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Memory center: The Lausanne model

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Abstract

We present the multidisciplinary approach toward the diagnostic and treatment of patients with cognitive complaints adopted within the Leenaards Memory Centre at the University Hospital of Lausanne in Switzerland. Our strategy combines clinical evaluation using standardized neuropsychological, biological, imaging, and genetic biomarkers, together with an integrated approach to care of the patient and his/her caregiver(s) that takes into account the individual environmental and socioeconomic circumstances. Tightly integrated with the clinical process is a centralized electronic information system—called CLEMENS—that maintains a database of detailed records of assessment results, actions, care plans and biomarker and imaging data of consulting patients. The CLEMENS system provides the translational bridge between the clinical activity and its projection into and from clinical research, enabling the in-depth and multivariate evaluation of all clinically measured aspects. We discuss how research outcomes can feed back into the clinical activity, allowing for more accurate patient evaluation, diagnostic stratification, and care

Keywords

Memory disorders, Alzheimer's disease, informatics, database, brain imaging, biomarkers, clinical standards, clinical research

Introduction

The Leenaards Memory Center (LMC) at the University Hospital of Lausanne is a clinical multidisciplinary ambulatory service that cares primarily for patients affected by memory or cognitive impairment that may be precursory or predictive for Alzheimer's disease (AD) or other types of cognitive disorders. The center focuses on early diagnostic of cognitive decline primarily in the elderly population and on treatment, care, and long-term follow-up. The LMC is also a translational center in which advanced clinical research programs are closely intertwined with state-of-the-art clinical practice.

The LMC has been established and is being funded through the joint financial efforts of the health authority in Canton of Vaud, the University Hospital of Lausanne, and the Leenaards Foundation. The center is leading a network of regional centers under the auspices of the cantonal and regional health authorities, with memory centers located at Yverdon-les-Bains, Vevey, and Rolle, each covering distinct population areas. The network of memory clinics has been established within the framework of the cantonal Alzheimer program, which aims to improve diagnostic, care, and prevention of dementia and its negative social impacts on the elderly population.

A network of multidisciplinary memory centers

One of the main aims of the creation of the network of memory centers (for which the LMC has a coordinator role) is to establish and put in practice a common set of

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procedures and standards for clinical evaluation, patient diagnostic, referral, and follow-up. The ultimate goal of this approach is to ensure equality in terms of quality of care across the geographic area of the canton for the concerned population. Taking into account the specificities of local and regional health-care structures, the strategy of the network is to introduce a multidisciplinary approach that involves specialists and professionals from all specialties concerned in the care act.

Within each center, neurologists, psychiatrists, geriatricians, and neuropsychologists consult patients and contribute to the multidisciplinary assessment. Each center has at least one associated liaison nurse who is in charge of coordinating the communication between the patient, his/her caregiver(s), his/her general practitioner, and health and socio-economic institutions such as care homes or social assistance providers. Centers may also benefit from the on-site presence of social assistance and psychological assistance specialists. The clinical staff participates in regular (daily at the LMC) multidisciplinary meetings where individual patient cases are discussed. These colloquia enable communication between professionals and foster experience and knowledge sharing to optimize individual patient's case assessment.

Similar to the LMC, but to a smaller scale, the regional centers are structured as multidisciplinary entities where medical professionals of distinct specialties may bring their individual contribution to each individual case diagnostic and treatment. The LMC counts an overall number of 40 members of staff and coordinates the activity of the regional centers that altogether employ a similar number of staff. Complex cases are discussed in joint meetings, and cases from the regional centers may also be evaluated by the LMC staff either on-site or at the LMC for more in-depth, complementary investigations (genetics, molecular imaging, and biomarkers).

The LMC and the regional centers cover a population basin of over 750,000 permanently resident individuals, out of which approximately 170,000 are 60 years of age or older. Annually, in average over 950 patients consult at the LMC, out of which 50% are new cases. The combined total number of patients consulted within 1 year by the three regional centers is similar to that of the LMC.

The function and operation of the LMC is similar to and takes model from a number of other memory clinics in Switzerland, Europe, and across the world. In Switzerland, the Association of Swiss Memory Clinics[1] joins a number of memory clinics, ranging from local practices to larger centers present in each of the major university hospitals (Lausanne, Geneva, Zurich, Basel, and Bern), but operating models may differ from canton to canton. The network of memory centers in the Canton of Vaud is similar to the French model setup following the national Alzheimer plans (2001/2004, 2004/2007, and 2008/2012[2]), where university-level centers lead and coordinate regional centers that provide a proximity mission for the diagnosis and monitoring of patients. Regional memory centers are a second-level consultation (after the GPs). The university-level center, in addition to being a second-level center in itself, acts at a third-level as a resource for centers and specialists in the region in complex diagnostic situations (e.g. for young onset cognitive disorder and atypical dementia) or for inclusion of patients in research protocols.

Pursuing translational research

In parallel to its clinical activity, the LMC is pursuing its academic role not only through training of junior medical doctors and neuropsychologists but also by participating within a number of research projects in the field of neurodegeneration. The latter develop thanks to the input of dedicated scientists specialized in clinical research. Research protocols span a wide spectrum, from clinical trials of new pharmaceutical drugs in phase 2 and 3 to prospective observational studies of patients and their caregiver(s) as well as to retrospective studies investigating existing patient data and biomarkers in research of novel diagnostic methods and improving approaches to care. In particular, retrospective research relies on the CLEMENS database registry that records the clinical events and outcomes related to care within the clinic. The LMC also shares facilities with the Neuroimaging Research Laboratory of UNIL[3] which provides access to a 3-Tesla Siemens MRI scanner exclusively dedicated to neuroimaging research, located in the same building as the LMC.

A number of institutes around the world follow similar approaches of combining patient care and long-term follow-up of dementia patients with clinical research backed by computerized multimodal patient registries. In Europe, we note the Alzheimer Center of the VU University Medical Center in Amsterdam.[4] In the United States, the National Institute of Aging,[5] part of NIH, funds a network of Alzheimer's Disease Research Centers; the Oregon Health & Science University's C. Rex and Ruth H. Layton Aging and Alzheimer's Disease Center[6] is one of the centers of reference in the network.

In the rest of this article, we present an overview of the clinical assessment protocols implemented at the LMC and the patient evaluation and care process. We continue by presenting the CLEMENS project and aspects related to information collection and management within the clinic. We conclude by presenting several translational research projects empowered by the CLEMENS database and their potential contribution toward improving patient care.

Clinical assessment of cognitive impairment in the elderly

The primary operating vision of the LMC and of the affiliated memory centers within the canton is to act as second-line specialist centers treating patients referred by first-line medical professionals. The majority of patients

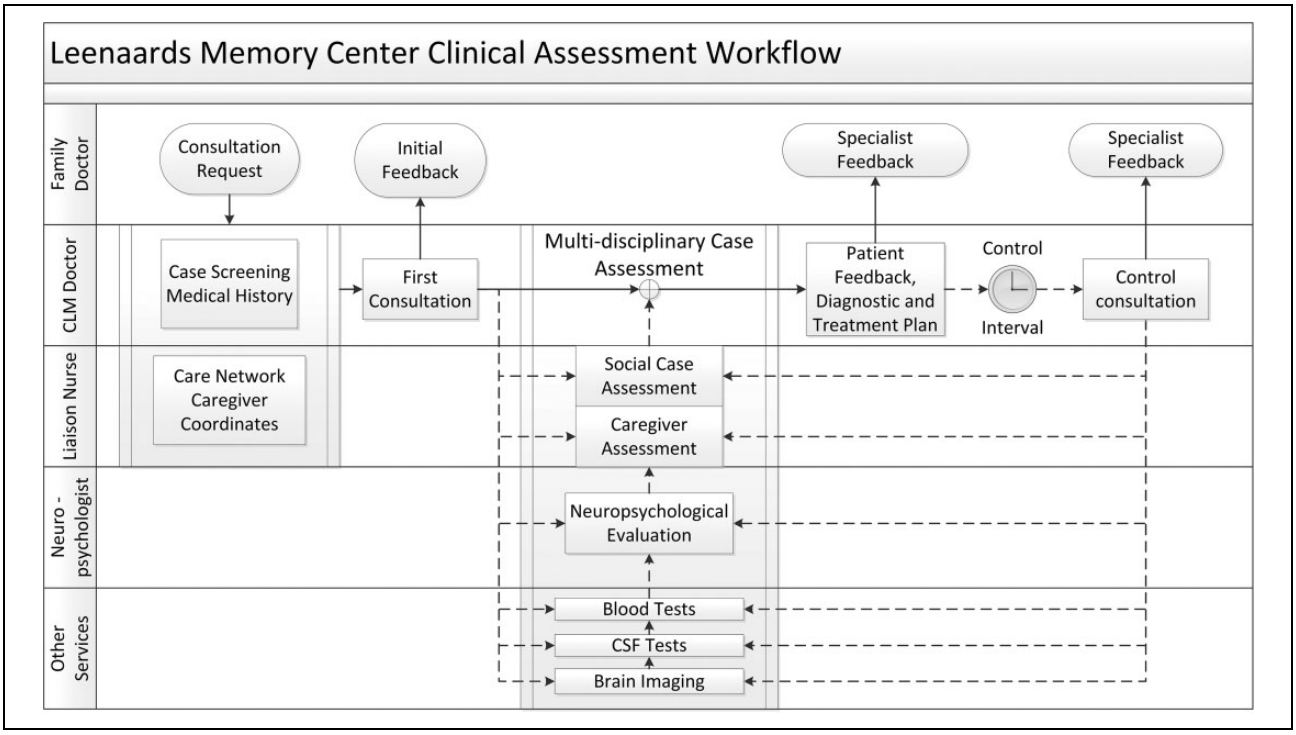

Figure 1. Clinical assessment workflow.

are referred to the LMC by family doctors or other specialists in the area who request a consultation at the memory center to assess signs of cognitive decline or impairment. At the same time, roughly a quarter of LMC's patients arrive through referrals from other Centre Hospitalier Universitaire Vaudois (CHUV) clinical units, mainly the Neurology Department. The LMC is an ambulatory care center; for the rare cases, where hospitalization may be required following a consultation, patients are referred to the appropriate structures at CHUV or within the area. In addition, the LMC provides neuropsychological and neurological consultations for hospitalized patients within CHUV; these are routinely performed within the geriatric and readaptation unit and carried out on request within other units.

We illustrate a synthesized view of the patient assessment and treatment workflow within the LMC in Figure 1, where, for brevity, a number of optional decision points and steps are omitted. Dashed lines within the workflow identify optional elements. We outline the main steps below.

A multidisciplinary medical team from the LMC performs an initial screening of consultation requests before a patient is seen—this includes, at the minimum, an assessment of the medical concerns by a doctor of the team (case competence and medical history) and a care network assessment by the liaison nurse (existence of caregiver or social network and/if social intervention is required). The multidisciplinary team also decides if the case merits the attention of a particular specialty (be it neurology, psychiatry, or geriatrics) which will be charged with carrying out the initial consultation.

Should a consultation request be accepted (which is the vast majority of cases), a series of visits are planned. These begin with an initial clinical consultation by a medical doctor. Following the consultation, an initial feedback letter is written to the requesting doctor and, in general, the multidisciplinary assessment follows with:

- in-depth neuropsychological evaluation with a neuropsychologist, typically carried out over one or two 1-h sessions (70% of patients);
- MRI brain imaging (40% of patients) or other neuroimaging investigations (PET/CT scan using either FDG or pathology-specific ligand—7% of patients);
- blood tests (50% of patients) and CSF tests (10% of patients); and
- consultation by the liaison nurse or social assistant with the primary caregiver/family (35% of cases).

The results of these assessments are distilled in a "feedback" meeting where a diagnostic is communicated to the patient and a therapeutic and care plan is established. This information is further transmitted in a letter to the general practitioner who requested the consultation. According to the care plan defined, follow-up control visits are planned at regular intervals of 1 year, however extra visits may be planned depending on specific needs, such as monitoring medication or other specialized treatment. Control consultations may be accompanied by reevaluations on all aspects (neuropsychological, imaging, and social), following a similar format of the initial evaluation.

A proportion of 50% of new patients are seen for at least one control consultation following the initial evaluation.

Evaluation methods and tools. The initial clinical interview identifies the type of cognitive and/or behavior complaint. In addition to a complete anamnesis, a set of core tests are performed to characterize the complaint (QPC[7]) and to assess functional autonomy in daily life activities (BADL and IADL,[8] DAD-6[9]), mood (HAD[10]), and global cognition (MoCA[11]). These core tests are used as screening tools in advance of a more detailed neuropsychological assessment that performs a thorough evaluation of all cognitive functions. In addition, a complete neurological examination is performed. Its aim is to identify the presence of parkinsonism (often present in dementia with Lewy bodies (DLB), PSP, and DCB) or of a focal deficit (often present in vascular disorders) which are typically not present in AD. This initial examination makes it possible to classify the severity of cognitive impairment and its functional repercussion as subjective complaint, minor disorder or major disorder (in agreement with DSM 5 classification). In parallel to the patient's evaluation, there is an evaluation of the caregiver's needs as well as his/her burden linked to the patient's health situation, (Zarit[12]), and interventions are prioritized accordingly.

The neuropsychological exam assesses clinically and formally all cognitive functions, in-line with the guidelines established by the Association of Swiss Memory Clinics. The formal testing includes an assessment of the main memory systems: episodic memory (RL/RI 16[13], Doors and People test[14]), short-term and working memory (digit span, forward and backward, and spatial span), and semantic memory (Pyramid and Palm tree test,[15] Becks[16]). Language is clinically analyzed and controlled at minimum by a naming test (BNT[17]) and a verbal fluency test. Executive functions are assessed by tests of inhibition control (Stroop[18]), mental flexibility (TMT A and B[19]), and programming (Luria alternating series[20]); verbal fluencies are also interpreted in this section. Praxis are evaluated using a short battery ("batterie brève d'évaluation des praxies gestuelles") and gnosis by the perception of entangled figures (BEN GEREN[21]) as well as by several subtests of a complete battery (VOSP[22]). Finally, elements of social cognition (recognition of emotional states and of the "Faux-Pas") are evaluated through the Mini-SEA battery. These outline the typical collection of tests administered to the LMC patients; additional tests or alternative tests may be used depending on the patient.

The neuropsychological assessment aims to identify the predominant cognitive deficit (classically amnestic in typical AD or dysexecutive in frontotemporal dementia (FTD)) or the cognitive pattern at the earlier stage of the disease (minor disorder and mild dementia); in general, a diffuse cognitive disorder is observed at the later stage of major cognitive disorder (moderate and severe dementia).

The comparison of clinical and structural (MRI)/functional (FDG PET) imaging data helps to give a topographical diagnosis of neurodegenerative disorder with the level of probability in agreement with validated criteria for each entity (e.g. amnestic syndrome and hippocampus atrophy/hypometabolism in probable typical AD, executive dysfunction and frontal atrophy or hypometabolism in FTD).

In cases suspected of AD, we use CSF biomarkers (amyloid Aβ42, total, and phosphorylated Tau) to improve the level of proof for the etiological diagnostic, particularly for patients with atypical symptoms or for patients with cognitive impairment less than 60 years of age. In rare cases, genetic test are performed in suspected patients with inherited dementia (AD, FTD, ALS-FTD, and CADASIL).

Outcomes of the evaluation are to communicate the diagnosis to the patient and his/her caregivers/relatives and to inform his/her general practitioner, to establish a care and psychosocial plan, and to initiate appropriate medical follow-up. Where suitable, patients are also proposed to participate in ongoing research protocols—whether academic or therapeutic research—depending on individual circumstances and compatibility with inclusion criteria.

The CLEMENS project and operational aspects of data collection

The inception of the LMC has been paralleled by the creation of an associated database of clinical records of patients consulting within the center. In the context of the generally slow and largely insidious development of cognitive impairment, the long-term follow-up of patients is necessary and can be of practical use only in an environment of accurate record keeping and monitoring of clinical parameters. In this digital age, we can benefit from the existence of electronic health record systems (EHRs) that automate the tasks of managing and consulting patient files. Such systems must be complemented with data recording procedures that are regular, routine and accurate, and fit within the limited resources of time and attention of clinical staff. The CLEMENS project is centered on the creation, maintenance, and management of the clinical records within the LMC.

In comparison to other standard cohort approaches, the distinguishing aspect of the CLEMENS registry is that it relies solely on medical data acquired as part of the clinical routine, meaning no additional data collection tasks are introduced and no additional tests or measurements are performed beyond what is prescribed by the medical staff. The key driver toward this approach is economical: Costs are being kept at a minimum by limiting/reducing additional effort required, which also is beneficial to ensuring the long-term sustainability of the project. On the other hand, the result of this approach is that there is no certainty on the availability of particular data points for each individual patient. As each patient's timing and planning of appointments as well as care and evaluation plan evolves

depending on its individual circumstances, a level of variability in the collected data is to be expected. Nevertheless, the data accurately record the actual clinical events and the measurements available to the medical practitioner in his routine activity and are free of bias that may result from preestablished selection criteria or other inclusion limitations that may be present in traditional cohorts.

To comply with existing ethical and legal regulations and to ensure the protection of the privacy of patient's medical data, a charter of usage and management of CLEMENS data has been established and approved together with the cantonal ethics committee and the hospital medical directorate. Patients consulting at the LMC are routinely informed of the research being carried out within the center and within the hospital at large and are solicited to participate in the Lausanne Biobank Project[23] and provide a general consent to the reuse of clinical data in the research, without their decision having an impact on their future care within the center. When patients provide their consent, their data may be used for retrospective research purposes under protocols approved by the cantonal ethics committee.

The approach taken by CLEMENS for the reuse of medical record data in clinical research is in itself well known.[24,25] The same approach has been and is being taken at pan-European scale by a number of initiatives on creating similar data and biobanks oriented toward dementia research. We list the DESCRIPA study,[26] EPAD[27], and EMIF-AD[28] as notable projects.

Data collection instruments. The CLEMENS project integrates data acquisition tools within the clinical process through intuitive web-based interfaces that facilitate the recording and consultation of data at key points in the clinical process. The data interfaces are accessible to clinical staff within the secured hospital network, allowing mobility and flexibility of access irrespective of the device used, while maintaining security and data confidentiality.

To minimize the effort of data collection, electronic forms are attached to key tasks or key time points in the assessment workflow such as:

- Consultation request screening: The system collects primary entry point data, including information about the main complaints, known co-morbidities, known medications, and other aspects relevant to the initial case evaluation. We also record estimated time of onset as well as other operational aspects (location, date of entry, etc.).
- Multidisciplinary meeting: At each visit of the patient, the system records key conclusions of the multidisciplinary assessment, changes observed since the last visit, core neuropsychological and screening tests (MoCA, BADL, HAD, etc.), coded diagnostic, and key follow-up decisions such as referral to other services or investigations.
- Psychometric testing: A dedicated form records detailed results of the neuropsychological evaluation. Along with patient education level data, it allows for interactive entry of score values that is context-dependent on complex test branching logic, adapting to patient's age, sex, education level, and other parameters. The system automates the generation of a formatted table of results that is included in the examination report.
- Liaison nurse intervention: The form captures key data concerning the social and quality-of-life situation of the patient and the burden on caregiver(s).

In addition to these data dedicated to the memory clinic assessment, medical staff has access to the hospital-wide EHR system that includes a wide range of clinical information including additional assessment forms, editing and management of medical letters as well as access to imaging results, laboratory tests, and other relevant medical data. All these data are being retrospectively included in the CLEMENS database.

BNA diagnostic coding model

To accurately record the result of the clinical assessment process, we have sought a structured model for recording patient diagnosis. While a coding system such as ICD-10 is widely used at the Lausanne University Hospital and elsewhere, we consider it relatively insufficient for describing the details of cognitive impairment, in particular the observable psychometrics and the potential etiologies involved in the apparition and development of cognitive disorders and dementia.

To address this issue, we have adopted a model created for the French Alzheimer National Database (BNA),[2,29] which describes the diagnostic on three axes:

- Stage: be it major, minor, subjective complaint or of other nature;
- Syndrome: whether memory, language, visual or executive functions are predominantly affected, or whether a diffuse form is observed; and
- Etiology: a choice of up to three contributing etiologies can be selected, given a panel of 43 etiologies predominantly present in the typical population of a memory clinic.

The panel of etiologies includes typical neurodegenerative diseases (Alzheimer's, Parkinson's, DLB, PSP, FTD, etc.) as well as vascular-related lesions (be it diffuse or focal), other causes of lesions (metabolic, traumatic, infectious, and toxic) or psychiatric disorders or neurodevelopmental disorders.

To bridge between the BNA codification and the ICD-10 standard, we have implemented a translation method that allows the clinician to directly map a BNA diagnostic into a corresponding set of ICD-10 codes. This mapping is

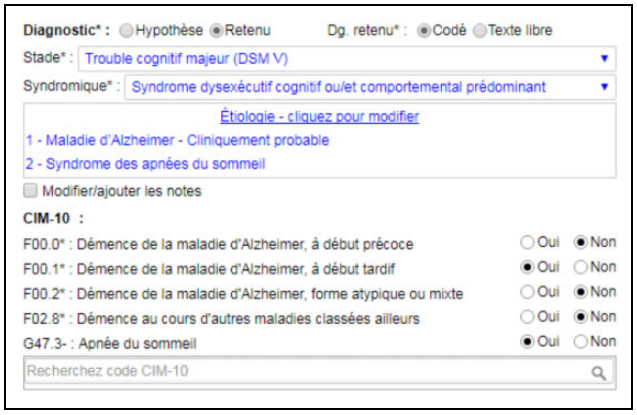

Figure 2. BNA coding interface with ICD-10 mapping (in French).

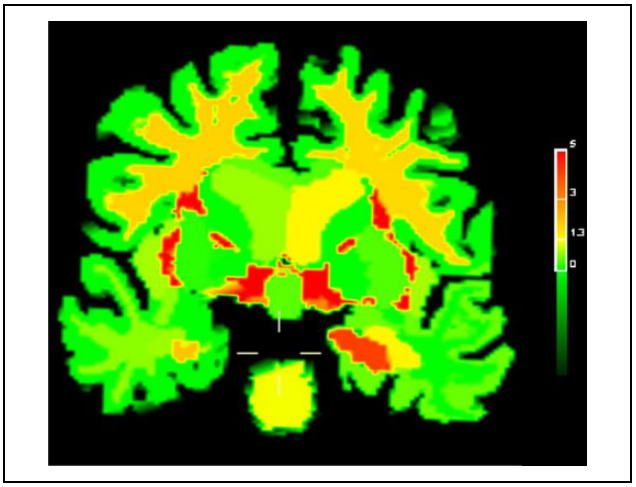

Figure 3. MorphoBox visualization of brain segmentation and volumetric deviation.

performed in a guided fashion—starting from a complete BNA model, the system proposes a set of compatible ICD-10 codes that are then individually validated by the clinician. This process accelerates data entry by limiting the scope of the search in the vast ICD-10 structure and by directing the user to what typically is a small set of compatible codes. A screenshot of the interface deployed to accomplish this task is presented in Figure 2.

Diagnostics are coded and updated within the daily multidisciplinary meetings for each visit of the patient. This approach ensures all participants involved in the care act agree with the diagnostic decision; it also promotes the internal validity of the proposed diagnostic with the use of current validated criteria.

The CLEMENS database in numbers

Since its creation in 2013, the CLEMENS registry has collected data of more than 2700 patients of the center spanning over 10,000 consultations. Patients are added at a rate of approximately 50 new patients per month. To date, the database includes over 45,000 psychometric tests scores as well as images for approximately 1000 MRI scans, 4000 blood sample, and 280 CSF sample analyses. Over 7000 medical letters and 2000 neuropsychological reports are included in hypertext form.

To complement data acquired in a structured fashion using process-oriented forms, natural language text from free-text fields or medical letters is also included in the database. Natural language text is indexed and searchable using a manually curated terminology set that reflects the key medical concepts used in the clinic. We have thus created a vocabulary of over 4000 distinct concepts with approximately 50,000 synonyms structured within an ontology that creates groups of high-level concepts such as medical observations, treatments, interventions as well as parameters such as anatomical locations, stages, severity, and so on. The 700,000 text paragraphs within the database are indexed using this terminology set allowing for faceted search and classification.

Translational research and the CLEMENS database

The wide range of parameters recorded within the database allows for multivariate approaches of retrospective analysis of the data. Several research projects have received ethical approval and are being carried out and we discuss two examples below.

The CLEMENS/PACS-MOLIS project: Impact of imaging and biological biomarkers on the diagnostic of memory impairment

The CLEMENS/PACS-MOLIS project involves the long-term evaluation of the contribution of various imaging and biological biomarkers in the clinical diagnostic and early detection of dementia. The project is specifically investigating the contribution of brain morphometry tools such as MorphoBox.[30] The MorphoBox tool provides automatic segmentation of the brain structures and calculates individual volumes for each brain region. A volume deviation estimate is provided by comparing measured volume with matching age and sex volumes from the ADNI dataset. Volume deviation is calculated and visualized in a color scale, which allows the rapid identification of atrophic regions. An example visualization is provided in Figure 3.

We include patients over 45 years of age who have given their general consent to the reuse of data and had a consultation and diagnostic at the LMC and brain MRI performed at CHUV with the associated brain morphometry data. At the end of 2016, a dataset for 699 subjects has been released for analysis. The dataset includes basic demographics, brain morphometry, clinical psychometrical scores, and diagnostic classification according to severity

and type of cognitive decline (Alzheimer, MCI, subjective complaint, with or without confounding comorbidities such as vascular, psychiatric, or other risk factors).

Preliminary analysis indicates a strong correlation between atrophy in specific brain regions (measured in terms of volume deviation from ADNI controls) and cognitive impairment; specificity can be obtained to distinguish between the various categories of diagnosis. Analysis of the dataset is ongoing with the aim to validate an automated image analysis tool that can assist the clinician in the diagnostic decision.

Comparison of poly-medications in the CLM population and the Lc65+ cohort

The project carried out with a master's student in medicine involves the evaluation of comorbidities and medications within the LMC patient population. The project aims to parallel recent research on poly-medication within the senior Canton Vaud population based on the Lc65+ cohort.[31,32]

The project included the semiautomated and manual review of over 15,000 medication labels (products, ingredients, or generic terms such as "anti-depressant") and their classification according to the WHO Anatomic Therapeutic Chemical drug classification (ATC). We identify medication labels within medical text, and focus, in particular, on specific sections of medical letters that list the current medications of the patient. Our evaluation of the quality of the data extraction has established an F1 score of 97%, which we consider highly accurate.

To date, data from the period spanning 2013 to 2016 has been exported for a subset of 447 patients for statistical analysis. Preliminary results indicate a significant level of hyper-medication within the LMC population in comparison to group-level, age- and gender-matched members of the Lc65+ cohort; this increased medication consumption involves a majority of domains of the ATC drug classification. The analysis and interpretation of the data is ongoing.

Concluding remarks

The creation of CLEMENS as a systematic database of patient records empowers translational clinical research within the LMC and facilitates the long-term follow-up and evaluation of clinical decisions and processes. It enables the emergence of research hypotheses, the creation of clinical studies, and the selection and identification of potential participants based on the existing clinical activity. On the reverse, results, tools, and conclusions of clinical research can quickly be applied into the clinic connecting to existing data and systems.

We are pursuing efforts to distribute the information systems supporting CLEMENS to the regional memory centers in the Canton of Vaud to enable distributing the data collection and increase the coverage of patients within the registry. Our goals are to ensure a uniform recording of data across the canton, and we are discussing with other homologous Swiss centers about adopting unified models of evaluation and data collection. Our work also contributes to the Human Brain Project[33] with which we closely collaborate through the provision of research data and expertise.

Declaration of conflicting interests

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References

1. Swiss Memory Clinics Association, http://www.swissmemoryclinics.ch/ (2018, accessed 10 March 2018).
2. Le Duff F, Develay AE, Quetel J, et al. The 2008-2012 French Alzheimer plan: description of the national Alzheimer information system. *J Alzheimers Dis* 2012; 29: 891–902. DOI: 10.3233/JAD-2012-111943.
3. LREN. Laboratoire de recherche en neuroimagerie (LREN), Faculté de biologie et de médecine, Université de Lausanne, https://www.unil.ch/lren/en/home.html (2017, accessed 10 March 2018).
4. van der Flier WM, Pijnenburg YA, Prins N, et al. Optimizing patient care and research: the Amsterdam Dementia Cohort. *J Alzheimers Dis* 2014; 41: 313–327. DOI: 10.3233/JAD-132306.
5. National Institute of Aging, https://www.nia.nih.gov/ (2018, accessed 10 March 2018).
6. The OHSU C. Rex and Ruth H. Layton aging and Alzheimer's disease center, http://www.ohsu.edu/xd/health/services/brain/getting-treatment/diagnosis/alzheimers-aging-dementia/index.cfm. (accessed 10 March 2018)
7. Thomas Antérion C, Ribas C, Honoré-Masson S, et al. Le questionnaire de plainte cognitive (QPC): un outil de recherche de plainte suspecte d'évoquer une maladie d'Alzheimer? *L'Année Gérontologique* 2003; 17: 56–65.
8. Lawton MP and Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontol* 1969; 9: 179–186.
9. de Rotrou J, Wu YH, Hugonot-Diener L, et al. DAD-6: A 6-Item version of the Disability Assessment for Dementia scale which may differentiate Alzheimer's disease and mild cognitive impairment from controls. *Dement Geriatr Cogn Disord* 2012; 33: 210–218. DOI: 10.1159/000338232.
10. Zigmond AS and Snaith RP. The hospital anxiety and depression scale. *Acta psychiatrica Scandinavica* 1983; 67: 361–370.
11. Nasreddine ZS, Phillips NA, Bedirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild

cognitive impairment. *J Am Geriatr Soc* 2005; 53: 695–699. DOI: 10.1111/j.1532-5415.2005.53221.x.
12. Zarit SH, Todd PA and Zarit JM. Subjective burden of husbands and wives as caregivers: a longitudinal study. *Gerontol* 1986; 26: 260–266.
13. Amieva H, Carcaillon L, Rouze L'Alzit-Schuermans P, et al. Cued and uncued memory tests: norms in elderly adults from the 3 Cities epidemiological study. *Revue Neurologique* 2007; 163: 205–221.
14. Davis D, Bradshaw CM and Szabadi E. The doors and people memory test: validation of norms and new correction formulae. *Br J Psychol* 1999; 38: 305–314.
15. Howard D and Patterson K. *The pyramids and palm trees test: test for semantic access from words and pictures*. Bury St Edmunds: Thames Valley Test Company, 1992.
16. Beck AT and Steer RA. *Manual for the beck depression inventory. San Antonio*: TX: Psychological Corporation, 1987.
17. Kaplan E, Goodglass H and Weintraub S. *Boston naming test*. Philadelphia, PA: Lea and Febiger, 1983.
18. Bayard S, Erkes J and Moroni C. Victoria Stroop Test: normative data in a sample group of older people and the study of their clinical applications in the assessment of inhibition in Alzheimer's disease. *Arch Clin Neuropsychol* 2011; 26: 653–661. DOI: 10.1093/arclin/acr053.
19. Tombaugh TN. Trail making test A and B: normative data stratified by age and education. *Archives of Clin Neuropsychol* 2004; 19: 203–214. DOI: 10.1016/S0887-6177(03)00039-8.
20. Luria AR. *Higher cortical functions in man*. New York: Basic Books, 1966.
21. Gainotti G, D'Erme P and Bartolomeo P. Early orientation of attention toward the half space ipsilateral to the lesion in patients with unilateral brain damage. *J Neurol Neurosurg Psychiatry* 1991; 54: 1082–1089.
22. Warrington EK and James M. *Visual Object and Space Perception Battery (VOSP)*. Suffolk, England: Thames Valley Test Company, 1991.
23. Mooser V and Currat C. The Lausanne Institutional Biobank: a new resource to catalyse research in personalised medicine and pharmaceutical sciences. *Swiss Med Wkly* 2014; 144: w14033. DOI: 10.4414/smw.2014.14033.
24. Meystre SM, Lovis C, Burkle T, et al. Clinical data reuse or secondary use: current status and potential future progress. *Yearb Med Inform* 2017; 26: 38–52. DOI: 10.15265/IY-2017-007.
25. Kohane IS, Churchill SE and Murphy SN. A translational engine at the national scale: informatics for integrating biology and the bedside. *J Am Med Inform Assoc* 2012; 19: 181–185. DOI: 10.1136/amiajnl-2011-000492.
26. Visser PJ, Verhey FR, Boada M, et al. Development of screening guidelines and clinical criteria for predementia Alzheimer's disease. The DESCRIPA study. *Neuroepidemiology* 2008; 30: 254–265. DOI: 10.1159/000135644.
27. The EPAD project, http://ep-ad.org/ (2018).
28. EMIF-AD Project, http://www.emif.eu/ (2018).
29. Anthony S, Pradier C, Chevrier R, et al. The French National Alzheimer database: a fast growing database for researchers and clinicians. *Dement Geriatr Cogn Disord* 2014; 38(5–6): 271–280.
30. Schmitter D, Roche A, Maréchal B, et al. An evaluation of volume-based morphometry for prediction of mild cognitive impairment and Alzheimer's disease. *Neuroimage Clin* 2015; 7: 7–17.
31. Santos-Eggimann B. Cardiovascular diseases: a target for prevention to thwart the effects of population aging. *Rev Méd Suisse* 2006; 56(653–654): 656–657.
32. Renard D, Fustinoni S, Seematter-Bagnoud L, et al. Médicaments chez les seniors vaudois à domicile: nombre et composition. In: (IUMSP) Iudmsep, (ed). *Raisons de santé*. 2015.
33. Frackowiak R and Markram H. The future of human cerebral cartography: a novel approach. *Philos Trans R Soc Lond B Biol Sci* 2015; 370(1668): 20–32.