**Evaluation of the framework for mono-resistant vs. MDR/XDR profiles**

To further illustrate the applicability of the framework beyond per-drug predictions, we evaluated its ability to distinguish composite resistance profiles using the CRyPTIC dataset.

* **Definitions**:
* Rifampicin mono-resistance was defined as resistance to rifampicin (RIF-R) with susceptibility to the other first-line drugs.
* MDR/XDR was defined as co-resistance to rifampicin and isoniazid (RIF-R and INH-R). Because second-line DST data were largely missing, XDR could not be precisely defined and was therefore merged with MDR in this analysis.
* **Results:**
* The framework showed strong performance for identifying MDR/XDR cases (precision = 0.969, recall = 0.888).
* For rifampicin mono-resistant isolates, the performance was lower (precision = 0.667, recall = 0.632) due to the very small sample size (n = 19).

**Confusion matrix for rifampicin in CRyPTIC dataset**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Predict True | RIF-R | MDR/XDR | Other | Sum |
| RIF-R | 12 | 6 | 0 | 18 |
| MDR/XDR | 2 | 247 | 6 | 255 |
| Other | 5 | 25 | 135 | 165 |
| Sum | 19 | 278 | 141 | 438 |

* **Interpretation**:

These results demonstrate that the framework can be applied to profile-level classification derived from per-drug predictions. However, estimates for mono-resistance should be interpreted with caution given the limited number of available isolates. Larger cohorts with more complete DST data will be needed to systematically validate performance across resistance profiles.