Identifying and Characterising Pathways to Clinical Diagnosis of Non-Alcoholic Fatty Liver Disease and Non-Alcoholic Steatohepatitis in Hospitals in England

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Introduction

- Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) have an estimated UK prevalence of 20-30% and 2-12% respectively. 1,2
- Challenges around diagnosis, such as non-specific symptoms and biopsy diagnosis, mean that NAFLD & NASH are often diagnosed in later stages of the disease.
- Identifying pathways to diagnosis may improve earlier diagnoses and identify cohorts suitable for inclusion in clinical trials.

Objectives

- To identify the pathways by which patients are diagnosed with NAFLD/NASH.
- To describe the patient characteristic, survival, laboratory testing and diagnostic testing of patients in the identified pathways.

Methods

Patient identification

Patients with NAFLD/NASH identified (ICD-10 codes: K74.6, K75.8 & K76.0) in The Arcturis Real World Data Network research database (**Figure 1**) using de-identified electronic hospital records from January 2015 to March 2024.

Patients entered (index date) on first NAFLD/NASH diagnosis and were excluded if they had any record for alcoholic liver disease or were first diagnosed prior to study start.

Analyses

Identify different pathways to diagnosis (**Figure 2**)

Describe each pathway's demographic and comorbidity profile

Calculate each pathway's 1-year and 5-year crude incidence rate of death

Describe use of 60 laboratory tests, biopsies, and imaging in pre-defined windows

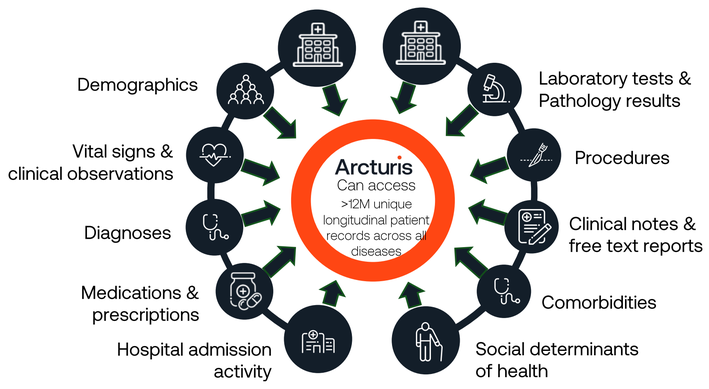

Figure 1: Data captured in The Arcturis Real World Data Network

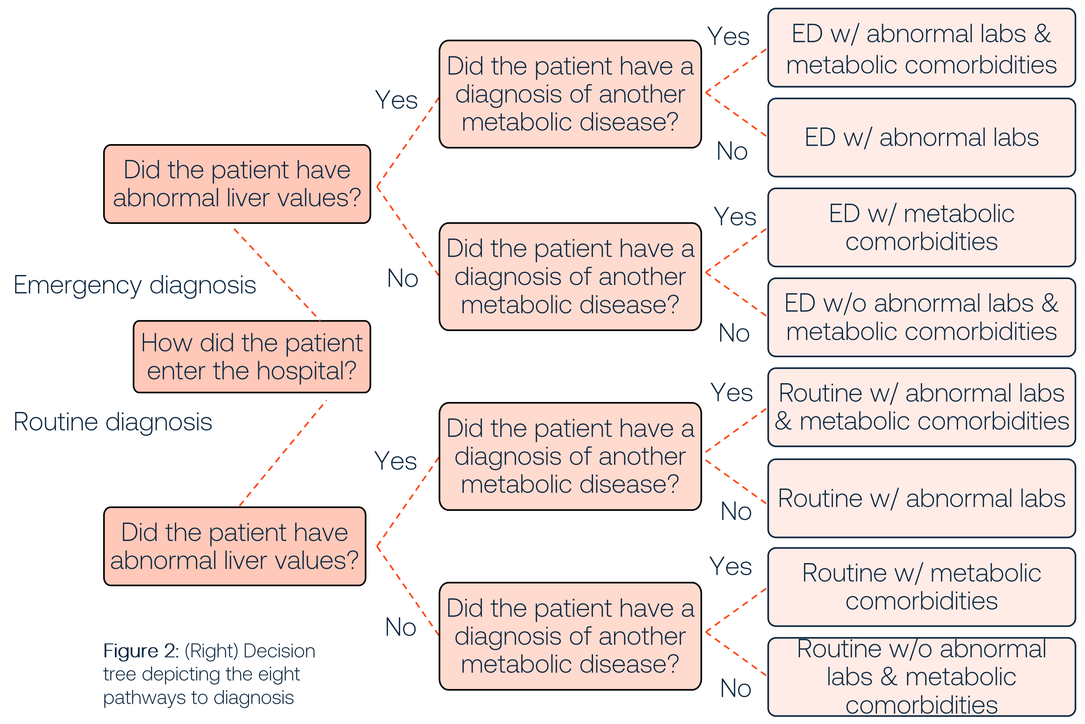

Figure 2: (Right) Decision tree depicting the eight pathways to diagnosis

Results - Characteristics

- Of 22,444 patients diagnosed with NAFLD/NASH, 8,855 had abnormal labs and metabolic comorbidities (59% emergency, 41% routine), 6,151 had just abnormal labs (58% emergency, 42% routine), 4,278 had just metabolic comorbidities (40% emergency, 60% routine), 3,160 had neither abnormal labs nor metabolic comorbidities (41% emergency, 59% routine).
- **Patients without comorbidities were on average ~10 years younger** than those with metabolic comorbidities.
- Other demographic characteristics between the pathways were broadly similar.
- The **1-year incidence rate varied** between 284.78 (95% CI 191.75, 377.81) and 2,839.77 (95% CI 2,662.60, 3,016.94) per 10,000 person years, **Figure 3,** with emergency department admissions and patients with abnormal labs having higher rates.

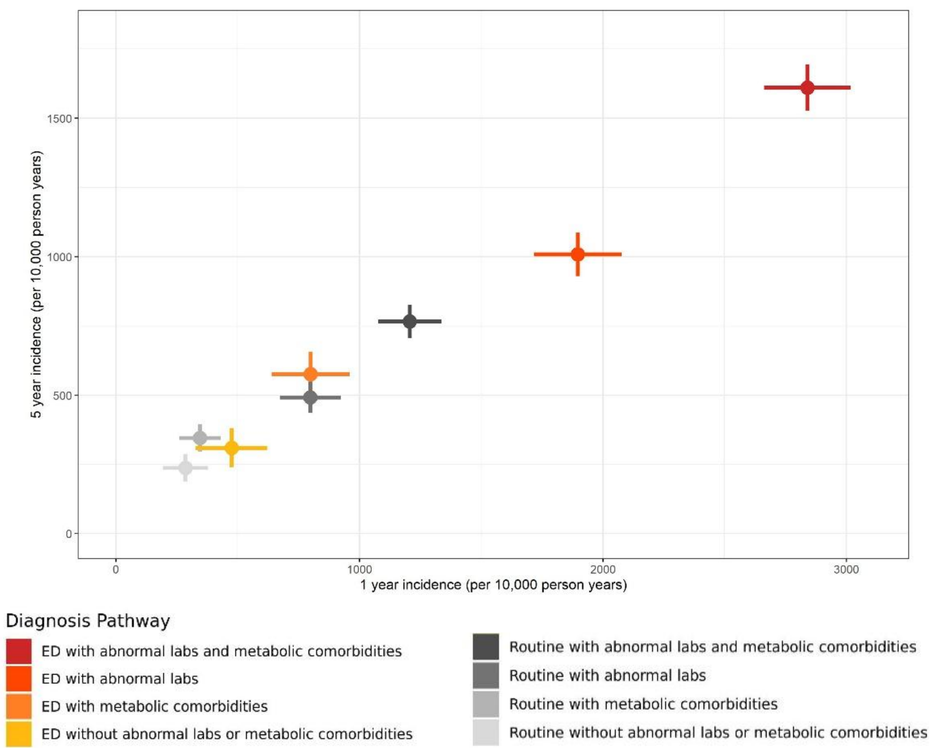

Figure 3: Overall survival incidence rate at 1 (x-axis) and 5 (y-axis) years after index date of all eight diagnosis pathways

Results - Testing

- **64.9%** of liver biopsies were undertaken in the month before index date, range: **15.4%** in the ED with metabolic comorbidities pathway to **81.3%** in the routine pathway with no abnormal liver labs or metabolic comorbidities, **Figure 4a.**
- Abdominal ultrasounds occurred frequently prior to diagnosis, **Figure 4b.**
- Around diagnosis abdominal ultrasound were more common in the emergency department.
- Liver laboratory tests, such as albumin and ALP, were frequently tested throughout the windows, with peak testing around the index date, **Figure 4c.**
- Testing for GGT, secondary liver test, was higher in routine care diagnosed patients, **Figure 4d.**

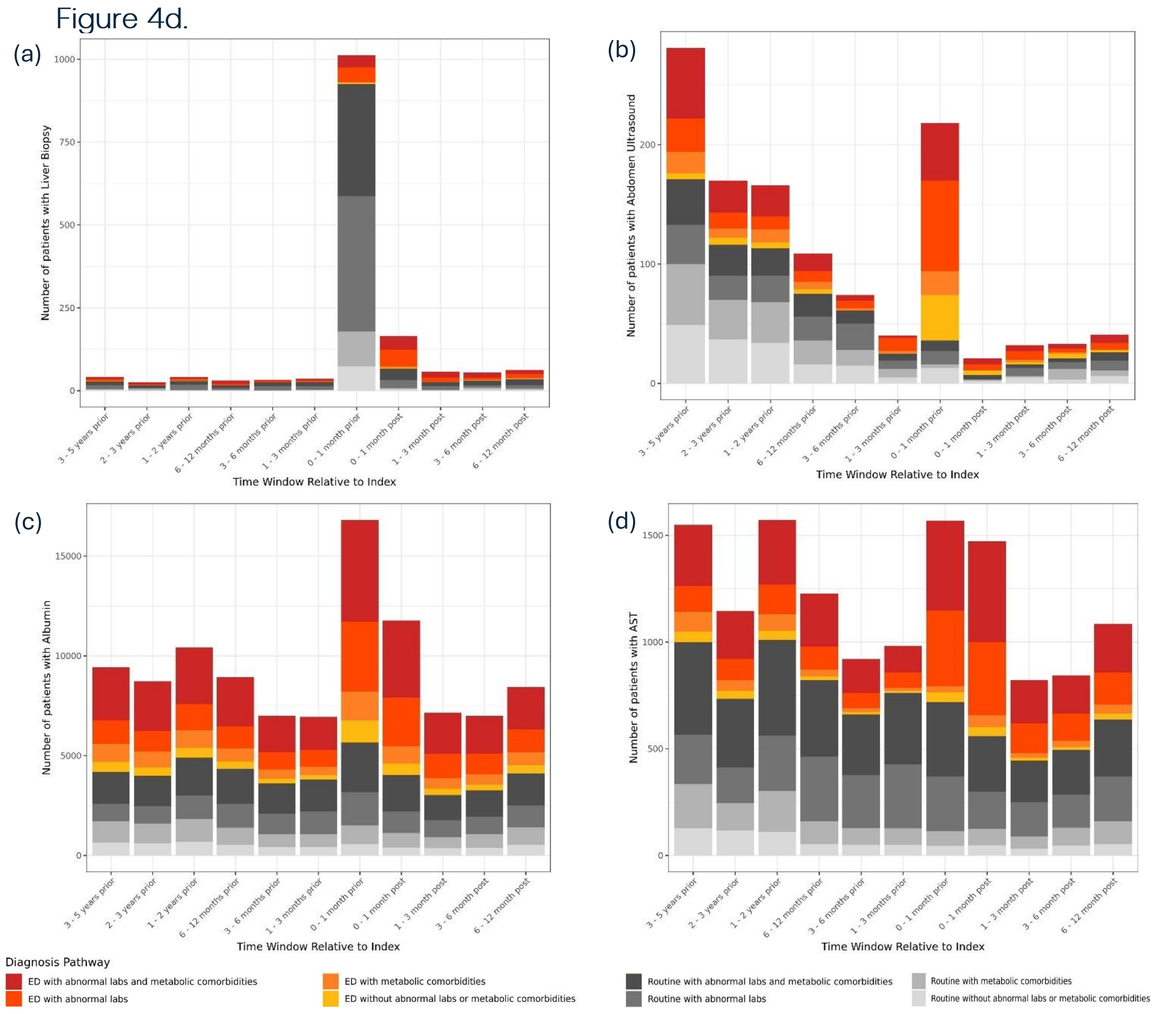

Figure 4: Stacked bar charts depicting number of patients with (a) liver biopsy, (b) abdominal ultrasound, (c) Albumin lab test and (d) GGT lab test

Conclusions

- We have identified and characterised 8 potential pathways to NAFLD/NASH diagnosis.
- Patient demographics were generally similar between pathways to diagnosis.
- Pathway to diagnosis impacted survival, likelihood of liver biopsy, imaging and liver laboratory tests.
- These pathways can help inform recruitment for clinical trials assessing novel therapies for NAFLD/NASH patients.

Acknowledgments & References

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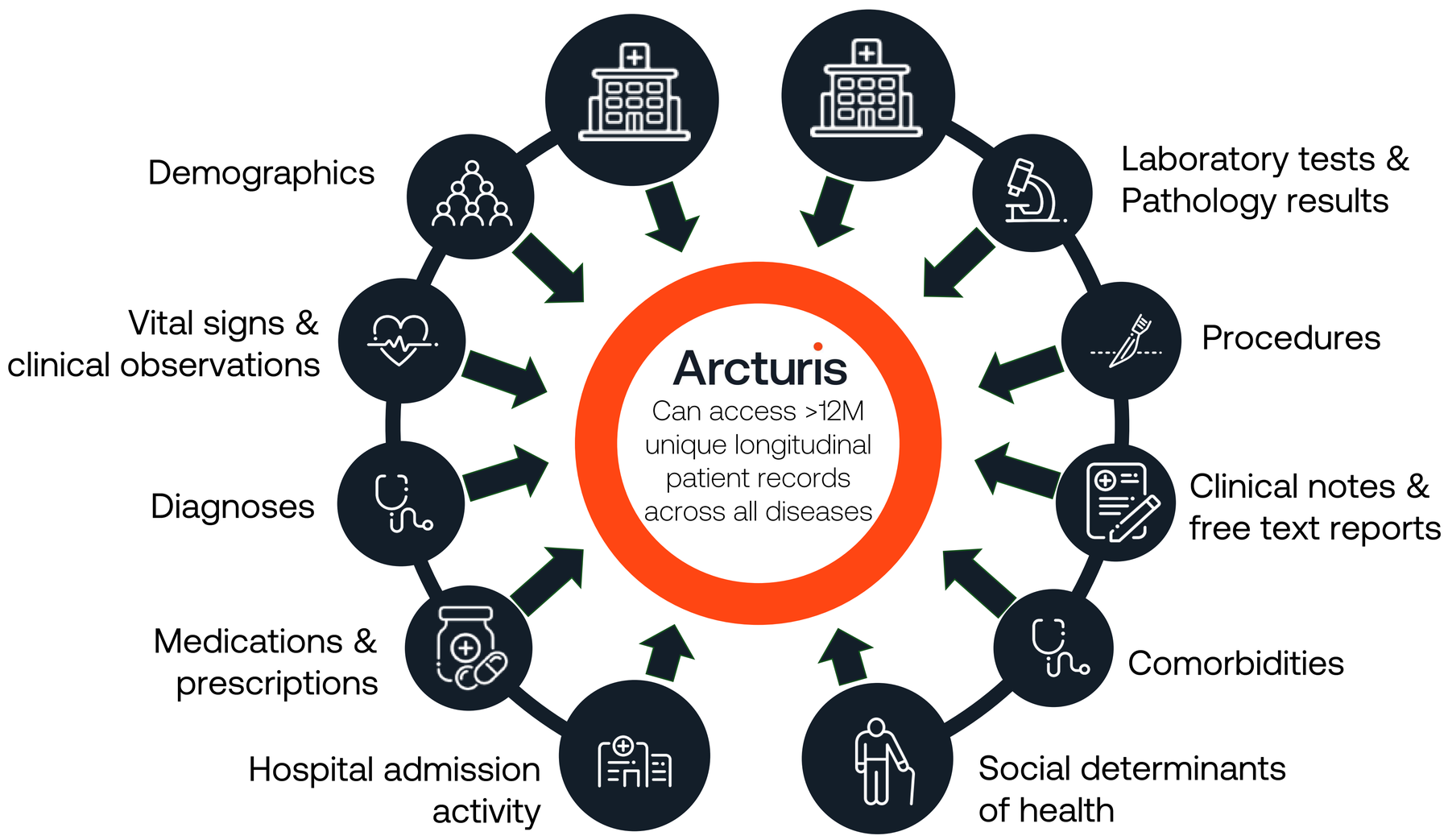

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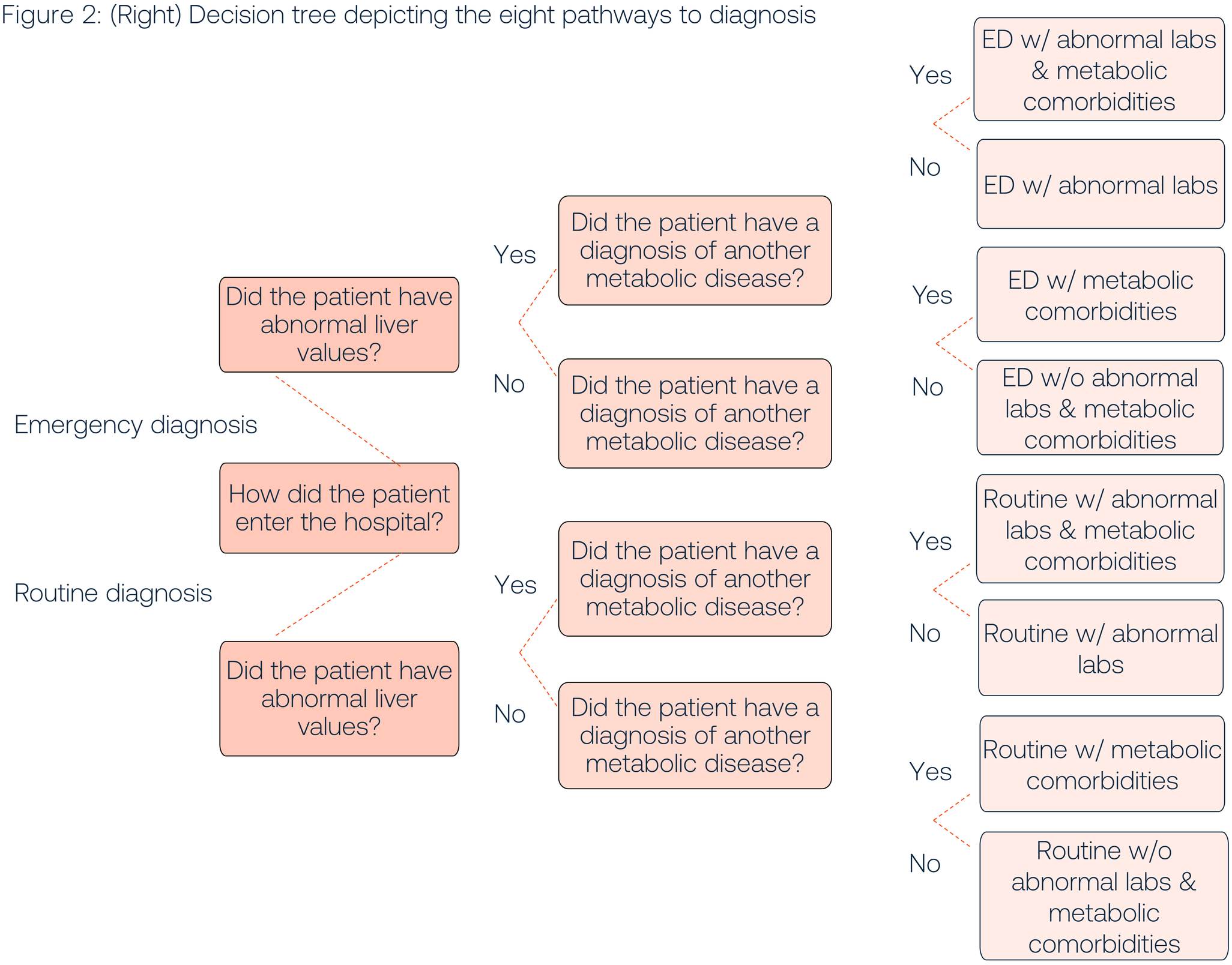

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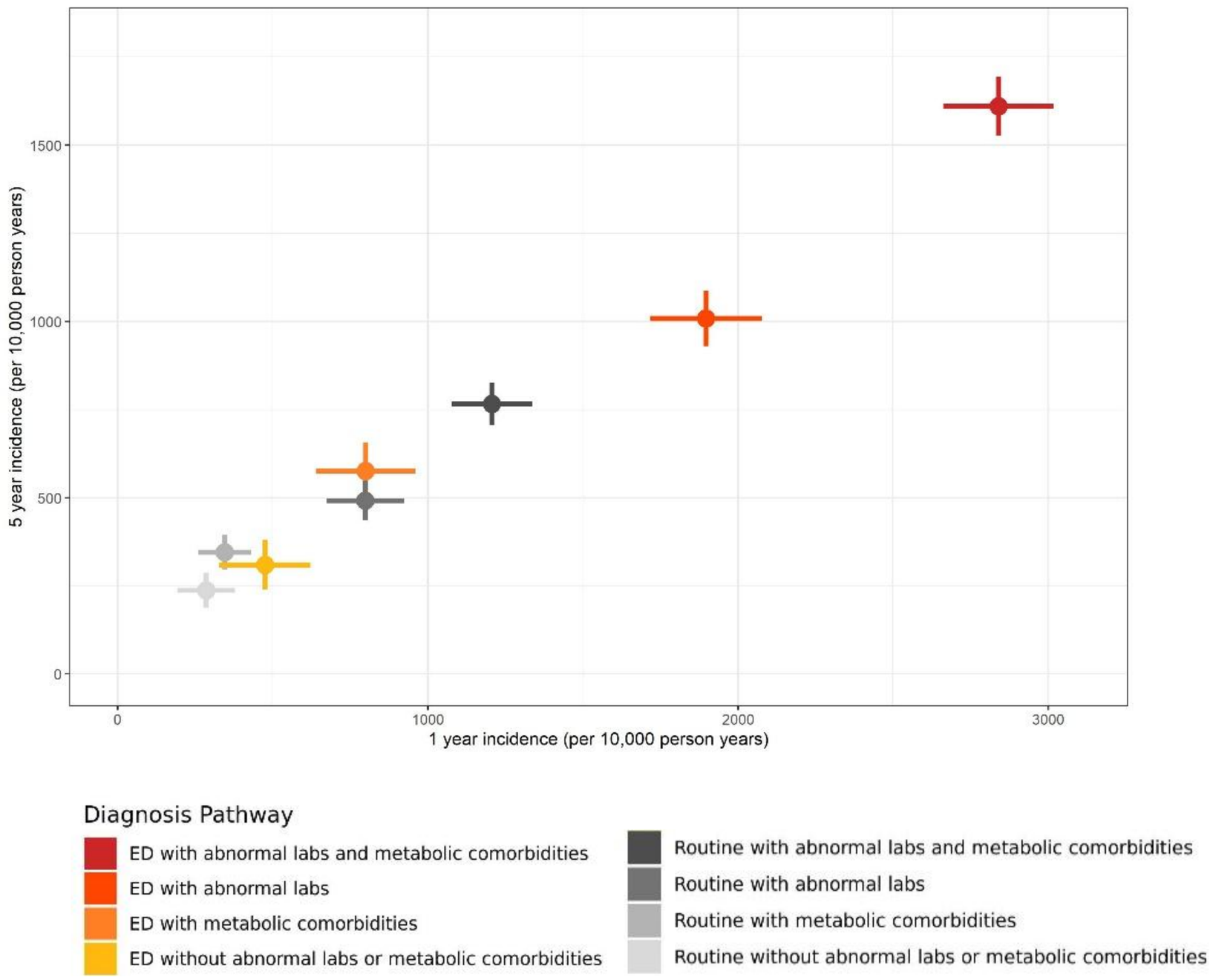

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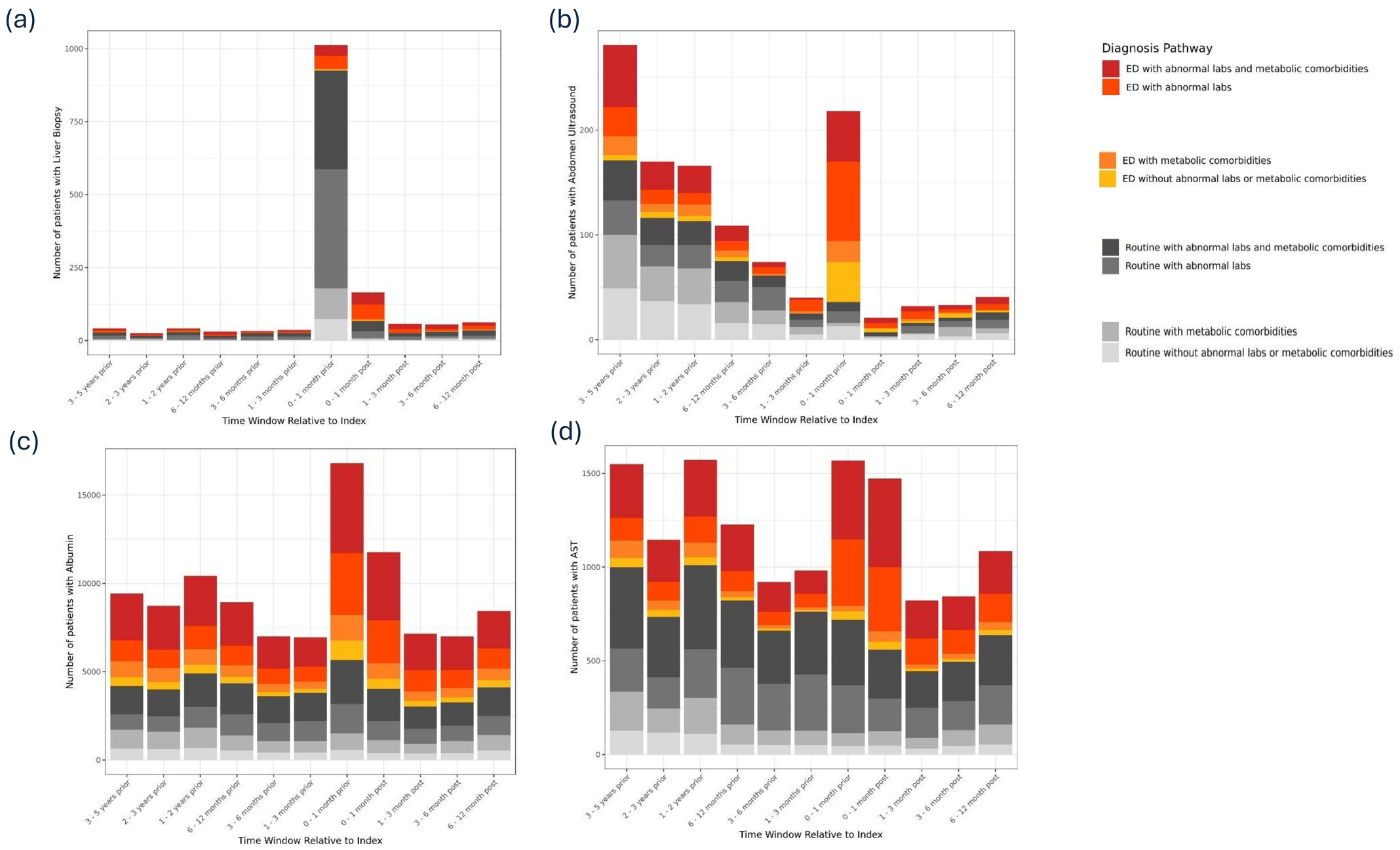


Results

- The model trained on the compounded MICS^2 dataset was evaluated against each of the independent test sets, achieving an average accuracy of 98.46% [95% CI = 0.5%] and required an average of 76.43 (±43.59) training examples per clinical feature.
- In comparison, an en masse approach that took all annotated data that was not partitioned into the independent test sets and used that for finetuning (242.63 ± 89.79 training examples per feature) resulted in a model with 95.46% average accuracy [95% CI = 1.6%]. This took an average of 13.15 (± 19.25) iterations per permutation.
- The poorest performance was associated with a random sampling approach. This took the same number of samples as was used in MICS^2 (76.43 ±43.59 samples per feature) but randomly sampled them from the remaining data not used in the test sets. This led to an Accuracy of 92.29%, [95% CI = 1.91%].
- MICS^2 took significantly longer to run (~32 hrs and 34 mins for all clinical features) compared to the en masse (~20 mins for all features) or random sampling (~29 mins for all features) approaches.
- MICS^2 s significantly longer run time is due to the iterative nature of the data sampling, and the requirement to retrain the model for each iteration which increases in length with each iteration due to the increasing finetuning set size.

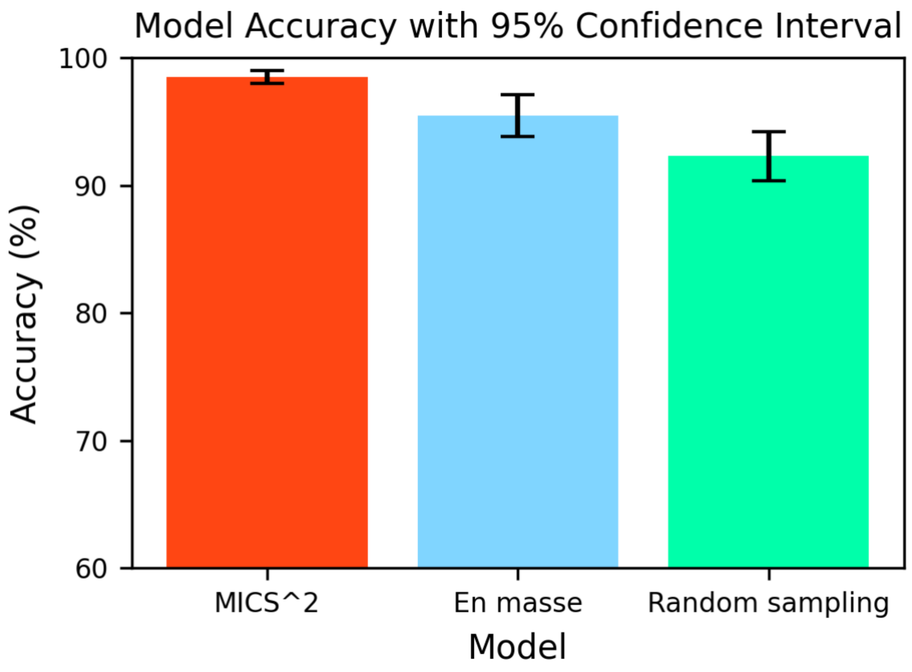
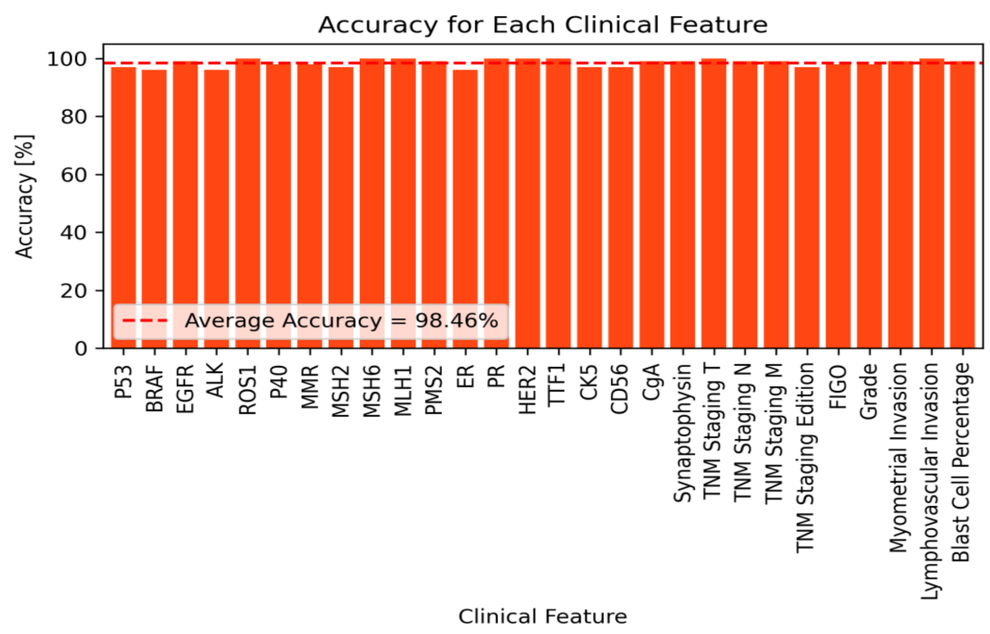


Fig. 3 (right) – Accuracy of MICS2 against the independent test set for each of the clinical features, with the average accuracy across all features displayed with the dashed line

Fig. 2 (left) – Accuracy of MICS2 (left, orange) compared with training a model with all remaining data (middle, blue), and randomly sampling the remaining data based off the number of training samples used in the MICS2 training set (right, green)



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