# ELSE KRÖNER-FORSCHUNGSKOLLEG MAINZ



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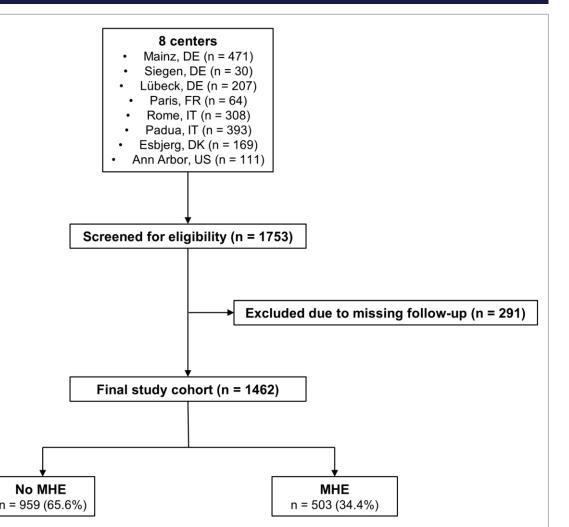
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### **Background & Aims**

Previous (smaller) studies suggest that patients with cirrhosis and minimal HE (MHE) are at high risk for developing overt HE (OHE)

#### Patients & Methods

- 8 centers (Europe, US); 1462 patients with cirrhosis
- MHE diagnosed by PHES
- A subgroup was also tested with S-ANT1



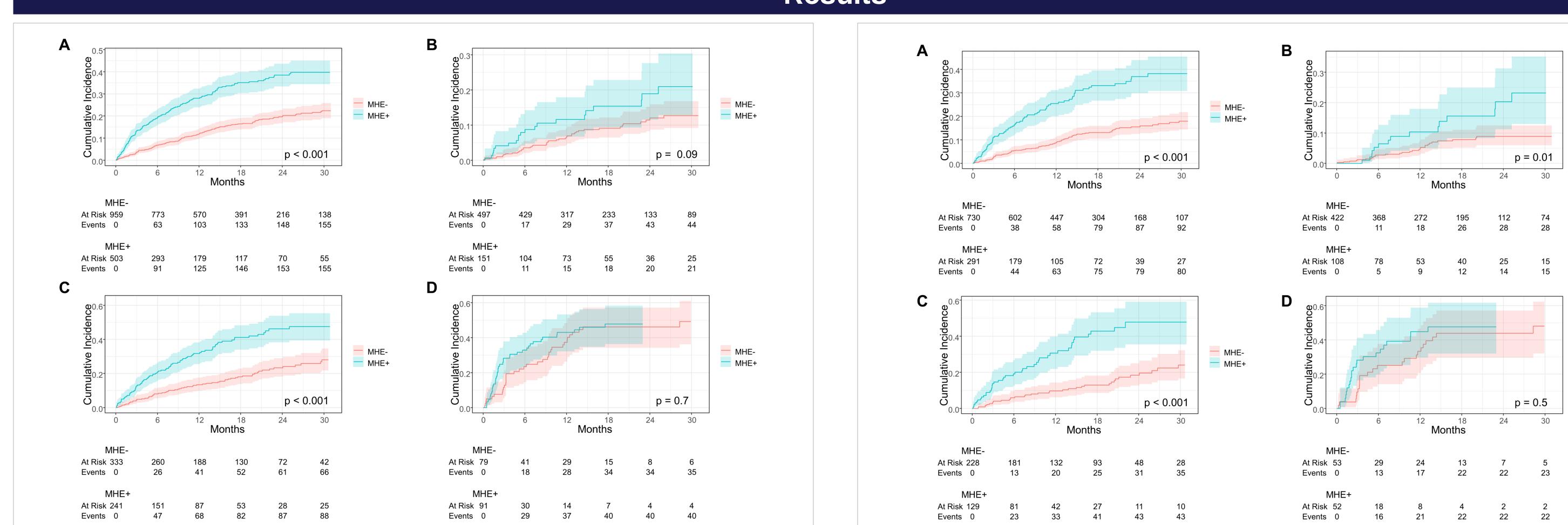
MHE-

MHE+

MHE-

MHE+

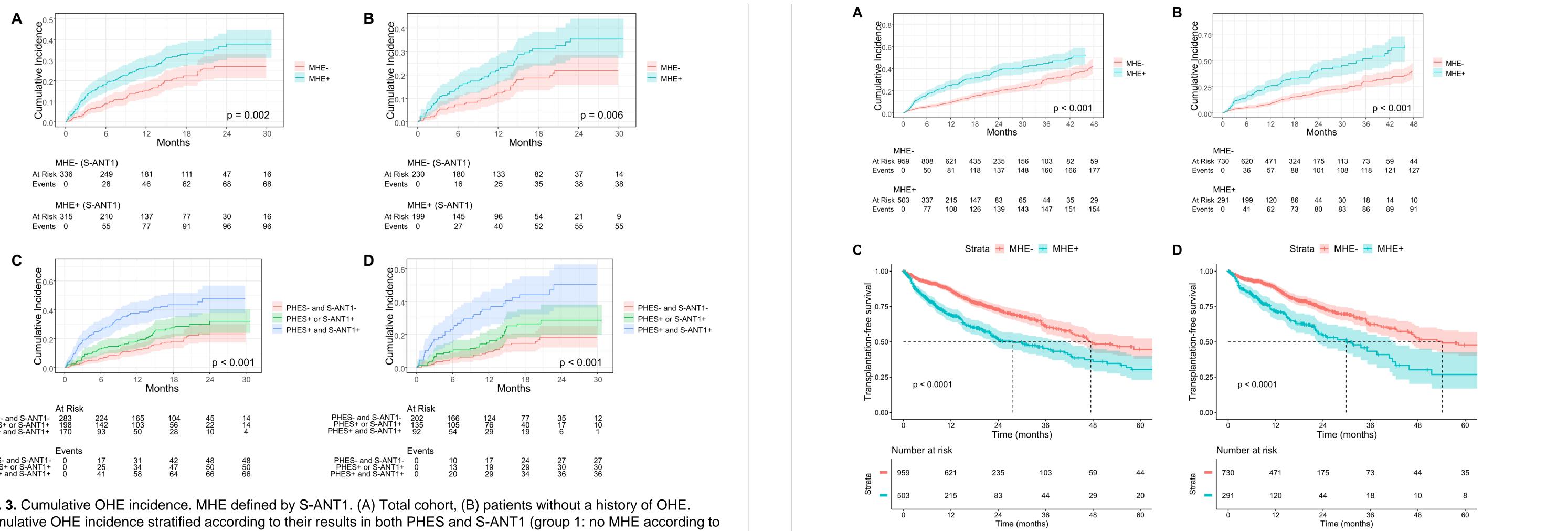
- However, multicenter, international studies including a large numbers of patients are lacking - in particular for adequate subgroup analysis
- **Aim:** To analyze the association of MHE with the development of OHE, liver transplantation (LTx), or death in a large multicenter study cohort with a focus on subgroup analysis
- Patients were followed for OHE development, death, or LTx
- Statistical analysis: multi-state models with three states were used to calculate OHE incidences and to fit Fine and Gray regression models



#### Results

Fig. 1. Cumulative OHE incidence. MHE status defined by PHES. (A) All patients, (B) patients with CP A, (C) patients with CP B, and (D) patients with CP C. Death and liver transplantation were fitted as competing events.

Fig. 2. Cumulative OHE incidence in patients without a history of OHE. MHE defined by PHES. (A) All patients without a history of OHE, (B) patients with CP A without a history of OHE (C) patients with CP B without a history of OHE, and (D) patients with CP C without a history of OHE.



At Ri PHES- and S-ANT1- 283 PHES+ or S-ANT1+ 198 PHES+ and S-ANT1+ 170	sk 224 142 93	165 103 50	104 56 28	45 22 10	14 14 4	At Risk PHES- and S-ANT1- 202 166 124 77 35 12 PHES+ or S-ANT1+ 135 105 76 40 17 10 PHES+ and S-ANT1+ 92 54 29 19 6 1	
Even PHES- and S-ANT1- 0 PHES+ or S-ANT1+ 0 PHES+ and S-ANT1+ 0	ts 17 25 41	31 34 58	42 47 64	48 50 66	48 50 66	Events PHES- and S-ANT1- 0 10 17 24 27 27 PHES+ or S-ANT1+ 0 13 19 29 30 30 PHES+ and S-ANT1+ 0 20 29 34 36 36	

Fig. 3. Cumulative OHE incidence. MHE defined by S-ANT1. (A) Total cohort, (B) patients without a history of OHE. Cumulative OHE incidence stratified according to their results in both PHES and S-ANT1 (group 1: no MHE according to PHES and S-ANT1; group 2: MHE according to PHES or S-ANT1; group 3: MHE according to both PHES and S-ANT1) in (C) total cohort and (D) patients without a history of OHE.

## Conclusion

- MHE is associated with an increased OHE risk, with the strongest association in patients with CP-B cirrhosis
- MHE is associated with poorer prognosis
- Combined testing with both PHES and S-ANT1 is superior to single testing for OHE prediction

Fig. 4. Survival of patients. MHE defined by PHES. Cumulative incidence of death in patients with vs without MHE with liver transplantation as a competing event in (A) total cohort and (B) subgroup of patients without a history of overt HE. (C) Kaplan-Meier curve showing Tx-free survival stratified according to MHE status (PHES) in (C) total cohort and (D) subgroup of patients without a history of overt HE.

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