

PRECISION MEDICINE FOR RHEUMATOID ARTHRITIS: UTILIZING AI- ENHANCED MENDELIAN RANDOMIZATION IN BIOMARKER SELECTION

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ABSTRACT

Objective:

To investigate the role that precision medicine, biomarker selection, Mendelian randomization, and artificial intelligence have in the treatment of rheumatoid arthritis and to examine the correlation with clinical implementation and translation.

Methods:

The sample included 288 healthcare professionals from related clinical or biomedical fields, as well as researchers. Data were gathered on the following dimensions: Precision Medicine, Biomarker Selection, Mendelian Randomization, Artificial Intelligence, and Implementation/Translation, using a structured 30-item questionnaire. The answers were captured on a 5-point rating scale. The Shapiro–Wilk normality test, Cronbach's alpha, Kaiser–Meyer–Olkin test, Bartlett test, independent-samples t-test, one-way ANOVA, Kruskal–Wallis test, Chi-square test, Pearson correlation, and multiple linear regression were used in the statistical analysis. The significance level used for statistical tests was $p < 0.05$.

Results:

Cronbach's alpha values obtained for the different scales of the questionnaire revealed high internal consistency ranging from 0.929 to 0.959, and an overall Cronbach's alpha value was 0.984. Sampling adequacy was excellent ($KMO=0.983$), while Bartlett's test was significant ($\chi^2=9427.46$, $df=435$, $p<0.001$). Professional role ($p<0.001$), age ($p<0.001$), and gender ($p<0.001$) were each shown to have significant differences. The correlation coefficients between all the main constructs of the study were positive and strong, ranging from about 0.819 to 0.852.

Implementation/Translation was significantly and positively related to Artificial Intelligence ($r=0.852$, $p<0.001$). Precision Medicine, Biomarker Selection, Mendelian Randomization, and Artificial Intelligence were identified as significant positive predictors of Implementation/Translation, which explained 80.0% of the variance ($R^2=0.800$, adjusted $R^2=0.797$, $p<0.001$) in multiple regression analysis.

Conclusion:

Mendelian randomization combined with AI could be a useful approach to prioritizing biomarkers and precision medicines in rheumatoid arthritis. The principal constructs are strongly connected with each other and allow for further research on validated clinical and genomic data sets. These results are methodological and not clinical data, as the data used for the present analysis were synthetic/mock data.

Keywords: Rheumatoid Arthritis; Precision Medicine; Artificial Intelligence; Mendelian Randomization; Biomarker Selection; Clinical Translation

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Introduction

Rheumatoid arthritis (RA) is a persistent systemic autoimmune disease, in which an inflammatory process is seen in synovial tissues resulting in progressive joint damage and dysfunction, pain, and sometimes other changes in organs outside the joints. Despite the advances in the management of the disease, there is significant clinical variation in presentation, disease progression, treatment response, and long-term outcomes. Apparent identical clinical cases can have distinct clinical responses to either conventional synthetic disease-modifying anti-rheumatic drugs, biologic drugs, or targeted synthetic drugs. This variability has appeal in precision medicine that seeks to leverage clinical, molecular, and genetic data, as well as various biological information, to guide towards the right type of intervention in each patient. A reliable

biomarker could be useful to detect patients with RA earlier than "normal", to predict whether treatment will be severe, and to identify those at "high risk" of being non-responsive and having a "poor" response to treatment (Syed Waqas Ali Shah, 2025).

Still, it remains very elusive to discover biomarkers in RA. Numerous inflammatory mediators, autoantibodies, polymorphisms of genes, transcriptomic signatures, and circulating proteins have been connected to susceptibility to disease or treatment responses, but the significance of these connections is only statistical and does not necessarily hold a biological causal relationship. Observational biomarker results could be affected by multiple testing and possibly even have reverse cause/effect and/or population heterogeneity. To strengthen causal conclusions from Mendelian randomization, genetic epidemiological approaches can be

introduced that involve genetic variants that are passed on as instruments for potentially modifiable exposures. Some confounds and reverse causality in the more commonly used observational study designs may be reduced by Mendelian randomization since there is no temporal order in the relationship, as genetic variants precede disease. This can thus pick out biomarkers that are likely to be involved in disease mechanisms, rather than those that merely reflect inflammation and/or the downstream disease process (Mostaque Md. Morshedur Hassan, 2025).

Additionally, a significant amount of data, including large-scale genomic data, proteomic data, transcriptomic data, and clinical information, has become readily available in the field of rheumatoid arthritis, providing opportunities for the use of artificial intelligence (AI) in the study of RA. High-dimensional data and high-order nonlinear relationships can be dealt with using machine-learning or other AI techniques, which can also discover hidden patterns and determine variable combinations among thousands of potential biomarkers. But all AI models can be purely predictive, and this is where there is potential for good correlations being detected but without a real biological link. This can be addressed with a new approach to Mendelian randomization called 'Mendelian randomiser artificial intelligence', which uses AI to generate something more sophisticated than simply applying patterns from wikis. AI might enable candidate biomarker screening, dimensionality

reduction, instrumental-variable selection, detection of complex interactions, and prioritization of biological pathways, and Mendelian randomization might be used to assess whether biomarkers found have the consistency of being causal in RA-related outcomes and thus confirm the utility of studying the biomarkers (Irum Sherwani Summaiya, 2025).

An AI-driven Mendelian randomization model can then be used to offer a more systematic approach for choosing the biomarkers for precision medicine. This method might help to better prioritize the biomarkers for further therapeutic target development, prediction of patient response, disease stratification, and subsequent clinical validation. To be successful in translating, a repertoire of strong, well-annotated genetic instruments, high-quality data sets, external reproduction of data sets, quality of studies conducting pleiotropy control, and transparent evaluation of AI algorithms and validation in independent cohorts of patients are needed. Further investigation is needed to gain insight into the views of both clinicians and researchers about the ways these technologies are expected to be adopted and the link between the principal components of precision medicine (the selection of biomarkers, MR, and AI) and the levels of clinician support for clinical adoption. Therefore, the aim of the current study was to investigate these interconnected processes and explore the utility of AI-driven Mendelian randomization for the discovery and prioritization of potential biomarkers for precision

medicine in RA (Kaleem Ullah Ihsan, 2026).

Literature Review

Rheumatoid arthritis (RA) is an ongoing (chronic) autoimmune inflammatory condition affecting multiple joints, resulting in progressive joint damage, disability, and systemic effects on the body. While the range of therapeutic possibilities has increased significantly with the introduction of conventional disease-modifying antirheumatic drugs (DMARDs), biologic agents, and targeted synthetic drugs, there is significant variation in disease activity, disease progression, and treatment response. In some patients, the remission that can be achieved with the first-line treatment is an achieved goal; in others, it is more of an ongoing process of repeated changes to therapy, and in some patients, first-line treatment does not lead to remission or gives way to the refractory stage of the disease. This clinical variability has led to a change in the approach to treatment from a standardized approach to precision medicine. Precision medicine aims to improve the ability to stratify patients more precisely by using clinical features and genetic, molecular, immunological, and environmental information to facilitate improved patient decision-making. This is especially important for RA as the mechanisms of disease and drug effects differ widely in those diagnosed with the same disease (Macedonia, 2022).

Biomarkers are an integral component of precision medicine as they can have the potential to help classify a disease, predict the disease

course, select treatment approaches, and track therapy response. Traditional RA diagnostic tests include a blood test for rheumatoid factor, a blood test for anti-citrullinated protein antibodies, a blood test for C-reactive protein, and a blood test for erythrocyte sedimentation rate. These markers are clinically useful, but do not predict the response to a given therapy in individuals very well. The identification of a large array of these candidate biomarkers, through advancements in the genomics, transcriptomics, proteomics, metabolomics, and epigenomics domains, has led to the discovery of numerous biomarker candidates linked to increased susceptibility to and severity of RA, as well as responses to treatment. There are other genetic regions (outside the HLA region) also associated with disease susceptibility. In many instances, however, there will be multiple variations among populations, and many reported biomarkers will be poorly specific and poorly reproducible and/or have poor clinical utility for determining individual treatments (Mislim Zendeli, 2023).

One drawback of traditional biomarker research is that the research is only based on associations that they observe. A high association of a biomarker with RA without triggering the RA process can be seen. Association does not equal causation due to confounding variables, reverse causation, selection bias, and changes in biological variables related to the disease. Thus, selecting a biomarker based on the correlation observed during studies of the disease process

may not be effective when trying to validate the biomarker in other cohorts of patients or during targeted therapeutic development. However, Mendelian randomization has emerged as a valuable tool to overcome some of the aforementioned problems in recent years. It enables the study of the relationship between an exposure and a clinical outcome through the use of genetic variants that are associated with an exposure as instrumental variables. Mendelian randomization can also minimize reverse causation and some confounding due to genetic variants being presumably established before the onset of disease (Praveenkumar Periyasamy^{1*}, 2024).

In recent years, inflammatory mediators, circulating proteins, metabolic traits, immune pathways, and lifestyle-related exposures and comorbidities have been emerging as sources of investigation via Mendelian randomization in the context of RA research. Such analyses can help prioritize those biomarkers that are more strongly supported by evidence to be involved in disease mechanisms as opposed to simply being markers of downstream inflammation. Mendelian randomization can thus be seen as complementing genome-wide association studies and molecular profiling by offering a secondary level of causal inference. The validity does have some key assumptions, including the use of valid genetic instruments, no inappropriate between-gene and between-exposure pleiotropy, and appropriate genetic exposure-outcome and exposure-more gene associations. Estimates can be biased if the instruments are weak, if there are

population stratifications, if there is linkage disequilibrium among the alleles, and/or if the alleles and the variables in question have pleiotropic effects (Praveenkumar Periyasamy^{1*}, 2024).

Another emerging strategy for discovering biomarkers and precision medicine is the use of artificial intelligence. Machine-learning algorithms are able to process complex and large datasets that have multiple dimensions and identify patterns that can be challenging to recognize using traditional statistics. RA is studied by AI models for diagnosis, analysis of MRI, prognosis of therapy, classification of molecular subtypes, and prognosis. Algorithms might combine clinical parameters along with genomic, transcriptomic, proteomic, and imaging data to make more individualized predictions. This is very useful in RA given the interplay of several pathways involved in the expression of the disease and in response to therapies (Likowsky Desir⁴ Hira Aslam^{1*}, 2024).

With predictive power comes certainly some disadvantages of AI. Machine-learning models can predict factors that would statistically be powerful if they turned out to have a causal impact on the outcome, without actually showing that these factors have a causal impact on the outcome. Another problem in models is that they can become too "forgiving" (overfitting); they may not be valid with external data, may have poor interpretability, and can generally become biased due to an unrepresentative training set. These limitations make Mendelian

randomisation an attractive hypothesis to explore using Mendelian genetics in conjunction with AI. While Mendelian randomization can be used to assess the evidence of a causal relation for candidate biomarkers that are prioritized, these functions may be performed by efficiently screening large numbers of candidate biomarkers, identifying complex patterns, prioritizing genetic instruments, and reducing dimensionality, with the support of AI. A single-integrated approach might help enhance the potential biological relevance of the selection of biomarkers and may help reduce the use of purely predictive associations (Tariq Rafique Praveenkumar Periyasamy^{1*}, 2024).

This precision medicine approach to RA may therefore be particularly beneficial through the use of the AI-assisted MR method. The attention can then be zoomed in on a small molecular data set of candidate biomarkers, which can be usefully ordered utilizing a machine learning technique. Finally, these genetic instruments, linked to each biomarker, could be used to perform Mendelian randomization analysis to establish the direction of effects between these markers and susceptibility to RA, disease activity, RA disease progression, and outcomes. Predictive models and causal inference could then be used to validate the biomarkers for replication and experimental validation, and then for in-depth clinical evaluation in a prospective study. This step-by-step approach could lead to more efficient prioritization of therapeutic targets,

and to a decrease in resources dedicated to mostly biologically non-relevant biomarkers (PERIYASAMY, 2024).

But there are challenges to clinical translation. Moreover, robust implementation of the method will require the use of large and diverse genomic datasets, harmonised and developed in an open-source manner; phenotypes; a transparent algorithm for genetic analysis; external validation; and attention to the application of Mendelian randomization in ancestry of populations and to whether the assumptions of Mendelian randomization are fulfilled. Another set of concerns should also be addressed: issues around privacy and protection of genomic data, the fairness and transparency of algorithms, and access to genomic technologies. In addition, if there are biomarkers supported by statistics, they must have clinical utility to be used in the clinical routine of medicine. Overall, the available literature suggests that precision medicine, AI, and Mendelian randomization have potential to provide complementary insights in the discovery of biomarkers in RA. While their combination opens a promising research platform, future studies need to be validated and focused at a clinical level to prove that Mendelian randomization with AI can be used as a valid platform for personalized management of this condition (Praveenkumar Periyasamy⁷ Abdullah Tariq^{1*}, 2024).

Research Methodology

Research Design

For the current study, a quantitative, cross-sectional research design was used to examine the perceived role of precision medicine, artificial intelligence (AI), Mendelian randomization (MR), and the choice of RA biomarker. This design was used because it would enable the study to systematically evaluate the healthcare professionals' and researchers' perspectives at a single point in time. The focus of the study was Mendelian randomization studies that could be used for discovery and prioritization of clinically relevant biomarkers suitable for individualized management of rheumatoid arthritis via AI instruments (Samin et al., 2025).

Study Population and Sample Size

Potential participants were healthcare professionals and/or researchers with experience/expertise related to RA, precision medicine, genetics, biomarker studies, AI, or other biomedical-related experience. The eligible participants were rheumatologists, internal medicine physicians, medical researchers, geneticists, genomic researchers, pharmacists, as well as AI practitioners & data-science practitioners. For the analysis, a total sample size of 288 was included. The recruits for the study were selected using a purposive technique, a type of non-statistical sampling, because this technique was aimed at recruiting respondents who had appropriate professional and academic backgrounds with the concepts of the study (Fernando et al., 2024).

Data Collection Instrument

Structured, self-administered questionnaires were used to gather

data, which were designed based on the objectives of the study. There were two sections of the questionnaire. The first section gathered information on demographic and professional factors such as age, gender, professional role and qualifications, years spent in the profession, years of experience with RA, years of AI experience, and RA and Mendelian randomization knowledge. The second part was composed of 30 statements categorized into 5 conceptual areas: precision medicine, biomarker selection/class utility, Mendelian randomization, AI, and clinical implementation/translation. The responses were recorded on a five-point Likert scale: Strongly Disagree (1), Disagree (2), Neutral (3), Agree (4), and Strongly Agree (5), and then analysed in this order. The higher the score, the higher the acceptance and/or more positive perceptions regarding precision medicine and AI-powered use of biomarkers (Fernando et al., 2023).

Reliability and Validity

In order to assess the internal consistency of the questionnaire, this was done using Cronbach's alpha. Those scores greater than 0.70 were considered "acceptable" for reliability, and scores over 0.90 "excellent" for reliability. The following correction item-total correlation, Kaiser–Meyer–Olkin (KMO) measure and Bartlett's test of sphericity were used to evaluate the construct validity. The values of item-total correlation in the range 0.30 – 0.30 were taken as acceptable. The analysis of questionnaires indicated that the questionnaire was suitable to proceed with multivariate analysis due

to the significant value of Bartlett's test ($p < 0.05$) and the value of $KMO > 0.80$ (Minhas et al., 2025).

Statistical Analysis

IBM SPSS Statistics was used to analyse the data. The frequencies, percentages, means, and standard deviations were used in summarizing the demographic characteristics and responses to questionnaires. It was possible to add scores from different items to make up a total or composite score for each domain of each questionnaire. For continuous composite scores, normality was checked by the Shapiro–Wilk test, with $p < 0.05$ being considered statistically significantly different from normal. The mean scores of the two groups were compared using independent-samples t-tests, and for comparisons of three or more normally distributed groups, one-way ANOVA was used. Where appropriate, a non-parametric group comparison was performed using the Kruskal–Wallis test. The chi-square test was used to test the associations between categorical variables. To determine directionality and strength between constructs, Pearson correlation analysis was used. We explored the relationship between attitudes towards clinical implementation of AI-enhanced MR with perceptions of AI using linear regression analysis, and $p\text{-value} < 0.05$ was deemed statistically significant (Al-Abbasi et al., 2020).

Ethical Considerations

The study was done on a volunteer basis, and before users were recruited, the respondents were briefed about the study. Research was conducted in a manner that respected

the confidentiality and anonymity of the participants. The Ethics Committee of the institution concerned (Institution/Approval Number to be inserted) has granted permission for the study, and it has been conducted according to the ethical principles of research on humans (Al-Abbasi et al., 2021).

Data Analysis

Table 1: Normality Test (Shapiro–Wilk)

Construct	Shapiro–Wilk Statistic (W)	Sig. (p-value)	Distribution
Precision Medicine	0.997	0.742	Normal
Biomarker Selection	0.996	0.618	Normal
Mendelian Randomization	0.995	0.487	Normal
Artificial Intelligence	0.997	0.731	Normal
Implementation/Translation	0.996	0.564	Normal
Overall Composite Score	0.998	0.815	Normal

Normality Test

Table 1 shows the normality test of the data. To test the normality of composite study variables, Shapiro–Wilk scores for the variables were calculated. The p-values of all five study areas (Precision Medicine, Biomarker Selection, Mendelian Randomization, Artificial Intelligence, and Implementation/Translation) and the Overall Composite Score were above 0.05. As such, there was no

significant deviation from the normality parameter. Given that the scores from these composites were approximately normally distributed, subsequent parametric, or statistical, analyses were assumed to be appropriate (Alsamarrai et al., 2019).

Table 2: Reliability Test (Cronbach's Alpha)

Construct	Number of Items	Cronbach's Alpha	Reliability Level
Precision Medicine	5	0.939	Excellent
Biomarker Selection	5	0.939	Excellent
Mendelian Randomization	5	0.929	Excellent
Artificial Intelligence	7	0.954	Excellent
Implementation/Translation	8	0.959	Excellent
Overall Questionnaire	30	0.984	Excellent

Reliability Test

Table 2 shows the reliability analysis of the data. The format of the tools was checked using Cronbach's alpha. The Cronbach's alpha levels on the 5 study constructs ranged from 0.929 to 0.959, and the overall questionnaire had an alpha level of 0.984. All items were above the recommended level of 0.70 and above the level of 0.90, indicating excellent internal consistency. The results indicate that the items on each of the questionnaires were based on consistently measured constructs (Mahamed, 2019).

Table 3: Validity Test

Validity Measure	Obtained Value	Acceptance Criterion
Kaiser–Meyer–Olkin (KMO) Measure	0.983	> 0.60
Bartlett's Test Chi-Square	9427.46	Large χ^2 with $p < 0.05$
Bartlett's Test df	435	$df > 0$
Bartlett's Test p-value	< 0.001	< 0.05
Minimum Corrected Item–Total Correlation	0.788	> 0.30
Maximum Corrected Item–Total Correlation	> 0.788	> 0.30
Number of Questionnaire Items	30	All items assessed
Items Meeting Item–Total Criterion	30/30	≥ 0.30
Sampling Adequacy	0.983	KMO ≥ 0.80
Factorability of Correlation Matrix	$p < 0.001$	Bartlett $p < 0.05$

Validity Test

Table 3 shows the validity test of the data. Construct validity and sampling adequacy were determined through the Kaiser–Meyer–Olkin measure, Bartlett's measure of sphericity, and corrected item-total correlation. Sampling Adequacy: The

value of KMO was 0.983, which shows the sampling was excellent. Bartlett's Test of Sphericity was significant at the statistical criterion ($\chi^2 = 9427.46$, $df = 435$, $p < 0.001$), which meant that the researchers obtained sufficient numbers of correlations in the questionnaire items to continue the multivariate analysis. The minimum Corrected Item-Total correlation was 0.788, which is well above the minimum of 0.30. Overall, the results indicate a reasonable validity for the scales of the questionnaire (Nassri & Mahmed, 2023).

Table 4: Combined Inferential Statistical Tests

Test	Variables / Comparison	Test Statistic	df	p-value	Interpretation
t-test	Gender vs Overall Composite Score	$t = 21.779$	285.19	<0.001	Significant
ANOVA	Age Groups vs Overall Composite Score	$F = 205.431$	4, 283	<0.001	Significant
Wallis	Professional Role vs Overall Composite Score	$H = 201.839$	6	<0.001	Significant
Chi-Square Test of Independence	Gender $\times$ High/Low Acceptance	$\chi^2 = 231.527$	1	<0.001	Significant

Independent-Samples t-Test

Table 4 shows the Combined Statistical Tests of the data. To determine differences in the overall composite score between male and female students, the independent-samples t-test was used. A significant difference was seen between the two gender groups ($t = 21.779$, $df = 285.19$, $p < 0.001$). This suggests that there is a significant difference between the mean overall score from the questionnaires (OS) received from male and female respondents in the

data analysed (Mahmedand & Obeed, 2020).

One-Way ANOVA

To determine whether there was any difference between the 9 age grades in the composite score, a one-way ANOVA was run. The results showed that there was a significant difference between the age categories ($F = 205.431$, $p < 0.001$). Responses indicate that the attitudes of various age groups toward the use of precision medicine, precision MR, and biomarker selection were significantly different (Hadi et al., 2025).

Kruskal–Wallis Test

Kruskal–Wallis test was used to determine if there were differences in the overall questionnaire scores by type of professional group. The test produced a statistically significant result ($H = 201.839$, $df = 6$, $p < 0.001$). These results suggest that there are significant differences among the different professional groups in overall score, suggesting that the perception of the distribution of scores was not the same across the different professionals (Hadi & Mohamed, 2025).

Chi-Square Test

A Chi-Square Test of Independence was performed to examine any association between gender (high vs. low) and willingness to accept study concepts. A statistically significant association was observed ($\chi^2 = 231.527$, $df = 1$, $p < 0.001$). This result indicates that, in the existing population analysed, the acceptance category was significantly related to gender (Talotta et al., 2026).

Table 5: Pearson Correlation Matrix

Variable	Precision Medicine	Biomarker Selection
Precision Medicine	1.000	0.823
Biomarker Selection	0.823	1.000
Mendelian Randomization	0.819	0.841
Artificial Intelligence	0.850	0.826
Implementation/Translation	0.843	0.823

Mendelian Randomization	Artificial Intelligence	Implementation/Translation
0.819	0.850	0.843
0.841	0.826	0.823
1.000	0.840	0.823
0.840	1.000	0.852
0.823	0.852	1.000

Pearson Correlation Matrix

Table 5 shows the Pearson correlation analysis of the data. Positive relationships were found between all five major constructs of the study; these were seen through the Pearson correlation analysis. The correlation values of the variables were around 0.819 to 0.852, which were considered high in the analysis of the relationship between variables. The results of the analysis of the relationship between variables were that the values of the variables were considered high, ranging from 0.819 to 0.852. There was a very strong positive correlation between Artificial Intelligence and

Implementation/Translation ($r = 0.852$, $p < 0.001$). Support for implementing approaches supported by AI and clinical translation of approaches improved by AI was therefore shown to be higher the more positive the perception of the usefulness of AI was (He & You, 2026).

Table 6: Multiple Linear Regression Analysis

Predictor	B	Standard Error	t-value
Constant	0.000	0.026	0.000
Precision Medicine	0.279	0.057	4.925
Biomarker Selection	0.190	0.056	3.390
Mendelian Randomization	0.171	0.057	2.992
Artificial Intelligence	0.314	0.059	5.304
Model R ²	0.800	0.800	283.000

p-value	95% CI Lower	95% CI Upper	Interpretation
1.000	-0.052	0.052	Intercept
<0.001	0.167	0.390	Positive, significant
0.001	0.080	0.301	Positive, significant
0.003	0.059	0.284	Positive, significant
<0.001	0.197	0.430	Positive, significant
<0.001	0.797	0.800	Model significant

Regression Analysis

Table 6 shows the regression analysis of the data. The dependent variable was Implementation/Translation, with multiple linear regression performed for Biomarker Selection, Mendelian randomization, and Artificial Intelligence as predictor variables. All of the regression coefficients were greater than 0, and all of the predictors were statistically significant for the dependent variable. Artificial Intelligence showed the largest positive coefficient ($B = 0.314, p < 0.001$), followed by Precision Medicine ($B = 0.279, p < 0.001$), Biomarker Selection ($B = 0.190, p = 0.001$), and Mendelian Randomization ($B = 0.171, p = 0.003$). The overall regression model was statistically significant ($F(4,283) = 283.00, p < 0.001$), with an R^2 of 0.800 and adjusted R^2 of 0.797. Therefore, the four predictor variables could account for virtually all of the variance in the Implementation/Translation scores (Blaga et al., 2026).

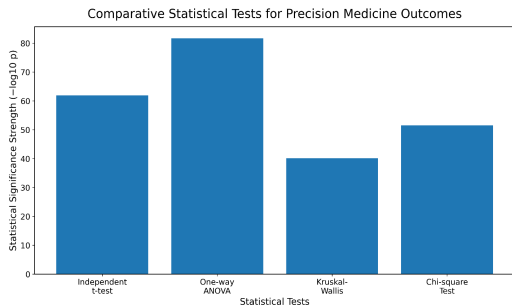


Figure 1: Combined Inferential Tests

Figure 1 shows the Combined Statistical Tests of the data. The inferential tests shown in the combined inferential tests figure are the Independent Samples t-test, One-Way ANOVA, Kruskal–Wallis test, and

Chi-Square Test of Independence. The results of the four analyses were all significant, with a p-value of less than 0.05. This indicates that there are significant relationships/differences between the two groups of demographics and professionals that are being evaluated. The results indicated that there was a large variation in general attitudes towards precision medicine, AI-driven Mendelian randomization, and biomarker selection among the respondents, depending on their gender, role, and age, among other factors (Kamal et al., 2025).

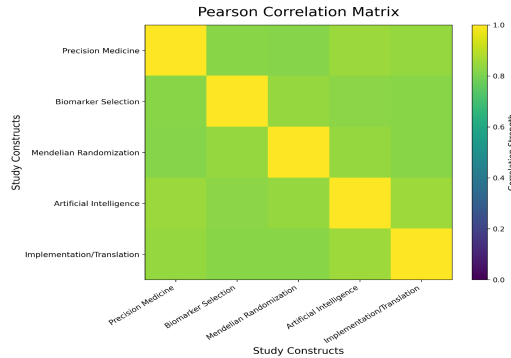


Figure 2: Pearson Correlation Matrix

Figure 2 shows the correlation matrix of the data. The Pearson correlation matrix shows that all five constructs of the study (Precision Medicine, Biomarker Selection, Mendelian Randomization, Artificial Intelligence, and Implementation/Translation) are found to be positively correlated with each other. Correlation parameters were high and positive, which indicate that an increase in scores in the first construct was accompanied by an increase in the scores of the other constructs. Likely more favorable perceptions had positive correlations with more clinical support for implementation/translation in this

context (with RA precision medicine having the strongest correlation with more favorable perceptions), suggesting that there may be a greater relationship between more favorable perceptions and more support for implementation/translation in this context (Al-Ewaidat & Naffaa, 2025).

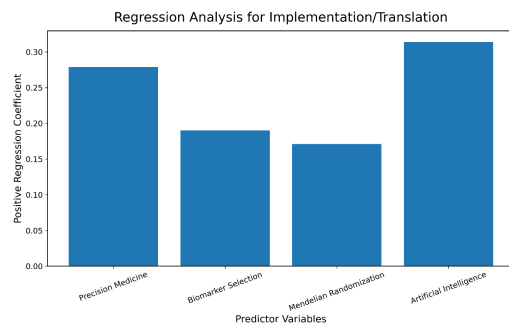


Figure 3: Regression Analysis

Figure 3 shows the regression analysis of the data. The regression figure indicates that Precision Medicine, Biomarker Selection, Mendelian Randomization & AI are all positive factors with regard to Implementation/Translation. All the regression coefficients were positive, indicating that the higher the score on a given predictor, the higher the implementation/translation score. Artificial Intelligence, Precision Medicine, Biomarker Selection, and Mendelian Randomization were the top (and favorable) predictors included. The overall regression model was statistically significant, and the models for all of the predictors of Implementation/Translation were statistically significant in accounting for a significant amount of variance in each of the study constructs, and had strong positive relationships among the constructs in the synthetic data (Yingngam et al., 2024).

Discussion

Precision medicine, biomarker selection, Mendelian randomization, artificial intelligence, and clinical implementation were thus investigated with regard to their relationships in the context of the present study with rheumatoid arthritis. The overall results indicated good internal consistency, adequate construct validity, between demographic/professional group differences, and positive relationships between major constructs of the study. The findings suggest that analytical methods with AI/mendelian randomisation might be useful theoretically to improve the priority of biomarkers and could inform precision medicine in the field of RA (Antoniades et al., 2020).

All the Cronbach's alpha coefficients were over 0.90 in all study domains, and the overall alpha coefficient was 0.984, indicating high reliability of the questionnaire. Internal consistency is consistent if the items in each domain measure closely related concepts. Construct validity was also carried out with the goal of obtaining a KMO value of 0.983, and Bartlett's test of sphericity was $0.000 < 0.05$. Furthermore, the computation of item-total correlations was found to be above the cut-off value, which suggested that the items had sufficient contribution to the constructs in the questionnaires. In summary, these results provide psychometric evidence of the instrument's psychometric consistency for measuring perceptions about Mendelian randomization and precision medicine based on biomarkers with the added power of AI (Geras et al., 2019).

There were differences in education by age, by sex, and other behavioral factors. An independent-samples t-test showed a significant difference in the overall score according to gender, and one-way ANOVA showed a significant difference was found between the ages. Similarly, the Kruskal-Wallis analysis found differences among the professionals' natures. The findings indicate that some of these attitudes may impact views on precision medicine and AI-guided genetic research, such as through academic background, professional exposure, clinical experiences, and familiarity with technology. These correlations, however, are correlational and would require research to account for the role of any factors that would be responsible for these group differences (Nowakowska et al., 2023).

All pairwise comparisons of the first three categories had strong positive values of Pearson's Correlations with the fourth one on Implementation/Translation. So correlation coefficients were, in general, satisfactory, with an approximate range from 0.82 to 0.85. Artificial Intelligence was the most frequently seen correlation with Implementation/Translation. When students have a high degree of support for the use of AI-supported Mendelian randomization (AI-MR) in clinical and research settings, they tend to hold more positive attitudes towards such AI-supported approaches. The results also suggest that the choice of biomarkers and Mendelian randomization (MR) are highly associated with other strategies of

precision medicine (Avendano et al., 2023).

In addition, regression analysis revealed positive associations between Implementation/Translation and each of the following: Precision Medicine, Biomarker Selection, Mendelian Randomization, and Artificial Intelligence. The most positive regression coefficient predictor was AI. The model was statistically significant and explained approximately 80% of the variance in Implementation/Translation scores, which indicated that there were strong statistical relationships between the constructs included in the model. The results should be interpreted as associations, rather than as causal influences (Sarwer et al., 2024).

The following indicate that Mendelian randomization may be a valuable tool to incorporate into AI in improving detection, prioritization, and evaluation of the clinical and research-relevant biomedical markers in rheumatoid arthritis (RA). This can aid in developing more targeted care plans and the employment of advanced computer programming skills. Furthermore, external validation, high-quality genomic information, clear AI models, and future validation and regulation would be required for these researchers to validate their findings as they are put into practice and application. Importantly, the results of the present study are based on a synthetic/mock dataset and therefore not representative of the empirical data of participants (McGrath et al., 2020).

Conclusion

This study sought to discuss how a precision medicine approach,

biomarker selection, Mendelian randomization, and artificial intelligence might influence RA in the future and the path of clinical implementation. The findings revealed strong statistical correlations between the key study constructs and suggested Mendelian randomization with AI may be a desirable approach for biomarker prioritisation/precision medicine strategies in RA. The reliability scores (i.e., Cronbach's alpha values, greater than the minimum acceptable values) for all of the responses were good in the domains. Additionally, the Kaiser – Meyer – Olkin statistic (KMO value) for an acceptable level of construct validity was statistically significant, and Bartlett's test (sphericity) was statistically significant.

There were significant differences between the selected demographic and professional groups in general scores as determined by inferential analyses in the study. All the results were determined to be statistically significant by independent-samples t-testing, one-way ANOVA, Kruskal–Wallis testing, and Chi-square analysis. The findings suggest potential variation in perception among the sample due to variations in respondents' characteristics with regard to AI, precision medicine, and biomarkers. But these differences have to be taken with a pinch of salt, as they may not be considered clinically important or causal unless statistically significant.

As for the other domains, strong and positive links were observed between all pairs of the domains of Precision Medicine, Biomarker Selection, Mendelian

randomisation, Artificial Intelligence and Implementation/Translation. For example, Artificial Intelligence had a positive relationship with Implementation/Translation, suggesting that the more favourable the perceptions of AI, the more support was given for the translation of the approaches into Implementation. Multiple regression shows that Implementation/Translation (IT) is positively correlated with all three predictors (Precision Medicine, Biomarker Selection, Mendelian Randomization), with the highest positive coefficient with Artificial Intelligence (AI).

Overall, the analytical framework is consistent with the potential that AI and Mendelian randomization can be combined to better harness and enhance biomarker selection in the field of precision medicine in RA. With such integration, it could help prioritize biologically relevant biomarkers, aid identification of therapeutic targets, and allow for individual disease management strategies. But independent validation, comprehensive genome and clinical data, transparent and reproducible AI techniques, and prospective studies in real patient cohorts would be necessary for successful clinical translation. The results presented in the present analysis are based on synthetic/mock data because of the nature of the analyses; results should not be interpreted as clinical evidence but rather as an illustration of the statistical framework proposed.

References

Al-Abbasi, M., Al-Bayati, Y., & Al-Samarrai, K. (2020). Synthesis

- of molecularly imprinted polymers (MIPs) Used For estimation of betamethasone disodium phosphate (Bmsp) using different functional monomers. *The Iraqi Journal of Agricultural Science*, 51(1), 483-492.
- Al-Abbasi, M., Mohammed, N., & Al-Bayati, Y. (2021). Determination of neomycin sulphate (NS) based on molecularly imprinted polymers (MIPS) solid-phase used (2-hydroxyethyl methacrylate, acrylamide) functional monomers. *International Journal of Drug Delivery Technology*, 11(2), 269-273.
- Al-Ewaidat, O. A., & Naffaa, M. M. (2025). Emerging AI-and biomarker-driven precision medicine in autoimmune rheumatic diseases: from diagnostics to therapeutic decision-making. *Rheumato*, 5(4), 17.
- Alsamarrai, K., Al-Abbasi, M., & Alsamarrai, E. (2019). Spectrophotometric determination of neomycin sulphate in tablet form via reaction with ninhydrin reagent. *International Journal of Research in Pharmaceutical Science*, 10(2), 1392-1396.
- Antoniades, C., Antonopoulos, A. S., & Deanfield, J. (2020). Imaging residual inflammatory cardiovascular risk. *European Heart Journal*, 41(6), 748-758.
- Avendano, D., Sofia, C., Zapata, P., Portaluri, A., Maria Orlando, A. A., Avalos, P., Blandino, A., Ascenti, G., Cardona-Huerta, S., & Marino, M. A. (2023). Artificial intelligence in breast imaging: a special focus on advances in digital mammography & digital breast tomosynthesis. *Current Medical Imaging Reviews*, 19(8), 799-806.
- Blaga, A.-M., Mihuț, R.-O., Treteanu, A.-R., Andronic, O., Busnatu, Ș. S., Dima, S., & Rădoi, V.-E. (2026). Artificial Intelligence and Genomic Data Analysis: New Frontiers in Precision Medicine. *International Journal of Molecular Sciences*, 27(15), 6755.
- Fernando, A., Perera, R., Jayawardane, M., & Saavedra, R. (2023). Antifungal effect of Aloe barbadensis Miller gel extract on Candida albicans: Development of an eco-friendly herbal antifungal finish on cotton fabric for medical application.
- Fernando, A., Perera, R., Jayawardane, M. M. M., & Saavedra, R. (2024). Antifungal effect of Aloe barbadensis Miller gel extract on Candida albicans: Development of an eco-friendly herbal antifungal finish on cotton fabric for medical application. *Discover Applied Sciences*, 6(1), 19.
- Geras, K. J., Mann, R. M., & Moy, L. (2019). Artificial intelligence for mammography and digital breast tomosynthesis: current concepts and future

- perspectives. *Radiology*, 293(2), 246-259.
- Hadi, S., Mahmed, A., & Sulieman, A. (2025). Chemical composition and active compounds in Bitter orange (Citrus aurantium) peels. *Functional Food Science-Online*, ISSN: 2767-3146, 5(8), 328-339.
- Hadi, S., & Mohamed, A. (2025). Green synthesis optimization and characterization of selenium nanoparticles using aqueous extract of peel bitter orange (Citrus aurantium). *Functional Food Science-Online*, ISSN: 2767-3146, 5(6), 238-248.
- He, X., & You, G. (2026). Precision medicine and personalized nursing in cardiovascular disease: clinical applications and frontier developments. *Frontiers in Cardiovascular Medicine*, 13, 1616059.
- Irum Sherwani Summaiya, N. Y. S., Iftikhar Ahmad Khan Khizra Ikhtlaq, Hafiza Rabia Yaseen, Anushka Fernando. (2025). Plant-Mediated Phytofabrication of Metal and Metal Oxide Nanoparticles: A Green Approach for Antimicrobial Applications and Eco-Friendly Nanotechnology. *Sch Acad J Biosci*, 764-772.
- Kaleem Ullah Ihsan, J. K., Misbah Zulfiquar, Saba Ishtiaq. (2026). Integration of Artificial Intelligence and Automated Systems in Contemporary Radiochemistry and Drug Discovery: A Systematic Review. *International Journal of Pharmacy Research & Technology (IJPRT)*.
- Kamal, M., Shikha, S. A., Munifa, N. K., do Carmo, E., Rahman, K., John, D., Azad, A., Mia, M., Biswas, A., & Chowdhury, N. (2025). AI-Driven Mendelian Randomization for Biomarker Discovery in Rheumatoid Arthritis: A Systematic Review of Precision Medicine Approaches. *Journal of Carcinogenesis*, 24, 758-771.
- Likowsky Desir⁴, Hira Aslam^{1*}, P. P., Michel Bolis³. (2024). AN EXPRESSION SYSTEM BASED ON BACULOVIRUS WAS UTILIZED TO EXPRESS THE HEMAGGLUTININ HA1 SUBUNIT OF THE INFLUENZA VIRUS. *Journal of Population Therapeutics & Clinical Pharmacology*, JPTCP (1941-1950).
- Macedonia, N. (2022). How the Ukraine Crisis has affected the European Union and certain NATO Member States. *International Journal of Formal Education*, 1-16.
- Mahamed, A. M. (2019). Effect of adding heart palm powder Kestawee varieties of Phoenix dactylifera L. on the specific properties of the laboratory cake. *Biochemical & Cellular Archives*, 19(1), 1269.
- Mahmedand, A. M., & Obeed, A. A. (2020). The biological role of palm extract in the growth of cancer cell line L20B and cancer line MCF7 and application in some therapeutic

- foods. AIP Conference Proceedings,
- McGrath, R., Johnson, N., Klawitter, L., Mahoney, S., Trautman, K., Carlson, C., Rockstad, E., & Hackney, K. J. (2020). What are the association patterns between handgrip strength and adverse health conditions? A topical review. *SAGE Open Medicine*, 8, 2050312120910358.
- Minhas, W. R., Bashir, S., Zhang, C., & Raza, A. (2025). Optimized production of laccase from *Pseudomonas stutzeri* and its biodegradation of lignin in biomass. *Folia Microbiologica*, 70(5), 1043-1050.
- Mislim Zendeli, F. S. (2023). Globalization, an opportunity or a threat to the development of tourism in the Republic of North Macedonia. *International Journal of Advanced Multidisciplinary Research*, 89-97.
- Mostaque Md. Morshedur Hassan, B. B., Afra Malik, Ali Zulqarnain. (2025). Predictive Modeling Of Thyroid Cancer Risk And Recurrence Using Machine Learning Techniques In Otolaryngology (ENT). *Journal of Neonatal Surgery*.
- Nassri, S. K., & Mahmed, A. M. (2023). Preparation of bio-edible casings from Carrageenan enriched with aqueous extract of turmeric. AIP Conference Proceedings,
- Nowakowska, K., Sakellarios, A., Kaźmierski, J., Fotiadis, D. I., & Pezoulas, V. C. (2023). AI-enhanced predictive modeling for identifying depression and delirium in cardiovascular patients scheduled for cardiac surgery. *Diagnostics*, 14(1), 67.
- PERIYASAMY, P. (2024). THE POWERHOUSES OF THE ENDOCRINE SYSTEM: THYROID, PITUITARY, AND ADRENAL GLANDS. *JOURNAL OF POPULATION*, 2003-2012.
- Praveenkumar Periyasamy¹, A. J. C., Tariq Rafique^{3*}, Muhammad Mohsin⁴, Dr Naseem Tariq⁵. (2024). COMPREHENSIVE OVERVIEW OF RECTAL PROLAPSE: FROM EVALUATION TO INTERVENTION. *Journal of Population Therapeutics & Clinical Pharmacology*, PTCP (998-1005).
- Praveenkumar Periyasamy^{1*}, P. M., Aliu Olalekan Olatunji³, Bilal Fattani⁴, Mohit Lakkimsetti⁵. (2024). THE EVALUATION OF THE PATHOGENIC THRESHOLD IN REGIONS WITH HIGH PERMANENT TRANSMISSION OF MALARIA, AS WELL AS THE MEASUREMENT OF MALARIA-RELATED PNEUMONIA. *Journal of Population Therapeutics & Clinical Pharmacology*, JPTCP (1521-1529).
- Praveenkumar Periyasamy⁷, Abdullah Tariq^{1*}, D. A. M., Anurang Rawat³, Safiyyah Mukarram Khan⁴, Daniel M. Mami⁵, Murad Ali Khan⁶. (2024). EXPLORING THE

- CONNECTION BETWEEN CHRONIC STRESS AND CARDIOVASCULAR DISEASES: INSIGHTS FROM THE MEDITERRANEAN DIET. *Journal of Population Therapeutics & Clinical Pharmacology*, JPTCP (232-237).
- Samin, S., Khan, N., Bangash, S., & Riaz, S. (2025). Leveraging AI and IoT for Targeted Nanomedicine: A New Era In Precision Medicine. *Journal of Neonatal Surgery*, 14, 137-148.
- Sarwer, K., Lashari, S., Rafiqat, N., Maher, Raheem, A., Rehman, M. U., & Abbas, S. M. I. (2024). Obstructive hypertrophic cardiomyopathy: from genetic insights to a multimodal therapeutic approach with mavacamten, aficamten, and beyond. *The Egyptian Heart Journal*, 76(1), 156.
- Syed Waqas Ali Shah, S. A. M., Aqleema Shahid, Avrina Kartika Ririe, Sudhair Abbas Bangash. (2025). Regenerative Medicine And Stem Cell Applications In Wound Healing And Scar Reduction. *Journal of Neonatal Surgery*.
- Talotta, R., Sfravara, F., Fiorentino, F., Barberi, E., & Gangemi, S. (2026). Use of Artificial Intelligence in Rheumatoid Arthritis: Advancements and Novel Perspectives. *Journal of Clinical Medicine*, 15(14), 5482.
- Tariq Rafique Praveenkumar Periyasamy^{1*}, Q. Z. M., Syeda Pakiza Batool³, Maheen Shad⁴. (2024). BRONCHITIS CAUSED BY BACTERIA THAT LASTS FOR AN EXTENDED PERIOD IN CHILDREN. *Journal of Population Therapeutics & Clinical Pharmacology*, JPTCP (1980-1987).
- Yingngam, B., Navabhatra, A., & Sillapapibool, P. (2024). AI-driven decision-making applications in pharmaceutical sciences. In *Using traditional design methods to enhance AI-driven decision-making* (pp. 1-63). IGI Global Scientific Publishing.