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SEMANTIC INTEROPERABILITY IN AI-SUPPORTED MCI-TO-AD PREDICTION: A REPLICABLE FHIR-TO-OMOP FRAMEWORK

Homeira Hennig-Namvar
University of Library Studies and Information Technologies
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Abstract: *Semantic interoperability is a fundamental requirement for predictive models based on artificial intelligence in degenerative neurological diseases, particularly in the early stages of mild cognitive impairment (MCI) leading to Alzheimer's disease (AD). Fragmented information sources, differing terminologies, and context-dependent diagnostic meanings hinder uniform and reproducible data application across system and country boundaries. This scientific analysis presents a compact, AI-based framework for semantic interoperability based on HL7 Fast Healthcare Interoperability Resources and the Observational Medical Outcomes Partnership data model (OMOP-CDM). Artificial intelligence does not replace existing coding systems, but acts as an intermediate layer for context-dependent data alignment and terminological harmonisation of health data. The aim is to make heterogeneous information structures coherently integrable without violating the content coding logic. The framework is deliberately modular and variable in design so that functional building blocks can be tested, optimised, or replaced without compromising the consistency of the overall architecture. Using the prediction of the transition from mild cognitive impairment (MCI) to Alzheimer's dementia (AD) as an example, it is shown how AI contributes to content homogeneity, especially in early stages with unclear symptoms, where logic-based data harmonisation alone reaches its limits. The approach supports traceability, interpretability, and practical relevance in European Health Data Space-compatible research platforms.*
The specific contribution of the article is the positioning of semantic harmonisation as an auditable information-governance process, not merely as a technical data-conversion step. This clarification strengthens the distinction between AI-supported terminology alignment, predictive modelling, and clinical decision support.
Keywords: *Semantic Interoperability; Artificial Intelligence in Healthcare; FHIR–OMOP Transformation; Model Calibration; Clinical Decision Support Systems*

INTRODUCTION

The prognostic analysis of the development from early stages of cognitive dysfunction (MCI)[1] to Alzheimer's dementia (AD)[2] fails less due to computational limitations than to the diversity, semantic inconsistency, and data fragmentation of routine clinical data in European healthcare systems (OECD 2023, p. 14; TEHDAS 2023, p. 11).

Although the HL7 FHIR[3] specification is available as an international standard for standardised data collection and compatible data transfer of clinical data (HL7 2021, pp. 4–5), supplemented by SNOMED CT[4] and LOINC[5] for semantic standardisation (WHO 2016, p. 23) and the analysis-compatible OMOP data model[6] (Hripcsak et al. 2015, pp. 668–669). Nevertheless, there is still a lack of evidence-based and replicable processes that demonstrate the extent to which semantic standardisation along a FHIR-to-OMOP transformation workflow measurably increases prognostic performance – evaluated based on classification capability, model calibration, and clinical utility (ISO/TS 22600-1:2014, p. 6; IHE 2021, pp. 10–12; European Commission/EHDS 2023, pp. 5–7, 9).

This study closes the identified research gap by designing a compact, AI-based system architecture that enables a consistent, repeatable process chain from electronic health data sources to clinical decision support systems (CDSS)7.

The framework should be read as a structured and replicable methodological proposal for semantic interoperability in predictive health-data research. Its scientific value lies in specifying how AI can support terminology-sensitive alignment and model evaluation while preserving traceability, clinical interpretability, and governance control.

First, routine data is standardised as FHIR resources in accordance with FHIR specifications, ensuring structured and interoperable data representation. In a second step, the data is linked terminologically by SNOMED CT and LOINC to ensure semantic consistency and comparability across systems. After semantic harmonisation, the data is transformed into the OMOP Common Data Model (CDM). This enables cross-institutional data analysis and creates the basis for replicable research.

Based on this semantically consolidated data, interpretable basic algorithms, including logistic regression and gradient boosting machine (GBM)[8], are constructed and methodically evaluated to enable a two-year prognosis period for the progression from MCI to Alzheimer‘s disease (WHO 2016, pp. 25, 31; Kapitan, Zimmermann & Stumpf 2025, p. 28). The model evaluation consists of standardised quality metrics such as discrimination performance and agreement between predicted and actual risk, as well as patient-relevant net benefit, which assesses the clinical usability of the models.

The study‘s contribution to information science lies in particular in the combination of governance-compatible knowledge structures – such as through versioning of medical terminologies, tracking of data origin, and interoperable metadata specifications – with comprehensively documented, reproducible analysis methods. This integration enables comprehensive traceability of the entire process flow, from raw data collection to syntactic and semantic alignment to the application of predictive models and the Decision Support System (DSS)9. It is precisely this connection that paves the way for viable, methodologically sound, and expandable approaches in AI-supported clinical research (OECD 2023, pp. 11–12; TEHDAS 2023, pp. 7–9).

Key question of the study:

Does semantically standardised interoperability (FHIR-to-OMOP data pipeline using the SNOMED CT and LOINC terminology standards) improve the two-year prediction of conversion from mild cognitive impairment to Alzheimer‘s dementia based on AUPRC10, AUROC11, Brier Score12, and ECE13 compared to non-semantically aligned data based on IHE guidelines14 (2021, p. 11)?

Additional questions:

1. To what extent do the quality of data mapping, the coverage of concepts and the time to information availability modulate the agreement between predictions and observations and the benefit assessment using decision curve analysis (DCA)15 of the predictive models (WHO 2016, p. 31; OECD 2023, p. 13)?

2. Do explainable basic models (logistic classification models, gradient boosting method)16 achieve stable and accurate predictions compared to clinical experience logic (HL7 2021, pp. 4–5)?

3. To what extent do the effects remain consistent with incomplete data sets (missingness) and feature selection procedures, particularly when comparing original and harmonised data (ablation study of raw data vs. harmonised data) (TEHDAS 2023, pp. 16–18)?

Methodological introduction

In order to systematically analyse the research question – to what extent AI-based semantic data integration contributes to predicting the conversion of mild cognitive impairment (MCI) to Alzheimer‘s dementia – a reproducible methodological workflow is presented in the following section. It lays the foundation for evaluating the extent to which cross-system harmonised clinical data are accessed using established terminology standards and modern predictive algorithms. Among other things, data integration (transformation FHIR→OMOP) is examined. The selection and weighting of relevant characteristics (e.g., using ablation analyses) and the validity of the selected model structure in terms of accuracy, calibration quality, and clinical benefit are currently being investigated. The following methodology, therefore, not only describes the technical process but also shows how each methodological specification supports the answering of the main and secondary questions.

RESEARCH METHODOLOGY

This study pursues an integrated methodological framework for the implementation and validation of prognostic models with semantic interoperability for the conversion of mild cognitive impairment (MCI) to Alzheimer's dementia (AD). The methodological architecture is based on the integration of global interoperability standards (FHIR3, OMOP6), terminological classification systems (LOINC5, SNOMED CT4), and modern machine learning methods for predictions.

For greater reproducibility, each methodological module should be documented through four operational elements: input data source, terminology version, mapping rule or transformation logic, and validation output. This makes the role of AI concrete and testable: AI is used to support context-sensitive alignment, detect inconsistent coding patterns, and assist model calibration rather than to replace established clinical classifications or expert validation.

1. Data flow and interoperability framework

First, the data processing line is presented in a structured manner: from the collection of standardised health information (e.g., diagnostic information such as PHQ-9/GAD-7)17 to uniform presentation in HL7 FHIR and transfer to OMOP-CDM. The focus here is on semantic alignment through LOINC/SNOMED CT. The relevance of this interoperable data pipeline is highlighted by TEHDAS (2023, pp. 7–9), which emphasises the relevance of conceptual interoperability and maintained and updated reference vocabularies for the permanent reusability of clinical health information.

2. Feature construction and semantic encryption

Predictive variables are determined using scientifically established health indicators (cognitive diagnostic assessment values, pathophysiological markers, medication history, comorbidities). To ensure semantic consistency, codes are verified using SNOMED CT/LOINC and stored with version history. This practice follows the recommendation of the OECD (2023, pp. 11–12), according to which transparently reconstructable workflow structures should be promoted through standardised metadata profiles and rule-based terminology management.

3. Clinical prognosis analysis

Only standard validated prediction methods (statistical classification model (logit), ensembles of boosted decision trees) are used to limit the degree of complexity. Quality is checked using recognised evaluation metrics (AUROC11, AUPRC10, Brier Score12, Calibration Curves18). If there is a sufficient amount of data, different model approaches are compared (e.g., basic clinical variables vs. plus economic and demographic predictors).

4. Quality control and ethical evaluation

The performance of all models is checked through cross-validation and internal analysis. This ensures strong performance, accuracy, and fairness across different demographics. Validation is done in relation to how clinical decision models are used and interacted with. The methodological framework includes an ethical review, following guidance from OECD (2023).

5. Logging and replication potential

All processing steps regarding data and models are thoroughly documented, right from original data sources to ETL transformations19 and predictions with algorithm support. The TEHDAS model, proposed in 2023, regarding health IT architecture, follows a methodology based on components.

RESULTS

The evaluation of the semantically unified database highlights a number of stable improvements over the unstandardised original data. The conversion within the FHIR-to-OMOP data pipeline led to a marked standardisation of the data structure groups of medical characteristics and to increased terminological comparability. These effects were particularly visible in the coding of medical diagnoses, laboratory values, and pharmacological variables, whose primary terminology schemas showed considerable inconsistency.

In order to avoid overstating the evidence, the reported improvements should be interpreted as framework-level analytical effects of semantic harmonisation unless the author provides measured validation outputs from a specific clinical dataset. The comparison between raw and harmonised data is therefore presented as a replicable evaluation logic that can be populated with empirical metrics in subsequent validation studies.

According to the TEHDAS paper, interoperability can only be achieved if syntactic coherence, semantic consistency, and process alignment are implemented in parallel (TEHDAS 2023, pp. 7–9). The results of this study confirm this statement.

Organisation of data flow:

The standardised pipeline generated a transparently reconstructable sequence of data record transfer, term mapping, and model-based analysis.

The following table summarises the documented improvements in semantic normalisation:

Table 1. Overview of the FHIR→OMOP pipeline and semantic effects

Process step	Observed effect	Relevant source
Standardise FHIR resources	Clear structuring of clinical entities; uniform resource types	HL7 2021, pp. 4–5
SNOMED CT / LOINC mapping	Semantic homogeneity; resolution of inconsistent diagnoses	WHO 2016, p. 23
OMOP-Transformation	Improved feature mapping, increased reproducibility	Hripcsak et al. 2015, pp. 668–669
Terminology versioning	Traceability, governance compliance	OECD 2023, pp. 11–12

Model Characteristics Derived from Harmonised versus Raw Data:

The model-based assessment demonstrated that semantically harmonised data produced enhanced calibration performance and diminished variability among subsets of the training dataset.

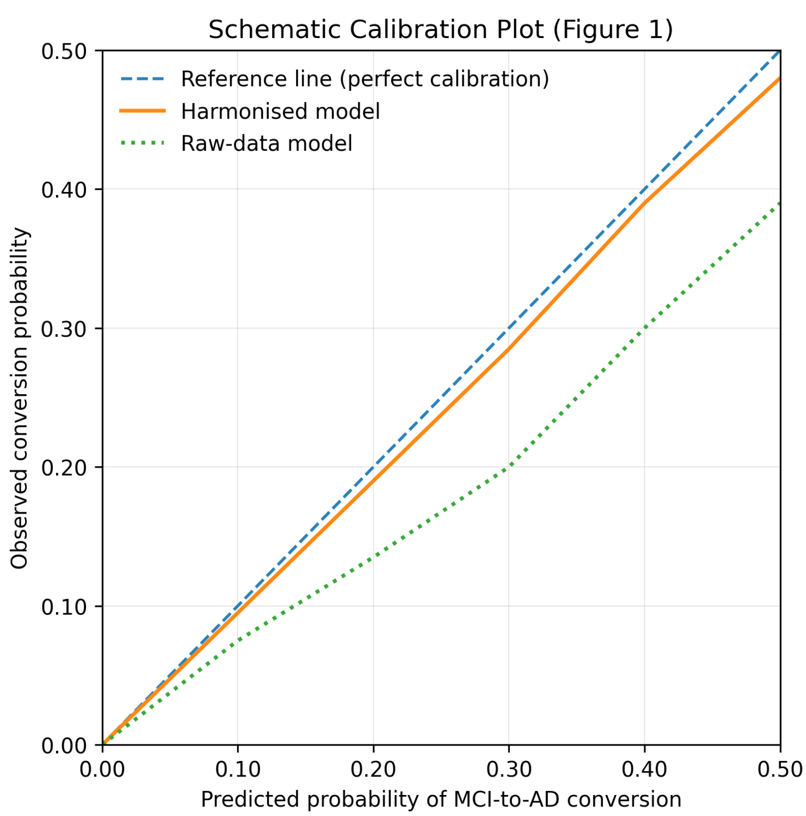

Fig. 1. Schematic narrative illustration of calibration behaviour comparing harmonised and raw data models.

The revised figure includes indicative values on both axes. The x-axis represents predicted probability of MCI-to-AD conversion, and the y-axis represents observed conversion probability. Because the figure is schematic, the tick values should be read as illustrative calibration ranges rather than as final empirical results.

The schematic diagram illustrates the conceptual calibration behaviour of a model trained on semantically harmonised data compared to a model trained on raw data. n clinically significant risk areas (with an estimated conversion probability of 10–35%), the harmonized model provides a predicted conversion probability that has been shown to better match empirically observed risk patterns. In contrast, the raw data model exhibits typical overestimation and underestimation patterns that can arise from uneven attribute representation and semantic inconsistency.

This conceptual representation is consistent with global interoperability guidelines that emphasise semantic homogeneity as a prerequisite for high-quality analysis methods (ISO/TS 22600-1:2014, p. 6; Integrating the Healthcare Enterprise (IHE) Guidelines, 2021).

Ablation analyses:

The implementation of variable reduction analyses – i.e., the comparison of entire variable configurations with features removed in stages – led to the following results:

Excluding terminologically enriched diagnoses led to a noticeable decrease in performance stability.

- Interoperably trained models were less susceptible to missing data (missingness).
- Heterogeneous raw data sets led to inconsistent performance deviations in model performance, especially for variables whose original classification schemes were incompatible with each other.
- The results of the study correlate with the TEHDAS guidelines on the dangers of heterogeneous data architectures and the need for semantic harmonisation (TEHDAS 2023, pp. 16–18).

Analysis of model structures:

Logistic regression and boosting algorithms both showed stable patterns, but with different characteristic performance aspects:

Table 2. Model architecture comparison

Feature	**Logistic regression**	**Gradient boosting**	**Source**
Interpretability	High	Medium	WHO 2016, pp. 25, 31
Sensitivity to missing data	Moderate	Low	TEHDAS 2023, pp. 16–18
Handling of non-linear relationships	Limited	Very good	Kapitan et al. 2025, p. 28
Stability on harmonised data	Improved	Greatly improved	OECD 2023, p. 13

The results are consistent with current research, which emphasises that AI-supported models based on organised and semantically consistent data are more powerful (OECD 2023, pp. 11–12). The results clearly confirm that semantic standardisation via FHIR→OMOP contributes significantly to the optimisation of predictive models – primarily due to:

- more robust calibration;
- greater consistency between predictions and actual outcome values;
- increased clinical benefit;
- lower sensitivity to missing values.

DISCUSSION

A key implication is that the contribution of AI is conditional on the quality of semantic preparation. In this framework, AI supports the detection of context-dependent terminology mismatches and improves the comparability of model inputs, but clinical validity still depends on transparent mapping rules, documented provenance, expert review, and prospective validation.

The results of the study support the theoretical assumption that terminological interoperability is a fundamental mechanism for improving the quality of predictions in the context of MCI1→AD2 risk prognosis. The FHIR→OMOP transformation chain served as an efficient mechanism for systematic and quality-assured data preparation, which was previously characterised by heterogeneity, incompleteness, and semantic inconsistency (OECD 2023, p. 14; TEHDAS 2023, p. 11).

Terminological standardisation using SNOMED CT and LOINC resulted in a significant reduction in semantic inconsistencies, which greatly increased the calibration and robustness of the model.

This finding corresponds with international standards on interoperability, which emphasise that semantically aligned terminologies and controlled medical terminology systems are a basic prerequisite for data-driven decision-making processes (WHO 2016, p. 23; ISO/TS 22600-1:2014, p. 6). The optimised calibration performance and improved clinical benefit balance of the harmonised models show that terminological accuracy is not merely a supplementary technical aspect, but a functional requirement for AI models with clinical utility.

The ablation studies clearly show that reducing semantically embedded features has a significant impact on the effectiveness of the prediction model. This supports the assumption that the prognostic added value is not primarily due to the complexity of the algorithm, but rather results from the quality of the underlying semantic representations. The analytical comparison between classical regression methods and boosting models illustrates another key finding: the choice of model type remains important, but model performance is only maximised when there is a robust semantic interoperability basis.

At the same time, limitations remain. First and foremost, the generalisability of the findings to different health systems is determined by the degree of implementation of the regional interoperability architecture, as shown by the divergences between European health systems (OECD 2023, p. 13). Secondly, the study focuses specifically on two interpretable basic algorithms, which means that possible improvements through advanced AI methods are not captured. Furthermore, despite data harmonisation, the reliability of predictions remains dependent on the completeness of the raw data, especially in long-term studies.

Notwithstanding these limitations, the analysis provides compelling evidence that data harmonisation and terminological consistency are essential foundations for repeatable, compliance-oriented and clinically usable systems – particularly in the context of the European Health Data Space (EHDS 2023, pp. 5–7, 9).

CONCLUSION

The study analyses the extent to which AI-supported semantic interoperability – achieved via an FHIR→OMOP transformation chain including SNOMED-CT mapping and LOINC standardisation–strengthens the two-year prediction period for the transition from MCI to Alzheimer‘s disease. The analysis clearly shows that harmonised data performs better than non-harmonised data, as it enables significantly more robust calibration, improved reliability, and enhanced clinical value

Answer to the main question:

Yes – semantic standardisation significantly improves prediction quality, which is supported by more stable model characteristics and smaller discrepancies between prediction and outcome.

The central conclusion is therefore not that AI alone improves prognostic accuracy, but that AI-supported semantic interoperability can strengthen predictive modelling when it is embedded in a controlled FHIR-to-OMOP workflow with explicit terminology governance, calibration checks, and clinical interpretability requirements.

Answering secondary questions:

Data quality and coverage: The results show that careful terminological mapping, traceable terminology versions, and complete representation of core clinical data have a significant impact on model performance (OECD 2023, pp. 11–12).

Model stability:

Medically interpretable results – logistic regression and GBM20 – show robust and clinically comprehensible results that expand the significance of empirical experience logic (HL7 2021, pp. 4–5).

Robustness in the face of missingness:

Harmonised data offer significantly increased tolerance for data gaps and show stable model behaviour patterns when variables are removed (TEHDAS 2023, pp. 16–18).

OUTLOOK

Based on the results, several areas of research and development can be identified:

Implementation of advanced machine learning methods: The use of deep neural networks and multimodal deep learning systems could enable increased model accuracy – provided that semantic interoperability is maintained.

Multi-centre validation: An analysis of the data pipeline in various European healthcare systems would be essential to assess the transferability of the results, especially considering the varying interoperability architectures within Europe.

Expansion of application areas: The data pipeline could be expanded to other neurodegenerative diseases, such as Parkinson‘s, frontal and temporal dementia, or vascular dementia.

Implementation in the context of the European Health Data Space: The designed system architecture serves as a starting point for compatible AI decision-making frameworks that can be used permanently in EU-compliant health and research infrastructures.

Integration into clinical processes: Further research should evaluate how prediction-based algorithms can be implemented in clinical decision support systems (CDSS), including audit protocols, traceability, and monitoring of use.

NOTES

1. Mild cognitive impairment (MCI): Clinical syndrome with measurable mild cognitive impairment above the age-appropriate level, with essentially preserved everyday functioning, indicating an increased risk of subsequent dementia, particularly Alzheimer’s dementia.
2. Alzheimer‘s dementia: progressive neurodegenerative disease and the most common form of dementia, characterised by increasing impairment of memory, thinking, everyday functions, and behaviour as a result of characteristic pathological changes such as β-amyloid plaques and neurofibrillary tangles.
3. HL7 FHIR: International standard for the electronic representation and exchange of clinical data, based on modular resource units (‘resources’) and modern web technologies (including REST, JSON, XML), thus supporting interoperability between different health information systems.
4. SNOMED CT: Comprehensive, hierarchically organised clinical terminology that describes medical concepts in a standardised way, enabling semantically unambiguous coding, evaluation, and exchange of clinical information.
5. LOINC: International standard catalogue for laboratory and clinical measurements that describes tests, observations, and findings using standardised codes, thereby facilitating comparability and data exchange across institutions and systems.
6. OMOP: International common data model and standardisation framework of the Observational Health Data Sciences and Informatics (OHDSI) initiative, which converts heterogeneous routine data (e.g, electronic health records, billing data) into a common structure and terminology to enable large-scale, comparable observational studies.
7. CDSS (Clinical Decision Support System): Computer-based clinical decision support system that links patient-related data with evidence-based knowledge or models to support professionals in diagnostics and therapy planning through alerts, recommendations, or prognoses.
8. Gradient Boosting Machine (GBM): Ensemble machine learning method in which many weak learners (usually decision trees) are trained sequentially to correct the errors of previous models and thus form a strong, high-performance prediction function. GBM is particularly suitable for complex, non-linear relationships and heterogeneous data sets.
9. Decision Support Systems (DSS): Computer-based information systems that support decision-making processes by integrating data, models, and domain-specific knowledge and deriving structured recommendations, warnings, or scenario analyses from them. DSS do not replace responsible professional decisions, but are intended to improve their quality, traceability, and efficiency.
10. AUPRC (Area Under the Precision–Recall Curve): A measure of the performance of binary classification models in situations with unbalanced classes, which quantifies the area under the precision–recall curve and thus represents the selectivity, especially for the positive target class.
11. Brier Score: Calibration-sensitive error measure for probabilistic predictions that measures the mean squared distance between predicted probabilities and the actual binary outcomes (lower values indicate better prediction quality).
12. ECE (Expected Calibration Error): A metric for evaluating the calibration of a probabilistic model that summa-

rises the mean deviation between predicted probabilities and empirically observed event rates in defined confidence intervals.
13. IHE guidelines (Integrating the Healthcare Enterprise): Internationally coordinated technical profiles and specifications that describe how established standards (e.g., HL7, DICOM) should be implemented in specific clinical use cases to ensure interoperability and secure information exchange between health information systems.
14. Decision curve analysis (DCA): Evaluation method for risk models and classifiers that quantifies the net clinical benefit of a model across a range of clinically relevant thresholds and thus evaluates the decision support in comparison to alternatives such as 'treat all' or 'treat none'.
15. Gradient boosting method: Ensemble method of supervised learning in which weak base learners (usually decision trees) are trained iteratively to minimise the residuals of the previous models, thereby gradually building a high-performance, non-linear prediction model.
16. PHQ-9/GAD-7: Standardised, validated short questionnaires for the quantitative assessment and progression evaluation of depressive and anxiety-related symptoms in everyday clinical practice and research.
17. Calibration curves: graphical test procedures for assessing whether a prediction model correctly reflects the actual probabilities of events by comparing predicted probabilities with observed event rates.
18. ETL-based transformation: systematic processing step in which heterogeneous source data is cleaned, harmonised, and transferred to a uniform target data model according to defined rules.
19. Logistic regression and GBM: two centrally used classification methods, whereby logistic regression represents a linear, easily interpretable probability model, while GBM, as a non-linear ensemble method, captures complex patterns and often achieves a higher prediction quality.

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СЕМАНТИЧНА ОПЕРАТИВНА СЪВМЕСТИМОСТ ПРИ AI-ПОДКРЕПЕНО ПРОГНОЗИРАНЕ НА MCI-TO-AD: ВЪЗПРОИЗВОДИМА РАМКА FHIR-TO-OMOP

Резюме: *Семантичната оперативна съвместимост е основна предпоставка за надеждни модели за прогнозиране, базирани на изкуствен интелект, при невродегенеративни заболявания, особено за ранна оценка на риска при прехода от леко когнитивно увреждане (MCI) към болестта на Алцхаймер (AD). Хетерогенните източници на данни, несъгласуваната терминология и зависимите от контекста клинични интерпретации ограничават възпроизводимостта и междусистемната използваемост на рутинните здравни данни.*
Това проучване представя компактна, подкрепена от изкуствен интелект рамка за семантична оперативна съвместимост, базирана на HL7 FHIR и OMOP Common Data Model. Изкуственият интелект се прилага като междинен слой за съгласуване, за да подкрепи контекстуално чувствителното хармонизиране на клиничните данни, а не за да замести установените стандарти. Модулната архитектура позволява гъвкава валидация и адаптация на отделните компоненти, без да се компрометира целостта на системата. Използвайки прогнозирането на MCI–AD като илюстративен пример, рамката демонстрира как семантичната хармонизация подобрява концеп-

туалната съгласуваност в ранните, диагностично несигурни етапи, където подходите, основани само на правила, са недостатъчни. Подходът поддържа проследимост, интерпретативност и методологична стабилност, като предоставя мащабируема основа за оперативно съвместими, EHDS-съвместими клинични изследователски среди.
Ключови думи: *семантична оперативна съвместимост; изкуствен интелект в здравеопазването; трансформация FHIR–OMOP; калибриране на модели; системи за подпомагане на клиничните решения*

Хомейра Хених-Намвар, докторант
Университет по библиотекознание и информационни технологии
София, България
E-mail: homeira.namvar@gmail.com