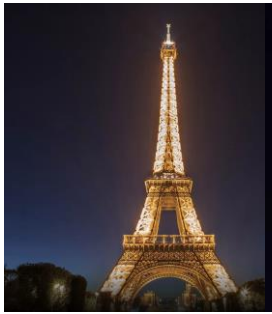


Hybrid PHC 2024

March 18-19, 2024

Institut Pasteur - Paris

Controversy: treat everyone with detectable HBV DNA?

Yes!

Jidong Jia, MD, PhD

March 18, 2024

Beijing Friendship Hospital, Capital Medical University

Disclosure

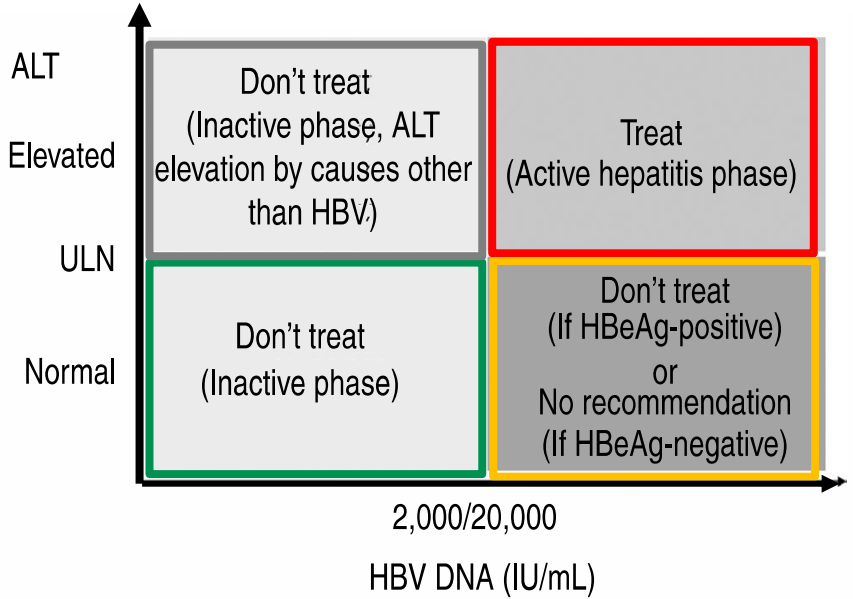
- **Investigator for clinical HBV trials of GSK, Gilead, BriiBiosciences and H&H pharmaceutical companies**

Outlines

- **The rationale to treat patients in immune tolerant phase**
- **The rationale to treat patients in inactive phase**
- **The rationale to treat patients in indeterminate phase**

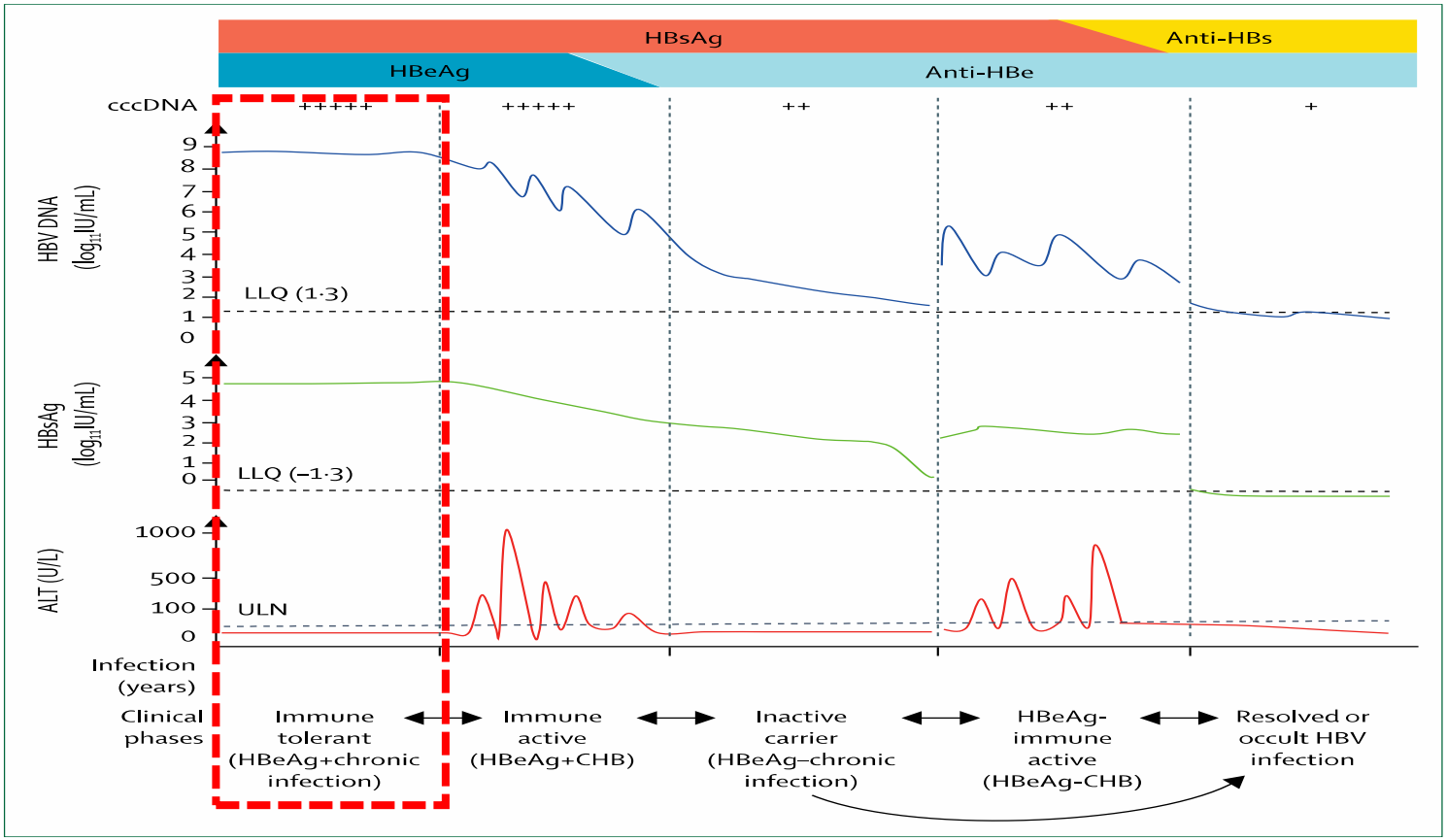
Rationale for not treating immune tolerant and inactive phases of CHB

- For Immune tolerant phase CHB
  - Minimal necroinflammation/ fibrosis
  - Slow disease progression
  - Low HBeAg &HBsAg seroconversion on current Tx
- For inactive phase CHB
  - Minimal necroinflammation/ fibrosis
  - Minimal disease progression



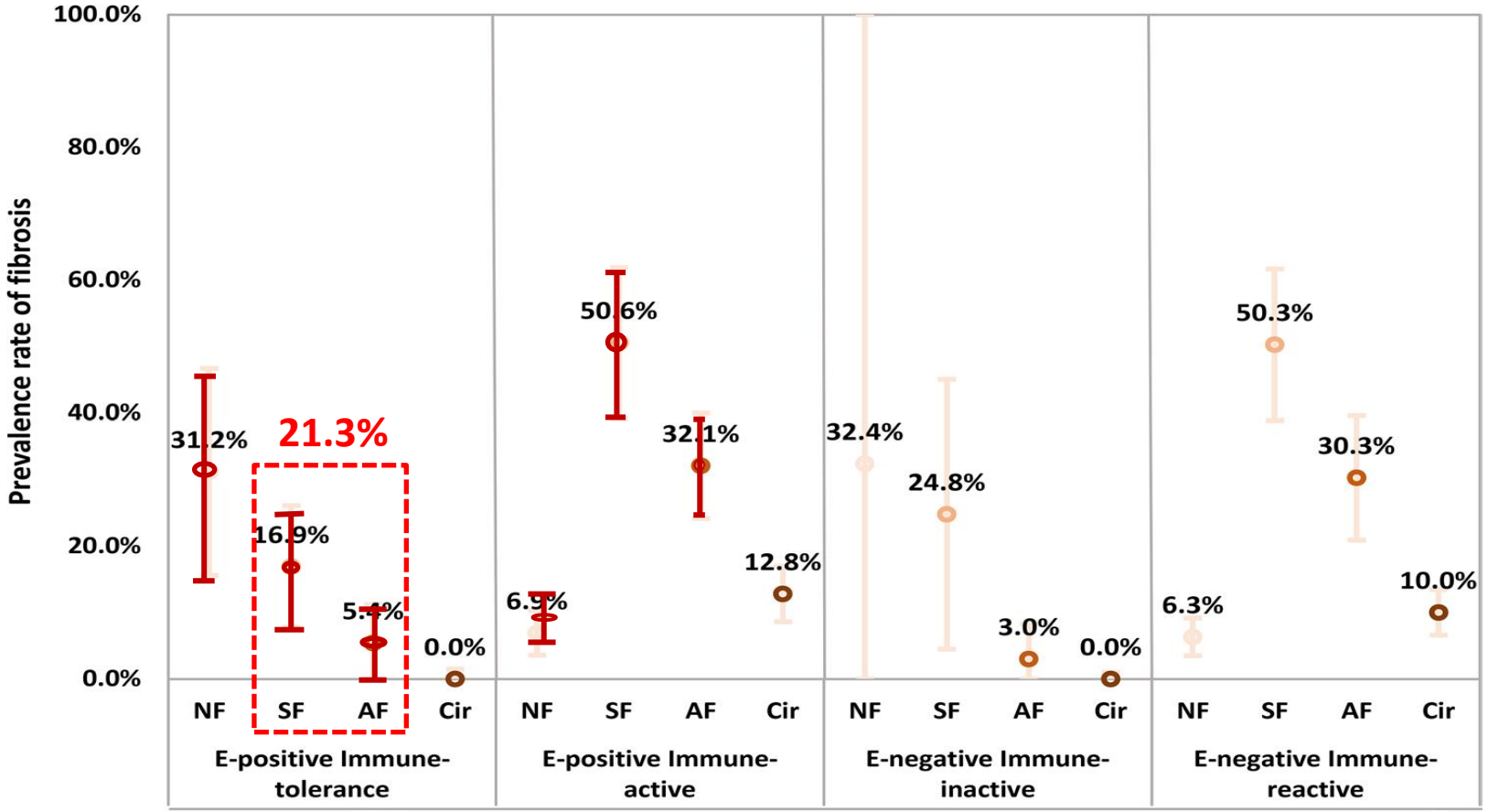
Kao JH, et al. Aliment Pharmacol Ther. 2020;52:1540-1550.

Immune tolerant phase: high HBV DNA and normal ALT



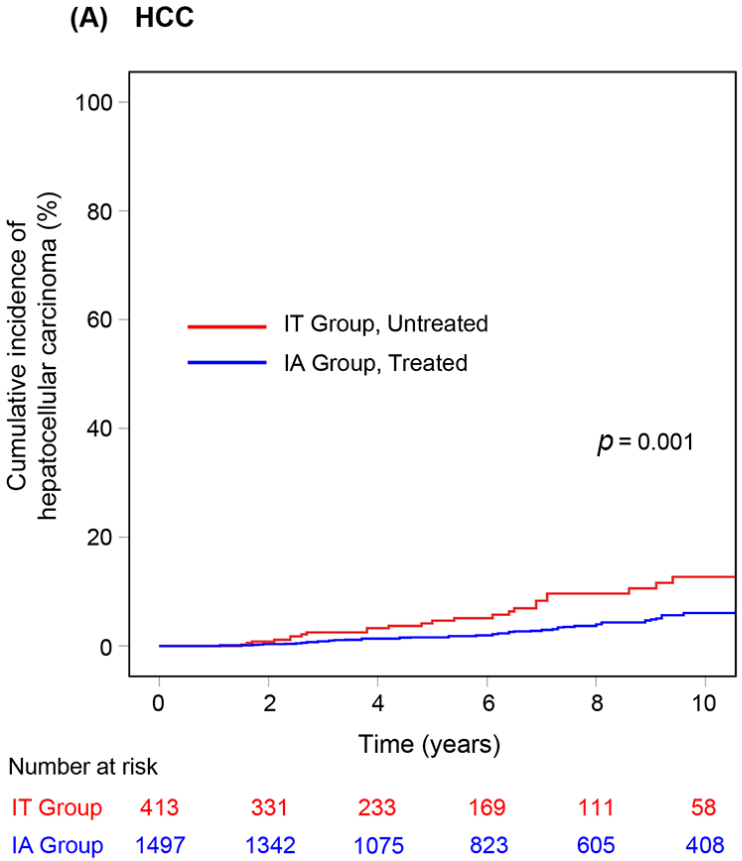
Jeng WJ,et al. Lancet. 2023

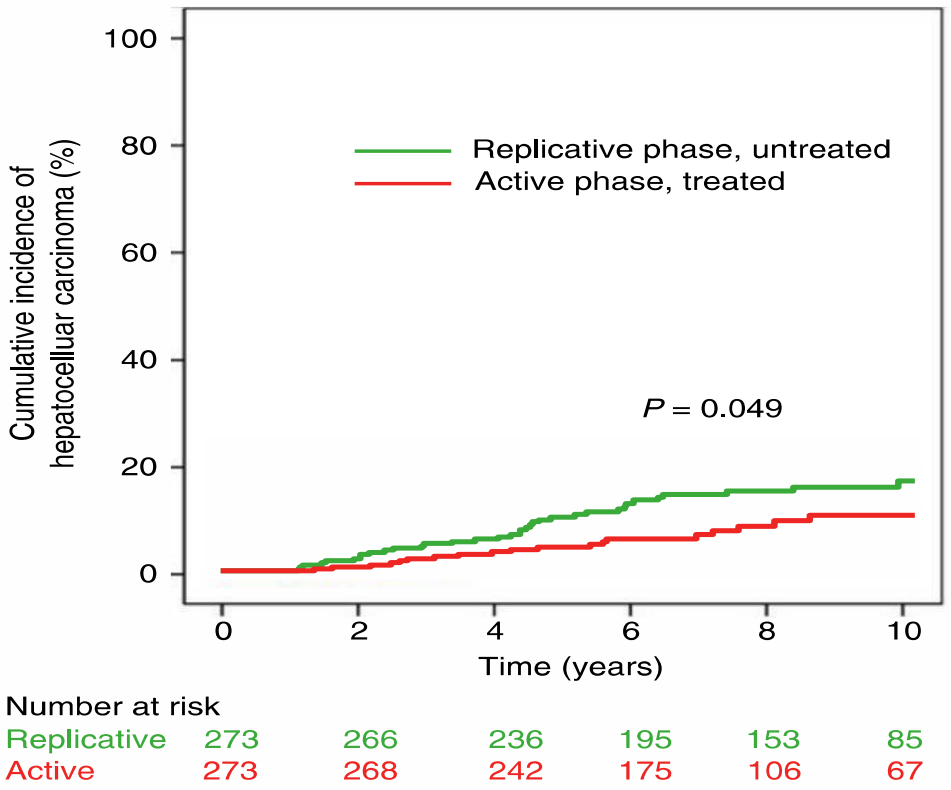
Immune tolerant phase is associated with significant fibrosis burden



Lin MH, et al. Dig Dis Sci. 2021

Higher risk of HCC in patients with untreated IT- than NA-treated IA-CHB

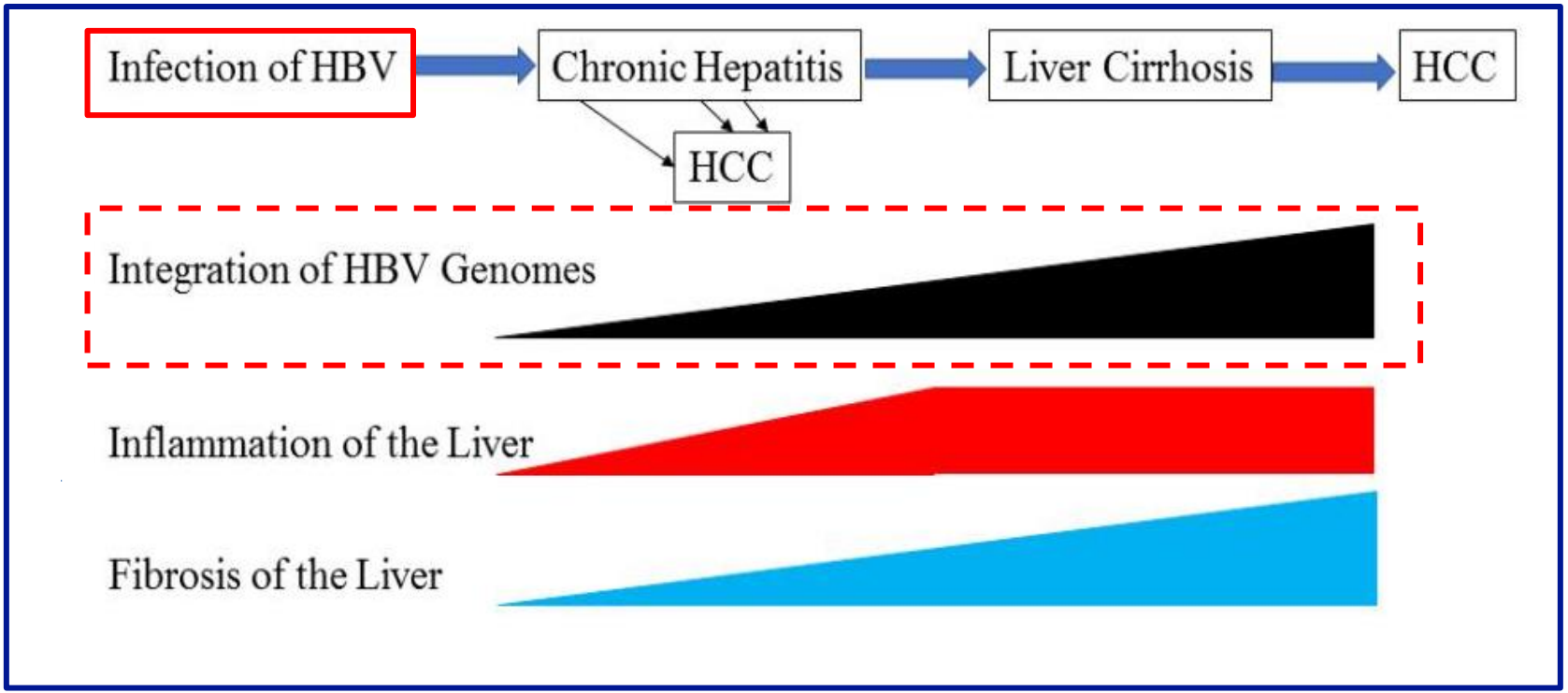




Kim GA, et al. Gut. 2018;67:945-52.

Choi GH, et al. Aliment Pharmacol Ther. 2019;50:215–26.

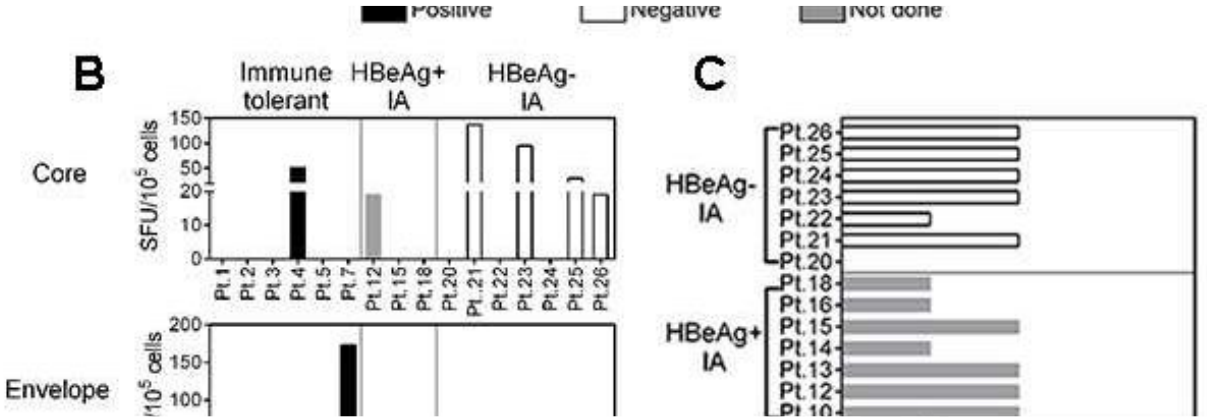
Integration of HBV genome is involved in the development of HCC



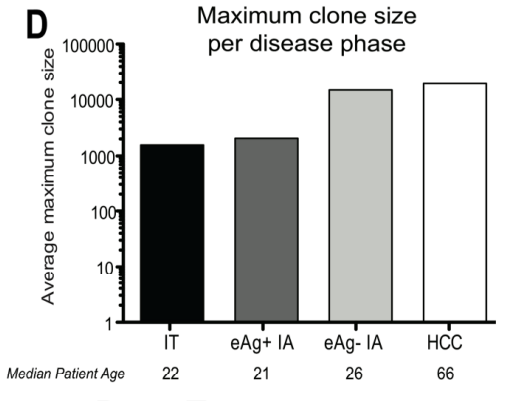
Kanda T, et al. Int J Mol Sci 2019;20:1358.

Similar HBV DNA integration & clonal hepatocyte expansion in IT & IA

HBV integration



Hepatocyte expansion

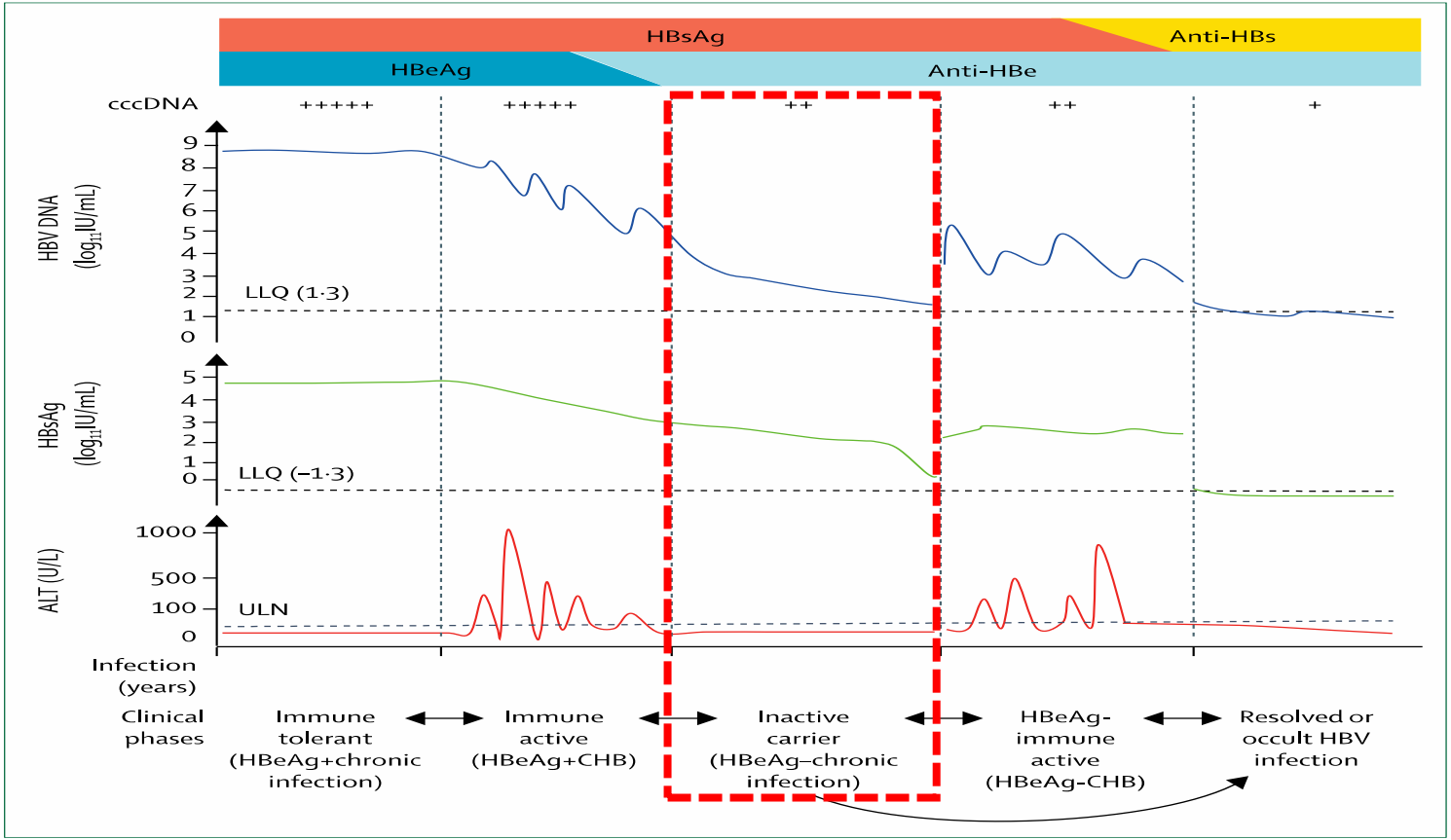


Mason WS, et al. Gastroenterology. 2016;151:986-98.

Outlines

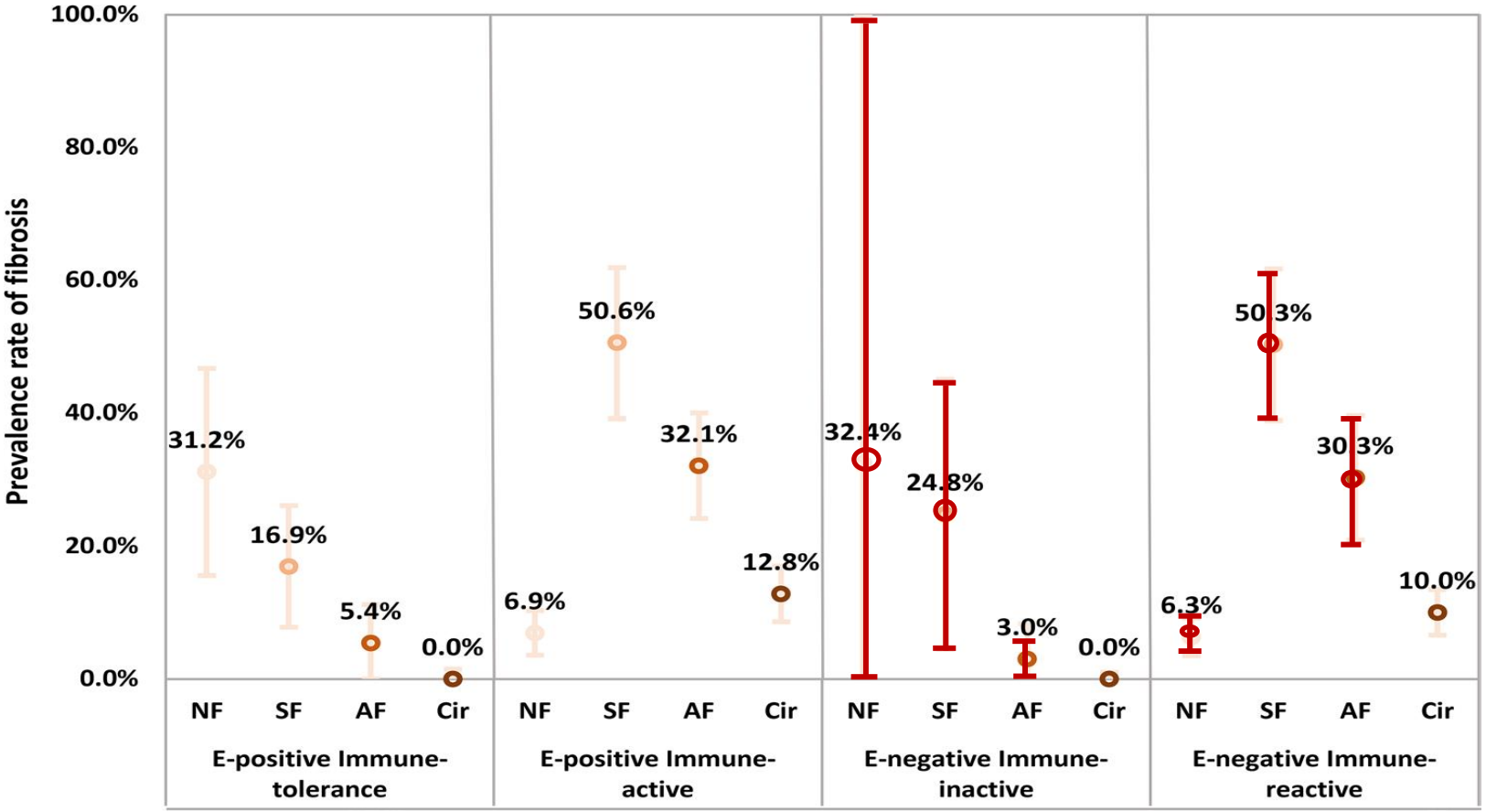
- **The rationale to treat patients in immune tolerant phase**
- **The rationale to treat patients in inactive phase**
- **The rationale to treat patients in indeterminate phase**

Inactive carriers phase-Low HBV DNA and normal ALT



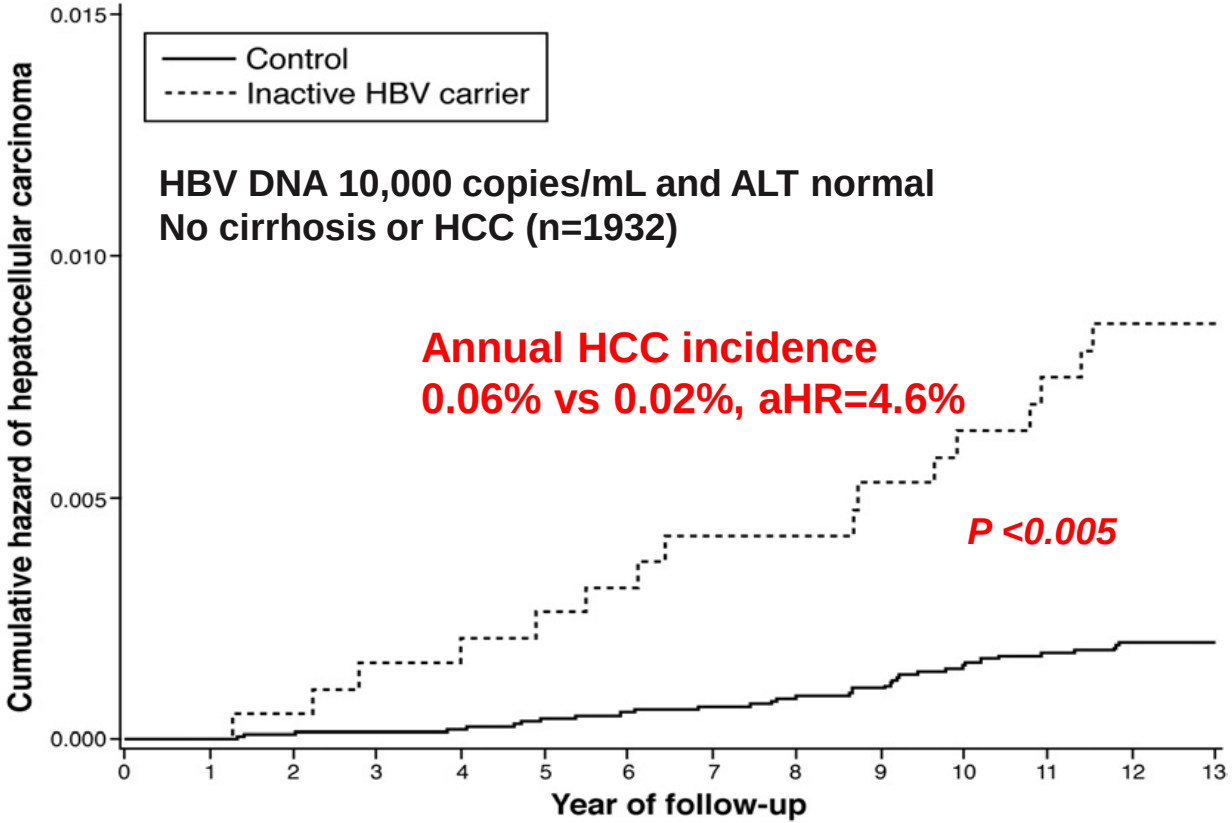
Jeng WJ,et al. Lancet. 2023

Inactive phase also associated with fibrosis burden



Lin MH, et al. Dig Dis Sci. 2021

REVEAL: inactive carriers have a higher HCC risk than those without HBV infection



Gastroenterology 2010;138:1747–1754

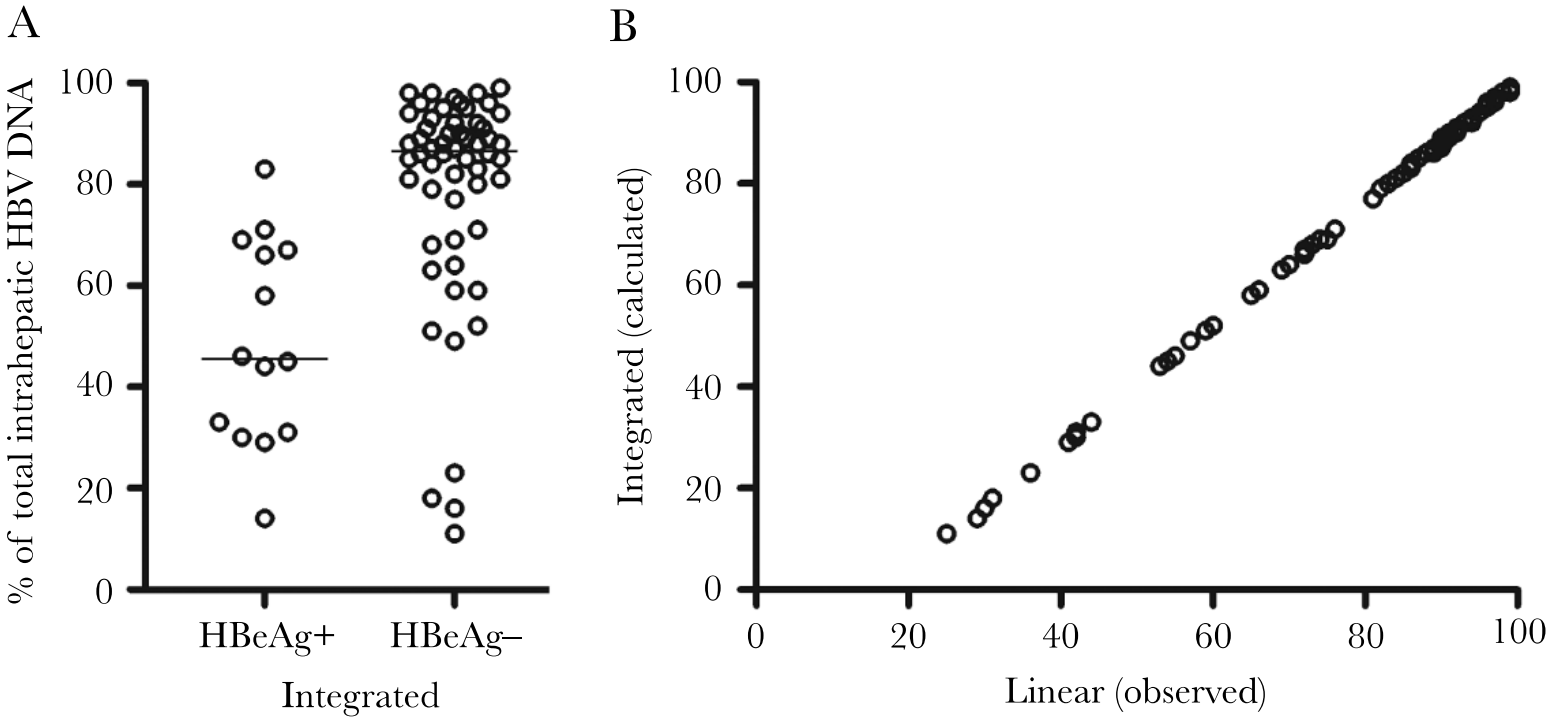
HCC occurred during long-term follow-up of inactive carriers

(HBeAg-, ALT <40 U/L, HBV DNA <10 000 copies/mL)

- **146 inactive carriers (mostly Asian) were followed up for 8±6.3 years**
  - ✓129 (88.4%) remained “inactive carriers”
  - ✓13 (8.9%) loss of HBsAg
  - ✓1 (0.7%) reactivation to HBeAg-negative CHB,
  - ✓ **2 (1.4%) developed HCC**

Tong MJ, et al. J Dig Dis 2013; 14; 311–317

The degree of integration of HBV DNA in HBeA(-) stage may be higher than previously anticipated



Rydell GE,et al. J Infect Dis. 2022;225:1982-90.

Outlines

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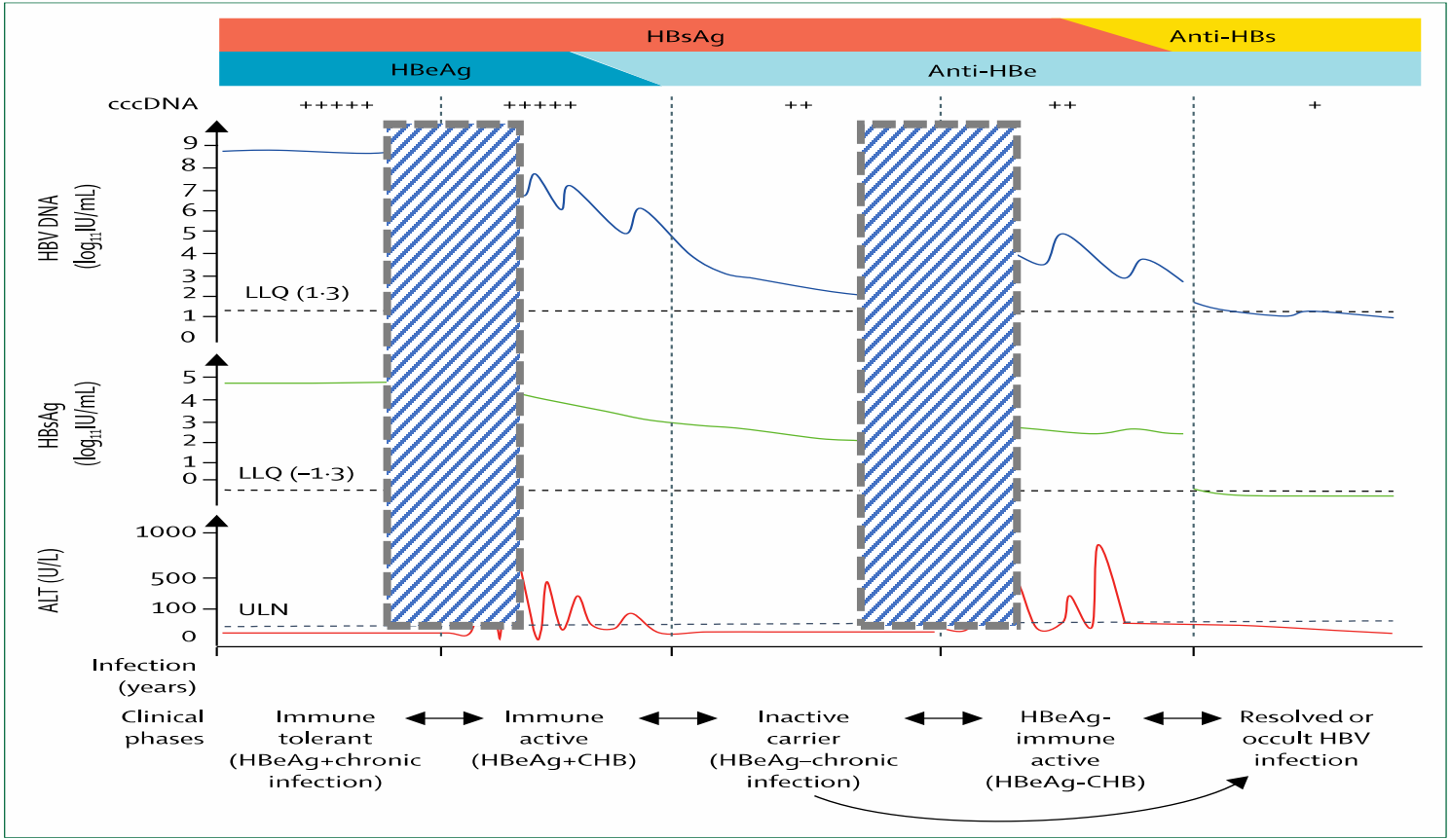
- **The rationale to treat patients in indeterminate phase**

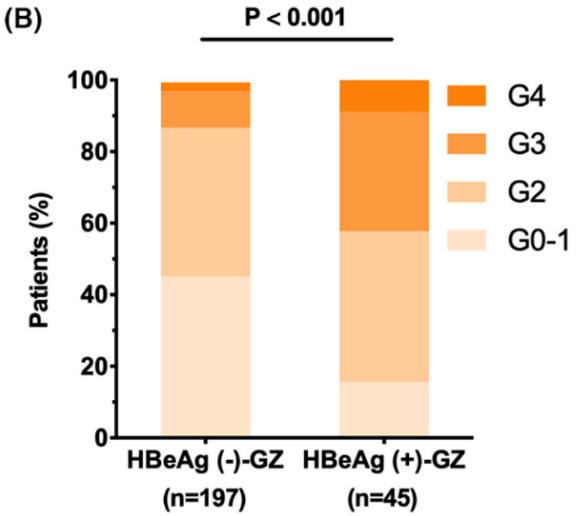
Grey-zone or Indeterminate phases of CHB

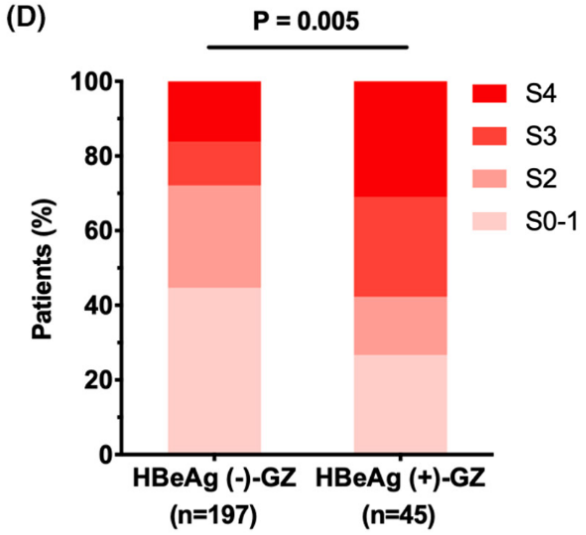


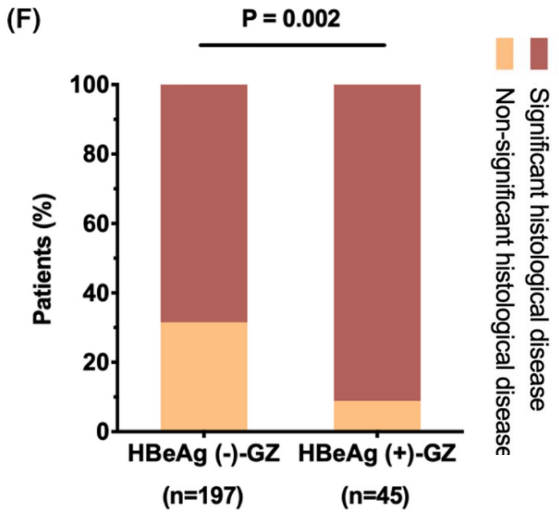
Jeng WJ, et al. Lancet. 2023

23.2% (242 /1043) CHB patients within grey zone

72.7%(176/242) of grey-zone pts had significant histological disease





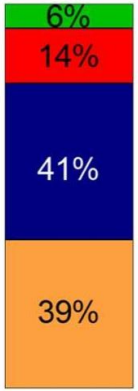


Wang J, et al. Aliment Pharmacol Ther. 2023;57:464-74.

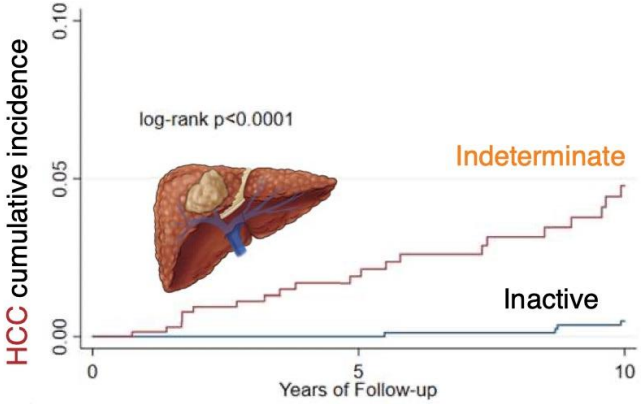
Natural History and HCC Risk in Chronic Hepatitis B Indeterminate Phase

3,366 treatment naïve CHB patients

- ✓ 39% were in the **indeterminate** phase at baseline
- ✓ **HCC** risk among **indeterminate** patients was 14X that of inactive patients



Immune Tolerant
Immune Active
Inactive
Indeterminate

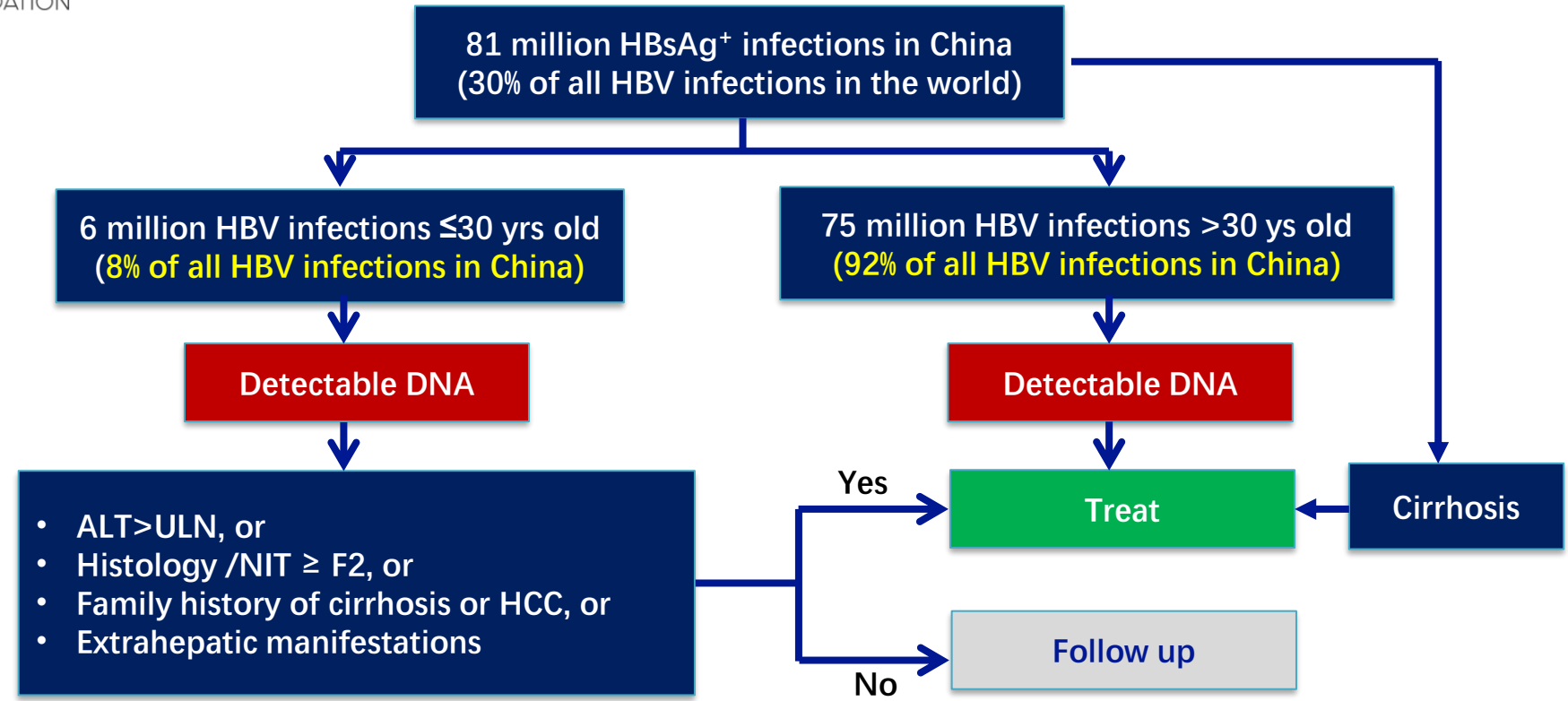


"Indeterminate phase": patients with elevated ALT but low HBV DNA, or elevated HBV DNA but low ALT levels, fall outside any of the 4 phases

Huang DQ, et al. Clin Gastroenterol Hepatol. 2021

China HBV Treatment Guidelines(2022)

-Test more, treat more, treat earlier and treat longer!



Center for Disease Analysis Foundation (@CDAFound) / X

Summary: the rationale for treating all with detectable HBV DNA

- Significant necroinflammation/fibrosis exists among a rather big proportion of patients with immune tolerant , inactive, or indeterminate phase
- HBV genome integration and hepatocyte clonal expansion occur during all these three phases
- Necroinflammation and fibrosis together with HBV genome integration pose a high risk of cirrhosis and HCC development
- Therefore, treat everyone with detectable HBV DNA would be critical to reduce the development of cirrhosis, HCC and the related deaths, which is the ultimate goal of antiviral therapy

Thanks for your attention !