM_relation theme/dist=bin solution;
  random intercept / subject=cluster_id type=un; run;
```

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Statistical challenges in measuring hindrance in activities and participation of clients with acquired brain injury

Richting: **Master of Statistics-Biostatistics**
Jaar: **2015**

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Voor akkoord,

Jouck, Peter

Datum: **27/08/2015**