

1 **SUPPLEMENT**

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3 **Costs and health-related quality of life in patients with NMO spectrum disorders and**

4 **MOG-antibody associated disease (CHANCE<sup>NMO</sup>-Study)**

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## 16 **eMethods:**

### 17 *Detailed description of cost valuation*

18 A comprehensive questionnaire provided detailed primary individual, patient-reported, and  
19 disease-related information on the consumption of medical and non-medical resources, care,  
20 and vocational occupation. Detailed data on patient demographics, education level, disease  
21 onset, disease severity, serostatus, symptoms, immunotherapy, and management of attacks were  
22 retrieved from the German Neuromyelitis Optica Study Group (NEMOS) database. Based on  
23 this utilization and individually reported frequencies, the consumption of resources was valued  
24 monetarily in a micro-costing approach by using unit prices based on the latest health economic  
25 recommendations for Germany<sup>1-4</sup> as already applied to former analyses.<sup>5,6</sup> As we assumed a  
26 stable consumption of resources, we extrapolated costs to one year where appropriate to estimate  
27 the annual cost of illness (COI) per patient. All costs before 2018 were inflation-adjusted.<sup>7</sup>

28 Direct medical costs reflect the consumption of direct medical and treatment resources.  
29 Hereunder, diagnostic tests that were performed in an outpatient setting were calculated on the  
30 basis of public price information given by the statutory, as well as by private health insurances  
31 in Germany.<sup>8-11</sup> Furthermore, outpatient physician consultations were estimated as costs per  
32 patient-doctor contact and were obtained from department-specific honoraria in 2018 divided  
33 through the number of patient contacts per year.<sup>4</sup> For medical domiciliary visits, the official  
34 value for travel compensation was added.<sup>12</sup> Inpatient hospital care comprised daily rates for  
35 normal ward and intensive care units, which were multiplied with the individual duration of  
36 stays. Moreover, rehabilitation in both the inpatient as well as outpatient sector was valued  
37 based on the latest Federal German Ministry Statutory Health Insurance Institutions reports.<sup>13-</sup>  
38 <sup>15</sup> Therefore, daily rates were estimated from German total expenditures in 2017 and inflation-  
39 adjusted. The respective daily rates were multiplied by the individual patient's duration of  
40 rehabilitation.<sup>4</sup> Medical aids were subcategorized into 33 superordinate categories.<sup>4</sup> The annual  
41 expenses of the German Statutory Health Insurance Institutions, divided by the number of

42 insured persons with a prescription for medical aids, approximated the mean costs for aids in  
43 these categories. Depending on the individual utilization of different medical aids, yearly per  
44 patient costs for aids were extrapolated.<sup>1,4</sup> For outpatient hospital consultations in specialized  
45 university-associated outpatient clinics, we used our own in-house remuneration as a rough  
46 estimation. Therapeutic healing included physio-, occupational, speech and psychotherapy, as  
47 well as lymphatic drainage and podiatry. The German “Heilmittelkatalog” (German catalog of  
48 evidence-based and reimbursed remedies/therapeutic healing)<sup>16</sup> provides detailed information  
49 on adequate further therapies for each disease. Based on this information, we used the  
50 remuneration agreements between care providers and health insurances to define costs per unit,  
51 depending on whether the patient had a statutory or private health insurance.<sup>2,17-26</sup> Drug costs  
52 were monetized based on public prices for Germany depending on daily dosage and package  
53 size.<sup>27</sup> As eculizumab (n=1) and inebilizumab (n=4) were applied as study medication in a few  
54 patients, we did not count any prize for these medications.

55 Patients stated their care level within the questionnaire. The care level according to the  
56 Germany health care system is stratified into five levels, while higher levels indicate a higher  
57 loss of autonomy and self-care ability (care level 1 = low impairment of individual autonomy,  
58 care level 5 = most severe impairment of individual autonomy with special demands for nursing  
59 care). Since German care levels were re-defined from 2017 to 2018, the care levels of all  
60 patients had to be adjusted to the new nomenclature.<sup>28,29</sup> Formal care costs included domestic  
61 help (costs per hour based on the statutory minimum wage in Germany inclusive employer’s  
62 contribution),<sup>30,31</sup> mobile nursing service (average basic care per hour cost of nearby mobile  
63 nursing services)<sup>32</sup>, and residential care (rates per day).<sup>33</sup> On the other hand, non-professional  
64 and non-trained persons provide informal care, mainly family members and/or friends. For the  
65 calculation of informal care costs, we substituted the time of care provided (hours per day) by  
66 informal caregivers by the statutory minimum wage for the caring sector in Germany (plus  
67 employer’s contribution) in order to estimate the costs that would have risen if the care had

68 been provided by formal caregivers instead.<sup>4,30,31</sup> Standards for classifying informal care costs  
69 into direct or indirect costs are not consistent internationally. As our study was located in  
70 Germany and we additionally used a substitutional cost approach, we classified them as direct  
71 non-medical costs in line with latest German recommendations for health economics  
72 evaluations.<sup>34</sup> In addition to informal care costs, the main contributors to direct non-medical  
73 costs were travel expenses (EUR 0.30 or USD 0.35 per kilometer according to German tax  
74 law<sup>35</sup>), investments into constructional adaptations of the house and car, as well as legal fees and  
75 other expenditures.

76 In contrast, indirect costs per definition arise from absenteeism, invalidity, or premature death,  
77 and thus represent the loss of productivity of an affected individual (and his or her caregiver).  
78 We used the human capital approach and calculated monetary losses due to reduction of  
79 working time, sick leaves, unemployment, and early retirement based on patient reported salary  
80 levels.<sup>2</sup> However, productivity loss due to premature death was not captured in this study  
81 because we did not collect death data.

82 Patients' own out-of-pocket expenses (eTable 1) were estimated according to patients' self-  
83 reported data or, if missing, based on the standardized co-payments to the German statutory  
84 health care insurance.<sup>36</sup>

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## 86 **eResults:**

### 87 ***Resource utilization***

88 Resource utilization was analyzed in order to estimate costs based on patients' retrospective  
89 consumption of medical resources and to depict an overview of the current care situation.

90 The detailed characterization of resource utilization is shown in eTable 4. In general, it becomes  
91 obvious that resource utilization drastically increased with increasing disability and loss of  
92 autonomy. Medication was the highest cost driver as 91% of all patients were treated with  
93 immunotherapies (eTable 3). Most of the patients (n=146, 69%) reported outpatient

94 consultations during the last three months. During this time periods mainly neurologists  
95 (n=137) were consulted (1.9 times per patient), followed by general practitioners (n=57, 3.7  
96 times). The same specialist distribution was noted for outpatient hospital consultations.  
97 Hundred and six patients (50%) were treated in hospital within the last 12 months, mainly in  
98 neurology departments, with a mean duration of 7 (95% bootstrap CI 5.6 to 8.9) days. Fourteen  
99 of these patients required 12 (95% bootstrap CI 5.6 to 18.9) days of intensive care unit (ICU)  
100 treatment. With increasing disease severity, the mean number of hospitalization days increased  
101 while the duration of stays in ICU decreased.

102 Therapeutic healing was the fourth highest cost driver of direct medical costs. Patients mainly  
103 used physiotherapy (n=109, 51%) with an increase according to disease severity and a direct  
104 correlation between hours of physiotherapy per week and a higher EDSS level ( $\rho=0.48$ , 95%  
105 CI 0.37 to 0.58). The same correlation between EDSS and occupational therapy was seen  
106 ( $\rho=0.41$ , 95% CI 0.29 to 0.52). Psychological therapy was obtained by only 13% (n=27),  
107 although at least 24% of the patients asked for more psychological support.

108 Every sixth patient (n=34, 16%) received rehabilitation treatment, which increased with disease  
109 severity: 12% (n=12) in the EDSS 0 - 3 group, 13% (n=9) in the EDSS 3.5 - 6 group, and 36%  
110 (n=12) in the EDSS 6.5 - 8.5 group ( $p=0.002$ , ANOVA group analysis). Moreover, there was a  
111 correlation between rising EDSS and the number of days in rehabilitation ( $\rho=0.18$ , 95% CI  
112 0.039 to 0.31). Additionally, there was a notable increase of resource utilization for care in the  
113 severely affected EDSS group, especially formal care. The number of patients who required  
114 formal care increased with disease severity (EDSS 0 - 3 4% vs. EDSS 6.5 - 8.5 88%,  $p<0.001$ ,  
115 non-parametric t-test), while the need of informal care was already more evident in the mild  
116 disease severity group. Nevertheless, the hours per day of informal care showed a correlation  
117 to disease severity ( $\rho=0.61$ , 95% CI 0.51 to 0.69).

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16 **eQuestionnaire:**

17 Please find below the English version of the original questionnaire for the survey of costs and  
18 health-related quality of life in patients with NMO spectrum disorders (NMOSD) and MOG  
19 antibody-associated disease (MOGAD) from the *CHANCE<sup>NMO</sup> Study*. A short letter addressed  
20 to the patients including some instructions on how to fill in the questionnaire is not presented.  
21 The patients were explicitly informed that all questions refer only to their neuromyelitis optica  
22 spectrum disorder and not to any additional diseases. Please note that at the time of the  
23 questionnaire survey, MOGAD was partially assigned to NMOSD according to diagnostic  
24 criteria of July 2015 (see reference 1, main manuscript). MOG antibody positive patients  
25 received the same questionnaire.

26

27 Clinical data on disease onset, severity, duration, serostatus, symptoms, immunotherapy, and  
28 management of attacks were retrieved from the NEMOS database in which all centers  
29 prospectively update the information of every individual patient.

30

31 **The questionnaire is protected by copyright.** Unauthorized use is not permitted. If you are  
32 interested in usage, please send a qualified request to [hueммert.martin@mh-hannover.de](mailto:hueммert.martin@mh-hannover.de).  
33 The use of the EuroQoL Group Five Dimension Five Level Scale (EQ-5D-5L) must be  
34 registered separately (<https://euroqol.org/>) and is not part of this supplement for copyright  
35 reasons.

## CHANCE<sup>NMO</sup>-Study Questionnaire

Site: \_\_\_\_\_

Patient-ID: \_\_\_\_\_

Date: \_\_\_\_\_

### Your demographics and professional occupation

Age: \_\_\_\_\_ years

Sex:  Female  Male

Are you employed at present?

Yes  No



If no:

- Seeking work
- Early retirement due to NMOSD
- Early retirement other reasons
- Reeducation
- Retirement
- Education/School
- Housewife/Househusband
- Other \_\_\_\_\_

Salary per month:

BEFORE NMOSD  
manifestation

\_\_\_\_\_ €/month

NOW

\_\_\_\_\_ €/month

If yes:

1. Occupational change needed due to NMOSD?  yes  no

2. Employment relationship:  Employed  Self-employed

3. Working hours per week: BEFORE NMOSD manifestation \_\_\_\_\_ hours/week  
NOW \_\_\_\_\_ hours/week

4. Salary per month: BEFORE NMOSD manifestation \_\_\_\_\_ €/month  
NOW \_\_\_\_\_ €/month

Family status:  Married  
 Living alone  
 Partnership  
 Divorced  
 Widowed

Medical insurance:  Statutory  Private

<b>Investments due to NMOSD</b>
---------------------------------

Have investments in structural modifications in your domestic environment been necessary since the onset of the disease (*e. g. stair lift, ramp, etc.*):

- Yes       No      If yes, which?

---

Approximate total costs: \_\_\_\_\_ €

Own out-of-pocket costs: \_\_\_\_\_ €

Have any investments/conversions been necessary on your car since the onset of the disease (*e. g. steering aids, brake boosters, etc.*)?

- Yes       No      If yes, which?

---

Approximate total costs: \_\_\_\_\_ €

Own out-of-pocket costs: \_\_\_\_\_ €

Did you purchase any mobility aids during the last 12 months?

(*Multiple answers possible*):

- Walking stick      (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- Crutches      (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- Walking frame      (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- Manual wheelchair      (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- Electric wheelchair      (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- None
- Other: \_\_\_\_\_

(quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )

---

(quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )

Did you purchase any daily living aids during the last 12 months?

*(Multiple answers possible):*

- Special cuterly (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- Key assistance (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- Non-slip underlay (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- Gripper (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- None
- Other: \_\_\_\_\_  
(quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )  
\_\_\_\_\_  
(quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )  
\_\_\_\_\_  
(quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )  
\_\_\_\_\_  
(quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )

Did you purchase any care aids during the last 12 months?

*(Multiple answers possible):*

- Nursing bed (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- Anti-decubitus-mattress (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- Toilet seat raiser (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- Toilet wheelchair (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- Bathtub insert (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )
- None
- Other: \_\_\_\_\_  
(quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )  
\_\_\_\_\_  
(quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )  
\_\_\_\_\_  
(quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )  
\_\_\_\_\_  
(quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )

<b>Medical treatment due to NMOSD</b>
---------------------------------------

Have you been under outpatient consultations within the last 3 months?

(If you have not received outpatient consultations within the last 3 months, please write the word "None" in the table.)

Reason for medical treatment <i>(e. g. laboratory test)</i>	Medical specialty <i>(e. g. Neurologist)</i>	Quantity <i>(e. g. 2 times a month)</i>	Out-of-pocket costs in €

Did you receive any home visits within the last 3 months?

No

Yes (If yes: quantity: \_\_\_\_\_; own out-of-pocket costs in € \_\_\_\_\_ )

Have you been under outpatient hospital consultations within the last 3 months?

(If you have not received outpatient hospital consultations within the last 3 months, please write the word "None" in the table).

Reason for outpatient hospital treatment <i>(e. g. specialist consultation for therapy evaluation)</i>	Medical specialty <i>(z. B. Neurology)</i>	Quantity <i>(e. g. 2x)</i>	Out-of-pocket costs in €

Have you been under inpatient hospital care within the last 12 months?

(If you have not received inpatient treatment within the last 12 months, please write the word "None" in the table.)

	Reason for inpatient hospital care (e. g. attack)	Medical specialty (e. g. Dept. of Neurology)	Number of overnight stays (e. g. 18 nights)	Out-of-pocket costs in €
1 <sup>st</sup> in-patient stay	Intensive care unit stay? <input type="checkbox"/> No <input type="checkbox"/> Yes (Number of overnight stays: _____ )			
2 <sup>nd</sup> in-patient stay	Intensive care unit stay? <input type="checkbox"/> No <input type="checkbox"/> Yes (Number of overnight stays: _____ )			
3 <sup>rd</sup> in-patient stay	Intensive care unit stay? <input type="checkbox"/> No <input type="checkbox"/> Yes (Number of overnight stays: _____ )			
4 <sup>th</sup> in-patient stay	Intensive care unit stay? <input type="checkbox"/> No <input type="checkbox"/> Yes (Number of overnight stays: _____ )			
5 <sup>th</sup> in-patient stay	Intensive care unit stay? <input type="checkbox"/> No <input type="checkbox"/> Yes (Number of overnight stays: _____ )			
6 <sup>th</sup> in-patient stay	Intensive care unit stay? <input type="checkbox"/> No <input type="checkbox"/> Yes (Number of overnight stays: _____ )			

Have you been under rehabilitation therapy within the last 12 months?

Inpatient rehabilitation

(If yes: Number of overnight stays: \_\_\_\_\_; out-of-pocket costs in € \_\_\_\_\_ )

Outpatient rehabilitation

(If yes: Number of overnight stays: \_\_\_\_\_; out-of-pocket costs in € \_\_\_\_\_ )

No

Have you been under one/some of the following therapies within the last 3 months:

*(Multiple answers possible):*

Physiotherapy

If yes, duration per week: \_\_\_\_\_ hours

Home visit:  No  Yes

Out-of-pocket costs : \_\_\_\_\_ €

Occupational therapy

If yes, duration per week: \_\_\_\_\_ hours

Home visit:  No  Yes

Out-of-pocket costs : \_\_\_\_\_ €

Speech therapy

If yes, duration per week: \_\_\_\_\_ hours

Home visit:  No  Yes

Out-of-pocket costs : \_\_\_\_\_ €

Psychology

If yes, duration per week: \_\_\_\_\_ hours

Home visit:  No  Yes

Out-of-pocket costs : \_\_\_\_\_ €

Other: \_\_\_\_\_

If yes, duration per week: \_\_\_\_\_ hours

Home visit:  No  Yes

Out-of-pocket costs : \_\_\_\_\_ €

No

Did you have any absent days from work due to NMOSD within the last 3 months?

Yes (If yes, number of days: \_\_\_\_\_ days)

No



**Transportation costs due to NMOSD**

Within the last 3 months, have you had any transportation due to your NMO spectrum disorder?

- No
- Yes - if yes, please fill in the following list:

Reason for transportation	Transportation Ambulance service	Private car	Cab	Public transport	Number of trips	Out-of-pocket costs in €	One way distance from home in kilometers
Outpatient consultations	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Outpatient hospital consultations	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Inpatient hospital care	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Inpatient rehabilitation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Outpatient rehabilitation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			

Reason for transportation	Transportation				Number of trips	Out-of-pocket costs in €	One way distance from home in kilometers
	Ambulance service	Private car	Cab	Public transport			
Visit to a physiotherapist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Visit to an occupational therapist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Visit to a speech therapist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Visit to a psychologist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Other: _____	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Other: _____	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			

<b>Care due to NMOSD</b>
--------------------------

**The following questions refer to the last month**

Do you have a care level?

- No       Yes    (if yes, which care level do you have: Level \_\_\_\_\_ )

Do you regularly use a care service?

- No  
 Yes (if yes, how often does the care service come?: \_\_\_\_\_ ;  
Total costs in €/month \_\_\_\_\_ ; out-of-pocket costs in €/month \_\_\_\_\_ )

Do you live in a nursing home?

- No  
 Yes (if yes, total costs in €/month \_\_\_\_\_ ; out-of-pocket costs in € \_\_\_\_\_ )

Do you use a home aid for support?

- No  
 Yes (if yes, how many hours per day: \_\_\_\_\_ ;  
Total costs in €/month \_\_\_\_\_ ; out-of-pocket costs in €/month \_\_\_\_\_ )

Enlist support from your family or friends for one of the following areas?

*(Multiple answers possible):*

- Care (if yes, how many hours per day: \_\_\_\_\_ )  
 Household help (if yes, how many hours per day: \_\_\_\_\_ )  
 Doing groceries (if yes, how many hours per day: \_\_\_\_\_ )  
 Other: \_\_\_\_\_ (if yes, how many hours per day: \_\_\_\_\_ )  
 Not applicable

Who supported you? *(Multiple answers possible):*

- Partner                       Son/Daughter  
 Father                         Other family member: \_\_\_\_\_  
 Mother                         Friend

Does this support require the reduction of a family member's or friend's occupation?

- No       Yes (if yes, for how many hours per week: \_\_\_\_\_ )



Have any of the following apparative / invasive tests been performed as **outpatient** examinations in the last 12 months?

*(Multiple answers possible, if you have any questions, please ask your study physician)*

- MRI examination of the head (if yes: quantity \_\_\_\_\_ )
- MRI examination of the spinal cord (if yes: quantity \_\_\_\_\_ )
- Evoked potentials (if yes: quantity \_\_\_\_\_ )
- Optical Coherence Tomography (OCT) (if yes: quantity \_\_\_\_\_ )
- Lumbar puncture (if yes: quantity \_\_\_\_\_ )
- Other: \_\_\_\_\_ (quantity \_\_\_\_\_ )
- Not applicable

**Other costs due to NMOSD**

Are there any other costs not listed in this questionnaire due to your NMO spectrum disorder? Please specify the reasons for additional expenses and their costs (*e.g. for artificial nutrition, etc.*).

Expenses	Costs in €



16 **eTables:**17 **eTable 1. Social, educational and occupational status of the CHANCE<sup>NMO</sup>-Study cohort**  
18 **stratified by disease severity**

	<b>All patients</b>	<b>EDSS 0 - 3</b>	<b>EDSS 3.5 - 6</b>	<b>EDSS 6.5 - 8.5</b>
<b>n<sup>a</sup> (%)</b>	<b>212 (100)</b>	<b>101 (48)</b>	<b>70 (33)</b>	<b>33 (16)</b>
<b>Family status, n<sup>b</sup> (%)</b>				
Married	127 (60)	54 (53)	48 (69)	19 (58)
Living alone	34 (16)	17 (17)	9 (13)	7 (21)
Partnership	29 (14)	22 (22)	4 (6)	2 (6)
Divorced	15 (7)	6 (6)	7 (10)	2 (6)
Widowed	5 (2)	2 (2)	0 (0)	3 (9)
Missing data	2 (1)	0 (0)	2 (2)	0 (0)
<b>Medical insurance, n<sup>c</sup> (%)</b>				
Statutory	197 (93)	94 (93)	65 (93)	31 (94)
Private	13 (6)	7 (7)	3 (4)	2 (6)
Missing data	2 (1)	0 (0)	2 (3)	0 (0)
<b>Education, n (%)</b>				
Higher education entrance qualification	49 (23)	30 (30)	13 (19)	6 (18)
Advanced technical college certificate	8 (4)	7 (7)	0 (0)	1 (3)
Vocational extension certificate	3 (1)	2 (2)	1 (1)	0 (0)
Secondary school	46 (22)	17 (17)	23 (33)	6 (18)
General school	16 (8)	9 (9)	4 (6)	3 (9)
Primary School	1 (<1)	0 (0)	1 (1)	0 (0)
Missing data	88 (42)	36 (36)	27 (39)	17 (52)
No graduation	1 (<1)	0 (0)	1 (1)	0 (0)
<b>Professional experience, n (%)</b>				
Completed vocational training	82 (39)	39 (39)	31 (44)	10 (30)
Completed higher education/ University education	36 (17)	23 (23)	8 (11)	5 (15)
Vocational extension studies	1 (<1)	1 (<1)	0 (0)	0 (0)
No education	11 (5)	3 (3)	6 (9)	2 (6)
Missing data	82 (39)	35 (35)	25 (36)	16 (48)
<b>Professional occupation, n<sup>e</sup> (%)</b>				
Patients of working age	181 (85)	97 (96)	57 (81)	22 (67)
<b>Total Employed</b>				
Employed	84 (40)	60 (60)	16 (23)	5 (15)
Employed	77 (92)	55 (92)	15 (94)	5 (100)
Self-Employed	5 (6)	4 (7)	1 (6)	0 (0)
Missing data	2 (2)	1 (1)	0 (0)	0 (0)
Occupational change needed	12 (6)	6 (6)	4 (6)	1 (3)
Absent days from work <sup>f</sup>	32.5 (23.5 to 41.3)	23.9 (15.5 to 32.6)	43.2 (24.4 to 62.1)	54.7 (3.3 to 76.4)
<b>Unemployed</b>				
Retirement	<b>128 (60)</b>	<b>41 (41)</b>	<b>54 (77)</b>	<b>28 (85)</b>
Retirement	29 (23)	5 (12)	13 (24)	8 (29)

Seeking work	5 (4)	3 (7)	1 (2)	1 (4)
On sick leave	11 (9)	4 (10)	6 (11)	1 (4)
Education/School	7 (5)	5 (12)	1 (2)	1 (4)
Parental leave	3 (2)	2 (5)	1 (2)	0 (0)
Early retirement due to NMO	41 (32)	9 (22)	22 (41)	8 (29)
Housewife/Househusband	12 (9)	7 (17)	2 (4)	3 (11)
Other	12 (9)	3 (7)	5 (9)	4 (14)
Reeducation	1 (<1)	0 (0)	1 (2)	0 (0)
Early retirement other reasons	7 (5)	3 (7)	2 (4)	2 (7)
Reduction of working time <sup>g</sup>				
All patients	2.6 (1.6 to 3.7)	2.8 (1.3 to 3.9)	2.3 (0.6 to 4.0)	3.2 (0.3 to 6.9)
Employed patients <sup>h</sup>	6.9 (4.2 to 9.2)	4.6 (2.6 to 6.8)	9.7 (3.8 to 17.1)	20.8 (8.5 to 33.0)

In some cases, percentages may not add exactly to 100% due to rounding.

Abbreviation: EDSS, expanded disability status scale.

<sup>a</sup>EDSS values of eight patients were missing.

<sup>b</sup>Data on the family status of two patients were missing in the entire cohort and the moderate affected EDSS group, respectively.

<sup>c</sup>Data on the medical insurance of two patients were missing.

<sup>d</sup>Data on employment status of two patients were missing in the entire cohort and of one patient in the mildly affected group.

<sup>e</sup>Absent days from work as mean number of days (bootstrap lower to upper 95% confidence interval of the mean [CI]) during the last three months; refer to the number of patients with absent days from work (All patients n=56, EDSS 0 – 3 n=34, EDSS 3.5 – 6 n=15, EDSS 6.5 – 8.5 n=7).

<sup>g</sup>Reduction of working time in hours per week; mean (bootstrap 95% CI)

<sup>h</sup>Employed patients: all n=84, EDSS 0 – 3 n= 60, EDSS 3.5 – 6 n= 16, EDSS 6.5 – 8.5 n= 5.

**eTable 2. Geographical distribution of inhabitants and CHANCE<sup>NMO</sup>-Study participants across the German federal states**

German federal states	German population in 2018 <sup>a</sup> (in 1 000)	%	Study participants (n)	%
<b>Baden-Wuerttemberg</b>	11 023.4	13	19	9
<b>Bavaria</b>	12 997.2	16	23	11
<b>Berlin</b>	3 613.5	4	45	21
<b>Brandenburg</b>	2 504.0	3	3	2
<b>Bremen</b>	681.0	<1	0	0
<b>Hamburg</b>	1 830.6	2	9	4
<b>Hesse</b>	6 243.3	8	0	0
<b>Mecklenburg-Western Pomerania</b>	1 611.1	2	6	3
<b>Lower Saxony</b>	7 962.8	10	34	16
<b>North Rhine-Westphalia</b>	17 912.1	22	60	28
<b>Rhineland-Palatinate</b>	4 073.7	5	0	0
<b>Saarland</b>	994.2	1	0	0
<b>Saxony</b>	4 081.3	5	7	3
<b>Saxony-Anhalt</b>	2 223.1	3	6	3
<b>Schleswig-Holstein</b>	2 889.8	3	0	0
<b>Thuringia</b>	2 151.2	3	0	0
<b>Total</b>	82 792.4	100	212	100

<sup>a</sup>Adapted from the German Federal Statistical Office.<sup>36</sup>



36 **eTable 3. Diversity of immunotherapies used by the CHANCE<sup>NMO</sup>-Study participants**

<b>Immunotherapy</b>	<b>n</b>	<b>%</b>
Rituximab	131	59
Azathioprine	35	16
Prednisolone	23	10
Tocilizumab	11	5
Mycophenolate mofetil	6	3
Intravenous immunoglobulin	4	2
Inebilizumab	4	2
Methothrexate	4	2
Belimumab	1	<1
Daclizumab	1	<1
Eculizumab	1	<1
Mitoxantrone	1	<1
Ocrelizumab	1	<1
All	223	100

37 193 patients (91%) were treated with one or more immunotherapies.

38

39 **eTable 4. Utilization of healthcare resources by CHANCE<sup>NMO</sup>-Study participants**  
40 **stratified by disease severity**

	<b>All patients</b>	<b>EDSS 0 - 3</b>	<b>EDSS 3.5 - 6</b>	<b>EDSS 6.5 - 8.5</b>
<b>n<sup>a</sup> (%)</b>	<b>212 (100)</b>	<b>101 (48)</b>	<b>70 (33)</b>	<b>33 (16)</b>
<b>Need for nursing care</b>	118 (56)	29 (29)	51 (73)	32 (97)
<b>Informal care</b>	111 (52)	26 (26)	50 (71)	29 (88)
Informal care total, hours/day <sup>b,c</sup>	1.8 (1.4 to 2.2)	0.6 (0.3 to 0.9)	2.1 (1.6 to 2.8)	4.4 (3.1 to 5.7)
Nursing care	40 (19)	1 (1)	15 (21)	22 (67)
Nursing care, hours/day <sup>b</sup>	0.6 (0.4 to 0.8)	0.01 (0.0 to 0.03)	0.6 (0.3 to 1.0)	2.1 (1.2 to 2.9)
Household	76 (36)	17 (17)	36 (51)	19 (58)
Houshold, hours/day <sup>b</sup>	0.7 (0.5 to 0.8)	0.3 (0.1 to 0.4)	0.8 (0.6 to 1.0)	1.5 (0.9 to 2.1)
Shopping assistance	98 (46)	20 (20)	47 (67)	26 (79)
Shopping assistance, hours/day <sup>b</sup>	0.4 (0.4 to 0.5)	0.2 (0.1 to 0.2)	0.6 (0.5 to 0.7)	1.0 (0.6 to 1.1)
<b>Formal care</b>	50 (24)	4 (4)	11 (16)	29 (88)
Domestic help	30 (14)	4 (4)	10 (14)	13 (39)
Domestic help, hours/day <sup>b</sup>	0.3 (0.1 to 0.6)	0.1 (0 to 0.4)	0.1 (0 to 0.1)	1.1 (0.1 to 2.6)
Nursing service	17 (8)	-	1 (1)	14 (42)
Nursing home	3 (1)	-	-	2 (6)
<b>Care degree</b>	54 (25)	1 (1)	23 (33)	26 (79)
Care level 1	3 (1)	-	1 (1)	2 (6)
Care level 2	18 (8)	-	13 (19)	4 (12)
Care level 3	16 (8)	1 (1)	6 (9)	8 (24)
Care level 4	11 (5)	-	2 (3)	8 (24)
Care level 5	6 (3)	-	1 (1)	4 (12)
<b>Therapeutic healing</b>	123 (58)	41 (41)	49 (70)	28 (85)
Physiotherapy	109 (51)	33 (33)	44 (63)	28 (85)

Physiotherapy, treatments/week <sup>b</sup>	1.4 (1.1 to 1.8)	2.1 (0.4 to 0.9)	1.8 (1.2 to 2.4)	2.8 (2.1 to 3.6)
Occupational therapy	28 (13)	1 (1)	12 (17)	14 (42)
Occupational therapy, treatments/week <sup>b</sup>	0.3 (0.2 to 0.4)	<0.1 (0 to 0.1)	0.3 (0.2 to 0.5)	1.2 (0.6 to 1.8)
Speech therapy	1 (<1)	-	-	-
Speech therapy, treatments/week <sup>b</sup>	<0.1 (0.0 to 0.04)	-	-	-
Psychology	27 (13)	11 (11)	12 (17)	3 (9)
Psychology, treatments/week <sup>b</sup>	0.3 (0.2 to 0.4)	0.3 (0.1 to 0.4)	0.3 (0.1 to 0.5)	0.3 (0 to 0.7)
Lymph drainage	6 (3)	-	-	6 (18)
Lymph drainage, treatments/week <sup>b</sup>	0.1 (0.01 to 0.2)	-	-	0.5 (0.1 to 0.9)
<b>Medication</b>	200 (94)	93 (92)	68 (97)	32 (97)
Immunotherapy	193 (91)	90 (89)	65 (93)	32 (97)
Treatment of attacks	61 (29)	29 (29)	19 (27)	12 (36)
Symptomatic therapy	184 (87)	82 (81)	64 (91)	32 (97)
<b>Medical aids</b>	72 (34)	8 (8)	32 (46)	28 (85)
Mobility aids	57 (27)	5 (5)	24 (34)	24 (73)
Daily living aids	31 (15)	3 (3)	13 (19)	13 (39)
Care aids	37 (17)	3 (3)	12 (17)	18 (55)
<b>Rehabilitation</b>	34 (16)	12 (12)	9 (13)	12 (36)
Inpatient admission, days <sup>b</sup>	9.4 (5.5 to 14.3)	4.9 (2.3 to 7.8)	5.3 (1.8 to 9.5)	24.7 (9.0 to 44.7)
<b>Inpatient hospital care<sup>d</sup></b>	106 (50)	55 (54)	28 (40)	18 (55)
Normal ward, days <sup>b</sup>	7.1 (5.6 to 8.9)	7.0 (5.0 to 9.2)	6.6 (3.5 to 9.6)	9.1 (4.4 to 15.3)
Intensive care unit, days <sup>b</sup>	0.8 (0.3 to 1.5)	1.1 (0.2 to 2.4)	0.2 (0.0 to 0.5)	1.4 (0.3 to 3.3)
<b>Outpatient hospital consultations<sup>e</sup></b>	85 (40)	34 (34)	33 (47)	17 (52)
Outpatient hospital consultations, last 3 months <sup>b</sup>	0.7 (0.6 to 0.9)	0.7 (0.4 to 1.0)	0.7 (0.5 to 0.9)	1.0 (0.6 to 1.4)
<b>Outpatient consultations<sup>f</sup></b>	146 (69)	60 (59)	59 (84)	23 (70)
Outpatient consultations, last three months <sup>b</sup>	1.5 (1.0 to 2.2)	1.2 (0.5 to 2.2)	1.3 (0.8 to 2.0)	3.1 (1.1 to 5.2)
<b>Outpatient diagnostic tests</b>	151 (71)	72 (71)	56 (80)	16 (48)
MRI brain	128 (60)	65 (64)	43 (61)	15 (45)
MRI spine	125 (59)	59 (58)	49 (70)	14 (42)
EP	29 (14)	17 (17)	7 (10)	3 (9)
OCT	43 (20)	24 (24)	13 (19)	4 (12)
LP	28 (13)	19 (19)	6 (9)	2 (6)
<b>Investments</b>	45 (21)	5 (5)	21 (30)	17 (52)
Home	43 (20)	5 (5)	19 (27)	17 (52)
Car	11 (5)	0 (0)	5 (7)	5 (15)

41 Abbreviations: EDSS, expanded disability status scale; MRI, magnetic resonance imaging; EP, evoked potentials; OCT, optical  
 42 coherence tomography; LP, lumbar puncture.

43 <sup>a</sup>EDSS values of eight patients were missing.

44 <sup>b</sup>mean (bootstrap 95% bootstrap confidence interval)

45 <sup>c</sup>Informal care costs in hours per day includes the category unspecific support next to nursing care, household, and shopping assistance.

46 <sup>d,e</sup>Inpatient hospital care during the last twelve months and outpatient hospital consultations within the last three months mainly took  
 47 place in neurology departments.

48 <sup>f</sup>Most outpatient consultations took place with neurologists (54%), followed by general practitioners (22%).

49 **eTable 5. Mean out-of-pocket money per patient of the CHANCE<sup>NMO</sup>-Study cohort**  
 50 **stratified by disease severity**

Out-of-pocket money of	Mean (95% bootstrap CI)			
	All patients	EDSS 0 - 3	EDSS 3.5 - 6	EDSS 6.5 - 8.5
<b>n<sup>a</sup></b>	<b>212</b>	<b>101</b>	<b>70</b>	<b>33</b>
<b>Direct medical costs</b>	<b>967 (570 to 1 399)</b>	<b>336 (247 to 450)</b>	<b>641 (424 to 898)</b>	<b>2 193 (915 to 4 224)</b>
Outpatient hospital consultations	15 (5 to 28)	16 (2 to 36)	18 (1 to 48)	7 (0 to 15)
Inpatient hospital care total	56 (35 to 83)	67 (37 to 108)	35 (18 to 54)	68 (9 to 167)
Medications	136 (115 to 158)	86 (70 to 107)	145 (114 to 177)	273 (201 to 360)
Rehabilitation	49 (28 to 73)	29 (13 to 49)	26 (11 to 47)	127 (48 to 237)
Therapeutic healing	105 (72 to 142)	49 (28 to 79)	131 (73 to 204)	176 (74 to 293)
Medical aids	101 (48 to 178)	16 (1 to 46)	211 (55 to 426)	132 (64 to 224)
Formal care	505 (135 to 893)	73 (14 to 148)	75 (0 to 178)	1 410 (146 to 3 471)
<b>Direct non-medical costs</b>	<b>2 581 (1 238 to 4 358)</b>	<b>165 (85 to 258)</b>	<b>3 392 (1 129 to 6 860)</b>	<b>8 855 (3 310 to 16 230)</b>
Transportation	157 (97 to 227)	112 (60 to 174)	230 (95 to 410)	178 (28 to 381)
Investments home	1 885 (690 to 3 440)	53 (0 to 129)	2 036 (482 to 4 495)	7 600 (2 263 to 14 908)
Investments car	539 (164 to 1 039)	0	1 126 (111 to 2 382)	1 077 (68 to 2 297)
<b>Total out-of-pocket money</b>	<b>3 548 (2 116 to 5 474)</b>	<b>501 (367 to 664)</b>	<b>4 033 (1 635 to 7 645)</b>	<b>11 048 (5 261 to 18 552)</b>
<b>Total costs incl. out-of-pocket money</b>	<b>59 574 (51 225 to 68 293)</b>	<b>34 991 (28 570 to 41 937)</b>	<b>60 037 (48 399 to 72 369)</b>	<b>129 688 (101 946 to 160 336)</b>

51 Mean out-of-pocket money (bootstrap 95% confidence interval) per patient per year in Euros.

52 Abbreviations: EDSS, expanded disability status scale.

53 <sup>a</sup>EDSS values of eight patients were missing.

54 <sup>b</sup>Proportion of total costs that had to be covered by patients. No out-of-pocket money was due for outpatient consultations and medical tests  
 55 within the direct medical cost category

56

57 **eTable 6. Detailed mean annual costs per patient of the CHANCE<sup>NMO</sup>-Study cohort stratified**  
 58 **by serostatus.**

	Mean (95% bootstrap CI)			
	MOGAD			
	AQP4-IgG (+) NMOsD	Double negative NMOsD	IPND (+)	IPND (-)
<b>n</b>	<b>141</b>	<b>25</b>	<b>25</b>	<b>21</b>
<b>Direct medical costs</b>	<b>26 136 (9 905 to 26 929)</b>	<b>17 000 (9 905 to 26 929)</b>	<b>25 037 (17 757 to 33 574)</b>	<b>32 907 (14 117 to 62 241)</b>
Outpatient consultations	530 (415 to 652)	409 (203 to 636)	808 (404 to 1 295)	975 (274 to 2 123)
Outpatient hospital consultations	287 (230 to 349)	130 (43 to 238)	280 (130 to 454)	283 (129 to 437)
Inpatient hospital care	5 183 (3 333 to 7 161)	2 315 (890 to 4 002)	6 375 (3 287 to 10 263)	7 345 (3 843 to 11 624)
Medication incl. apheresis	9 455 (7 884 to 11 356)	5 989 (3 767 to 8 517)	10 130 (4 880 to 17 789)	16 111 (5 430 to 32 018)
Immunotherapy	7 582 (6 175 to 9 403)	5 223 (3 040 to 7 823)	7 034 (3 198 to 12 919)	12 799 (3 807 to 28 554)
Treatment of attacks	1 042 (538 to 1 653)	296 (20 to 784)	2 345 (772 to 4 216)	2 780 (369 to 6 353)
Symptomatic therapy	830 (593 to 1 102)	470 (213 to 771)	751 (116 to 1 936)	532 (184 to 950)
Outpatient diagnostic tests	248 (200 to 304)	324 (169 to 535)	398 (250 to 542)	425 (276 to 616)
Rehabilitation	1 750 (902 to 2 687)	2 506 (0 to 6 948)	1 883 (371 to 4 073)	821 (0 to 1 906)
Therapeutic healing	3 531 (2 660 to 4 541)	3 576 (1 744 to 6 206)	3 333 (1 633 to 5 250)	3 335 (1 151 to 6 380)
Medical aids	592 (395 to 811)	454 (129 to 970)	341 (86 to 662)	317 (21 to 692)
Formal care	4 540 (2 068 to 8 077)	1 296 (0 to 3 611)	1 488 (119 to 3 242)	3 294 (0 to 8 535)
<b>Direct non-medical costs</b>	<b>22 729 (17 222 to 28 916)</b>	<b>14 346 (5 432 to 25 079)</b>	<b>17 910 (6 004 to 32 478)</b>	<b>11 923 (4 562 to 20 897)</b>
Informal care	18 220 (14 239 to 22 686)	12 621 (4 891 to 22 931)	15 009 (5 182 to 27 992)	10 946 (4 297 to 18 403)
Transportation	379 (243 to 557)	324 (36 to 720)	414 (203 to 647)	262 (86 to 469)
Investments home	3 596 (1 540 to 6 247)	0	848 (41 to 1 868)	714 (0 to 2 000)

Investments car	534 (79 to 1 223)	1 400 (0 to 4 200)	1 640 (0 to 4 398)	0
<b>Indirect costs</b>	<b>11 992 (8 645 to 16 037)</b>	<b>17 534 (8 473 to 29 011)</b>	<b>19 391 (9 409 to 31 506)</b>	<b>15 569 (5 569 to 26 979)</b>
Loss of salary for employed	3 529 (2 012 to 5 259)	1 603 (0 to 4 749)	3 146 (0 to 9 201)	2 642 (0 to 7 925)
Loss of salary for unemployed	4 512 (2 384 to 7 137)	5 242 (834 to 11 518)	6 756 (874 to 14 933)	1 923 (0 to 4 533)
Loss of salary as an indicator for productivity loss - days of sick leave	3 488 (1 558 to 5 886)	6 460 (301 to 16 205)	9 219 (2 680 to 19 679)	9 876 (2 581 to 19 008)
Loss of salary - working time reduction	462 (12 to 1 049)	4 228 (0 to 10 621)	271 (0 to 812)	1 128 (0 to 2 899)
<b>Total costs</b>	<b>60 857 (51 448 to 71 889)</b>	<b>48 879 (30 267 to 71 780)</b>	<b>62 339 (40 498 to 89 542)</b>	<b>60 398 (32 400 to 97 376)</b>

Mean costs (bootstrap 95% confidence interval) per patient per year including out-of-pocket money expenses in Euros. Abbreviations: NMOSD, neuromyelitis optica spectrum disorders; AQP4-IgG(+), aquaporin-4 immunoglobulin G antibody (positive patients); MOGAD IPND (+), myelin oligodendrocyte glycoprotein immunoglobulin G antibody positive disease fulfilling the International Panel for NMO Diagnosis criteria 2015; MOGAD IPND (-), MOGAD not fulfilling the IPND criteria.

### eTable 7. Patients' satisfaction with care supply stratified by disease severity

Care satisfaction	All patients	EDSS 0 - 3	EDSS 3.5 - 6	EDSS 6.5 - 8.5
<b>n<sup>a</sup> (%)</b>	194 (92) <sup>b</sup>	94 (93)	62 (89)	31(94)
<b>Very satisfied</b>	96 (49) <sup>c</sup>	55 (59)	31 (50)	9 (29)
<b>Mostly satisfied</b>	77 (40)	31 (33)	23 (37)	18 (58)
<b>Moderately dissatisfied</b>	20 (10)	8 (9)	7 (11)	4 (13)
<b>Very dissatisfied</b>	1 (<1)	0 (0)	1 (2)	0 (0)

<sup>a</sup>Eighteen values for care satisfaction and eight EDSS values were missing.

<sup>b</sup>Percentage in this row refer to the total number of patients in the respective group; All patients n= 212, EDSS 0 - 3 n=101, EDSS 3.5 - 6 n=70, EDSS 6.5 - 8.5 n=33.

<sup>c</sup>All other percentages refer to the percentages shown in the column above.

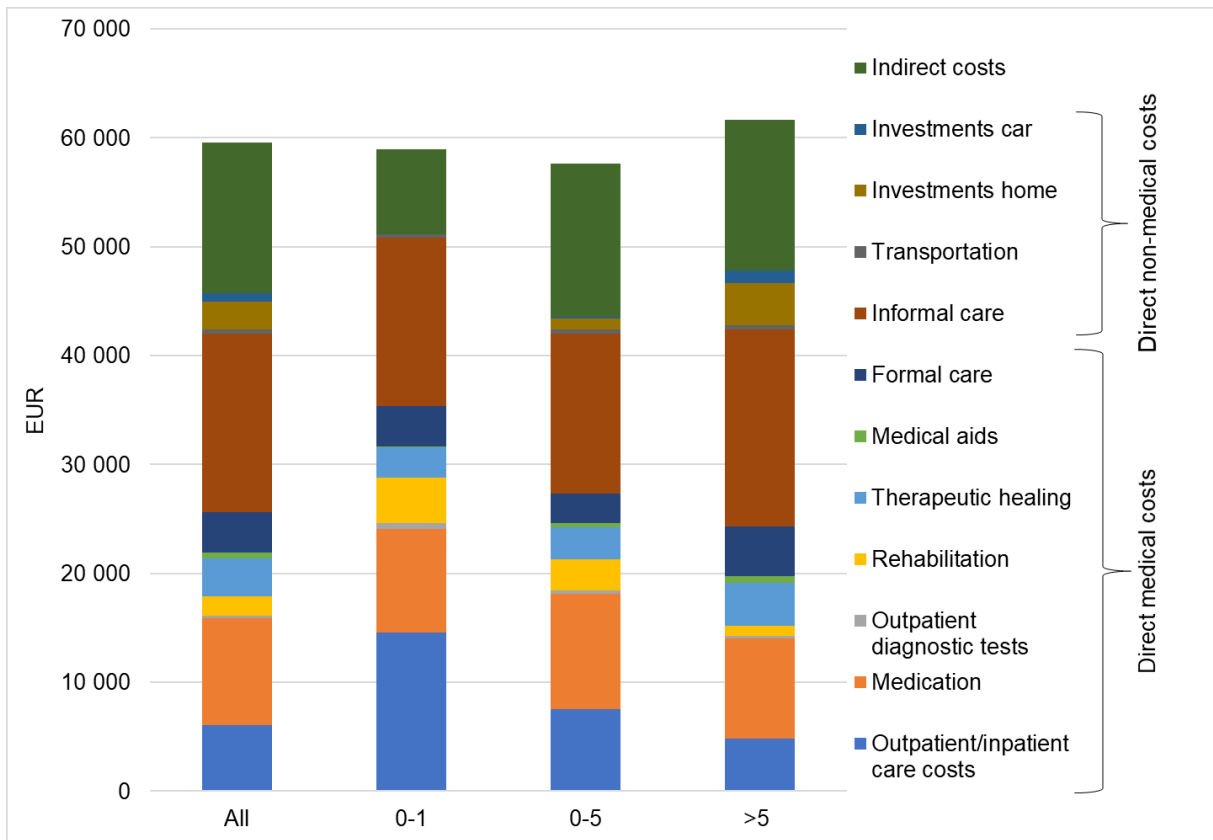
Percentages may not add exactly to 100% due to rounding.

### eTable 8. Specification of the time periods for the categories queried in the CHANCE<sup>NMO</sup>-Study questionnaire

Before disease manifestation	Ever since disease manifestation	Last 12 months	Last 3 months	Last 1 month	Current state
State of vocational occupation	Investments in house adaption	Medical aids	Outpatient consultations	Formal care	State of vocational occupation
Salary	Investments in car adaption	Inpatient hospital care	Outpatient hospital consultations	Informal care	Salary
Working hours a week		Rehabilitation	Therapeutic healing	Working time reduction of relatives	Working hours a week
		Outpatient diagnostic tests	Transportation costs		Further costs
		Attacks	Absent days from work		Care satisfaction
		Immunotherapy			Health-related quality of life

16 **eFigures:**

17 **eFigure 1. Mean annual costs per patient subdivided by disease duration**

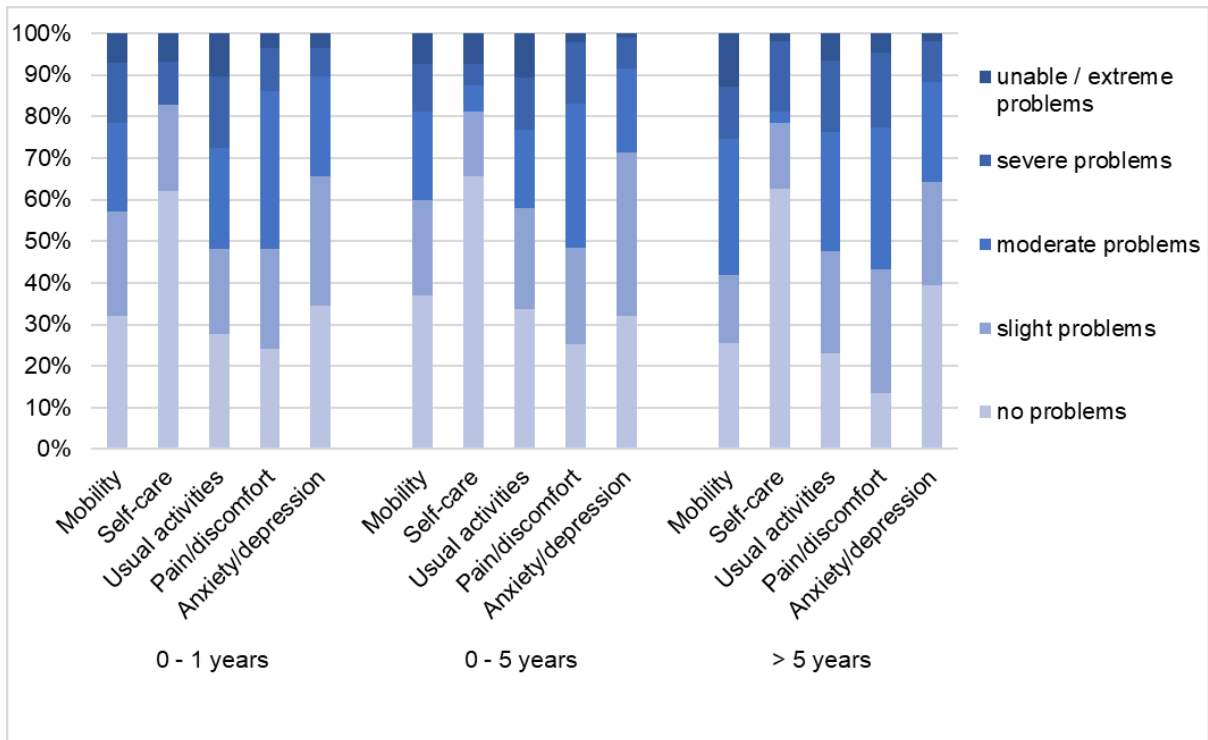


18

19 Mean total annual costs per patient per year of the entire study population and related to disease duration. In one patient, the disease duration  
 20 was unknown. Bar 2 (0-1 year disease duration, n=30) and bar 3 (0-5 years disease duration, n=97) both include patients who became ill less  
 21 than one year ago and serve for comparison with patients who became ill more than five years ago (n=114, bar 4). The total annual costs per  
 22 patient in the different disease duration groups were the same, but some individual cost categories differed (0-1 years of illness vs. >5 years of  
 23 illness): outpatient consultations and inpatient hospital care costs (p<0.001), outpatient diagnostic tests (p<0.001), rehabilitation costs  
 24 (p<0.001), investments home (p=0.03), and indirect costs (p=0.05). Abbreviations: EUR, Euros (2018).

25

26 **eFigure 2. Level of problems experienced by patients with different disease duration**



27

28 Patients were able to provide levels on a scale from 0-5 (0 = no problems, 5 = unable / extreme problems) for each of the five dimensions of  
 29 the EQ-5D-5L (EuroQoL five dimensions five levels). There was no statistically significant difference regarding the development of problems  
 30 in relation to disease duration.