

BMJ Open Protocol: Prospective evaluation of feasibility, added value and satisfaction of remote digital self-assessment for mild cognitive impairment in routine care with the neotivCare app

Emrah Duzel ^{1,2}, Michael Schöttler,³ Harriet Sommer,³ Martin Griebe⁴

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¹German Center for Neurodegenerative Diseases, Magdeburg, Germany

²Institute of Cognitive Neurology and Dementia Research, Otto von Guericke University Magdeburg, Magdeburg, Germany

³Roche Pharma AG, Grenzach-Wyhlen, Germany

⁴Department of Neurology, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany

Correspondence to

Dr Emrah Duzel;
emrah.duezel@dzne.de

ABSTRACT

Introduction Timely diagnosis of mild cognitive impairment (MCI) in Alzheimer's disease is crucial for early interventions, but its implementation is often challenging due to the complexity and time burden of required cognitive assessments. To address these challenges, the usability of new unsupervised digital remote assessment tools needs to be validated in a care context.

Methods and analysis This multicentric healthcare research evaluation survey, *re.cogni.ze*, aims to evaluate physician satisfaction with a remote digital assessment solution (neotivCare) in primary and specialised routine care in Germany. Over a period of 22 months, physicians in different regions of Germany will recommend the application (app) to approximately 1000 patients for a 12-week self-assessment of cognition. The primary endpoint is the evaluation of physicians' and patients' overall satisfaction with neotivCare and with neuropsychological questionnaires/standard procedures using a Likert scale, while secondary endpoints include user-friendliness, qualitative assessment of acceptance and potential improvements on medical routine services. The study also aims to evaluate the proportion of physicians or patients attributing added value to neotivCare compared with standard paper-pencil tests. The study results will provide insights into the feasibility, efficiency and acceptance of new digital tools for MCI diagnosis in routine care. The *re.cogni.ze* survey will thus provide proof-of-concept information for the implementation of remote digital cognitive assessment apps for MCI into medical routine care.

Ethics and dissemination This study was approved by the ethics committee of the State Medical Association (Landesärztekammer) Baden-Württemberg, (F-2021-161) as the leading committee and nine ethics committees local to the participating healthcare professionals (Lower Saxony, North Rhine, Westphalia-Lippe, Hesse, Bremen, Berlin, University of Göttingen, Charité, University of Rostock). The results can be shared (upon reasonable quest) to improve routine clinical processes and holistic approaches.

INTRODUCTION

In Alzheimer's disease (AD), cognitive complaints typically precede the onset of

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Large-scale assessment of feasibility, satisfaction and added value of remote digital self-assessment of mild cognitive impairment in routine care.
- ⇒ Outcome measures obtained from general practitioners, specialists as well as patients.
- ⇒ The study is limited by a single application and absence of a control group.

dementia by several years. Mild cognitive impairment (MCI) is defined as significant impairment relative to an age norm in one cognitive domain, typically episodic memory,¹ with no or only minimal impairment in activities of daily living.² Cognitive complaints associated with normal cognitive performance are referred to as subjective cognitive decline (SCD).³ A timely distinction between SCD and MCI is important to initiate preventive interventions and early treatment in case of MCI and to ease concerns in case of SCD.^{4 5} Additionally, early diagnosis might facilitate the research of effective agents in clinical studies when irreversible neurodegeneration is still limited.⁶

In routine care, patients with memory complaints are typically assessed by paper-pencil screening tools like the Clock-drawing Test or the Mini Mental State Examination which have been primarily developed to detect dementia and have low sensitivity and specificity for MCI.^{7 8} More comprehensive paper-pencil tests such as the Free and Cued selective reminding test are time-intensive and resource-intensive⁹ because they require trained neuropsychologists. Paper-pencil tests are performed only once in a clinical setting which can be stressful for patients and potentially unrepresentative of their true cognitive abilities.

Remote methods for extensive cognitive testing and self-monitoring of cognitive impairment using digital application (app)-based solutions can help to overcome these challenges and simplify the diagnosis of MCI in routine care.^{10–14} Favourable sensitivity and specificity of digital tests compared with paper–pen assessments have been reported.¹⁵

As an emerging technology, remote self-assessment of cognition using digital tools is a new approach in healthcare, and knowledge about feasibility, handling by physicians and patients, acceptance and satisfaction of use by physicians and patients in a healthcare setting is much needed.¹⁶ In particular, it is unclear how physicians would rate their satisfaction with such a tool in comparison with standard paper–pencil tests, to what extent they would see an added value in the diagnostic assessment of cognitive impairment compared with paper–pencil tests, whether a digital solution would simplify MCI assessment from a physician perspective, whether a digital solution would alter the number of MCI diagnoses physicians believe they would make in their practice, whether a digital solution would improve the communication between physicians and patients, how well app results would be taken into account regarding further diagnostic and therapeutic decisions and how the user-friendliness of a digital solution would be rated. From the perspective of patients, it is unclear how acceptable they would rate self-assessment, how much concern handling and using an app would induce, how self-assessment would influence their concerns and uncertainties about cognitive deficits, how much instruction and training users would require to use the app but also to understand the outcome of the app results.

These questions are addressed in the re.cognize study (figure 1), which is an open-label, cross-sectional, survey-based evaluation of user satisfaction and experienced added value of a remote, smartphone-based self-assessment tool for MCI, neotivCare. The app is designed to simplify and accelerate the diagnostic process for patients, treating physicians and specialised memory clinics while offering comprehensive testing of episodic memory over a longer period of time.

neotivCare uses a set of anatomically informed and non-verbal, memory-centred tasks, which have been implemented for remote assessment in prospective cohort studies—including the DELCODE Study of the German Center for Neurodegenerative Disease,¹³ the BioFinder Study, the US Wisconsin Registry for Alzheimer's Prevention cohort of the Alzheimer's Disease Research Center in Wisconsin¹⁷ as well as in studies at University College London (COVID-19)¹⁸ and Citizen Science studies.¹⁴ The tests target cognitive processes in brain regions that are affected by early tau and amyloid pathology,^{19 20} and analyse the ability of short-term mnemonic discrimination of object and scene representations, short-term and long-term cued-recall of object–scene association and long-term scene recognition memory.²¹ Its diagnostic accuracy in remote and unsupervised use and feasibility to be used by memory-impaired persons in a memory clinic context have been recently reported.¹³

Performance in the tests implemented in neotivCare is summarised into a composite score, the Remote Digital Memory Composite (RDMC). The RDMC is robustly correlated with in-clinic measurements of the Preclinical Alzheimer's Cognitive Composite 5 (PACC5) and shows sensitivity of over 80% and specificity of over 70%

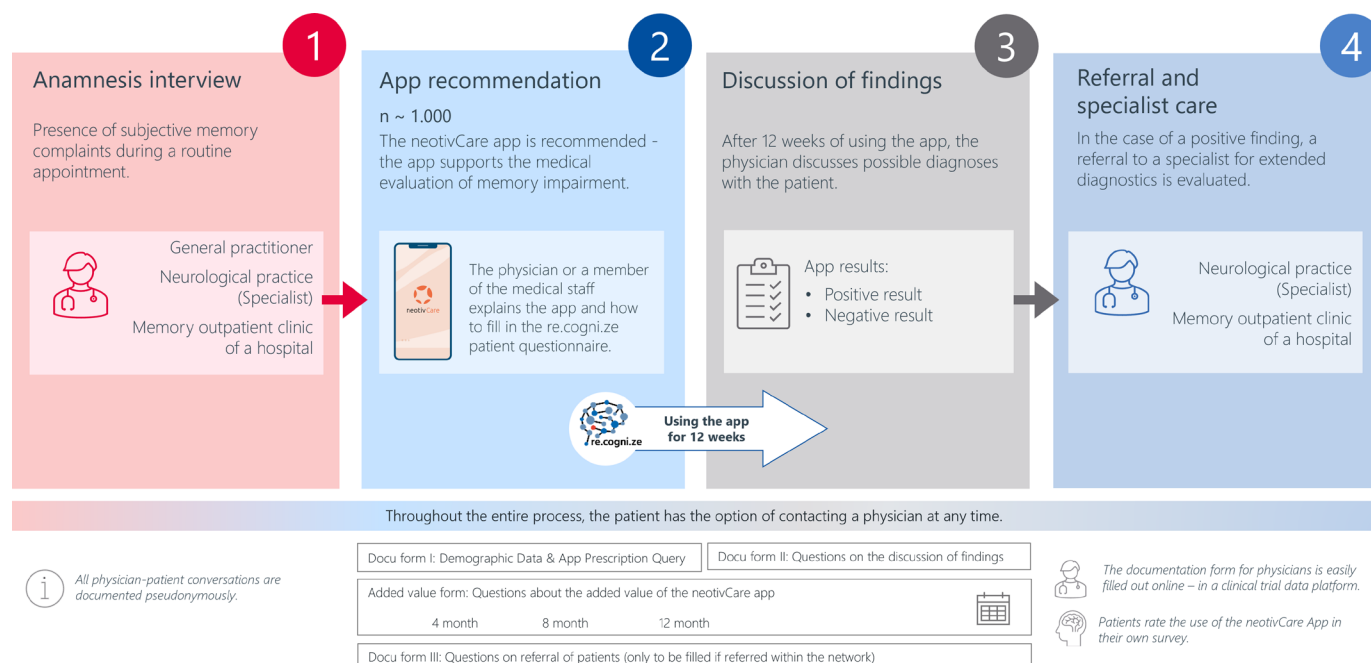


Figure 1 Study design of the evaluation study re.cognize.

for a PACC5-based classification into MCI or cognitively normal. The retest reliability across repeated RDMC tests is high.¹³ After completion of self-assessment with neotivCare, RDMC results are summarised in a patient report within the app.

The re.cogni.ze study started in April 2022 and will be completed in January 2024. As illustrated in [figure 1](#), general practitioners (GPs) and specialists prescribed the app to patients who reported memory complaints in a routine appointment if they suspected MCI. Patients completed self-assessment within 12 weeks and then discussed the neotivCare app report with their physician during a follow-up appointment. The physician then decided about further patient management. Physicians and patients documented their use of the app and responded to app-independent electronic and paper-based questionnaires on satisfaction and added value of neotivCare.

METHODS

Study design

re.cogni.ze is an open-label, cross-sectional, survey-based evaluation of user satisfaction and experienced added value of neotivCare for physicians and their patients with memory complaints in a healthcare research setting. It is currently actively recruiting. First patient in was in April 2022. Last patient out is planned for December 2023. The evaluation survey targets the physicians prescribing neotivCare as well as the patients using neotivCare. There is no control group. The study design is shown in [figure 1](#). The study questionnaire has been developed by the authors in cooperation with a panel of recruiting physicians and patients.

Study setting

We are conducting the survey in routine care, in five regional multicentric networks of doctors' offices as well as memory clinics in Germany. A total of 43 physicians including neurologists, psychiatrists and primary care physicians participate in the trial.

Study population

The study population includes (a) the doctors who prescribe the app and evaluate the app results and communicate the results to the patients, and (b) the patients—predominantly between 60 and 80 years—who consult the doctor due to subjectively perceived disturbances of memory. Approximately 1000 app recommendations are intended. The sample sizes were calculated for the physicians' responses to the primary endpoints ([table 1](#)).²²

Inclusion and exclusion criteria

Patients with subjectively perceived disturbances of memory are eligible. The memory problems can be raised by the patients, their relatives or by the physicians. The physicians' recommendation is based on standardised

information material about test principles, certified indication of the app, age range, scheduling and scientific validation of neotivCare. Manifest dementia, which is defined as a clinical diagnosis of dementia made by a physician based on standardised diagnostic criteria such as the Diagnostic and Statistical Manual of Mental Disorders or the International Classification of Diseases, is an exclusion criterion for the use of neotivCare. Patients under the age of 18 years are excluded from the study. Patients deemed eligible, as well as reasons for not prescribing or refusal of the patients, are recorded. Patients might be unsuitable due to medical, social or technical reasons.

Patient and public involvement

The study questionnaires have been developed by the authors in cooperation with physicians and patients.

Study duration

22 months.

Study protocol

The primary and secondary endpoints and additional endpoints of re.cogni.ze are listed in [table 1](#) separately for physicians and patients. Physicians' and patients' experiences are enquired with documentation forms and a survey questionnaire (using the Software Marvin by XClinical, Germany), respectively, which was endorsed by an ethics committee (Landesärztekammer Baden-Württemberg, Ethik-Kommission, F-2021-161). First, the participating physicians will document patient demographic and anamnestic information in eligible patients, regardless of whether the app was prescribed or not.

After discussion and recommendation, patients give informed consent, receive an app access code and the patient questionnaire to be completed independently at home. The physicians will document each contact with the included patients, beginning with the app recommendation. In addition, they will fill in the added value questionnaire after months 4, 8 and 12.

App procedures

Upon prescription, patients will start the app-based assessment unsupervised and self-administered in their everyday environment for a time course of 12 weeks, once a week for 15–20 min. Out of these measurements, the app generates a medical report including the RDMC relative to the age-dependent reference group in order to distinguish between normal cognitive abilities and MCI-typical impairment of memory. Patients are recommended discussing the results of this report with their treating physician to understand it properly and to plan further actions, jointly with their physician. In addition to the RDMC, the medical report shows contextual information for each single app test: the time at which each app test was conducted together with a self-rating by the patients regarding concentration, distraction and performance and a free comment field that shows subjectively relevant issues that patients felt they would like their

Table 1 Excerpt of the main endpoints in re.cogni.ze

Endpoint	Definition
Primary	
Satisfaction with neotivCare and with neuropsychological standard tests (physician and patient reported)	Endpoint 1: binary yes/no response to the question: ‘Does the app has an added value to standard test procedures?’ Endpoint 2: two 7-item Likert scales regarding satisfaction (from very dissatisfied to very satisfied): one for the app and one for standard test procedures
Secondary	
Added value of neotivCare in comparison with neuropsychological standard tests (physician and patient reported)	Proportion of physicians or patients attributing added value to neotivCare in comparison with neuropsychological standard tests
Specific aspects regarding the added value of neotivCare in comparison with neuropsychological standard tests (physician and patient reported)	Proportion of physicians or patients attributing added value regarding, for example, accelerated diagnosis, simplified diagnosis, active involvement of the patient, better doctor–patient communication and others
Further endpoints	
Patient compliance	Proportion of patients who discussed the app results with the physician after agreeing to use it following the doctor’s recommendation
Likelihood that neotivCare will be used again (physician reported)	Mean of an 11-item Likert scale regarding reuse (from not likely to very likely)
Network effect of neotivCare (physician reported)	Proportion of physicians attributing an improved effect in terms of, for example, network collaboration and the respective reasons for improved collaboration
Changes in diagnoses due to neotivCare in the current quarter compared with the previous quarter without neotivCare (physician reported)	Proportion of physicians attributing an effect in terms of, for example, frequency of MCI diagnosis
Findings 12 weeks after using neotivCare (physician and patient reported)	Several questions regarding the memory performance falling within/outside the normal range, for example, education about preventive measures, explanation of a potential diagnosis following preparation of a therapy plan, referral to a specialist for further differential diagnostic assessment
User-friendliness of neotivCare (patient reported)	Several questions regarding, for example, prescription, handling, frequency of use, time expenditure
Overall assessment of neotivCare (patient reported)	Several questions regarding, for example, concerns and uncertainties about cognitive deficits, classification of memory problems, reuse, handling, recommendation to a friend, potential for improvement (in, for example, usability of the memory tests, adequacy of training before memory tests, preparation or explanations of findings, other functions of the app such as reminder or support functions)
app, application; MCI, mild cognitive impairment.	

physicians to know (for instance, ‘I did not sleep well last night’).

Outcomes and analyses

The primary endpoint in re.cogni.ze is the evaluation of overall satisfaction with neotivCare and with standard neuropsychological tests. It will be assessed with two 7-item Likert scales (from very dissatisfied to very satisfied). The secondary endpoint evaluates the proportion of physicians or patients attributing added value to neotivCare compared with standard paper–pencil tests. Further endpoints include user-friendliness, qualitative assessment of acceptance and potential improvements on medical routine services. The most relevant endpoints,

their definitions and its assignment for patients and doctors are shown in [table 1](#).

To represent the patients’ as well as the physicians’ point of view in supporting the diagnosis of MCI, analyses will be performed for both groups. We will also explore potential demographic and clinical predictors of the app’s feasibility and user compliance. This will include factors age, sex, education level and whether a person lives alone or not.

Ethics and dissemination

This study was approved by the ethics committee of the State Medical Association (Landesärztekammer) Baden-Württemberg, (F-2021-161) as the leading committee

and nine ethics committees local to the participating healthcare professionals (Lower Saxony, North Rhine, Westphalia-Lippe, Hesse, Bremen, Berlin, University of Göttingen, Charité, University of Rostock). The results will be published in a peer-reviewed journal.

DISCUSSION

The standard-of-care diagnostic tools for patients with memory complaints are neuropsychological paper-pencil tests, which are highly time-intensive and resource-intensive. Consequently, in-depth neuropsychology cannot meet the existing and emerging needs due to the demographic change in the context of diseases affecting cognition. Furthermore, GPs play a minor role in the diagnosis of MCI today, although they are often contacted first. Consequently, there is a need to empower GPs with efficient tools for MCI assessment and to improve the handover of affected patients from GPs to specialists.

Unsupervised remote digital assessment may effectively relieve the diagnostic burden on both patients and healthcare providers and improve accessibility and availability of extensive cognitive testing over time periods rather than a single moment. Widespread implementation of digital assessment can improve case finding at the GPs for in-depth diagnostic work-up in specialised settings. The same technology integrated in the everyday life can also improve the feasibility of high-frequency monitoring of cognition and open new avenues for integrating digital companion technologies to facilitate preventive and therapeutic interventions. Moreover, patients' health-related competencies and sovereignty can be enhanced.

The implementation of remote digital assessment offers flexibility regarding testing schedules and duration that is not available in a primary care setting as well as for on-site neuropsychology. In the case of neotivCare, patients perform weekly tests at home lasting 15–20 min, with the time of day left up to them. Each of the three test types implemented in neotivCare is repeated four times over a period of 12 weeks. For the composite test result (RDMC) calculation, at least two of the four repetitions need to be completed and the lowest performance is excluded. This redundancy in the test scheduling is aimed to reduce patient anxiety towards single tests and to improve the feasibility of obtaining a composite after prescription. The 12-week testing period places the completion of the assessment and the provision of the report close to the regular 3-month rescheduling of physician appointments. This form of implementation has been shown to be feasible in pilot studies in healthcare settings and has received acceptance by study participants and in Citizen Science settings.¹⁴

The purpose of digital assessment of MCI with neotivCare is to provide decisive guidance for the timely detection of prodromal stages of AD with less effort and burden for all concerned parties. With the advent of disease-modifying treatments in prodromal and preclinical AD, the identification of patients with MCI becomes

an important healthcare challenge. Digital tools that help to distinguish between SCD and MCI may facilitate both, treatments in prodromal AD as well as preclinical treatments in SCD. Therefore, by screening and continuous monitoring of cognitive functions of patients with potential AD, a patient-relevant improvement of healthcare structures and processes may be expected.^{23 24}

The healthcare research re.cogni.ze will evaluate the integration of neotivCare in routine care settings and provide insights about the benefit and acceptance of digital, remote self-assessment in routine care. It will help to close knowledge gaps for digital assessment regarding feasibility, handling by physicians and patients, acceptance and satisfaction of use by physicians and patients in a healthcare setting. It will inform about how physicians rate their satisfaction with such a tool in comparison with standard paper-pencil tests, to what extent they see an added value in the diagnostic assessment of cognitive impairment compared with paper-pencil tests, whether they believe that this digital tool will simplify MCI assessment, whether the number of MCI diagnoses in their practice increases or decreases with this tool, whether this digital solution improves their communication with patients regarding MCI, how well they can take app results into account regarding further diagnostic and therapeutic decisions and how the user-friendliness the digital solution was felt to be. From the perspective of patients, the study will provide insights into how they rate self-assessment with neotivCare, how much concern handling and using the app creates, how self-assessment influences their concerns and uncertainties about cognitive deficits, whether instruction and training they received are sufficient to use the app but also to understand the outcome of the app results.

Strengths and limitations of this study

A major strength of re.cogni.ze is that it is the first large-scale assessment of feasibility, satisfaction and added value of remote digital self-assessment of MCI in routine care. Another strength is that it includes both GP and specialist settings. Therefore, it will provide first large-scale insights into how GPs, specialists and their patients handle and rate remote digital self-assessment. Limitations include that it focuses on a single app and therefore some of the results may be specific to this solution. A second limitation is that there is no control group. As such, re.cogni.ze cannot provide quantitative data about the impact of neotivCare on the care pathways of patients with suspected MCI. We see such an assessment as a follow-up study requiring a complex design such as cluster randomisation of GPs and specialists into standard of care or digital assessment arms.

CONCLUSION

While re.cogni.ze will evaluate several specific outcomes regarding user satisfaction and added value of neotivCare and its way of implementation, we also expect the

results to be important for understanding the usability and acceptance of remote digital assessment in general. The findings can be shared with future app users, developers and healthcare providers to improve routine clinical processes and holistic approaches.

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Contributors MS and ED designed the study. HS served as biostatistician for all aspects of the study design and outcome measures. MG is the PI of the study. All authors will analyse the results jointly. ED, MS, MG and HS wrote the manuscript together.

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Competing interests ED is co-founder of neotiv and holds shares of neotiv; is CMO at neotiv; and has done paid consultancy work for Biogen, Roche, Rox Health, UCLC, Lilly and Heptares. MS and HS are employed by Roche Pharma AG, Germany and are stakeholders of Roche. MG received honoraria from Roche Pharma AG, Germany.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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ORCID iD

Emrah Duzel <http://orcid.org/0000-0002-0139-5388>

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