Supplementary Information

Knowledge Graph Definition

Knowledge graphs (KGs) can be conceptualized as labeled, directed multigraphs [25]. Formally, we define a KG as KG $= (V, L, F)$, where V represents the set of entity vertices, L denotes the collection of relation labels, and $F \subseteq V \times L \times V$ constitutes the set of factual triples. Each triple $\langle h, r, t \rangle$ represents a directed edge from the head entity h to the tail entity t via relation r.

Link Prediction in Graphs

Link prediction within KG reasoning addresses incomplete queries of the form $\langle h, r, ? \rangle$, aiming to identify missing connections. This task requires estimating whether an unobserved triple $\langle h, r, t \rangle$ represents a true relationship in the underlying knowledge domain. Given a partial query $\langle h, r, ? \rangle$, the objective is to assign scores to all potential tail entities $v \in V$ within the inference graph KG $= (V, L, F)$, ranking them according to the probability $P(t = v \mid h, r)$.

In the domain of drug repurposing, link prediction specifically focuses on discovering novel Drug $\xrightarrow{\text{treats}}$ Disease relationships [26]. The task involves identifying potential therapeutic applications for existing medications beyond their currently known or approved indications, leveraging patterns embedded within the knowledge graph structure [27].

Within the *transductive link prediction* framework, both training and inference occur on an identical graph structure $G_{\text{train}} = G_{\text{inf}}$. Under this paradigm, the model learns to predict previously unobserved connections between entities that existed during training, without requiring generalization to entirely new entities or relation types. Formally, where $G_{\text{train}} = (V_{\text{train}}, L_{\text{train}}, F_{\text{train}})$ and $G_{\text{inf}} = (V_{\text{inf}}, L_{\text{inf}}, F_{\text{inf}})$:
$\mathrm{V}_{\text{train}} = V_{\text{inf}}$
$L_{\text{train}} = L_{\text{inf}}$
$F_{\text{train}} \subset F_{\text{inf}}$

Training configuration of Foundation Model

For our foundation model, we trained ULTRA with a 6-layer architecture (64-dimensional hidden representations) for both relation and entity embedding. Using DistMult message passing with sum aggregation, we enhanced training stability through layer normalization and residual connections. We trained for 100 epochs (500 batches/epoch, batch size 512) using binary cross-entropy loss with logits for link prediction. Optimization used AdamW (lr=$5 \cdot 10^{-4}$, weight decay=10^{-4}) with a ReduceLROnPlateau scheduler and early stopping (patience=6). Each positive triplet generated 10 strict negative samples during training to ensure challenging and meaningful training signals. This approach enabled our foundation model to effectively capture biomedical relationships before patient-specific fine-tuning.

Fine-tuning configuration of Patient-Specific Models

Our fine-tuning strategy preserves knowledge in the pre-trained foundation model while adapting to individual patient data through a parameter-efficient approach. Rather than retraining the entire graph, we freeze all 168,705 foundation model parameters and train only 1,733 patient-specific weights within our personalized loss function (a 97.3× reduction in trainable parameters). This helps us preserve the essential domain information already learned from the biomedical knowledge graph. Fine-tuning for 3 epochs with 100 batches per epoch yielded stable loss values that confirm effective learning without overfitting (lr=10^{-4}, weight decay=10^{-4}, patience=5, gradient clipping=1).

Selection of Patients for Case Studies

To demonstrate our approach's effectiveness, we selected representative patients from the UK Biobank's Alzheimer's disease population for detailed case studies.

We analyzed four patient data categories: (i) protein biomarkers, (ii) medical history including prescriptions and diagnoses, (iii) PRS for comorbidities, and (iv) lifestyle and demographic information. For each category, we applied k-means clustering to partition patients into groups by minimizing within-cluster sum of squares:

$$\text{Minimize} \quad WCSS = \sum_{i=1}^{k} \sum_{p \in S_i} ||p - \mu_i||^2 \tag{2}$$

where μ_i represents the centroid of cluster S_i. We determined optimal cluster numbers using the elbow method and merged these initial clusters to form three distinct final groups $\{F_1, F_2, F_3\}$.

From each final cluster, we selected one patient who maximized differentiation from other clusters:

$$p_j^* = p \in F_j \arg\max \left(\sum_{m=1 m \neq j}^{6} d(p, \mu_m) \right) \tag{3}$$

where $d(p, \mu_m)$ represents Euclidean distance between patient p and centroid μ_m. This yielded three patients (anonymized as Zoro, Robin and Usopp) with diverse characteristics but all having prescription histories to enable medication comparisons (Figure 5).

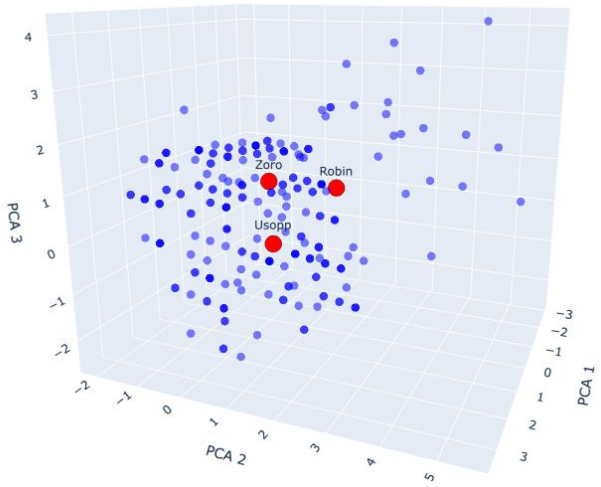

Figure 5: **Chosen Patients for Case Study in Final Final Cluster**

Binary Cross Entropy

$L_{pred} = -\frac{1}{N} \sum_{i=1}^{N} [y_i \log(p_i) + (1 - y_i) \log(1 - p_i)]$ which is the binary cross-entropy loss for link prediction widely used; N is the number of samples, y_i is the true label (0 or 1), and p_i is the predicted probability.

Expanded Results for Patient-Specific Models

Patient: *Zoro*	Description	λ_1 (PRS)	λ_2 (Biomarker)	MR	MRR	Hits@1	Hits@3	Hits@10	ROC AUC	AUPRC
Baselines	No personalized factors in loss	0	0	739.09216	0.13328	0.06175	0.13592	0.27811	0.99953	0.27152
	PRS only	0.5	0	739.09216	0.13328	0.06175	0.13592	0.27811	0.99562	0.12277
	Biomarkers only	0	0.5	739.09393	0.13328	0.06175	0.13593	0.27812	0.99948	0.00657
Equal Influence	Low equal influence	0.1	0.1	739.09387	0.13328	0.06175	0.13593	0.27809	0.99451	0.29228
	Medium equal influence	0.5	0.5	739.09741	0.13327	0.06175	0.13596	0.27808	0.99921	0.02617
	High equal influence	2	2	739.11365	0.13323	0.06174	0.13587	0.27784	0.99933	0.00833
	Extreme equal influence	10	10	739.26581	0.13326	0.06169	0.13606	0.27781	0.99959	0.05697
Balanced Ratios	Slight PRS emphasis (3:2)	0.3	0.2	739.09534	0.13327	0.06175	0.13595	0.27811	0.99532	0.09079
	Slight biomarker emphasis (2:3)	0.2	0.3	739.09619	0.13327	0.06173	0.13593	0.27811	0.99623	0.30918
PRS-Dominant	Moderate dominance (2:1)	0.2	0.1	739.09412	0.13327	0.06175	0.13595	0.27811	0.99960	0.09906
	Strong dominance (5:1)	**0.5**	**0.1**	**739.09711**	**0.13327**	**0.06175**	**0.13595**	**0.27807**	**0.99462**	**0.36033**
	Very strong dominance (10:1)	1	0.1	739.10736	0.13326	0.06176	0.13588	0.27802	0.99977	0.20119
	High-value dominance (5:1)	2.5	0.5	739.12659	0.13320	0.06169	0.13588	0.27786	0.99941	0.10552
Biomarker-Dominant	Moderate dominance (1:2)	0.1	0.2	739.09332	0.13328	0.06175	0.13594	0.27811	0.99927	0.11634
	Strong dominance (1:5)	0.1	0.5	739.09497	0.13327	0.06174	0.13595	0.27810	0.99974	0.11751
	Very strong dominance (1:10)	0.1	1	739.09778	0.13327	0.06174	0.13592	0.27811	0.99575	0.30088
	High-value dominance (1:5)	0.5	2.5	739.10992	0.13325	0.06172	0.13594	0.27814	0.99952	0.09117
Fixed Sum (=1.0)	PRS emphasis	0.7	0.3	739.10370	0.13327	0.06175	0.13595	0.27808	0.99987	0.05412
	Biomarker emphasis	0.3	0.7	739.09644	0.13327	0.06174	0.13596	0.27809	0.99947	0.18790
High Influence	PRS emphasis	5	1	739.13019	0.13315	0.06166	0.13579	0.27781	0.99964	0.25313
	Biomarker emphasis	1	5	739.11554	0.13328	0.06177	0.13594	0.27801	0.99989	0.33618

Table 4: Expanded link prediction results for the patient-specific model trained on patient Zoro's data. Best performing model is in bold.

Patient: *Robin*	Description	λ_1 (PRS)	λ_2 (Biomarker)	MR	MRR	Hits@1	Hits@3	Hits@10	ROC AUC	AUPRC
Baselines	No personalized factors in loss	0	0	739.14075	0.13111	0.06202	0.13227	0.26895	0.99938	0.07406
	PRS only	0.5	0	739.14539	0.13109	0.06202	0.13218	0.26891	0.99974	0.04463
	Biomarkers only	0	0.5	739.14069	0.13112	0.06202	0.13227	0.26894	0.99883	0.06116
Equal Influence	**Low equal influence**	**0.1**	**0.1**	**739.14069**	**0.13111**	**0.06201**	**0.13225**	**0.26895**	**0.99949**	**0.24593**
	Medium equal influence	0.5	0.5	739.14484	0.13109	0.06200	0.13222	0.26891	0.99933	0.04087
	High equal influence	2	2	739.16327	0.13110	0.06205	0.13222	0.26887	0.99881	0.17639
	Extreme equal influence	10	10	739.56982	0.13129	0.06223	0.13249	0.26895	0.99856	0.14527
Balanced Ratios	Slight PRS emphasis (3:2)	0.3	0.2	739.14282	0.13111	0.06202	0.13223	0.26893	0.99934	0.06943
	Slight biomarker emphasis (2:3)	0.2	0.3	739.14093	0.13111	0.06203	0.13224	0.26894	0.99952	0.03898
PRS-Dominant	Moderate dominance (2:1)	0.2	0.1	739.14191	0.13111	0.06203	0.13225	0.26894	0.99912	0.12281
	Strong dominance (5:1)	0.5	0.1	739.13965	0.13111	0.06203	0.13220	0.26894	0.99899	0.17109
	Very strong dominance (10:1)	1	0.1	739.14685	0.13110	0.06201	0.13224	0.26890	0.99853	0.01306
	High-value dominance (5:1)	2.5	0.5	739.15717	0.13112	0.06205	0.13224	0.26885	0.99924	0.15363
Biomarker-Dominant	Moderate dominance (1:2)	0.1	0.2	739.14001	0.13111	0.06202	0.13226	0.26895	0.99858	0.06073
	Strong dominance (1:5)	0.1	0.5	739.14105	0.13112	0.06203	0.13226	0.26894	0.99924	0.12697
	Very strong dominance (1:10)	0.1	1	739.13989	0.13111	0.06201	0.13226	0.26897	0.99918	0.12097
	High-value dominance (1:5)	0.5	2.5	739.14117	0.13108	0.06199	0.13224	0.26894	0.99859	0.01774
Fixed Sum (=1.0)	PRS emphasis	0.7	0.3	739.14368	0.13108	0.06201	0.13222	0.26893	0.99940	0.09553
	Biomarker emphasis	0.3	0.7	739.14130	0.13111	0.06204	0.13223	0.26893	0.99908	0.03496
High Influence	PRS emphasis	5	1	739.22253	0.13120	0.06213	0.13240	0.26892	0.99934	0.08840
	Biomarker emphasis	1	5	739.14722	0.13109	0.06201	0.13221	0.26887	0.99876	0.03611

Table 5: Expanded link prediction results for the patient-specific model trained on patient Robin's data. Best performing model is in bold.

Patient: *Usopp*	Description	λ_1 (PRS)	λ_2 (Biomarker)	MR	MRR	Hits@1	Hits@3	Hits@10	ROC AUC	AUPRC
Baselines	No personalized factors in loss	0	0	734.69550	0.12432	0.05689	0.12459	0.25866	0.25866	0.06349
	PRS only	0.5	0	734.69739	0.12431	0.05690	0.12458	0.25862	0.99926	0.00796
	Biomarkers only	0	0.5	734.69525	0.12432	0.05690	0.12458	0.25866	0.99946	0.02944
Equal Influence	Low equal influence	0.1	0.1	734.69574	0.12432	0.05690	0.12460	0.25866	0.99965	0.11948
	Medium equal influence	0.5	0.5	734.69550	0.12430	0.05688	0.12458	0.25857	0.99942	0.03496
	High equal influence	2	2	734.70740	0.12430	0.05693	0.12461	0.25856	0.99959	0.05247
	Extreme equal influence	10	10	734.72241	0.12440	0.05701	0.12473	0.25865	0.99965	0.29938
Balanced Ratios	Slight PRS emphasis (3:2)	0.3	0.2	734.69617	0.12431	0.05690	0.12458	0.25863	0.99974	0.18224
	Slight biomarker emphasis (2:3)	0.2	0.3	734.69653	0.12432	0.05690	0.12460	0.25866	0.99889	0.03188
PRS-Dominant	Moderate dominance (2:1)	0.2	0.1	734.69617	0.12432	0.05690	0.12460	0.25867	0.99976	0.20703
	Strong dominance (5:1)	0.5	0.1	734.69556	0.12432	0.05691	0.12458	0.25863	0.99976	0.10501
	Very strong dominance (10:1)	1	0.1	734.69745	0.12432	0.05691	0.12458	0.25857	0.99945	0.11105
	High-value dominance (5:1)	**2.5**	**0.5**	**734.71130**	**0.12428**	**0.05689**	**0.12460**	**0.25857**	**0.99972**	**0.34562**
Biomarker-Dominant	Moderate dominance (1:2)	0.1	0.2	734.69580	0.12432	0.05690	0.12460	0.25866	0.99963	0.08188
	Strong dominance (1:5)	0.1	0.5	734.69611	0.12432	0.05690	0.12460	0.25867	0.99965	0.05587
	Very strong dominance (1:10)	0.1	1	734.69476	0.12432	0.05691	0.12460	0.25867	0.99940	0.00680
	High-value dominance (1:5)	0.5	2.5	734.69690	0.12432	0.05691	0.12457	0.25864	0.99870	0.07360
Fixed Sum (=1.0)	PRS emphasis	0.7	0.3	734.69519	0.12430	0.05688	0.12455	0.25859	0.99846	0.01958
	Biomarker emphasis	0.3	0.7	734.69458	0.12432	0.05690	0.12459	0.25866	0.99968	0.22430
High Influence	PRS emphasis	5	1	734.70190	0.12430	0.05690	0.12468	0.25853	0.99972	0.12006
	Biomarker emphasis	1	5	734.68201	0.12432	0.05691	0.12458	0.25857	0.99962	0.04227

Table 6: Expanded link prediction results for the patient-specific model trained on patient Usopp's data. Best performing model is in bold.