# A multifaceted approach to understand cognitive impairment in MS: exploring the nonlinearity of cognition

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# 6

# The impact of cognitive impairment on daily life

# 6.1

# Cognitive functioning in everyday life: The development of a questionnaire on instrumental activities of daily living in multiple sclerosis

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## ABSTRACT

Neuropsychological test scores in people with MS (PwMS) do not fully reflect cognitive functioning in daily life. Therefore, in this study we developed a questionnaire based on instrumental activities of daily living (IADL), using the Amsterdam IADL-Q© for Alzheimer's disease as starting point. Forty-eight items were evaluated on relevance and clarity by (inter)national experts (n = 30), PwMS (n = 61) and proxies (n = 30). Consequently, four items were omitted and seven items were added. In total, 50 items were included in the IADL questionnaire specific to cognitive functioning in MS (the MS-IADL-Q). Future studies are warranted to assess the psychometric properties of the MS-IADL-Q.

## INTRODUCTION

Up to 70% of the people with Multiple Sclerosis (PwMS) experience cognitive impairment,[1] which substantially impacts daily functioning, work participation and quality of life.[2]

Neuropsychological examination is currently the "gold standard" to assess cognitive functioning, although its ecological validity is being questioned.[1] Cognitive tasks in daily life often have to be performed in an environment with distractors and are consequently more demanding than cognitive tests in a clinical setting.[1] Alternatively, self-report questionnaires on cognitive performance (e.g., Multiple Sclerosis Neuropsychological Questionnaire (MSNQ)) are only weakly correlated with neuropsychological test scores and seem to reflect fatigue and mood instead.[3] In Alzheimer's disease (AD) and neuro-oncology, questionnaires measuring "instrumental activities of daily living" (IADL) bridge the gap between functioning in daily life and neuropsychological test scores.[4-6] IADLs are defined as complex tasks that require multiple cognitive processes to be active,[4] and are known to be susceptible to early signs of cognitive decline.[7] In AD, this questionnaire has been correlated with neuropsychological test results[6] and enabled the detection of small changes in daily cognitive functioning (pre-disease status).[8] Therefore, an IADL questionnaire for PwMS (the MS-IADL-Q) is expected to link cognitive functioning in everyday life to clinical measures of cognition enabling timely detection of cognitive decline.



## METHODS

**Step 1: Item-selection for the MS-IADL-Q**

The first step included the composition of the MS-IADL-Q based on the short version of the well-validated Amsterdam IADL Questionnaire (A-IADL-Q) developed for people with AD[9] and the recently developed IADL questionnaires for patients with brain tumors[5] and patients with HIV (in preparation; Figure 1, Appendix A).

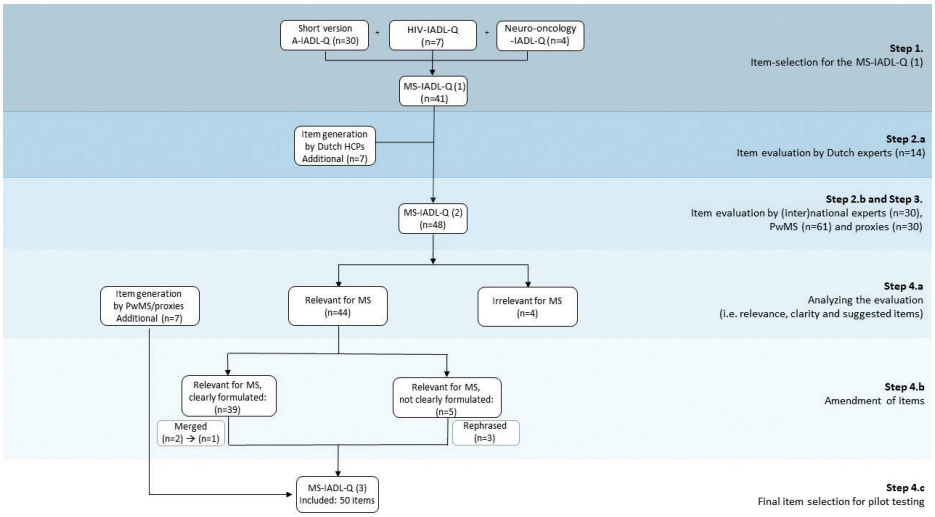


**Figure 1.** Flowchart reflecting the steps taken to develop and evaluate the MS Instrumental Activities of Daily Living Questionnaire (the MS-IADL-Q). *Abbreviations: PwMS = People with MS.*

### Step 2: Item evaluation by experts

To ensure content validity, the items for the questionnaire were evaluated by national (step 2a) and international experts (step 2b), i.e., neurologists, neuropsychologists, neuroscientists, nurses, rehabilitation physicians and occupational therapists. The relevance of the items was evaluated on a visual analogue scale ranging from 0 ("not relevant at all") to 100 ("very relevant"). Additionally, the clarity of the item description was evaluated and potential missing items could be added (Appendix B).

### Step 3: Evaluation by PwMS and proxies

The version of the MS-IADL-Q adjusted by the experts (Appendix C) was then evaluated by PwMS and their proxies as described in step 2. Medical Ethical approval was obtained from the VU University Medical Center.

### Step 4: Final item selection

The feedback from step 2 and step 3 was merged. Items with a mean rating of ≥ 75 were classified as "highly relevant", items with a score of ≥ 60 and < 75 were classified as "moderately relevant", and items with a score of < 60 were classified "little relevance".[9] If items received a score of < 60 (i.e., "irrelevant") by all groups, exclusion from the questionnaire was justified.[9] All items with a "moderate to high" rating (> 60) and no more than six "unclear" ratings were included in the final selection. Unclear items were evaluated and subsequently omitted or rephrased. Suggestions were incorporated in the questionnaire if the suggestion was mentioned at least three times by an independent rater.

## RESULTS

**Step 1: Item-selection for the MS-IADL-Q**
Thirty items of the A-IADL-Q, four items of the neuro-oncology list and seven items of the HIV list were included in the first version of the MS-IADL-Q (41 items) covering the following IADL: household, appliances, administration, work, devices, leisure, transport, and "other" activities (Appendix A).

**Step 2: Item evaluation by experts**
Seven items were added to the list: "keeping appointments", "focusing attention while performing tasks at work", "dealing with distractions at work", three items related to smartphone-use, and "other participation in traffic". The new MS-IADL-Q (48 items) was evaluated by the international experts (n = 15) and one more national expert (Appendix C). No differences in expert ratings were found between national and international experts (Appendix B).

**Step 3: Evaluation by PwMS and proxies**
Sixty-one PwMS (67% female, mean age = 49.0 ± 10.2 SD, relapsing-remitting MS (60%), progressive MS (28%), other (12%)) and 30 proxies (57% female, mean age = 51.4 ± 12.8 SD) evaluated the 48 items of the MS-IADL-Q (Figure 1).

**Table 1.** Evaluation of the MS-IADL-Q (version 2) by experts (national and international), People with MS (PwMS) and their proxies (ordered from highest average relevance to lowest average relevance). The average relevance per group is displayed, together with the mean. For relevance, scores range from 0 ("not relevant at all") to 100 ("very relevant"). For clarity of the item, frequency per group is displayed, together with the sum.

| | | **Relevance (0 – 100)** | | | | **Clarity** | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Category** | **Activity** | Experts (n = 30) | PwMS (n = 61) | Proxies (n = 30) | Mean | Experts (n = 30) | PwMS (n = 61) | Proxies (n = 30) | Sum |
| 4 | 3. Focusing attention while performing tasks at work | 91.10 | 88.03 | 76.87 | 85.33 | 1 | 2 | 1 | 4 |
| 3 | 5. Keeping appointments | 78.80 | 88.80 | 82.73 | 83.45 | 0 | 3 | 2 | 5 |
| 5 | 1. Using a computer | 80.80 | 86.77 | 82.60 | 83.39 | 1 | 1 | 3 | 5 |
| 3 | 4. Making appointments | 79.70 | 86.67 | 80.67 | 82.35 | 1 | 3 | 2 | 6 |
| 5 | 6. Using a mobile phone or smartphone | 79.70 | 83.97 | 82.00 | 81.89 | 0 | 0 | 1 | 1 |
| 8 | 2. Being responsible for his/her own medication | 75.80 | 88.34 | 81.07 | 81.74 | 0 | 1 | 0 | 1 |
| 8 | 5. Learning new things (such as a course, computer program, or appliance) | 84.50 | 83.00 | 75.70 | 81.07 | 1 | 0 | 1 | 2 |
| 4 | 1. Working | 89.20 | 81.51 | 70.80 | 80.50 | 1 | 2 | 4 | 7 |
| 8 | 4. Having a conversation with multiple people at the same time | 82.60 | 81.03 | 77.57 | 80.40 | 2 | 0 | 1 | 3 |
| 3 | 6. Using a PIN-code | 69.30 | 85.90 | 85.90 | 80.37 | 0 | 0 | 0 | 0 |
| 7 | 1. Driving a car | 78.90 | 83.08 | 78.67 | 80.22 | 0 | 1 | 3 | 4 |
| 3 | 1. Paying bills | 75.20 | 83.48 | 81.23 | 79.97 | 0 | 1 | 1 | 2 |
| 6 | 4. Reading a book or newspaper | 78.40 | 82.26 | 78.90 | 79.85 | 0 | 1 | 0 | 1 |
| 4 | 4. Dealing with distractions at work | 86.70 | 83.39 | 69.13 | 79.74 | 1 | 3 | 1 | 5 |
| 3 | 2. Managing the household budget | 78.00 | 82.97 | 77.20 | 79.39 | 0 | 1 | 1 | 2 |
| 7 | 4. Other participation in traffic (for instance by foot, bike, or scoot mobile) | 65.40 | 89.48 | 82.40 | 79.09 | 2 | 1 | 3 | 6 |
| 3 | 3. Using electronic banking | 69.50 | 84.16 | 80.37 | 78.01 | 0 | 0 | 0 | 0 |
| 5 | 2. E-mailing | 68.30 | 84.61 | 80.73 | 77.88 | 0 | 0 | 3 | 3 |
| 3 | 9. Filling in forms | 69.50 | 84.54 | 78.43 | 77.49 | 2 | 1 | 1 | 4 |
| 1 | 4. Cooking | 74.20 | 80.23 | 77.33 | 77.25 | 0 | 1 | 2 | 3 |
| 6 | 3. Following a TV program or movie | 72.60 | 78.25 | 80.37 | 77.07 | 0 | 1 | 0 | 1 |
| 8 | 3. Doing multiple things at the same time (multitasking) | 80.80 | 78.15 | 71.37 | 76.77 | 1 | 0 | 1 | 2 |

**Table 1.** Continued

| | | Relevance (0 – 100) | | | | Clarity | | | |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 1. Carrying out household duties | 74.50 | 79.44 | 75.80 | 76.58 | 4 | 3 | 4 | 11 |
| 5 | 7. Making phone calls with a mobile phone or smartphone | 67.30 | 82.87 | 78.73 | 76.30 | 0 | 0 | 0 | 0 |
| 1 | 3. Buying the correct groceries | 70.20 | 81.36 | 76.23 | 75.93 | 0 | 0 | 3 | 3 |
| 1 | 2. Grocery shopping independently | 72.50 | 80.13 | 75.13 | 75.92 | 0 | 1 | 2 | 3 |
| 5 | 4. Operating devices | 68.20 | 80.64 | 76.17 | 75.00 | 8 | 5 | 7 | 20 |
| 4 | 2. Finishing work on time | 83.10 | 77.43 | 63.07 | 74.53 | 3 | 1 | 5 | 9 |
| 6 | 5. Organizing/initiating social activities | 76.50 | 76.51 | 69.97 | 74.32 | 0 | 1 | 1 | 2 |
| 7 | 3. Using public transport | 73.50 | 77.67 | 70.80 | 73.99 | 0 | 2 | 3 | 5 |
| 3 | 10. Making online purchases (on any device) | 66.70 | 83.48 | 70.30 | 73.49 | 0 | 2 | 1 | 3 |
| 7 | 2. Using a navigation system | 66.80 | 78.85 | 73.57 | 73.07 | 0 | 1 | 1 | 2 |
| 8 | 1. Using keys | 58.80 | 79.02 | 77.13 | 71.65 | 2 | 0 | 0 | 2 |
| 8 | 6. Writing in any format | 68.10 | 73.16 | 71.20 | 70.82 | 4 | 0 | 4 | 8 |
| 5 | 5. Operating the television remote control | 58.20 | 76.67 | 75.83 | 70.24 | 0 | 0 | 1 | 1 |
| 2 | 2. Operating the microwave oven | 59.50 | 72.95 | 77.13 | 69.86 | 0 | 0 | 3 | 3 |
| 2 | 1. Operating domestic appliances | 59.20 | 76.18 | 73.67 | 69.68 | 1 | 1 | 3 | 5 |
| 1 | 5. Preparing cold meals | 58.70 | 71.18 | 69.70 | 66.53 | 3 | 0 | 2 | 5 |
| 2 | 3. Operating the coffee maker | 58.30 | 67.98 | 73.20 | 66.49 | 1 | 0 | 3 | 4 |
| 2 | 4. Operating the washing machine | 60.00 | 72.07 | 63.43 | 65.17 | 1 | 4 | 8 | 13 |
| 3 | 7. Obtaining money from an ATM | 66.60 | 67.46 | 60.40 | 64.82 | 0 | 0 | 0 | 0 |
| 5 | 9. Sending out e-mails on a smartphone | 54.90 | 68.82 | 66.93 | 63.55 | 0 | 1 | 3 | 4 |
| 5 | 8. Using social media on a smartphone | 53.40 | 69.02 | 67.27 | 63.23 | 0 | 1 | 2 | 3 |
| 5 | 3. Printing documents | 55.40 | 62.23 | 65.57 | 61.07 | 0 | 0 | 1 | 1 |
| 3 | 8. Paying with cash | 59.20 | 63.92 | 56.47 | 59.86 | 0 | 0 | 0 | 0 |
| 6 | 1. Playing card and board games | 57.60 | 59.57 | 59.83 | 59.00 | 0 | 1 | 1 | 2 |
| 1 | 6. Making minor repairs to the house | 44.70 | 64.67 | 62.07 | 57.15 | 0 | 1 | 2 | 3 |
| 6 | 2. Playing computer games | 55.20 | 51.80 | 56.57 | 54.52 | 0 | 1 | 1 | 2 |

**Step 4: Final item selection**

***Relevance.*** The experts considered 35/48 items (73%) relevant to PwMS, whereas PwMS and proxies considered 46/48 items (96%) and 45/48 items (94%) as relevant, respectively (Table 1). Four items (i.e., "playing card and board games", "playing computer games", "paying with cash" and "making minor repairs to the house") received a score < 60 by all groups and were therefore omitted from the questionnaire.

***Clarity.*** 39 relevant items were clearly formulated (Table 1; Appendix D). Five items were unclear, of which three items were rephrased and two items were improved by editing the format of the questionnaire. Due to the overlap, two items ("E-mailing" and "Sending out e-mails on a smartphone") were merged into one item ("sending out e-mails").

***Suggested items.*** Seven novel items were suggested by at least three participants (Figure 1, Table 1, Appendix D). The final version of the MS-IADL-Q consists of 50 items (Appendix E).

## DISCUSSION

A questionnaire for PwMS was developed to investigate cognitive performance in daily life using IADL. Relevant items were selected by (inter)national experts, PwMS and their proxies, resulting in 50 items for the final MS-IADL-Q. National and international experts did not differ in their ratings, suggesting that the MS-IADL-Q can be used in an international setting.

During the item-selection, concerns were expressed that physical problems, rather than cognitive problems, would interfere with IADL. Therefore, in the final version of the MS-IADL-Q, a question will be added to differentiate between physical and cognitive problems.

The A-IADL-Q was used as a starting point for questionnaire development because of its previously confirmed psychometric properties,[4, 6] such as the ability to detect treatment effects and small cognitive changes between groups and over time.[9, 10] We expect that the MS-IADL-Q has similar psychometric properties in PwMS. Next, the MS-IADL-Q needs to be validated in different MS-subtypes, disease durations and over time. Ideally, this will be done in an international set-up.

## REFERENCES


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## SUPPLEMENTARY MATERIALS

**Appendix A. First version of the MS-IADL-Q (after step 1; 41 items) From the Alzheimer's questionnaire (30 items):[1]**

1. Household duties

- (1.1) Carrying out household duties
- (1.2) Grocery shopping independently
- (1.3) Buying the correct groceries
- (1.4) Cooking
- (1.5) Preparing cold meals
- (1.6) Making minor repairs to the house

2. Using household appliances

- (2.1) Operating domestic appliances
- (2.2) Operating the microwave oven
- (2.3) Operating the coffee maker
- (2.4) Operating the washing machine

3. Administration

- (3.1) Paying bills
- (3.2) Managing the household budget
- (3.3) Using electronic banking
- (3.4) Making appointments
- (3.5) Using a PIN code
- (3.6) Obtaining money from an ATM
- (3.7) Paying with cash
- (3.8) Filling in forms

4. Working

- (4.1) Working

5. Devices

- (5.1) Using a computer
- (5.2) E-mailing
- (5.3) Printing documents
- (5.4) Operating devices
- (5.5) Operating the television remote control
- (5.6) Using a mobile phone or smartphone

6. Leisure time
· (6.1) Playing card and board games

7. Transport
· (7.1) Driving a car
· (7.2) Using a navigation system
· (7.3) Using public transport

8. General
· (8.1) Being responsible for his/her own medication

**From the HIV questionnaire (7 items):**
3. Administration
· (3.9) Making online purchases (on any device)

6. Leisure time
· (6.2) Playing computer games
· (6.3) Reading a book or newspaper
· (6.4) Organizing/initiating social activities

8. General
· (8.2) Using keys
· (8.3) Doing multiple things at once (multitasking)
· (8.4) Writing in any format

**From the neuro-oncology questionnaire (4 items):**
4. Working
· (4.2) Finishing work on time

6. Leisure time
· (6.2) Following a TV program or movie

8. General
· (8.5) Having a conversation with several people at the same time
· (8.6) Learning new things (such as a course, computer program, or appliance)

**Appendix B. Item evaluation by experts**
Evaluation of the MS-IADL-Q went twofold:

Step 2.a. A first version of the questionnaire (Appendix B) was sent out to sixteen Dutch experts. Experts were asked to anonymously rate the relevance of each item of the questionnaire on a visual analogue scale ranging from 0 (“not relevant at

all") to 100 ("very relevant").[1] Additionally the clarity of the item description was evaluated and potential missing items could be added.

Step 2.b. After incorporating the suggested items by the Dutch experts, a second version MS-IADL-Q (Appendix C) was sent out to twenty international experts (European and North-American) to investigate cross-cultural relevance of the included items. The international experts needed to indicate relevance of each of the items in a similar fashion as was described in step 2.a. Independent samples *t*-test or Mann-Whitney U tests (in case of non-normal distributions) were used to assess cross-cultural validation. Statistical significance was set at $p < .05$. SPSS version 24 was used to perform statistical analyses. No significant differences were found between the Dutch and the non-Dutch expert ratings for any of the activities in the survey (data not shown).

The final expert group (n = 30) consisted of 12 neurologists, six neuropsychologists, two clinical neuropsychologists, two scientists, three nurses, three rehabilitation physicians and two occupational therapists.

**Appendix C. Second version of the MS-IADL-Q (after step 2.a; 48 items)**

1. Household duties
- (1.1) Carrying out household duties
- (1.2) Grocery shopping independently
- (1.3) Buying the correct groceries
- (1.4) Cooking
- (1.5) Preparing cold meals
- (1.6) Making minor repairs to the house

2. Using household appliances
- (2.1) Operating domestic appliances
- (2.2) Operating the microwave oven
- (2.3) Operating the coffee maker
- (2.4) Operating the washing machine

3. Administration
- (3.1) Paying bills
- (3.2) Managing the household budget
- (3.3) Using electronic banking
- (3.4) Making appointments
- (3.5) Keeping appointments (added by Dutch experts)
- (3.6) Using a PIN code
- (3.7) Obtaining money from an ATM
- (3.8) Paying with cash

- (3.9) Filling in forms
- (3.10) Making online purchases (on any device)

4. Working
- (4.1) Working
- (4.2) Finishing work on time
- (4.3) Focusing attention while performing tasks at work (added by Dutch experts)
- (4.4) Dealing with distractions at work (added by Dutch experts)

5. Devices
- (5.1) Using a computer
- (5.2) E-mailing
- (5.3) Printing documents
- (5.4) Operating devices
- (5.5) Operating the television remote control
- (5.6) Using a mobile phone or smartphone
- (5.7) Making phone calls with a mobile phone or smartphone (added by Dutch experts)
- (5.8) Using social media on a smartphone (added by Dutch experts)
- (5.9) Sending out e-mails on a smartphone (added by Dutch experts)



6. Leisure time
- (6.1) Playing card and board games
- (6.2) Playing computer games
- (6.3) Following a TV program or movie
- (6.4) Reading a book or newspaper
- (6.5) Organizing/initiating social activities

7. Transport
- (7.1) Driving a car
- (7.2) Using a navigation system
- (7.3) Using public transport
- (7.4) Other participation in traffic (for instance by foot, bike, or scoot mobile; added by Dutch experts)

8. General
- (8.1) Using keys
- (8.2) Being responsible for his/her own medication
- (8.3) Doing multiple things at the same time (multitasking)
- (8.4) Having a conversation with multiple people at the same time
- (8.5) Learning new things (such as a course, computer program, or appliance)
- (8.6) Writing in any format

**Appendix D. Amendment of items**

***Clarity.*** The two items "operating domestic appliances" and "operating devices" were considered to be vague and too broad. Therefore, the order of items was changed so that these activities would be the last in their respective categories (Appendix E). Addition of the word "other" (Appendix E, activity 2.4) allows for participants to answer the question the way they see fit to their personal circumstances. The item "finishing work on time" was rephrased to "completing your tasks at work on time". Lastly, most of the comments on the two items "working" and "writing in any format" were considered to raise confusion as those items were considered to be mostly hampered by physical functioning". This was solved by editing the format of the questionnaire: in the final version of the MS-IADL-Q, PwMS will first have to fill out whether items are applicable or not, and secondly whether its function is hampered by physical or cognitive problems.

***Suggested items.*** Three items were suggested by all groups: "the ability to express your thoughts" "dealing with environmental stimuli" and "taking care of children". The latter was merged with the suggestion "taking care of pets" to yield "taking care of others". Additionally, "activities relating to self-care" was added to the questionnaire. One IADL that was mentioned remarkably often by PwMS was "planning daily activities" (n = 11) and was therefore included in the questionnaire. We decided to split this item into two new items (i.e., "planning daily activities" and "carrying out this planning of daily activities").

Finally, "dealing with environmental stimuli" and "doing puzzles" were listed as missed items by PwMS and proxies. Since two items were omitted from the category "leisure" (i.e., "playing card and board games" and "playing computer games"), the latter suggestion was combined with other hobbies such as sports and games to create a broader item: "undertaking hobbies and social activities as you wish to".

**Appendix E. Final version of the MS-IADL-Q (50 items)**

<u>1. Household duties</u>

- Carrying out household duties
- (1.2) Grocery shopping independently
- (1.3) Buying the correct groceries
- (1.4) Cooking
- (1.5) Preparing cold meals

<u>2. Using household appliances (change of order as suggested by PwMS/proxies)</u>

- (2.1) Operating the microwave oven
- (2.2) Operating the coffee maker
- (2.3) Operating the washing machine
- (2.4) Operating other domestic appliances (rephrased)

3. Administration
- (3.1) Paying bills
- (3.2) Managing the household budget
- (3.3) Using electronic banking
- (3.4) Making appointments
- (3.5) Keeping appointments (added by Dutch experts)
- (3.6) Using a PIN code
- (3.7) Obtaining money from an ATM
- (3.8) Filling in forms
- (3.9) Making online purchases (on any device)

4. Working
- (4.1) Working
- (4.2) Completing your tasks at work on time (rephrased)
- (4.3) Focusing attention while performing tasks at work (added by Dutch experts)
- (4.4) Dealing with distractions at work (added by Dutch experts)

5. Devices
- (5.1) Using a computer
- (5.2) Sending out e-mails (merged)
  - (5.2.1) On a computer
  - (5.2.2) On a smart phone (added by Dutch experts)
- (5.3) Printing documents
- (5.4) Operating the television remote control
- (5.5) Using a mobile phone or smartphone
- (5.6) Making phone calls with a mobile phone or smartphone (added by Dutch experts)
- (5.7) Using social media on a smartphone (added by Dutch experts)
- (5.8) Operating other devices

6. Leisure time
- (6.1) Following a TV program or movie
- (6.2) Reading a book or newspaper
- (6.3) Undertaking leisure activities (added by PwMS/proxies)
- (6.4) Initiating social activities

7. Transport
- (7.1) Driving a car
- (7.2) Using a navigation system
- (7.3) Using public transport
- (7.4) Other participation in traffic (for instance by foot, bike, or scoot mobile; added by Dutch experts)

8. General

- (8.1) Using keys
- (8.2) Planning daily activities (added by PwMS/proxies)
- (8.3) Carrying out this planning of daily activities (added by PwMS/proxies)
- (8.4) Taking care of self (added by PwMS/proxies)
- (8.5) Taking care of others (children, pets, others) (added by PwMS/proxies
- (8.6) Being responsible for his/her own medication
- (8.7) Doing multiple things at the same time (multitasking)
- (8.8) Dealing with environmental stimuli (added by PwMS/proxies)
- (8.9) Expressing your thoughts and feelings clearly (added by PwMS/proxies)
- (8.10) Having a conversation with multiple people at the same time
- (8.11) Learning new things (such as a course, computer program, or appliance)
- (8.12) Writing in any format

## SUPPLEMENTAL REFERENCES

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