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RESEARCH ARTICLE

The adherence of memory clinics to consensus recommendations for dementia diagnosis: A multicentric study in Italy

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Abstract

INTRODUCTION: Quantitative evaluations of how recommendations influence clinical practice are limited. This study assessed changes in the diagnostic pathways after the 2020 Italian Intersocietal Consensus Recommendations (IICR) for biomarker-based dementia diagnosis.

METHODS: Medical charts of new patients referred to three Italian memory clinics were reviewed for 2018 and 2019 (pre-IICR) and 2022 and 2023 (post-IICR). Sociodemographic and clinical data were extracted. Adherence to IICR was measured using

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an adherence index (AI, range 0–5). Deviations from recommended pathways were analyzed.

RESULTS: We analyzed 601 pathways in pre-IICR and 434 in post-IICR. Biomarker-based diagnoses increased from 23% to 41% post-IICR, with a significant redistribution of diagnostic categories and greater biomarker use. The AI increased modestly (2.09 ± 1.04 to 2.28 ± 1.04; $p = 0.04$), driven by improved neuropsychological assessment and biomarker selection ($p < 0.001$). Deviation analyses showed that adherence remained heterogeneous, with reduced biomarker use in older patients.

DISCUSSION: Diagnostic practices partially aligned with IICR, reflecting a progressive shift toward standardized, biologically informed dementia diagnosis in Italian expert centers.

KEYWORDS
diagnosis, neurocognitive disorders, practice, recommendations, validation study

Highlights

- A multicentric study evaluated real-world feasibility of dementia recommendations.
- Adherence to diagnostic workflows was measured using a quantitative index.
- Biomarker-based diagnoses increased after guideline publication.
- Real-world deviations reflect system-level barriers to implementation.

1 | BACKGROUNDS

Neurodegenerative disorders, such as Alzheimer's disease (AD), Lewy body dementia (LBD), and frontotemporal lobar degeneration (FTLD), are progressive conditions characterized by significant cognitive and behavioral impairment.[1–5] These disorders, affecting millions of individuals globally, pose a substantial burden on health-care systems and society. Timely and accurate diagnosis is essential to future disease management, including symptom handling, home-based caring, disease-modifying drug administration, insurance and reimbursement issues, and treatment trial access.[6,7] Guidelines and recommendations are crucial for improving diagnoses' accuracy and consistency, facilitating effective patient care, and advancing research. For these reasons, numerous national and international organizations and scientific societies have published diagnostic criteria statements[1,2] and recommendations for biomarker-appropriate use in the diagnostic process.[8–11]

In this context, in 2020 six Italian scientific societies published the Italian Intersocietal Consensus Recommendations (IICR), including a diagnostic workflow promoting an integrated and rational use of validated biomarkers for the etiological diagnosis of the major forms of neurocognitive disorders[12] (see details in Figure 1). The workflow suggests two consecutive assessments, that is, the baseline and the biomarker-based assessment. The baseline assessment includes four domains of assessment (i.e., clinical visit, blood tests, neuropsychological assessment, and structural imaging—computed tomography or magnetic resonance imaging [MRI]) and aims at formulating a syndromic diagnostic hypothesis among the main forms of neurocognitive disorders (i.e., AD, LBD, FTLD). The biomarker-based assessment recommended the best biomarker according to the syndromic diagnostic, among cerebrospinal fluid (CSF) analysis, positron emission tomography (PET) with amyloid tracer (amyloid), or with 2-deoxy-2-[18F]fluorodeoxyglucose (2-[18F]FDG), dopamine transporter (DaT) single-photon emission computed tomography (SPECT), or [^{123}I]metaiodobenzylguanidine ([^{123}I]-MIBG) cardiac scintigraphy.

Despite their potential impact, the real-world implementation of diagnostic guidelines in clinical practice remains largely unexamined. To the best of our knowledge, only a few studies systematically evaluated implementation and adherence to guidelines in clinical practice.[13–15] These studies share several methodological features: they adopted retrospective designs and reviewed medical records systematically. Typically, they focused on key diagnostic procedures (e.g., cognitive assessments, neuroimaging, and laboratory exams) documented at the time of diagnosis. However, most did not account for factors that could influence adherence, such as resource availability, local protocols, or clinician preferences. More importantly, they rarely explored the extent and type of deviations from guidelines, particularly regarding the use of advanced diagnostic tools such as biomarkers.

This pilot study was conceived as a proof-of-concept implementation analysis to examine how the IICR translate into routine diagnostic practice. We assessed adherence to the IICR workflow in three Italian memory clinics, comparing diagnostic practices before and after their publication. Additionally, we characterized patterns of non-adherence to the recommended use of biomarkers to identify how real-world

RESEARCH IN CONTEXT

1. **Systematic review**: The authors reviewed the literature using traditional sources (e.g., PubMed) to examine how the feasibility of diagnostic guidelines and recommendations for dementia is assessed in clinical practice. Available studies primarily assessed feasibility through retrospective designs, using quantitative adherence or compliance measures. However, these investigations were limited in number, heterogeneous in approach, and generally restricted to single-center experiences or selected diagnostic components rather than the full recommended diagnostic workflow.
2. **Interpretation**: This study provides a multicentric, quantitative evaluation of the real-world feasibility of the Italian Intersocietal Consensus Recommendations for biomarker-based dementia diagnosis (Boccardi et al., 2020), applying a structured adherence index to entire diagnostic pathways. The findings show modest but significant improvements in adherence after recommendation publication, alongside persistent organizational and logistical constraints.
3. **Future directions**: These results extend existing knowledge by empirically documenting both progress and barriers in guideline translation. Future research should examine whether the implementation barriers observed in Italy are shared across other European health-care systems, in line with ongoing efforts to harmonize biomarker-based diagnostic workflows at the European level.

clinical practices and center-specific factors may have influenced such deviations. By providing an initial empirical assessment of guideline implementation in specialized centers, this study aims to generate hypotheses and methodological insights for future broader evaluations of diagnostic practice.

2 | METHODS

We retrospectively analyzed clinical data from consecutive new patients referred for cognitive complaints to three regionally representative Italian memory clinics (Padua, Rome, and Chieti) in 2018 and 2019 (P1, before IICR publication) and 2022 and 2023 (P2, after IICR publication) to examine diagnostic pathways and determine etiological diagnoses.

Two independent clinicians per center were identified for the data collection (i.e., three neuropsychologists, two neurology residents, and one psychologist researcher) and trained to use an ad hoc built online platform specifically developed using LAMP technology (Linux, Apache, PHP, MySQL). An inter-rater reliability procedure was developed to prevent rater bias. Briefly, the clinicians were required to enter data into the platform from 10 anonymized medical charts provided by the coordinating center (IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli). The inter-rater reliability procedure was judged completed when the data imputed by each clinician agreed 100% with the data imputed by the coordinating center's personnel (i.e., S.O., a geriatrician and C.F., a senior researcher). Collected data included demographic and clinical variables (i.e., age, sex, Mini-Mental State Examination [MMSE] score), the number and timing of clinical visits and diagnostic procedures (i.e., neuropsychological assessment, blood tests, MRI, 2-[18F]FDG PET, amyloid PET, CSF analysis, DaT SPECT, cardiac [^{123}I]-MIBG scintigraphy), diagnostic hypothesis, and final diagnosis.

Clinical pathways were categorized as (1) non-diagnostic, for example, visit for disability assessments, tax benefits, second opinion visit, and drug prescriptions; (2) diagnostic without biomarkers, that is, when the diagnostic pathway only consisted of neuropsychological assessment and structural imaging; (3) biomarker-based diagnostic, when at least a biomarker exam was prescribed.

The study was approved by the IRCCS Fatebenefratelli Ethics Committee (approval date: January 25, 2022; Approval No.: 2/2022) and it was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

2.1 | Statistical analyses

Descriptive statistics were computed for all variables. Means and standard deviations were reported for continuous variables, while frequencies and percentages were calculated for categorical variables. Normality was assessed using the Shapiro–Wilk test.

Diagnostic pathway adherence to IIRC was assessed using the adherence index (AI), modified from Turró-Garriga et al.[13] Global AI was computed based on the adherence score of the baseline and biomarker-based assessment. For baseline assessment, a weighted AI was computed to assess the completeness and clinical relevance of the diagnostic pathway across the four domains, that is, blood exams, clinical and neuropsychological assessment, and structural imaging (Figure 1). For each domain the IICR specified the essential features to be included for a comprehensive evaluation (e.g., specific cognitive domains to be assessed in neuropsychological assessment, or acquisition and analysis parameters for MRI). Each feature was independently rated by three expert neurologists (L.B., G.B., A.C.), using a three-point scale based on clinical utility (i.e., 1 "useful," 2 "important," 3 "essential"). This weighting procedure was introduced to refine the original adherence framework proposed by Turró-Garriga et al.,[13] allowing the index to better reflect the relative diagnostic relevance of individual components of the clinical work-up rather than treating all procedures as equally informative. The mean of these ratings represented the diagnostic weight of each feature (see Figure S1 in supporting information for more details). The adherence score ranged from 0 (i.e., not used

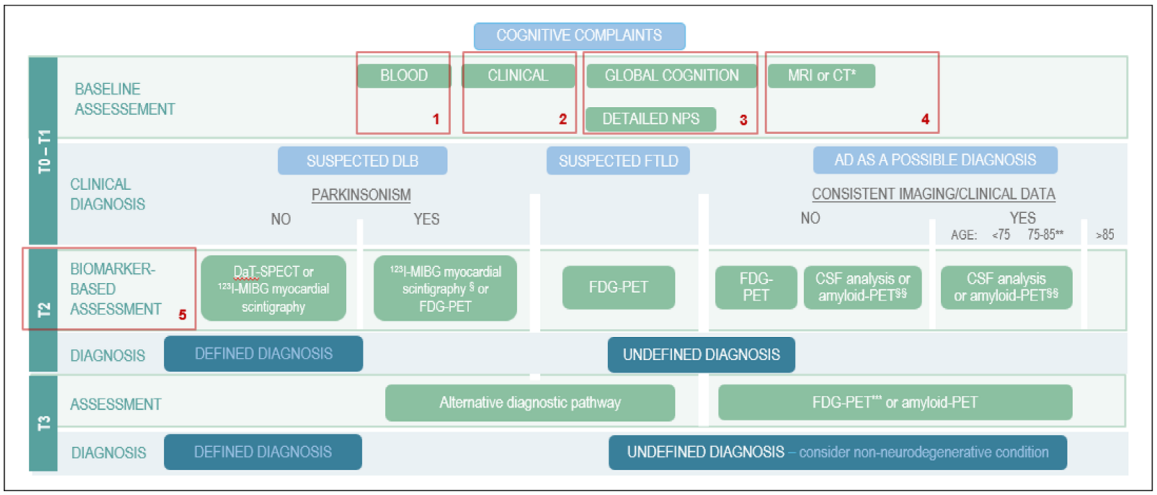

FIGURE 1 Computation of adherence index based the Italian Intersocietal Consensus Recommendations (IICR, graph modified from Boccardi et al, 2020). The IICR diagnostic pathway includes two consecutive levels: a baseline assessment (T0–T1), including four domains (i.e., blood exams, clinical and neuropsychological assessment, and structural imaging), followed by a biomarker-based assessment (T2 & T3). Numbered boxes indicate the data used to compute the adherence index (see Methods for details). AD, Alzheimer's disease; CSF cerebrospinal fluid; CT, computed tomography; DaT, dopamine transporter; DLB, dementia with Lewy bodies; FDG, fluorodeoxyglucose; FTLD, frontotemporal lobar degeneration; MIBG, metaiodobenzylguanidine; MRI, magnetic resonance imaging; NPS, neuropsychiatric symptoms; PET, positron emission tomography; SPECT, single-photon emission computed tomography.

after the IICR) to 1 (i.e., used after the IICR) for each domain, with the contribution of each feature proportionally weighted according to its assigned diagnostic relevance. Similarly, the adherence index for the biomarker-based assessment was scored by assigning a value of 0 (i.e., biomarker not used or not used according to the IICR) or 1 (i.e., biomarker used according to the IICR).

Thus, the global AI score was calculated by summing these five domain scores (i.e., the four domains of baseline assessment and the domain of the biomarker-based assessment), ranging from 0 to 5, with higher scores indicating greater adherence to IICR. Differences in global AI scores between the two periods (P1 and P2) were tested using the Mann–Whitney *U* test.

To further characterize real-world diagnostic practices, each biomarker-based diagnostic pathway was classified along two independent binary dimensions, adherence and deviation. Adherence referred to the appropriateness of biomarker selection with respect to the IICR. A pathway was considered adherent when the biomarker recommended for the specific diagnostic hypothesis (e.g., CSF for AD, FDG PET for FTLD, DaT SPECT for LBD) was used exactly as prescribed, without omission or addition of other biomarkers. Pathways were classified as non-adherent when biomarker use diverged from the IICR, for instance through omission of the recommended biomarker, substitution with a non-indicated test, or combination of multiple biomarkers when only one was indicated.

Deviation, in contrast, referred to the structural conformity of the overall diagnostic workflow. A pathway was defined as deviant when it departed from the expected sequence or completeness of the IICR diagnostic process, including the omission of a baseline domain (i.e., clinical, neuropsychological, blood, or imaging assessment) or the use of a biomarker not indicated for that diagnostic hypothesis. Pathways that fully respected the recommended structure were classified as non-deviant.

Cross-classifying adherence and deviation yielded four mutually exclusive groups: adherent/non-deviant (biomarker and workflow both aligned with the IICR), adherent/deviant (correct biomarker but incomplete or structurally inconsistent workflow), non-adherent/non-deviant (correct structure but inappropriate biomarker use), and non-adherent/deviant (both biomarker and workflow diverging from the IICR). This framework allowed the disentanglement of content-related deviations (inappropriate biomarker use) from process-related deviations (structural omissions or workflow errors).

The relationship between adherence and deviation was examined using 2×2 contingency tables, visualized through mosaic plots in which cell areas represented group frequencies and colors encoded Pearson residuals from χ^2 tests (blue indicating overrepresentation and red underrepresentation).

UpSet plots were used to visualize the most frequent combinations of biomarkers used in clinical practice and identify the most frequent deviations.

All statistical analyses were conducted using R software version 4.3.2. Statistical significance was set at a two-tailed p value < 0.05.

3 | RESULTS

Data collection started in June 2023 and ended in July 2025. In P1 601 medical charts were reviewed. Among them, 201 (33.4%) described non-diagnostic visits, 271 (45.1%) a no biomarker–based diagnostic pathway, and the remaining 129 (21.5%) a biomarker-based diagnostic pathway. The P2 cohort comprised 434 patients' medical charts,

TABLE 1 Patient sociodemographic characteristics of the reviewed charts before (P1, 2018–2019) and after (P2, 2022–2023) publication of the IICR (*N* = 722).

	P1 *N* = 400		P2 *N* = 322	
Diagnostic pathways	**Without biomarkers**	**Biomarker based**	**Without biomarker**	**Biomarker based**
N	271	129	217	105
Age (mean ± SD)	75.7 ± 9.3	69.3 ± 9.2	70.1 ± 12.1	69.5 ± 7.9
Sex (female %)	60.1%	46.5%	60.4%	47.6%
MMSE (mean ± SD)	22.8 ± 5.8	22.6 ± 4.9	24.0 ± 6.3	23.5 ± 4.3
Biomarker used (*n*, %)				
2-[18F]FDG PET	–	68 (52.7%)	–	42 (40.0%)
CSF	–	31 (24.0%)	–	30 (28.6)
Amyloid PET	–	14 (10.8)	–	26 (24.8)
DaT SPECT	–	16 (12.5)	–	7 (6.6)
Cardiac [^{123}I]-MIBG scintigraphy	–	0 (0%)	–	0 (0%)
Final diagnosis (*n*, %)				
Alzheimer's disease	61, 22.5%	49, 38.0%	47, 21.7%	51, 48.6%
Lewy bodies disease	12, 4.4%	24, 18.6%	29, 13.4%	21, 20.0%
Frontotemporal dementia	3, 1.1%	23, 17.8%	8, 3.7%	14, 13.3%
Subjective cognitive complain	54, 19.6%	10, 7.8%	47, 21.7%	11, 10.5%
Vascular disease	53, 19.2%	6, 4.7%	20, 9.2%	0, 0%
Other	88, 33.2%	17, 13.2%	66, 30.4%	8, 7.6%

Abbreviations: CSF, cerebrospinal fluid; DaT, dopamine transporter; FDG, fluorodeoxyglucose; IICR, Italian Intersocietal Consensus Recommendations; MIBG, metaiodobenzylguanidine; MMSE, Mini-Mental State Examination; PET, positron emission tomography; SD, standard deviation; SPECT, single-photon emission computed tomography.

of whom 105 (24.2%) were diagnostic pathways with biomarkers and 217 (50.0%) were diagnostics pathways without. Table 1 shows the sociodemographic and clinical characteristics of the patients across the diagnostic pathways. The distribution of final diagnoses differed significantly between pathways with and without biomarkers in both cohorts (P1: $\chi^2[5] = 98.3$, $p < 0.0001$; P2: $\chi^2[5] = 59.1$, $p < 0.0001$). In each period, AD was more frequently diagnosed within biomarker-based pathways (P1: 38.0% vs. 22.5%; P2: 48.6% vs. 21.7%), confirming the preferential use of biomarkers where etiological confirmation is most established. Similar trends were observed for LBD and frontotemporal dementia (FTD), whereas subjective cognitive complaints and vascular diagnoses predominated in non-biomarker pathways.

Between cohorts, the proportion of biomarker-supported AD diagnoses increased from 38.0% to 48.6%, paralleled by a reduction in non-specific or "other" categories (13.2% to 7.6%). These findings indicate a gradual consolidation of biomarker-guided diagnostic practice after the IICR publication, with a more targeted and hypothesis-driven application of biomarkers across major neurocognitive disorders.

The following analyses focus only on biomarker-based diagnostic pathways. Overall, 2-[^{18}F]FDG PET was the most frequently used biomarker, accounting for 115 out of 249 total biomarkers (46.2%). However, CSF remained the most selected first-choice biomarker, used in 52 cases (20.9%). The most common final diagnosis was AD (P1: *N* = 49, 37.9%; P2: *N* = 51, 48.6%) followed by LBD (P1: *N* = 24, 18.6%; P2: *N* = 21, 20.0%).

The Mann–Whitney *U* test revealed a modest but statistically significant increase in global AI scores in P2 compared to P1, with mean values increasing from 2.09 ± 1.04 in P1 to 2.28 ± 1.04 in P2 ($U = 8107$, $p = 0.047$; Figure 2). When examining AI scores across baseline assessment domains (Figure 3), the improvement was primarily driven by enhanced adherence to neuropsychological assessments, which rose from 0.40 ± 0.36 in P1 to 0.48 ± 0.43 in P2 ($U = 9\,492$, $p < 0.001$). In contrast, no significant differences were observed in adherence to clinical visits, structural imaging, or blood tests between the two periods (all $p > 0.12$).

We examined the relationship between biomarker adherence and diagnostic deviation (Figure 4). Each diagnostic pathway was classified according to the two independent binary dimensions described above. A significant association emerged between adherence and deviation ($\chi^2 = 84.4$, $p < 2.2 \times 10^{-16}$). In both cohorts, the most frequent profile was adherent and non-deviant, representing pathways in which both biomarker selection and overall workflow were fully aligned with the IICR (P1: 119 [66.9%]; P2: 92 [66.2%]). The second most common category was non-adherent and deviant (P1: 37 [20.8%]; P2: 22 [15.8%]), indicating diagnostic pathways diverging from IICR both in biomarker use and in process structure. Less frequent profiles included adherent but deviant pathways (P1: 13 [7.3%]; P2: 16 [10.8%]), in which

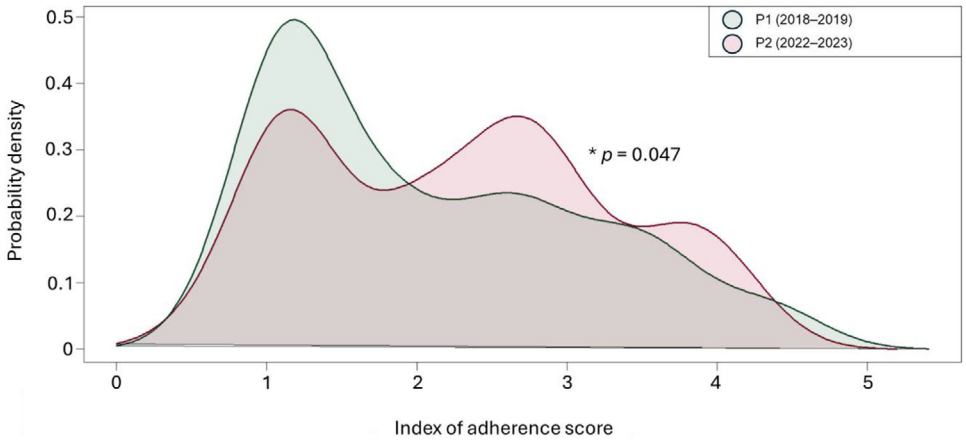

FIGURE 2 Distribution of the global AI score in P1 and P2. Kernel density plots show a rightward shift in P2, indicating improved adherence to diagnostic recommendations. Mean (SD) global AI increased from 2.09 (1.04) in P1 to 2.28 (1.04) in P2 (Mann–Whitney $U = 8107$). AI, adherence index; SD, standard deviation.

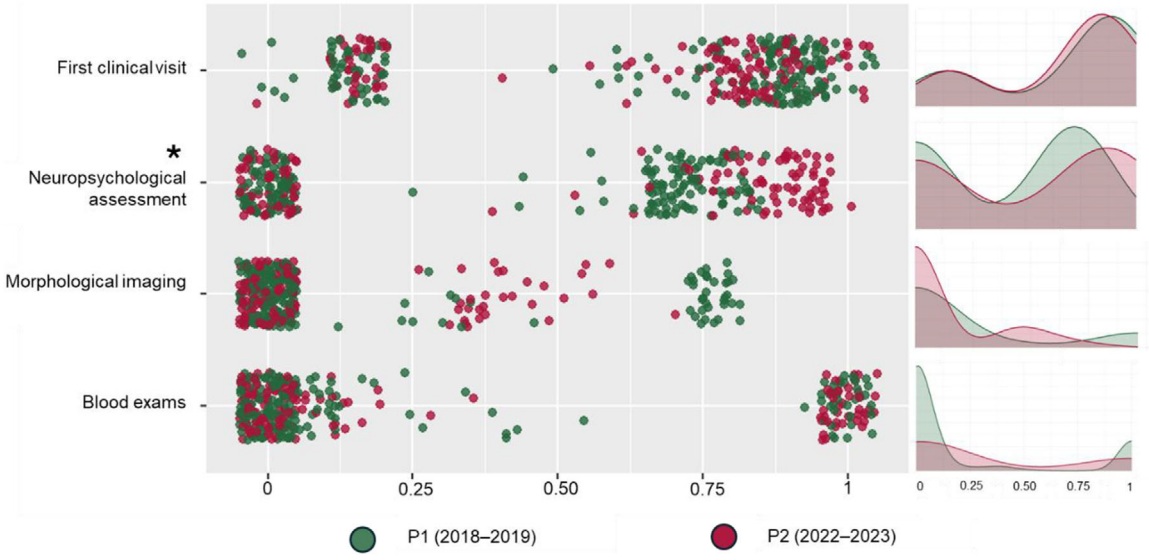

FIGURE 3 Adherence to IICR across baseline assessment domains in P1 and P2. Higher adherence levels were observed in P2 (red dots) versus P1 (green dots), only for neuropsychological assessment domain (Mann–Whitney *U* test; $^*P < 0.05$), suggesting improved compliance after the IICR implementation. IICR, Italian Intersocietal Consensus Recommendations.

biomarker choice was correct but the diagnostic process omitted one or more baseline domains. These distributions underscore that adherence to biomarker recommendations was strongly associated with the structural integrity of the diagnostic pathway.

To further characterize how clinical practice diverges from IICR, Figure 5 displays the frequency and overlap of diagnostic examinations within the P2 cohort, stratified by diagnostic hypothesis. Each intersection represents a specific combination of tests performed across patients, allowing visual identification of pathways consistent with, or deviating from, IICR recommendations. This graphical analysis provides a detailed view of adherence and deviation patterns in real-world diagnostic workflows. In FTLD (Figure 5A), the most common pattern ($n = 11$) omitted 2-[18F]FDG PET, suggesting underuse of this recommended exam. In LBD (Figure 5B), patterns were more heterogeneous: CSF was overused in four pathways, (DaT) SPECT was omitted in seven, and eight pathways lacked at least one baseline assessment. Among AD patients aged ≤ 75 years (Figure 5C), deviation included omission of the IICR-recommended biomarker in eight cases. In AD patients aged 75 to 85 years (Figure 5D), for which guidelines allow clinical discretion to use biomarkers or rely solely on syndromic diagnosis, biomarker use was less frequent overall. Nevertheless, deviations were still observed, with 27 pathways missing at least one domain of the baseline assessment. Advanced biomarker use was less frequent overall in this older group, potentially reflecting concerns regarding invasiveness or access.

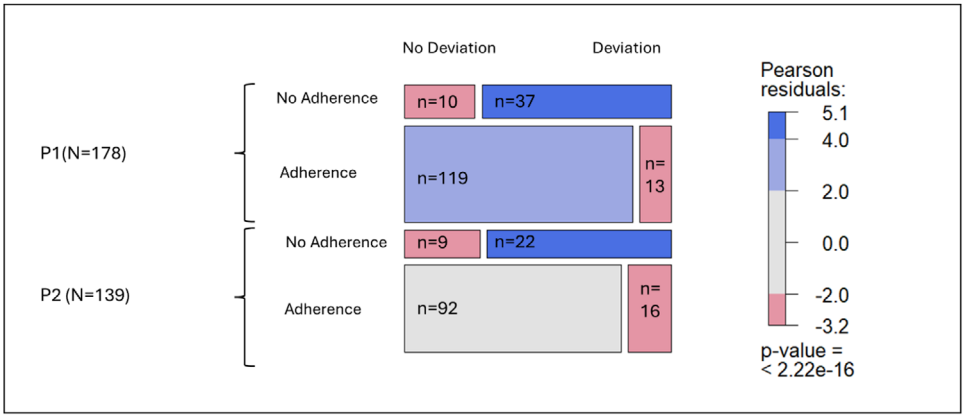

FIGURE 4 Distribution of diagnostic pathways by biomarker adherence and deviation status. Mosaic plot illustrating the distribution of diagnostic pathways according to two independent binary dimensions: biomarker adherence (adherent vs. non-adherent) and diagnostic deviation (deviant vs. non-deviant). Cell areas represent the relative frequency of each combination, and color intensity encodes Pearson residuals from the χ^2 test of independence (blue: cells occurring more frequently than expected; red: less frequent). The most prevalent profile in both cohorts was adherent and non-deviant, indicating full alignment with IICR recommendations in both biomarker selection and workflow structure. Adherent but deviant pathways reflect correct biomarker choice but incomplete diagnostic workflows, whereas non-adherent and deviant pathways show divergence from IICR on both dimensions. A significant association between adherence and deviation was observed ($\chi^2 = 84.4$, $p < 2.2 \times 10^{-16}$). IICR, Italian Intersocietal Consensus Recommendations.

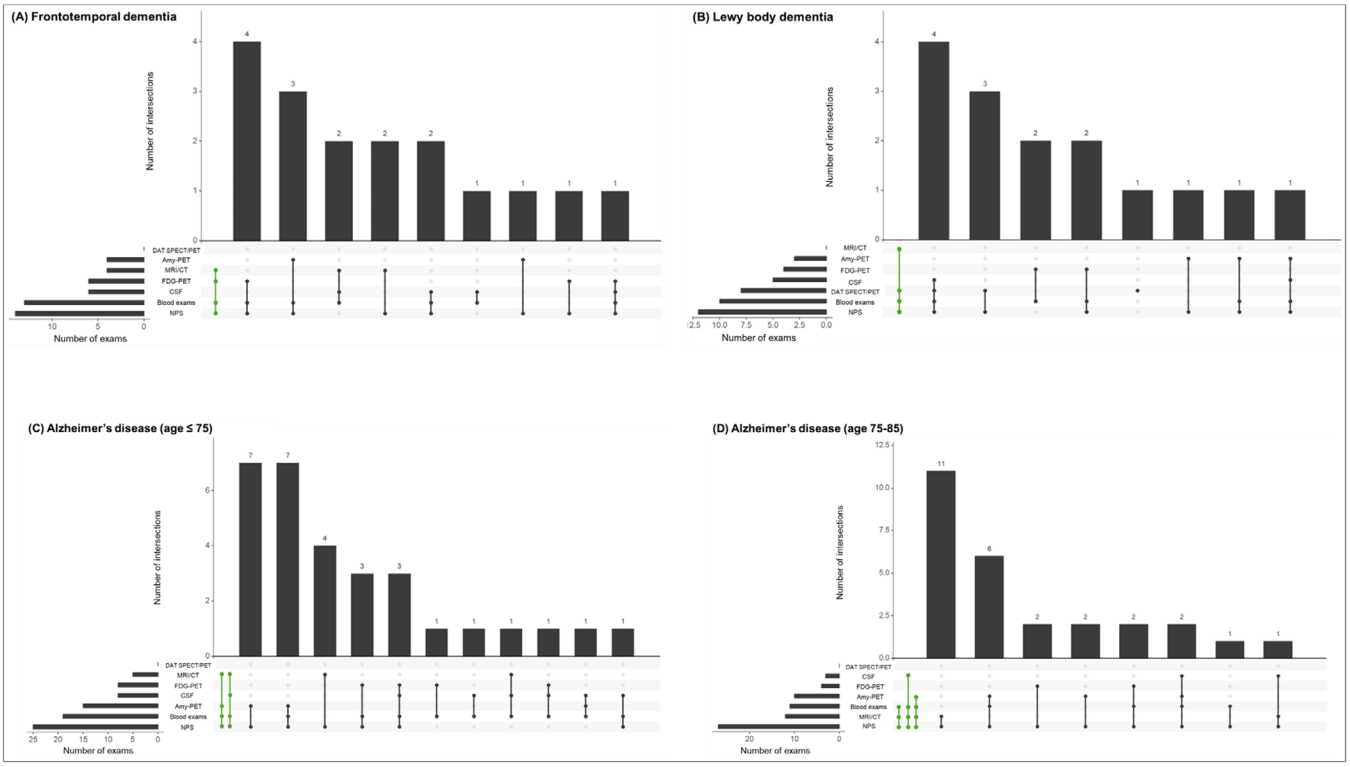

FIGURE 5 Patterns of biomarker use and deviations from IICR across diagnostic hypotheses (P2 cohort). The UpSet plot displays the most frequent deviant combinations of diagnostic exams used in patients with a working diagnosis of FTD (A), LBD (B), patients with a diagnosis of AD aged ≤ 75 years (C), patients with AD aged 75 to 85 years (D) during the 2022 to 2023 period. Green bars highlight exam combinations fully consistent with IICR recommendations; black intersections represent deviations. Horizontal bars show exam frequency; vertical bars show combination counts. For FTD (A), the main deviation was underuse of FDG PET. In LBD (B), patterns were heterogeneous, with frequent omission of DaT SPECT and occasional overuse of CSF. In younger AD patients (C), deviations mainly reflected omission of CSF or amyloid PET, while in older AD patients (75–85 years; D) advanced biomarker use declined overall, suggesting their potential underuse. AD, Alzheimer's disease; CSF cerebrospinal fluid; CT, computed tomography; DaT, dopamine transporter; DLB, dementia with Lewy bodies; FDG, fluorodeoxyglucose; FTD, frontotemporal dementia; IICR, Italian Intersocietal Consensus Recommendations; LBD, Lewy body dementia; MRI, magnetic resonance imaging; NPS, neuropsychiatric symptoms; PET, positron emission tomography; SPECT, single-photon emission computed tomography.

4 | DISCUSSION

Evaluating adherence to guidelines in real-world clinical contexts is essential, as guidelines must be not only scientifically sound but also feasible, reliable, and beneficial in routine practice. A biomarker-based diagnostic pathway can enhance diagnostic precision, support appropriate patient management, and reduce unnecessary procedures, ultimately contributing to the sustainability of health-care systems.[11,16] Quantifying the discrepancies between recommended and actual practices is therefore crucial to inform targeted improvement strategies.

In this multicentric study, we assessed the real-world impact of the IICR for the biomarker-based diagnosis of cognitive complaints in the Italian clinical practice of three academic memory clinics. Our findings reveal modest but statistically significant improvements in adherence after the IICR publication reflected in higher AI scores driven by more comprehensive neuropsychological assessments and an increased, though variably applied, use of biomarkers across diagnostic groups and age ranges.

Real-world validation studies, such as this, provide critical insights into practical barriers to implementation that can hinder the implementation of clinical guidelines. The aim of the present study was not to establish causal effects of the IICR but to describe implementation dynamics and deviations in real-world clinical workflows. They help identify areas requiring clarification or adaptation and assess whether diagnostic recommendations are effectively translated into improved patient outcomes.[17,18] In this context, the observed improvement in neuropsychological assessments may reflect heightened clinician awareness, with potential cost-effectiveness implications, as comprehensive cognitive profiling is central to differential diagnosis, patient stratification, and therapeutic planning.[19] This trend may be attributable not only to the publication of the IICR but also to broader national efforts to harmonize dementia care, such as those led by the Italian Network of Neuroscience and Neurorehabilitation.[20] By supporting shared protocols and fostering professional alignment, these structural developments may have contributed to the increased adherence observed in this diagnostic domain.

The formal analysis of non-adherent diagnostic pathways highlighted recurring deviations from the recommended workflow. Most notably, a substantial proportion of diagnostic trajectories lacked one or more domains of the baseline assessment. Structural neuroimaging and blood tests emerged as the most frequently undocumented procedures. According to the clinicians involved, this pattern may not reflect a true omission of examinations, but rather a failure in the systematic integration of results into the medical records, pointing to deficiencies in standardized reporting practices. MRI was particularly affected, and clinicians hypothesized that post-COVID restructuring, for example, the outsourcing of imaging to territorial facilities to address backlog, might have contributed to incomplete documentation within institutional archives. Although such reorganization improved access, it may have inadvertently compromised data traceability, with potential implications for clinical continuity, auditability, and research reproducibility. The observed gaps in systematic reporting of assessments underscore the need for improved digital infrastructures. Incorporating structured templates and decision-support tools into electronic health records could facilitate adherence monitoring and traceability of diagnostic procedures, therefore promoting research reproducibility and standardization across centers.

Another key observation was the heterogeneity in biomarker combinations, even within the same diagnostic hypothesis. The reduced biomarker use in older adults and the heterogeneity across centers may reflect not only clinical discretion but also disparities in resource allocation and reimbursement policies. For example, among patients with suspected AD, there was a clear tendency to favor amyloid PET over CSF analysis. When stratifying by center (results not shown), however, greater consistency was noted in the selection of first-line biomarkers, suggesting that local protocols may play a stabilizing role. According to participating clinicians, logistical constraints and center-specific resource availability were central in shaping biomarker use, often taking precedence over purely diagnostic considerations. The choice and timing of examinations were frequently dictated by institutional workflows and test accessibility. Some deviations may reflect not only logistical barriers but also areas of uncertainty within the IICR workflow itself. For instance, the recommendations allow clinical discretion in older patients, for whom biomarker use is not strictly mandated. Such flexibility, while clinically justified, may also contribute to variability in practice. Refining the guidelines to provide clearer decision trees for specific clinical scenarios, such as advanced age, multimorbidity, functional status and frailty, or suspected mixed etiologies, could reduce heterogeneity and strengthen their clinical utility.

These findings highlight the enduring tension between recommendations and real-world system constraints, an aspect that should be more explicitly addressed in future efforts to promote guideline implementation and equity of access.

Finally, while our findings point to measurable improvements in adherence after the IICR publication, they must be interpreted considering the scope and context of the study. All three participating centers are academic, highly specialized memory clinics, with privileged access to advanced biomarkers and research infrastructures. As such, the results may not reflect the broader landscape of memory services in Italy, particularly those based in non-academic or community settings. Extrapolations to national practice should therefore be made with caution, and further multicenter work including community-based facilities is advised to capture the full spectrum of real-world implementation.

In this sense, the present study should be interpreted as a pilot, proof-of-concept implementation analysis aimed at providing an initial empirical assessment of how consensus-based diagnostic workflows translate into routine practice in expert centers. In this context, the present study can be interpreted as the Italian pilot phase of a broader European validation effort (EUROVALICO), aimed at assessing the implementation of consensus-based diagnostic workflows across European memory clinics within a harmonized methodological framework. Future research should extend this framework to larger and more heterogeneous samples of memory clinics, including cross-

national comparisons, to better characterize structural determinants of guideline implementation across health-care systems.

In addition, the present study did not include patient-centered outcomes (e.g., diagnostic accuracy, time to diagnosis, or downstream clinical decisions), and future prospective studies will be needed to assess whether improved adherence to diagnostic workflows translates into measurable clinical or health-system benefits.

The present results may also have relevance beyond the Italian setting. Similar challenges in guideline implementation have been reported in other European countries, with studies highlighting underuse of biomarkers and variability in diagnostic completeness.[21,22] Comparative analyses across nations could clarify whether the barriers we observed are context specific or represent broader systemic issues, in line with the recent effort in the development of a European workflow for harmonization of diagnostic biomarker use in the dementia setting.[11] Ensuring that guideline-based diagnostic opportunities are equitably available across age groups and geographic areas should be a public health priority, particularly in view of the imminent implementation of disease-modifying therapies in Europe.

In conclusion, while the IICR fostered measurable improvements in diagnostic practice, their full realization in clinical routines remains contingent upon addressing practical barriers, standardizing reporting frameworks, and integrating logistical feasibility into implementation policies. Future research should build upon these insights, using prospective designs linking adherence indices to patient outcomes, and incorporating economic evaluations to optimize biomarker-based diagnostic strategies in neurodegenerative disorders and evaluate whether guideline implementation directly improves prognosis and quality of life.

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CONFLICT OF INTEREST STATEMENT

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CONSENT STATEMENT

Informed consent specific to this study was not required, as this was a retrospective observational study based on the review of routinely collected clinical data. At all participating centers, patients had previously provided written informed consent for the use of their clinical data for research purposes at the institutional level. The study protocol was approved by the competent ethics committee and conducted in accordance with the Declaration of Helsinki and applicable national and institutional regulations on research involving human subjects.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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