Pediatric Working Group

Liver Forum 2024

Focus Group Participants - 9/4/2024

- Stavra Xanthakos, MD
- Miriam Vos, MD, MSPH
- Bart Koot, MD
- Jake Mann, MD
- Bryan Rudolph, MD – Boehringer Ingelheim
- Mark Hartman, MD – Eli Lilly
- Becky Taub, MD – Madrigal
- Jan Taminiau, MD - EMA
- Veronica Miller – Forum for Collaborative Research

Focus Group Outcomes

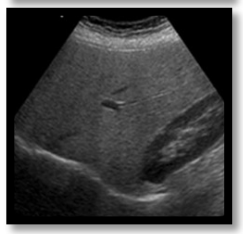
- Reviewed current state of pediatric MASLD clinical trial development
- Developed catalog of barriers, challenges to development
- Plan for next steps

Framework – Need for pediatric therapeutics

- Children have unique phenotypic differences in liver disease patterns and progression, severity of obesity and associated comorbidity risk compared to adults
- Unclear if results from adult trials can be extrapolated to youth without additional (clinical trial) data

Prevalence of MASLD (aka NAFLD) ↑ in adolescents

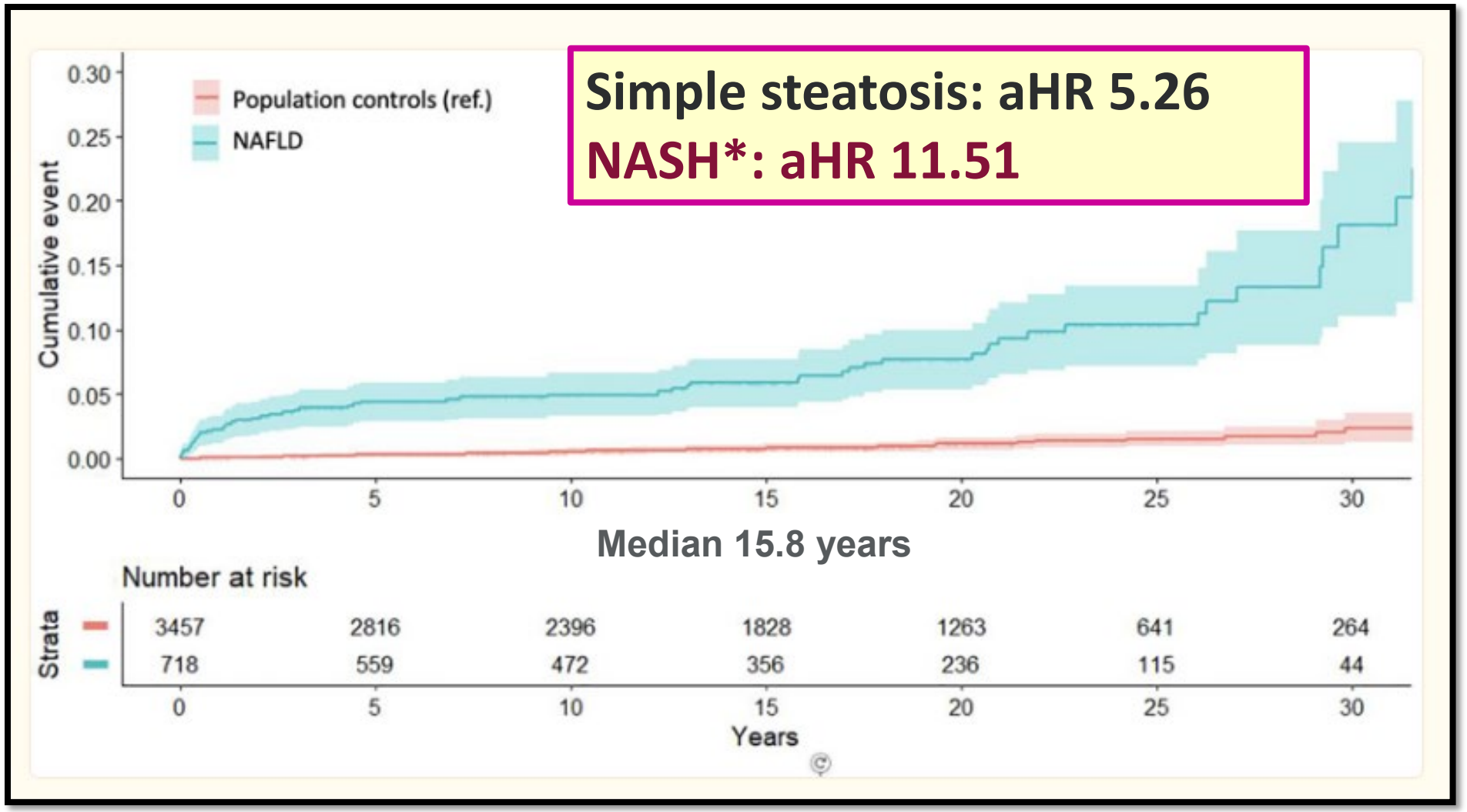
Global Burden of Disease Study



Hartmann P et al. Hepatology 2023

↑mortality in adulthood youth-onset MASLD

(n=718, biopsy-confirmed NAFLD, mean age 17, Sweden)



Cancer
- aHR 15.6

Liver Disease
- aHR 16.5

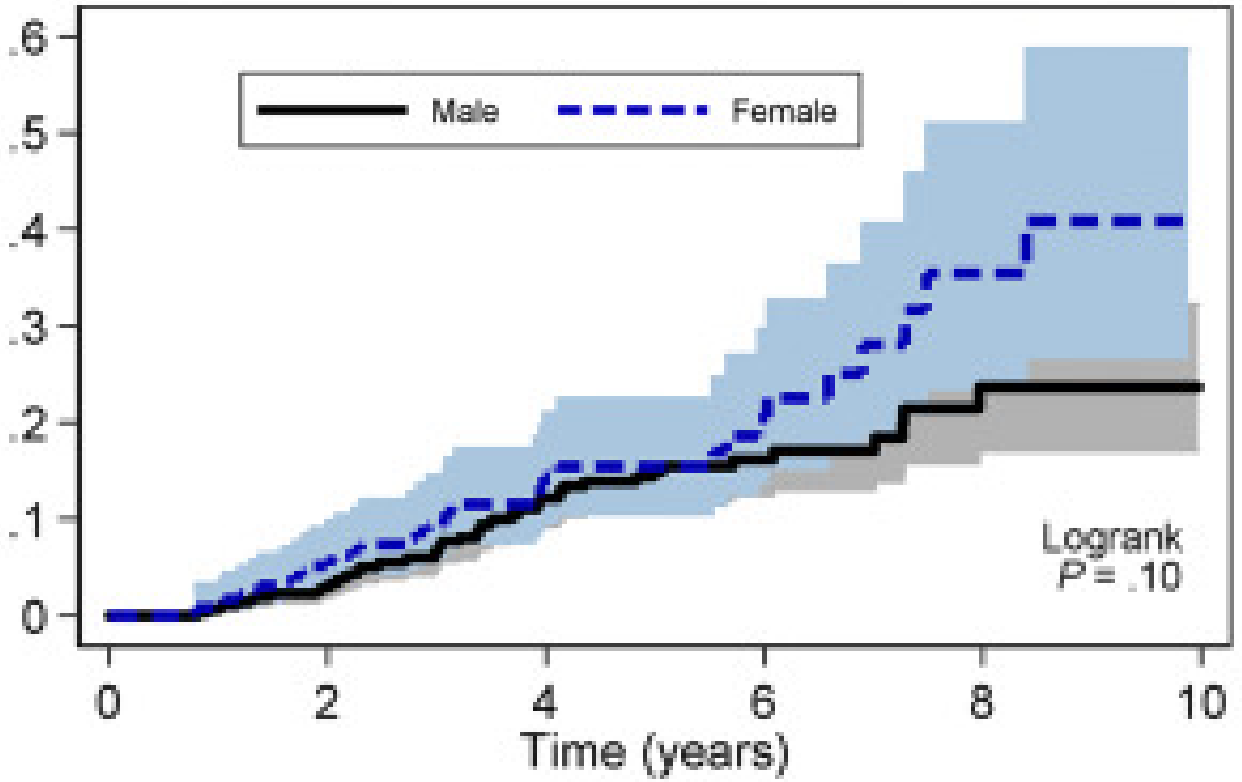
CVD
- aHR 4.32

*NASH did not distinguish between fibrotic (n=166)) vs. non-fibrotic (n=106)

Simon TG. J Hepatol 2021;75:1034

↑ risk of incident T2 diabetes in children with biopsy-confirmed NAFLD (NASH CRN cohort)

- **3000 cases/100,000 person years of risk**
- **5% incidence diabetes risk in clinical trials (1 to 2 year duration)**
  - **8% incidence in adolescents vs. 2% in pre-adolescents**
- **Overall, 17% period prevalence** of T2DM over 3.8 years of follow -up



Newton KP. Clinical Gastroenterol Hepatol 2022 epub 13 June 2022 https://doi.org/10.1016/j.cgh.2022.05.028

Important Questions

- What is the best approach for studies in adolescents – how much can be extrapolated and modeled from adult studies?
- Which age groups (12-17 yrs), 7-11 yrs, very young?
- What are the endpoints? Are there RLSE in children? Role of biopsy?
- What clinical outcomes are meaningful in adolescents when liver-related clinical outcomes mostly occur in adulthood?
- Patient selection – who needs treatment during childhood?
- Treatment duration?
- Control groups – are they feasible? Historical cohorts? Master protocols? Virtual controls? Or open-label transition?

Next Steps/Future Plans

- Summarize areas that require consensus
- Identify experts in these areas to provide data/summarize literature
- In-person consensus developing meeting planned Nov 2024 with all parties at the table
- Develop white paper, EMA, and FDA co-authorship with working group