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Development and Validation of a Prediction Model for 6-Month Societal Costs in Older Community Care-Recipients in Multiple Countries; the IBenC Study

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ABSTRACT: This study aims to develop and validate a prediction model of societal costs during a period of 6-months in older community care-recipients across multiple European countries. Participants were older community care-recipients from 5 European countries. The outcome measure was mean 6-months total societal costs of resource utilisation (healthcare and informal care). Potential predictors included sociodemographic characteristics, functional limitations, clinical conditions, and diseases/disorders. The model was developed by performing Linear Mixed Models with a random intercept for the effect of country and validated by an internal-external validation procedure. Living alone, caregiver distress, (I)ADL impairment, required level of care support, health instability, presence of pain, behavioural problems, urinary incontinence and multimorbidity significantly predicted societal costs during 6 months. The model explained 32% of the variation within societal costs and showed good calibration in Iceland, Finland and Germany. Minor model adaptations improved model performance in The Netherland and Italy. The results can provide a valuable orientation for policymakers to better understand cost development among older community care-recipients. Despite substantial differences of countries' care systems, a validated cross-national set of key predictors could be identified.

KEYWORDS: Prediction model, elderly people, societal costs, Linear Mixed Models

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Background

The number of disabled older individuals in need of long-term health and social care increases steeply in Europe.[1,2] Most of them prefer to stay at home independently for as long as possible with appropriate support instead of going to a nursing home.[3] This policy is also promoted by many European governments, as it is generally assumed that community care is associated with better self-reported quality of life and with lower costs than institutionalised care.[4,5]

Despite this, governmental expenditures on health and long-term community care have grown faster than can be expected based on demographic trends only.[6] Developments other than aging that probably contributed to this include: a decline in the availability of informal caregiving due to societal developments, higher expectations in terms of quality of life as people become wealthier, and high investments in science and technology (both medical and non-medical) that enable people to stay at home longer.[2] In combination with existing budget constraints, this has led to high pressure on care systems across Europe. Many community care systems fall short to meet current care demands. This may lead to premature institutionalisation and unnecessary hospital admissions, which in turn increases costs, leads to premature mortality and reduces quality of life.[7,8] This situation exacerbates as Europe is facing increasing shortages of home health aides and home nurses.[9] It is a major challenge for policymakers to organise care in such a way that available resources are used optimally.

For a comprehensive view on total costs of care, it is important to take a societal perspective on costs meaning that not only costs of health and social care should be included, but also informal care. This is important because a large percentage of community care-recipients receive informal care regularly.[8,10] We have only limited understanding of factors predicting costs of utilisation of formal and informal care services by older community care-recipients. Previous studies on predictors of societal costs found that country of residence, being married, functional limitations, limitations of going out, cognitive impairment, number of medication intake, arthritis and

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cerebrovascular accident and comorbidity predicted societal costs.[11-17] However, these studies mainly focused on disease-specific groups such as people with dementia and not on people who receive community care in general. Since funding systems in long-term care are not designed based upon disease-specific groups, insight into the populations and the costs is essential for the sustainability of long-term care settings. Modifiable conditions that are found to predict costs, might be targeted by interventions to curtail rising costs. Therefore, this study aimed to develop and validate a prediction model of societal costs of care utilisation during a period of 6-months in older community care-recipients across multiple European countries.

Methods

Design

Data were collected as part of the cross-European IBenC ('Identifying best practices for care-dependent elderly by Benchmarking Costs and outcomes of community care') study. IBenC had a prospective longitudinal design and aimed to identify best practices in community care for care-dependent elderly people by benchmarking the cost-effectiveness of community care delivery systems in Europe.[18] Data collection was performed between January 2014 and August 2016.

The study was approved by all relevant medical ethical committees. When required, written informed consent was obtained from participants prior to the assessments.

Setting and sample

The IBenC sample consisted of 2884 community-dwelling care-recipients aged 65 years and older from 6 European countries (Belgium, Finland, Germany, Iceland, Italy and the Netherlands), who received professional community care and were expected to receive care for at least 6 months after inclusion. Terminally ill care-recipients and care-recipients with a planned admittance to a nursing home within 6 months after the start of the study were not included in the study.

Procedure

Community care organisations were invited to participate by the national study centres. Eligible care-recipients were invited by the care organisations or automatically enrolled, depending on the local ethical regulations. Care-recipient outcome data were collected using the interRAI Home Care (HC) instrument. Data were collected at the homes of care-recipients by trained (research) nurses, using licensed software.[19] InterRAI-HC assessments were performed at baseline, after 6 and after 12 months.

Data

Data on care-recipient characteristics and resource utilisation were collected with the interRAI-HC. The interRAI-HC is a standardised and reliable comprehensive geriatric assessment instrument designed to assist in care planning, outcome measurement, quality improvement and resource allocation for care-recipients who receive care at home.[20-22]

Measures

Dependent variable. The primary outcome measure was the mean total societal costs based on resource utilisation over a 6 months follow-up period. Societal costs included the utilisation of community care, physician visits, other healthcare services, hospital admissions, supportive care services, number of days in institutionalised care, and informal caregiver time. Resource utilisation was registered over 3, 7 or 90 days prior to the assessment, depending on the type of service. The length of hospital stay in days was estimated by multiplying the reported number of events with country-specific averages of length of hospital stay during the year 2012 (Table 1).[23] For both assessments, resource utilisation was extrapolated to reflect a period of 3 months. Subsequently, units of resource utilisation were multiplied by Dutch standard costs in order to calculate cost of resource utilisation (Table 1).[24] Standard costs from a single country were used in order to eliminate differences due to country-specific prices. Costs between measurements were linearly interpolated by multiplying costs at baseline assessment by 0.5; costs at 6 months after baseline by 1.5.[25] Total costs over the period of 6 months were calculated by summing the extrapolated baseline and 6-month cost estimates. This approach had good convergent validity as compared with the Resource Utilization in Dementia Lite instrument,[25,26] and is, therefore, considered to be valid to estimate societal costs over 6 months.

Independent variables. Potential predictors of societal costs were derived from previous prediction and costing studies, and from what experts assumed about the interrelationship between the characteristics of older community care-recipients and societal costs.[11-17] Information on predictors was collected at baseline and included sociodemographic characteristics, functional limitations, clinical conditions and diseases/disorders of the care-recipients. Predictors are described briefly below and described in more detail in Supplemental Appendix 1.

Sociodemographic characteristics included age, gender, living alone, loneliness and caregiver distress. The interRAI-HC includes several functional scales, which were used to assess *functional limitations*, including functional impairments, difficulty in performing instrumental activities, cognitive impairment, presence of depressive symptoms, required level of formal and informal care support, health instability and presence of pain.[27-33] Other functional limitations that were considered, included behavioural problems and any falls. *Clinical conditions* included anxiety, dehydration, dizziness, major skin problems, pressure ulcer, unintended weight loss and urinary incontinence.

Table 1. Overview of used unit cost (in €2015) and average length of stay (days).

CARE SERVICE	COSTS[24]	RECALL PERIOD	EXTRAPOLATION
Community care			
Home health aide (per hour)	€50	7d	*13
Home nursing (per hour)	€73	7d	*13
Physician visits			
General practitioner visit/Outpatient clinic visit (per visit)	€92	90d	*1
Other healthcare services			
Physical therapy (per session)	€33	7d	*13
Occupational therapy (per session)	€34	7d	*13
Social worker (per session)	€64	7d	*13
Hospital admissions			
Hospital admission with overnight stay (per day with overnight stay)	€479	90d	*1
Average length of hospital stay[23]			
Finland	11.0d	NA	
Germany	9.2d	NA	
Iceland	5.8d	NA	
Italy	7.7d	NA	
Netherlands	5.2d	NA	
Emergency room visit without overnight stay (per visit)	€261	90d	*1
Supportive care services			
Home making services (per hour)	€23	7d	*13
Meals on wheels (per day)	€7.50	7d	*13
Institutionalised care			
Nursing home (per day)	€168	NA	
Informal care			
Informal care (per hour)	€14.08	3d	/3*90

Abbreviation: NA, not applicable.

Clinically established *diseases/disorders* included Alzheimer's disease, cancer, chronic obstructive pulmonary disease, congestive heart failure, coronary artery disease, diagnosis of urinary tract infection, dementia other than Alzheimer's disease, depression, diabetes, hemiplegia, multiple sclerosis, Parkinson's disease, pneumonia, stroke (Cardio Vascular Accident) and any fracture in the past 30 days.[34] Multimorbidity was defined as the presence of 2 or more chronic diseases.[35]

Sample size

All data available from this sample were used to maximise the power of the results. To ensure accurate prediction in subsequent subjects, 2 to 20 subjects per predictor are required.[36-38] Our sample exceeds these minimum sample size requirements and is therefore expected to provide robust estimates.

Analysis strategy

Data from Belgium were excluded from analyses as information on informal care hours was not available (n = 525). Also, data from 224 Dutch respondents were excluded because data collection of interRAI-HC was put on hold in one Dutch organisation due to a software switch.

Socio-demographic and clinical characteristics at baseline were described using descriptive statistics and frequencies. Differences in baseline characteristics on country level were evaluated using Chi-square tests and ANOVAs. A histogram and a Normal Quantile plot were used to visually check the normality of societal costs. Log-transformation was used to account for skewness of the outcome measure. Distributions of all potential predictors were investigated using frequencies, descriptive statistics, boxplots and histograms. Linearity between potential predictors and the outcome measure were determined by using scatterplots. Also, normality of the distribution of regression residuals was checked.[39]

Imputation of missing cost data was performed using Multivariate Imputation by Chained Equations (MICE),[40] stratified for country to increase the validity of the imputation. Predictive mean matching was used during imputation to account for the skewed distribution of costs.[41] For participants who passed away, costs were set at zero after death. Costs of institutionalised care for participants who were admitted between baseline and follow-up were assumed to be equal to the standard cost per admission day in a nursing home. These events were assumed to have taken place halfway between 2 assessments. Characteristics included in the multiple imputation model were baseline characteristics that differed significantly between participants and drop-outs, and baseline characteristics that were significantly associated with costs after 6 months. Ten imputed datasets were generated and separately analysed. The results were pooled using Rubin's rules.[42]

Correlations between potential predictors were investigated using Pearson correlation coefficients. In case of collinearity ($r > 0.8$), only the strongest associated variable was retained in the analysis.[43] Although common, univariable linear regression analyses to preselect predictors were not performed, since important predictors may be rejected using this approach owing to nuances in the dataset or because they are confounded by other predictors.[44-46]

A Linear Mixed Model was developed with fixed effects for all predictors plus a random intercept for country effects. Predictors were removed stepwise until all variables showed a statistically significant association with the outcome ($P \leq .05$). In case one of the dummies of a categorical predictor variable showed no significant association with the outcome, and the other(s) did, a likelihood ratio test was performed to compare models with and without that predictor variable and to assess their fit.[47] The model with the best fit determined whether the predictor was in- or excluded.

Model validation. An internal-external validation procedure was performed, which enables optimal use of sample size and allows dealing with potential heterogeneity between different IBenC countries.[48,49] Data from all countries, but the validation country were iteratively used to develop a prediction model. This model was then validated against the validation country sample. This process was repeated until every country had functioned as validation country. Relevant predictors from the multivariable analyses were entered in each development sample. Subsequently, the intercept and regression coefficients were extracted and combined to create a linear predictor function and used to calculate a linear predictor score for every respondent in the validation sample. Different scenarios were created to investigate consistent model performance when applied in another country sample that was not included during its development.[48,50]

The quality of the prediction model was expressed as the explained variance (R^2). Various R^2 were calculated: R^2 for each country and R^2 as proposed by Snijders and *Bosker*[51,52] based on the multilevel model including all countries.

The predictive performance (ie, the agreement between predicted costs and observed costs) was assessed with ratios of predicted costs divided by mean observed costs (E/O-ratios) and calibration curves. In an ideal situation, E/O-ratios are 1 and all points of the calibration curve lie on the 45° slope.[44] To take clustering into account, the predictive performance in individual countries (within-cluster performance) was assessed.[53] Predicted and observed costs were back transferred using the exponential function. To calculate the calibration plot, groups of deciles were created based on predicted costs. Subsequently, mean predicted and observed costs were calculated for each group and plotted in a single figure.[54] The calibration curve was estimated as best-fit straight line through the calibration plot points.

Model optimisation. A final validation step was model optimisation. For countries in which model performance was low, the following options were considered to improve the model: updating the intercept or removal of predictors with predictive importance that have heterogeneous effects across countries.[48]

The intercept was re-estimated using an offset procedure via Generalised Linear Models with an identity link. First, the linear predictor scores were re-calculated without the intercept. Second, the intercept was estimated by adding the linear predictor (as offset) as only variable in the model in the validation sample.

To provide insight into heterogeneous predictor effects across countries, regression coefficients from relevant predictor variables were estimated by country by linear regression analyses and plotted in a single figure. Higher between-county variability in regression coefficients indicate more heterogeneity for that predictor.[50]

Results

Study sample

A total of 2135 participants from the original IBenC sample (n = 2884) were included in the analyses. Excluded respondents were statistically significantly older than the included respondents.

Between the baseline and 6-month follow up assessments 94 participants were admitted to a care facility, 78 deceased, 16 were discharged from home care, and 53 participants were lost to follow-up due to lack of interest or time (n = 16), or without reason (n = 37).

Two-thirds of the participants in the study sample were female and the mean age was 83.0 years. Significant differences ($P < .001$) were found between countries in all baseline characteristics (Table 2).

Societal costs

Six-month societal costs per participant were on average €18 467 (SE = 332). The highest societal costs were found in Italy (€26 980 (SE = 644) per participant per 6 months), followed by the Netherlands (€19 353 (SE = 1202), Germany (€17 402 (SE = 649) and Finland (€14 245 (SE = 587), and the lowest societal costs were found in Iceland (€13 622 (SE = 623) per participant per 6 months). The distribution of societal costs per country can be found in Supplemental Appendix 2.

Multivariable analyses

The multivariable analyses showed that living alone, caregiver distress, ADL and iADL impairment, required level of care support, health instability, presence of pain, behavioural problems, urinary incontinence and multimorbidity statistically significantly predicted 6-months societal costs (Table 3).

ADL and IADL impairment and required level of care support were found to be the strongest predictors of high societal costs. Compared to care-recipients without ADL impairment, care-recipients with total ADL dependency and limited to extensive ADL dependency had 32% and 23% higher societal costs, respectively. Further, one point increase on the IADL impairment scale (ie, more dependency in performing instrumental activities) and on the required level of care were associated with respectively 13% and 21% higher societal costs.

Model validation

The total variance in 6-month societal costs explained by the final model was 32%. For individual countries, the explained variance ranged from 19% for Italy, 25% for the Netherlands, 34% for Finland, 34% for Iceland to 36% for Germany.

Figure 1 shows the predicted and observed societal costs for the different countries. Visual inspection of these calibration plots indicates that the model performed well for Iceland, Finland and Germany, but poorly for the Netherlands and Italy. Overall, E/O-ratios (Figure 1) were smaller than 1 in all validation countries. Figure 2 provides an overview of between-country variability in regression coefficients between countries. The predictors ADL and multimorbidity showed substantial between-country variability.

Model optimisation

For the Netherlands, estimated costs were much lower than observed costs (E/O = 0.51). Also, mean estimated costs for the different groups of deciles in the calibration plot were clustered around €15 000 (Figure 1). Predictor effects for the Netherlands deviated from the other countries for the predictors living alone, presence of pain, multimorbidity (stronger effects) (Figure 2). Model performance was improved by updating its intercept from 8.55 to 8.90 (Figure 3), resulting in an E/O-ratio of 0.72.

The calibration plot for Italy showed that costs were underestimated for people with relatively low observed societal costs and overestimated for people with relatively high observed societal costs. This led to a reasonably well E/O-ratio. However, considering the low explained variance and the poor calibration, we updated the model by removing predictors with overall the highest heterogeneity (ADL and multimorbidity). The updated model performed better as shown by the calibration plot (Figure 3), although the E/O-ratio deteriorated (0.69). The explained variance of the updated model was 19%.

Discussion

In this study, we focused on predictors of costs that are directly related to care utilisation. Predictors of 6-month societal costs in a sample of older community care-recipients from 5 European countries included living alone, caregiver distress, ADL and iADL impairment, required level of formal and informal care support, health instability, presence of pain, behavioural problems, urinary incontinence and multimorbidity. The final model performed satisfactory for Iceland, Finland and Germany and sufficiently for the Netherlands and Italy after optimisation. For the latter 2 countries, optimal model performance was achieved by increasing the intercept (the Netherlands) and by removing predictors with high heterogeneity (Italy).

The initial model predicted lower than observed costs for the Netherlands. Dutch care-recipients had the highest societal costs after Italy, although the average level of impairment in the Dutch sample was relatively low. Across all country samples, the Italian sample experienced on average the highest functional impairments. In Italy disabled people tend to live in the community longer than in other countries, which may be the result of cultural factors and of policy. Also, older adults in Italy were highly supported by informal care and they used relatively little professional home care compared with older adults in the other countries under study.[55] Such cultural and policy factors were not included in this study, which might be an explanation for the poor initial model performance in Italy. Future studies could investigate whether adding these factors can further improve the prediction model.

We found rather heterogeneous effects in the extent to which ADL impairment predicted societal costs. This may be explained by the fact that resource allocation policies in home care differs across countries. Although assessment of ADL and IADL impairment were key aspects for determining eligibility to receive home nursing care in all countries, in some countries the availability of informal caregivers is also taken

Table 2. Characteristics of the study population per country and of the total sample.

VARIABLES	TOTAL (N = 2135)	ITALY (N = 499)	THE NETHERLANDS (N = 267)	ICELAND (N = 420)	FINLAND (N = 456)	GERMANY (N = 493)	CHI²/F	*P* VALUE
Socio-demographics								
Country of residence, n (%)	Italy 499 (23%) Netherlands 267 (13%) Iceland 420 (20%) Finland 456 (21%) Germany 493 (23%)							
Mean age (SD)	83 (7.5)	81.8 (7.9)	82 (7.5)	83.7 (7)	82.9 (7)	84.2 (7.6)	8.3	<.001
Female, n (%)	1434 (67%)	286 (57%)	192 (72%)	292 (70%)	313 (69%)	351 (71%)	29.8	<.001
Living alone, n (%)	1259 (59%)	82 (16%)	193 (72%)	256 (61%)	369 (81%)	359 (73%)	523.3	<.001
Loneliness, n (%)	484 (23%)	43 (9%)	98 (37%)	85 (20%)	120 (26%)	138 (28%)	94.6	<.001
Caregiver distress, n (%)	278 (15%)	76 (15%)	22 (8%)	134 (32%)	22 (6%)	24 (8%)	141.3	<.001
Functional limitations								
Mild impairment (ADLH <2), n (%) Limited to extensive impairment (ADLH 2-4), n (%) Dependent in ADLs (ADLH ⩾5), n (%)	1141 (53%) 702 (33%) 292 (14%)	54 (11%) 237 (47%) 208 (42%)	221 (83%) 38 (14%) 8 (3%)	341 (81%) 77 (18%) 2 (1%)	359 (79%) 85 (19%) 12 (3%)	166 (34%) 265 (54%) 62 (13%)	947.9	<.001
Mean iADLCH score (SD)	3.9 (1.8)	5.1 (1.4)	2.7 (1.7)	3.5 (1.5)	3.9 (1.5)	3.8 (2.1)	103.1	<.001
Cognitive impairment (CPS ⩾3), n (%)	407 (19%)	179 (37%)	4 (1%)	40 (10%)	49 (11%)	135 (27%)	221,1	<.001
Depressive symptoms (DRS ⩾3), n (%)	303 (14%)	73 (15%)	54 (20%)	47 (11%)	37 (8%)	92 (19%)	33.1	<.001
Mean Case Mix Index, informal care (SD)	1.1 (0.7)	1.8 (0.7)	0.7 (0.4)	0.7 (0.5)	0.8 (0.5)	1.2 (0.7)	259.8	<.001
Mean CHESS score (health instability) (SD)	1.1 (1.1)	1.6 (1.3)	1.0 (1.0)	1.2 (1.0)	0.7 (0.9)	0.6 (0.9)	78.6	<.001
Presence of pain (Pain Scale >0), n (%)	1085 (51%)	217 (43%)	126 (47%)	252 (60%)	277 (61%)	213 (43%)	55.9	<.001
Behavioural problems, n (%)	344 (16%)	65 (13%)	31 (12%)	42 (10%)	73 (16%)	133 (27%)	62.2	<.001
Any falls, n (%)	472 (22%)	156 (31%)	72 (27%)	80 (19%)	98 (21%)	66 (13%)	52.1	<.001
Clinical conditions								
Anxiety, n (%)	198 (9%)	51 (10%)	7 (3%)	120 (29%)	14 (3%)	6 (1%)	258.7	<.001
Dehydrated, n (%)	69 (3%)	26 (5%)	15 (6%)	6 (1%)	6 (1%)	16 (3%)	20.8	<.001

(Continued)

Table 2. (Continued)

VARIABLES	TOTAL (N=2135)	ITALY (N=499)	THE NETHERLANDS (N=267)	ICELAND (N=420)	FINLAND (N=456)	GERMANY (N=493)	CHI²/F	*P* VALUE
Dizziness, n (%)	860 (40%)	230 (46%)	111 (42%)	197 (47%)	178 (39%)	144 (29%)	40.3	<.001
Major skin problems or skin tears or cuts, n (%)	159 (7%)	76 (15%)	16 (6%)	12 (3%)	24 (5%)	31 (6%)	61.6	<.001
Any stasis ulcer, n (%)	196 (9%)	153 (31%)	5 (2%)	10 (2%)	10 (2%)	18 (4%)	361.3	<.001
Unintended weight loss, n (%)	196 (9%)	107 (21%)	28 (10%)	16 (4%)	7 (2%)	38 (8%)	138.3	<.001
Urinary incontinence, n (%)	1063 (50%)	326 (66%)	124 (47%)	182 (43%)	181 (40%)	250 (51%)	76.2	<.001
Diseases/disorders								
Alzheimer's Disease, n (%)	260 (12%)	37 (7%)	9 (3%)	36 (9%)	143 (31%)	35 (7%)	203.3	<.001
Dementia other than Alzheimer, n (%)	346 (16%)	93 (19%)	7 (3%)	53 (13%)	46 (10%)	147 (30%)	123.5	<.001
Cancer, n (%)	273 (13%)	81 (16%)	48 (18%)	48 (11%)	42 (9%)	54 (11%)	19.0	<.001
COPD, n (%)	234 (11%)	73 (15%)	48 (18%)	64 (15%)	24 (5%)	25 (5%)	60.6	<.001
Congestive heart failure, n (%)	486 (23%)	103 (21%)	75 (28%)	128 (30%)	101 (22%)	79 (16%)	32.2	<.001
Coronary artery disease, n (%)	557 (26%)	128 (26%)	41 (15%)	168 (40%)	147 (32%)	73 (15%)	98.8	<.001
Diagnosis of urinary tract infection, n (%)	170 (8%)	53 (11%)	40 (15%)	36 (9%)	32 (7%)	9 (2%)	48.9	<.001
Depression, n (%)	286 (13%)	52 (10%)	29 (11%)	100 (24%)	36 (8%)	69 (14%)	56.6	<.001
Diabetes, n (%)	561 (26%)	129 (26%)	74 (28%)	61 (15%)	142 (31%)	155 (32%)	43.1	<.001
Hemiplegia, n (%)	111 (5%)	48 (10%)	7 (3%)	7 (2%)	20 (4%)	29 (6%)	35.1	<.001
Multiple sclerosis, n (%)	17 (1%)	6 (1%)	7 (3%)	3 (1%)	0 (0%)	1 (0%)	18.2	<.001
Parkinson's disease, n (%)	150 (7%)	56 (11%)	18 (7%)	23 (5%)	22 (5%)	31 (6%)	18.8	<.001
Pneumonia, n (%)	85 (4%)	25 (5%)	22 (8%)	24 (6%)	7 (2%)	7 (1%)	32.8	<.001
Stroke (CVA), n (%)	271 (13%)	65 (13%)	45 (17%)	41 (10%)	55 (12%)	65 (13%)	7.8	<.001
Any fracture during last 30 d, n (%)	87 (4%)	46 (9%)	10 (4%)	9 (2%)	11 (2%)	11 (2%)	45.4	<.001
Multimorbidity (presence of 2 or more disease diagnosis), n (%)	1202 (56%)	293 (59%)	139 (52%)	278 (66%)	256 (56%)	236 (48%)	34.1	<.001

Abbreviations: ADLH, Activities of Daily Living Hierarchy Scale; CHESS, Changes in Health, End-Stage Disease, Signs, and Symptoms Scale; chi²/F, test statistics Chi-square tests and ANOVAs; COPD, Chronic obstructive pulmonary disease; CPS, Cognitive Performance Scale; DRS, Depression Rating Scale; iADLCH, Instrumental ADL Capacity Hierarchy Scale; SD, standard deviation.
P-value <.05 indicates statistically significant differences between participants between countries.

Table 3. Results of the Linear Mixed Model analyses with fixed effects for the predictors plus a random intercept for the effects of country.

PREDICTOR	β (95% CI)	*P*-VALUE
Living alone (item 0-1)	−0.18 (−0.26; −0.11)	<.001
Caregiver distress (item 0-1)	0.15 (0.05; 0.25)	<.001
ADLH (limited to extensive ADL assistance (ADLH score 2-4) versus ADL independent (ADLH score 0-1))	0.21 (0.11; 0.3)	<.001
ADLH (ADL dependent (ADLH score 5-6) versus ADL independent (ADLH score 0-1))	0.28 (0.13; 0.43)	<.001
iADL (IADLCH, scale 0-6)	0.12 (0.09; 0.14)	<.001
Required level of care support (CMI informal care, 0.23-8.97)	0.19 (0.12; 0.27)	<.001
Health instability (CHESS, scale 0-6)	0.05 (0.02; 0.08)	<.001
Presence of pain (Pain Scale, item 0-1)	0.08 (0.02; 0.15)	.01
Behavioural problems (item 0-1)	0.11 (0.02; 0.2)	.01
Urinary incontinence (item 0-1)	0.1 (0.03; 0.17)	.01
Multimorbidity (item 0-1)	0.09 (0.02; 0.15)	.01
Intercept	8.61 (8.43; 8.79)	<.001
Random-effects parameters		
Random intercept for country	Estimate (SE)	
SD (Intercept)	0.1472 (0.0512)	
SD (Residual)	0.7052 (0.012)	

Abbreviations: ADL, Activities of Daily Living; CHESS, Changes in Health, End-Stage Disease, Signs and Symptoms Scale; iADL, Instrumental ADL; IADLCH, Instrumental ADL Capacity Hierarchy Scale; SD, standard deviation; SE, Standard Error; β, regression coefficient.
The β's are expressed in log-transformed values.
Predictors that showed a statistically significant association with the outcome are included (cut-off point $P = .05$).

into account.[55] Consequently, individuals with the same level of need do not necessarily receive the same level and mix of care services across countries.[55]

The predictors caregiver distress, ADL and IADL impairment, health instability, presence of pain, behavioural problems and urinary incontinence may be modifiable to a certain degree and could be targeted by interventions in an attempt to curtail future increases in societal costs. ADL and IADL impairment are frequently identified as being key predictors of societal costs across (multi)national samples, our results confirm this.[11,13,15-17,56] Interventions could, for example, aim to enhance self-efficacy and adaptive coping.[57] Early interventions to promote an active life can also be beneficial, as it helps to maintain (I)ADL independence and prevent disability in older age.[58] Behavioural problems was also identified as a predictor of societal costs in an earlier study.[13] Health instability was included as a risk score for negative outcomes such as mortality, hospitalisation, pain, caregiver distress and poor self-rated health which may predict resource utilisation and costs. Health instability relates to identified conditions that require rapid action to prevent further deterioration and is therefore well suited to flag interventions.[32]

The other, non-modifiable predictors found in this study may be used by policymakers for optimal resource allocation. Living alone significantly predicted lower 6-month societal costs; required level of care support and multimorbidity were associated with higher 6-month societal costs, which is in line with previous research.[13,16,59-61] The measure for required level of care support was developed by the interRAI-group based on the case-mix classification system 'Resource Utilization Groups III Home Care'[31,62] and was shown to explain 33.7% of the variance in resource use in the home care setting.[31] Our findings confirm that the required level of care support is an important predictor of societal costs.

Most previously conducted studies focused on community-dwelling older adults with dementia, a subgroup in our sample.[11,13,15-17] Only 2 earlier studies on predictors of societal costs reported information on model performance.[11,16] In these studies, a pooled R^2 of 32% to 37% for dementia care costs was found based on the predictors ADL impairment, multimorbidity and falls; one is in line with the R^2 found in the present study (32%), the other is slightly higher (37%). However, no model validation was performed in these studies, leaving its predictive performance uncertain. Our study adds to these

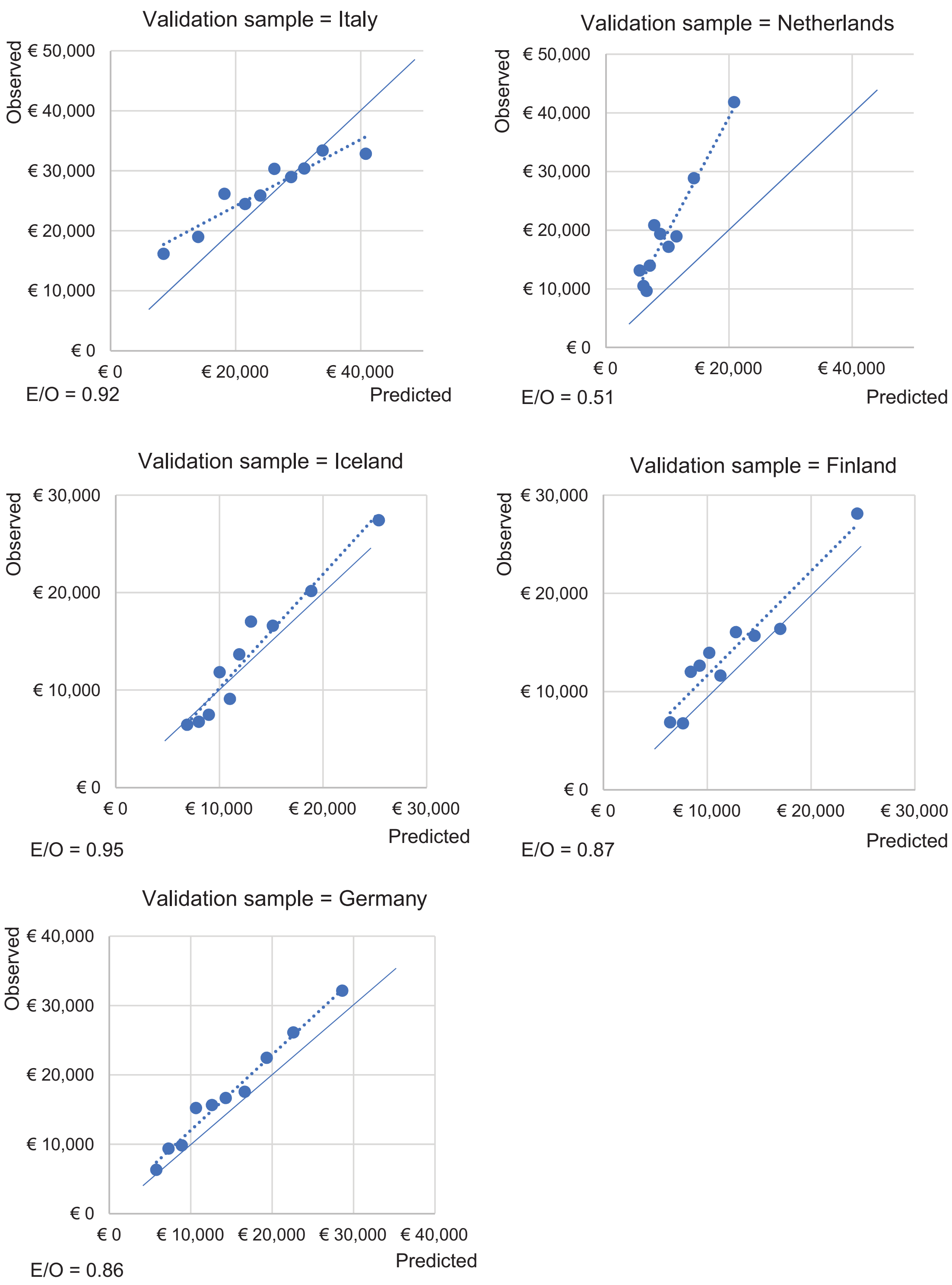
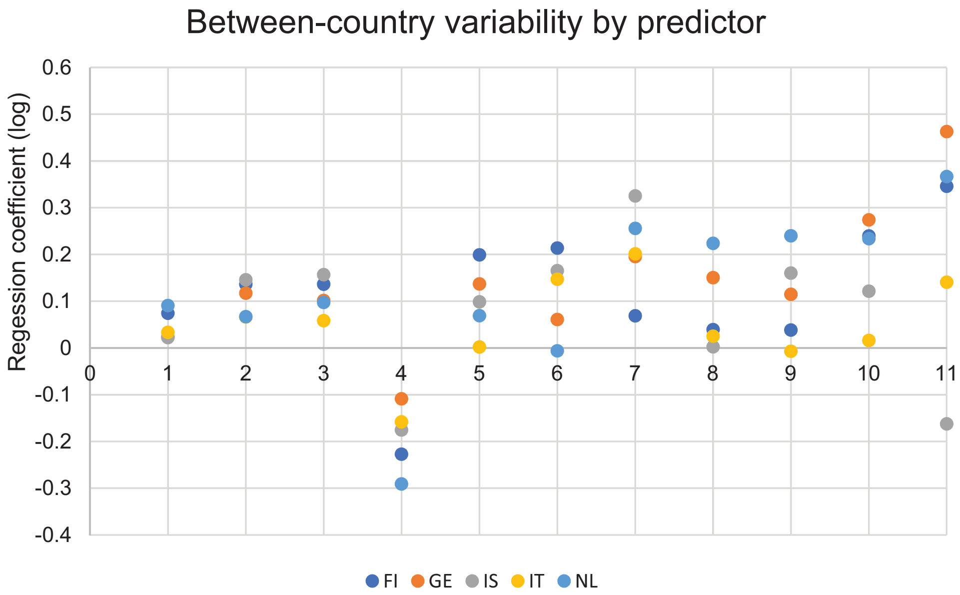


Figure 1. Graphical representation of predicted and observed societal costs.
E/O = ratio of predicted and observed costs. Solid line indicates the 45° line. Dotted line is the calibration curve (best fit of data points).

findings by confirming that most of the identified predictors are also predictive of societal costs in older community care-recipients and are not country-specific.

Strengths and limitations

Strengths of this study are the large multinational sample, and the use of random effects to account for heterogeneity across countries. Further, the approach of this study was similar to an individual participant data (IPD) meta-analysis, since the various countries in our dataset were treated as individual samples.[48,63] Prediction models based on IPD meta-analysis may be more generalisable than prediction models based upon single samples since the inclusion of multiple study samples addresses a wider range of study populations and increases the variation in the characteristics of the included participants.[50]



Legend x-axis

1 Health instability (CHESS)
2 Urinary incontinence
3 iADL (iADLCH)
4 Living alone
5 Behavioural problems
6 Caregiver distress
7 Required level of care support (CMI)
8 Presence of pain (Pain Scale)
9 Multimorbidity
10 ADL (ADLH, limited to extensive ADL assistance vs. ADL independent)
11 ADL (ADLH, ADL dependent vs. ADL independent)

Figure 2. Heterogeneity among predictors included in the final multivariable model.
Predictors are ordered based on their variability between countries (low to high).

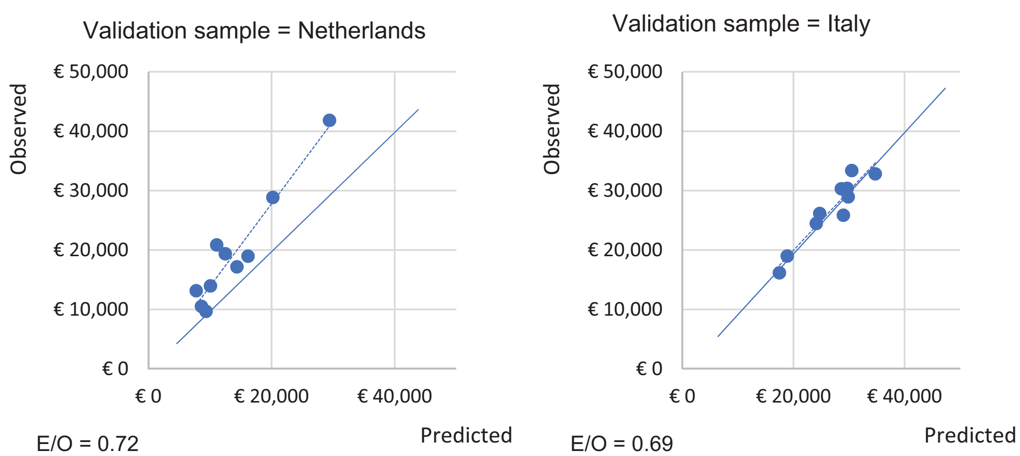


Figure 3. Model optimisation for the Netherlands and Italy.
Solid line indicates the 45° line. Dotted line is the calibration curve (best fit of data points).

IPD meta-analysis also allows researchers to synthesize country-data to develop and validate a single prediction model. An advantage of our study over an IPD meta-analysis is that all data were collected at the same time in a population selected using similar inclusion and exclusion criteria. Another strength of the study is the internal-external validation procedure. This approach allows for optimal use of sample size and enabled us to deal with heterogeneity.[48,49] Maximizing sample size leads to more robust predictions compared to the more traditional approach of randomly splitting the sample for development and validation.[50] We evaluated whether the prediction models had good prognostic performance in individual countries and updated the country-specific models if necessary. Further, all data (care-recipient characteristics and resource utilisation) could be collected by a single instrument that is widely implemented in routine care practice. Finally, costs were estimated from a societal perspective, including costs of health care, social care and informal care, thereby providing a comprehensive view of the total costs for society.

For the cost calculation, some assumptions were made, which can be considered a potential limitation of the study. In case of admission to a long term care institution or death, we assumed that it took place halfway between 2 measurements, which is common practice in health economic models.[64] Another potential limitation is that Dutch standard costs were used to value resource utilisation for all countries under study. By using this approach, cost estimates of the various countries do not reflect 'actual' care costs per country. An advantage of this approach is that it enables a relative benchmark of resource utilisation across countries, eliminating differences caused by factors related to national contexts rather than resource utilisation, like wages. Further, 8% of the total societal cost estimates were missing, which is a limitation of the study. To minimise the impact of bias due to selective dropout, multiple imputation was used, which is currently the recommended approach to account for missingness.[65] Another limitation is that our cost measurements did not include all categories included in the societal perspective. For example, costs of day-care utilisation are not recorded with the interRAI-HC and therefore not taken into account in this study, although costs of day-care may be substantial amongst this group. Also, lost productivity costs of informal care givers and pharmacy costs were not taken into account. In a study conducted among Spanish informal caregivers of community care-recipients with dementia, lost productivity costs were observed in 28% of the informal caregivers, with an estimated average monthly loss of €441.[66] In our sample, the impact of lost productivity costs is expected to be lower as only a small proportion of the care-recipients experienced severe cognitive impairment (16%).

Pharmacy costs is expected to account for up to 5% of societal costs.[67] Care-recipients who have high pharmacy costs, usually also incur high care costs, therefore we expect that the relative contribution of pharmacy costs to societal costs is low. Further, participants from Belgium were excluded from the analyses because information on informal care hours was not available. Belgian participants were on average older than the included sample. However, we expect that the effect on the results is limited, since age was not a relevant predictor. Finally, for some countries, the study samples are not necessarily representative of the national community care population, as the general aim of IBenC required a diverse sample of care organisations.[18] However, dependency levels in our samples closely reflect previously reported dependency levels among home healthcare-recipients.[68] Therefore, we expect that the developed model will perform satisfactorily in future samples. The representativeness of the IBenC study sample is described in more detail elsewhere.[18]

Implications

Our study may support policymakers across Europe to better understand predictors of societal costs among older adults receiving community care services. Potentially modifiable predictors may be targeted in interventions in attempt to curtail increases in societal costs. In addition, the prediction model may be used to optimise resource allocations for the countries under study. Despite substantial differences of countries' care systems, a validated cross-national set of key predictors could be identified. Especially for Finland, Iceland and Germany, the prediction model performed well.

Conclusion

In this study, we derived and validated a model to predict societal costs in a sample of older community care-recipients in 5 European countries. Living alone, caregiver distress, (I)ADL impairment, required level of care support, health instability, presence of pain, behavioural problems, urinary incontinence and multimorbidity significantly predicted societal costs during 6 months. The model explained 32% of the variation within societal costs and showed good calibration in Iceland, Finland and Germany. Minor model adaptations improved model performance in The Netherland and Italy.

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Author Contributions

LL, MH, JB, HR and HH designed the study. LL conducted the analyses and drafted the manuscript. All authors revised and approved the final manuscript.

Ethical Approval and Consent to Participate

The study was performed in accordance with the Declaration of Helsinki and was approved by relevant legal authorised medical ethical committees in the countries that participated in the IBenC project (Belgium, Finland, Germany, Iceland, Italy and the Netherlands). Prior to the start of the assessments, written informed consent was obtained from the participants. When a participant was known to be cognitively impaired, informed consent from a close relative, legal representative or legal guardian on behalf of the participant was obtained.

Names and Reference Numbers

Belgium: Commissie Medische Ethiek van de universitaire ziekenhuizen KU Leuven, reference number: ML10265
Finland: Tutkimuseettinen työryhmä (TuET), reference number: THL/796/6.02.01/2014
Germany: Ethikkommission des Institut für Psychologie und Arbeitswissenschaft (IPA) der TU – Berlin, reference number: GH_01_20131022
Iceland: Vísindasiðanefnd, reference number: 13-176-S1
Italy: Comitato Etico, reference number: 2365/14
The Netherlands: Medical Ethics Review Committee of the VU University Medical Center (METc VUmc), reference number: 2013.333

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Availability of Data and Materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Supplemental Material

Supplemental material for this article is available online.

REFERENCES

1. Lanzieri G. *The Greying of the Baby Boomers. A Century-long View of Ageing in European Populations*. Eurostat: Statistics in focus; 2011.
2. Rechel B, Grundy E, Robine JM, et al. Ageing in the European Union. *Lancet*. 2013;381:1312-1322.
3. Kasper JD, Wolff JL, Skehan M. Care arrangements of older adults: What they prefer, what they have, and implications for quality of life. *Gerontologist*. 2019;59:845-855.
4. Kok L, Berden C, Sadiraj K. Costs and benefits of home care for the elderly versus residential care: a comparison using propensity scores. *Eur J Health Econ*. 2015;16:119-131.
5. Colombo F, Llena-Nozal A, Mercier J, Tjadens F. *Help Wanted? Providing and Paying for Long-Term Care*. OECD Publishing; 2011.
6. De la Maisonneuve C, Oliveira Martins J. The future of health and long-term care spending. *OECD Econ Stud*. 2015;2014:61-96.
7. Global Coalition on Aging. *A sustainable solution for Europe's elder care crisis*. Accessed November 4, 2019. https://globalcoalitiononaging.com/wp-content/uploads/2018/06/RHBC_Report_DIGITAL.pdf
8. Genet N, Boerma WG, Kringos DS, et al. Home care in Europe: a systematic literature review. *BMC Health Serv Res*. 2011;11:207. doi:1472-6963-11-207
9. Eurostat Statistics Explained. Healthcare personnel statistics - nursing and caring professionals. Accessed September 2, 2019. https://ec.europa.eu/eurostat/statistics-explained/index.php/Healthcare_personnel_statistics_-_nursing_and_caring_professionals#Healthcare_personnel_.E2.80.94_nursing_professionals
10. Broese van Groenou MI, De Boer A. Providing informal care in a changing society. *Eur J Ageing*. 2016;13:271-279. doi:10.1007/s10433-016-0370-7
11. Leicht H, Konig H, Stuhldreher N, Bachmann C, Bickel H, Fuchs A. Predictors of costs in dementia in a longitudinal perspective. *PloS One*. 2013;8:e70018. doi:10.1371/journal.pone.0070018
12. Handels RL, Wolfs CA, Aalten P, Verhey FR, Severens JL. Determinants of care costs of patients with dementia or cognitive impairment. *Alzheimer Dis Assoc Disord*. 2013;27:30-36.
13. Gustavsson A, Brinck P, Bergvall N, Kolasa K, Wimo A, Winblad B. Predictors of costs of care in Alzheimer's disease: a multinational sample of 1222 patients. *Alzheimers Dement*. 2011;7:318-327.
14. Jonsson L, Eriksdotter Jonhagen M, Kilander L, Soininen H, Hallikainen M, Waldemar G. Determinants of costs of care for patients with Alzheimer's disease. *Int J Geriatr Psychiatry*. 2006;21:449-459.
15. Joling KJ, Schöpe J, van Hout HP, van Marwijk HW, van der Horst HE, Bosmans JE. Predictors of societal costs in dementia patients and their informal caregivers: a two-year prospective cohort study. *Am J Geriatr Psychiatry*. 2015;23:1193-1203.
16. Dodel R, Belger M, Reed C, Wimo A, Jones R, Happich M. Determinants of societal costs in Alzheimer's disease: GERAS study baseline results. *Alzheimers Dement*. 2015;11:933-945.
17. Van Lier LI, van der Roest HG, Oosten BS, Garms-Homolová V, Onder G, Finne-Soveri H. Predictors of societal costs of older care-dependent adults living in the community in 11 European Countries. *Health Serv Insights*. 2019;12:1-13.
18. Van der Roest H, Van Eenoo L, Van Lier L, et al. Development of a novel benchmark method to identify and characterize best practices in home care across six European countries: design, baseline, and rationale of the IBenC project. *BMC Health Serv Res*. 2019;19:310.
19. interRAI group. Licensing with interRAI. Accessed November 15, 2016. https://www.interrai.org/licensing.html
20. Hirdes JP, Ljunggren G, Morris JN, et al. Reliability of the interRAI suite of assessment instruments: a 12-country study of an integrated health information system. *BMC Health Serv Res*. 2008;8:277-278.
21. Landi F, Tua E, Onder G, et al. Minimum data set for home care: a valid instrument to assess frail older people living in the community. *Med Care*. 2000;38:1184-1190.
22. Morris JN, Fries BE, Steel K, et al. Comprehensive clinical assessment in community setting: applicability of the MDS-HC. *J Am Geriatr Soc*. 1997;45:1017-1024.
23. OECD. Statistics Length of hospital stay Acute Care, days. Updated 2016. Accessed January 15, 2016. https://data.oecd.org/healthcare/length-of-hospital-stay.htm
24. Hakkaart-van Roijen L, van der Linden N, Bouwmans C, Kanters T, Swan Tan S. *Kostenhandleiding: methodologie van kostenonderzoek en referentieprijzen voor economische evaluaties in de gezondheidzorg*. Accessed February 4, 2016. https://www.zorginstituutnederland.nl/publicaties/publicatie/2016/02/29/richtlijn-voor-het-uitvoeren-van-economische-evaluaties-in-de-gezondheidszorg
25. van Lier LI, van der Roest HG, van Hout HP, et al. Convergent validity of the interRAI-HC for societal costs estimates in comparison with the RUD Lite instrument in community dwelling older adults. *BMC Health Serv Res*. 2016;16:440-1702.
26. Wimo A, Gustavsson A, Jonsson L, Winblad B, Hsu MA, Gannon B. Application of resource utilization in dementia (RUD) instrument in a global setting. *Alzheimers Dement*. 2013;9:429-435.
27. Morris JN, Fries BE, Morris SA. Scaling ADLs within the MDS. *J Gerontol A Biol Sci Med Sci*. 1999;54:M546-M553.
28. InterRAI. Scales: Status and Outcome Measures. *Updated* 2016. Accessed December 15, 2019. http://www.interrai.org/scales.html
29. Morris JN, Fries BE, Mehr DR, et al. MDS cognitive performance scale. *J Gerontol*. 1994;49:M174-M182.
30. Burrows AB, Morris JN, Simon SE, Hirdes JP, Phillips C. Development of a minimum data set-based depression rating scale for use in nursing homes. *Age Ageing*. 2000;29:165-172.
31. Poss JW, Hirdes JP, Fries BE, McKillop I, Chase M. Validation of Resource Utilization Groups version III for Home Care (RUG-III/HC): evidence from a Canadian home care jurisdiction. *Med Care*. 2008;46:380-387.
32. Hirdes JP, Frijters DH, Teare GF. The MDS-CHESS scale: a new measure to predict mortality in institutionalized older people. *J Am Geriatr Soc*. 2003;51:96-100.
33. Fries BE, Simon SE, Morris JN, Flodstrom C, Bookstein FL. Pain in U.S. Nursing Homes: validating a pain scale for the minimum data set. *Gerontologist* 2001;41:173-179.
34. Foebel AD, Hirdes JP, Heckman GA, Kergoat MJ, Patten S, Marrie RA. Diagnostic data for neurological conditions in interRAI assessments in home care, nursing home and mental health care settings: a validity study. *BMC Health Serv Res*. 2013;13:457.
35. Calderón-Larrañaga A, Vetrano DL, Onder G, Gimeno-Feliu LA, Coscollar-Santaliestra C, Carfí A. Assessing and measuring chronic multimorbidity in the older population: a proposal for its operationalization. *J Gerontol A Biol Sci Med Sci*. 2017;72:1417-1423.
36. Green S. How many subjects does it take to do a regression analysis. *Multivariate Behav Res*. 1991;26:499-510.
37. Harrell FE. *Regression modeling strategies: with applications to linear models, logistic regression and survival analysis*. Springer; 2001.
38. Austin PC, Steyerberg EW. The number of subjects per variable required in linear regression analyses. *J Clin Epidemiol*. 2015;68:627-636.
39. Twisk JWR. *Inleiding in de toegepaste biostatistiek*. 3rd ed. Reed Business Education; 2014.
40. van Buuren S. *Flexible imputation of missing data*. Chapman & Hall/CRC; 2012.
41. Rubin DB. Statistical matching using file concatenation with adjusted weights and multiple imputations. *J Bus Econ Stat*. 1986;4:87-94.
42. Rubin DB. Inference and missing data. *Biometrika*. 1976;62:581-590.
43. Franke GR. *Multicollinearity*. John Wiley & Sons Ltd; 2010.
44. Moons KGM, Altman DG, Reitsma JB, et al. Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): explanation and Elaboration. *Ann Intern Med*. 2015;162:W1-W73. doi:10.7326/M14-0698
45. Steyerberg EW. *Clinical prediction models: a practical approach to development, validation, and updating*. Springer; 2009.
46. Sun GW, Shook TL, Kay GL. Inappropriate use of bivariable analysis to screen risk factors for use in multivariable analysis. *J Clin Epidemiol*. 1996;49:907-916.
47. Mistler SA. A SAS® macro for computing pooled likelihood ratio tests with multiply imputed data. *SAS Global Forum*. Accessed November 10, 2016. https://support.sas.com/resources/papers/proceedings13/440-2013.pdf
48. Debray TPA, Riley RD, Rovers MM, Reitsma JB, Moons KGM; group CIM-aM. Individual participant data (IPD) Meta-analyses of diagnostic and prognostic modeling studies: guidance on their use. *PLoS Med*. 2015;12:e1001886.
49. Steyerberg EW, Bleeker SE, Moll HA, Grobbee DE, Moons KGM. Internal and external validation of predictive models: a simulation study of bias and precision in small samples. *J Clin Epidemiol*. 2003;56:441-447.
50. Debray TPA, Moons KGM, Ahmed I, Koffijberg H, Riley RD. A framework for developing, implementing, and evaluating clinical prediction models in an individual participant data meta-analysis. *Statist Med*. 2013;32:3158-3180.
51. Snijders TAB, Bosker RJ. Modeled variance in two-level models. *Sociol Methods Res*. 1994;22:342-363.
52. Snijders TAB, Bosker RJ. *Multilevel Analysis. An Introduction to Basic and Advanced Multilevel Modeling*. Sage; 1999.

53. Bouwmeester W, Twisk JWR, Kappen TH, van Klei WA, Moons KGM, Vergouwe Y. Prediction models for clustered data: comparison of a random intercept and standard regression model. *BMC Med Res Methodol*. 2013;13:19.
54. Harrell FE, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med*. 1996;15:361-387.
55. van Eenoo L, Declercq A, Onder G, et al. Substantial between-country differences in organising community care for older people in Europe-a review. *Eur J Public Health*. 2016;26:213-219.
56. Gillespie P, O'Shea E, Cullinan J, Lacey L, Gallagher D, Ni Mhaolain A. The effects of dependence and function on costs of care for Alzheimer's disease and mild cognitive impairment in Ireland. *Int J Geriatr Psychiatry*. 2013;28:256-264.
57. Gitlin LN, Winter L, Dennis MP, Corcoran M, Schinfeld S, Hauck WW. a randomized trial of a multicomponenet home intervention to reduce functional difficulties in older adults. *JAGS*. 2016;54:809-816.
58. WHO. *Active ageing: a policy framework*. 2002. Accessed September 15, 2018. https://apps.who.int/iris/bitstream/handle/10665/67215/WHO_NMH_NPH_02.8.pdf;jsessionid=BB81621DCC7E02F295592F575DF1A924?sequence=1
59. Dueñas M, Ojeda B, Salazar A, Mico JA, Failde I. A review of chronic pain impact on patients, their social environment and the health care system. *J Pain Res*. 2016;9:457-467.
60. Zhu CW, Torgan R, Scarmeas N. Home health and informal care utilization and costs over time in Alzheimer's disease. *Home Health Care Serv Q*. 2008;27:1-20.
61. Picco L, Achilla E, Abdin E, Chong SA, Vaingankar JA, McCrone P. Economic burden of multimorbidity among olders adults: impact on healthcare and societal costs. *BMC Health Serv Res*. 2016;16:703.
62. Björkgren MA, Fries BE, Shugarman LR. A RUG-III case-Mix system for home care. *Can J Aging*. 2000;19:106-125.
63. Riley RD, Lambert PC, Abo-Zaid G. Meta-analysis of individual participant data: rationale, conduct, and reporting. *BMJ*. 2010;340:c221.
64. Naimark DM, Bott M, Krahn M. The half-cycle correction explained: two alternative pedagogical approaches. *Med Decis Making*. 2008;28:706-712.
65. Oostenbrink JB, Al MJ. The analysis of incomplete cost data due to dropout. *Health Econ*. 2005;14:763-776.
66. M. Farré, B. Kostov, J.M. Haro, et al. Costs and burden associated with loss of labor productivity in informal caregivers of people with dementia:results from Spain. *J Occup Environ Med* 2018;60:449-456.
67. van Leeuwen KM, Bosmans JE, Jansen AP, et al. Cost-effectiveness of a chronic care model for frail older adults in primary care: economic evaluation alongside a stepped-wedge cluster-randomized trial. *J Am Geriatr Soc*. 2015;63:2494-2504.
68. Carpenter I, Gambassi G, Topinkova E, et al. Community care in Europe. The Aged in Home Care project (AdHOC). *Aging Clin Exp Res*. 2004;16:259-269.