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Original Study

Clinical Pathways for Diagnosing Neurocognitive Disorders: Insights From Process Mining a Memory Clinic Cohort

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ABSTRACT

Objectives: Process mining (PM) has only recently been used in medicine. Its implementation in the dementia field could be valuable, considering the epidemiologic breadth of the condition and its economic implications. This proof-of-concept study aims to apply PM in the context of dementia to provide a realistic picture of patients' diagnostic pathways in a memory clinic.
Design: Retrospective observational study.
Setting and Participants: A total of 539 medical charts were reviewed to obtain sociodemographic data and type and timing of diagnostic evaluations (eg, clinical or neuropsychological visits, imaging scans, and fluid biomarker analyses).
Methods: We used a PM approach to create a process map from the clinical events and visualize the most common diagnostic pathways in the total cohort and subcohort of patients. PM techniques represent the temporal and dynamic sequence of clinical events in the patients' journeys, overcoming the traditional frequency analyses focused only on aggregate statistics and event distributions.
Results: The results showed that the diagnosis was typically reached during the third clinical visit, following the results of instrumental examinations (ie, morphologic imaging, routine blood and neuropsychological examinations) and a first-line diagnostic biomarker. In mild cognitive impairment (MCI) and mild dementia (DEM) subcohorts, cerebrospinal fluid analyses are the most frequently used first-line biomarkers to ascertain a suspicion of Alzheimer disease (23%). Differential PM analyses revealed that the DEM subcohort underwent morphologic imaging before accessing the memory clinic more often than the MCI subcohort ($P < .05$).
Conclusions and Implications: This preliminary use of PM algorithms in memory clinics shows promising results in visualizing and measuring real-world diagnostic pathways.

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Process mining (PM) consists of data-driven techniques that are an easy and effective tool for exploring the real-world patient clinical journey, allowing the integration of a comprehensive and individualized view of the pathways and facilitating data visualization. Originally developed to enhance business and industry processes, PM merges the Business Process Management perspective with Machine Learning to develop fully data-driven software systems that describe how an institution operates.[1,2]

From a conceptual standpoint, PM is positioned at the intersection of data science, which focuses on extracting value from structured and unstructured data, and process science, which aims to understand and optimize organizational workflows and dynamics.[3] PM methodologies enable retrospective analyses—such as bottleneck identification, root cause analysis, and compliance checking—and prospective applications, including process prediction, anomaly detection, and adaptive decision support.

PM emerged at the beginning of the 2000s, primarily in response to perceived limitations in traditional business intelligence approaches, which heavily relied on aggregated metrics and predefined models that often failed to reflect real-world processes' complexity accurately. The pioneering work of Wil van der Aalst and colleagues[4] provided essential theoretical foundations for the field, leading to the development of the first algorithms specifically designed for automated process discovery. A key advancement in the field occurred in 2004 with the introduction of ProM, an open-source software platform that significantly increased the accessibility of PM techniques within the research community. Thanks to its modular plug-in architecture, ProM facilitated numerous practical applications and now comprises more than 1500 plug-ins. Concurrently, the commercial availability of platforms such as Celonis, Disco, and UiPath Process Mining has facilitated the mainstream adoption of PM techniques in various business sectors.[3]

PM application within health care has notably advanced through the Process Mining for Healthcare (PM4HC) workshop series 2008. PM4HC has consistently promoted interdisciplinary collaboration among computer scientists, clinicians, and health informatics professionals, significantly influencing research direction and encouraging PM implementation in clinical practice.[5] One of the earliest documented health care applications of PM was published in 2008, and since then, its use in health care settings has rapidly grown.[6]

Health care represents a particularly complex and rich environment for PM, owing to its inherent variability, patient heterogeneity, and intricate interdependencies among health care providers and organizational resources. These characteristics have established health care as both a challenging domain and an inspiring source of use cases for PM research.[5,7] Reflecting its increasing relevance, numerous literature reviews published since 2016 have synthesized the expanding body of PM research within health care, covering general overviews and in-depth analyses of specific clinical domains such as oncology, intensive care, and emergency medicine.[8–10] Practical benefits demonstrated by PM applications in health care include the optimization of patient care pathways, monitoring adherence to clinical guidelines, improved care coordination, and streamlined administrative processes.[7,11]

Many PM algorithms have been implemented to describe and optimize patients' diagnostic processes and therapeutic prescriptions.[12] For instance, some algorithms allow for learning process models underlying the provided data, computing the probabilities of the different processes and graphically representing them.[4,13] The detected diagnostic processes of specific sample subcohorts could be statistically compared, highlighting their similarities and differences.[14] Lastly, more frequent diagnostic pathways could be explored in depth to assess their prognostic value.[15] In dementia, PM algorithms can aid in reconstructing patients' diagnostic pathways, accounting for the heterogeneity due to different performed examinations and execution times.[11] However, to our knowledge, dementia is an application field poorly investigated by these techniques.

Despite significant advances in diagnostic tools for neurocognitive disorders, clinical practices often struggle with inaccurate, inconsistent, or delayed diagnoses—particularly in the early stages of the disease.[16–18] Raising awareness of real-world diagnostic processes aligns with the need for biological diagnosis of neurocognitive disorders[19] and the upcoming availability of disease-modifying drugs.[20,21] Quantifying the differences between actual and intended practices knowledge may guide reform activities. Given the complexities of real-world health care procedures, acquiring accurate information on how they unfold in practice is difficult. Exploring patients' clinical pathways by reviewing the medical charts could be valuable from clinical and economic points of view, providing data on real-world sustainability and using a biomarker-based diagnosis in neurodegenerative disorders as a reference. However, simple descriptive analyses of biomarkers use (eg, frequency of use and type of biomarker) in clinical settings provide limited information, as they fail to capture the complexity of the diagnostic process in the neurocognitive disorder context.[22] PM techniques may offer a promising solution by enabling the integration and analysis of large, heterogeneous data sets (eg, neuroimaging, cognitive tests, genetic data, EHRs). These methods can uncover hidden patterns, enhance early detection, and support more personalized diagnostic pathways.

This proof-of-concept study aims to test PM techniques to delineate the diagnostic pathway of patients in a memory clinic setting, detailing visits and instrumental examinations performed and their temporal sequence. Moreover, we performed some of the analyses by dividing the sample into 3 groups according to the stage of cognitive decline (ie, subjective cognitive decline, mild cognitive impairment, and mild dementia). The European recommendation suggested different pathways according to the patient's clinical severity[23]; therefore, the comparison analyses could be valuable to show the potential of PM in the dementia context. We aim to provide a comprehensive understanding of the activities performed, process sequences and diagnostic results, which can serve as a foundation for clinical and organizational discussions and decisions.

Method

Participants and Data Source

In this retrospective study, we reviewed data from 724 medical charts of consecutive new patients evaluated for cognitive complaints at the Geneva Memory Clinic between July 1, 2021, and December 31, 2022. For this study, we selected patients with a Mini-Mental State Examination score higher than 17,[24] a global score at Clinical Dementia Rating scale equal to 0.5/1,[25] and whose diagnostic workup included at least 1 diagnostic biomarker, including magnetic resonance imaging (MRI), [^{18}F]-fluorodeoxyglucose (FDG) positron emission tomography (PET), amyloid PET, tau-PET, cerebrospinal fluid (CSF), dopamine active transporter (DAT) single-photon emission computed tomography (SPECT)/PET, and cardiac [^{123}I]-meta-iodobenzylguanidine scintigraphy.

Although the diagnostic pathway can be tailored to each patient's clinical presentation, it is not entirely discretionary. Clinicians' choices are guided by national clinical guidelines, which are also linked to insurance coverage and reimbursement policies.[26] These constraints define a set of recommended and often necessary diagnostic steps to ensure eligibility for specific procedures and facilitate diagnostic standardization. Specifically, in suspected Alzheimer disease (AD), the recommended biomarker pathway follows a stepwise approach: CSF analysis is generally performed first, followed—if necessary—by amyloid PET. In cases of suspected non-Alzheimer dementia, clinicians had more flexibility to select the diagnostic workup based on clinical judgment.[23]

After the filtering, our analytic sample consisted of 539 subjects. For some analyses, we divided the total sample into 3 groups according to the stage of cognitive decline.

- Subjective cognitive decline (SCD) (n = 96) refers to a perceived decline in cognitive abilities compared with previous performance without objective cognitive deficits.[27]
- Mild cognitive impairment (MCI) (n = 308) refers to a cognitive decline that is greater than expected for a person's age but does not interfere significantly with daily life or functional abilities.[28]
- Mild dementia (DEM) (n = 135) is a more advanced stage of cognitive impairment in which the deficits interfere with daily function, and there is a need for assistance with some tasks.[29]

Two independent clinicians (S.B. and F.R.) inserted data in Google Forms, suitable for online questionnaires. This platform allows for the design of customizable surveys and automatically collects responses in a structured format, facilitating data organization and export. From each medical chart, we collected (1) the patient's demographic and clinical data (ie, age, gender, Mini-Mental State Examination, anxiety and depressive symptomatology, diagnostic hypotheses, and final clinical or biomarker-based etiologic diagnosis) and (2) details of diagnostic examinations (ie, types and timing of clinical visits and instrumental examinations from the baseline, until the communication of the diagnosis).

Potential diagnostic hypotheses and final diagnosis were categorized according to the European consensus for the biomarker-based diagnosis of neurocognitive disorders.[23] Access to the data was approved by the Service de la pharmacienne cantonale – Commission cantonale d'éthique de la recherche (CCER) (approval no.: 2023-02028, January 8, 2024).

Analysis Pipeline

The analysis followed a computational pipeline structured as follows:

1. Data preprocessing: evaluation of data quality, handling of missing data through removal, and formatting the data into an Event Log (EL), the basic standard input format for PM analysis[4,30]
2. Descriptive statistics: computation of descriptive average analyses on the cohort
3. Process discovery: application of process discovery algorithms to explore the main clinical workups of the Geneva Memory Clinic and compare the most frequent pathways in the subcohort (ie, SCD, MCI, DEM)

Tools and Data Analyses

All statistical analyses were conducted in R 4.3.2. Descriptive data of demographic and clinical variables were reported as mean (M) supplemented by the standard deviation (SD) or as the number of participants (N) with the percentage in parentheses.

To conduct PM analyses, we used *pMineR*,[31] an open-source R library (freely available at https://github.com/PMLiquidLab/pMineR.v046) mainly built to be applied in health care. This represents a comfortable development environment for data analysis because it is suitable for statisticians, physicists, and physicians, and, therefore, it increases the number of potential users. The choice of *pMineR* was also based on the kind of PM algorithm it proposes. Because of the nature of the analysis, in this study, we used the following 2 specific algorithms for PM: the First-Order Markov Model (FOMM) and the CareFlow Miner (CFM).

The FOMM algorithm builds a directly follows graph (DFG), an intuitive graphical language that connects 2 events (ie, nodes) if they consecutively appear in at least 1 clinical workup (ie, trace). Even if DFGs have some well-known limitations,[32] they are very intuitive and can be helpful in sharing with clinicians and experts a first representation of the data. To mitigate the spaghetti effect (ie, the graphical effect that occurs when analyzed processes are unstructured, irregular, flexible, and variable, making the reading of the graphical visualization of data complex)[33] and simplify the reading of results, the DFG can be pruned by implementing various thresholds, such as those based on the absolute or relative number of transitions, timing considerations, and more.

The CFM algorithm builds a process tree graph of all the clinical pathways followed by the patient.[34] One first graphical visualization that partially used the CFM algorithm is the Between Stacked Nodes (BSN) diagram, which intuitively represents the development of a variable that could assume different values over time. The second graphical visualization that used the CFM algorithm is the CFM diagram. This graph starts with an initial node (ie, root), which includes all the patients (ie, that corresponds to all possible workups), and splits into n subsequent nodes that represent all possible first events in all traces. Each graph node represents a specific visit or instrumental examination and encapsulates the count of patients passing through it. The CFM algorithm is repeated recursively for each new node until we reach the final nodes when all corresponding traces in the EL are exhausted. To mitigate the spaghetti effect, the tree graph can be pruned, either by setting a threshold for the minimum number of patients that have to pass through the node or by limiting the depth of the tree. The CFM algorithm facilitates the creation of descriptive and inferential trees, detailing in each node various statistics such as the number of patients passing through the node (ie, hits) and the likelihood of progressing to specific outcomes in one node (prediction). Related to the CFM algorithm, we also applied the Differential Process Mining (ΔPM) feature,[14] which statistically compares the variance in the workup process of 2 subcohorts (eg, in our study, MCI and DEM subsamples) with a different number of patients passing through the same process tree. The general tree was built using all the patients, as in a standard CFM tree graph. However, each node contains few features for each event, allowing the comparison between 2 subcohorts passing through this general process tree. For instance, the node indicates the proportion of hits in the 2 different subcohorts on the total number of patients in each subcohort, the ratio of hits between the 2 subcohorts, the relative change of this ratio compared to the ratio of initial cardinalities (ie, root node ratio), and the *P* value of a Fisher exact test indicating the level of statistical significance between hits ratio and the root node ratio.

Results

Data preprocessing procedures are reported in Supplementary Material 1.

Descriptive Statistics

Supplementary Table 1 reports the main demographic and clinical characteristics of the total samples and the 3 subcohorts.

Supplementary Table 2 shows the frequencies of examinations available before the start of the clinical workup (ie, available examinations) and after the first visit (ie, performed examinations). There were no statistically significant differences in the frequencies of available examinations among SCD, MCI, and DEM. However, there is a statistically significant difference for performed examinations between the 3 subcohorts in neuropsychological assessment, $\chi^2(2) =$

16.119, $P < .001$; MRI, $\chi^2(2) = 10.668$, $P = .005$; Tau-PET, $\chi^2(2) = 6.553$, $P = .038$; DAT SPECT/PET, $\chi^2(2) = 7.985$, $P = .018$; and CSF, $\chi^2(2) = 31.748$, $P < .001$.

Process Discovery Analyses

The FOMM algorithms

Before presenting the results, we briefly orient to reading the FOMM maps. These maps are based on DFGs, where each node represents a clinical event (eg, a visit or an examination), and each arrow represents a direct temporal transition from one event to the next in at least 1 patient's diagnostic pathway. The thickness and the number in the label of the arrows indicate how frequently that transition occurs in the data set. This representation allows for identifying the most common sequences of diagnostic steps and points of divergence or variability in the clinical workup.

In the overall cohort (Figure 1), the diagnostic itinerary in our memory clinic typically begins with a first clinical visit, moves on to structural neuroimaging (MRI or CT) and formal neuropsychological testing, and culminates in a second visit at which the diagnosis is disclosed. When uncertainty persists, CSF biomarkers are requested—an eventuality that arose in roughly one-quarter of patients—followed by a third visit where the final diagnosis is established. Rare investigations such as FDG-PET contributed little to the main flow and are therefore presented only in Supplementary Figure 1.

Subcohort analyses (Figure 2) showed that patients with SCD underwent a streamlined process. Almost four-fifths (79%) reached a definitive diagnosis by the second visit after completing MRI or CT and neuropsychological assessment, with few requiring additional tests. By contrast, the trajectories of individuals with MCI or DEM were broadly similar to each other: most received imaging and cognitive testing between the initial 2 visits, whereas CSF analysis was usually introduced only when the second visit failed to yield a conclusive diagnosis.

The BSN algorithms

Before presenting the results, we briefly orient to reading the BSN map. This graph represents the set of different pathways between the first diagnostic hypothesis and the final diagnosis. In each pathway, nodes correspond to an event (ie, clinical visits), and each label (eg,

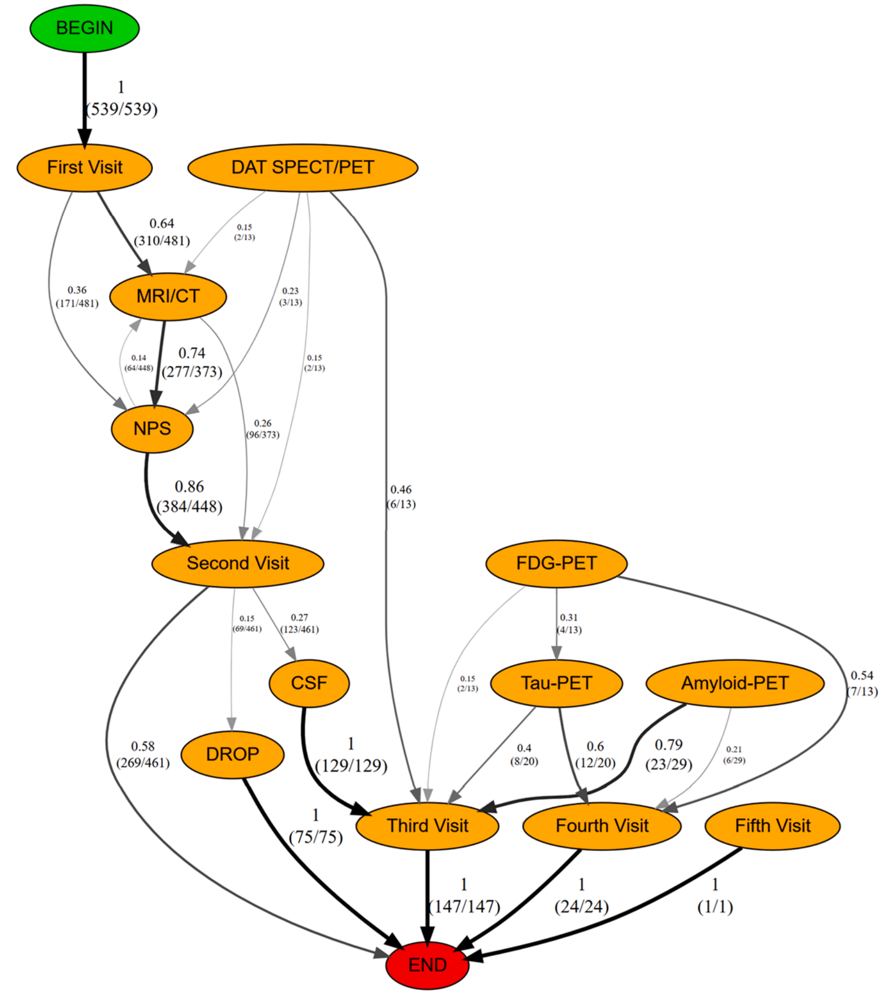
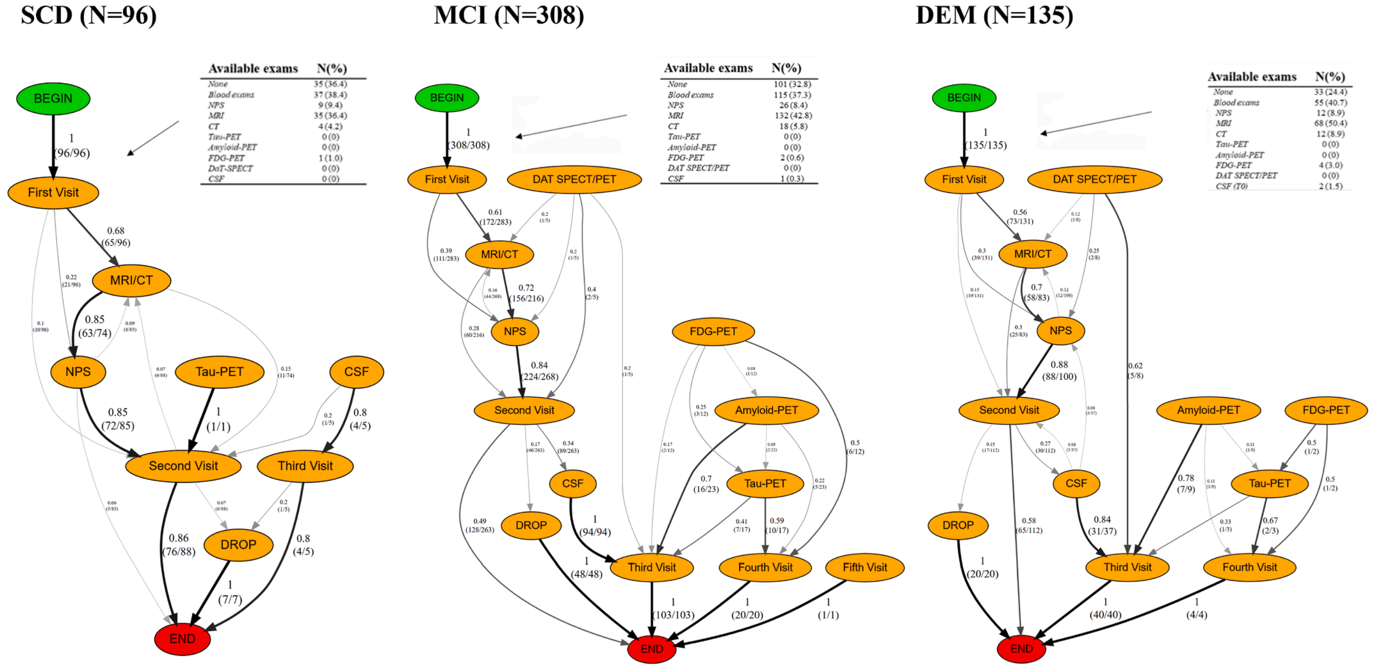


Fig. 1. The First-Order Markov Model (FOMM) algorithms: The graph shows the more frequent connections between events. Each arrow connecting 2 events (represented by orange ovals) shows the most common sequence of events over time, accompanied by the ratio (eg, first visit → MRI/CT: 0.58) and the number of patients following this pathway relative to the total number who completed the previous event (eg, first visit → MRI/CT: 310/530). The bolder the arrow, the more frequent the pathway. If the association between 2 events is rare (frequency <0.20), the arrows were not represented to avoid an overload of nonrepresentative information in the graph. * The event "Fifth Visit" appears isolated in the graph because only 1 patient progressed to the fifth visit before receiving a diagnosis, indicating that a single individual followed this specific pathway and fell below the predefined threshold (ie, frequency <0.20). Consequently, the algorithm included the event in the output chart and connected it to the "End" node; however, the previous steps and their temporal sequence are not displayed because of their extreme rarity compared to other pathways. Amyloid-PET, amyloid positron emission tomography; CSF, cerebrospinal fluid analyses; DAT SPECT/PET, dopamine active transporter scan; FDG-PET, fluorodeoxyglucose positron emission tomography; MRI/CT, magnetic resonance imaging/computed tomography; NPS, neuropsychological assessment; Tau-PET, tau–positron emission tomography.



Available exams	N(%)
None	35 (36.4)
Blood exams	37 (38.4)
NPS	9 (9.4)
MRI	35 (36.4)
CT	4 (4.2)
Tau-PET	0 (0)
Amyloid-PET	0 (0)
FDG-PET	1 (1.0)
DaT-SPECT	0 (0)
CSF	0 (0)

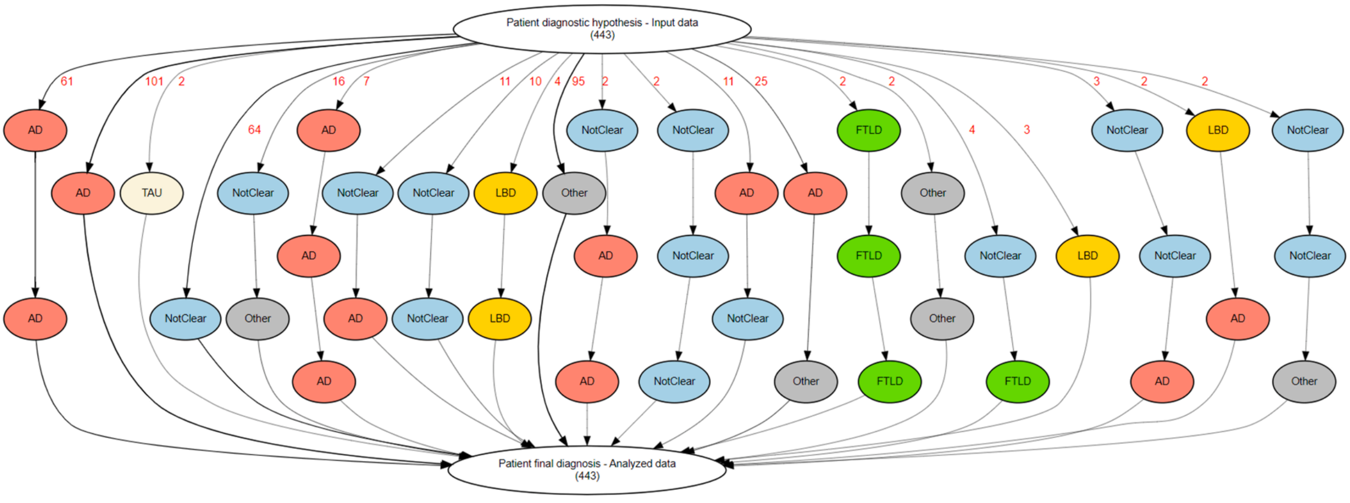
Available exams	N(%)
None	101 (32.8)
Blood exams	115 (37.3)
NPS	26 (8.4)
MRI	132 (42.8)
CT	18 (5.8)
Tau-PET	0 (0)
Amyloid-PET	0 (0)
FDG-PET	2 (0.6)
DAT SPECT/PET	0 (0)
CSF	1 (0.3)

Available exams	N(%)
None	33 (24.4)
Blood exams	55 (40.7)
NPS	12 (8.9)
MRI	68 (50.4)
CT	12 (8.9)
Tau-PET	0 (0)
Amyloid-PET	0 (0)
FDG-PET	4 (3.0)
DAT SPECT/PET	0 (0)
CSF (T0)	2 (1.5)

Fig. 2. The First-Order Markov Model (FOMM) algorithms: The graphs show the more frequent connections between events (ie, visits/instrumental examinations) according to their temporal sequence by cognitive decline stage (ie, SCD, MCI, DEM). Each arrow between 2 events (orange circles) indicates the main temporal movement between the 2 events, supplemented by the ratio and the number of patients moving in this direction on the total number of patients that performed the previous event. The bolder is the arrow, the more frequent is the pathway. If the association between 2 events was rare (<0.20), the arrows were not represented to avoid an overload of nonrepresentative information in the graph. The tables titled "Available exams" reported in the figure for each graph show the number (n) and percentage (%) of examinations performed before the first visit, namely, the examinations that the patient brought to the doctor's attention and that were not prescribed during the diagnostic workup at the Geneva memory clinic. Amyloid-PET, amyloid positron emission tomography; CSF, cerebrospinal fluid analyses; DAT SPECT/PET, dopamine active transporter scan; DEM, mild dementia; FDG-PET, fluorodeoxyglucose positron emission tomography; MCI, mild cognitive impairment; MRI/CT, magnetic resonance imaging/computed tomography; NPS, neuropsychological assessment; SCD, subjective cognitive decline; Tau-PET, tau−positron emission tomography.

AD) and node's color (eg, red) represents a specific category of the variable (ie, diagnostic hypothesis). The number above each pathway reflects the number of patients following this pathway over time. This visualization tracks how clinical impressions or hypotheses evolve along the diagnostic process.

In our study, we used the BSN diagram to visualize changes in the diagnostic hypothesis until the final diagnosis (Figure 3). Excluding the 91 patients (20.5%) who finished their diagnostic pathway with an unclear diagnosis (mainly dropouts), in 278 patients (62.8%), the first diagnostic hypothesis was corroborated at the end of their



Notes: ● NotClear: No clear hypothesis; ● AD: Alzheimer's disease; ● FTLD: Frontotemporal disease; ● LBD: Lewy body disease; ● TAU: Motor tauopathy; ● Other: Other diseases (e.g., psychiatric condition, vascular cognitive impairment, toxic-metabolic or system disease, etc.).

Fig. 3. The Between Stacked Nodes (BSN) algorithms: the graph shows the change of diagnostic hypothesis in MCI and DEM (N = 443). Each pathway represents the specific change through the different clinical visits according to their temporal sequence. In particular, each node (colored ovals) reported the diagnostic hypothesis after each visit. The starting node (white oval, "Patients diagnostic hypothesis—Input data") contains the number of patients the algorithm considers. The final node (white oval, "Patient's final diagnosis—Analyzed data") contains the patients that reach a final diagnosis, confirming the last diagnostic hypothesis reported in the pathway. The red number at the start of each pathway represents the absolute number of patients following that pathway. If the pathway is rarely performed (frequency <2), the processes were not represented to avoid an overload of nonrepresentative information in the graph.

pathway. For instance, in 169 patients (38.1%), the diagnostic hypothesis of AD received on the first visit was confirmed at the end of the diagnostic workup. On the other hand, in 74 patients (16.7%), the first hypothesis was modified after the execution of instrumental examinations. We excluded the rare pathways to provide a more straightforward and readable graph; however, the complete graph is reported in the supplementary material (Supplementary Figure 2).

The CFM algorithms

Before presenting the results, we briefly reference the CFM maps. These graphs are structured as tree diagrams, where each node represents a specific event (eg, a visit or examination), and each branch indicates a possible transition to the next event in the diagnostic process. The root node includes all patients; each subsequent level represents a step further along the diagnostic pathway. The label of each arrow indicates the number of patients who passed through that specific step. This representation allows for exploring all the potential clinical sequences in the diagnostic pathways, identifying more or less common branches, and comparing diagnostic trajectories across subgroups.

Subsequently, we used the CFM algorithm to represent the evolution of workups in our sample. This method allowed us to visualize how specific diagnostic pathways evolve over time and the number of patients following the specific sequence of visits and examinations. The CFM algorithm builds a graph tree starting from an initial virtual state called the root through the events of their clinical pathways (Figure 4). To reduce the *spaghetti effect* and consider the co-occurrence of neuropsychological assessment and morphologic imaging in many patients, we propose to add a new event that aggregates “NPSY” and “MRI/CT” events. The most common clinical pathway started with a first visit, followed by a neuropsychological assessment and a morphologic imaging examination; then, there was a second visit in which the clinician prescribed a CSF examination that was performed before the third visit, in which the patient received the final diagnosis.

Before interpreting the results, we briefly introduce how to read the ΔPM map. This representation compares 2 process models (eg, different subcohorts). The map highlights in yellow only the significant ($P < .05$) differences between the 2 processes: nodes indicate the absolute and relative frequency rates of clinical events between the 2 subcohorts. This visualization identifies the main shifts in diagnostic or care pathways across groups or over time.

In our study, we applied the ΔPM function to compare the clinical workup of 2 subcohort of patients (MCI vs DEM) (Figure 5). The most remarkable differences between the 2 groups concern the first part of their clinical pathways. Specifically, more patients carried out a morphologic imaging examination in the DEM subcohort before accessing the memory clinic than in the MCI subcohort (−20.72%). Indeed, the MCI subcohort is more likely to perform a neuropsychological and morphologic imaging assessment between the first and second visit (40.26%).

Discussion

This proof-of-concept study shows the usefulness of implementing PM techniques on real-world data of memory clinic patients. Indeed, PM algorithms help to map the diagnostic processes for patients with cognitive complaints effectively and elucidate the most commonly performed examinations and their temporal order. As in other cohorts of patients,[14,15] PM is a tool for enhancing the clarity and comprehension of typical diagnostic procedures and a potential foundation for informed clinical and organizational decision-making in memory care settings.

The FOMM Algorithms

The FOMM algorithms led to having a first idea of the general and most common pathways in the Geneva memory clinic, finding that, on average, the most common diagnostic pathways led to the final diagnosis at the second visit after a neuropsychological assessment

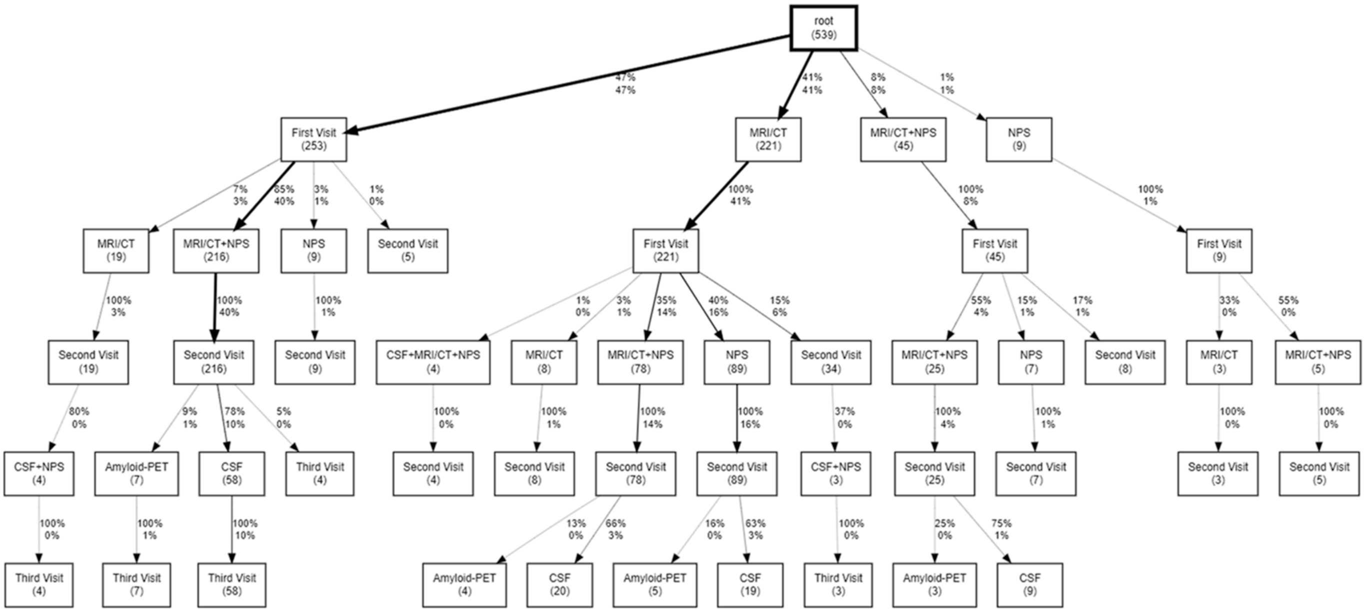


Fig. 4. The CareFlow Miner (CFM) algorithms: The graph describes the evolution of pathways of patients, considering both examinations performed before and after the first visit. The number in parentheses in each node shows the absolute count of patients passing through the node (frequency threshold in the graph = each presented event has a frequency ≥3). On each arrow, the upper percentage shows the proportion of patients following that arrow relative to the total number of patients exiting the node above. The lower percentage shows the proportion of patients following that arrow relative to the total number of patients in the *root* node (for system approximations, if the percentage is <1%, the algorithm returns a percentage of 0%). A second available threshold in CFM is the depth (depth threshold in the graph = 5), namely, the maximum number of events shown for each process (if the event complies with the frequency threshold). Amyloid-PET, amyloid positron emission tomography; CSF, cerebrospinal fluid analyses; NPS, neuropsychological assessment; MRI/CT, magnetic resonance imaging/computed tomography.

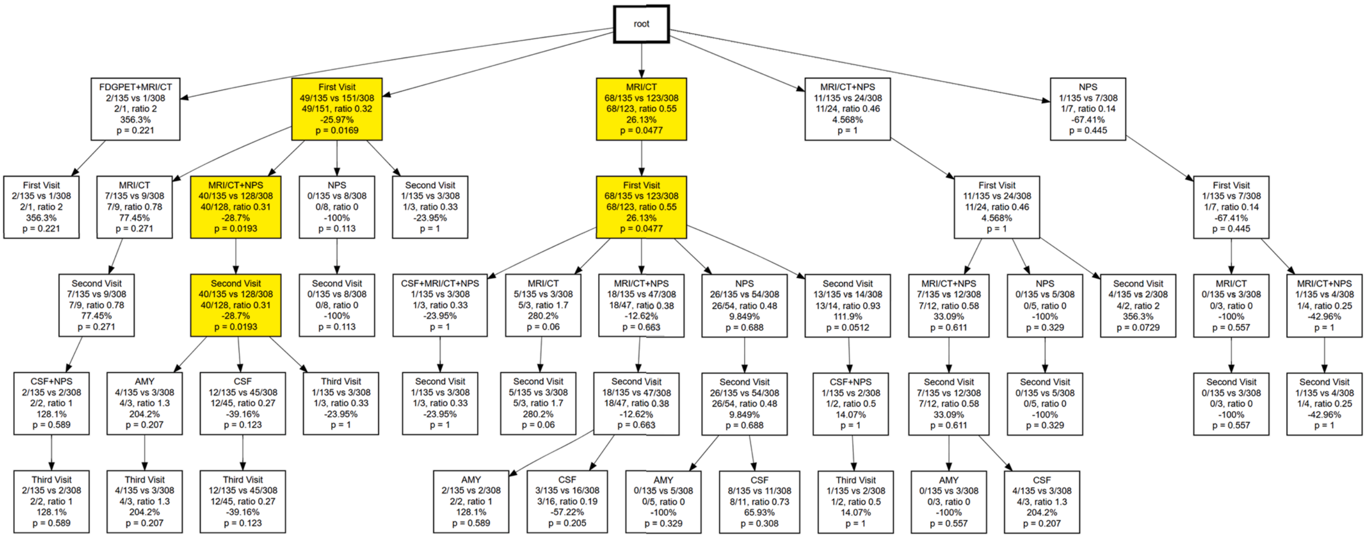


Fig. 5. The CareFlow Miner (CFM) with Differential Process Mining (ΔPM) algorithms: the graph shows differences in hits between 2 subcohorts (MCI vs DEM). The tree graph is constructed as in standard CFM using the whole considered cohort (MCI and DEM, N = 443). Each node (rectangle) contains the following information: the number of patients for each subcohort that performed the event (eg, First Visit, 151/308 vs 49/135 on the total MCI and DEM, respectively), the ratio between MCI and DEM that performed that event in 2 similar expressions (eg, 151/49, ratio 3:1), the ratio expressed in percentage difference with respect to MCI group (eg, 35.07%) between the ratio of MCI and DEM that performed the examination (ie, 151/49) and the initial ratio at the root of the tree (ie, 308/135), and the *P* value on Fisher exact test on the contingency table created by the frequencies of participants who perform or not perform the event in the 2 groups (eg, *P* = .0169). Nodes with a *P* value lower than 0.05 are colored in yellow. Amyloid-PET, amyloid positron emission tomography; CSF, cerebrospinal fluid analyses; MRI/CT, magnetic resonance imaging / computed tomography; NPS, neuropsychological assessment.

and a morphologic imaging examination or at the third visit after the addition of the CSF analyses. However, the graph also suggests a moderate grade of heterogeneity in the data, with a few biomarker examinations (ie, mainly FDG-PET and DAT SPECT/PET) placed at different time points of the diagnostic pathways. The computation of 3 FOMMs according to the severity of the cognitive decline stage (ie, SCD, MCI, DEM) provides a potential explanation for the 2 most frequent diagnostic pathways of the main FOMM. Indeed, the SCD group commonly obtains the diagnosis on the second visit without prescribing biomarkers, whereas the MCI group performs a CSF analysis more often. The DEM group contributed to both pathways, potentially owing to the different ages, clinical symptoms, and severity of cognitive decline.

The BSN Algorithms

The BSN algorithms and graph showed another aspect of the patient cohort: the change in the diagnostic hypothesis until the final diagnosis. The more frequent pathway in our analyses involved the AD hypothesis for MCI and DEM. Therefore, these analyses could help determine the most frequent neurocognitive disorders considered by the Geneva Memory Clinic, adding new information on the evolution of the diagnostic hypothesis during the patient's journey. The change in the diagnostic hypothesis through the different visits is focal information for clinicians, considering its impact on the following prescribed examinations to the patient. Therefore, the BSN graph could be an intuitive tool for clinicians to see how they manage patient care and an opportunity to discuss the most uncommon hypothesis changes and those pathways ending with no precise diagnosis. Indeed, the EL allows us to trace the patients with specific features—for instance, patients ending with no precise diagnosis—and see the specific medical chart of the patient, clarifying reasons for the uncertainty. Otherwise, FOMM algorithms and graphs could be implemented in a subset of the database (eg, patients with uncommon or multiple diagnostic hypothesis changes) to understand better the performed instrumental examinations that caused these changes.

The CFM Algorithms

The CFM algorithms and graph increase the granularity of the data, moving the focus to the most frequent specific pathways. These analyses are the natural extension of FOMM algorithms, providing a view beyond the general and average pathways all patients follow. In our cohort of patients, the first information provided by the CFM is the moderate heterogeneity of individual diagnostic pathways. There are a few frequent temporal sequences of visits/examinations (eg, first visit, MRI/CT+NPS, second visit, CSF, third visit), but no consistent and predominant pathway exists among the others. Interesting in-depth analyses involve the ΔPM function embedded in CFM algorithms. The function allows us to compare 2 data subsets—in our example, MCI and DEM—and highlight the statistically significant difference in the most frequent specific pathways between the 2 considered groups. The results showed more examinations (ie, MRI/CT+NPS) before the first visit in the DEM group than in the MCI group. The last group performed the same examinations significantly after the first memory clinic visit. These results align with general practitioners' standard prescription of neuropsychological assessment and morphologic imaging when they have a clear neurocognitive disorder hypothesis on the patient.[35,36] For the MCI group, in which clinical and cognitive symptoms are often more shaded, general practitioners prefer to prescribe a visit to a memory clinic for a specialized assessment. Memory clinic professionals could find these algorithms valuable in delineating the most repeated sequence of visits and examinations in their cohorts and determining if some subgroups present different pathways, facilitating a more targeted analysis to enhance the effectiveness of clinical procedures.

Taken together, the findings of this proof-of-concept study highlight several key take-home messages. First, PM techniques—through the application of different algorithms—provide complementary and actionable insights into the diagnostic workup of memory clinic patients. Specifically, FOMM graphs enable the identification of common diagnostic trajectories and their timing, offering a high-level overview of how diagnoses are reached across different stages of cognitive impairment. BSN analyses, on the other hand, can capture the evolution of diagnostic hypotheses, allowing clinicians to reflect on how initial clinical diagnoses evolve into final etiological diagnoses and how these transitions may influence the choice of further investigations. Finally, CFM and ΔPM algorithms deepen the level of granularity, offering a dynamic view of how different subgroups (eg, MCI vs DEM) may follow distinct diagnostic paths—potentially because of clinical uncertainty or severity of symptoms—and allowing for statistically grounded comparisons.

These findings underline that PM is not merely a descriptive tool but a method capable of enhancing clinical understanding, supporting decision making, and identifying variability or inefficiencies in routine practice. By providing structured, data-driven visualizations, PM can foster interdisciplinary dialogue and inform future organizational and policy-level decisions in dementia care.

This study also touches on a broader consideration relevant to clinical practice: the trade-off between diagnostic sensitivity and specificity. Clinicians may prioritize different diagnostic goals depending on the clinical stage and presentation. In the early stages of cognitive decline (eg, SCD), the primary concern is often not to miss a potentially progressive neurodegenerative condition, thus requiring higher sensitivity. In intermediate stages (eg, MCI), where uncertainty is greater, sensitivity and specificity must be balanced to avoid over- or underdiagnosis. In more advanced stages (eg, DEM), where impairment is already evident, the focus tends to shift toward specificity, aiming to clarify etiology and inform appropriate care planning. This rationale aligns with recent clinical frameworks that recommend adapting diagnostic strategies based on disease stage and phenotype.[37] Our stratified analysis and process mining outputs reflect these shifting priorities, offering a data-driven view of how diagnostic strategies may differ across the cognitive continuum.

Strengths and Limitations

The study has some strengths, namely, the use of open-source software (*pMineR*) to perform the PM analyses and the relatively easy implementation of the package functionalities after correctly creating the EL. Moreover, the applied technique holds promise to unravel the process underlying the diagnostic pathway of patients in a memory clinic setting, highlighting adherence and deviations from an ideal pathway (eg, international guidelines, internal protocols) and producing a real-world picture of how the diagnosis is achieved. Therefore, this approach offers the opportunity to update and improve clinical protocols, making them more realistic and practical in everyday practice. This process can also help to optimize resources, enhance the quality of care, and ultimately ensure a more effective and targeted diagnostic approach. However, there are some limitations. First, the achieved results using PM analysis techniques in health care could be affected by organizational, administrative, bureaucratic, or insurance constraints that might overlap or replace clinical decision making. Second, for health care professionals, the reading of these graphs could be disorienting and complicated at the first view. However, adopting cutting-edge statistical and visualization technologies (eg, process mining, artificial intelligence) in health care is essential and will be the norm in the coming years. Third, PM relies heavily on the quality and completeness of the data provided by the clinic's IT systems. Incomplete data, missing records, or inaccuracies in recorded events could significantly affect the results and lead to misleading conclusions about diagnosis changes. In our study, we tried to minimize these aspects by entrusting data collection to 2 clinicians supervised by a third expert neurologist; however, mistakes and oversights are possible. Fourth, the ΔPM—at the moment—allows only a comparison between 2 different subsamples of the main population. For this reason, discussions are ongoing with the developers of the software tool to communicate user requirements and guide further enhancements of the software library.

Conclusions and Implications

PM has proven to be an effective, intuitive, and relatively easy-to-use tool for mapping and analyzing memory clinic patients' diagnostic pathways. In addition to traditional descriptive outputs, PM techniques provided a visual and statistical representation of diagnostic pathways, adding value to the representation of these data and potentially contributing to clarity and comprehension of typical diagnostic procedures. Moreover, the PM will allow for tracking and analyzing the actual pathways followed by patients within a memory clinic, detecting any discrepancies between the actual and expected diagnostic processes and allowing for recognizing potential critical areas or bottlenecks that could impact system efficiency. Therefore, these techniques could help to optimize resources, enhance the quality of care, and ultimately ensure a more effective and targeted diagnostic approach. To better understand PM analyses' value and limitations, more studies are needed on implementing these algorithms in other memory clinics.

Disclosure

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Supplementary Data

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