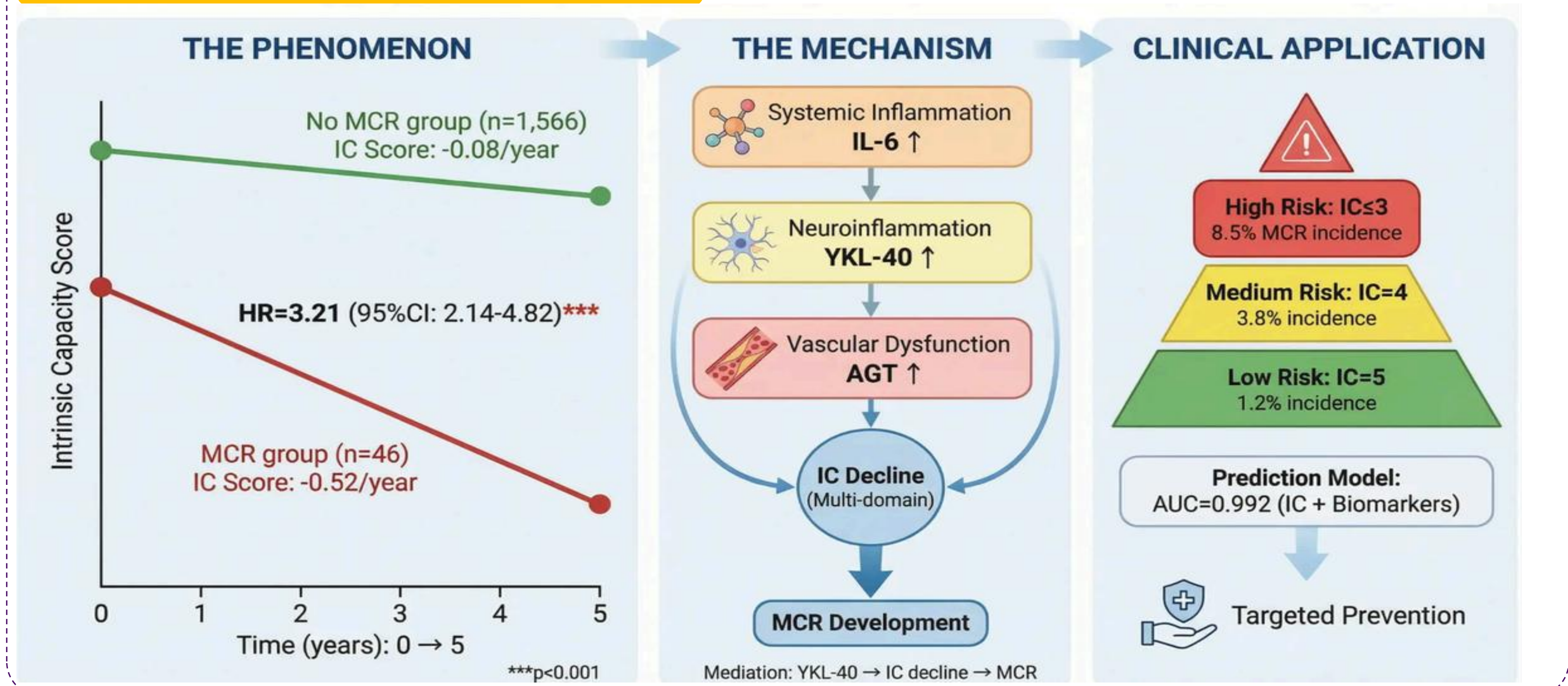


Accelerated Intrinsic Capacity Decline Predicts Incident Motoric Cognitive Risk: Trajectory Analysis and Neuroinflammatory Mechanisms in a 5-Year Prospective Cohort

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GRAPHICAL ABSTRACT



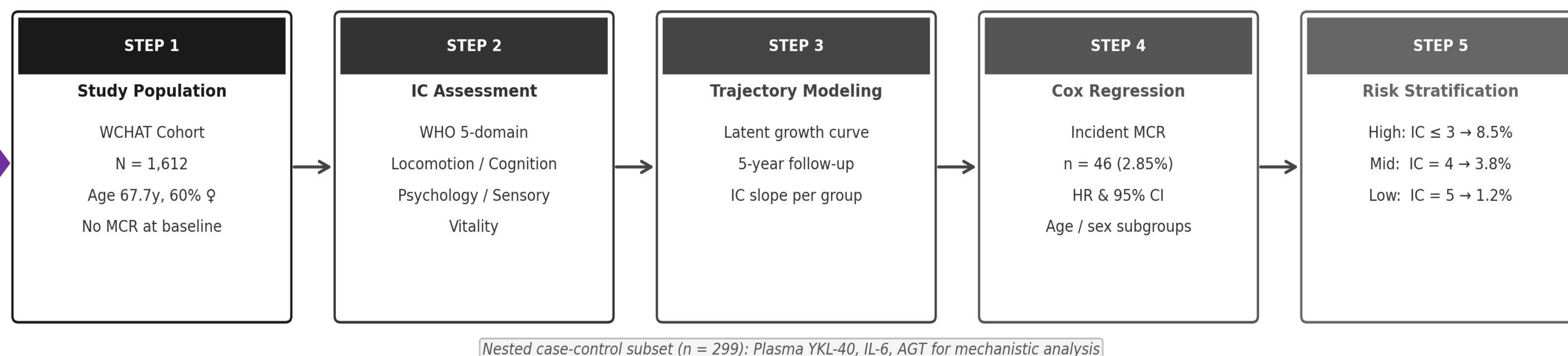
KEY TAKE AWAY :

- Accelerated IC decline (slope -0.52/yr) confers a 3.2-fold elevated MCR risk (HR = 3.21, 95% CI: 2.14-4.82).
- Elevated YKL-40 predicts both IC decline and MCR onset, implicating neuroinflammation as a mechanistic pathway.
- IC-based stratification identifies a 7-fold difference in 5-year MCR incidence (8.5% vs 1.2%).

INTRODUCTION

- Motoric Cognitive Risk (MCR) syndrome defined by slow gait and subjective cognitive complaints is a pre-dementia state strongly predicting cognitive decline, falls, and mortality.
- The WHO Intrinsic Capacity (IC) framework (ICOPE) captures five domains of physical and mental reserve: Locomotion, Cognition, Psychology, Vitality, Sensory.
- Hypothesis**
Accelerated IC decline predicts incident MCR, mediated in part by neuroinflammatory pathways (YKL-40/CHI3L1).

Study Design and Analytical Framework



RESULTS

Key Results Summary

Finding	Result	Statistical Detail
Sample Size	n = 1,612 (MCR-free at baseline)	WCHAT cohort, 2018-2023
Incident MCR	46 cases (2.85%)	5-year follow-up
IC Trajectory (MCR group)	Slope: -0.52/year	vs -0.08/year in Non-MCR; p < 0.001
Cox Regression (Overall)	HR = 3.21	95% CI: 2.14-4.82; per 1-SD IC decline
Age ≥ 70 Subgroup	HR = 4.18	95% CI: 2.61-6.71; stronger effect
Male Subgroup	HR = 3.76	95% CI: 2.21-6.39; stronger in males
YKL-40 (Neuroinflammation)	HR = 2.87	95% CI: 1.74-4.73; nested subset n = 299
Risk Stratification	High risk (IC ≤ 3): 8.5% MCR incidence	vs 1.2% in low risk (IC = 5); 7-fold difference
Prediction Model (AUC)	AUC = 0.992	IC + biomarkers composite model

HR, hazard ratio; CI, confidence interval; IC, intrinsic capacity; MCR, motoric cognitive risk syndrome; AUC, area under the ROC curve; SCC, subjective cognitive complaints.

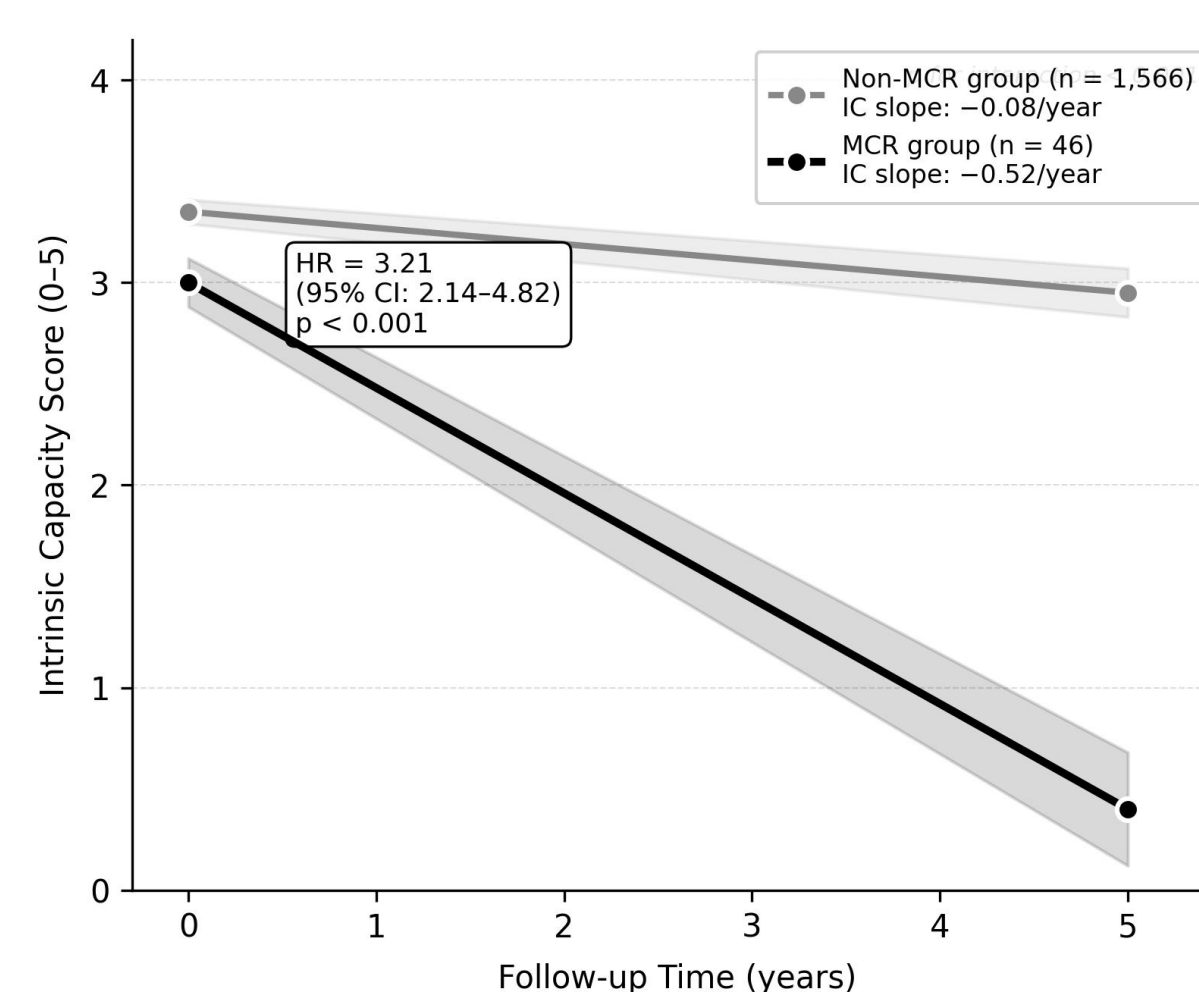


Figure 1. IC Trajectories in Participants Who Developed MCR vs. Those Who Did Not
IC trajectories estimated by latent growth curve analysis. Shaded areas represent 95% confidence intervals. HR, hazard ratio; CI, confidence interval; IC, intrinsic capacity; MCR, motoric cognitive risk syndrome.

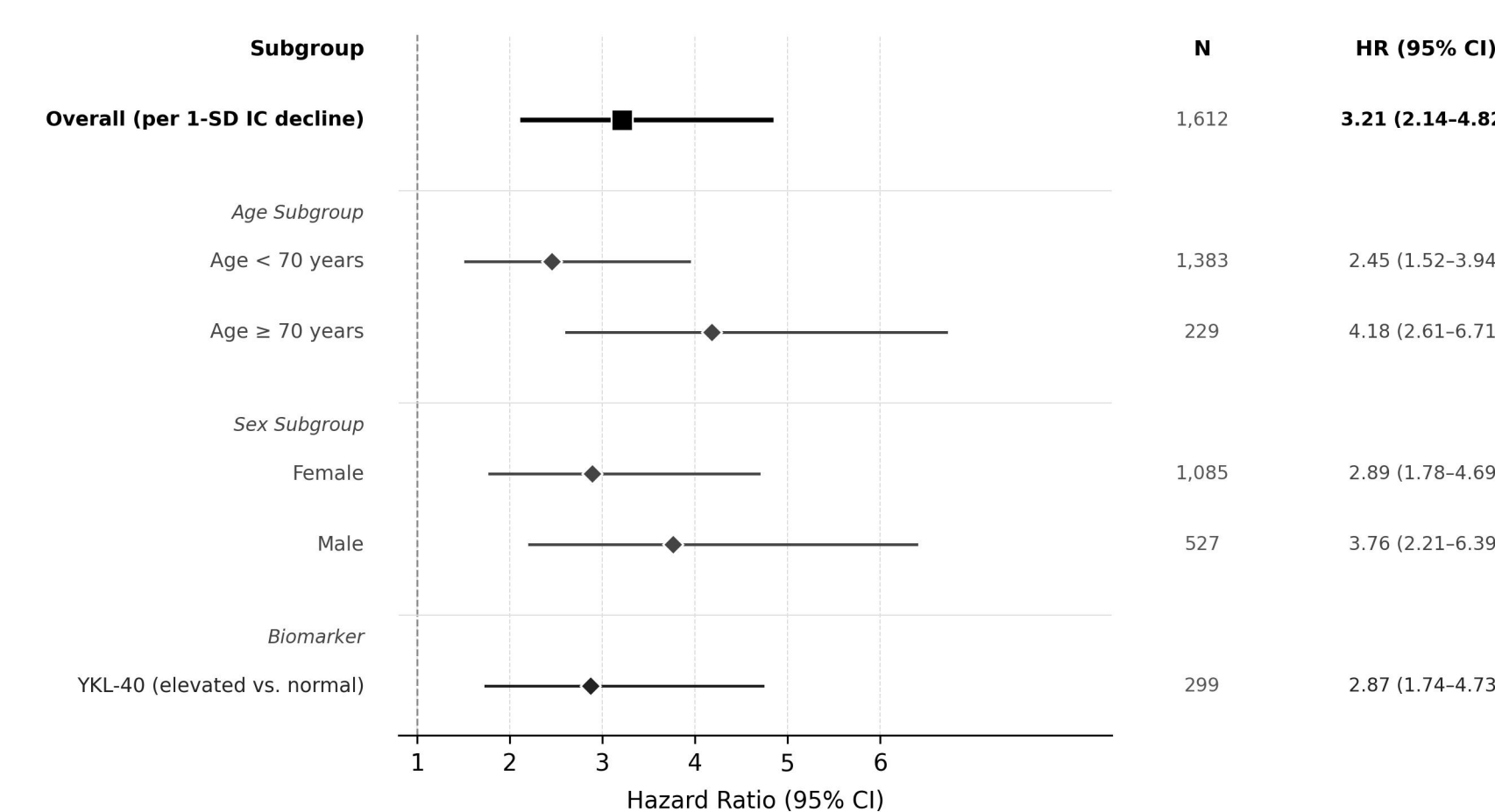


Figure 2. Cox Regression: IC Decline Rate and Risk of Incident MCR
HRs represent risk per 1-SD increase in IC decline rate, adjusted for age, sex, education, and comorbidities. YKL-40 (CHI3L1): elevated vs. normal baseline concentration (nested case-control subset, n = 299). HR, hazard ratio; CI, confidence interval; IC, intrinsic capacity; MCR, motoric cognitive risk syndrome.

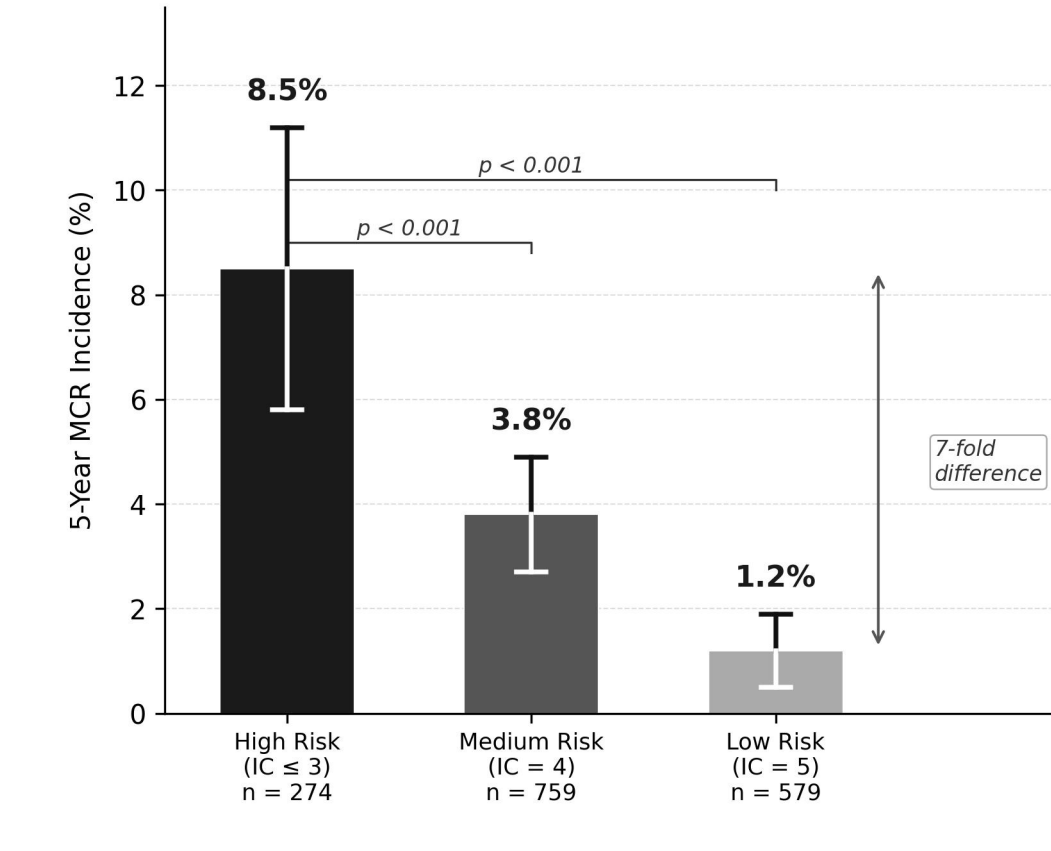


Figure 3. MCR Incidence by Baseline IC Risk Stratification
MCR incidence rates across three IC-based risk strata. Error bars represent 95% confidence intervals. High risk: IC score ≤ 3 (lowest 27th percentile). Low risk: IC score = 5 (top 28%). IC, intrinsic capacity; MCR, motoric cognitive risk syndrome.

CONCLUSIONS

- Each 1-SD increase in IC decline rate confers a 3.2-fold elevated MCR risk (HR = 3.21, 95% CI 2.14-4.82).
- Elevated baseline YKL-40 predicts both IC decline and MCR onset, implicating neuroinflammatory pathways.
- A 7-fold difference in MCR incidence between high-risk (IC 3: 8.5%) and low-risk (IC = 5: 1.2%) groups.
- Integrating WHO ICOPE assessment into primary care enables early, multi-domain preventive interventions.