LUND UNIVERSITY
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Effectiveness of the Digital Platform, Support, Monitoring and Reminder Technology for Mild Dementia (SMART4MD) for People with Mild Cognitive Impairment and Their Informal Caregivers

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Abstract

Background: As the population ageing increases, the dramatic rise in cognitive disorders such as mild cognitive impairment and dementia has become a public health priority. Mobile health technology is a unique non-pharmacological intervention for dementia and cognitive disorders. A digital platform (Support Monitoring and Reminder for Mild Dementia: SMART4MD) is created for persons with mild cognitive impairment (MCI) and informal caregivers. A randomized controlled trial was conducted on the SMART4MD application.

Objective: The objective was to study the effects of the SMART4MD compared to standard care in Sweden and Spain over an 18-month follow-up period.

Methods: One thousand and seventy-eight dyads were enrolled: 537 dyads in the intervention group and 541 dyads in the control group. The primary outcome measure was health-related quality of life using the European Quality of Life 5 dimensions, 3 Levels, (EQ-5D-3L) index. Mean differences were analyzed with independent samples T-test. Simple and multiple linear regression analyses were conducted for continuous outcomes and logistic regression analyses for the categorical outcomes. Age, gender, education, living arrangements and baseline scores were adjusted for.

Results: There were no significant difference observed in the health-related outcomes between the intervention and the control group at follow-up. For PwMCI, the mean differences of the outcomes were: EQ-5D-3L (EVAS) = 0.00 (p = 0.84), total QALYs gained = 0.01 (p = 0.77), composite QoL-AD = 0.42 (p = 0.30), MMSE scores = 0.40 (p = 0.22). For the informal caregivers, the mean differences were EQ-5D-3L (EVAS) = 0.02 (p = 0.13), total QALYs gained = 0.03 (p = 0.12), ZBI = 0.31 (p = 0.61).

Conclusion: The effect of the SMART4MD for PwMCI and the caergivers was insignificant and inconclusive. Further studies are needed to add on the evidence.

Trial registration: ClinicalTrials.gov: NCT03325699

1 Table of Contents

2 Introduction

Population ageing is increasing, and the number of people aged 60 years and above was 1 billion in 2019 and is expected to reach 2.1 billion by 2050 (1). WHO recognizes dementia as a public health priority alongside the ageing population rise (2). An estimated 50 million people live with dementia worldwide, and it is expected to double every 20 years, reaching 75 million by 2030 (3). Dementia is a syndrome which affects cognitive abilities beyond the normal biological ageing (2). There is an intermediate stage between the normal cognitive ageing and dementia named mild cognitive impairment (4).

People with MCI (PwMCI) have different dependency levels, which associate with decreased health-related quality of life (HRQoL) (5). In individuals with MCI, basic daily activities such as eating and bathing are not affected. Still, as cognitive abilities become impacted, the more complex actions which need cognitive skills are affected (5). These activities include telephone use, driving, shopping, cooking food, and managing medication (5). Consequently, the effect on daily living due to cognitive impairment significantly impacts the quality of life (6). Furthermore, it exerts pressure on the health system, services, and support system for older people (7).

As the dependency increases in individuals with MCI, the burden falls upon their caregivers, primarily informal caregivers, usually a spouse or a child (8). The carers of people with dementia bear the highest burden compared to caring for other diseases such as heart/lung disease, stroke, fracture, and depression (9). As the person copes with reduced autonomy due to MCI, the informal caregiver's role is essential to assist and support the person. For example, one of the crucial aspects of independence is the daily medication management of the PwMCI. Cognitive impairment and impaired memory make PwMCI challenging to manage in their medication-taking (10). Medication errors such as under-dosing or overdosing are common in PwMCI (10), and caregivers need to learn about several medications the individuals with MCI are taking. Technology can support the independent living of the PwMCI and reduce the caregiver's burden.

Mobile health (mHealth) has developed with the high rise of mobile application uses (11). According to the National Institutes of Health (NIH) Consensus Group, mHealth is defined as "the use of mobile and wireless devices to improve health outcomes, health care services, and

health research" (11). Mobile technology can effectively monitor people with chronic medical diseases, including mental health conditions such as psychosis, depression, and bipolar disorder (12). Furthermore, technology has proven facilitated patient self-management and screening for depression and assessing cognitive function in older adults (12). Interventions that boost autonomy and help cope with reducing independence have been proven beneficial (6). Up to date, MCI is incurable; therefore, mHealth offers a way of non-pharmacological intervention with a great potential to improve the QoL of both the PwMCI and their caregivers (11). To people with the cognitive condition, good quality of life refers to the experience of independence to a certain extent and managing daily-life activities (7).

Currently, a few different telemedicine and mHealth intervention studies on cognitive conditions exist (13-25). There are studies on the efficacy of the telemedicine intervention on caregivers of persons living with dementia and Alzheimer's disease using videoconferencing (13) and computer-mediated automated interactive voice response (IVR) intervention (14) and telephone-based cognitive behaviour therapy (22). However, the outcomes of these studies were inconsistent, only caregivers were included, and the sample sizes were relatively small (13, 14, 22). Scullin et al. conducted a 4-week RCT to study the feasibility and efficacy of a digital voice recorder app and a reminder app on prospective memory functioning in 52 older adults with MCI/mild dementia (24). Results showed that persons with mild dementia could use smartphones adequately trained (24).

Furthermore, the training on smartphone strategies was found to have advantages in prospective memory and quality of life (24). Another RCT was evaluated for a computerised platform, a technology platform for the assisted living of people with dementia and their carers (ALADDIN). There were significant improvement results in the quality of life of the carers (20). ALADDIN provides educational information about dementia to carers and offers social networking opportunities through a forum (20). A systematic review categorised health outcomes and efficacy of mHealth apps for persons with cognitive impairment and found that most mHealth app interventions that evaluated health outcomes had shown improvements in PwMCI, Alzheimer's disease, and dementia (11). However, due to the quality of these studies, more randomised controlled trials with large sample sizes and trial designs that minimise bias were recommended (11).

The SMART4MD (support, monitoring and reminder technology for mild dementia) is a tabloid application primarily created to support PwMCI to live a structured life in everyday life and reduce the stress of PwMCI and the informal caregivers (7). The application sends reminders about medication, healthcare appointments, and social appointments (7). It supports cognitive function by activities such as clock, calendar, brain games and photos (7). The PwMCI can share information about their health status and mood as an option to family and informal carers (7). The SMART4MD trial was a pragmatic, multicenter, randomised controlled trial involving PwMCI and informal caregivers. This study aims to study the effects of the SMART4MD app on the health-related quality of life and cognitive function for PwMCI and health-related quality of life and the burden on their informal caregivers.

3 Objectives

The research objectives are as follows:

For PwMCI, to estimate the effectiveness of the SMART4MD app in addition to standard care on:

1. health-related quality of life measured by generic European quality of life, five dimensions, three levels (EQ-5D-3L) with European Visual Analogue Scale (EVAS) and the UK Tariff
2. quality of life measured by the dementia-related quality of life – Alzheimer's disease (QoL-AD) questionnaire
3. cognitive impairment function measured by mini-mental state examination (MMSE) questionnaire
4. medication adherence

For informal caregivers, to estimate the effectiveness of the SMART4MD app in addition to standard care on:

1. health-related quality of life measured by EQ-5D-3L (EVAS) and UK Tariff
2. carer burden measured by Zarit Burden Interview (ZBI) scores

The research hypotheses were tested as follows:

- Null hypothesis

There is no difference between the two groups in EQ5D (EVAS, UK Tariff), QoL-AD, QALY, and medication adherence in PwMCI, and there is no difference between the two groups in EQ5D (EVAS, UK Tariff), ZBI scores and QALY in the caregiver at 18 months follow up.

- Alternative hypothesis

The SMART4MD application causes a difference between the two groups in EQ5D (EVAS, UK Tariff), QoL-AD, QALY, medication adherence in PwMCI, and EQ5D (EVAS, UK Tariff), ZBI scores and QALY in the caregiver at 18 months follow up.

4 Method

4.1 The SMART4MD trial

This trial was a pragmatic, multicenter, randomised, controlled trial (registration number: NCT03325699). The consolidated standards of reporting trials (CONSORT) guidelines were followed (7). The study sought to evaluate the impact of the SMART4MD tablet app on people with mild cognitive impairment and their informal caregivers (7).

4.1.1 Setting

The trial was conducted in 3 European countries: Spain, Sweden, and Belgium, and 4 participant sites, which are Consorci Sanitari de Terrassa (Catalonia, Spain), Servicio Andaluz de Salud (Andalusia, Spain), Blekinge Institute of Technology (Karlskrona, Sweden) and University College Leuven-Limburg (Belgium) from December 2017 to September 2020. This study used data from 3 participant sites in Spain and Sweden. The fourth site in Belgium recruited too few participants (n=4); therefore, it was excluded from this study.

4.1.2 Participants

Participants were recruited from primary care, secondary care services (memory clinics), outpatient clinics, day hospitals, specialist mental health care units, geriatric medicine units, and neurology services units in Region Blekinge in Southeast Sweden and Catalonia and Andalusia in Spain. There were 1,078 dyads of PwMCI and their informal caregivers in the trial, randomised 1:1 block randomisation to control (n=541) and intervention group (n=539) at baseline. At 18-month follow-up, there were 650 dyads with control group (n= 337) and intervention group (n= 313).

Patients and their family caregivers were selected with the following criteria:

4.1.3 Inclusion Criteria:

Participants were recruited if

- they score 20 to 28 points on the MMSE,
- assessed to have experience memory problems for more than six months,
- who are older than 55years, receiving home care, and have an informal carer,
- if they take prescribed medication and self-manage their medication use,
- no impairments (visual, hearing or motor) might hinder the app usage.

4.1.4 Exclusion Criteria:

Participants were not eligible if any of the following conditions apply:

- Have a terminal illness with less than three years of expected survival
- Geriatric depression scores >11 or cognitive impairment due to abuse and other psychiatric diagnoses such as bipolar disorders, schizophrenia, and developmental disorders. The detailed participation at sites throughout the trial can be observed in Figure1.

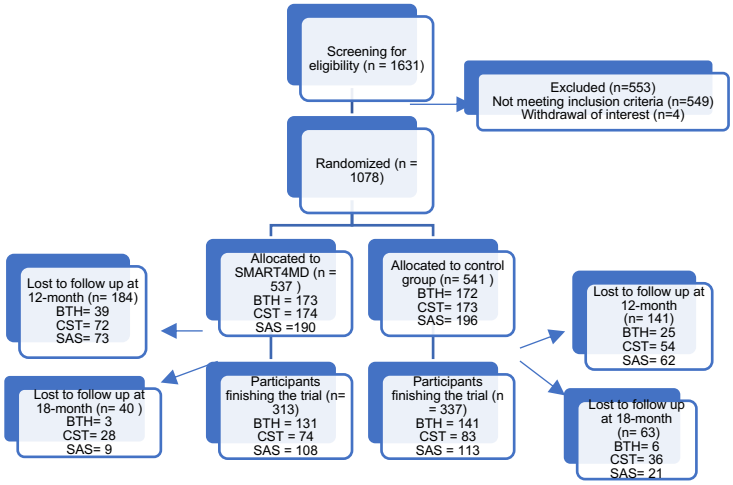

Figure 1. Flow chart of the participation at sites information

4.1.5 Intervention

Participants in the intervention group received standard care plus the SMART4MD app. Data-enabled tablets with the SMAR4MD app installed were provided to the participants. The application was meant to be used daily with the assistance of informal caregivers if needed. The dyads in the intervention group received a 1.5-h training session on application usage by a research nurse (26).

4.1.6 Control

The control group only received their treatment as usual. Treatment as usual, mainly involves standard health care from the primary health care centre. In Sweden, routine care for the elderly includes a yearly check-up visit to a physician and refilling prescriptions (26). In Spain, every person is assigned a general practitioner (GP), and the GP refers to the specialist (27). In the case of retired persons, almost every medicine, including anti-dementia drugs, is paid for by the government (27). The participants' standard care outside the trial is different individually if individuals have various comorbidities, health-seeking behaviours, etc. (27).

4.2 Ethical consideration

The trial followed the principles of the declaration of Helsinki. Generally, as this is a randomised controlled trial involving humans, no harm should be done, and the benefit of the intervention should outweigh the risk. As this is a pragmatic RCT comparing treat as usual, the risk is minimal (28). Ethical approval was granted at the participating sites by the regional ethical review boards. Informed consent was obtained from the dyads. For PwMCI, consent was actively sought and reaffirmed on every time the data were obtained. For informal carers, consent was gained at the start of the trial. Participants can withdraw from the study for reasons, details were described somewhere in the protocol of the trial (7). Data protection and confidentiality are ensured to comply with the laws of each EU member state. The anonymity of the participants was maintained.

4.3 Statistical Analysis of Data

4.3.1 Outcome measures

4.3.1.1 For PwMCI

4.3.1.1.1 Health-related quality of life (HRQoL)

The primary outcome was the EQ-5D-3L scores using the European EQ-5D VAS valuation (EVAS) (28). The EVAS was used as the study data was from two European countries, Spain and Sweden. The UK tariff is also used as it is commonly used in the scientific literature to increase comparability (29). The scores were then used to calculate the accumulated quality-adjusted life years (QALYs) using the area-under-the-curve approach (30).

4.3.1.1.2 Quality of life-Alzheimer's disease (QoL-AD)

The QoL-AD is commonly used in measuring the quality of life for dementia (31). The two versions, the self-report in interview format to the PwMCI and proxy report version, a questionnaire completed by caregivers, were used. A weighted composite score is calculated

twice the weight of the PwMCI self-reported scores plus the caregiver's assessment, divided by 3 (26).

4.3.1.1.3 Mini-mental state examination (MMSE)

MMSE is widely used for screening the cognitive status (31) and is valuable for serially documenting the cognitive change (32). The score ranges from 0 to 30, with higher scores showing better cognitive functioning (32).

4.3.1.1.4 Medication adherence

Adherence to prescribed medication was assessed at the 6-, 12- and 18-month visits. The PwMCI's documented prescription for medicines was compared with the number of pills taken in the previous 30 days before the assessment at each follow-up month. A maximum of 2 drugs for each participant in the pill count was chosen.

Pill count is the number of pills taken divided by the prescribed number of pills/doses per day multiplied by the number of specified days between two visits (7). Medication adherence was assessed as a binary variable 1: if the medication adherence rates were between 80% (20% doses/pills missed) and 110% (taking 10 % more doses/pills) and 0: if they were not. The cut-off was used at 80%, commonly used in MCI (33) and as described in the protocol (7).

4.3.1.2 For informal caregivers

4.3.1.2.1 Health-related quality of life (HRQoL)

Quality of life for the caregivers was assessed by the EQ5D-3L index using EVAS and the UK tariff and calculation of the accumulated QALYs.

4.3.1.2.2 Zarit Burden Interview (ZBI)

To monitor the mental wellness of informal caregivers, the Zarit burden interview short-form (ZBI-12) was used (34). The lower the score, the better the outcome is; therefore, the scores were inverted to be aligned with the other index scores.

4.3.2 Data Analysis

Simple descriptive statistics (arithmetic mean and standard deviation) were used to summarise continuous variables and frequency for categorical variables. Intergroup differences were checked for balance for both demographic characteristics and outcome scores at baseline and follow up by independent samples T-test and presented as mean difference with standard deviation and p-value. Intragroup differences between baseline and follow-up were estimated using paired t-test. Medication adherence was estimated as mean values at each follow up 6-, 12- and 18-month period using the Chi-squared test. The analysis used intention to treat principle.

The effect of the SMART4MD app on the index scores and medication adherence was then analysed with an ordinary least squares (OLS) regression model for the continuous variables of outcome measures and logistic regression for medication adherence. As the prevalence of MCI was found to be increased with age, being women, living alone, low education attainment (4) and a previous study has evidence that old age, being female, single, low education and living alone may have a negative association with the HRQoL, in general, more senior adults (35), these factors were considered as potential confounders and adjusted for the regression analyses. For linear regression, coefficient, p-value, and 95 % confidence interval were reported. For logistic regression, the odds ratio, p-value and 95 % confidence intervals were reported with significant levels shown with stars.
The data analysis was done with Stata software, version 17. All p-values less than 0.05 were considered significant.

5 Result

5.1 Demographic characteristics

Table 1 shows the summary statistics for demographic characteristics of PwMCI and informal caregivers both at baseline and follow-up. Demographic characteristics were not significantly different between the two groups (Table 1).

There were 40 % drop-out rates at 18 month (Figure 1). For PwMCI, there was a significant age difference (p- value= 0.0008), the mean age of dropouts was 75.88, and the non-drop-out was 73.76 in the intervention group in those who dropped out. 62.22 % were females in the intervention group who dropped out. (p-value= 0.005). In the control group 65.35 % had at least elementary school education (p = 0.029). 60.89 % of the intervention group who dropped out were either married or with a partner (p= 0.024), while, in the control group who dropped out, 62.87 % were married/partnered (p= 0.002). There was no difference in the EQ-5D baseline scores; however, the QoL-AD scores at baseline differ significantly in the dropouts of the control group (p = 0.0007, mean difference = 2.01). Lastly, MMSE scores at baseline were significantly different in the intervention group dropouts with a difference of 1.50, p= 0.00 and in the control group, the mean difference was 0.98, p = 0.00.

As for the informal caregivers, there was a significant age difference, with a mean difference of 3.599, p= 0.006, in the intervention groups who dropped out. ZBI scores at baseline

differed significantly in the dropouts; intervention group mean difference = 1.72, p= 0.008 and in the control group, the mean difference = 2.02, p= 0.0038. There was no significant difference in the sex, education and EQ-5D baseline scores.

At baseline, the average age of PwMCI was around 74 years old, and their carers were around 61-62 years old. Over 50 per cent of participants were female for PwMCI, and nearly 70 per cent of the caregivers were female. Most of the PwMCI had elementary education at least, and the caregivers' education was distributed evenly across elementary, secondary, and higher education. Most of the dyads were either married or with a partner, with being single less than 30 per cent and over 60 per cent living with their partners. Overall, there is no significant difference between the groups at baseline and randomisation was successful.
Similarly, there is no significant difference in demographic characteristics observed between the groups at follow-up. The groups were still balanced even though there were drop-outs at follow-up, and there was no selection bias at follow-up.

5.2 Intergroup Differences in outcome measures

5.2.1 Baseline

In addition to demographic characteristics, the outcome measures at the baseline were checked for balance and were presented in Table 2. Results suggest no significant differences in outcome measures of EQ5D-3L (EVAS and UK Tariff), composite-QoL- AD, and MMSE scores for PwMCI. Similarly, no significant differences were seen in the caregivers' EQ5D-3L scores and ZBI scores.

5.2.2 Follow up

At follow-up, there were no significant differences observed in EQ-5D-3L (EVAS and UK Tariff), composite-QoL-AD and MMSE scores observed between the two groups for PwMCI and the informal caregivers (Table2).

5.3 Intragroup difference of effect measures

5.3.1 PwMCI

To compare the baseline and follow-up differences, paired t-tests were used. The results obtained from the paired T-tests are set out in Table 3. There were no significant differences between baseline and follow-up within intervention groups. What stands out in Table 3 is a small effect seen on the EQ-5D-3L scores in the control group for PwMCI. There was a significantly small reduction in EQ-5D-3L scores in the control group, with a mean difference

of -0.03 (p-value= 0.01) with the EVAS scale. This is confirmed with a mean difference of -0.04 (p-value= 0.01) with the UK Tariff. Similarly, in the intervention group, EQ-5D-3L EVAS scores were reduced but not significant, with a mean difference of -0.02 (p-value= 0.08). The difference is consistent with UK Tariff which is -0.03 (p-value= 0.07).

5.3.2 Informal caregivers

No significant changes were seen between baseline and follow-up within intervention and control groups for the informal caregivers.

5.4 Medication adherence

Table 4 reports results from the chi-squared test on the difference in adherence to two drugs chosen for pill counts. There was no significant difference found in adherence between the groups.

5.5 Effect of SMART4MD on health-related outcome measures using regression analyses

5.5.1 Health-related outcomes for PwMCI

The SMART4MD application has no significant impact on quality-of-life scores, mini-mental state examination scores and QALYs on PwMCI (Table 5). Controlling for age, sex, education, living arrangement, and baseline scores, QoL AD scores have an 0.55 increase in the SMART4MD group at a p-value of 0.05 level. All baseline scores (EQ5D EVAS and UK Tariff, QoL-AD, and MMSE) significantly positively impact the outcomes of each. Being female persons with mild cognitive impairment has a negative impact on EQ5D (EVAS and UK Tariff) and QALY(EVAS and Tariff) except on MMSE. Higher education has a significant positive effect on EQ5D (EVAS and UK Tariff), MMSE, and QALY (EVAS and UK Tariff); however, it did not significantly impact QoL-AD. Surprisingly, no significant effect was seen with age and living with a spouse or children on quality of life and cognitive function.

5.5.2 Health-related outcomes for Informal Caregivers

Linear regression analyses of the SMART4MD application use on health outcomes in informal caregivers are presented in Table 6. The SMART4MD application has a significant positive effect on the QALY (UK Tariff) of the informal caregivers (beta= 0.08, 95 % CI 0.02 to 0.13, p-value = 0.01) in model 1. The effect reduced to 0.05 in model 2 (beta= 0.05, 95 % CI 0.00 to 0.11, p-value = 0.04), all else being equal. However, there was no significant relationship between SMART4MD and the QALY (EVAS). The caregiver's age significantly affects the EQ5D (EVAS and TTO) and QALY (EVAS and TTO), except for the ZBI score.

Being a female caregiver has a significant negative relationship with all the outcome measures, with the largest effect on ZBI score (beta= -1.19, 95 % CI -2.34 to -0.05, p-value= 0.04). Higher education has a significant positive effect on the QALYs (EVAS) (beta = 0.08, 95 % CI 0.03 to 0.13, p-value <0.01) and UK Tariff (beta = 0.12, 95 % CI 0.05 to 0.18, p-value <0.01). Baseline scores for EQ5D (EVAS and UK Tariff) and ZBI scores have a significant positive relationship with the follow-up scores.

5.5.3 Medication adherence

Logistic regression analyses of the SMART4MD application use on medication adherence are presented in Table 7. There was no significant increase in odds of adherence seen in the SMART4MD group at all follow-up points. The odds of adhering to medication to drug 1 were 1.84 times higher for people living with their spouses than the singles at the 12-month follow-up (95 % CI 1.01 to 3.35, p-value = 0.04). Similarly, living with a spouse has 2.06 higher odds of adherence to drug2 at 12- month follow-up but not significant (95 % CI 0.93 to 4.53, p-value = 0.07). Significantly, PwMCI with carers whose education had at least secondary education showed 2.04 higher odds of adherence to drug 1 at 18- month follow-up (95 % CI 1.19 to 3.49, p-value= 0.01).

6 Discussion

6.1 Main findings

The effectiveness of the SMART4MD app on the quality of life of PwMCI and their informal caregivers were studied. The study could not find enough evidence that the application improves the quality of life of PwMCI and their informal caregivers and the reduced burden on the caregiver regarding mean differences. The intergroup mean differences were not significant; however, the intragroup differences between baseline and follow-up showed a significant decline in the EQ-5D index in the control group. The intervention group had a fewer decrease in the EQ-5D index (both EVAS and UK Tariff) which is not statistically significant. This may be explained by the difference in the number of observations at baseline and follow-up between the independent T-test and the paired T-test. In the paired T-test, the number of observations was less than the observations in the groups when analysed with an independent t-test for the intergroup difference. The calculation only took account of the participants for baseline values present at the follow-up in the paired T-test.

Furthermore, regression analyses with the additional controls for baseline scores, age, sex, education, and living arrangement revealed some improvement in informal caregivers' QALYs (UK Tariff). The age of caregivers has a significant negative impact on EQ-5D and QALYs except the burden ZBI scores. Being female has a significant negative impact on the EQ5D indexes and QoL-AD. This result is different from the findings of Song et al., which did not show significant relationships between females and HRQoL (35). This may be due to the different sample sizes and study designs between the two studies. The current study has a larger sample size (n= 1078 vs n= 204), and the study design is a randomised controlled trial vs a cross-sectional design.

The significant positive effect found in the informal caregiver's QALY (UK Tariff) suggests that the application is probably more beneficial for the caregiver than the PwMCI. This result is aligned with the previous short-term economic evaluation of the trial (26). However, the effect was inconsistent with QALYs (EVAS). This inconsistency between the two values could be due to the difference between the two methods of visual analogue scale, which use the rating scale and the time trade-off (the UK Tariff), a choice-based (36). However, rescaling could increase the comparison between the two (36). It is also noteworthy that the R squared for the models in Table 5 were relatively low (below 30), and the low percentage of explanation of the model should be considered when interpreting the result.

Being a female caregiver has a significant negative association with the HRQoL and the increased burden of caregiving. This highlights the burden on the female caregivers of individuals with mild cognitive impairment and the need for support to reduce the carer burden and maintain their quality of life.

Regarding education, higher education positively affects the quality of life of the PwMCI and the caregivers over time. There is a piece of previous evidence on higher education as a good prognostic factor in MCI to return to normal cognition instead of the progression into dementia (37). The current study supports the fact, and findings suggest that education is a supportive factor for the caregivers managing and supporting the family members with mild cognitive impairment.

Results from this study on improvement in medication adherence contradict the study of the Perx smartphone application on medication adherence in a 12-month randomised controlled

trial (38). The differences in the study population and the demographic characteristics may account for this. The Perx trial was assessed on the average age of 59.5 for chronic conditions such as cardiovascular disease, type 2 diabetes, obesity, or other endocrine disorders taking polypharmacy (38). In comparison, the current study examined the effect of the application on mild cognitive impaired older adults with a mean age of 74-75 (38). Regarding the intervention, the Perx application has an incentive for the users by providing gift cards, in-app forums and weekly medication reports, which more likely enables the user's engagement with the application in various ways (38).

Other recent studies were conducted in the telehealth (13, 14, 22) and computerised platforms (20) and analyses the caregivers alone (22). Extensive trials with longer duration were lacking. This study provides novel evidence on the long-term effectiveness of the tabloid app on the quality of life of both PwMCI and their informal caregivers and medication adherence.

6.2 Implications and explanations

This study did not find enough evidence to reject the null hypothesis of no changes in the outcome measures between the groups. The trial duration could explain the fact that the effects were not evident in this study. 18- months may not capture the long-term impact on the quality of life as the application primarily aimed for. In addition, the application was aimed principally to support persons with mild cognitive impairment in coping with the disease in the later stages of potential progression to dementia. In that way, the persons will be familiar with the application usage and could assist in their later disease stage.

Another probable explanation could be the heterogenous levels of familiarity with technology and the application's usability among the participants, which could lead to different engagement with the application. On the contrary, this study did not have information on the actual use of the application and random assignment to the group was regarded as the use of the application. Moreover, the information on whether the application use was as intended is unknown.

Furthermore, the application was supposed to be used daily; however, for older people with mild cognitive impairment, forgetfulness influences the use of the application itself, and mild cognitive impairment has also affected the ability of telephone usage (5).

The intervention itself could have been an additional burden for PwMCI and their caregivers. The reminders from the application may have caused a nuisance in the daily life of the PwMCI by causing a distraction. Moreover, the study did not have information on different subtypes of MCI, which could be amnesic or non-amnesic MCI (4), and participants with amnesic MCI may have felt more confusion from the application functions.

The mHealth applications for dementia are more likely to be adopted if the features are simple (18). It is possible that the SMART4MD application's functions might not have been simple enough for PwMCI. A review of mHealth apps reported a high association between the simple, easy and interactive features of the applications and the usability and acceptability (39). If the app functions are complex and PwMCI are not familiar with the app, it could even lead to distress for them (39).

In addition, the application is a behaviour change intervention, and it may be possible for more interest and more use of the application if the gamification (reward) system were incorporated.

6.3 Methodological considerations

The study uses randomised controlled trial data and randomised assignments to make the compared groups ceteris paribus (40). When checking for balance, randomisation was found to be successful at baseline. This suggests there is no selection bias in the samples. The mean difference in outcome measures between the two groups is the average causal effect of the intervention plus selection bias due to an unbalanced randomisation (40). A causal inference could be made from this study. Secondly, the study used the intention to treat principle, and this, in one way, handled the effect of dropouts of the study, which are approximately 40 per cent (Figure1). However, the groups were still in the balance at follow-up with similar dropout rates, suggesting the study results were unbiased. Multiple imputations could be considered another method to account for missing values for the regression analyses (41). This study did not use multiple imputations.

Although randomisation eliminates selection bias (40) and the study was controlled for potential confounder for omitted variable bias, there could still be inadequate controls such as

comorbidities, subtypes of MCI, number of medications taken at present and the actual use of the application.

Lastly, Hussenoeder et al. highly recommended the differentiated approach, using facets of QoL instead of the total scores in their study of the burden of MCI on the older population (6). This study, however, used the total scores, and the results could be interesting to observe if the approach had been different.

6.4 Strengths and Limitations

During the application development, the PwMCIs and the caregivers were involved in the process. It is essential to be user-centred in the design and development of mHealth applications. The trial is a long-duration randomised trial (18 months), and the sample size was large. As this study examined data from two different European countries, Sweden and Spain, the results are generalisable to the European population with a similar population. In addition, quality of life was measured with several different indexes, such as QoL-AD, EQ-5D-3L, and total QALYs gained using the European visual analogue scale and the UK Tariff.

The study focused on health-related quality of life only. The results might differ if the QOL was assessed with a different index, such as WHOQOL-OLD, specifically designed for older adults over 60 (6). The information on the actual use of the application was lacking in this study, and the potential association with the application's actual use on health outcomes was not examined.

There were some limitations. This study had equal dropouts between the groups. However, there were significant differences in the QoL-AD baseline scores between the dropouts and completers in PwMCI. Comparable dropout rates do not always imply unbiased treatment effect estimates and vice versa. (42) In the current study, missing at non-random cannot be excluded, and the study may have an attrition bias (43). Using mixed models to estimate unbiased estimates is recommended (41). However, the study controlled for baseline scores in the OLS regression models, which could account for missingness at complete random. Therefore, the effect of the SMART4MD application may be underestimated, and this finding is consistent with the previous short-term economic evaluation of the SMART4MD application (26). Furthermore, attrition analysis was not performed in this study. Future

research should account for the missingness with the mixed model or another method such as a multiple imputation approach.

7 Conclusion

The effect of the SMART4MD application is inconclusive, and the treatment effect may be underestimated. Although the application may benefit informal caregivers more than persons with mild cognitive impairment, the results should be considered cautiously. Further studies are needed to examine the effect of the SMART4MD application.

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Table 1
Sociodemographic characteristics of persons with mild cognitive impairment (PwMCI) and informal caregivers at baseline and follow-up at 18 month

Characteristics	PwMCI				Informal caregiver			
	Baseline		Follow up		Baseline		Follow up	
	Intervention (n= 537)	Control (n= 541)	Intervention (n= 313)	Control (n= 337)	Intervention (n= 537)	Control (n= 541)	Intervention (n= 313)	Control (n= 337)
Age [a]	74.65 (7.24)	74.33 (7.23)	75.34 (6.97)	75.63 (6.77)	61.82 (15.00)	62.70 (14.36)	64.79 (14.04)	65.19 (14.47)
Gender [b]								
Male	241 (44.88)	265 (48.98)	156 (49.84)	174 (51.63)	166 (30.91)	178 (32.90)	88 (28.12)	110 (32.64)
Female	296 (55.12)	276 (51.02)	157 (50.16)	163 (48.37)	371 (69.09)	363 (67.10)	225 (71.88)	227 (67.36)
Education [b]								
Elementary education	313 (58.61)	333 (61.78)	180 (57.69)	200 (59.52)	175 (33.52)	201 (37.92)	110 (36.07)	121 (36.56)
Secondary education	124 (23.22)	100 (18.55)	74 (23.72)	58 (17.26)	186 (35.63)	156 (29.43)	111 (36.39)	101 (30.51)
Higher education	97 (18.16)	106 (19.67)	58 (18.59)	78 (23.21)	161 (30.84)	173 (32.64)	84 (27.54)	108 (32.63)
Civil status [b]								
Unmarried	181 (33.71)	159 (29.44)	100 (31.95)	86 (25.52)	105 (19.63)	95 (17.59)	54 (17.25)	63 (18.81)
Married/Partnered	356 (66.29)	381 (70.56)	213 (68.05)	251 (74.48)	430 (80.37)	445 (82.41)	259 (82.75)	272 (81.19)
Living arrangements [b]								
Single	117 (21.99)	102 (18.96)	73 (23.32)	50 (14.88)	52 (9.74)	43 (7.95)	28 (8.95)	19 (5.65)
Spouse/Common law	327 (61.47)	356 (66.17)	205 (65.50)	243 (72.32)	357 (66.85)	378 (69.87)	226 (72.20)	254 (75.60)
Children	56 (10.53)	41 (7.62)	21 (6.71)	14 (4.17)	53 (9.93)	48 (8.87)	29 (9.27)	20 (5.95)
Other	32 (6.02)	39 (7.25)	14 (4.47)	28 (8.33)	72 (13.48)	72 (13.31)	29 (9.27)	41 (12.20)

Note. [a] Mean (SD),
[b] n(%), ; no significant differences between the two groups were found.

Table 2

Change in health effects between (inter-group differences) intervention and control group at baseline and follow-up at 18-month

Variables	Baseline			Follow up		
	Intervention (n = 537)	Control (n = 541)	Difference (p-value)	Intervention (n= 311)	Control (n= 334)	Difference (p-value)
	M (SD)	M (SD)		M (SD)	M (SD)	
PwMCI						
EQ-5D-3L index scores (EVAS) [a, b]	0.77 (0.19)	0.77 (0.21)	-0.00 (0.87)	0.76 (0.20)	0.76 (0.20)	0.00 (0.84)
EQ-5D-3L index scores (UK Tariff) [a, b]	0.74 (0.28)	0.74 (0.29)	-0.00 (0.96)	0.72 (0.29)	0.71 (0.30)	0.01 (0.77)
Total QALYs gained (EVAS)				1.14 (0.24)	1.13 (0.25)	0.01 (0.77)
Total QALYs gained (UK Tariff)				1.09 (0.34)	1.08 (0.35)	0.01 (0.69)
Composite QoL-AD [c, d]	35.69 (5.94)	35.53 (6.17)	0.16 (0.66)	36.48 (5.19)	36.05 (5.06)	0.42 (0.30)
MMSE scores	25.38 (2.51)	25.49 (2.40)	-0.11 (0.48)	26.01 (4.23)	25.61 (3.90)	0.40 (0.22)
Informal Caregiver						
EQ-5D-3L index scores (EVAS) [e, f]	0.80 (0.18)	0.79 (0.21)	0.02 (0.21)	0.80 (0.18)	0.78 (0.20)	0.02 (0.13)
EQ-5D-3L index scores (UK Tariff) [e, f]	0.78 (0.25)	0.75 (0.29)	0.03 (0.77)	0.78 (0.25)	0.74 (0.28)	0.04 (0.08)
Total QALYs gained (EVAS)				1.20 (0.23)	1.17 (0.25)	0.03 (0.12)
Total QALYs gained (UK Tariff)				1.17 (0.30)	1.12 (0.35)	0.05 (0.06)
ZBI [g, h]	41.24 (7.43)	41.14 (7.88)	0.11 (0.82)	41.50 (7.78)	41.20 (7.46)	0.31 (0.61)

Note. Abbreviations: M, mean; SD, standard deviation; PwMCI, person with mild cognitive impairment; EQ-5D-3L, European quality of life index, five dimension, 3 levels, EVAS, European visual analogue scale; QALYs, quality adjusted life years; QoL-AD, Quality of life-Alzheimer's disease; MMSE, mini-mental state examination scores; ZBI, Zarit burden caregiver inventory. Independent sample t-test is used to examine the difference between the two groups. No statistically significant difference was found between the two groups at baseline and follow-up. For PwMCI: [a] n = 536 for intervention, n= 541 for control at baseline, [b] n= 312 for intervention, n= 333 for control at follow-up; [c] n= 532 for intervention, n= 536 for control at baseline; [d] n= 302 for intervention, n= 327 for control at follow-up. For informal caregiver: [e] n= 535 for intervention, n= 535 for control at baseline; [f] n= 312 for intervention, n= 333 for control at follow-up; [g] n= 536 for intervention, n= 538 for control at baseline; [h] n= 305 for intervention, n= 330 for control at follow-up.

Table 3

Baseline to 18-month change in health effects within (intragroup differences) intervention and control groups

	Intervention Group (n= 310)			Control Group (n= 335)		
	Baseline	Follow-up	Difference (p-value)	Baseline	Follow-up	Difference (p-value)
	M (SD)	M (SD)		M (SD)	M (SD)	
PwMCI						
EQ-5D-3L index scores (EVAS) [a]	0.78 (0.19)	0.76 (0.20)	-0.02 (0.08)	0.78 (0.20)	0.75 (0.20)	-0.03 (0.01)*
EQ-5D-3L index scores (UK Tariff)[b]	0.75 (0.27)	0.72 (0.29)	-0.03 (0.07)	0.75 (0.30)	0.71 (0.28)	-0.04(0.01)*
Total QALYs gained (EVAS)		1.14 (0.24)			1.13 (0.25)	
Total QALYs gained (UK Tariff)		1.09 (0.34)			1.08 (0.35)	
Composite QoL-AD [c]	36.16 (6.20)	36.54 (5.16)	0.38 (0.14)	36.23 (6.23)	36.00 (5.10)	-0.23(0.29)
MMSE scores	26.03 (2.11)	26.00 (4.24)	-0.03 (0.88)	25.89 (2.20)	25.62 (3.90)	-0.27 (0.08)
Informal caregiver						
EQ-5D-3L index scores (EVAS) [d]	0.81 (0.17)	0.80 (0.18)	-0.01 (0.46)	0.78 (0.20)	0.77 (0.21)	-0.01 (0.38)
EQ-5D-3L index scores (UK Tariff)	0.80 (0.23)	0.78 (0.24)	-0.02 (0.28)	0.75 (0.29)	0.73 (0.29)	- 0.02 (0.35)
Total QALYs gained (EVAS)		1.20 (0.23)			1.17 (0.25)	
Total QALYs gained (UK Tariff)		1.17 (0.30)			1.12 (0.35)	
ZBI scores [e]	41.96 (7.44)	41.57 (7.77)	-0.39 (0.33)	41.79 (7.41)	41.09(7.48)	-0.70 (0.11)

Note. Statistically significant difference was found for EQ5D in the control group between baseline and follow-up. For PwMCI, [a] n= 311 for intervention, n= 333 for control, [b] n= 312 for intervention, n= 333 for control, [c] n= 299 for intervention, n= 324 for control. For caregiver, [d] n= 307 for intervention, n= 330 for control , [e] n= 304 for intervention, n= 329 for control. Number of observations were the same for baseline and follow-up. Abbreviations: M, mean; SD, standard deviation; PwMCI, person with mild cognitive impairment; EQ-5D-3L, European quality of life index, five dimension, 3 levels, EVAS, European visual analogue scale; QALYs, quality adjusted life years; QoL-AD, Quality of life-Alzheimer's disease; MMSE, mini-mental state examination scores; ZBI, Zarit burden caregiver inventory. Paired t-test is used to examine the difference between the two groups. Significance levels: p <0.05 *,0.01 ** and 0.001 ***.

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Table 4

Change in medication adherence (within 80 and 110 percent) between (inter-group differences) between intervention and control groups for drug 1 and drug 2 at 6, 12, 18 month follow-up

		Adherence for drug1			Adherence for drug 2		
		Adherence N (%)	No adherence N (%)	P -Value	Adherence N (%)	No adherence N (%)	P- value
M6	Intervention	171 (56.81)	130 (43.19)	0.44	114 (58.76)	80 (41.24)	0.71
	Control	173 (53.73)	149 (46.27)		138 (57.02)	104 (42.98)	
M12	Intervention	138 (62.16)	84 (37.84)	0.44	84 (64.12)	47 (35.88)	0.79
	Control	149 (65.64)	78 (34.36)		104 (62.65)	62 (37.35)	
M18	Intervention	142 (64.25)	79 (35.75)	0.56	89 (60.96)	57 (39.04)	0.57
	Control	133 (61.57)	83 (38.43)		93 (57.76)	68 (42.24)	

Note. This table reports frequencies and percentages of adherence between 80 and 110 per cent at 6-, 12-, and 18-month follow-ups. Chi-squared test was used to estimate the difference between the groups and p-values are shown with stars for significance. None of the results was significant.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 5

Linear regression of SMART4MD on health effects in PwMCI in model 1 (unadjusted) and model 2 (adjusted) for demographic characteristics and baseline scores

VARIABLES	(1) EQ5D (EVAS)	(2) EQ5D (EVAS)	(1) EQ5D (UK Tariff)	(2) EQ5D (UK Tariff)	(1) QoL AD	(2) QoL AD	(1) MMSE	(2) MMSE	(1) QALY (EVAS)	(2) QALY (EVAS)	(1) QALY TTO	(2) QALY TTO
SMART4MD group	0.00	0.00	0.01	0.00	0.42	0.55*	0.40	0.22	0.01	0.01	0.01	0.02
	(0.84)	(0.82)	(0.77)	(0.88)	(0.30)	(0.05)	(0.22)	(0.36)	(0.77)	(0.64)	(0.69)	(0.55)
	[-0.03, 0.03]	[-0.02, 0.03]	[-0.04, 0.05]	[-0.04, 0.04]	[-0.38, 1.23]	[-0.00, 1.10]	[-0.23, 1.02]	[-0.25, 0.69]	[-0.03, 0.05]	[-0.03, 0.05]	[-0.04, 0.07]	[-0.04, 0.07]
PWD - Age		-0.00		-0.00		-0.03		-0.02		0.00		0.00
		(0.86)		(0.99)		(0.13)		(0.35)		(0.54)		(0.20)
		[-0.00,0.00]		[0.00, 0.00]		[-0.07, 0.01]		[-0.05, 0.02]		[-0.00, 0.00]		[-0.00, 0.01]
Female		-0.03**		-0.05**		0.17		-0.31		-0.12***		-0.16***
(Male reference)		(0.03)		(0.02)		(0.58)		(0.22)		(0.00)		(0.00)
		[-0.06, -0.00]		[-0.10, -0.01]		[-0.42, 0.76]		[-0.82, 0.19]		[-0.17, -0.08]		[-0.22, -0.10]
Secondary School		0.03		0.04		0.07		0.62*		0.04		0.05
(Elementary reference)		(0.11)		(0.11)		(0.85)		(0.05)		(0.13)		(0.19)
		[-0.01, 0.06]		[0.01, 0.09]		[-0.65, 0.79]		[-0.00, 1.24]		[-0.01, 0.09]		[-0.02, 0.12]
Higher education		0.04**		0.06**		0.07		0.65**		0.06**		0.09**
(Elementary reference)		(0.04)		(0.03)		(0.85)		(0.04)		(0.01)		(0.01)
		[0.00, 0.07]		[0.00, 0.11]		[-0.67, 0.82]		[0.02, 1.27]		[0.01, 0.11]		[0.02, 0.16]
Spouse/Common law		-0.01		-0.01		-0.00		-0.36		-0.01		-0.00
(Single reference)		(0.46)		(0.59)		(1.00)		(0.28)		(0.82)		(0.92)
		[-0.05, 0.02]		[-0.07, 0.04]		[-0.75, 0.75]		[-1.00, 0.29]		[-0.06, 0.05]		[-0.08, 0.07]
Children		-0.05*		-0.06		0.10		0.24		-0.06		-0.06
(Single reference)		(0.09)		(0.20)		(0.88)		(0.67)		(0.21)		(0.39)
		[-0.11, 0.01]		[-0.15, 0.03]		[-1.16, 1.35]		[-0.84, 1.32]		[-0.15, 0.03]		[-0.18, 0.07]
Other		-0.02		-0.03		-1.56**		-1.28**		-0.04		-0.05
		(0.49)		(0.51)		(0.02)		(0.03)		(0.39)		(0.44)
		[-0.09, 0.04]		[-0.13, 0.06]		[-2.89, -0.24]		[-2.43, -0.13]		[-0.14, 0.05]		[-0.19, 0.08]
Score at baseline		0.53***		0.48***		0.61***		1.20***				
		(0.00)		(0.00)		(0.00)		(0.00)				
		[0.46, 0.60]		[0.41, 0.56]		[0.56, 0.65]		[1.09, 1.32]				
Constant	0.76***	0.37***	0.71***	0.37***	36.05***	16.35***	25.61***	-4.12*	1.13***	1.11***	1.08***	0.95***
	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.06)	(0.00)	(0.00)	(0.00)	(0.00)
	[0.73, 0.78]	[0.20, 0.54]	[0.68, 0.75]	[0.13, 0.62]	[35.50, 36.61]	[12.79, 19.91]	[25.17, 26.05]	[-8.46, 0.22]	[1.11, 1.16]	[0.88, 1.35]	[1.04, 1.12]	[0.62, 1.27]
Observations	645	643	645	643	629	621	645	643	600	598	600	598
R-squared	0.00	0.32	0.00	0.26	0.00	0.55	0.00	0.46	0.00	0.09	0.00	0.08

Note: This table shows dependent variables in the heading row and independent variables in the first column. Coefficient estimates, p-value in parentheses and 95 % confidence intervals in brackets

were presented. R-squared and number of observations are reported. The same baseline scores were controlled for each outcome variable.*** p<0.01, ** p<0.05, * p<0.1

Table 6

Linear regression of SMART4MD on health effects in informal caregivers in model 1 (unadjusted) and model 2 (adjusted) for demographic characteristics and baseline scores

	(1)	(2)	(1)	(2)	(1)	(2)	(1)	(2)	(1)	(2)
VARIABLES	EQ5D EVAS		EQ5D (UK Tariff)		ZBI score		QALY EVAS		QALY TTO	
SMART4MD group	0.02	0.02	0.04*	0.03	0.31	0.36	0.03	0.03*	0.08***	0.05**
	(0.13)	(0.18)	(0.08)	(0.16)	(0.61)	(0.50)	(0.12)	(0.08)	(0.01)	(0.04)
	[-0.01, 0.05]	[-0.01, 0.05]	[-0.00, 0.08]	[-0.01, 0.07]	[-0.88, 1.50]	[-0.68, 1.39]	[-0.01, 0.07]	[-0.00, 0.07]	[0.02, 0.13]	[0.00, 0.11]
Age Carer		-0.00***		-0.00**		-0.00		-0.00***		-0.00***
		(0.00)		(0.01)		(0.97)		(0.00)		(0.00)
		[-0.00, -0.00]		[-0.00, -0.00]		[-0.04, 0.04]		[-0.01, -0.00]		[-0.01, -0.00]
Female		-0.08***		-0.11***		-1.19**		-0.15***		-0.19***
(Male reference)		(0.00)		(0.00)		(0.04)		(0.00)		(0.00)
		[-0.11, -0.05]		[-0.15, -0.06]		[-2.34, -0.05]		[0.19, -0.11]		[-0.25, -0.14]
Secondary School		-0.02		-0.03		-0.23		0.03		0.05
(Elementary reference)		(0.24)		(0.30)		(0.73)		(0.16)		(0.14)
		[-0.05, 0.01]		[-0.07, 0.02]		[-1.52, 1.06]		[-0.01, 0.08]		[-0.02, 0.11]
Higher education		0.01		0.02		-0.22		0.08***		0.12***
(Elementary reference)		(0.67)		(0.54)		(0.74)		(0.00)		(0.00)
		[-0.03, 0.04]		[-0.03, 0.07]		[-1.54, 1.10]		[0.03, 0.13]		[0.05, 0.18]
Spouse/Common law		-0.01		-0.02		0.26		-0.04		-0.06
(Single reference)		(0.83)		(0.48)		(0.78)		(0.20)		(0.17)
		[-0.05, 0.04]		[-0.09, 0.04]		[-1.57, 2.08]		[-0.11, 0.02]		[-0.15, 0.03]
Children		-0.00		-0.00		-1.68		-0.01		0.00
(Single reference)		(0.91)		(0.97)		(0.19)		(0.89)		(0.99)
		[-0.07, 0.06]		[-0.10, 0.09]		[-4.21, 0.85]		[-0.10, 0.08]		[-0.13, 0.13]
Other		-0.02		-0.05		-1.29		-0.08*		-0.11*
(Single reference)		(0.52)		(0.30)		(0.28)		(0.07)		(0.07)
		[-0.08, 0.04]		[-0.13, 0.04]		[-3.64, 1.06]		[-0.16, 0.01]		[-0.23, 0.01]
Score at baseline		0.33***		0.32***		0.50***				
		(0.00)		(0.00)		(0.00)				
		[0.26, 0.41]		[0.25, 0.40]		[0.43, 0.57]				
Constant	0.78***	0.70***	0.74***	0.72***	41.20***	21.23***	1.17***	1.51***	1.11***	1.52***
	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)
	[0.76, 0.80]	[0.58, 0.82]	[0.71, 0.77]	[0.57, 0.88]	[40.37, 42.02]	[16.52, 25.94]	[1.14, 1.20]	[1.38, 1.64]	[1.07, 1.15]	[1.34, 1.69]
Observations	642	624	642	624	635	620	580	569	613	569
R-squared	0.00	0.21	0.00	0.18	0.00	0.28	0.00	0.16	0.01	0.14

Note: This table shows dependent variables in the heading row and independent variables in the first column. Coefficient estimates, p-value in parentheses and 95 % confidence interval in brackets were presented. R-squared and number of observations are reported. The same baseline scores were controlled for each outcome variable. *** p<0.01, ** p<0.05,

* p<0.1

Table 7

Logistic regression of SMART4MD application use on medication adherence of two drug (1,2) at 6-, 12-, 18- month follow-up periods in models (1) unadjusted and (2) adjusted for demographic characteristics

	Adherence Drug 1 M6		Adherence Drug 1 M12		Adherence Drug 1 M18		Adherence Drug 2 M6		Adherence Drug 2 M12		Adherence Drug 2 M18	
	(1)	(2)	(1)	(2)	(1)	(2)	(1)	(2)	(1)	(2)	(1)	(2)
	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR
Control group (reference)	1	1	1	1	1	1	1	1	1	1	1	1
Intervention group	1.13	1.16	0.86	0.86	1.12	1.15	1.07	0.9	1.07	1.2	1.14	1.19
	(0.44)	(0.38)	(0.44)	(0.47)	(0.56)	(0.5)	(0.71)	(0.96)	(0.79)	(0.48)	(0.57)	(0.48)
	[0.83, 1.55]	[0.84, 1.61]	[0.58, 1.26]	[0.58, 1.29]	[0.76, 1.65]	[0.77, 1.73]	[0.73, 1.57]	[0.66, 1.47]	[0.66, 1.71]	[0.73, 1.99]	[0.72, 1.8]	[0.73, 1.93]
Age of PwMCI		1.02		1		1.01		0.9		1.01		1
		(0.26)		(0.94)		(0.59)		(0.18)		(0.62)		(0.84)
		[0.99, 1.04]		[0.97, 1.04]		[0.98, 1.05]		[0.95, 1.01]		[0.97, 1.06]		[0.95, 1.04]
Male (reference)		1		1		1		1		1		1
Female		1.08		1.06		1.03		1.0		1.15		1.97*
		(0.73)		(0.83)		(0.91		(0.97)		(0.7)		(0.06)
		[0.68, 1.72]		[0.61, 1.86]		[0.57, 1.89]		[0.58, 1.76]		[0.55, 2.4]		[0.96, 4.04]
Elementary school (reference)		1		1		1		1		1		1
Secondary School		0.94		0.74		0.95		0.8		0.74		0.88
		(0.78)		(0.28)		(0.86)		(0.4)		(0.38)		(0.71)
		[0.6, 1.47]		[0.43, 1.27]		[0.55, 1.65]		[0.47, 1.35]		[0.38, 1.44]		[0.46, 1.7]
Higher education		1.1		1.15		0.96		(0.91)		0.97		0.98
		(0.69)		(0.63)		(0.9)		(0.74)		(0.94)		(0.95)
		[0.68, 1.79]		[0.64, 2.08]		[0.54, 1.72]		[0.51, 1.62]		[0.48, 1.96]		[0.48, 1.97]
Living arrangement Single (reference)		1		1		1		1		1		1

Spouse/Common law		1.45		1.84**		1.47		0.57*		2.06*		1.38
		(0.15)		(0.04)		(0.25)		(0.08)		(0.07)		(0.43)
		[0.88, 2.39]		[1.01, 3.35]		[0.77, 2.79]		[0.3, 1.06]		[0.93, 4.53]		[0.62, 3.03]
Children		1.29		1.52		0.57		0.69		1.53		0.44
		(0.48)		(0.37)		(0.27)		(0.39)		(0.47)		(0.15)
		[0.64, 2.59]		[0.6, 3.85]		[0.21, 1.53]		[0.29, 1.61]		[0.48, 4.88]		[0.14, 1.36]
Other		1.84		0.87		1.36		0.6		2.49		1.07
		(0.17)		(0.77)		(0.56)		(0.38)		(0.17)		(0.91)
		[0.77, 4.35]		[0.34, 2.24]		[0.049, 3.79]		[0.2, 1.86]		[0.68, 9.14]		[0.3, 3.83]
Age carer		0.99		1		0.99		1		0.99		1
		(0.07)		(0.6)		(0.18)		(0.74)		(0.46)		(0.85)
		[0.97, 1]		[0.98, 1.01]		[0.97, 1.01]		[0.98, 1.01]		[0.97, 1.02]		[0.97, 1.02]
Male carer (reference)		1		1		1		1		1		1
Female		1.01		0.65		0.6		1.15		0.84		1.56
		(0.97)		(0.13)		(0.1)		(0.62)		(0.64)		(0.22)
		[0.64, 1.59]		[0.37, 1.13]		[0.32, 1.11]		[0.66, 2.01]		[0.41, 1.73]		[0.77, 3.14]
Carer education		1		1		1		1		1		1
Elementary school (reference)												
Secondary School		1.29		1.32		2.04***		1.21		1.35		1.42
		(0.24)		(0.3)		(0.01)		(0.48)		(0.36)		(0.28)
		[0.84, 1.98]		[0.78, 2.23]		[1.19, 3.49]		[0.72, 2.03]		[0.71, 2.57]		[0.75, 2.68]
Higher education		1.12		0.99		1.4		0.9		1.21		1.29
		(0.65)		(0.97		(0.26)		(0.73)		(0.6)		(0.48)
		[0.69, 1.8]		[0.56, 1.76]		[0.78, 2.51]		[0.51, 1.6]		[0.6, 2.44]		[0.63, 2.65]
Constant	1.16	0.54	1.91***	1.87	1.6***	1.44	1.33**	13.5**	1.68***	0.68	1.37	0.85
	(0.18)	(0.54)	0	(0.63)	(0)	(0.78)	(0.03)	(0.04)	(0)	(0.82)	(0.05)	(0.92)
	[0.93, 1.45]	[0.08, 3.87]	[1.45, 2.51]	[0.15, 24]	[1.22, 2.11]	[0.11, 19.62]	[1.03, 1.71]	[1.1, 165.12]	[1.22, 2.3]	[0.02, 19.98]	[1, 1.87]	[0.04, 19.08]

Note: This table shows dependent variables in the heading row and independent variables in the first column. Odds ratio (OR), p-value in parentheses and 95 % confidence interval in brackets were presented. *** p<0.01, ** p<0.05, * p<0.1

Popular Science Summary

“Is SMART4MD application effective for improving the lives of persons with mild cognitive impairment and reducing the burden on the caregivers?”

The SMART4MD (Support Monitoring and Reminder Technology for Mild Dementia) application may benefit the family caregivers of persons with mild cognitive impairment. The possible underestimation may have caused a minimal effect observed of the application on persons with mild cognitive impairment.

The early use of the application in the disease's initial stage may provide familiarity with the application. It may benefit coping with everyday life in the later stage of disease progression. The caregivers may benefit from the application's support in managing the person’s daily tasks, such as medication management and healthcare appointments. The quality of life may improve because of reduced stress. However, there were differences in the baseline quality of life scores in persons with mild cognitive impairment who dropped out of the trial. Therefore, it is vital to interpret the result with caution. It is necessary to have future research to analyse the effectiveness of the SMART4MD application accounting for the differences between the trial completers and drop-outs.

Mobile technology plays an essential role in providing an innovative way of supporting persons with impaired cognitive conditions and the family members who care for them. As the population of older adults has increased, the rise of mild cognitive impairment conditions and dementia in older adults has been problematic for the persons with the condition and their family caregivers. It is essential to have a sound support system for persons with mild cognitive impairment and caregivers to maintain or improve their quality of life.