

# The Economic Burden of Visual Impairment and Comorbid Fatigue: A Cost-of-Illness Study (From a Societal Perspective)

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**PURPOSE.** To investigate the burden of visual impairment and comorbid fatigue in terms of impact on daily life, by estimating societal costs (direct medical costs and indirect non-health care costs) accrued by these conditions.

**METHODS.** This cost-of-illness study was performed from a societal perspective. Cross-sectional data of visually impaired adults and normally sighted adults were collected through structured telephone interviews and online surveys, respectively. Primary outcomes were fatigue severity (FAS), impact of fatigue on daily life (MFIS), and total societal costs. Cost differences between participants with and without vision loss, and between participants with and without fatigue, were examined by (adjusted) multivariate regression analyses, including bootstrapped confidence intervals.

**RESULTS.** Severe fatigue (FAS  $\geq 22$ ) and high fatigue impact (MFIS  $\geq 38$ ) was present in 57% and 40% of participants with vision loss ( $n = 247$ ), respectively, compared to 22% (adjusted odds ratio [OR] 4.6; 95% confidence interval [CI] [2.7, 7.6]) and 11% (adjusted OR 4.8; 95% CI [2.7, 8.7]) in those with normal sight ( $n = 233$ ). A significant interaction was found between visual impairment and high fatigue impact for total societal costs (€449; 95% CI [33, 1017]). High fatigue impact was associated with significantly increased societal costs for participants with visual impairment (mean difference €461; 95% CI [126, 797]), but this effect was not observed for participants with normal sight (€12; 95% CI [-527, 550]).

**CONCLUSIONS.** Visual impairment is associated with an increased prevalence of high fatigue impact that largely determines the economic burden of visual impairment. The substantial costs of visual impairment and comorbid fatigue emphasize the need for patient-centered interventions aimed at decreasing its impact.

Keywords: fatigue, visual impairment, economic analysis, burden of illness, prevalence

In 2015, the number of visually impaired people worldwide was estimated to be 253 million.<sup>1</sup> The worldwide societal costs of visual impairment have been estimated at \$3 trillion in 2010,<sup>2</sup> partially explained by direct medical costs related to health care utilization,<sup>3,4</sup> and indirect costs characterized by loss in work participation.<sup>5</sup> The prevalence and economic burden of visual impairment are projected to increase by 20% in 2020 owing to demographic growth and aging of populations in Western society.<sup>2</sup>

Fatigue is an important problem for patients with irreversible visual impairment,<sup>6</sup> and is often referred to as an overwhelming sense of tiredness associated with impaired physical and/or cognitive functioning.<sup>7</sup> Patients with visual impairment described fatigue as an indirect result of vision loss through/by a high cognitive load, the effort that is necessary for visual perception, difficulties with light intensity, and negative cognitions related to negative thoughts.<sup>8</sup> Vision loss seems to

be related to increased symptoms of fatigue. Mojon-Azzi et al.<sup>9</sup> report a positive association between self-reported vision impairment and severity of fatigue. Also, in comparison with matched controls without ocular disease<sup>10-12</sup> and with regard to vision problems in patients with chronic conditions,<sup>13,14</sup> this relationship has been supported. However, no studies have investigated the prevalence of fatigue in persons with visual impairment.

The consequences of vision-related fatigue have been described by a qualitative approach, including difficulties with emotional functioning, the ability to carry out roles, societal participation, cognitive functioning, and maintaining daily activities.<sup>8,15</sup> Therefore, fatigue may increase the individual burden of visual impairment, but this has not been previously studied. This notion is supported by research in depression; Robinson et al.<sup>16</sup> report greater use of medication and health care utilization for patients with clinical levels of fatigue,



resulting in an increased economic burden for society. Fatigue also generates societal costs due to the negative implications for employment and work productivity.<sup>17,18</sup> Studies in patients with cancer and multiple sclerosis, for example, have identified fatigue as the key symptom influencing work capacity and preventing return to work.<sup>19,20</sup>

A greater understanding of the costs of vision-related fatigue will help inform health care decision-makers in setting up and prioritizing health care policies and interventions for people with visual impairment. Cost-of-illness studies are an essential measure in health care that allow for an evaluation of the economic burden of a disease on society as a whole.<sup>21</sup> Our study aimed (1) to determine the individual burden of fatigue in visually impaired adults compared with normally sighted adults, in terms of severity, impact on daily functioning, need for recovery after work, and prevalence; and (2) to estimate the societal burden of visual impairment and comorbid fatigue in terms of direct health care costs and indirect non-health care costs.

## METHODS

### Design

This study focussed on cost-of-illness (in Euros) of visual impairment and fatigue and was part of a larger cross-sectional survey on fatigue among visually impaired adults and normally sighted adults. The study was approved by the Medical Ethics Committee of the VU University Medical Center (Amsterdam, The Netherlands) and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All participants gave written consent to participate in the present study.

### Data Collection

Cross-sectional data of visually impaired adults and normally sighted adults were collected by two researchers (MSc and BSc in psychology) at the VU University Medical Center between August 2015 and June 2016 through structured telephone interviews and online surveys, respectively.

### Participants

Visually impaired adults were recruited from two multidisciplinary low vision rehabilitation centers in The Netherlands: Royal Dutch Visio and Bartiméus. The eligibility criteria for referral to these centers are described in the Dutch guideline "Vision Disorders, Rehabilitation and Referral,"<sup>22</sup> and are in correspondence with the World Health Organization criteria. Invitations were sent by letter to a random sample drawn from adult patients who received rehabilitation in 2015 and/or 2016. Eligibility criteria were sufficient mastery of the Dutch language, no severe cognitive impairment as assessed by the six-item version of the Mini Mental State Examination (MMSE),<sup>23</sup> and no diagnosis or treatment in the past year for (1) cancer, (2) multiple sclerosis, (3) chronic fatigue syndrome, or (4) psychiatric disorders. By excluding these comorbidities known for fatigue symptomatology, it was expected that more certainty could be obtained for the experienced fatigue to be related to visual impairment rather than other chronic illnesses.

The control group consisted of normally sighted adults, who were sampled to resemble the study population regarding age and sex distribution. Participants were recruited by means of purposive and snowball sampling through their own and the researcher's social networks and social media. Eligibility criteria were similar for controls, with the addition of sufficient

self-reported vision ability as assessed by a subset of the Organization for Economic Cooperation and Development long-term disability indicator.<sup>24</sup>

## Clinical Outcome Measures

**Fatigue.** Both severity and impact of fatigue were used for our analysis, since economic analyses with fatigue are scarce. Until now it is not clear whether the perceived severity or the self-reported impact (which incorporate the coping efforts) represents the best indicator for this type of analyses. Results of both indicators of fatigue will be reported and discussed.

Fatigue severity was measured by using the Dutch version of the Fatigue Assessment Scale (FAS), consisting of 10 items rated on a 5-point Likert-scale.<sup>25</sup> Total scores ranged from 10 to 50; higher scores indicate greater fatigue severity. We used the cutoff score of FAS  $\geq 22$  to categorize individuals with severe symptoms of fatigue.<sup>26</sup> The FAS is a valid scale and has high internal consistency reliability.<sup>27</sup>

The impact of fatigue was assessed with the Dutch version of the Modified Fatigue Impact Scale (MFIS), originally developed to measure the impact of fatigue on physical, cognitive, and psychosocial functioning in patients with chronic illness, with multiple sclerosis in particular.<sup>28</sup> The questionnaire consists of 21 items that are answered on a 5-point scale from 0 (never) to 4 (almost always). Total scores range from 0 to 84, with higher scores reflecting greater fatigue impact. A cutoff score of 38 was used to discriminate individuals with high fatigue impact from individuals with low fatigue impact as described in previous studies.<sup>29,30</sup>

A subscale of the Dutch Questionnaire on the Experience and Evaluation of Work was administered to evaluate need for recovery after work.<sup>31</sup> The questionnaire measures occupationally induced fatigue by 11 dichotomous items (yes/no). Scores were summed and transformed into a range of 0 to 100, with higher scores indicating higher levels of work-related fatigue. Scores equal to or higher than 54 were used as a cutoff to classify problematic need for recovery, indicating an increased risk of psychological complaints.<sup>32</sup>

**Cost Measures and Valuation.** Cost estimations were conducted from a societal perspective and included both direct health care costs and indirect non-health care costs. Direct health care costs included formal care such as admission to the hospital and medication use (informal care was not included). Indirect non-health care costs consisted of loss of work participation due to the secondary consequences of health problems or its treatment. All costs were adjusted to the year 2015, using consumer price indices.<sup>33</sup> Table 1 presents the cost categories and prices used in this economic evaluation.

Health care utilization was assessed by using the Trimbos and iMTA questionnaire for Costs associated with Psychiatric Illness (TiC-P) with a recall period of 4 weeks.<sup>34</sup> Participants were asked about the number of contacts with primary health care professionals (e.g., general practitioner), secondary care (e.g., medical specialist), and the use of prescribed medication. Costs were calculated by multiplying the units of resource use by their corresponding reference prices. Standard costs from the Dutch costing guideline were used to value health care utilization.<sup>35</sup> Medication costs were valued by using prices of the royal Dutch Society for Pharmacy.

Lost productivity and work-related characteristics were assessed with the Short Form-Health and Labour Questionnaire (SF-HLQ) with a recall period of 4 weeks.<sup>36</sup> A distinction is made between productivity losses due to absence from work, reduced efficiency at work (presenteeism), and productivity losses for unpaid work (i.e., substitution for domestic tasks). Costs for absenteeism and presenteeism were calculated

**TABLE 1.** Cost Categories and Prices (€, 2015) Used in This Economic Evaluation

Cost Category	Costs per Unit (2015)
Direct health care costs	
General practitioner	€30.98
Mental health care	€88.50
Psychologist or psychiatrist	
Private practice	€99.57
Outpatient – academic	€142.71
Outpatient – general	€70.80
Outpatient – other*	€79.65
Occupational physician	€100.31
Medical specialist	€34.85
Physiotherapist	€39.83
Social worker	€71.91
Domiciliary care	€38.72
Alternative healer	€49.89
Day-care treatment	€277.68
Hospitalization	
General hospital	€481.23
Academic hospital	€636.11
Mental hospital	€256.66
Nursing home	€263.30
Rehabilitation center	€376.14
Other health care institution	€84.59
Indirect non-health care costs	
Absenteeism (paid work: hour)	Depending on age and sex
Presenteeism (paid work: hour)	Depending on age and sex
Paid help/informal care (hour)	€14

\* Weighted average of the unit costs for a psychologist or psychiatrist at a psychiatric hospital, nursing home, rehabilitation center, or another health care institution.

with the human capital method that assumes the entire period of absence from work due to health problems, and valued according to Dutch averaged income values specified for sex and different age groups. Replacement costs for unpaid productivity losses were valued by applying the hourly wage for household care.<sup>35</sup>

**Analyses.** Sociodemographic comparisons between the visually impaired and control group were made by using  $\chi^2$  tests for dichotomous variables, independent samples *t*-tests for continuous variables, and nonparametric tests in case of nonnormally distributed data. Differences in fatigue measures were evaluated with adjusted (linear and logistic) regression models to allow for correction of potential confounders.

Linear regression models were used to estimate cost differences between people with and without vision loss (control versus visually impaired). Since costs have a highly skewed distribution, bias-corrected and accelerated bootstrapping was applied to estimate 95% confidence intervals [CIs] around the mean cost differences (5000 replications). Predictive mean matching was used to account for the skewed distribution of costs. Two models were built up to assess whether (1) fatigue severity or (2) impact of fatigue added to societal costs. First, differences between groups were evaluated in separate models with societal costs as the dependent variable and visual impairment as the determinant. Second, variables related to fatigue were included in the models. Third, models were adjusted for relevant confounders (age, sex, education in years, living status, and comorbidity). Fourth, the interaction between visual impairment and the fatigue variables were analyzed, and implemented in a separate model in case of significant interactions. Multiple comparisons were performed on subgroup level when significant interactions

were detected. We used multiple imputation methods with chained equations (MICE) to replace missing data on costs and outcomes.<sup>37</sup> Five imputed datasets were generated and analyzed separately, and the results of the analyses were pooled by using Rubin's rules.<sup>38</sup> All data were analyzed by using SPSS for Windows version 22 (SPSS IBM, New York, NY, USA) and STATA version 14.1 (Stata Corp LP, College Station, TX, USA).

## RESULTS

### Participants

Of the 1281 invited visually impaired adults, 321 (25%) accepted to participate and gave written informed consent. Fifty-nine participants did not meet the eligibility criteria and 15 refrained from participation or could not be reached for the interview, resulting in 247 visually impaired adults of whom data were included in the analysis. Comorbid psychiatric disease was the most common cause of exclusion, which was present in 69% of the excluded participants. A total of 253 controls showed interest to participate, data of 233 (92%) normally sighted adults were included in the analysis; 18 participants did not (completely) respond and 2 refrained from participation.

Table 2 shows the characteristics of both study populations. Participants with vision loss were significantly older, were more likely to be male, had a lower education level, had more comorbid conditions, and were more likely to use prescribed medication. The majority of the visually impaired sample had low vision and a progressive course of their eye disease. The most common causes of visual impairment were macular degeneration and retinitis pigmentosa and the median time of onset was 9 years.

### Fatigue

FAS scores (mean difference 5.0; 95% CI [4.0, 6.0]) and MFIS scores (mean difference 11.8; 95% CI [9.0, 14.5]) were significantly higher for participants with vision loss than for normally sighted participants. These differences (FAS: mean difference 4.3; 95% CI [3.8, 4.8] and MFIS: mean difference 11.1; 95% CI [7.6, 14.5]) remained significant after controlling for potential confounders. Severe fatigue (FAS  $\geq$  22) and high fatigue impact (MFIS  $\geq$  38) were present in 57% and 40% of participants with vision loss, respectively, which was significantly higher compared to 22% and 11% in those with normal sight (odds ratio [OR] 4.7; 95% CI [3.1, 7.0] and OR 5.3; 95% CI [3.3, 8.6], respectively), also after adjustment for confounders (severe fatigue: OR 4.6; 95% CI [2.7, 7.6] and high fatigue impact: OR 4.8; 95% CI [2.7, 8.7]).

### Work

Work-related characteristics of the visually impaired ( $n = 58$ ) and normally sighted participants with paid employment ( $n = 189$ ) are presented in Table 3. The employment rate in the visually impaired sample was low compared to global estimates,<sup>39,40</sup> and significantly lower than for participants with normal vision, also after adjustment for age (OR 0.09; 95% CI [0.06, 0.15]). Furthermore, percentage of absenteeism from work, mean need for recovery, problematic need for recovery, and mean hindrance during unpaid work were significantly higher for participants with visual impairment than for those with normal sight. Need for recovery remained significant after adjustment for confounding (mean difference 23.5; 95% CI [14.0, 32.0]).

TABLE 2. Demographic Characteristics of the Study Population ( $n = 480$ )

Participant Characteristic	Visually Impaired ( $n = 247$ )			Normally Sighted ( $n = 233$ )			<i>P</i>
	<i>N</i>	%	Range	<i>N</i>	%	Range	
Sex, female	152	62		171	73		0.006
Age, mean $\pm$ SD, y	57 $\pm$ 14		19-91	45 $\pm$ 17		18-78	<0.001
Working status: paid employment	58	24		189	81		<0.001
Living situation: living together	152	62		155	67		0.256
Nationality: Dutch	243	98		232	99		0.199
Education, mean $\pm$ SD, y	12 $\pm$ 3		0-16	14 $\pm$ 2		6-16	<0.001
Somatic comorbidity: $\geq 1$	118	48	0-4	83	36	0-4	<0.001
Using medication	193	78		83	36		<0.001
No. of prescribed medications, median, 25th-75th percentile	3		1-5	0		0-1	
Vision-specific characteristics							
Visual acuity*							
Mild vision loss	36	15					
Low vision	116	49					
Blind	86	36					
Eye disease course							
Stable	71	29					
Progressive	176	71					
Time of onset of visual impairment, median, 25th-75th percentile, y	9		7-36				
Causes of visual impairment							
Macular degeneration	58	24					
Retinitis pigmentosa	46	19					
Glaucoma	44	18					
Cataract	31	13					
Diabetic retinopathy	17	7					
Hemianopia	12	5					
Retinal vein occlusion	3	1					
Other	94	38					
Fatigue							
FAS severity score, mean $\pm$ SD	23 $\pm$ 6		10-44	18 $\pm$ 5		10-37	<0.001
Prevalence severe fatigue†	140	57		51	22		<0.001
MFIS impact score, mean $\pm$ SD	31 $\pm$ 17		0-71	20 $\pm$ 13		0-59	<0.001
Prevalence high fatigue impact‡	99	40		26	11		<0.001

SD, standard deviation.

\*  $n = 238$ : nine missing values.† Severe fatigue: FAS score  $\geq 22$ .‡ High fatigue impact: MFIS score  $\geq 38$ .

### Societal Costs of Visual Impairment and Fatigue Severity

Model 1 in Table 4 shows significantly increased direct health care costs for participants with vision loss compared to controls (€401; 95% CI [161, 567]). When fatigue severity was taken into account in model 2, total societal costs were found to be significantly higher for the visually impaired sample (€458; 95% CI [68, 726]). After adjusting for relevant confounders in model 3, indirect costs were significantly higher for participants with vision loss than for those with normal sight (€305; 95% CI [112, 636]). Model 4 and model 5 revealed no significant interactions between visual impairment and severe fatigue on all cost measures. Model 5 demonstrated the highest explained variance and accounted for 4.3% of the variance in total societal costs.

### Societal Costs of Visual Impairment and Fatigue Impact

Direct medical costs (€339; 95% CI [120, 499]) and total societal costs (€388; 95% CI [150, 594]) were significantly higher for participants with vision loss after the addition of high fatigue impact in model 2 (Table 5). Furthermore,

significantly increased direct costs (€212; 95% CI [17, 474]), indirect costs (€ 147; 95% CI [9, 367]), and total societal costs (€359; 95% CI [108, 689]) were observed for participants with high fatigue impact. In the corrected model (model 3), total societal costs remained significantly higher for participants with high fatigue impact (€337; 95% CL [49, 665]), explained by significantly increased indirect non-health care costs (€201; 95% CI [60, 446]). After correction, only indirect costs (€267; 95% CI [99, 531]) appeared to be significantly higher for participants with vision loss than for normally sighted participants.

Model 4 showed a significant interaction between the effect of visual impairment and high fatigue impact on total societal costs (€469; 95% CI [70, 973]), which remained significant after correction for potential confounders in model 5 (€449; 95% CI [33, 1017]). The corrected interaction effect is graphically presented in the Figure. Post hoc analyses in model 5 revealed significant differences between all pairwise contrasts, with the exceptions of normal sight with low fatigue compared to normal sight with high fatigue impact, and visually impaired with low fatigue compared to normal sight with high fatigue impact. Model 5 explained the highest proportion of the variance of total societal costs (5.1%).

TABLE 3. Work Characteristics of the Study Population With Paid Employment

Work Characteristic	Visually Impaired (n = 58)			Normally Sighted (n = 189)			P
	N	%	Range	N	%	Range	
Absenteeism in the last month, yes	19	33		10	5		<0.001
Absenteeism exceeding 1 month, yes	4	7		3	2		0.033
Need for recovery, mean $\pm$ SD	54 $\pm$ 30		0-100	32 $\pm$ 28		0-100	<0.001
Problematic need for recovery*	31	53		48	25		<0.001
Hindrances in performing paid work due to health problems†							
Absent period > month	4	7		5	3		
No, not at all	20	34		150	79		
Yes, slightly	25	43		33	17		
Yes, very much	9	16		1	1		
Self-reported work efficiency‡	6.6 $\pm$ 1.7		3-10	7.3 $\pm$ 1.6		2-10	0.407
Hindrances paid work§, mean $\pm$ SD	9.8 $\pm$ 2.8		6-18	9.1 $\pm$ 2.4		6-15	0.282
Hindrances unpaid work  , mean $\pm$ SD	2.7 $\pm$ 1.5		0-4	0.4 $\pm$ 1.0		0-5	<0.001

\* Problematic need for recovery: need for recovery (NFR) score  $\geq$  54.

† "Was your job performance adversely affected by health problems during the last month?"

‡ Self-reported work efficiency: "Please rate how well you performed on the days you went to work even though you were bothered by health problems" (1 = much worse performance than usual, 10 = work was not affected).

§ Hindrance experienced as result of health problems during paid work: score range, 6 to 24; higher score indicates more hindrance.

|| Hindrance experienced as result of health problems during unpaid work: score range, 0 to 8; higher score indicates more hindrance.

## DISCUSSION

This cost-of-illness study showed that fatigue is a highly prevalent problem in visually impaired adults with a high impact for society. In addition to the individual burden, our study clearly demonstrated an additional economic burden of high impact of fatigue specific for adults with visual impairment.

One of the most important findings of this study was the interaction found between visual impairment and high impact of fatigue for total societal costs. This indicates an additional economic burden of fatigue that was present in visually impaired participants, but not in the normally sighted ones. The presence of high fatigue impact was associated with an economic significant double-fold increase of the societal costs for a person with visual impairment (€552 versus €1043). As far as we know, this relationship has not been evaluated in a cost-of-illness study before. Our novel findings are similar to those of a recent study that investigated the economic burden of fatigue in patients with depression. Robinson et al.<sup>16</sup> have found greater mean annual total costs for patients with clinically significant fatigue than for those without fatigue (\$14,462 vs. \$9971). Only a small proportion of our visually impaired sample was employed, but in this subset, indirect costs were substantial and were characterized by absenteeism, but less by presenteeism and substitution for unpaid work (data not shown). Furthermore, the problematic need for recovery after work among those with visual impairment is indicative of high work-related fatigue, which may explain why fatigue impact was only associated with elevated costs in this cohort. People with vision loss already are at a higher risk of

not working or not optimally working,<sup>40</sup> and when fatigue is involved, it may become increasingly difficult to continue employment. In support of this hypothesis, fatigue has been associated with loss in work participation in other chronic patient populations,<sup>19,41-43</sup> but more research is needed to investigate this role in working adults with visual impairment. In contrast, direct costs were less affected by vision loss and fatigue, which may be reflected by the relatively low monthly

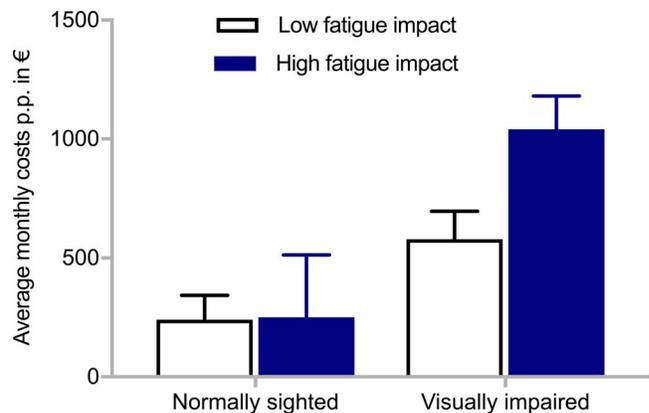


FIGURE. Interaction effect of visual impairment and high impact of fatigue on total societal costs, corrected for age, sex, education, living situation, employment, and comorbidity. Average monthly costs per person are represented in marginal means with estimated standard errors.

**TABLE 4.** Regression Analysis for the Societal Costs (€, 2015) of Visual Impairment and Severe Fatigue for the Whole Study Population ( $n = 480$ )

Fatigue Severity (FAS)	Direct Costs		Indirect Costs		Total Costs	
	$\beta$	95% CI*	$\beta$	95% CI*	$\beta$	95% CI*
Model 1						
Visually impaired	<b>401</b>	<b>161, 567</b>	92	-20, 229	<b>492</b>	<b>228, 710</b>
Model 2						
Visually impaired	367	-27, 591	90	-24, 265	<b>458</b>	<b>68, 726</b>
Fatigued†	96	-127, 556	4	-163, 123	99	-172, 544
Model 3‡						
Visually impaired	191	-502, 446	<b>305</b>	<b>112, 636</b>	496	-152, 874
Fatigued	4	-241, 314	43	-91, 172	47	-244, 382
Model 4						
Visually impaired	<b>529</b>	<b>322, 892</b>	122	-35, 391	<b>650</b>	<b>367, 1063]</b>
Fatigued	<b>369</b>	<b>25, 1898</b>	57	-72, 182	<b>426</b>	<b>58, 1838</b>
Visually impaired* fatigued	-452	-1783, -10	-88	-375, 134	-540	-1776, -31
Model 5‡						
Visually impaired	<b>340</b>	<b>49, 635</b>	<b>327</b>	<b>102, 718</b>	<b>667</b>	<b>281, 1145</b>
Fatigued	260	-41, 1387	81	-51, 216	<b>341</b>	<b>8, 1473</b>
Visually impaired* fatigued	-420	-1517, -8	-63	-328, 171	-483	-1586, 5

Bolded values are significant at  $P \leq 0.05$ .

\* For cost measures bootstrapped 95% confidence intervals were used.

† Severely fatigued: FAS score  $\geq 22$ .

‡ Corrected for age, sex, education, living situation, employment, and comorbidity.

costs for expenditure on vision-related medication (mean costs €8, 25th to 75th percentile: 0-3).

Furthermore, our results showed that visual impairment is associated with increased fatigue severity and impact of fatigue on daily life, which means a tremendous individual burden for patients. This is in correspondence with a few previous studies that have compared fatigue of persons with visual impairment to a control group with normal sight.<sup>10-12</sup> However, they assessed fatigue with the vitality subscale of SF-36 quality of life questionnaire, which does not involve a thorough inventory of the consequences of fatigue. Furthermore, as far as we know, these studies do not include a cutoff score to estimate a prevalence of fatigue. Our study revealed a fatigue prevalence

of 40% and 57% in the visually impaired sample with regard to fatigue severity and fatigue impact, respectively, which was significantly higher than in the normally sighted sample. These results are similar to prevalence rates described in studies with other chronic patient populations.<sup>44,45</sup>

It should be noted that we found different results when fatigue was measured in terms of severity by the FAS. The societal costs of severe fatigue were relatively low and the observed differences were not significant. Higher FAS scores are indicative of higher levels of fatigue, but this may not always lead to reduced daily functioning because the ability to cope with fatigue can differ between individuals.<sup>46</sup> The MFIS may have been more sensitive to societal costs because it

**TABLE 5.** Regression Analysis for the Societal Costs (€, 2015) of Visual Impairment and High Fatigue Impact for the Whole Study Population ( $n = 480$ )

Fatigue Impact (MFIS)	Direct Costs		Indirect Costs		Total Costs	
	$\beta$	95% CI*	$\beta$	95% CI*	$\beta$	95% CI*
Model 1						
Visually impaired	<b>401</b>	<b>161, 567</b>	92	-20, 229	<b>492</b>	<b>228, 710</b>
Model 2						
Visually impaired	<b>339</b>	<b>120, 499</b>	49	-50, 175	<b>388</b>	<b>150, 594</b>
Fatigued†	<b>212</b>	<b>17, 474</b>	<b>147</b>	<b>9, 367</b>	<b>359</b>	<b>108, 689</b>
Model 3‡						
Visually impaired	158	-420, 349	<b>267</b>	<b>99, 531</b>	425	-93, 725
Fatigued	136	-98, 362	<b>201</b>	<b>60, 446</b>	<b>337</b>	<b>49, 665</b>
Model 4						
Visually impaired	<b>283</b>	<b>17, 473</b>	15	-97, 154	<b>298</b>	<b>17, 530</b>
Fatigued	4	-275, 147	18	-99, 151	22	-255, 218
Visually impaired* fatigued	290	-19, 699	179	-50, 486	<b>469</b>	<b>70, 973</b>
Model 5‡						
Visually impaired	97	-537, 314	<b>242</b>	<b>77, 503</b>	339	-275, 147
Fatigued	-94	-671, 88	105	-25, 260	12	-502, 232
Visually impaired* fatigued	318	-14, 836	132	-88, 433	<b>449</b>	<b>33, 1017</b>

Bold values are significant at  $P \leq 0.05$ .

\* For cost measures bootstrapped 95% confidence intervals were used.

† High fatigue impact: MFIS score  $\geq 38$ .

‡ Corrected for age, sex, education, living situation, employment, and comorbidity.

measures the impact of fatigue on physical, cognitive, and psychosocial functioning. These concepts have been associated with substantial work productivity losses in patients with multiple sclerosis.<sup>43</sup> In turn, the dichotomization of patients in the regression models, based on the common cutoff scores used for the FAS and MFIS, may either have over- or underestimated the economical differences found.

There were some limitations that should be mentioned as well. First of all, the participation rate in the visually impaired sample was much lower than expected, which may have increased the risk of selection bias and decreased the generalizability of our results. Nonetheless, most nonresponders declined because participation was expected to be too burdensome, which may have led to an underestimation of fatigue in this sample. Second, the observed demographic differences between our samples may have accounted for the increased fatigue rate among participants with visual impairment. Fatigue is a common symptom in chronic disease,<sup>47-49</sup> and older individuals with a low education level could potentially have fewer resources necessary to effectively cope with fatigue. However, the corrected regression models revealed a strong association between visual impairment and fatigue. Nevertheless, future interventions should be tailored to senior age and related difficulties and comorbid conditions that are inherent for this population. Furthermore, the relatively short recall period for work productivity (4 weeks) may have led to an underestimation of the indirect costs. Chronic health conditions can lead to longer periods of absenteeism, which may have been left unnoticed in our study. Last, the exclusion of fatigue-related chronic conditions may have led to an underestimation of the medical costs, especially for participants with visual impairment, considering the high prevalence of depression.<sup>50</sup>

The presence of fatigue with high impact on daily functioning appears to specifically add to the economic burden of visual impairment. The societal costs seem substantial and emphasize the need for evidence-based interventions aimed at coping with the consequences of vision-related fatigue. In light of the quest for sustainable employability, increasing work participation for patients with visual impairment becomes even more important because of the increasing retirement age. Currently, no specified interventions are available for low vision professionals because the etiology of vision-related fatigue is still poorly understood. Potential treatment options may include cognitive behavioral therapy and exercise therapy because they have been shown to reduce fatigue in patients with chronic disease,<sup>51-53</sup> but more research is required to evaluate these interventions in the visually impaired population. The association between visual impairment and increased need for recovery suggests that successful treatment of vision-related fatigue may potentially improve work productivity and the likelihood of continued employment for employees with visual impairment. Health care providers and researchers in the field of low vision should acknowledge fatigue as an important problem, and should prioritize future resources to reduce and manage its impact on the individual level and society as a whole.

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