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Conference report: Trends, new technologies and implications for dementia diagnostics, treatment and care in Switzerland

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Summary

Dementia diseases represent a major burden for the directly affected people, their relatives and modern society. Despite considerable efforts in recent years, early and accurate disease diagnosis and monitoring is still a challenge while no cure is available in most cases. New drugs, in particular disease-modifying therapies, and recent technological advancements offer promising perspectives. The integration of novel biomarkers, artificial intelligence and digital health tools has the potential to transform dementia care, making it more personalised, efficient and adapted to the living conditions and needs of older people. In November 2023, the 7th Dementia Summit convened a panel of experts from geriatrics, neurology, neuropsychology, psychiatry, ethics as well as general medicine to discuss interdisciplinary challenges, advancements and their implications for the future of dementia care in Switzerland. The conference underscored the importance of a multidisciplinary approach to successfully integrate new technologies in both clinical-translational research and dementia prevention, diagnosis and care. While recent innovations represent major steps forward, their implementation also comes with important challenges including questions on healthcare system preparedness and adaptation, ethical aspects, technology literacy, acceptance and appropriate use.

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Introduction

Dementia presents significant challenges to both the directly affected people, their relatives and the healthcare system. Currently, around 156,900 people live with dementia in Switzerland, with 33,800 new cases annually [1]. However, early and accurate diagnosis is still a challenge, and a sizeable proportion of people affected by dementia remains undiagnosed. Relevant aspects such as neuropsychiatric symptom detection, monitoring and specific treatment are often not addressed. Innovative approaches to diagnostics, prevention, treatment and care are urgently needed. New drugs, in particular disease-modifying therapies, and recent technological advancements offer promising perspectives. The integration of novel biomarkers, artificial intelligence and digital health tools has the potential to transform dementia care, making it more personalised, efficient and adapted to the living conditions and needs of older people. Implementing new technologies and multidomain prevention and treatment interventions is essential for reducing the symptom burden and improving function – ultimately enhancing the quality of life of dementia patients – and for supporting their caregivers. However, important questions related to validation, costs, acceptance and technology literacy need to be addressed. The 2023 Dementia Summit brought together a panel of experts to discuss these advancements and their implications for the future of dementia care in Switzerland. The two-day conference addressed recent progress and innovation in different fields with high clinical relevance including nutrition and multidomain non-pharmacological interventions for the prevention and early treatment of cognitive disorders, but also the development of biomarkers for the early prediction and treatment of persisting neuropsychiatric symptoms (day 1). A further important topic was the ethics of use of innovative approaches and new technologies. Day 2 first focused on progress in neuropsychological and biomarker diagnosis, then addressed the opportunities and challenges related to the upcoming anti-amyloid drugs, and digital and robot-

ic technologies in the hospital and at the patient's home. Finally, the importance of literacy and attitudes of patients and caregivers regarding innovations and new technologies was highlighted.

Role of nutrition in prevention and treatment of cognitive decline in older people

Reto W. Kressig

A healthy diet has potential in preserving brain and cognitive health. Depending on adherence, the Mediterranean-DASH Diet Intervention for Neurodegenerative Delay (MIND diet) has been shown to be possibly associated with improved cognitive function in older adults [2]. The MIND diet recommends nuts, leafy green and other vegetables, berries, beans, whole grains, fish and poultry, olive oil and wine as cognitively healthy components, whereas red meat, butter, pastries and sweets, fast food and fatty cheese are considered unhealthy. As a possible mechanistic model for the MIND diet-cognitive relationship, the healthy diet components are supposed to decrease brain inflammation and brain oxidative stress by their anti-inflammatory and anti-oxidant properties. In the FINGER study [3], in which general lifestyle changes in regard to physical and cognitive activity also included the MIND diet as a specific brain-protective nutritional intervention, participants showed improvements in several cognitive domains after two years, whereas the most recent MIND diet single intervention trial for prevention in cognitive decline among older persons did not reveal any cognitive benefits after three years [4]. Not surprisingly, the MIND diet as a single intervention for preservation of cognitive health seems significantly empowered when combined with other healthy interventions such as exercise, cognitive training and strict monitoring of vascular risk factors.

Another, more recent strategy to prevent and manage neurodegenerative disease is to modify the diet and microbiota [5]. Published evidence indicates that fermented foods, including kefir, and foods that are high in bioactive polyphenols and complex carbohydrates, such as grapes, pomegranates and seaweed, may be effective at reducing neuroinflammation, oxidative stress, neurotransmitter dysfunction, and neuronal death associated with Alzheimer's and Parkinson's diseases. A phase 3 clinical trial in China with a drug derived from marine brown algae, a seaweed that is supposed to recondition dysbiosis of gut microbiota showed significant cognitive benefits in patients with mild-to-moderate Alzheimer's dementia after 36 weeks [6]. The same drug is currently being tested for motor improvements in phase 2 studies among patients with Parkinson's disease.

Recently, ketogenic therapies have been tested in randomised controlled trials, focusing on delaying disease progression and ameliorating cognitive function [7]. It is hypothesised that the brain energy gap, created by worsened glucose metabolism in early cognitive decline, is covered by the only alternative brain energy source: keto bodies. In general, the ketogenic diet (sometimes shortened to "keto diet") is a low-carbohydrate, high-fat diet that focuses on reducing carbs and increasing fats to encourage the body to enter a state of ketosis. In ketosis, the body uses fat as its primary energy source instead of carbohydrates. Study interventions were heterogeneous, acute or long-term (45–180 d), including adherence to a ketogenic diet, intake of ready-to-consume drinks, medium-chain triglyceride powder for drinks preparation, yoghurt enriched with medium-chain triglycerides, medium-chain triglyceride capsules and ketogenic formulas/meals. The use of isolated ketoneurotherapeutics in combination with continued habitual eating patterns proved effective in improving general cognition using the Alzheimer's Disease Assessment Scale-Cognitive, in interventions of either duration. In a six-month randomised controlled trial of ketogenic medium-chain triglyceride versus placebo in patients with mild cognitive impairment, the ketogenic medium-chain triglyceride drink improved three cognitive domains – executive function, memory and language [8]. Although research on the subject is still in the early stages and highly heterogeneous in terms of study design, interventions and outcome measures, ketogenic therapy appears promising in improving both acute and long-term cognition among patients with Alzheimer's disease and mild cognitive impairment.

For clinicians, it is a most common phenomenon that accelerated weight loss may precede diagnosis in Alzheimer's disease [9]. This weight loss is mainly due to a decrease in lean body mass possibly leading to sarcopenia. The most recent data confirm that intramuscular adipose tissue [3] – often seen in sarcopenia – may predict cognitive decline over the next six years, independent of overall adiposity or muscle health [10]. This disease-related muscle loss underlines the increased protein need among patients with dementia [11], which seems to be best prevented early on by leucine-enriched whey protein supplementation [12].

Dementia prevention with multidomain non-pharmacological interventions

Mélanie Bieler-Aeschlimann

The demographic evolution of Switzerland and the number of elderly people affected by neurodegenerative disease are quite alarming and require the implementation of risk-reduction strategies before reaching the stage of dementia [13]. Among people referred to memory clinics, about one third report subjective cognitive complaints, i.e. complaints without objective cognitive impairment in neuropsychological tests. These people have an increased risk of developing a neurodegenerative disease and there is growing evidence that targeted interventions can have a positive influence on the ageing cognitive functions of these individuals [3]. Relying on modifiable lifestyle factors [14] currently appears to be an excellent and largely available opportunity for seniors and especially for those with subjective cognitive complaints. Non-pharmacological interventions aim to strengthen brain and cognitive reserves, i.e. optimise structural and functional brain networks by training and/or adopting virtuous behaviours. Multidomain interventions seem promising: they act on several modifiable risk factors at once and optimise brain protection [15, 16]. While everyone can be recommended to follow a Mediterranean diet and stay active, the type of cognitive training recommended depends on the individual patient's cognitive profile.

Primary prevention targets older people in good cognitive health and proposes a programme designed to keep them

cognitively fit. For those with subjective cognitive complaints or mild cognitive impairment, we rely on symptoms and apply the principles of secondary prevention, proposing two types of approach: a restorative approach to train attention and executive functions (such as inhibition), and a compensatory approach based on strategies to improve (memory) performances. Improving metacognition seems particularly appropriate for patients with subjective cognitive complaints [17]. New technologies can assist in training cognition, but their efficiency depends on whether they rely on both neuroscience models and therapeutic knowledge [18]. The people who stand to benefit most from non-pharmacological interventions are the frail or pre-frail older adults. At the Leenaards Memory Centre, CHUV, Lausanne (CLM) we have set up three specific projects to support these populations.

Firstly, in a randomised controlled trial, we showed that a multidomain intervention containing a digitised programme of cognitive and physical activities, enhanced by motivational factors, and reinforcing social cohesion between users, improved overall cognition and information processing speed in pre-frail participants [19, 20]. This intervention was carried out at home and gave participants a certain degree of autonomy to choose their training programme. This study therefore demonstrates both the feasibility and the efficacy of a digitised home-based training programme, based on sound neuropsychological concepts.

Secondly, as part of CareMENS, a programme supported by the "Promotion Santé Suisse" foundation, the Leenaards Memory Centre has been offering nosognosic memory clinic patients the opportunity to undergo non-pharmacological interventions. To maintain the intervention's quality of life improvements [21], patients are then accompanied by a Care Manager to start a community leisure activity. Non-pharmacological interventions (neuropsychological, speech and/or physiotherapeutic therapy) are proposed to patients with subjective cognitive complaints or mild cognitive impairment. Over 1000 patients from all over French-speaking Switzerland have been referred to us so far, and more than half of them have joined the CareMENS programme, which has been yet extended to most memory centres in French-speaking cantons.

Thirdly, numerous young patients with Long COVID symptoms referred to the Leenaards Memory Centre first went through a rigorous multidisciplinary assessment, then were offered a 5-session holistic neuropsychological intervention. The symptoms of Long COVID on three cognitive domains (memory, attention and executive functions) were explained. Basic information on current research and the impact of symptoms such as fatigue, stress and sleep disorders on daily, professional and social life were also addressed in two sessions. As Long COVID patients in most cases have subjective cognitive complaints, the intervention is based on psychoeducation to reinforce patients' metacognitive skills and provide them with a large range of tools to help them better understand and overcome their difficulties [22]. Further investigations are needed to explore the subjective benefit of the intervention.

In a nutshell, non-pharmacological interventions enable patients to become active agents in their own health and should be recommended in practice, and even reimbursed by our healthcare system.

Multimodal biomarkers of neuropsychiatric symptoms

Miriam Rabl

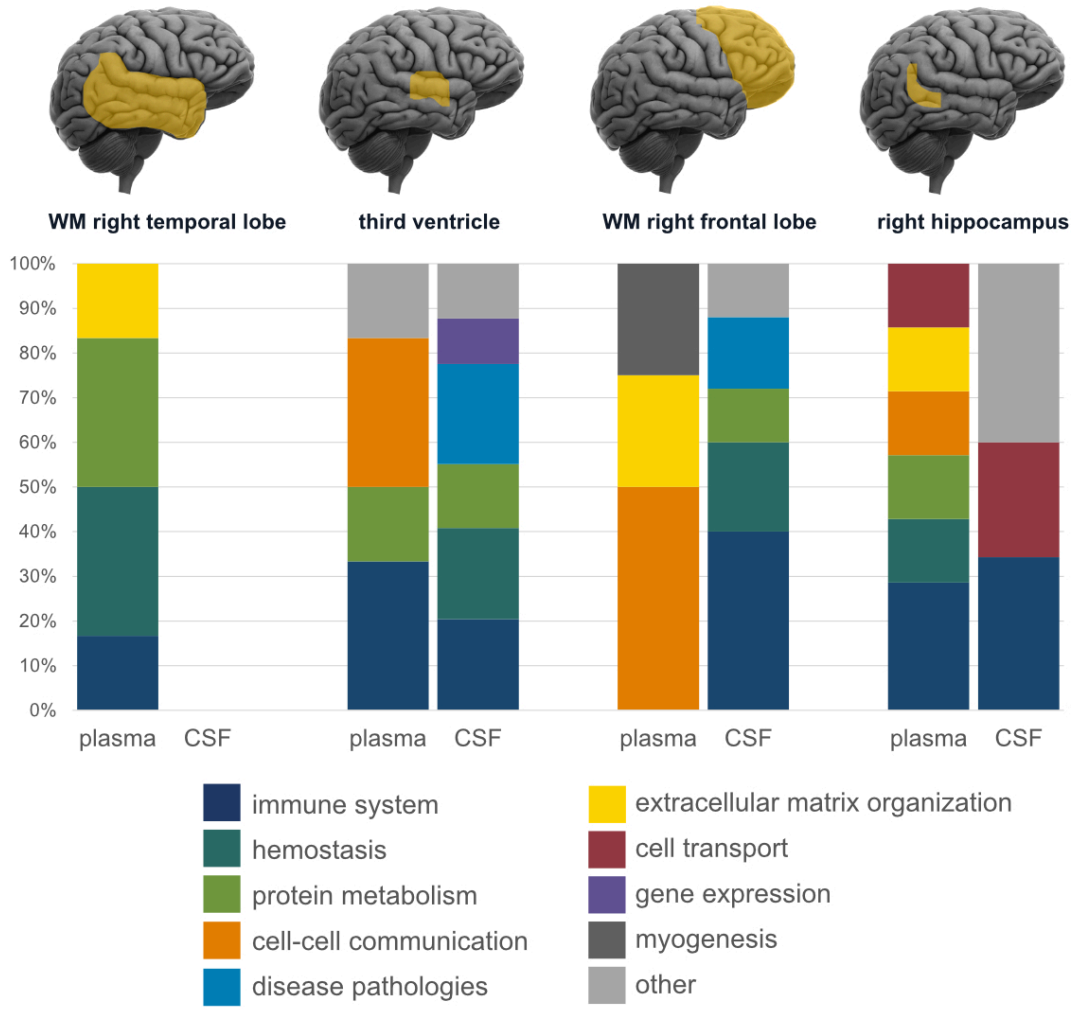
Neuropsychiatric symptoms such as depression, apathy, agitation or hallucinations are very frequent in older people, with a prevalence of up to 97% in people with dementia [23]. The presence of neuropsychiatric symptoms is the most common reason why patients with dementia are being admitted to psychiatric hospitals. Also, having neuropsychiatric symptoms is associated with worse outcomes such as more rapid cognitive decline and earlier death [24–26].

Little is known about the neurobiology underlying neuropsychiatric symptoms yet, and no biomarkers to detect the underlying pathology in neuropsychiatric symptoms are available. Neuropsychiatric symptoms may evolve as part of the core Alzheimer's disease biology and/or may be caused by environmental stress factors, or by other still-unknown pathologies. Different aetiologies may often be present at the same time and contribute to the clinical symptoms to a different extent. An aetiological differentiation based on the clinical manifestation is generally not possible. Also, no biomarkers for the detection of the pathologies underlying neuropsychiatric symptoms are available to date.

Some studies investigated the association between neuropsychiatric symptoms and biomarkers of the Alzheimer's disease core pathology (cerebrospinal fluid levels of total tau, phosphorylated tau and amyloid beta) with inconsistent findings [27]. Also, neuropsychiatric symptoms seem to not be robustly associated with markers of neurodegeneration like neurogranin, neurofilament light chain and GAP-43 [28, 29].

Using a data-driven untargeted proteomics approach in a memory clinic cohort, our group at the University of Zurich recently identified a panel of 15 plasma and 27 cerebrospinal fluid biomarker candidates for neuropsychiatric symptoms. These biomarkers also predicted long-term outcomes such as persistence of neuropsychiatric symptoms and associated cognitive decline [30, 31]. When combining findings from cerebrospinal fluid and plasma with structural MRI data, we found region-specific pathophysiological changes related to neuropsychiatric symptoms (figure 1). The most common enriched biological pathways related to neuropsychiatric symptoms were immune reaction, protein metabolism and haemostasis (Rabl et al., in preparation). Using a more targeted approach and quantifying 38 markers of inflammation and vascular injury in paired blood and cerebrospinal fluid samples, we confirmed that neuroinflammatory processes play an important role in neuropsychiatric symptoms [32]. Further, we partially replicated the findings in the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort. Different biomarker candidates were identified as being associated with neuropsychiatric symptoms and future neuropsychiatric symptoms up to two years later. Specific involved biological pathways were identified for the most common single symptoms of neuropsychiatric symptoms, whereas again the immune system was among the enriched pathways related to overall neuropsychiatric symptoms [33]. Overall, we found evidence suggesting that there are pathological changes underlying neuropsychiatric symp-

Figure 1: Distribution of enriched biological pathways (based on the Reactome database) of plasma and cerebrospinal fluid (CSF) proteins (expressed as percentages) in four brain regions are shown. The higher the percentage of enriched pathways of neuropsychiatric symptoms (NPS), the stronger its association with atrophy in the respective brain region. Regions and proteins were selected based on their associations with NPS. WM: white matter.



toms that are distinct from the core Alzheimer's disease pathology and independently contribute to more rapid cognitive decline [30].

Easily available biomarkers to detect neuropsychiatric symptoms and its underlying pathology would be helpful for the early detection of patients at risk of worse longitudinal outcomes such as persistence of neuropsychiatric symptoms over time and more rapid cognitive decline. This may be helpful in a memory clinic setting to provide personalised treatment recommendations. Also, knowing more about the involved pathophysiological mechanisms of neuropsychiatric symptoms opens the perspective for the development of new treatment targets. Nevertheless, research on this topic is still at the beginning and additional research is required before the results might be available for clinical application. Further and more targeted investigations and validation studies in independent and larger cohorts are needed.

Digital health and artificial intelligence for dementia: Balancing potential with ethics

Marcello Ienca

As the global population ages, dementia becomes increasingly prevalent, necessitating innovative care approaches. Digital health, encompassing artificial intelligence and Intelligent Assistive Technologies (IATs), offers transformative potential [34, 35]. These technologies can enhance the quality of life of dementia patients, reduce healthcare costs and promote social inclusion [35, 36]. Artificial intelligence-driven tools like predictive analytics, personalised care plans and automated monitoring systems exemplify how technology can support dementia care.

The integration of digital health technologies and artificial intelligence in dementia care represents a transformative but ethically sensitive frontier. Ethical considerations are especially pertinent as dementia patients are a vulnerable group with unique needs. This section examines the ethical dimensions of applying new technologies in dementia care, supported by concrete examples to illustrate both the opportunities and the ethical challenges involved. For in-

stance, artificial intelligence-driven predictive analytics can assist healthcare providers in forecasting disease progression, allowing for timely and personalised interventions [37]. However, such predictive capabilities bring concerns about patient autonomy and the potential for misinterpretation or misuse of predictive data [38]. Similarly, wearable monitoring devices can enhance patient safety by tracking movements and alerting caregivers to falls or risky behaviours [39] yet these devices may infringe upon privacy, raising questions about the balance between patient safety and personal freedom [38].

Issues like privacy, consent and data security are paramount, especially given the vulnerable nature of dementia patients. Ethical design principles must guide the development of these technologies, ensuring they respect human rights and dignity [38]. Additionally, addressing the digital divide is crucial to avoid exacerbating healthcare inequalities [40].

To ensure ethical compliance and effectiveness, the development of digital health tools must proactively involve stakeholders, particularly patients and caregivers [41, 42]. User-centred design principles can help create solutions that are not only technically sound but also empathic and practical [43]. Figure 2 provides a visual overview of user-centred design for assistive digital systems for people with dementia.

Ethically aligned innovation, which balances technological advancement with ethical considerations, is critical in this domain. The integration of digital health and artificial intelligence in dementia care holds immense promise for improving patient outcomes and healthcare efficiency. However, this must be navigated with a strong ethical compass. As we advance technologically, the human aspect of care should remain at the forefront. Ethical considerations, including privacy, consent and equity, must guide the development and application of these technologies. By prioritising ethically aligned innovation and user-centred design, we can harness the potential of artificial intelligence and digital health to transform dementia care, making it more effective, inclusive and humane.

Figure 2: Proactive user-centred design for assistive technologies. From: Ienca M, Kressig RW, Jotterand F, Elger B. Proactive Ethical Design for Neuroengineering, Assistive and Rehabilitation Technologies: the Cybathlon Lesson. J Neuroeng Rehabil. 2017 Nov;14(1):115 [84], https://doi.org/10.1186/s12984-017-0325-z, distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/).

Cognitive assessment of neurocognitive disorders and new developments

Andreas U. Monsch

Current neurocognitive assessment

The current neuropsychological examination of brain disorders in older people focuses on the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [44] and requires the assessment and classification of brain performance in the following six domains: learning and memory, language, perceptual-motor function, executive function, complex attention and social cognition. The examination often follows a two-stage process of screening and actual, in-depth neuropsychological examination. The brief screening examination (i.e. less than 15 minutes) allows for detecting possible brain disorders, must be performed by trained healthcare providers and does not provide a definite diagnosis. The assessment is based on normative data (with correction for age, education and sex) and has an established sensitivity and specificity. It provides guidance for the more detailed neuropsychological assessment.

This neuropsychological assessment evaluates all six cognitive domains and allows for a specific diagnosis based on the cognitive deficit profile (figure 3, [45]). However, it takes several hours and can only be carried out competently by certified neuropsychologists. The results are not only quantitative, but also qualitative in nature. The neuropsychological examination makes an important contribution to finding the cause of the brain disorder and is an important basis for treating patients and providing counselling for their relatives.

Strengths and weaknesses of the current neuropsychological assessment

The strength of the current, paper-pencil-based, neuropsychological assessment method encompasses the availability of extensive norms and knowledge of the influence of demographic factors (age, education, sex). Weaknesses are that single test scores rarely reflect a specific single brain activity; thus, interpretation is demanding. Moreover, the field of neuropsychology is methodologically rather weak with respect to meaningfully assessing change. Most likely, the currently available diagnostic criteria (ICD-11, DSM-5, etc.) reflect rather poorly the complexity of human brain function. Also, our brains usually work in everyday life, not only in a well-controlled laboratory setting.

Clearly, new development to better understand, assess and diagnose human brain functions is needed.

New developments in the neuropsychology of dementia

The development of an improved neuropsychological assessment must adopt findings from neuroscience research and integrate them into its framework. Moreover, neurocognitive processes must be understood within the everyday environment. And, lastly, newly available tools and sophisticated analytical methods must find their way into a new and improved methodology. New digital technologies offer tremendous potential for shifting from traditional face-to-face paper-pencil-based neuropsychological assessments to e.g. smartphone-based and thus remote gathering of data in an everyday environment. Several new "toys" have become available to serve this endeavour [46]. One such example is the remote digital memory composite (RDMC) score from an unsupervised remote cognitive assessment battery focusing on episodic memory and long-term recall [47] Participants perform cognitive assessments in a fully remote and unsupervised setting via a smartphone app. In addition to new tools to collect (big) data from study participants and patients, new analytical methods with artificial intelligence using e.g. machine learning are becoming more and more available.

New biomarkers? – What to expect

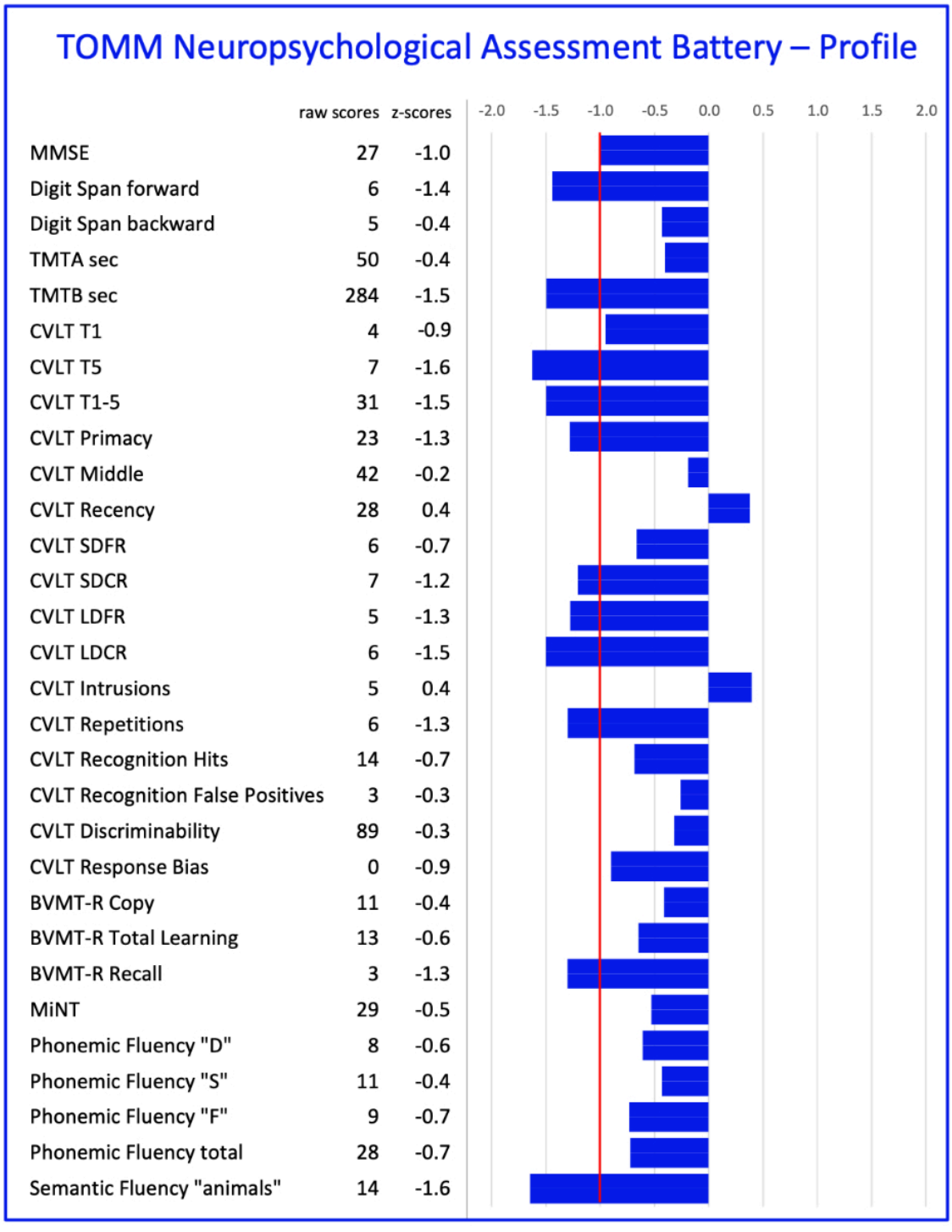
Julius Popp

Molecular cerebrospinal fluid biomarkers in particular amyloid beta (Aβ)1–42, the Aβ1–42/Aβ1–40 ratio, tau and p-tau181 and amyloid-PET are now established tools for the early and accurate detection of the specific Alzheimer pathology. While they are both recommended by Swiss Memory Clinics and covered by health insurance in Switzerland, these markers are still restrictively used in clinical practice, mostly due to the relative invasiveness of lumbar puncture and the costs and availability of amyloid-PET. The use of biomarkers results in a change in the previous diagnosis and the management plan in a large proportion of the investigated memory clinic patients [48, 49]. Accordingly, these markers are now increasingly often used as an additional investigation in the diagnostic workup of cognitive decline, including at the mild cognitive impairment stage [50, 51]. This trend may be due to a growing awareness about more personalised diagnosis and prognosis, and related treatment and management options when first signs of cognitive decline occur. It will likely be further accelerated by the upcoming anti-amyloid therapies which require the clear detection of amyloid pathology along with clinical syndrome due to cerebral Alzheimer's disease pathology.

Current research includes the identification of biomarker candidates for additional clinically relevant aspects of the cerebral pathologies, such as neuroinflammation and cholesterol metabolism [52, 53]. In addition, data-driven omics and integrative multi-omics are deployed to both detect and better understand the involved biological pathways, and to identify related biomarkers and intervention targets [54, 55].

Blood-based biomarkers such as plasma p-tau indicating the presence of Alzheimer's disease pathology in the brain may be used to accurately identify those patients that have a high or a low likelihood of having Alzheimer's disease pathology in the brain. Accordingly, only the remaining group of patients with inconclusive results may require additional lumbar puncture for cerebrospinal fluid analysis and/or PET to confirm or exclude Alzheimer's disease [56]. If validated, this approach will likely lead to a much broader utilisation of biomarkers and make early and accurate diagnosis available for a larger population while reducing costs for individual diagnostic workup. This trend may also accelerate the development of effective and individually tailored prevention and treatment interventions.

Figure 3: Current paper-pencil-based neuropsychological assessment profile. Example of a comprehensive neuropsychological assessment using the TOMM-Neuropsychological Assessment Battery [45]. Normative data are based on 198 cognitively healthy adults. A cognitive profile is shown of a patient with a mild neurocognitive disorder due to Alzheimer's disease. CVLT-II: California Verbal Learning Test; BVMT-R: Brief Visuospatial Memory Test–Revised; TMT: Trail Making Test; MiNT: Multilingual Naming.



The use of easily available, accurate and scalable biomarkers will also allow for repeated measurements not only to confirm diagnosis but also to monitor the evolution of relevant pathologies. This aspect may become particularly important when using disease-modifying interventions including, but not limited to, the new anti-amyloid antibody treatments [57]. Given the fact that the development of brain pathologies leading to dementia, especially in Alzheimer's disease, start in most cases more than a decade before the onset of symptoms, biomarkers may be deployed in the absence of any symptoms to identify preclinical disease and assess the risk of cognitive decline [58]. So far, the use of biomarkers is currently not recommended neither in older people in the general population nor in patients with subjective cognitive decline, i.e. cognitive complaints in the absence of objective cognitive impairment according to standard cognitive testing [50, 51]. However, we expect blood-based biomarkers to be used in

the near future as part of individual risk profiling in people without any cognitive symptoms. Guidance and counselling will be needed for the appropriate interpretation of the results.

New drug approvals? What to expect

Hans Pihan

In July 2023, lecanemab received regular approval from the US Food and Drug Administration and is expected to receive Swissmedic authorisation in 2024. Following the controversial approval of aducanumab in 2021, there have been many critical discussions in the specialist and lay press about the efficacy, tolerability, side effects and costs of the new therapy. An exploratory prompt sent to chatGPT on 9 November 2023 ("Negative expectations of new Alzheimer's therapies?") showed that there are particular concerns about long-term efficacy, side effects, patient safety, the cost-benefit ratio, diagnostic status and a fundamentally poor understanding of the aetiological factors.

The long-awaited stabilisation of the disease with positive therapeutic effects on the preservation of cognition and quality of life now appears to be within reach. However, efficacy and safety still need to be substantiated with real-world data.

Two anti-amyloid beta antibodies will be available in the near future for the treatment of Alzheimer's disease. Both the Clarity study (lecanemab) and the Trailblazer study (donanemab) showed positive results in terms of clinical endpoints, with lecanemab reducing decline by 27% on the CDR-SB (Clinical Dementia Rating - Sum of Boxes) and donanemab by 35% on the iADRS (integrated Alzheimer's Disease Rating Scale) [59, 60]. Limited data from extension trials suggest that this effect may increase when treatment is extended to two years or beyond [61].

One of the important questions that needs to be answered is which patient characteristics are predictive of a good response to anti-amyloid treatment. An extension study of aducanumab, which is not approved in Europe, showed that patients who were "amyloid-negative" on amyloid-PET after 18 months of treatment had a significantly slower decline on the CDR-SB during the further treatment course [62].

Post-hoc analyses from the Clarity (lecanemab) study showed that patients with low baseline amyloid levels had a significantly slower decline in cognitive parameters as compared to the whole group. The majority of patients with low initial tau levels (Braak stage I and II) developed no decline in cognitive performance over two years of treatment, and around half even showed an improvement on the CDR-SB [61].

These results must be interpreted with great caution given the post-hoc nature of the analysis and the relatively small number of patients. For example, it is unclear whether patients with low tau and low amyloid pathology represent an earlier stage of the disease or whether unknown resilience factors slow the progression of histopathology in this group. Despite the many uncertainties, the latest data give hope that questions about treatment initiation, efficacy, potential harm and treatment duration can be answered in the future.

Treatment adverse events in the form of Amyloid-Related Imaging Abnormalities (ARIAs) have occurred in all studies of anti-amyloid antibodies. Vasogenic oedema (ARIA-E) and microbleeds (ARIA-H) can occur, particularly during the first 6–9 months of treatment. Their incidence depends on Apolipoprotein E (ApoE) status and increases significantly with the number of ApoE4 alleles [63]. In the Trialblazer study (donanemab), they were detected in 36.8% of patients (24% ARIA-E; 31.4% ARIA-H). In the Clarity study (lecanemab) in 21.5% (12.6% had ARIA-E and 17.3% had ARIA-H). ARIAs are visible on MRI in the FLAIR and SWI sequences and require treatment to be interrupted or stopped once they reach a certain size or if symptoms occur. The percentage of symptomatic ARIAs was 6.1% in the donanemab study and 2.8% in the lecanemab trial. Typical symptoms were headache and confusion. In Clarity AD ARIA-E generally occurred in the first 3 months, was mild and asymptomatic, did not lead to discontinuation of lecanemab or placebo if mild, and resolved within 4 months. In Trailblazer 57.9% of first ARIA-E occurred after receiving up to 3 donanemab infusions [59, 60]. The first data on the subcutaneous administration of lecanemab suggest a similar risk of developing ARIA-E or ARIA-H [64].

Depending on the Swissmedic decision, which is expected in early 2025, the first approved anti-amyloid drug may be available in Switzerland in the near future. The new treatments bring new hopes, but also new challenges. Some of these challenges can be addressed as follows:

- Access: An estimated maximum of 20% of patients assessed in memory clinics will meet eligibility criteria or receive insurance coverage. However, 100% of people with Alzheimer's disease need high-quality care and the resources to provide services at all stages of the disease.
- Cost: Treatment costs are estimated at CHF 25,000 per year, an order of magnitude higher than the drug costs of about CHF 1000 for currently available anti-dementia pharmacological therapies. Do we need new standards for diagnosis and treatment? What will be the role of primary care, specialists and memory clinics? Do we need new reimbursement models?
- Efficacy and safety: How does 27% disease slowing (43% in men, 12% in women) with 18 months of treatment (lecanemab) translate into quality of life (QoL)? Preliminary data from the Clarity study point towards QoL benefits associated with treatment of lecanemab [59]. What is the significance of the sex effect? Are the therapeutic effects scalable to long-term therapy? Does low tau/low amyloid indicate earlier disease stages or different disease pathogenesis (more individual resilience)? What are the indicators of a good treatment response in individual patients? What impact do ARIAs have on treatment outcome?

New technologies for dementia treatment and care in the hospital setting

Stefan Klöppel

The predicted shortage of staff in the Swiss healthcare system warrants new approaches. Technology-based solutions hold promise with two developments in particular.

Robots to help lift patients or humanoids and pet robots to engage patients have entered long-term care and hospitals, particularly in the dementia-care setting. Paro is a baby seal robot and is often used to emotionally engage individuals affected by dementia. When introduced more than ten years ago, Paro caused ethical concerns as its appearance may deceive demented individuals in perceiving Paro as a real pet. While early studies were positive, a more recent meta-analysis found disappointing short- and long-term effects [65]. Best supported by data is the role of Paro in the treatment of agitation. While acceptance of robots is certainly influenced by cultural background, reports on robots in care even from technology savvy Japan recently sounded negative and listed time-consuming transfers as well as rebooting and maintenance of robots. In addition, only a fraction of patients consistently reacted positively to the robots [66].

Besides robots, sensor technology is another new technology with the potential to reduce the burden on professional care. In-bed sensors, for example, might alert nurses to imminent falls when a frail patient attempts to stand up. When the same sensors are set to a higher sensitivity, phases of restlessness can be detected and again result in alerting staff. In these scenarios, alerting staff serves to prevent more resource-intensive events (e.g. a fall) or enables them to better structure their ward round (visiting an agitated patient when walking past the room rather than reacting to the patient calling for help). While studies consistently show the ability of sensors to monitor sleep and activity of inpatients [67], there is a lack of studies on the effectiveness of modern sensor technology to prevent falls [68].

In summary, while solutions to battle staff shortage are urgently needed, robots and sensor technology still have to prove that they may meaningfully contribute.

Clearly, sensor technology can also aid patient monitoring outside hospitals, e.g. when the aim is to monitor patients with dementia at an increased risk of developing behavioural and psychological symptoms [69]. While reports of patients and relatives during a given consultation tend to focus on symptoms or the recent past, sensor-based monitoring could provide a more balanced view and thus support better treatment decisions. Lastly, sensors can guide just-in-time adaptive interventions (JITAIs) and thus a dementia risk-reducing lifestyle [70]. An example could be the smartphone detecting elevator use resulting in a push message to encourage taking the stairs.

Hospital at Home for persons with cognitive impairment

Tatjana Meyer-Heim

The emergence of hospitals in the early 19th century advanced medicine and to this day hospitals are considered the standard of care for acute illness. However, hospitals do not only have high maintenance costs, but can also, in particular in older people, carry a high risk of developing a delirium or functional decline.

In 1995, the first Hospital at Home service was set up at Johns Hopkins hospital in Baltimore – initiating a worldwide movement. Hospital at Home – also called home treatment or virtual wards – provides hospital-level care in the patient's home environment, combining telemonitoring and in-person care.

In many ways, the COVID-19 pandemic was a catalyst for an increase in demand for home-based acute care. In the context of the pandemic, the use of telemedicine technology has been the ideal solution in many countries, and patients realised that hospitals are not always the safest haven.

Telemedicine combined with other new technologies can play an increasingly important role in the diagnosis and treatment of acute illnesses such as heart failure, pneumonia, complicated urinary tract infections, exacerbated chronic obstructive pulmonary disease or COVID-19. In the near future, the service could expand to support people with an even wider range of conditions.

Wireless sensors are capable of monitoring heart rate, respiration rate, heart rate variability, temperature, oxygen saturation and 1-lead ECG. In some brands, an accelerometer is integrated into the sensor. Wireless blood pressure devices are used for comprehensive monitoring.

Patients' vital signs are continuously collected by sensors, then digitised and analysed. Real-time patient data and early warning alerts are transmitted to central monitoring stations and integrated with the provider's system. Telemonitoring is accompanied by in-person visits by nurses and physicians at the patient's home. Face-to-face visits are crucial.

Especially persons living with dementia tend to do poorly in a hospital setting. Hospital admissions harbour the risk of under- and overstimulation, sleep disruption, immobility, malnutrition, loneliness and functional decline [71]among other negative outcomes. The risk of developing a delirium in the hospital is particularly high for patients with preexisting neurocognitive disorders.

Person-centred care in the patient's home does improve patient satisfaction without jeopardising safety.

Both a recently published cohort study with more than 11,000 patients [72] and a Cochrane review [73] confirmed the results of other studies showing that mortality in a Hospital at Home setting was not higher than in patients treated in a conventional hospital setting. Besides admission avoidance, a Hospital at Home service can decrease admissions to long-term residential care at 6 months [74].

In late 2019, Spital Zollikerberg in Zurich launched the first Swiss Hospital at Home service for patients with acute internal medical diseases, called "Visit – Spital Zollikerberg Zuhause". Patients aged 19 to 99 years were included.

In agreement with already published studies [75], there were no safety issues and high patient and caregiver satisfaction were demonstrated (5.8. and 5.7, respectively, on a scale from 1 to 6). These are preliminary results of an ongoing pilot study.

Due to the small number of cases (n = 78), no subgroup of patients with cognitive impairment could be formed. However, individuals with dementia and their relatives reported a positive experience. Further studies are needed.

Larger randomised controlled trials which address the feasibility of Hospital at Home treatment for patients with cognitive impairments are needed. NICE 2017 guidelines recommend taking into account keeping a person living

with dementia in a familiar environment before a hospital admission. In the UK, so far over 240,000 people have been treated in a Hospital at Home setting since April 2022 [76].

In addition to finding ways of reimbursement and addressing other topics [77], healthcare systems have to ensure that nobody is left behind because of digital illiteracy while the use of digital tools is increasing [78].

Technology literacy in old age – a neglected prevention strategy in dementia care

Stefanie Becker

So-called gerontechnologies are increasingly penetrating the everyday lives of dementia patients [79–81]. An ever-wider range of technological solutions – from electronic bracelets with geolocalisation to intelligent rollators, communication supporting devices or smart homes – have emerged as pivotal allies. They offer innovative solutions and help to promote values such as freedom of choice and autonomy, thus aiming to reduce the impact of dementia-related impairments.

But they can only fully unfold their positive and supporting effects if they are tailored and suited for the use of the individual and work for the person. Unfortunately, despite the possible advantages for independent living, the reality is that use of technology in dementia has been poor. A main concern in connecting patients with dementia with gerontechnologies is the digital divide that excludes individuals from benefiting from these resources. The elderly population exhibits apprehension or difficulty in adopting new technologies, often stemming from a lack of digital literacy. So, despite the many potentially positive effects in empowering those affected by dementia and supporting the family carers, (new) technologies are not yet widely used. Today, among older adults, it is mainly those with a high interest in technology who use digital services. Research shows that especially expectations like perceived ease of use are related to age and interest in technology predict their use. Only a few seniors have an overall positive attitude towards these digital services [82].

Technology acceptance and use – attitude as a crucial factor

Nevertheless, potential for greater use is evident. To foster the use of better technology, acceptance, access, explanation, guidance and support to *learn* the helpful use of new technologies in everyday life are crucial. It is expected that the next generations of elderly people will be much more used to the daily adaptation of technologies. But even with that future perspective, technology acceptance or use are not just an "organic" development but require awareness-raising and motivational linkage to the individuals' preferences and needs. Challenging current models of technology acceptance, [83] found that attitude was the most important factor which is influenced by facilitating conditions and social influence. This had a direct effect on behavioural attitude and intention of use.

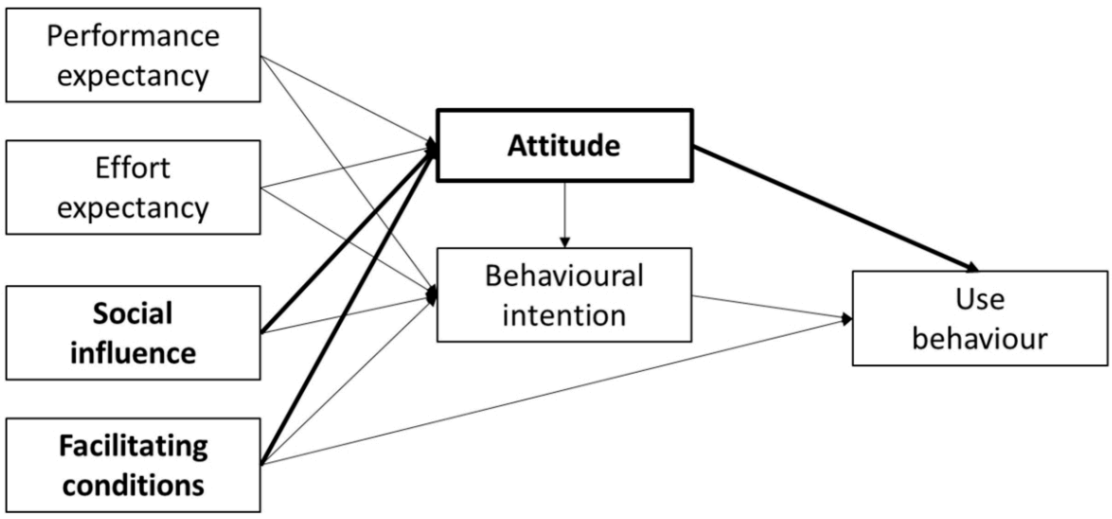
Technology literacy – a neglected prevention path

As a prerequisite for active and healthy ageing, older people must also be able to use the potential of technological innovations. But it is precisely this ideal of autonomy that is put to the test in the case of dementia. Digital literacy is therefore considered a key competence for active participation in an increasingly digital society. The acceptance and the safe and beneficial use of technologies are promoted by teaching digital skills to older people today to prepare them for a possible future life with dementia.

Consequently, there is a pressing need for user-centred design principles that prioritise intuitive interfaces and ease of use. This also means the inclusion of people with dementia and their caregivers in the developmental process of technologies to become real solutions instead of obstacles.

Ethical considerations also loom large, particularly regarding privacy and autonomy. The use of surveillance tech-

Figure 4: Model of technology acceptance: different factors influencing use behaviour; in bold the factors with the most important influence. Adapted from: Dwivedi YK, Rana NP, Jeyaraj A, Clement M, Williams MD. Re-examining the Unified Theory of Acceptance and Use of Technology (UTAUT): Towards a Revised Theoretical Model. Inf Syst Front. 2019;21(3):719–34 [83], https://doi.org/10.1007/s10796-017-9774-y, distributed under the terms of the Creative Commons CC BY license (https://creativecommons.org/share-your-work/cclicenses/).



nologies, while bolstering safety, concurrently raises questions about consent and the right to privacy. It is imperative that ethical frameworks are developed to navigate these issues, ensuring that the dignity of the individual with dementia is upheld and that motivation and trust can be built in cognitive healthy periods of life.

In summary, the strategic use of technology in dementia care is promising, offering tools that can improve safety, cognitive function, independence and quality of life. However, the translation of these technological advances into widespread clinical and home use must be approached with caution. Interdisciplinary collaboration among technologists, healthcare providers, patients and caregivers and inclusion of the target group of the respective technology are essential to optimise the use of technology in dementia care and to ensure that it serves as a bridge to a better quality of life for those affected. This implies that approaches to shape the attitudes of individuals for influencing intentions and behaviours will be an even more important pathway for (primary, secondary and tertiary) prevention for a good and self-determined life with dementia. But no matter how good the new technology is, it will always have to serve the individual and will never replace personal contact or human attention. Fostering the motivation to use and an interest in new technologies in older adults can however be an additional path of prevention for a self-determined life, especially in case of a dementia diagnosis.

Conclusion

The conference underscored the importance of a multidisciplinary approach for successfully integrating new technologies in both clinical-translational research and dementia prevention, diagnosis and care. Recent developments in the field of clinical, neuropsychological and biomarker diagnosis, along with digital remote assessment methods will substantially change both attitudes and clinical practice regarding individual risk profiling, and early diagnosis and monitoring of dementia diseases. This will allow for personalised counselling and tailored lifestyle, pharmacological and psychosocial interventions, and improve the quality of care. Upcoming disease-modifying interventions such as anti-amyloid antibodies will require precise identification of the targeted pathology and assessment of treatment-related risks. While these innovations represent major steps forwards, their implementation also comes with important challenges to be addressed including questions on ethical aspects, healthcare system preparedness and adaptation, resource availability, technology literacy, acceptance and appropriate use.

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