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NASH  
Meeting

September 7 & 8, 2023

9<sup>th</sup> edition

# Course of NAFLD from Childhood to Adulthood



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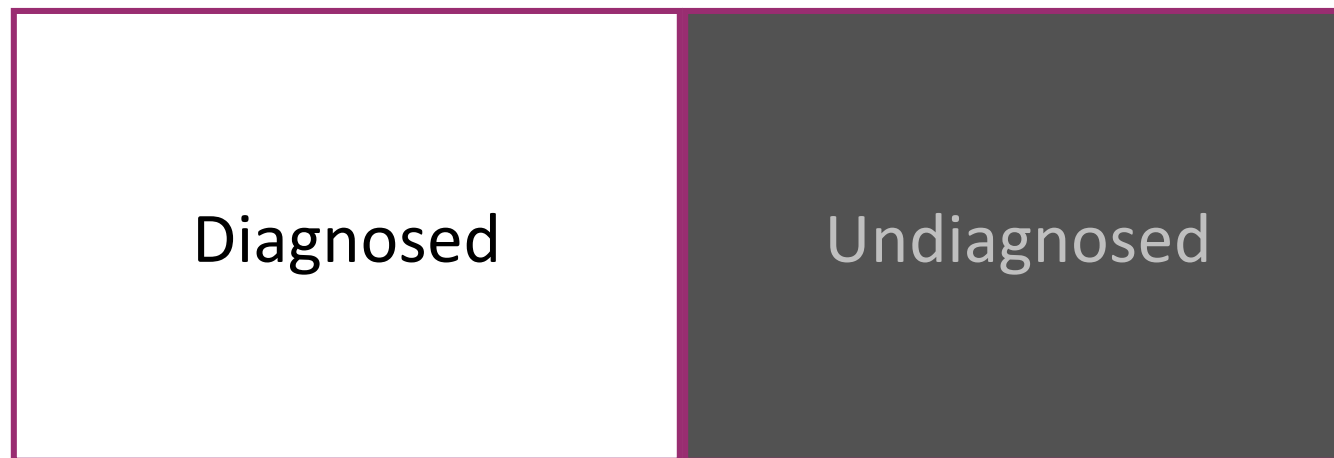
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## Conflict of interest disclosure

- Grants to UC San Diego: Intercept, Genfit, Seraphina
- Consultant: Merck



# What happens to children with NAFLD as they become adults?

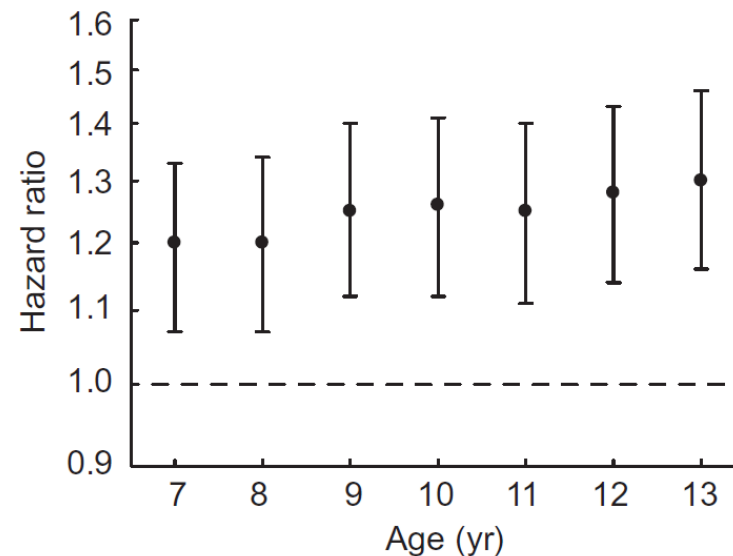


Undiagnosed

# Body mass index in childhood and adult risk of primary liver cancer



- N = 285,884
- Yearly exams: 7 to 13
- BMI z-score



[Berentzen et al. J. Hepatology 60:325-330, 2014](#)

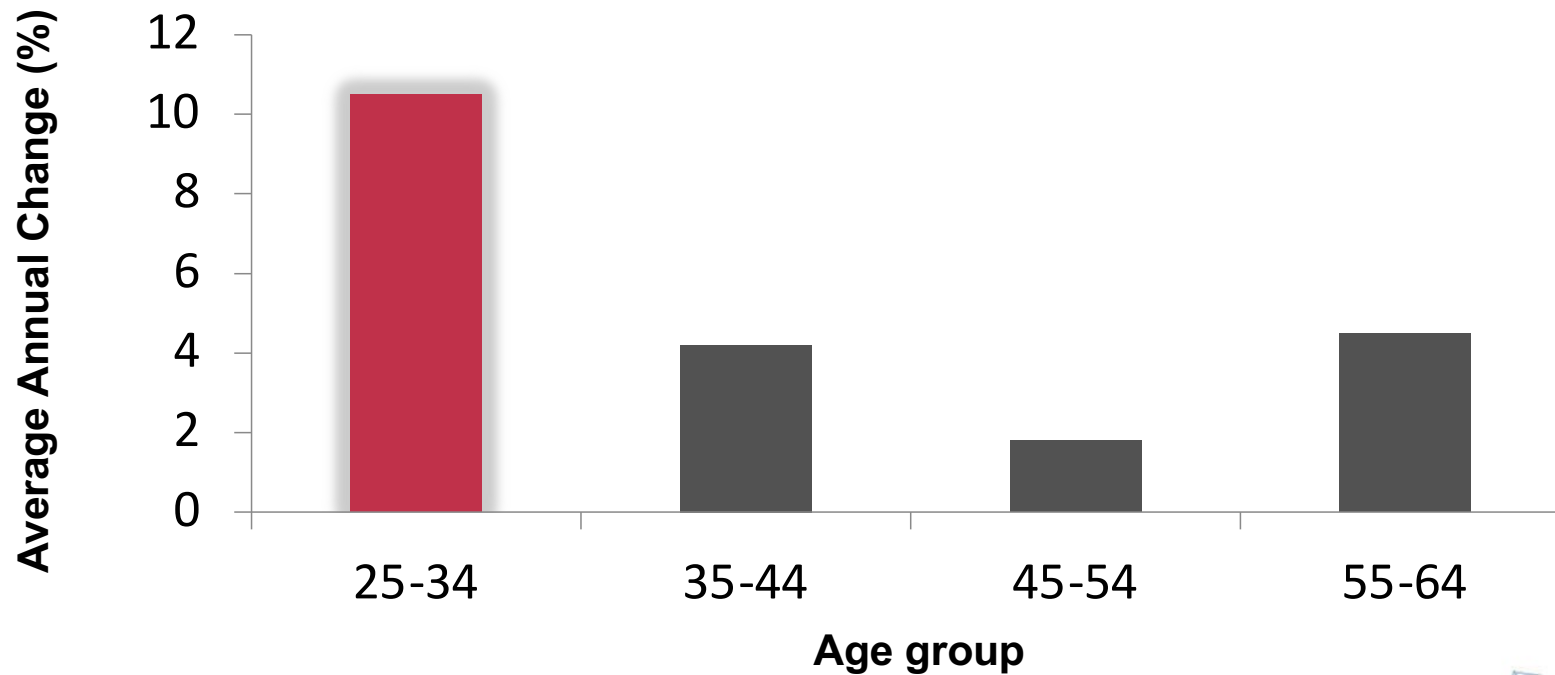
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Undiagnosed

## Increasing Cirrhosis-related Deaths: 2009-2016



Tapper and Parikh. *BMJ* 2018;362:k2817

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# Characteristics of Children vs Adults at Diagnosis

Diagnosed

	Children	Adults
<b>Age</b>	13 years	52 years
<b>Weight</b>	84.4 Kg	96 Kg
<b>BMI</b>	32.4	33
<b>ALT</b>	101	51
<b>AST</b>	62	38
<b>GGT</b>	45	47

[Goyal et al. Hepatology 77:197-212, 2023](#)

[Neuschwander-Tetri et al. Hepatology 52:913-924, 2010](#)



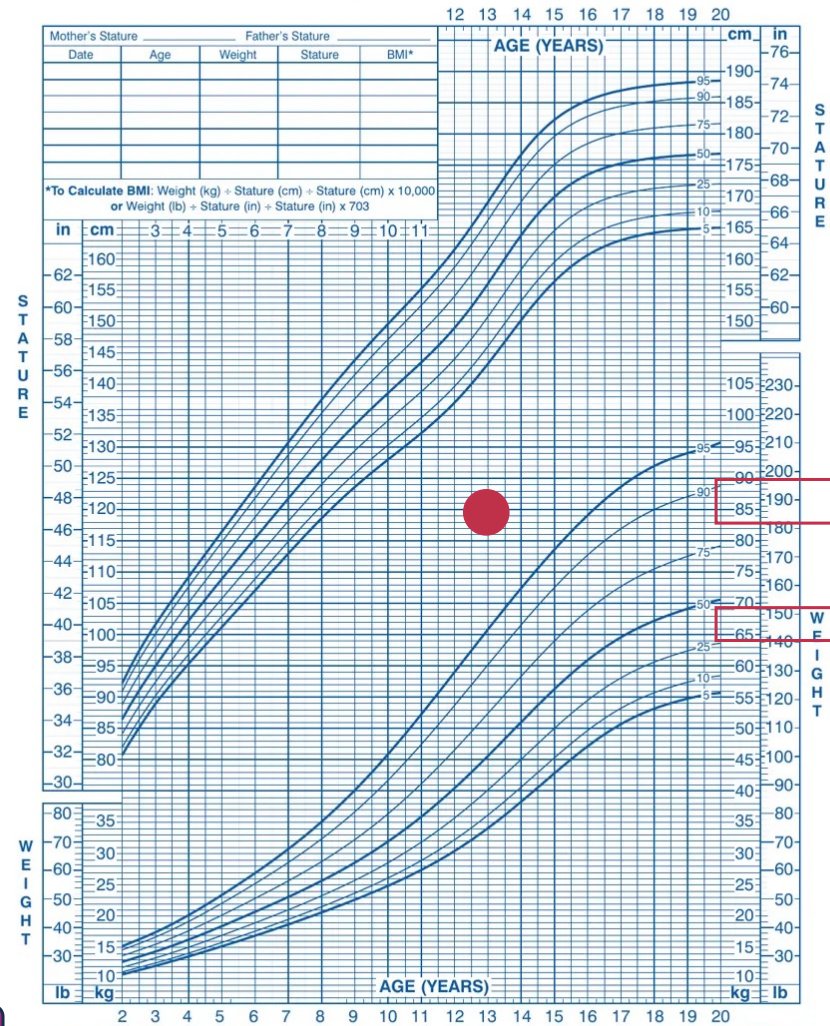
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2 to 20 years: Boys  
Stature-for-age and Weight-for-age percentiles

NAME \_\_\_\_\_

RECORD # \_\_\_\_\_



Published May 30, 2000 (modified 11/21/00).  
SOURCE: Developed by the National Center for Health Statistics in collaboration with  
the National Center for Chronic Disease Prevention and Health Promotion (2000).  
<http://www.cdc.gov/growthcharts>



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# Characteristics of Children vs Adults at Diagnosis

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[Goyal et al. Hepatology 77:197-212, 2023](#)

[Neuschwander-Tetri et al. Hepatology 52:913-924, 2010](#)



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# Characteristics of Children vs Adults at Diagnosis

Feature	Category	Children	Adults
Steatosis	1	28%	44%
	2	30%	33%
	3	<b>42%</b>	23%
NASH	NAFLD	27%	25%
	Borderline Zone 3	21%	18%
	Borderline Zone 1	<b>28%</b>	1%
	Definite	25%	<b>56%</b>

[Goyal et al. Hepatology 77:197-212, 2023](#)

[Neuschwander-Tetri et al. Hepatology 52:913-924, 2010](#)



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# Characteristics of Children vs Adults at Diagnosis

	Stage	Children	Adults
<b>Fibrosis</b>	0	31%	25%
	1a	7%	11%
	1b	5%	11%
	1c	<b>28%</b>	4%
	2	16%	18%
	3	13%	<b>21%</b>
	4	2%	<b>10%</b>

Goyal et al. *Hepatology* 77:197-212, 2023

Neuschwander-Tetri et al. *Hepatology* 52:913-924, 2010



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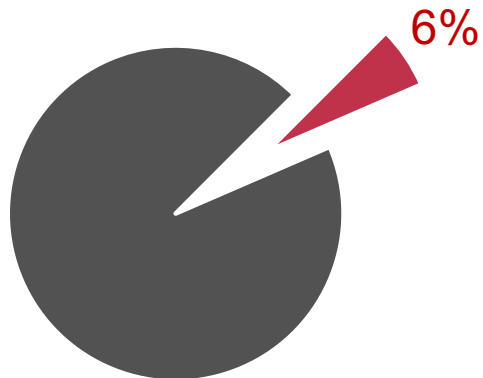
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# Mortality

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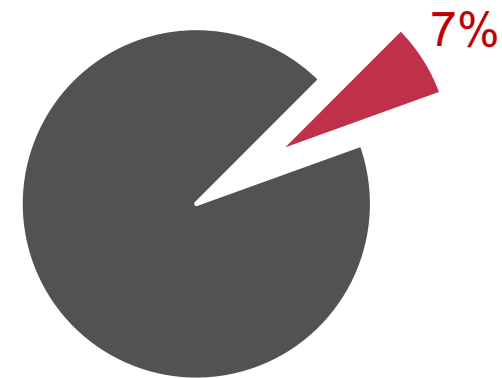
# In small studies, children with NAFLD had 6-7% mortality over 4 to 6 years

- Minnesota
- N = 66
- Follow-up 6.4 years



Feldstein et al. *GUT* 58:1538-1544, 2009

- Georgia
- N = 44
- Follow-up 4.5 years



Cioffi et al. *Children* 4:34, 2017

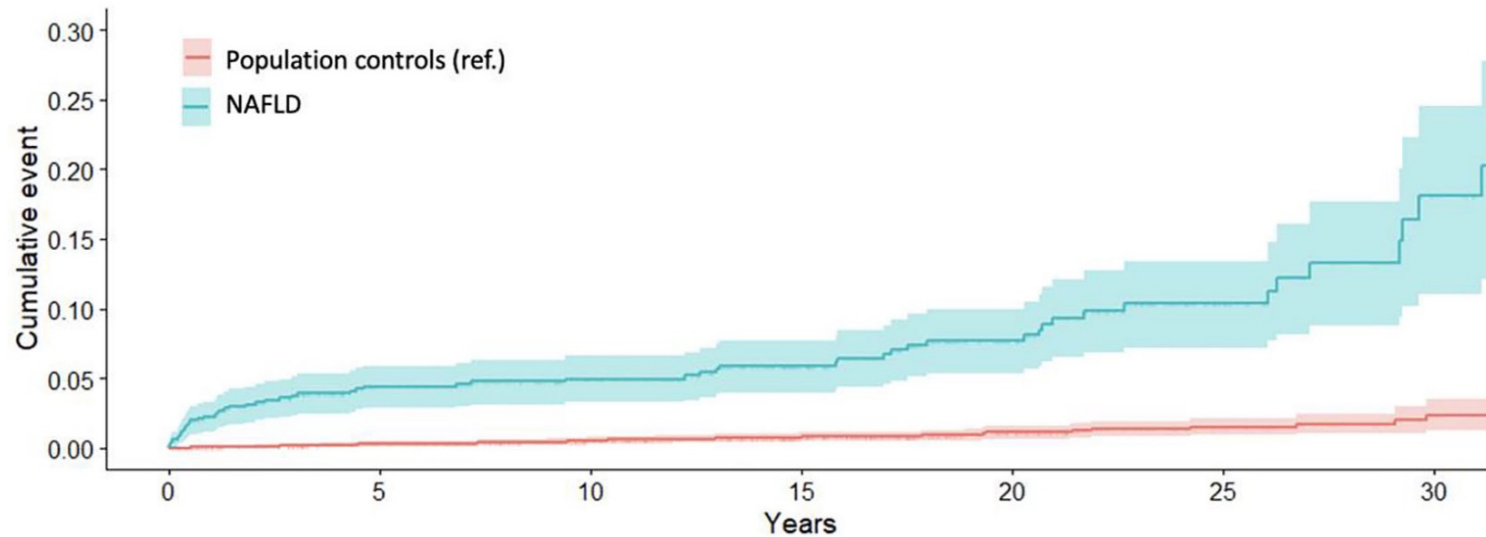


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# NAFLD at ages 17-25 is associated with increased long-term mortality

N = 718. Follow-up 15.8 years. Mortality = 5.5 per 1000 person-years

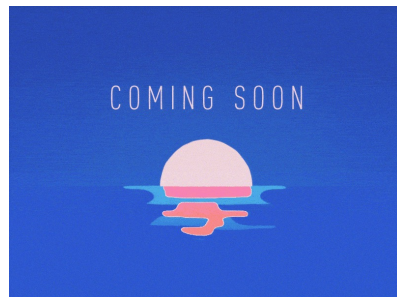




# Mortality of Childhood NAFLD

## The CALIFORNIA Study

- N = 1605
- Mean age 12.7 years
- Mean follow-up 7.3 years



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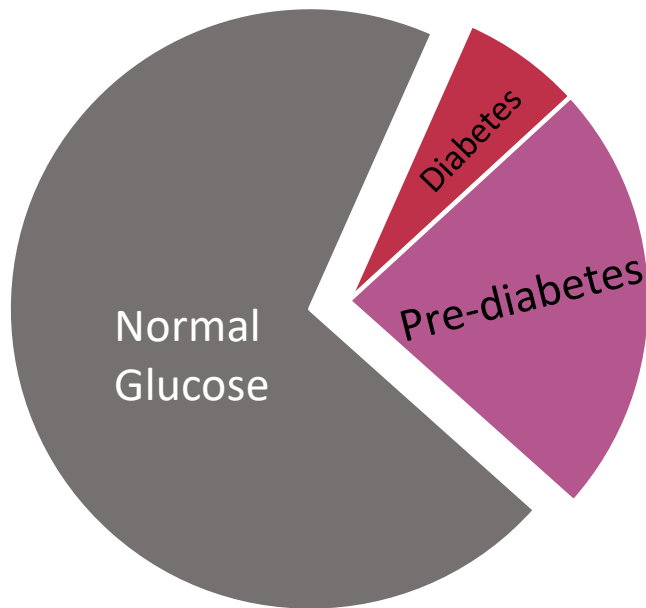


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# Diabetes

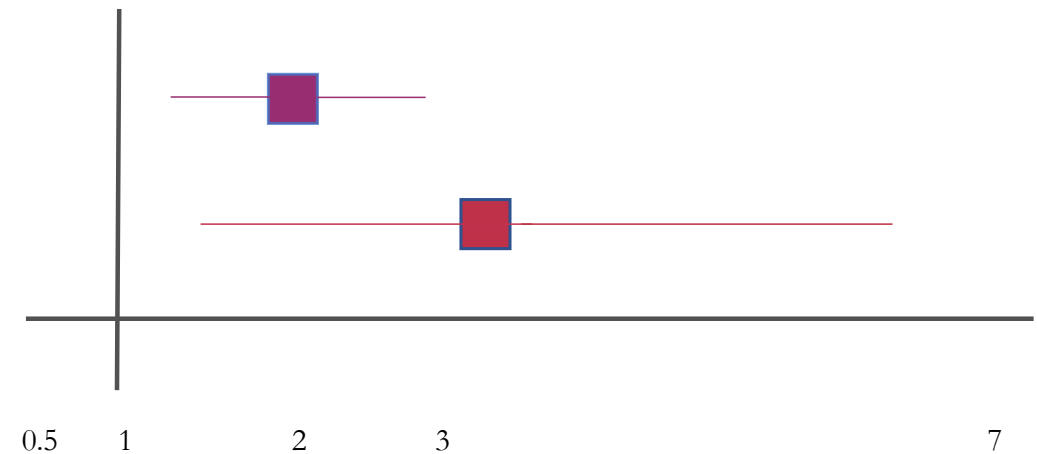
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# Type 2 Diabetes in Children with NAFLD



N = 675

Odds Ratio for NASH



Newton et al. *JAMA Pediatrics* 170:e161971, 2016

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# Incident Type 2 Diabetes in Children with NAFLD

- N = 892
- Age 12.8 years
- Follow-up 3.8 years

**3000 per  
100,000 person-years**

	Hazard Ratio	95% CI
Age	1.2	1.1-1.3
Female	1.8	1.2-2.8
BMI z-score	1.8	1.0-3.0
Steatosis grade	1.7	1.0-2.8
Ballooning grade	1.7	1.0-2.9
Fibrosis stage	1.8	1.1-2.8

Newton et al. *Clin Gastroenterol Hepatol* 21:1261-1270, 2023.



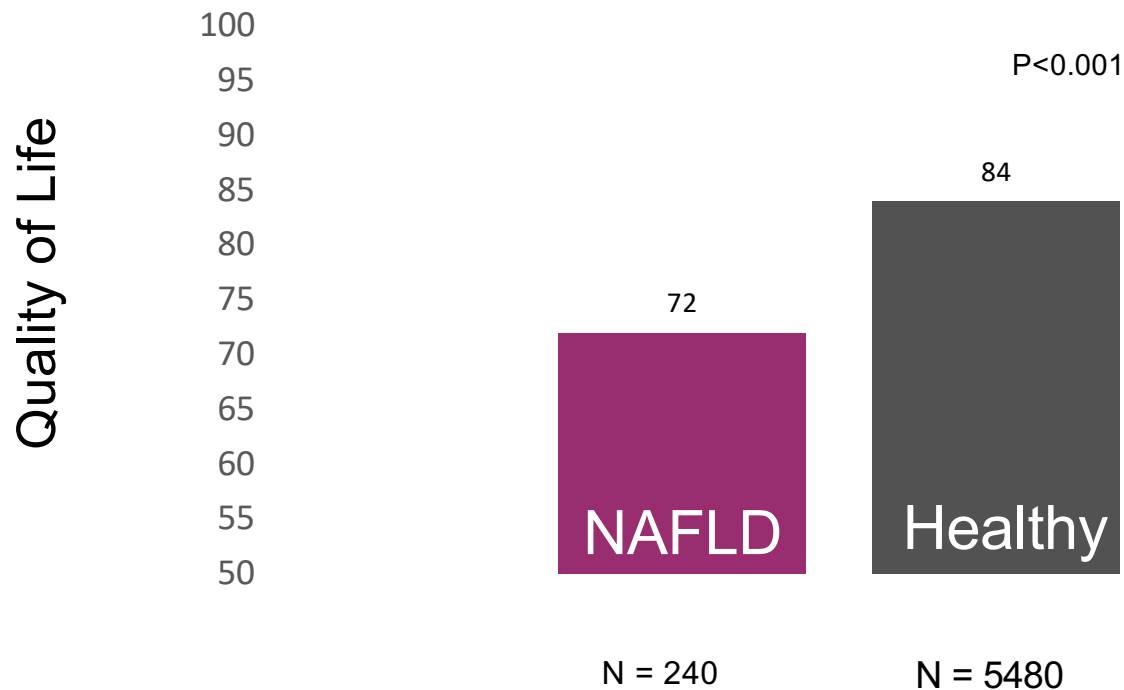
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# Mental Health

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# Children with NAFLD have lower Health Related Quality of Life



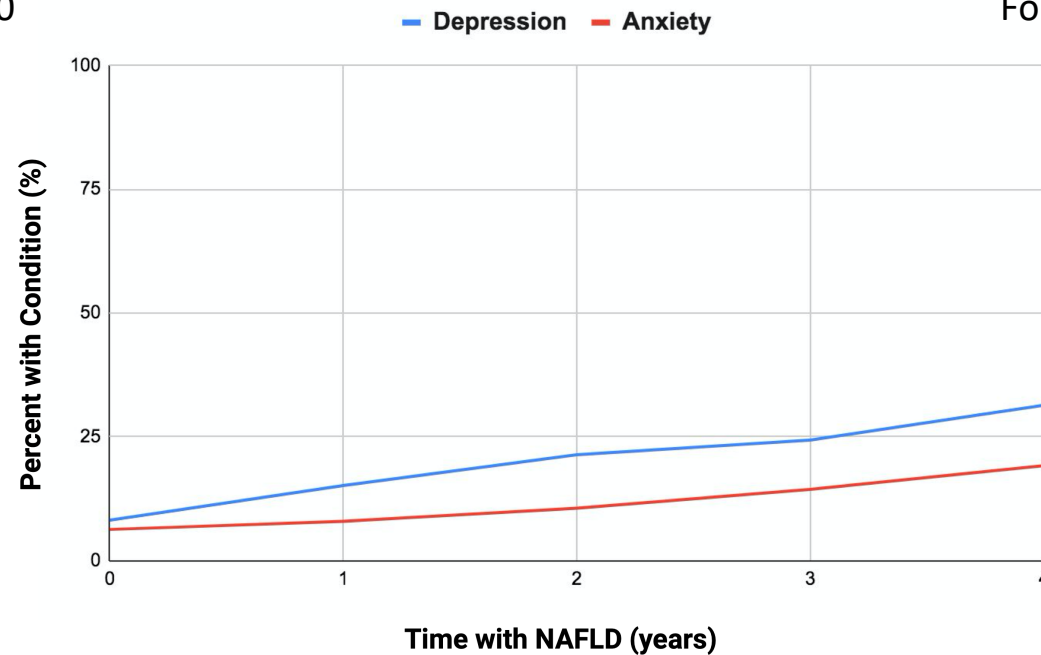
Kistler et al. *Alimentary Pharmacol Ther* 31: 396-406, 2010



# Adolescents with NAFLD have Higher Incident Depression and Anxiety

N = 160

Follow-up 3.8 years



Noon et al. *JPGN* 72(4):579-583, 2021.

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# Bone Health

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# Osteoporosis Prevention is a Pediatric Problem

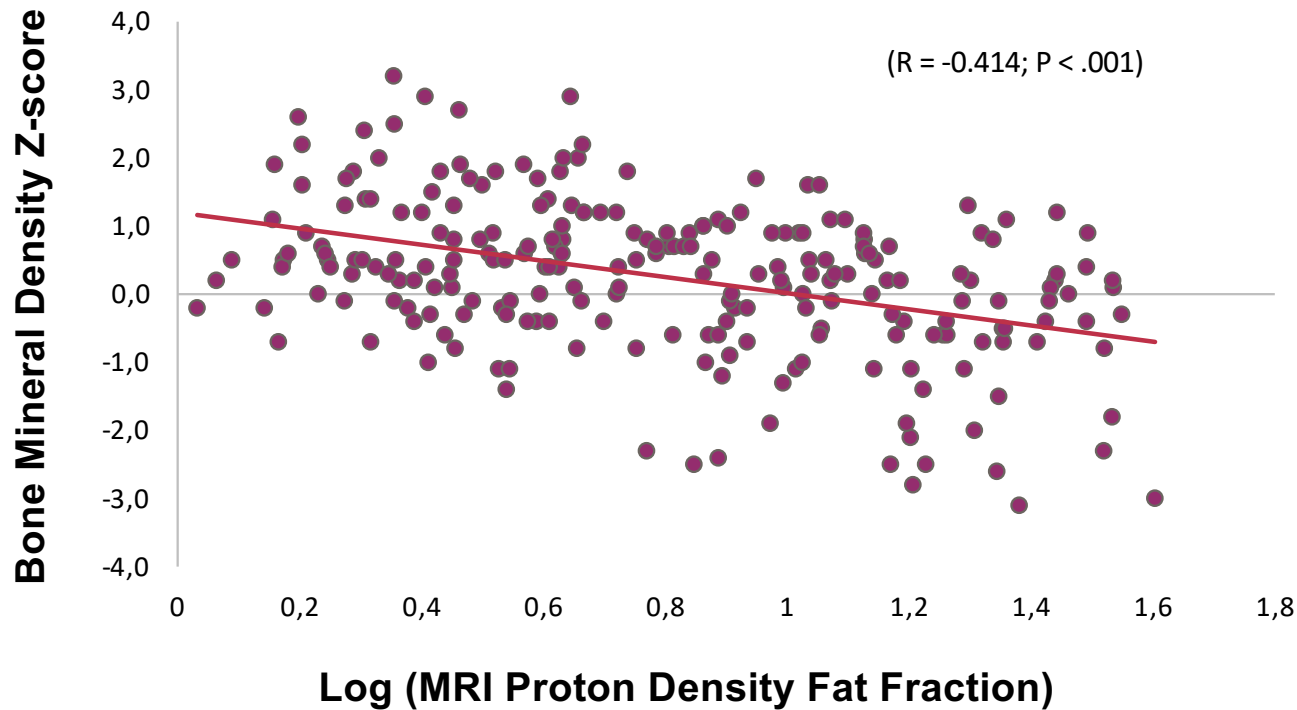


90% of Bone Mass Acquired  
Before Age 21



\$25 Billion per Year  
in USA

# Hepatic Steatosis is Negatively Correlated with Bone Mineral Density z-score in Children



# Risk Factor Accumulation

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International Think Tank

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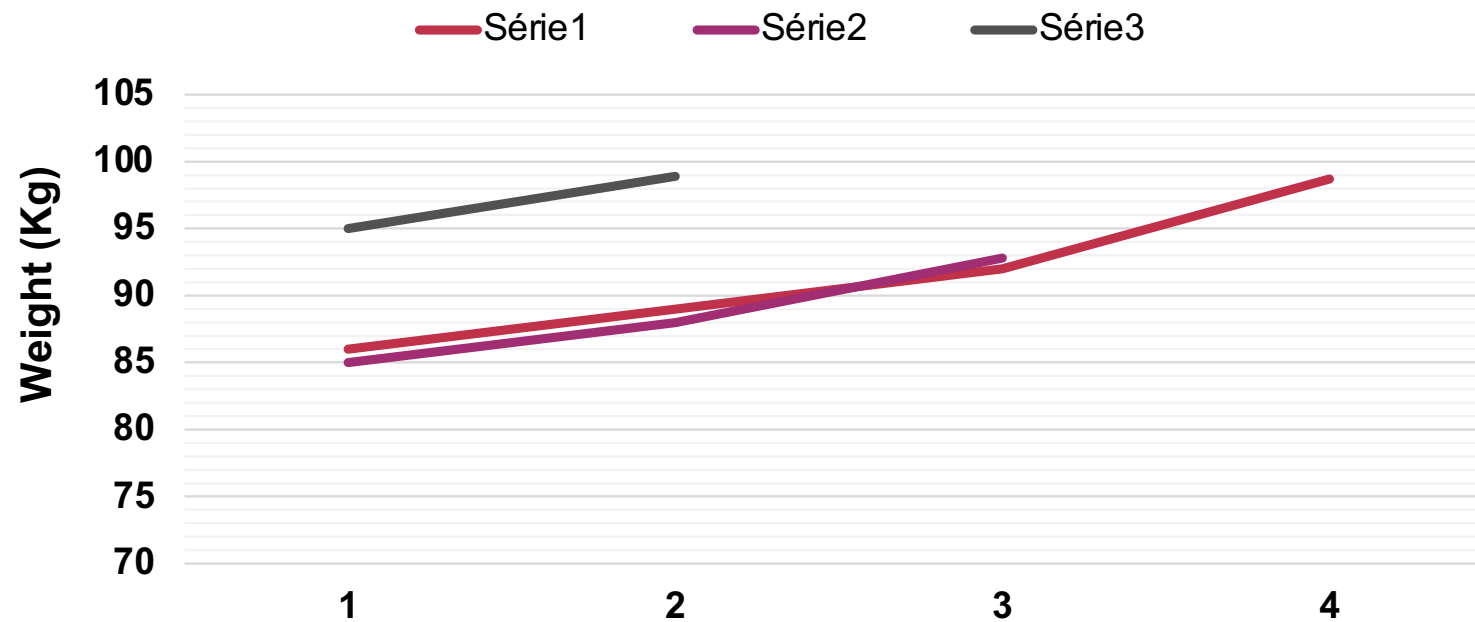


# Weight Gain

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# Children with NAFLD gain weight rapidly



[JAMA 305:1659-68, 2011](#)

[Gastro 151:1141-1154, 2016](#)

[Hepatology 76:429-444, 2002](#)

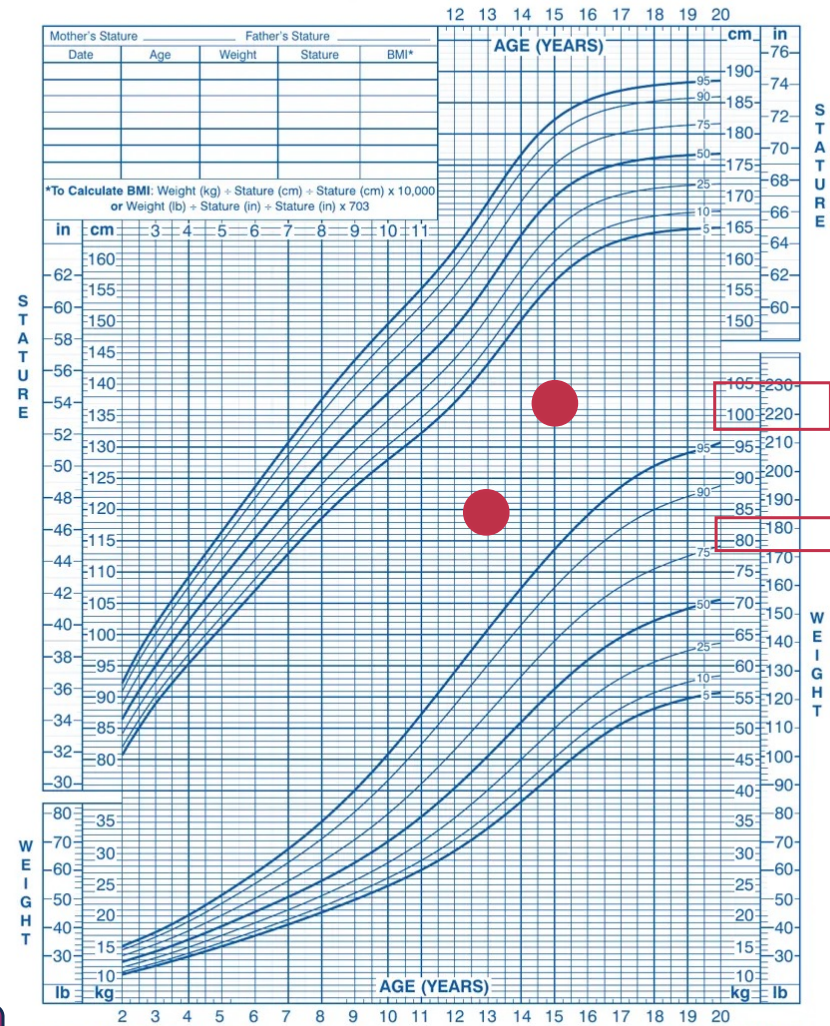


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## RECORD # \_\_\_\_\_

	BMI	
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27

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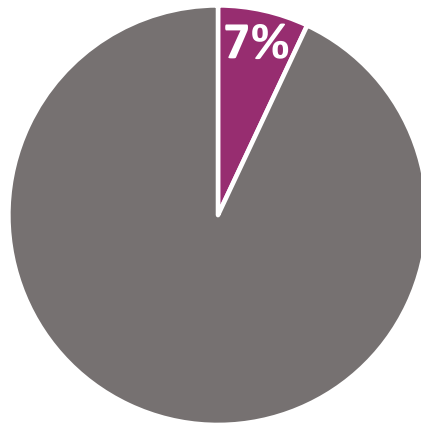
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# Alcohol Use

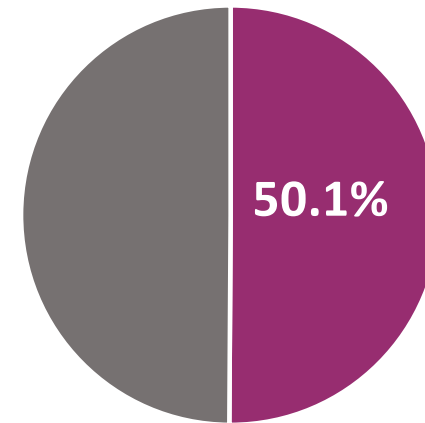
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# Alcohol Use: Adolescents vs Young Adults

**Age 12-17**



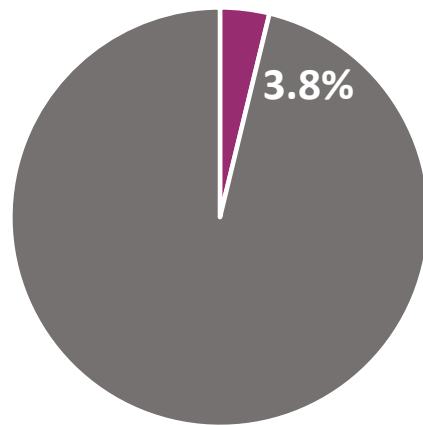
**Age 18-25**



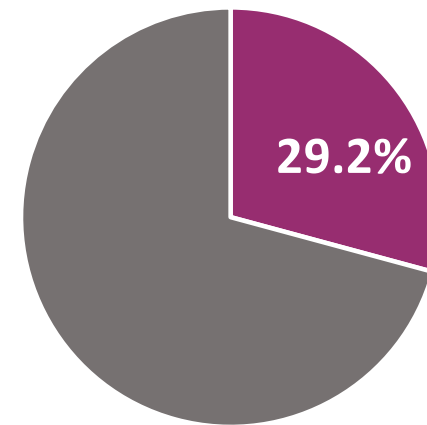
SAMHSA, National Survey on Drug Use and Health, 2021

# Binge Alcohol Use: Adolescents vs Young Adults

**Age 12-17**



**Age 18-25**

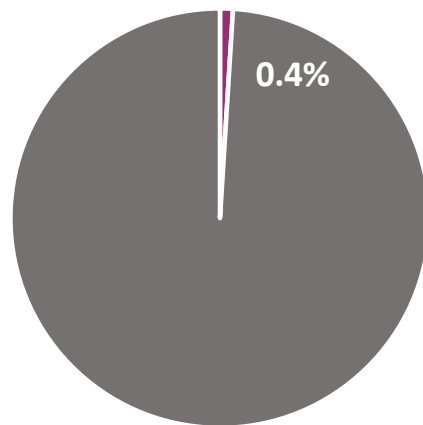


SAMHSA, National Survey on Drug Use and Health, 2021

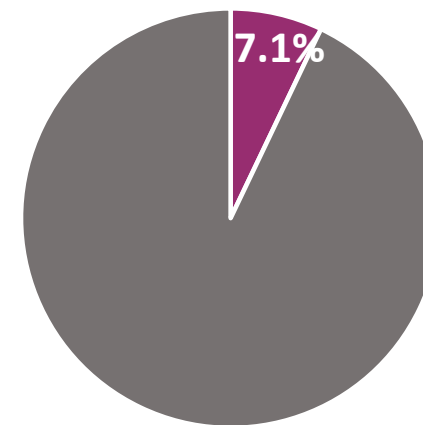


# Heavy Alcohol Use: Adolescent vs Young Adults

**Age 12-17**

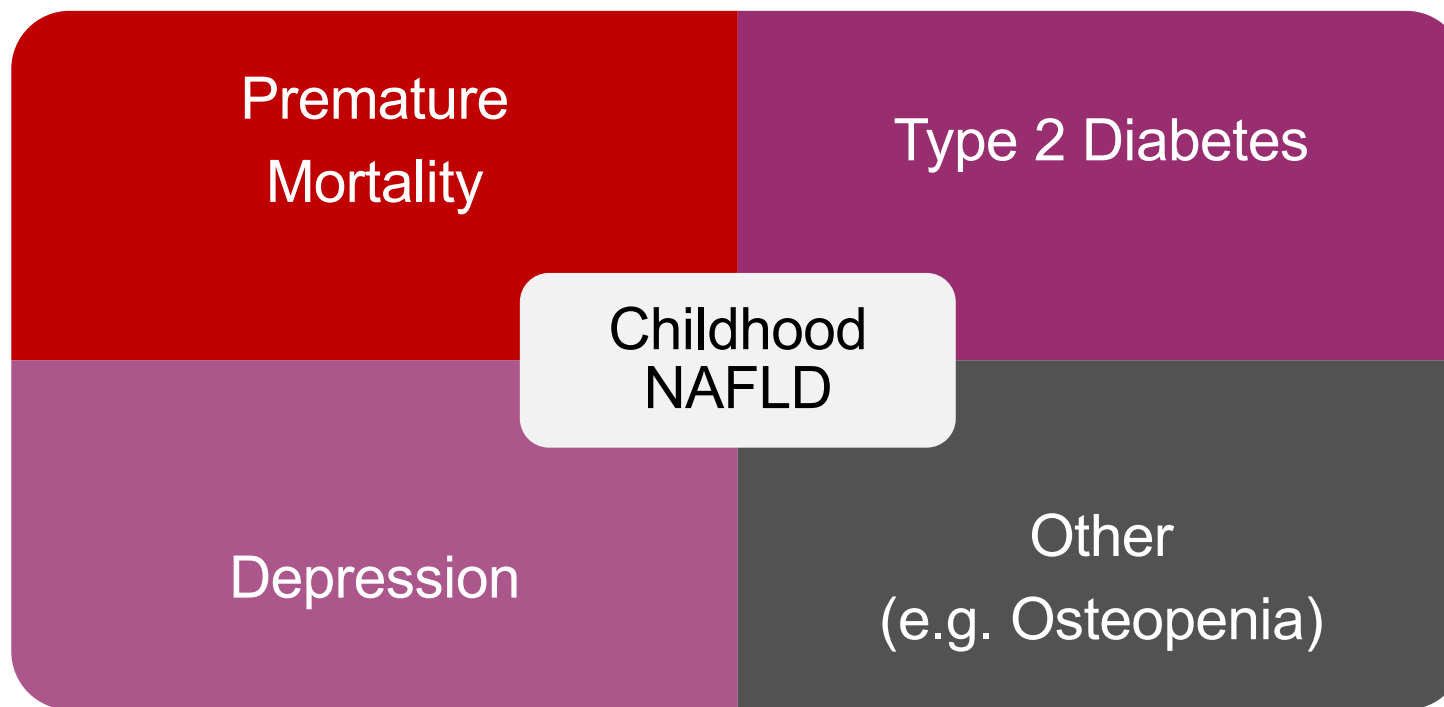


**Age 18-25**

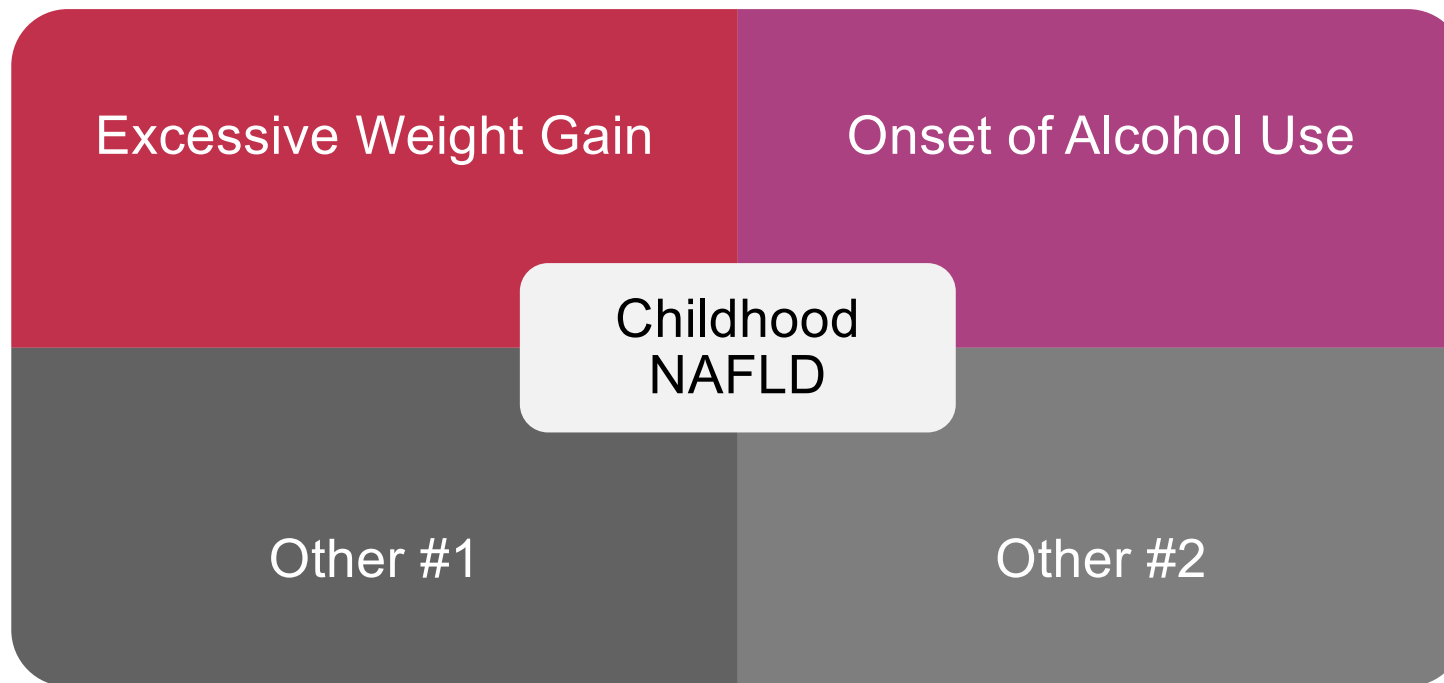


SAMHSA, National Survey on Drug Use and Health, 2021

# Clinical outcomes of childhood NAFLD are multi-dimensional



# Additional risk factors for adverse outcomes are accumulating





# Children with NAFLD Need Your Attention

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