

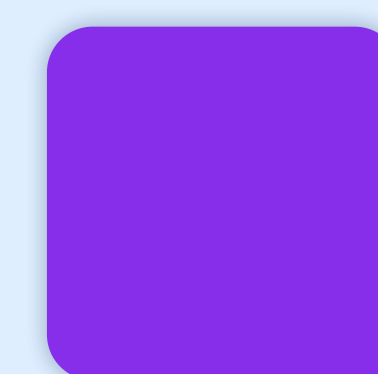
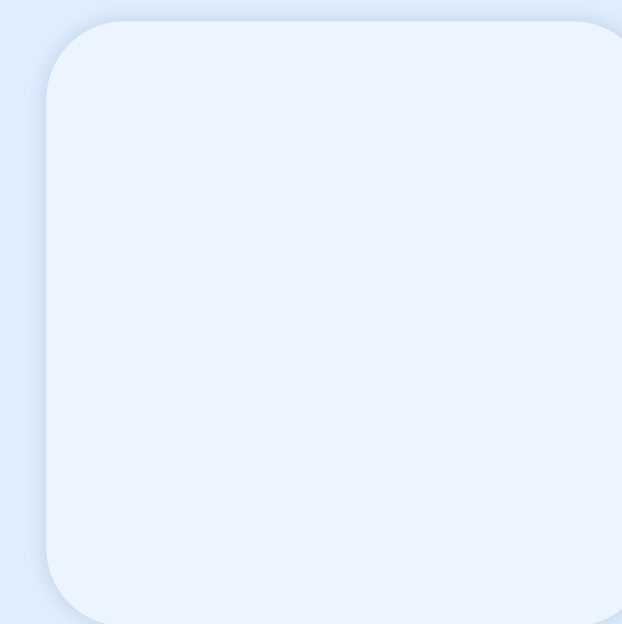
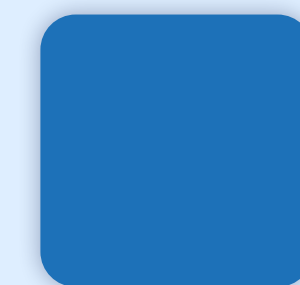
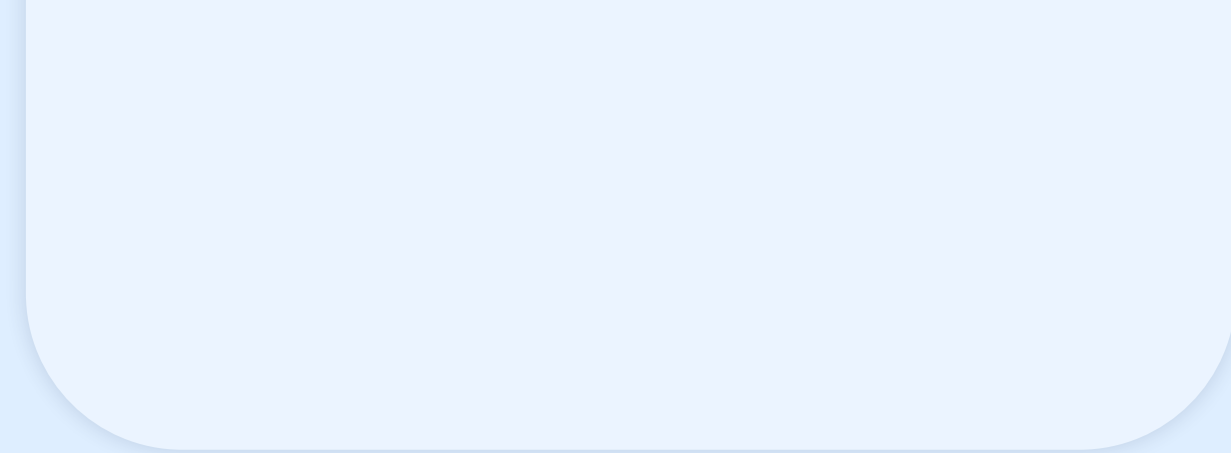


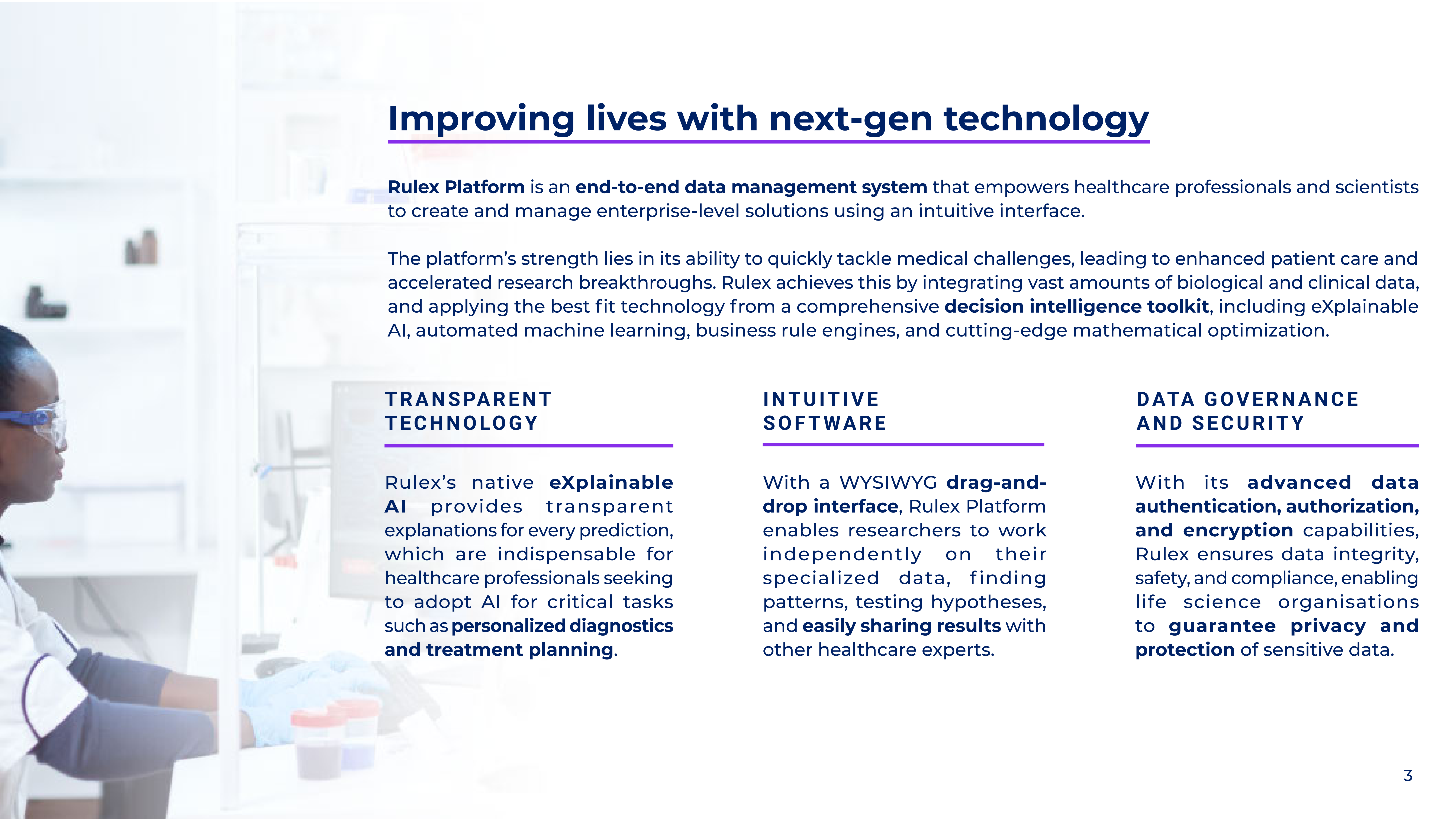
RuleX

Life Sciences & Healthcare

CASE STUDIES

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Improving lives with next-gen technology

Rulex Platform is an **end-to-end data management system** that empowers healthcare professionals and scientists to create and manage enterprise-level solutions using an intuitive interface.

The platform's strength lies in its ability to quickly tackle medical challenges, leading to enhanced patient care and accelerated research breakthroughs. Rulex achieves this by integrating vast amounts of biological and clinical data, and applying the best fit technology from a comprehensive **decision intelligence toolkit**, including eXplainable AI, automated machine learning, business rule engines, and cutting-edge mathematical optimization.

TRANSPARENT TECHNOLOGY

Rulex's native **eXplainable AI** provides transparent explanations for every prediction, which are indispensable for healthcare professionals seeking to adopt AI for critical tasks such as **personalized diagnostics and treatment planning**.

INTUITIVE SOFTWARE

With a WYSIWYG **drag-and-drop interface**, Rulex Platform enables researchers to work independently on their specialized data, finding patterns, testing hypotheses, and **easily sharing results** with other healthcare experts.

DATA GOVERNANCE AND SECURITY

With its **advanced data authentication, authorization, and encryption** capabilities, Rulex ensures data integrity, safety, and compliance, enabling life science organisations to **guarantee privacy and protection** of sensitive data.

Case studies



CASE STUDY

Error detection in health records

Improving the quality of large volumes of data

**13x
more effective
error detection**

compared to
random sampling
selection criteria

THE CHALLENGE

Inaccuracies in medical records can lead to consequences that vary widely in severity, from minor billing errors to serious issues such as **incomplete or incorrect diagnoses**, or **delays** in scheduling vital surgical procedures.

OUR SOLUTION

Rulex used **its native eXplainable AI (XAI) to automate the validation** of coding used in hospital discharge forms for a regional health authority in Italy. Specifically:

- ✓ The study evaluated the feasibility of implementing new automated logical-clinical checks to hospital discharge records to provide a more comprehensive and nuanced analysis of clinical variable correlations. Previously, automated checks were limited to ensuring compatibility between sex-diagnosis or age-diagnosis.
- ✓ Rulex's XAI-powered data quality tool, RDC, autonomously generated corrective rules from historical data and proposed corrections for expert validation, improving the reliability of the error detection process. Consequently, inconsistencies in diagnoses, surgeries, medical procedures, and Diagnosis-Related Groups (DRGs) could be effectively identified.
- ✓ By expressing rules in an *if-then* format, Rulex's RDC clarified why a specific entry was flagged as potentially incorrect.
- ✓ Precisely defined validation rules improved the efficiency of record checks by pinpointing probable error locations, and significantly reducing the workload of hospital personnel.
- ✓ Following the successful application of the approach on a test data, automatic checks were extended to all surgical discharge records.

LEARN MORE:

[Case study's paper \(in Italian\)](#)

[Rulex's data quality](#)

CASE STUDY

Tailored diagnostic predictions

Enhancing traditional models with XAI and cluster analysis for novel insights

4 new patient subgroups

identified, with different phenotypes and prognoses

LEARN MORE:

[Case study's paper](#)

[Rulex's native eXplainable AI](#)

THE CHALLENGE

The unpredictable progression of Primary Biliary Cholangitis (PBC), the lack of precise biomarkers, and the limited **availability of comprehensive patient data** makes accurate prognostication particularly challenging. While machine learning models can be accurate, their opacity poses **ethical and practical challenges** in clinical practice.

OUR SOLUTION

Rulex and the medical department of Milano-Bicocca University conducted a study to optimize PBC risk stratification and prognostication. The data-driven approach **combined eXplainable AI (XAI) with cluster analysis** to complement traditional risk models. Using unsupervised machine learning, the solution could analyze large-scale datasets, while XAI-generated findings were easily understood and validated by clinicians. Specifically:

- ✓ Rulex's proprietary XAI algorithm was applied to an international dataset of PBC patients to rank the most relevant features for liver-related death or transplantation. The dataset was split into a training set of 11,819 subjects and a validation set, with key clinical values like age, sex, UDCA treatments, serum total bilirubin, ALP, and serum albumin.
- ✓ The algorithm generated clear predictive *if-then* rules and ranked the most relevant features for outcome classification.
- ✓ Clustering was used to categorize individuals by the most relevant features. Standard survival analyses were performed to evaluate the prognostic discrimination of clusters. Results were then compared to the predicted risk from the UK PBC risk score.
- ✓ The analysis identified 4 distinct patient clusters, each characterized by unique phenotypes and long-term prognoses. Further sub-analyses revealed a correlation between albumin protein levels and the probability of transplant-free survival.



CASE STUDY

Genetic risk stratification

Using XAI for the analysis of genomic data

71.7%

accuracy in
model predictions

LEARN MORE:

[Case study's paper](#)

[Rulex's native eXplainable AI](#)

THE CHALLENGE

Precision medicine aims to personalize diagnosis, monitoring, and treatment based on each individual's **unique genetic makeup and environmental background**.

This is challenging due to the intricate nature of medical traits and the numerous genetic variants involved. For rare diseases, the **lack of historical data** adds a further level of difficulty.

OUR SOLUTION

In collaboration with the medical departments of Humanitas and Milano-Bicocca Universities, Rulex conducted a pioneering study to evaluate the feasibility and accuracy of predicting the risk of Primary Biliary Cholangitis (PBC) by **analyzing genomic data with eXplainable AI (XAI)**. Specifically:

- ✓ Rulex's proprietary XAI algorithm was applied to an extensive dataset of European-ancestry subjects, comprising 1,345 individuals, including 444 PBC cases and 901 healthy controls. The study utilized quality-checked, imputed genotype data.
- ✓ Data pre-processing identified 41,899 genetic variants for analysis. Several parameter configurations for feature selection were simulated, and supervised classification of PBC by genotype was performed.
- ✓ Rulex's proprietary XAI technology generated 38 rules for disease prediction, expressed in a clear *if-then* format, with the most prominent rule involving the RIN3, KANSL1, TIMMDC1, and TNPO3 genes.
- ✓ Validated on a cohort of 834 individuals, the model achieved over 71% accuracy, a Matthews correlation coefficient of 0.29, a Youden's index of 0.21, sensitivity of 0.28, specificity of 0.93, a Positive Predictive Value of 0.66, and a Negative Predictive Value of 0.72.
- ✓ Unlike "black-box" algorithms, Rulex's proprietary XAI technology adheres to strict data privacy regulations, such as GDPR, by providing transparent explanations for each prediction.



CASE STUDY

Treatment of therapeutic inertia in type 2 diabetes

Identifying new parameters associated with TI and failure of metformin monotherapy

High discriminatory ability

among the inertia-YES/
inertia-NO groups
(ROC-AUC = 0.81)

2 new sub-types

of therapeutic inertia
identified

LEARN MORE:

[Case study's paper](#)

[Paper on achieving optimal metabolic control while maintaining target HbA1c levels](#)

[Rulex's native eXplainable AI](#)

THE CHALLENGE

Therapeutic inertia occurs when physicians delay starting or adjusting treatment for uncontrolled type 2 diabetes, often due to limited guideline awareness, concerns about potential side effects, poor treatment adherence, or **inadequate monitoring of glucose levels (HbA1c)**. This affects insulin and other therapies, leading to poor glycemic control, increased healthcare costs, and a higher risk of complications.

OUR SOLUTION

The Italian Association of Medical Diabetologists used Rulex to **identify and categorize factors associated with therapeutic inertia in type 2 diabetes patients** and suboptimal blood glucose control despite metformin monotherapy. Combining native eXplainable AI (XAI) with traditional statistics, the analysis provided a deeper understanding of complex medical data, especially HbA1c values and related variables. Specifically:

- ✓ The study analyzed extensive raw data, including the medical records of 1.5 million diabetic patients treated at 271 diabetes clinics, and the data collected from medical visits over a 14-year period. Inclusion criteria focused on patients on metformin monotherapy with two consecutive mean HbA1c levels above 7.0%. The cohort was then divided into patients with or without inertia.
- ✓ Rulex's XAI analyzed patient responses by building models that identified the most relevant variables, even without prior knowledge. This approach matched or exceeded the accuracy of leading machine learning algorithms, including Decision Trees, Artificial Neural Network, and K-Nearest Neighbor classifiers.
- ✓ The study considered a wide range of variables and identified two main distinct sub-types of therapeutic inertia, marked by either a steady increase in HbA1c levels over time, or a moderate, non-uniform increase, rather than just absolute levels.
- ✓ The identification of novel parameters that can mitigate therapeutic inertia paves the way for personalized treatment strategies.



CASE STUDY

Short-term glycemic control in type 2 diabetes

*Improving glycemic control
with a what-if, ML-based
scenario simulator*

**17%
increase**

in patients meeting
recommended
metabolic targets

LEARN MORE:

[Case study's paper](#)

[Paper on metabolic control without weight gain
in type 2 diabetes](#)

[Rulex's native eXplainable AI](#)

THE CHALLENGE

International diabetes care guidelines stress the need for prompt and effective glycemic control to lower the risk of macrovascular complications in type 2 diabetes (T2DM). However, data from the Italian Association of Medical Diabetologists (AMD) shows **only 47% of patients meet glycemic targets**, with around 30% using insulin.

OUR SOLUTION

In collaboration with the Italian AMD, Rulex conducted a study using real-world data to **simulate the impact of timely insulin initiation** for all eligible patients, with the aim of improving the quality of care for T2DM patients. Specifically:

- ✓ The study was based on a large database comprising over 1 million patients with T2DM, considering variables such as demographics, medical history, and biomarkers. The effects on glycemic control were projected over a 12-month period, aligning with the frequency of patient visits to Italian diabetes centers.
- ✓ Rulex's eXplainable AI (XAI) technology simulated the impact of timely insulin use for all eligible patients. In the simulated scenario, introducing timely insulin therapy resulted in a projected 17% increase in patients achieving the recommended metabolic target (hemoglobin A1c <7.5%) within 12 months of starting treatment.
- ✓ Rulex's XAI predicted which patients could have reached the desired outcomes, if timely therapeutic measures had been implemented. The model projected over a 34% improvement in the number of patients achieving the target compared to actual real-world results.
- ✓ By generating clear, intelligible rules for medical experts without specialized statistical or mathematical skills, Rulex's XAI fostered greater trust in its predictions.
- ✓ The study reaffirmed the critical role of early intervention in therapeutic inertia, showing that prompt initiation of insulin therapy significantly improved patient metabolic outcomes after 12 months.



CASE STUDY

Differential diagnosis of pleural mesothelioma

Achieving accurate disease classification with minimal computational resources

**77.5%
global accuracy
increase,**

closely aligning with
established knowledge
of tumor markers' role

LEARN MORE:

[Case study's paper](#)

[Rulex's native eXplainable AI](#)

THE CHALLENGE

Malignant pleural mesothelioma (MPM) is a **rare and highly lethal tumor**. Diagnosing MPM is difficult due to its atypical symptoms, often causing **misdiagnoses** with other cancers or benign pleurisy. While combining data from various markers using techniques like ROC curve analysis improves accuracy, some markers and methods typically underperform or **fail to provide clinically relevant insights**.

OUR SOLUTION

In collaboration with Gaslini Children's Hospital, Rulex developed an **eXplainable AI solution** for the accurate classification of MPM patients. Unlike "black-box" methods that produce opaque results, this approach provided clear, actionable insights in an easy-to-understand *if-then* format, enhancing clinical utility for medical experts. Specifically:

- ✓ A cohort of 177 patients from two pulmonary departments in Italy (2009-2011) was analyzed. The study evaluated tumor markers like SMRP, CYFRA 21-1, and CEA for their effectiveness in distinguishing MPM from pleural metastasis (MTX) and benign conditions.
- ✓ Cytological exams were positive in about one-third of MPM patients and half of MTX patients, confirming the technique's low sensitivity.
- ✓ Rulex technology generated 29 classification rules from historical data, all associated with high values of SMRP and low values of CEA, using distinct cut-off values for each.
- ✓ Comparative analyses with other supervised data mining techniques such as Decision Trees (DT), K-Nearest Neighbors (KNN), and Artificial Neural Networks (ANN) showed that Rulex's XAI consistently outperformed them in classification accuracy. While DT could extract meaningful information from tumor markers and convert them into rules, Rulex's XAI delivered a more comprehensive and detailed picture with its ability to generate partially overlapping rules.



CASE STUDY

New prognostic classifier for neuroblastoma patients

Supporting clinical decisions with a transparent, weighted classification model

New **NB-hypo-II** signature identified

LEARN MORE:

[Case study's paper](#)

[Previous paper on hypoxia's prognostic value in neuroblastoma](#)

[Rulex's native eXplainable AI](#)

THE CHALLENGE

Cancer patients' prognosis is partly determined by the **tumor's gene expression profile**. A prior study identified a 62-probe set (NB-hypo) for detecting hypoxia in neuroblastoma, effectively stratifying patients by outcomes. Developing a prognostic classifier from this signature is crucial for risk categorization and personalized therapy selection.

OUR SOLUTION

In collaboration with Gaslini Children's Hospital, a **novel weighted classification method** using Rulex's proprietary eXplainable AI (XAI) technology was applied to predict outcomes in neuroblastoma patients based on the NB-hypo gene signature. This approach improved prediction accuracy and provided robust clinical decision support tools. Specifically:

- ✓ The initial dataset included gene expression data from 182 neuroblastoma tumors, obtained through microarray analysis.
- ✓ The Attribute Driven Incremental Discretization (ADID) preprocessing method transformed continuous variables into simpler, discrete categories, improving pattern recognition across different classes.
- ✓ After feature selection, Rulex's XAI identified a new 11-probe set signature (NB-hypo-II) as the most significant for outcome prediction out of the original 62 probe sets in the NB-hypo signature.
- ✓ Rulex's XAI generated nine clinically applicable *if-then* rules, which clearly articulated the relationship between premises and outcomes.
- ✓ When validated on an independent dataset, these rules demonstrated efficiency comparable to that of Prediction Analysis of Microarray (PAM) and Support Vector Machine (SVM), and outperformed other algorithms such as Decision Trees.
- ✓ By applying weighted classification, the method improved the accuracy of classifying underrepresented groups in highly imbalanced datasets – in this case, patients with poor outcomes.



CASE STUDY

Gene expression analysis for cancer diagnosis

Classifying patients with neuroblastoma with an innovative, supervised method

**sAUC = 0.99, 95%
CI: 0.98–1.0
accuracy**

demonstrated by Rulex's XAI, outperforming any other method except SVM (comparable accuracy)

LEARN MORE:

[Case study's paper](#)

[Rulex's native eXplainable AI](#)

THE CHALLENGE

High-risk neuroblastoma (NB) carries a grim prognosis, with nearly **50% of patients not surviving treatment**. A key area for developing better stratification strategies lies in understanding that hypoxia – low oxygen levels in poorly vascularized tumor regions – is linked to worse outcomes.

OUR SOLUTION

Rulex participated in a study to **develop a prognostic classifier for pediatric and adult neuroblastoma**, integrating clinical and molecular risk factors. Specifically:

- ✓ Rulex's proprietary eXplainable AI technology was employed to classify neuroblastoma patients based on key risk factors: age at diagnosis, INSS stage, MYCN amplification, and NB-hypo (a gene expression signature measuring tissue hypoxia in neuroblastoma).
- ✓ Unlike most traditional methods of supervised data analysis, Rulex's XAI algorithm successfully generated clear, explicit rules that were directly applicable in a clinical setting. Additionally, the partially overlapping nature of these rules allowed for the identification of small, significant subgroups that often go undetected by univariate analysis or divide-and-conquer methods.
- ✓ The classification method was highly accurate in predicting outcomes for both good and poor prognosis patients.
- ✓ The method's performance was further validated on an independent dataset, where Rulex's XAI was compared to several supervised methods for cancer diagnosis, using microarray data from multiple cancer types. Rulex's technology outperformed most standard machine learning methods, including Decision Trees (DT), Artificial Neural Network (ANN), and K-Nearest Neighbor (KNN).
- ✓ Notably, the NB-hypo signature proved to be a key element in the rules, showing predictive strength comparable to traditional tumor staging.

CASE STUDY

Validation of multiple osteochondromas classification

Identifying key factors and MO pathogenesis with a user-friendly tool

85%
mean
accuracy

of the model across
the 3 MO classes

LEARN MORE:

[Case study's paper](#)

[Rulex's native eXplainable AI](#)

THE CHALLENGE

Multiple osteochondromas (MO) is an autosomal dominant disorder marked by the development of benign cartilage-capped bone growths, known as osteochondromas or exostoses. Although there have been **various attempts to classify the condition clinically**, experts have not yet reached an agreement on a standard classification system.

OUR SOLUTION

Rulex's study, conducted in collaboration with the Rizzoli Orthopaedic Institute of Bologna, validated a **user-friendly eXplainable AI** tool to identify key factors in three classes of MO and explore its pathogenesis. The method was reproducible, objective, and required no expert intervention. Specifically:

- ✓ The input dataset consisted of 289 individuals with MO, including data from physical exams, X-Rays, molecular screenings, and follow-ups. Patients were classified into groups, based on the presence or absence of deformities and/or functional limitations.
- ✓ This study analyzed 150 variables grouped into several categories: affected sites, severity of clinical manifestations, genetic data, family history, and other factors such as age, gender, weight, and height.
- ✓ Rulex's XAI technology generated clear *if-then* rules, identifying 30 key variables in MO classes using relevance scores.
- ✓ Ankle valgism, Madelung deformity, and limitations in hip external rotation were identified as distinctive markers ("tags") for the three clinical classes, facilitating the evaluation of patient phenotypes.
- ✓ Testing revealed that the model achieved high mean accuracy across the three MO classes, confirming its effectiveness in defining homogeneous groups. Additionally, the classification analysis demonstrated that Class III encompassed the discriminators of both Class II and Class I, effectively tracking disease progression.



CASE STUDY

Simple OSA diagnosis in individuals with Down syndrome

*Accurately predicting OSA
with XAI and simpler
procedures*

90%

cross-validated negative
predictive value for
moderate/severe OSA

LEARN MORE:

[Case study's paper](#)

[Rulex's native eXplainable AI](#)

THE CHALLENGE

Obstructive sleep apnea (OSA) is highly prevalent in individuals with Down Syndrome (DS), affecting between **55% and 97% of this population**, compared to just 1–4% in the neurotypical population. Early detection can prevent comorbidities and assess its impact on behavioral and mental health. However, **traditional sleep studies are often costly and poorly tolerated**, complicating diagnosis and management.

OUR SOLUTION

In a study with Massachusetts General Hospital and Boston Children's Hospital, Rulex developed an innovative prediction model to effectively **identify individuals with DS who are unlikely to have significant apnea**, potentially allowing them to forgo a diagnostic polysomnogram. Specifically:

- ✓ A dataset was compiled from 130 patients with DS, aged 3 to 24 years.
- ✓ Rulex's eXplainable AI technology was then used to create a predictive model with a set of clear *if-then* rules, demonstrating high predictive accuracy.
- ✓ Rulex identified the 15 most relevant variables out of a total of 101. These included survey questions (e.g., "Does your child snore loudly while sleeping?"), medication history, anthropometric measurements, vital signs, patient age, and physical examination findings. Each variable was assigned a quantitative score to determine its importance in the predictive model.
- ✓ The proposed model, utilizing simple and cost-effective procedures, could predict which patients with DS were unlikely to develop moderate to severe obstructive sleep apnea and would therefore most likely not require a diagnostic sleep study.





We are a fast-growing, dynamic team working every day to make technology accessible to everyone. Investing significantly in training, research, and innovation, we not only meet but anticipate the evolving needs of our clients and partners.

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