View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by White Rose Research Online

This is a repository copy of *Predicting Productivity Losses from Health-Related Quality of Life Using Patient Data.*.

White Rose Research Online URL for this paper:
http://eprints.whiterose.ac.uk/114481/

Version: Accepted Version

Article:
Mukuria, C., Rowen, D., Hernández-Alava, M. et al. (2 more authors) (2017) Predicting Productivity Losses from Health-Related Quality of Life Using Patient Data. Applied Health Economics and Health Policy. ISSN 1175-5652

https://doi.org/10.1007/s40258-017-0326-x

Reuse
Unless indicated otherwise, fulltext items are protected by copyright with all rights reserved. The copyright exception in section 29 of the Copyright, Designs and Patents Act 1988 allows the making of a single copy solely for the purpose of non-commercial research or private study within the limits of fair dealing. The publisher or other rights-holder may allow further reproduction and re-use of this version - refer to the White Rose Research Online record for this item. Where records identify the publisher as the copyright holder, users can verify any specific terms of use on the publisher's website.

Takedown
If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

White Rose university consortium
Universities of Leeds, Sheffield & York

eprints@whiterose.ac.uk
https://eprints.whiterose.ac.uk/

Predicting productivity losses from health related quality of life using patient data

Clara Mukuria, Donna Rowen, Mónica Hernández-Alava, Simon Dixon, Roberta Ara
School of Health and Related Research (ScHARR), University of Sheffield

Correspondence to: Clara Mukuria, Health Economics and Decision Science, University of Sheffield, Regent Court, 30 Regent Street, Sheffield, S1 4DA, UK.
Email: c.mukuria@sheffield.ac.uk
Telephone: + 44 114 222 6395
Fax: + 44 114 222 0749

Abstract

Objectives: This paper estimates productivity loss using the health of the patient in order to allow indirect estimation of these costs for inclusion in economic evaluation.

Methods: Data were used from two surveys of inpatients (HODaR sample n=42,442 and HIPO sample n= 6,046). The number of days off paid employment or normal activities excluding paid employment was modelled using the health of the patients measured by EQ-5D, International Classification of Diseases (ICD) chapter and other health and sociodemographic data. Two part models (TPM) and zero inflated negative binomial (ZINB) models were identified as the most appropriate specifications given large spikes at the minimum and maximum days for the dependent variable. Analysis was undertaken separately for the two datasets to account for differences in recall period and identification of those who were employed.

Results: Models were able to reflect the large spike at the minimum (zero days) but not the maximum with TPM doing slightly better than the ZINB model. EQ-5D was negatively associated with days off employment and normal activities in both data sets but ICD chapters only had statistically significant coefficients for some chapters in HODaR.

Conclusions: TPM can be used to predict productivity loss associated with the health of the patient to inform economic evaluation. Limitations include recall and response bias and identification of who is employed in HODaR while HIPO suffers from small sample size. Both samples exclude some patient groups.

Key points for Decision Makers:

- Productivity losses are important indirect costs of poor health and they can be estimated from the health of the patient
- Models based on EQ-5D and diagnosis using the international classification of diseases (ICD) can be used to predict productivity loss including time off work and time off unpaid activities
- Estimates can be included in economic evaluation where productivity has not been measured directly

1 INTRODUCTION

Economic evaluation combines information on costs and benefits to inform priority setting in health care and to inform decisions on the reimbursement of health care interventions. Costs are typically the direct costs of providing health care but where a societal perspective is taken, then outcomes beyond the patients' health and direct costs of health care should be taken into account [1].

Productivity refers to the economic output associated with both paid and unpaid work. The health of patients impacts upon their ability to work, often resulting in either having to take time off work (absenteeism) or returning to work at reduced capacity causing productivity losses (presenteeism) [2]. In the United Kingdom (UK), days off paid employment due to ill-health are estimated to be 140 million working days per year with costs to employers valued at £9 billion while the government spends £13 billion on health-related welfare payments [3]. The inclusion of productivity costs can have a substantial impact on the results of an economic evaluation [4] and these costs therefore warrant consideration. The exclusion of productivity costs has often been justified based on supporting decision makers in the health sector whose objective is to maximise health therefore non-health costs and outcomes need not be considered. However, it can be argued that exclusion of the wider economic costs and outcomes can lead to suboptimal resource allocation. From a welfarist perspective, inclusion of all costs and outcomes in economic evaluation would be the recommended approach where the objective is to maximise social welfare [5]. A societal perspective may also be preferred as it reflects decision making under a 'veil of ignorance' which would be more acceptable to members of the public who are not aware of which conditions will affect them in the future and therefore where the costs would fall [6].

Productivity loss is typically measured using time-off paid employment, time-off unpaid employment, or time-off usual activities due to ill health. For absenteeism, this can be self-reported by patients or objective data reported by employers [2]. Questionnaires such as the Health Labour

Questionnaire [7] have been developed to ask about time-off work or away from unpaid work over a specific period e.g. the last 7 or 14 days. However, it can be difficult for respondents to separate leisure from unpaid work and an alternative approach focusing on the time spent by others doing the work of the person who is ill has been advocated to minimise this problem [5]. Some productivity loss questionnaires also include questions to measure presenteeism. However, where questions related to productivity have not been asked, estimating productivity loss may not be possible.

A potential solution to estimating productivity losses where productivity questions have not been asked is to predict them indirectly using health related quality of life (HRQoL) measures used in cost utility analysis such as EQ-5D. Brouwer et al [8] present a theoretical model of a U shaped relationship between productivity loss and HRQoL which included periods of presenteeism before and after a period of absenteeism. Empirical studies support this relationship with associations found between productivity loss and EQ-5D including Lamers, et al. [9] in patients with lower back pain and Bouwmans et al [10] in patients with depression and anxiety for absenteeism while Kawalec and Malinowski [11] found a negative association between EQ-5D and presenteeism in patients with ankylosing spondylitis. Krol, et al. [12] used a representative general population Dutch sample to collect data on EQ-5D and productivity in order to develop models to predict productivity indirectly. Their results showed good external validity although they were not based on actual time-off paid employment but rather on hypothetical estimates made by the respondents on whether they would go to work given a particular EQ-5D state. Bouwmans et al [10] found differences in the relationship based on whether patients had anxiety, depression or both indicating that disease status may be important.

The aim of this current study was to model the relationship between EQ-5D and productivity using a large mixed patient sample in order to allow for indirect estimation of productivity losses for inclusion in economic evaluation.

2 METHODS

2.1 Data

This study uses two alternative UK patient datasets: Health Outcomes Data Repository (HODaR) and Health Improvement and Patient Outcomes (HIPO). Both datasets were from inpatients attending Cardiff and Vale NHS Hospitals Trust, a large University hospital in South Wales, UK. HODaR covers the period between 2002 and January 2009 [13] while HIPO data were restricted to 2014.

The same data collection methodology was used in both datasets. Surveys were sent six weeks after discharge to all subjects aged 18 years or older. People with a primary diagnosis of a psychological illness or learning disability on admission were excluded. The survey was linked to existing routine hospital health data to provide a dataset with socio-demographic, HRQoL and diagnosis data provided without any personal identifiers. Informed consent was obtained from survey participants. Both surveys were reviewed by ethics committees (Bro Taf Local REC 02/4685 and NRES Committee North West Chester 12/NW/0535).

HODaR reported employment status but this did not include whether the respondent was retired. Those who said they were employed or self-employed and aged 65 and under (pre-retirement age) were selected to represent the employed group in HODaR. The HIPO questionnaire was designed to ensure that employment status included 'retired' as a separate option.

2.2 Measures

Survey respondents were asked two single item questions about employment and normal activities: "How many days off have you had to take off paid employment due to your health …?" and "Other than paid employment, how many days have you had to spend away from your normal activities, e.g. gardening, housework, due to your health …?". Recall was 6 weeks in HODaR and 4 weeks (paid employment) and 1 week (normal activities) in HIPO. The revised recall period used in HIPO was designed to reduce recall bias and so that health as measured by the EQ-5D (which relates to health 'today') would be more closely aligned to the health experienced during the recall period.

Health was measured using the self-reported EQ-5D as well as primary diagnosis based on the International Classification of Diseases (ICD). EQ-5D is a preference-based HRQoL measure which has five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. There are two versions: the 3 level version which has three severity levels (no/moderate and severe problems) for each dimension and the more recently developed 5 level version (includes mild and extreme) both with a recall period for 'today' [14;15]. The 3-level version has utility values elicited from the general population that range from -0.594 to 1, [16] and the cross-walk algorithm was used to generate EQ-5D-3L utility values using the same valuation survey for the EQ-5D-5L [17]. HODaR used EQ-5D-3L while HIPO used EQ-5D-5L. The EQ-5D is the recommended HRQoL measure for health technology assessment (HTA) in England [18] and is widely used. It is therefore useful to use it as the basis of linking health to productivity losses.

ICD 10th version (ICD-10) [19] was used to record clinical diagnosis in the hospital. ICD classifications were recorded as primary diagnosis (reason for admission) as well as for secondary diagnoses in the hospital data and these were linked to survey data along with routine data on surgical procedures.

2.3 Analysis

Descriptive statistics of sample characteristics across the samples used to estimate productivity losses were generated. Spearman rank correlation between days off work/normal activities and EQ-5D was assessed. Regression analysis was used to estimate the relationship between HRQoL of the patient and days off paid employment due to illness and days off normal activities.

2.3.1.1 Explanatory variables

The main explanatory variables included EQ-5D utility score and ICD categories. Dummy variables were used to represent the different ICD groups with Chapter 21 (factors influencing health status and contact with health services) excluded as the reference, presence of comorbidities (at least one secondary diagnosis) and for surgical procedures (operation) during their most recent hospitalisation. Gender and age were also added to the models as these can be related to productivity.

2.3.1.2 Dependent variables

The dependent variables were days off paid employment or days off normal activities which are count data. In HODaR, although the 6-week recall period gave a maximum of 42 days some respondents reported up to 45 days; these were recoded to 42. In HIPO, the recall period was 4 weeks (maximum 28 days) for days off paid employment or 1 week for days off normal activities. Very few respondents (1.8%) reported over 20 days in HIPO so days above this number were recoded to 20. There was a large proportion of respondents in both datasets who reported zero days off paid employment or zero days off normal activities. The spike at zero is usual in this type of data and is a reflection of the large number of people who do not need to take any days off. There were also spikes at the maximum number of days as well as smaller spikes at multiples of 5 and 7 days which potentially reflects a number of issues, including measurement errors and real phenomena. For example, when answering the question, people may have used a heuristic based that was based on calendar weeks or working weeks. Alternatively, it may reflect individuals rounding off responses or due to behavioural factors that result in individuals taking whole, rather than partial, weeks off work when ill.

2.3.1.3 Models

Different count models can be used to assess the relationship between productivity and health. In a study examining the effect of health on informal care time, Rowen et al [20] compared Poisson, negative binomial, two-part and zero-inflated negative binomial models where the explanatory variable was the number of days receiving care. That study showed that the two part model and zero-inflated negative binomial models outperformed the others. The distribution for the number of days receiving care was similar to the number of days off paid work with a large spike at zero and the maximum number of days and positively skewed data. Therefore, we focus on models able to deal with these two characteristics: two-part models (also known in the literature as hurdle models) and zero inflated models. The distribution for positive counts was positively skewed with a long tail and the variance exceeded the mean which was evidence of overdispersion and in parallel to the Rowen study, we use negative binomial specifications for both.

Both the two-part models (TPM) and zero-inflated negative binomial (ZINB) are similar in that they can generate a large number of zeros. They differ, however, in the way those zeros are generated. The TPM assumes that the zeros and the positive outcomes are generated by two completely different processes, zeros are a hurdle to overcome before positive counts can be attained. The ZINB assumes that the zeros can be the outcome of two processes due to two different groups of individuals. One group will always have a count of zero, never a positive count, the second group might happen to have a zero count but there is a positive probability that s/he could have a positive count.

The TPM in this paper combines a binary probit model to predict the zeros with a zero truncated negative binomial regression for the positive counts defined by the following two equations:

$$\Pr(y_i = 0 \mid \mathbf{z}_i) = \Phi(\mathbf{z}_i'\boldsymbol{\gamma}) \tag{1a}$$

and

$$\Pr(y_i \mid y_i > 0, \mathbf{x}_i) = \frac{\Pr(y_i \mid \mathbf{x}_i)}{1 - \left(1 + \alpha e^{\mathbf{x}_i'\boldsymbol{\beta}}\right)^{-1/\alpha}} \tag{1b}$$

where $\mathbf{z}_i$ is a vector of random variables which determine the probability of a zero in the data, $\boldsymbol{\gamma}$ is the corresponding parameter vector and $\Pr(y_i \mid \mathbf{x}_i)$ is:

$$\Pr(y_i = m \mid \mathbf{x}_i) = \frac{\Gamma(y_i + \alpha^{-1})}{y_i!\,\Gamma(\alpha^{-1})}\left(\frac{\alpha^{-1}}{\alpha^{-1} + e^{\mathbf{x}_i'\boldsymbol{\beta}}}\right)^{\alpha^{-1}}\left(\frac{e^{\mathbf{x}_i'\boldsymbol{\beta}}}{\alpha^{-1} + e^{\mathbf{x}_i'\boldsymbol{\beta}}}\right)^{y_i} \quad (2)$$

where $\Gamma(\ )$ is the gamma function and α is the degree of dispersion. The vector $\mathbf{z}_i$ could in principle be identical to $\mathbf{x}_i$.

The expected counts for the TPM are found using the formula below:

$$E(y_i \mid \mathbf{x}_i, \mathbf{z}_i) = (1 - \Phi(\mathbf{z}_i'\boldsymbol{\gamma}))*\left(\frac{e^{\mathbf{x}_i'\boldsymbol{\beta}}}{1 - (1 + \alpha e^{\mathbf{x}_i'\boldsymbol{\beta}})^{-1/\alpha}}\right) \quad (3)$$

The ZINB models can be estimated using either constant inflation or allowing inflation to be a function of explanatory variables. The zero-inflated negative binomial model can be defined by the negative binomial in equation (4):

$$\eta_i = \exp(\mathbf{x}_i'\boldsymbol{\beta} + \xi_i) \quad (4)$$

together with a logit model for the probability of group membership:

$$\Pr(\text{group } 1 \mid \mathbf{z}_i) = \frac{e^{\mathbf{z}_i'\boldsymbol{\gamma}}}{1 + e^{\mathbf{z}_i'\boldsymbol{\gamma}}} \quad (5)$$

The expected counts for the model are found using the formula below:

$$E(y_i \mid \mathbf{x}_i, \mathbf{z}_i) = \left(1 - \frac{e^{\mathbf{z}_i'\boldsymbol{\gamma}}}{1 + e^{\mathbf{z}_i'\boldsymbol{\gamma}}}\right)e^{\mathbf{x}_i'\boldsymbol{\beta}} \quad (6)$$

The models were assessed to identify which fitted the data best based on the predictive performance of the models as well as Akaike Information Criterion (AIC) [21] and the Schwarz Bayesian Information Criterion (BIC) [22]. To aid interpretation, marginal effects for the models are reported and the model coefficients are reported in the Appendix. STATA version 12 was used for all the statistical analyses.

3 RESULTS

3.1 Descriptive statistics

Mean EQ-5D utility scores were higher for those were aged 65 and under who were employed in both samples (0.730 and 0.795 in HODaR and HIPO respectively) compared to the full sample (Table 1). Mean age for employed respondents was lower than for the full samples (48.6 vs. 58.2 and 49.0 vs. 60.3 for HODaR and HIPO respectively). Around 50% of the samples were female and a majority had a comorbidity and operation (Table 1). Mean length of stay ranged from 1.5 days in HIPO to 4.5 days in HODaR. However, despite selection based on being an inpatient, a large proportion (43% in HODaR and 57% in HIPO) had less than a day stay in hospital. Across the samples, the largest ICD Chapters included those for neoplasms, diseases of the circulatory, digestive, musculoskeletal and genitourinary systems and systems not classified elsewhere (Table 1).

[Insert Table 1]

Mean number of days off work was 8.5 in HODaR and 9.10 in HIPO while mean days off normal activities was 4.8 and 1.1 respectively across the two samples (Table 2). Majority reported 0 days off work and normal activities (Table 2). In HODaR, there was a weak negative correlation between days off paid employment and EQ-5D score (*rho*=-0.1222 $p<0.001$) compared to -0.3866 $p<0.001$ in HIPO. There was little variation in mean days off paid employment for those with EQ-5D scores less than 1 in HODaR whereas in HIPO, mean days off paid employment fell as EQ-5D scores increased (Table 2). The correlation between EQ-5D scores and days off normal activities was stronger in HODaR (*rho*=-0.3668 $p<0.001$) with similar results in HIPO (*rho*=-0.3378 $p<0.001$). Mean days off normal activities based on EQ-5D score reflected these correlations in HODaR but slightly less so in HIPO (Table 2).

[Insert Table 2]

3.2 Regression results

3.2.1 Days off paid employment

AIC and BIC indicated that the ZINB with variable inflation (HoDAR: AIC=121,875 BIC=122,129; HIPO AIC=7,887 BIC=8,043) were slightly better than the ZINB with constant inflation (HoDAR: AIC 123,654 BIC=123,876; HIPO AIC=8,110 BIC=8,244) so only the former models are reported. In both HODaR and HIPO, the two-part model (TPM) and zero-inflated negative binomial (ZINB) model predicted the

spike at zero well for days off paid employment (Figure 1). The other spike was at the maximum (42 and 20 days respectively) which was under-predicted. The TPM did slightly better at predicting the maximum number of days off paid employment but this was still below the observed maximum number. The models either over-predicted or under-predicted the number of days off for the number of days off paid employment greater than zero but less than the maximum (Figure 1).

[Insert Figure 1]

In HODaR, Chapters 2 (neoplasms), 5 (mental health), 6 (nervous system), 9 (circulatory system), 13 (musculoskeletal), 17 (congenital malformations), and 19 (injury, poisoning external causes) were statistically significant at the 10% level and associated with more days off paid employment than Chapter 21 (Table 3). Chapters 3 (diseases of the blood), 12 (skin and subcutaneous tissue) and 18 (symptoms not classified elsewhere) were statistically significant and associated with fewer days off paid employment compared to Chapter 21 (Table 3).

In contrast, very few of the ICD coefficients were statistically significant in HIPO with the exception being in the first part of the TPM (Table 3). Only coefficients for Chapters 3 (blood) and 8 (ear and mastoid) in HIPO were statistically significant for part 2 of the TPM and in the ZINB model but coefficients were larger compared to coefficients for other variables and may reflect the small samples for the ICD chapters (n = 20 and 19 respectively). Coefficients for ICD chapters in HIPO generally had the same sign as those in HODaR but the number of days off associated with each Chapter varied by sample which is expected given the different recall periods (Table 3).

Higher EQ-5D scores were associated with fewer days off paid employment in both HODaR and HIPO with a unit increase in EQ-5D resulting in reduced days off work of 7 to 14 days depending on the sample and model (Table 3). Increasing age was associated with more days off paid employment (and a lower probability of reporting zero days off paid employment) and this was at a decreasing (increasing) rate (Table 3). Being female was associated with fewer days off paid employment while having a comorbidity was associated with more days off in HODaR while in HIPO these were not statistically significant apart from in the first part of the TPM (Table 3). Having an operation was associated with more days off paid employment in HIPO but not HODaR. In the ZINB models, both the constant and variables (EQ-5D, age and female) are statistically significant in HODaR but age is not statistically significant in HIPO. There were also differences in coefficient direction for the constant and female inflation variables in the two samples (Appendix Table 5).

[Insert Table 3]

3.2.2 Days off normal activities

As with the days off paid employment regressions, the ZINB with variable inflation regressions (HoDAR: AIC=261,909 BIC=262,186; HIPO AIC=12,841 BIC=13,028) were preferred to the ZINB with constant inflation (HoDAR: AIC=267,396 BIC=267,637; HIPO AIC=13,434 BIC=13,595) so the latter models are not reported. Predicted days off normal activities showed a similar pattern to days off paid employment in HODaR. The TPM and ZINB model predicted the spike at zero reasonably well but under-predicted the spike at 42 days (Figure 2). There was also under and over-prediction for days off normal activities greater than zero but less than the maximum. In HIPO, prediction of the spike at zero was also good for both the models. However, the TPM predicted the spike at 7 days well (7.18 vs observed of 8.6). Although this was better than the ZINB model, overall there was over-prediction in the TPM compared to observed days off normal activities.

[Insert Figure 2]

There were more ICD chapters that were statistically significant in HODaR compared to HIPO in the days off normal activities regressions with some similarities with which ICD chapters were statistically significant with Chapters 2, 5, 9, 13, 17, and 19 along with Chapter 10 (respiratory system) associated with more days off normal activities than Chapter 21 in HODaR (Table 4). In addition, Chapter 7 (eye and adnexa) and 15 (pregnancy and childbirth) were associated with fewer days off normal activities in HODaR. The number of days off normal activities associated with each ICD chapter was generally less than the number of days off paid employment apart from for Chapter 15 (pregnancy) and 17 (congenital mal/deformations). In HIPO, only Chapter 11 (digestive system) was statistically significant and the number of days was less than 1 for all the ICD chapters.

Higher EQ-5D scores were associated with fewer days off normal activities in both samples (Table 4), and this is the key parameter of interest. Age was statistically significant and positive but age squared was also positive in the ZINB model indicating that days off normal activities increased at a higher rate as age increased. Having a comorbidity was associated with fewer days off normal activities in the ZINB model in contrast to more days off as seen for paid employment in HODaR. The inflation variables in HODaR and HIPO were statistically significant (Appendix Table 6).

[Insert Table 4]

4 DISCUSSION

This paper presents regression analyses that enable the estimation of productivity losses associated with the health of the patient. Such an approach enables productivity loss data to be estimated indirectly for individual economic evaluations, by allowing estimates to be derived from EQ-5D data.

In terms of predictive performance, there was little to choose from between the TPM and ZINB but the TPM did slightly better than the ZINB when considering the prediction of the maximum days off either paid employment or normal activities therefore this model is recommended for use. The coefficients for the recommended models are reported in Appendix Table 7. The choice of which sample to use should be informed by the sample where results will be applied although both data sets used in the analysis have limitations which are highlighted later in the discussion.

Further external validation is recommended to ascertain whether the TPM would work as well in other samples. This is important as at the aggregate, the models used to estimate productivity loss were able to accurately predict the spike at zero but under-predicted the number of days off at the maximum in both samples. The only exception was predictions of days off normal activities in HIPO, the smaller sample. However, these predictions were associated with errors of overall over-prediction which would be amplified out-of-sample.

The relationship between EQ-5D and productivity losses was consistent and significant, where lower EQ-5D score meant higher productivity losses. This result is broadly similar to that reported by Krol, et al. [12] although models were different. There were some differences in the coefficient sizes particularly for paid employment in the ZINB variable inflation models. This may reflect differences in sample size and/or recall period. Some ICD chapters had statistically significant associations with productivity mainly in HODaR. Compared to the Krol et al. [12] model, the results presented here are based on real data and also account for different diseases as well as characteristics such as the presence of a comorbidity or whether respondents have had an operation which can be considered to have an impact on absenteeism. Furthermore, the results can also be used to predict days off normal activities in addition to days off work.

The results presented here enable productivity loss to be estimated using available data, yet it should be recognised that these are only predictions and are unlikely to be as accurate as collecting productivity data directly from respondents in studies. However one advantage of this technique is that productivity loss can be estimated for studies retrospectively where this information was not collected. A further advantage is that the same methodology can be used to produce comparable

estimates of productivity loss for all studies involving EQ-5D. These comparable estimates can then be used to inform economic evaluation.

4.1 Limitations

This study used EQ-5D score as the independent variable relating to health, in order that the results could be applied to data that are commonly reported in economic evaluations. However, the correlations between EQ-5D and days off work/normal activities were weak to moderate. This is a limitation to the approach where EQ-5D is the key parameter of interest but this was not the only parameter included in the models and overall the models had good predictive performance apart from the maximum number of days off. Under-prediction would under-estimate the level of productivity loss but this is likely to be for a small sub-sample (10% or less) based on the datasets used in this analysis.

Although HODaR and HIPO data provided a large sample of patients with different conditions, there were limitations associated with these samples. Some conditions based on ICD codes had very small groups which may limit applicability of results in these groups. Furthermore, the datasets did not include patients with a primary diagnosis on admission of a psychological illness or learning disability, and therefore these estimates are not recommended for use in health interventions for these patients. The analysis was based on patients who had been recently hospitalised and they may be significantly different from other patient populations In addition all data was collected in the UK and hence may not be representative in countries with different payment compensation schemes for days off work. Therefore the results may not be generalisable. While EQ-5D has been used for all patients, it may not be an appropriate measure of health for all patient groups and estimating productivity losses using EQ-5D data would also be inappropriate.

A further related limitation of using the HODaR data is that retired individuals reported past employment which was addressed by excluding those who are above retirement age but this may not have captured everyone. Mean age for those who were employed in HODaR and HIPO was 48.6 and 49.0 and EQ-5D scores were 0.730 and 0.795 in HODaR and HIPO respectively (note use of EQ-5D-3L in HODaR and EQ-5D-5L cross-walked to 3L in HIPO) which may indicate that the selected ‘employed’ sample in HODaR was comparable in terms of age and health. However, as noted, correlation between health and days off paid employment was weak in HODaR which suggests that although summary statistics were similar, there was more variation in HODaR which may be as a result of individuals in the ‘employed’ sample who were not employed.

The spikes in the data where full weeks have been counted e.g. 7, 14 etc. indicate that respondents were rounding off days which may indicate some form of recall bias although it may also reflect the number of days that patients are signed-off from work. In the literature recommended recall periods of 3 months for productivity have been suggested [2] but the evidence in HODaR suggests that there is some bias over a longer period. In addition HIPO finds less evidence of a spike at the maximum days off paid employment. However, shortening the recall period in HIPO may have resulted in under-estimation of the number of days off work as it may have excluded the period immediately after discharge.

While this study provides a means to estimate the productivity losses associated with HRQoL in terms of predictions of days, the valuation of these losses can be challenging where there is no information on the type of work or usual activities which have not been undertaken. In addition, whilst our study did include productivity losses outside paid employment, our productivity losses did not include presenteeism. Estimating these effects would require additional data collection.

Finally, this study used EQ-5D utility scores to enable productivity losses to be estimated. However, better specified relationships may be possible by using responses to the individual EQ-5D questions. Dixon et al [23] used this approach when examining the impact of EQ-5D responses on carer time and found that those models outperformed those using EQ-5D scores as the independent health variable. This may suggest that whilst the use of the EQ-5D score is a convenient approach to estimating production losses, more accurate estimates are possible.

4.2 Conclusion

Models to predict days off work and days off normal activities were estimated using large patient datasets. These allow productivity losses associated with HRQoL to be estimated for inclusion in economic evaluation using a wider societal perspective. These estimates of productivity losses can be obtained for a dataset including the EQ-5D of patients alongside sociodemographic characteristics, and using the same methodology informal care need can also be estimated using the models reported in Rowen et al [20]. The use of large patient datasets in the estimation of the models reported here has the benefit that the models are based on HRQoL from a number of conditions. However there are a number of limitations associated with each dataset used to model the relationship and further research is needed to address this.

Compliance with Ethical Standards

1. This is an independent study commissioned and funded by the Policy Research Programme in the Department of Health. The study was undertaken by the Policy Research Unit in Economic Evaluation of Health and Care interventions (EEPRU) funded by the Department of Health Policy Research Programme. The views expressed are not necessarily those of the Department.

2. Clara Mukuria, Donna Rowen, Mónica Hernández-Alava, Simon Dixon and Roberta Ara have no conflicts of interest to declare.

3. The HODaR study was ethically reviewed by the Bro Taf Local Research Ethics Committee (02/4685) and the HIPO study was ethically reviewed by the NRES Committee North West – Cheshire (REC REF: 12/NW/0535). All procedures performed in studies involving human participants were in accordance with the ethical standards of the research committees and with the 1964 Helsinki declaration and its later amendments.

4. Informed consent was obtained from all study participants

Author Contributions

All authors were involved in design of the study. CM, DR and MHA prepared and analysed the data; SD and RA reviewed results. CM and DR drafted the manuscript and SD, MHA and RA reviewed and made changes to the manuscript.

Reference List

1. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-effectiveness in Health and Medicine. Jama 1996; 276(15):1253-1258.

2. Zhang W, Bansback N, Anis AH. Measuring and valuing productivity loss due to poor health: a critical review. Social science & medicine 2011; 72(2):185-192.

3. Black CD, Frost D. Health at work-an independent review of sickness absence. 8205 ed. The Stationery Office; 2011.

4. Johannesson M, Jonsson B, Jonsson L, Kobelt G, Zethraeus N. Why should economic evaluations of medical innovations have a societal perspective? Office of Health Economics Briefings 2009.

5. Krol M, Brouwer W, Rutten F. Productivity costs in economic evaluations: past, present, future. Pharmacoeconomics 2013; 31(7):537-549.

6. Russell LB, Gold MR, Siegel JE, Daniels N, Weinstein MC. The role of cost-effectiveness analysis in health and medicine. Jama 1996; 276(14):1172-1177.

7. Van Roijen L, Essink-Bot ML, Koopmanschap MA, Bonsel G, Rutten FF. Labor and health status in economic evaluation of health care: The Health and Labor Questionnaire. International journal of technology assessment in health care 1996; 12(03):405-415.

8. Brouwer WB, Meerding WJ, Lamers LM, Severens JL. The relationship between productivity and health-related QOL. Pharmacoeconomics 2005; 23(3):209-218.

9. Lamers LM, Meerding WJ, Severens JL, Brouwer WB. The relationship between productivity and health-related quality of life: an empirical exploration in persons with low back pain. Quality of life research 2005; 14(3):805-813.

10. Bouwmans CAM, Vemer P, van Straten A, Tan SS, Hakkaart-van Roijen L. Health-related quality of life and productivity losses in patients with depression and anxiety disorders. Journal of Occupational and Environmental Medicine 2014; 56(4):420-424.

11. Kawalec P, Malinowski K. Disease activity, quality of life and indirect costs of reduced productivity at work, generated by Polish patients with ankylosing spondylitis. Reumatologia 2015; 53(6):301-308.

12. Krol M, Stolk E, Brouwer W. Predicting productivity based on EQ-5D: an explorative study. The European Journal of Health Economics 2014; 15(5):465-475.

13. Currie CJ, McEwan P, Peters JR, Patel TC, Dixon S. The routine collation of health outcomes data from hospital treated subjects in the Health Outcomes Data Repository (HODaR): descriptive analysis from the first 20,000 subjects. Value in health 2005; 8(5):581-590.

14. Brooks R, Group E. EuroQol: the current state of play. Health policy 1996; 37(1):53-72.

15. Herdman M, Gudex C, Lloyd A, Janssen MF, Kind P, Parkin D et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Quality of life research 2011; 20(10):1727-1736.

16. Dolan P. Modeling valuations for EuroQol health states. Medical care 1997; 35(11):1095-1108.

17. van Hout B, Janssen MF, Feng YS, Kohlmann T, Busschbach J, Golicki D et al. Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets. Value in health 2012; 15(5):708-715.

18. National Institute for Health and Care Excellence. Guide to the methods of technology appraisal. 2013.
Ref Type: Generic

19. World Health Organization. International statistical classification of diseases and related health problems. 2 ed. World Health Organization; 2010.

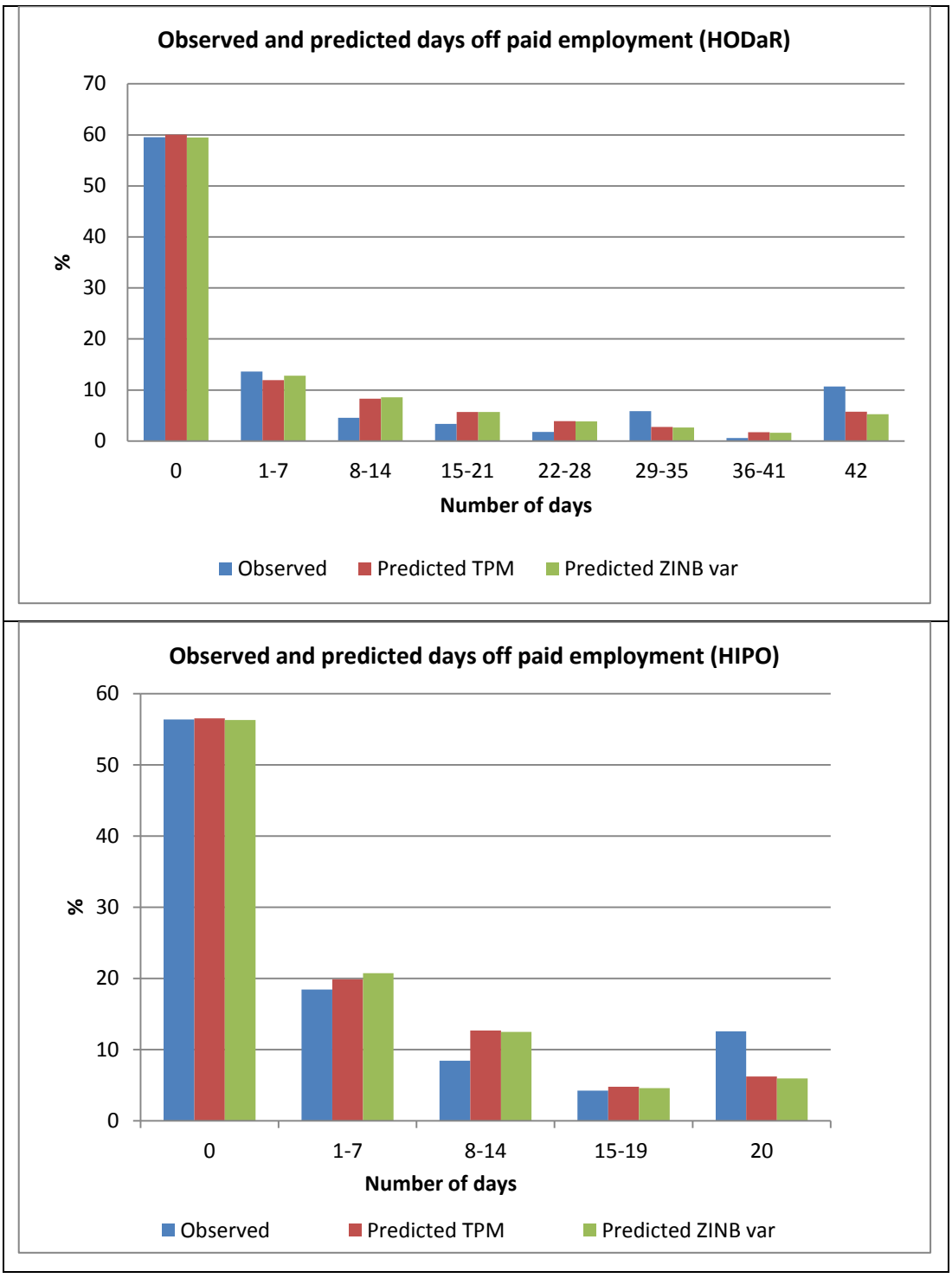
20. Rowen D, Dixon S, Hernández-Alava M, Mukuria C. Estimating informal care inputs associated with EQ-5D for use in economic evaluation. The European Journal of Health Economics 2015;1-12.

21. Akaike H. Information theory and an extension of the maximum likelihood principle. Selected Papers of Hirotugu Akaike. Springer; 1998. p. 199-213.

22. Schwarz G. Estimating the dimension of a model. The annals of statistics 1978; 6(2):461-464.

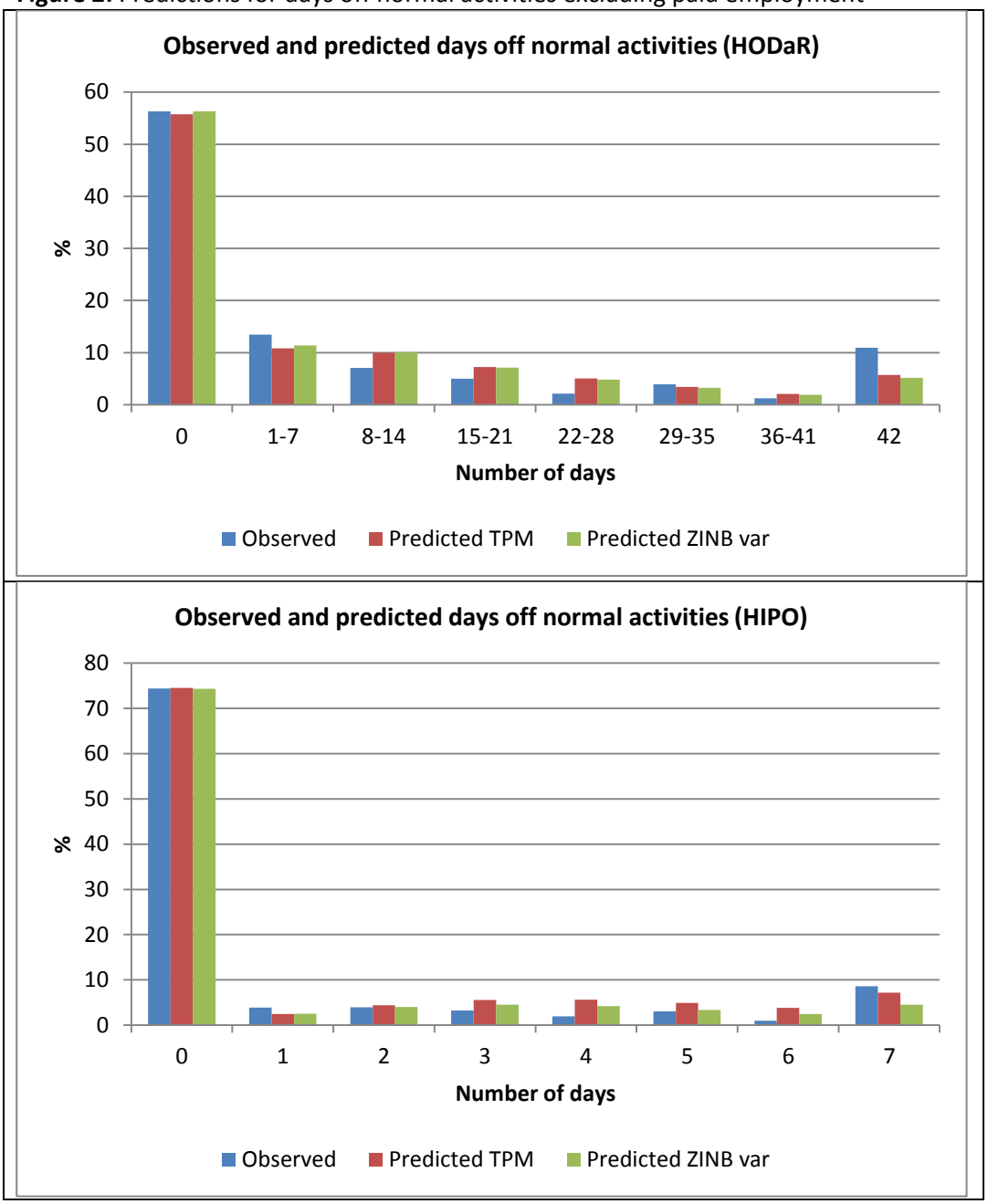
23. Dixon S, Walker M, Salek S. Incorporating carer effects into economic evaluation. Pharmacoeconomics 2006; 24(1):43-53.

Figure 1: Predictions for days off paid employment



HODaR - Health Outcomes Data Repository; HIPO - Health Improvement and Patient Outcomes; TPM – two part model; ZINB – zero inflated negative binomial

Figure 2: Predictions for days off normal activities excluding paid employment



HODaR - Health Outcomes Data Repository; HIPO - Health Improvement and Patient Outcomes; TPM – two part model; ZINB – zero inflated negative binomial

Table 1: Summary of sample characteristics of HODaR and HIPO (employed and full sample)

Sample	HODAR		HIPO	
	Aged < 66 , likely to be employed	Full sample	Employed	Full sample
n	27,124	55,726	1,921	6,046
Mean EQ-5D (SD)	0.730 (0.290)	0.673 (0.311)	0.795 (0.196)	0.674 (0.287)
Mean age (SD)	48.58 (12.13)	58.15 (17.20)	49.03 (11.88)	60.25 (16.45)
Female	52.6%	50.3%	52.8%	50.1%
Comorbidity	67.7%	72.8%	78.0%	84.2%
Operation	78.2%	74.5%	89.3%	85.3%
Length of hospital stay (SD)	3.41 (10.02)	4.54 (11.58)	1.48 (3.73)	2.35 (5.93)
ICD Chapter				
1 Certain infectious and parasitic diseases	168 (0.6%)	325 (0.6%)	28 (1.4%)	69 (1.1%)
2 Neoplasms	2,866 (10.6%)	5,795 (10.4%)	206 (12.2%)	741 (12.3%)
3 Diseases of the blood	312 (1.2%)	757 (1.4%)	20 (1%)	141 (2.33%)
4 Endocrine, nutritional and metabolic diseases	508 (1.9%)	988 (1.8%)	32 (1.7%)	104 (1.7%)
5 Mental and behavioural disorders	50 (0.2%)	86 (0.2%)	-	-
6 Nervous system	803 (3.0%)	1,443 (2.6%)	56 (2.9%)	174 (2.9%)
7 Eye and adnexa	780 (2.9%)	2,938 (5.3%)	65 (3.4%)	308 (5.1%)
8 Ear and mastoid process	174 (0.6%)	265 (0.5%)	19 (1%)	39 (0.7%)
9 Circulatory system	3,474 (12.8%)	8,612 (15.5%)	167 (8.7%)	658 (10.9%)
10 Respiratory system	1,048 (3.9%)	2,362 (4.2%)	75 (3.9%)	264 (4.4%)
11 Digestive system	3,814 (14.1%)	7,393 (13.3%)	311 (16.2%)	833 (13.8%)
12 Skin and subcutaneous tissue	877 (3.2%)	1,564 (2.8%)	56 (2.9%)	149 (2.5%)
13 Musculoskeletal system	3,393 (12.5%)	6,337 (11.4%)	320 (16.7%)	826 (13.7%)
14 Genitourinary system	2,127 (7.8%)	3,629 (6.5%)	158 (8.2%)	438 (7.2%)
15 Pregnancy, childbirth	767 (2.8%)	1,003 (1.8%)	-	-
17 Congenital malformations, deformations	100 (0.4%)	141 (0.3%)	-	-
18 Symptoms not classified elsewhere	2,817 (10.4%)	6,024 (10.8%)	189 (9.8%)	613 (10.1%)
19 Injury, poisoning and certain external causes	1,721 (6.3%)	3,284 (5.9%)	117 (6.1%)	343 (5.7%)
21 Factors influencing health status and contact with health services	1,325 (4.9%)	2,780 (5.0%)	102 (5.3%)	346 (5.7%)

Chapters 16 Certain conditions (perinatal period), 20 External causes of morbidity and mortality and 22 Codes for special purposes did not have any respondents

SD – standard deviation; HODaR - Health Outcomes Data Repository; HIPO - Health Improvement and Patient Outcomes

Table 2: Mean days off paid employment and normal activities

	Days off paid employment		Days off normal activities	
	HODaR (6 weeks)	**HIPO (4 weeks)**	**HODaR (6 weeks)**	**HIPO (1 week)**
Mean Days Off (SD)	8.50 (14.50)	9.10 (14.50)	4.80 (7.48)	1.10 (2.21)
Mean Days Off Range, n(%)				
0 days	16,154 (59.6%)	31,398 (56.3%)	1,083 (56.4%)	0 days 4,497 (74.4%)
1-7 days	3,694 (13.6%)	7,493 (13.5%)	354 (18.4%)	1 day 236 (3.9%)
8-14 days	1,239 (4.6%)	3,922 (7.0%)	162 (8.4%)	2 days 238 (3.9%)
15-21 days	914 (3.4%)	2,792 (5.0%)	287 (14.9%)	3 days 194 (3.2%)
22-28 days	479 (1.8%)	1,168 (2.1%)	35 (1.8%)	4 days 118 (2.0%)
29-35 days	1,581 (5.8%)	2,191 (3.9%)	-	5 days 184 (3.0%)
36-41 days	163 (0.6%)	670 (1.2%)	-	6 days 59 (1.0%)
42 days	2,900 (10.7%)	6,092 (10.9%)	-	7 days 520 (8.6%)

	HODaR (6 weeks)		**HIPO (4 weeks)**		**HODaR (6 weeks)**		**HIPO (1 week)**	
EQ-5D range	**N**	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**Mean (SD)**
-0.594 - 0	1215	10.1 (16.9)	9	14.0 (10.3)	3433	21.5 (18.2)	234	2.2 (3.1)
0.001 - 0.199	1474	10.3 (16.3)	18	13.4 (8.9)	4034	16.9 (17.6)	240	2.5 (3.2)
0.2 - 0.399	783	15.7 (18.0)	67	11.5 (9.0)	1983	19.2 (18.6)	545	2.4 (2.9)
0.4 - 0.599	1486	10.4 (16.5)	127	8.3 (9.0)	4681	14.9 (17.0)	713	1.9 (2.7)
0.6 - 0.799	10971	10.0 (15.3)	727	6.2 (7.9)	23298	8.1 (13.3)	2179	1.1 (2.1)
0.8 - 0.999	2739	9.4 (14.8)	414	3.8 (6.8)	5043	6.0 (11.6)	988	0.4 (1.3)
1	8456	4.8 (10.5)	559	1.7 (4.7)	13254	2.9 (7.7)	1147	0.2 (0.8)

SD – standard deviation; HODaR - Health Outcomes Data Repository; HIPO - Health Improvement and Patient Outcomes

Table 3: Days off paid employment HODaR and HIPO (marginal effects)

	HODaR			HIPO		
	TPM part 1	TPM part 2	ZINB variable	TPM part 1	TPM part 2	ZINB variable
1 Certain infectious & parasitic	-0.0848	-2.324	-0.731	-0.197*	-1.799	-0.582
	(0.0438)	(2.211)	(0.931)	(0.0999)	(2.567)	(1.187)
2 Neoplasms	-0.157***	5.193***	2.550***	-0.279***	2.472	1.392
	(0.0157)	(1.026)	(0.437)	(0.0519)	(1.882)	(0.876)
3 Diseases of the blood	-0.0296	-4.094*	-1.622*	-0.175	-7.036***	-2.880***
	(0.0303)	(1.830)	(0.776)	(0.108)	(1.850)	(0.860)
4 Endocrine, nutritional, metabolic	-0.0447	0.101	0.208	-0.0943	-3.461	-1.443
	(0.0252)	(1.657)	(0.704)	(0.0886)	(3.044)	(1.395)
5 Mental and behavioural	-0.0441	10.03*	4.281*			
	(0.0830)	(4.525)	(1.944)			
6 Nervous system	-0.107***	2.971*	1.520**	-0.199*	0.346	0.337
	(0.0218)	(1.315)	(0.559)	(0.0785)	(2.231)	(1.032)
7 Eye and adnexa	-0.0514*	0.621	0.435	-0.102	-0.362	-0.0405
	(0.0218)	(1.431)	(0.611)	(0.0711)	(2.717)	(1.258)
8 Ear and mastoid process	-0.0723	-0.916	-0.166	-0.108	-8.274***	-3.435***
	(0.0383)	(2.237)	(0.951)	(0.112)	(1.935)	(0.877)
9 Circulatory system	-0.171***	5.742***	2.825***	-0.247***	1.489	0.933
	(0.0156)	(1.032)	(0.441)	(0.0543)	(1.932)	(0.902)
10 Respiratory system	-0.0348	-1.019	-0.307	-0.107	0.830	0.525
	(0.0198)	(1.275)	(0.540)	(0.0675)	(2.315)	(1.078)
11 Digestive system	-0.0693***	-0.600	-0.0139	-0.120*	-1.220	-0.410
	(0.0148)	(1.032)	(0.440)	(0.0484)	(1.870)	(0.871)
12 Skin and subcutaneous tissue	-0.0166	-2.864*	-1.180	-0.0457	-2.853	-1.277
	(0.0202)	(1.428)	(0.606)	(0.0753)	(2.440)	(1.135)
13 Musculoskeletal system	-0.159***	4.925***	2.463***	-0.203***	1.848	1.077
	(0.0152)	(0.998)	(0.426)	(0.0495)	(1.802)	(0.839)
14 Genitourinary system	-0.0800***	-1.848	-0.540	-0.155**	-0.470	-0.00886
	(0.0162)	(1.083)	(0.460)	(0.0549)	(1.919)	(0.893)
15 Pregnancy, childbirth	0.00601	0.691	0.275			
	(0.0202)	(1.556)	(0.657)			
17 Congenital mal/deformations	-0.160**	4.842	2.455*			
	(0.0497)	(2.692)	(1.153)			
18 Symptoms not classified elsewhere	-0.0516**	-2.963**	-1.088*	-0.0684	-2.059	-0.895
	(0.0157)	(1.068)	(0.453)	(0.0531)	(1.971)	(0.916)
19 Injury, poisoning, external	-0.213***	4.940***	2.526***	-0.305***	2.478	1.416
	(0.0175)	(1.057)	(0.451)	(0.0610)	(1.913)	(0.891)
EQ-5D	0.0727***	-14.67***	-8.109***	0.754***	-7.278***	-11.54***
	(0.0114)	(0.607)	(0.340)	(0.0616)	(1.212)	(0.780)
Age/10	-0.359***	6.216***	9.736***	-0.0312	4.137*	2.130*
	(0.0188)	(1.217)	(0.623)	(0.0561)	(1.639)	(0.846)
Age/10 squared	0.0501***	-0.525***	-1.213***	0.00493	-0.436*	-0.240**
	(0.00206)	(0.136)	(0.0689)	(0.00601)	(0.179)	(0.0905)
female	0.0107	-1.046**	-0.856***	-0.0811***	-0.486	0.536
	(0.00657)	(0.380)	(0.205)	(0.0216)	(0.563)	(0.311)
comorbid	-0.0401***	4.580***	1.977***	-0.0602*	-0.185	0.00976
	(0.00687)	(0.445)	(0.187)	(0.0266)	(0.754)	(0.345)
operation	0.0311***	-0.116	-0.153	-0.0537	1.610	0.750
	(0.00785)	(0.459)	(0.192)	(0.0358)	(1.112)	(0.504)
N	27124	10970	27124	1921	838	1921

Standard errors in parentheses * $p<0.1$; ** $p<0.05$; *** $p<0.01$

HODaR - Health Outcomes Data Repository; HIPO - Health Improvement and Patient Outcomes; TPM – two part model; ZINB – zero inflated negative binomial

1-19 – has condition in ICD chapter; Age/10 – age divided by 10; Comorbid – has comorbidity; Operation - has had an operation

Table 4: Days off normal activities HODaR and HIPO (marginal effects)

	HODaR			HIPO		
	TPM part 1	TPM part 2	ZINB variable	TPM part 1	TPM part 2	ZINB variable
1 Certain infectious & parasitic	-0.117***	1.053	-0.731	0.0221	-0.284	-0.0838
	(0.0331)	(1.484)	(0.931)	(0.0516)	(0.533)	(0.147)
2 Neoplasms	-0.117***	4.341***	2.550***	-0.0334	0.292	0.0862
	(0.0111)	(0.620)	(0.437)	(0.0267)	(0.319)	(0.0859)
3 Diseases of the blood	-0.0315	0.103	-1.622*	0.0357	-0.726	-0.204
	(0.0202)	(1.171)	(0.776)	(0.0389)	(0.457)	(0.126)
4 Endocrine, nutritional,	-0.0421*	0.798	0.208	0.0477	-0.731	-0.225
metabolic	(0.0188)	(1.038)	(0.704)	(0.0413)	(0.493)	(0.138)
5 Mental and behavioural	0.0459	-2.624	4.281*			
	(0.0518)	(2.733)	(1.944)			
6 Nervous system	-0.104***	2.300**	1.520**	-0.0453	-0.280	-0.0680
	(0.0163)	(0.806)	(0.559)	(0.0380)	(0.362)	(0.0963)
7 Eye and adnexa	-0.00102	-2.008**	0.435	0.00633	-0.493	-0.138
	(0.0128)	(0.745)	(0.611)	(0.0325)	(0.428)	(0.116)
8 Ear and mastoid process	0.00802	-1.941	-0.166	0.00578	-0.436	-0.127
	(0.0302)	(2.130)	(0.951)	(0.0614)	(0.591)	(0.155)
9 Circulatory system	-0.143***	4.314***	2.825***	-0.0680*	0.276	0.0845
	(0.0109)	(0.602)	(0.441)	(0.0278)	(0.312)	(0.0839)
10 Respiratory system	-0.0592***	2.146**	-0.307	-0.0306	0.127	0.0421
	(0.0145)	(0.765)	(0.540)	(0.0344)	(0.393)	(0.106)
11 Digestive system	-0.0630***	0.438	-0.0139	-0.00419	-0.532	-0.142
	(0.0107)	(0.611)	(0.440)	(0.0258)	(0.305)	(0.0822)
12 Skin and subcutaneous tissue	-0.0227	-0.388	-1.180	0.0529	-0.326	-0.116
	(0.0154)	(0.917)	(0.606)	(0.0381)	(0.526)	(0.146)
13 Musculoskeletal system	-0.196***	5.544***	2.463***	-0.0776**	0.392	0.117
	(0.0111)	(0.582)	(0.426)	(0.0265)	(0.289)	(0.0776)
14 Genitourinary system	-0.0754***	0.326	-0.540	-0.0234	0.00496	0.00905
	(0.0121)	(0.682)	(0.460)	(0.0292)	(0.351)	(0.0945)
15 Pregnancy, childbirth	0.00310	-3.206**	0.275			
	(0.0172)	(1.054)	(0.657)			
17 Congenital mal/deformations	-0.129**	6.763**	2.455*			
	(0.0426)	(2.370)	(1.153)			
18 Symptoms not classified	-0.0504***	-1.107	-1.088*	-0.0319	-0.219	-0.0510
elsewhere	(0.0112)	(0.622)	(0.453)	(0.0278)	(0.315)	(0.0847)
19 Injury, poisoning, external	-0.185***	8.553***	2.526***	-0.0497	0.549	0.156
	(0.0127)	(0.651)	(0.451)	(0.0315)	(0.329)	(0.0883)
EQ-5D	0.427***	-16.03***	-8.109***	0.382***	-3.322***	-2.358***
	(0.00737)	(0.323)	(0.340)	(0.0176)	(0.165)	(0.0903)
Age/10	-0.0439***	2.446***	9.736***	-0.0723***	0.0674	0.0855
	(0.00775)	(0.417)	(0.623)	(0.0186)	(0.234)	(0.0522)
Age/10 squared	0.00701***	-0.159***	-1.213***	0.0102***	0.00352	0.0207
	(0.000702)	(0.0371)	(0.0689)	(0.00165)	(0.0202)	(0.0467)
female	-0.0453***	-1.961***	-0.856***	-0.0313**	-0.151	0.377***
	(0.00465)	(0.236)	(0.205)	(0.0106)	(0.116)	(0.0946)
comorbid	-0.0416***	3.558***	1.977***	-0.00853	0.312	-0.0471***
	(0.00509)	(0.292)	(0.187)	(0.0151)	(0.196)	(0.00844)
operation	0.00296	0.540*	-0.153	-0.0430**	0.0542	0.0970
	(0.00536)	(0.271)	(0.192)	(0.0165)	(0.174)	(0.0523)
N	55726	24328	55726	6046	1549	6046

Standard errors in parentheses * $p<0.1$; ** $p<0.05$; *** $p<0.01$

HODaR - Health Outcomes Data Repository; HIPO - Health Improvement and Patient Outcomes; TPM – two part model; ZINB – zero inflated negative binomial

1-19 – has condition in ICD chapter; Age/10 – age divided by 10; Comorbid – has a comorbidity; Operation - has had an operation

APPENDIX

Table 5: Days off paid employment HODaR and HIPO

	HODaR (6 weeks recall period)			HIPO (4 weeks recall period)		
	TPM part 1	TPM Part 2	ZINB variable	TPM part 1	TPM part 2	ZINB variable
1 Certain infectious and parasitic	-0.245**	-0.138	-0.105	-0.586**	-0.203	-0.147
	(0.122)	(0.138)	(0.138)	(0.287)	(0.295)	(0.303)
2 Neoplasms	-0.442***	0.253***	0.297***	-0.813***	0.225	0.283
	(0.046)	(0.054)	(0.056)	(0.163)	(0.186)	(0.199)
3 Diseases of the blood	-0.088	-0.257**	-0.249*	-0.526*	-1.262***	-1.129***
	(0.089)	(0.124)	(0.128)	(0.310)	(0.296)	(0.282)
4 Endocrine, nutritional,	-0.132*	0.006	0.028	-0.295	-0.435	-0.414
	(0.073)	(0.092)	(0.094)	(0.270)	(0.432)	(0.446)
5 Mental and behavioural	-0.130	0.442***	0.458***	-	-	-
	(0.239)	(0.166)	(0.172)			
6 Nervous system	-0.307***	0.153**	0.188***	-0.592**	0.035	0.076
	(0.062)	(0.068)	(0.069)	(0.231)	(0.224)	(0.235)
7 Eye and adnexa	-0.151**	0.034	0.057	-0.318	-0.038	-0.010
	(0.063)	(0.078)	(0.080)	(0.219)	(0.283)	(0.297)
8 Ear and mastoid process	-0.210*	-0.052	-0.023	-0.335	-1.853***	-1.644***
	(0.108)	(0.130)	(0.132)	(0.333)	(0.595)	(0.448)
9 Circulatory system	-0.479***	0.276***	0.325***	-0.724***	0.141	0.198
	(0.045)	(0.055)	(0.057)	(0.169)	(0.192)	(0.205)
10 Respiratory system	-0.103*	-0.058	-0.043	-0.332	0.081	0.116
	(0.059)	(0.073)	(0.075)	(0.209)	(0.228)	(0.241)
11 Digestive system	-0.202***	-0.034	-0.002	-0.370**	-0.133	-0.101
	(0.044)	(0.058)	(0.060)	(0.157)	(0.195)	(0.208)
12 Skin and subcutaneous tissue	-0.050	-0.173*	-0.175*	-0.148	-0.344	-0.357
	(0.061)	(0.088)	(0.092)	(0.241)	(0.303)	(0.328)
13 Musculoskeletal system	-0.446***	0.241***	0.288***	-0.603***	0.173	0.226
	(0.044)	(0.054)	(0.056)	(0.157)	(0.181)	(0.194)
14 Genitourinary system	-0.232***	-0.108*	-0.076	-0.471***	-0.049	-0.002
	(0.047)	(0.062)	(0.064)	(0.172)	(0.197)	(0.210)
15 Pregnancy, childbirth	0.018	0.038	0.037	-	-	-
	(0.062)	(0.084)	(0.087)			
17 Congenital mal/deformations	-0.448***	0.238*	0.288**	-	-	-
	(0.134)	(0.122)	(0.122)			
18 Symptoms not classified	-0.152***	-0.180***	-0.160**	-0.218	-0.235	-0.236
	(0.047)	(0.063)	(0.064)	(0.172)	(0.214)	(0.229)
19 Injury, poisoning, external	-0.590***	0.242***	0.295***	-0.884***	0.225	0.287
	(0.050)	(0.056)	(0.058)	(0.185)	(0.189)	(0.201)
EQ-5D	0.201***	-0.724***	-0.746***	2.192***	-0.699***	-0.674***
	(0.032)	(0.029)	(0.031)	(0.201)	(0.117)	(0.123)
Age/10	-0.996***	0.307***	0.282***	-0.091	0.397**	0.392**
	(0.053)	(0.060)	(0.060)	(0.163)	(0.157)	(0.162)
Age/10 squared	0.139***	-0.026***	-0.023***	0.014	-0.042**	-0.042**
	(0.006)	(0.007)	(0.007)	(0.017)	(0.017)	(0.018)
female	0.030	-0.052***	-0.041**	-0.236***	-0.047	-0.045
	(0.018)	(0.019)	(0.019)	(0.063)	(0.054)	(0.055)
comorbid	-0.111***	0.226***	0.236***	-0.175**	-0.018	0.002
	(0.019)	(0.022)	(0.022)	(0.078)	(0.072)	(0.075)
operation	0.086***	-0.006	-0.018	-0.156	0.155	0.163
	(0.022)	(0.023)	(0.023)	(0.104)	(0.107)	(0.110)
Constant	1.761***	2.423***	2.444***	-0.597	1.788***	1.712***
	(0.125)	(0.144)	(0.145)	(0.450)	(0.420)	(0.433)
Inflated Variables			$\hat{\gamma}$			$\hat{\gamma}$
EQ5D			0.412***			4.216***
			(0.051)			(0.397)
Age/10			-1.635***			-0.165
			(0.089)			(0.286)
Age/10 squared			0.226***			0.024
			(0.010)			(0.031)
Female			0.115***			-0.371***

	HODaR (6 weeks recall period)			HIPO (4 weeks recall period)		
	TPM part 1	TPM Part 2	ZINB variable	TPM part 1	TPM part 2	ZINB variable
			(0.030)			(0.106)
Constant			2.234***			-2.811***
			(0.194)			(0.723)
Dispersion		0.946	0.966		0.562	0.584
N	27,124	10,970	27,124	1,921	838	1,921
Log likelihood	-17141	-43518	-60906	-1158	-2725	-3915
AIC	34333	87088	121875	2360	5497	7886
BIC	34538	87277	122129	2483	5606	8041

Standard errors in parentheses * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

HODaR - Health Outcomes Data Repository; HIPO - Health Improvement and Patient Outcomes; TPM – two part model; ZINBv – zero inflated negative binomial with variable inflation

1-19 – has condition in ICD chapter; Age/10 – age divided by 10; Comorbid – has comorbidity; Operation - has had an operation

Table 6: Days off normal activities HODaR and HIPO

	HODaR (6 weeks recall period)			HIPO (1 week recall period)		
	TPM part 1	TPM part 2	ZINB variable	TPM part 1	TPM part 2	ZINB variable
1 Certain infectious and parasitic	-0.328***	0.058	0.071	0.087	-0.071	-0.080
	(0.091)	(0.080)	(0.079)	(0.201)	(0.135)	(0.142)
2 Neoplasms	-0.328***	0.219***	0.234***	-0.115	0.073	0.080
	(0.032)	(0.033)	(0.034)	(0.096)	(0.075)	(0.076)
3 Diseases of the blood	-0.092	0.006	0.011	0.139	-0.191	-0.204
	(0.058)	(0.066)	(0.067)	(0.155)	(0.126)	(0.132)
4 Endocrine, nutritional, metabolic	-0.122**	0.044	0.049	0.191	-0.193	-0.228
	(0.054)	(0.057)	(0.057)	(0.171)	(0.137)	(0.149)
5 Mental and behavioural disorders	0.140	-0.160	-0.178	-	-	-
	(0.163)	(0.180)	(0.186)			
6 Nervous system	-0.293***	0.122***	0.136***	-0.159	-0.070	-0.064
	(0.046)	(0.043)	(0.043)	(0.132)	(0.090)	(0.090)
7 Eye and adnexa	-0.003	-0.120***	-0.126***	0.024	-0.126	-0.134
	(0.038)	(0.045)	(0.046)	(0.122)	(0.112)	(0.115)
8 Ear and mastoid process	0.024	-0.116	-0.126	0.022	-0.111	-0.122
	(0.090)	(0.134)	(0.139)	(0.231)	(0.155)	(0.155)
9 Circulatory system	-0.399***	0.218***	0.234***	-0.234**	0.064	0.074
	(0.031)	(0.033)	(0.033)	(0.098)	(0.073)	(0.074)
10 Respiratory system	-0.170***	0.114***	0.123***	-0.107	0.029	0.037
	(0.041)	(0.041)	(0.041)	(0.122)	(0.093)	(0.094)
11 Digestive system	-0.181***	0.024	0.034	-0.019	-0.141*	-0.142*
	(0.031)	(0.034)	(0.035)	(0.095)	(0.076)	(0.078)
12 Skin and subcutaneous tissue	-0.066	-0.022	-0.022	0.213	-0.082	-0.111
	(0.045)	(0.052)	(0.053)	(0.159)	(0.134)	(0.145)
13 Musculoskeletal system	-0.543***	0.272***	0.291***	-	0.090	0.101
	(0.032)	(0.031)	(0.032)	(0.094)	(0.068)	(0.069)
14 Genitourinary system	-0.215***	0.018	0.030	-0.084	0.001	0.008
	(0.035)	(0.038)	(0.039)	(0.106)	(0.084)	(0.085)
15 Pregnancy, childbirth	0.009	-0.200***	-0.214***	-	-	-
	(0.051)	(0.070)	(0.071)			
17 Congenital mal/deformations	-0.361***	0.323***	0.338***	-	-	-
	(0.116)	(0.099)	(0.099)			
18 Symptoms not classified	-0.145***	-0.065*	-0.058	-0.112	-0.054	-0.048
	(0.033)	(0.036)	(0.036)	(0.100)	(0.077)	(0.078)
19 Injury, poisoning, external	-0.512***	0.394***	0.410***	-0.173	0.123	0.132*
	(0.036)	(0.033)	(0.033)	(0.111)	(0.076)	(0.076)
EQ-5D	1.198***	-0.779***	-0.780***	1.331***	-	-0.816***
	(0.023)	(0.015)	(0.016)	(0.067)	(0.043)	(0.046)
Age/10	-0.123***	0.119***	0.178***	-	0.016	0.013
	(0.022)	(0.020)	(0.014)	(0.065)	(0.056)	(0.056)
Age/10 squared	0.020***	-0.008***	0.024*	0.036***	0.001	0.001
	(0.002)	(0.002)	(0.013)	(0.006)	(0.005)	(0.005)
female	-0.127***	-0.095***	0.116***	-	-0.036	-0.033
	(0.013)	(0.011)	(0.020)	(0.037)	(0.028)	(0.028)
comorbid	-0.117***	0.173***	-0.008***	-0.030	0.074	0.076
	(0.014)	(0.014)	(0.002)	(0.053)	(0.047)	(0.047)
operation	0.008	0.026**	-0.094***	-0.144**	0.012	0.017
	(0.015)	(0.013)	(0.011)	(0.058)	(0.041)	(0.042)
Constant	-0.237***	2.772***	2.764***	0.269	1.656***	1.661***
	(0.067)	(0.063)	(0.064)	(0.217)	(0.179)	(0.179)
Inflation variables						
EQ5D			2.110***			2.130***
			(0.041)			(0.114)
Age/10			-0.286***			-0.533***
			(0.035)			(0.113)
Age/10 squared			0.040***			0.071***
			(0.003)			(0.010)
female			-0.175***			-0.196***
			(0.021)			(0.064)

	HODaR (6 weeks recall period)			HIPO (1 week recall period)		
	TPM part 1	TPM part 2	ZINB variable	TPM part 1	TPM part 2	ZINB variable
Constant			-0.919***			0.237
			(0.099)			(0.322)
Dispersion		0.653	0.659		0.0233	0.0255
N	55,726	24,328	55,726	6,046	1,549	6,046
Log likelihood	-34,794	-95,635	-130,924	-3,088	-3,280	-6,557
AIC	69,638	191,322	261,909	6,219	6,605	12,841
BIC	69,861	191,533	262,186	6,367	6,728	13,028

Standard errors in parentheses * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

HODaR - Health Outcomes Data Repository; HIPO - Health Improvement and Patient Outcomes; TPM – two part model; ZINBv – zero inflated negative binomial with variable inflation

1-19 – has condition in ICD chapter; Age/10 – age divided by 10; Comorbid – has comorbidity; Operation - has had an operation

Table 7: Coefficients for TPM to allow predictions of days off work or days off normal activities

Days off work				
	HODaR		HIPO	
	TPM part1	TPM part 2	TPM part1	TPM part 2
1 Certain infectious and parasitic diseases	-0.24508431	-0.13794693	-0.58587641	-0.20253513
2 Neoplasms	-0.44196263	0.25308716	-0.81296505	0.22469750
3 Diseases of the blood	-0.08807063	-0.25748607	-0.52603158	-1.26238533
4 Endocrine, nutritional, metabolic	-0.13206202	0.00558699	-0.29546461	-0.43493427
5 Mental and behavioural disorders	-0.13034625	0.44228184		
6 Nervous system	-0.30730500	0.15250512	-0.59230927	0.03465576
7 Eye and adnexa	-0.15103577	0.03384859	-0.31789851	-0.03754577
8 Ear and mastoid process	-0.21015407	-0.05212614	-0.33488613	-1.85272609
9 Circulatory system	-0.47895778	0.27642237	-0.72430845	0.14129737
10 Respiratory system	-0.10321344	-0.05817031	-0.33164145	0.08123540
11 Digestive system	-0.20176801	-0.03383309	-0.37004283	-0.13277972
12 Skin and subcutaneous tissue	-0.04998003	-0.17296831	-0.14823411	-0.34358400
13 Musculoskeletal system	-0.44638718	0.24146286	-0.60301682	0.17255406
14 Genitourinary system	-0.23188857	-0.10809127	-0.47079657	-0.04903272
15 Pregnancy, childbirth	0.01834339	0.03760131		
17 Congenital mal/deformations	-0.44835238	0.23782896		
18 Symptoms not classified elsewhere	-0.15175235	-0.17950138	-0.21796800	-0.23547081
19 Injury, poisoning, external	-0.59014383	0.24214064	-0.88363333	0.22518297
EQ-5D	0.20144421	-0.72436821	2.19197953	-0.69924506
Age/10	-0.99626379	0.30698379	-0.09071621	0.39742346
Age/10 squared	0.13875395	-0.02592483	0.01434990	-0.04191095
Female	0.02977747	-0.05165029	-0.23574510	-0.04672291
Comorbidity	-0.11123936	0.22619982	-0.17513219	-0.01780249
Operation	0.08624032	-0.00571200	-0.15610999	0.15467928
Constant	1.76077781	2.42285513	-0.59688067	1.78829541
Dispersion (α)		0.9462932		0.5623412
Days off Normal Activities				
1 Certain infectious and parasitic diseases	-0.32786713	0.05771232	0.08670380	-0.07367897
2 Neoplasms	-0.32811405	0.21903631	-0.11926633	0.06786809
3 Diseases of the blood	-0.09161548	0.00579628	0.13934071	-0.19125374
4 Endocrine, nutritional, metabolic	-0.12176296	0.04401712	0.19116868	-0.19355829
5 Mental and behavioural disorders	0.13992641	-0.16020950		
6 Nervous system	-0.29333664	0.12197855	-0.15925119	-0.06977515
7 Eye and adnexa	-0.00300514	-0.12024362	0.02364103	-0.12567657
8 Ear and mastoid process	0.02383457	-0.11594762	0.02215244	-0.11058757
9 Circulatory system	-0.39850584	0.21781476	-0.23382296	0.06382162
10 Respiratory system	-0.17005568	0.11427064	-0.10745245	0.02782909
11 Digestive system	-0.18071168	0.02441086	-0.01451493	-0.13671081
12 Skin and subcutaneous tissue	-0.06631625	-0.02215379	0.21341741	-0.08204150
13 Musculoskeletal system	-0.54254914	0.27213061	-0.26457574	0.08992269
14 Genitourinary system	-0.21496289	0.01824900	-0.08410712	0.00051135
15 Pregnancy, childbirth	0.00919058	-0.19952601		
17 Congenital mal/deformations	-0.36127705	0.32319440		
18 Symptoms not classified elsewhere	-0.14522172	-0.06450461	-0.11327288	-0.05542834
19 Injury, poisoning, external	-0.51218389	0.39371337	-0.17335731	0.12320991
EQ-5D	1.19834117	-0.77909880	1.33120016	-0.78713305
Age/10	-0.12319003	0.11890256	-0.25319571	0.01639363
Age/10 squared	0.01965632	-0.00771880	0.03565989	0.00079459
Female	-0.12712540	-0.09531266	-0.10921793	-0.03583822
Comorbidity	-0.11663993	0.17295911	-0.02939702	0.07354753
Operation	0.00829142	0.02625400	-0.14470939	0.00783676
Constant	-0.23710103	2.77182424	0.26886470	1.65875542
Dispersion (α)		0.6528781		0.0233346