From predictions to error-controlled decisions

Zitnik Lab



Towards actionable foundation models in medicine



Intae Moon

Ying Jin*, Intae Moon*, and Marinka Zitnik *Co-first authors

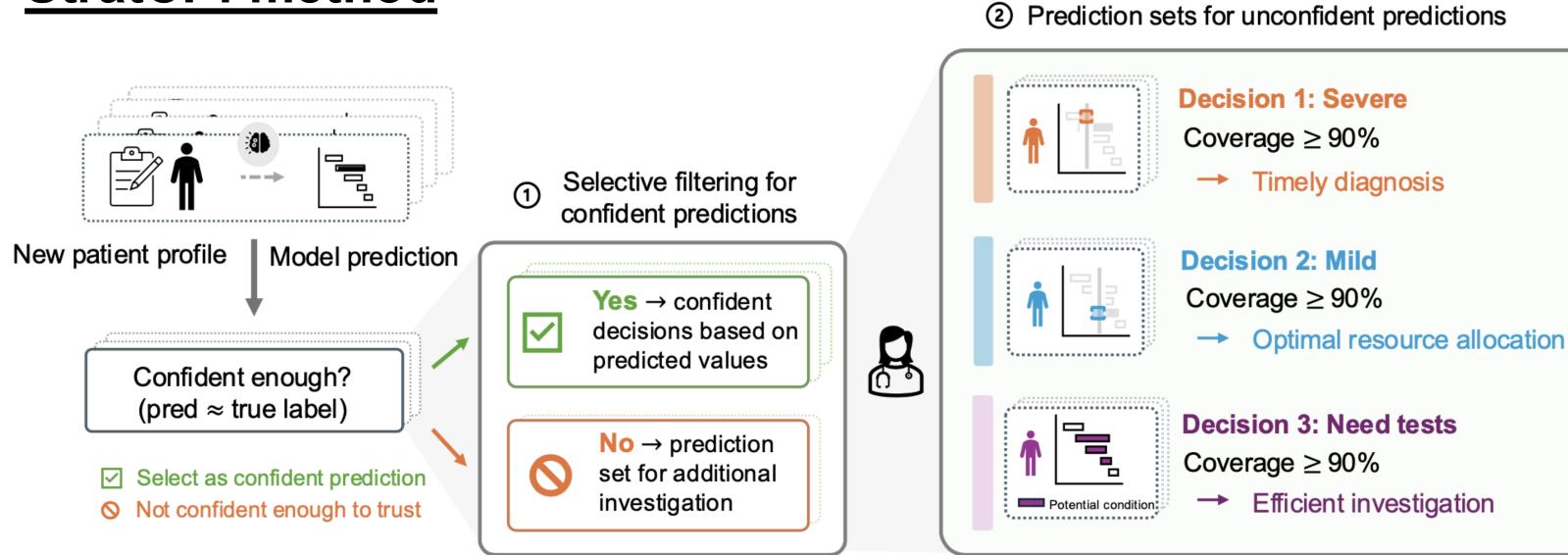
Motivation

- Foundation models (FMs) show broad promise and are increasingly evaluated prospectively in medicine
- Deployment in clinical practice requires outputs that clinicians can act on under pre-specified error budgets (e.g., a cap on false-positive calls)

We introduce **StratCP**, which wraps any existing foundation model to deliver

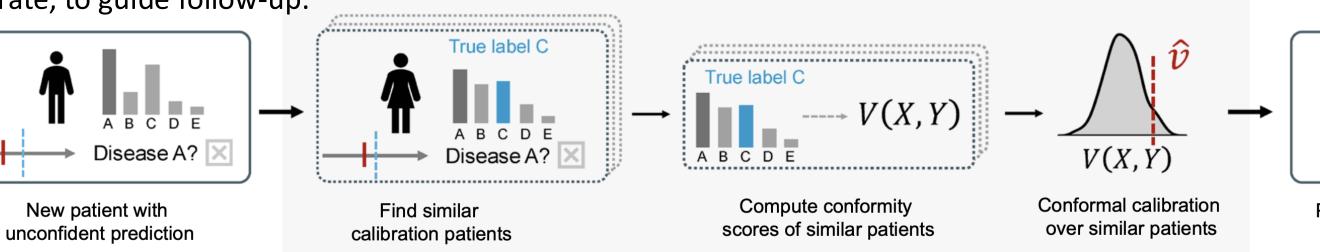
- patient-level diagnosis/outcome within a pre-specified false discovery rate (FDR)
- calibrated, clinically coherent differentials for deferred patients

StratCP: method



Step (1): select patients for confident calls using a calibrated cutoff τ that keeps selection within a prespecified FDR budget (act vs abstain). For theoretical details, see Jin and Candès (JMLR, 2023) Patient m — Disease A? ✓ Patient 2 → Disease B? Disease A? Patient m Disease A? → Disease A? 1-d confidence measure Calibrate cutoff

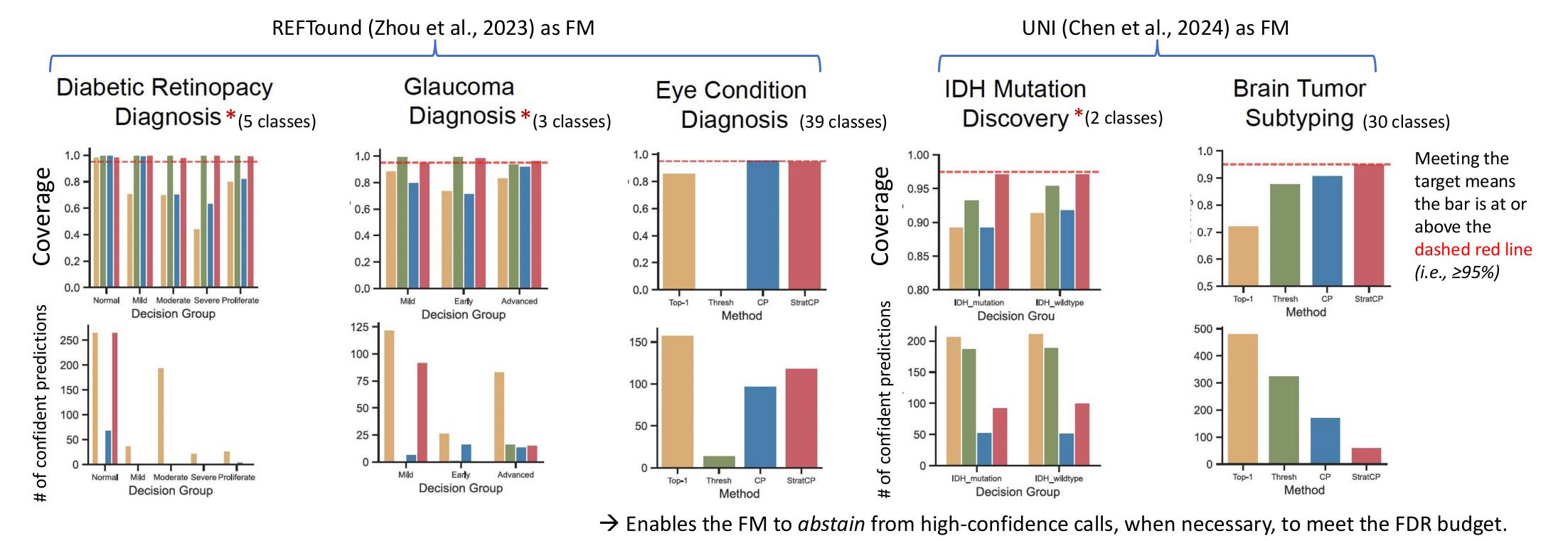
Step (2): build calibrated prediction sets for the remaining patients, that contain the true label at a pre-specified error rate, to guide follow-up.



given unconfident prediction

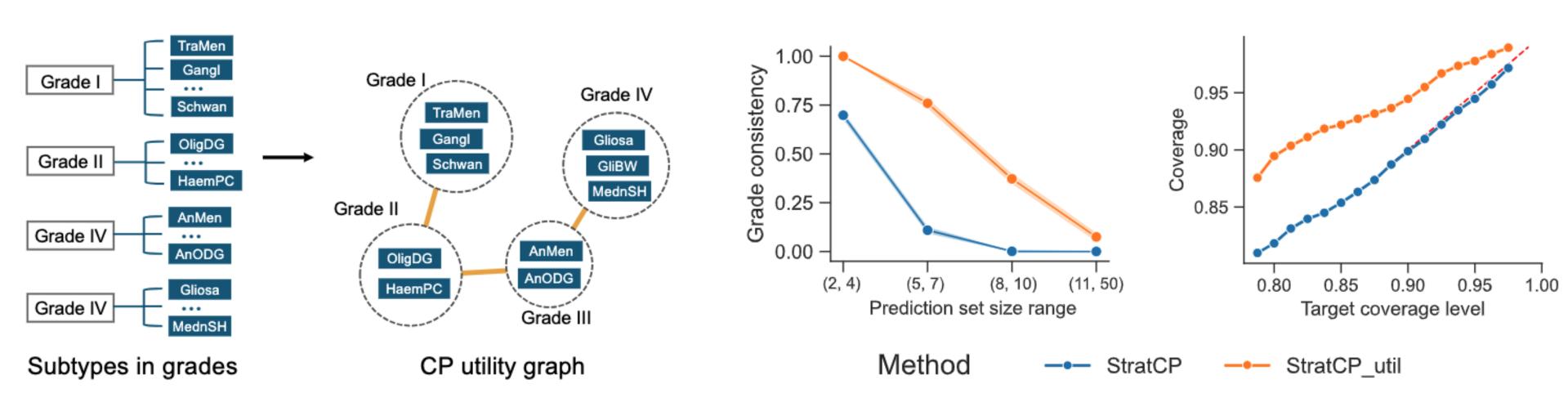
StratCP: main results

StratCP selects high-confidence patients under a pre-specified FDR budget (5% error rate) across ophthalmology and neuro-oncology, providing action-conditional guarantees*.



StratCP provides utility-enhanced prediction sets for deferred patients, which respect clinical adjacency and shared management, while still satisfying coverage guarantees.

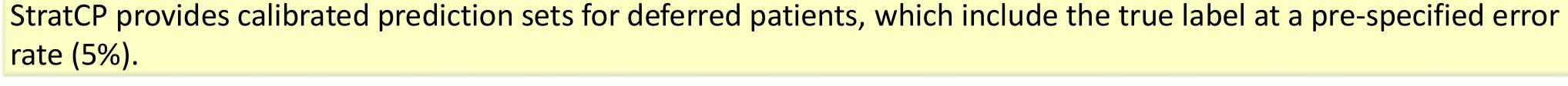
Order labels using model scores + a utility graph and add the next most useful label until the calibrated coverage target is met.

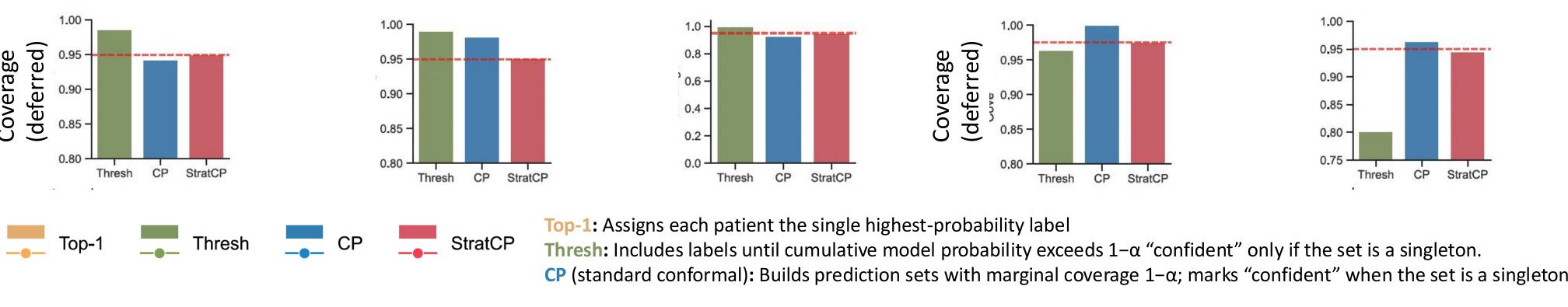


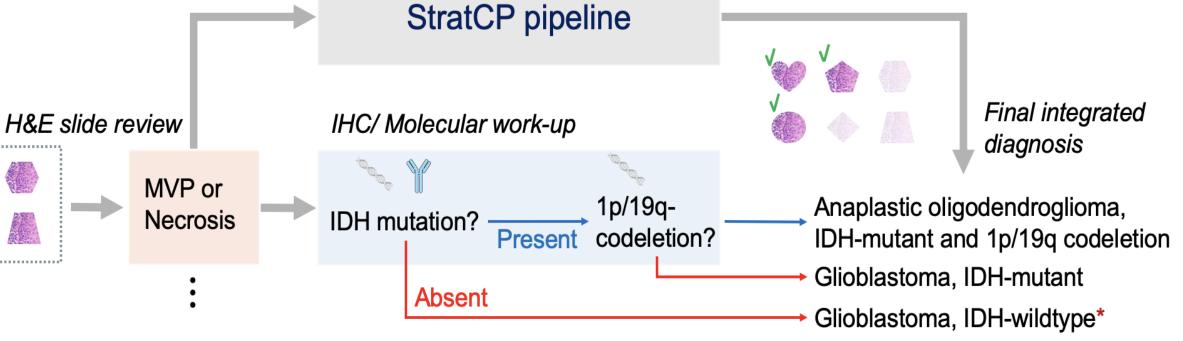
For suspected adult-type diffuse glioma cases, StratCP enables H&E-only calls under a pre-specified FDR budget (5% error rate), reducing confirmatory assays and turnaround.

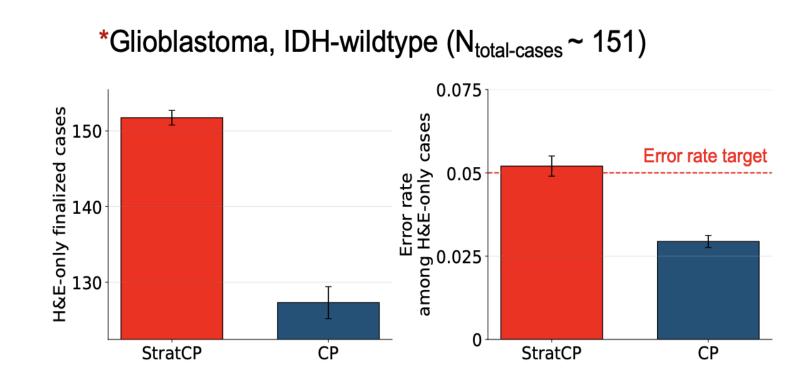
H&E-only selection with

error rate control





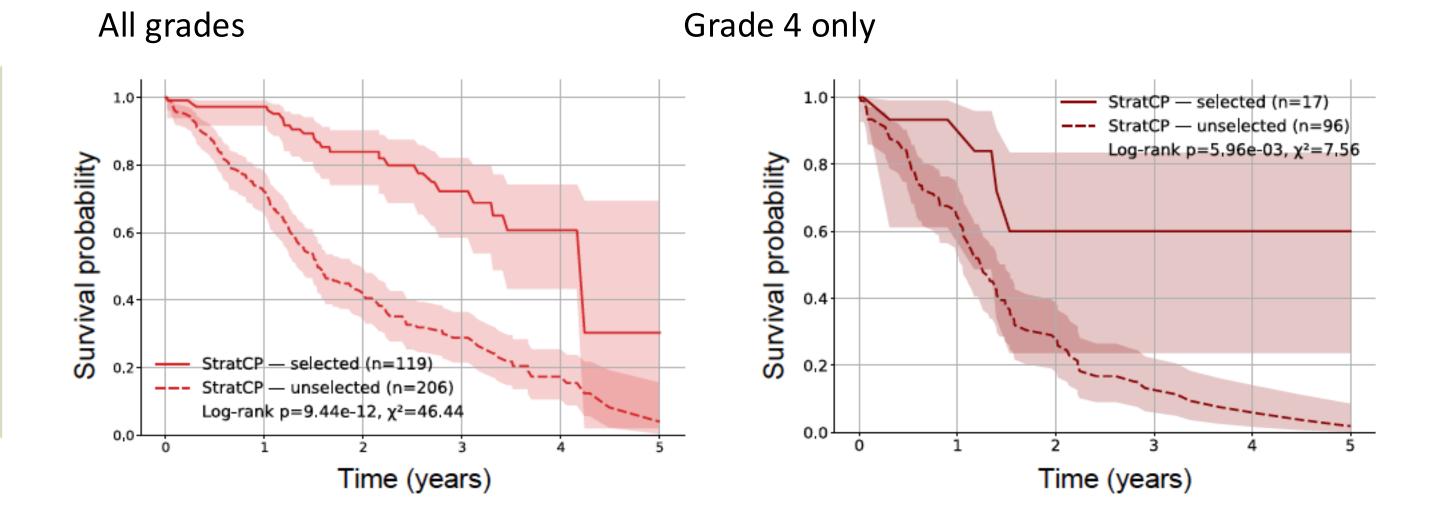




H&E-only finalization reduces time (2) and cost (5) \rightarrow ~8.7 lab-days + \$1,650 saved per case (GBM, IDH-wildtype)

 \rightarrow ~66,000 lab-days + \$12.5M saved annually in the US (CBTRUS 2024)

Time-to-event prediction task: StratCP's selection of long survivors (≥18 months) demonstrates clinically meaningful stratification compared to unselected (deferred) patients.



Key Takeaways:

- StratCP is a drop-in, model-agnostic layer that makes foundation model outputs decision-ready with per-patient error control at key points in the clinical workflow (triage, diagnosis, prognosis).
- StratCP incorporates a utility graph to generate clinically and biologically coherent prediction sets for deferred patients.
- Future work includes prospective trials (e.g., biomarker triage for IDH, TP53, and hormone receptor status) to assess StratCP in clinical deployment.