Welcome to the 53rd Annual Conference

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Drug & Alcohol Abuse Under the Radar

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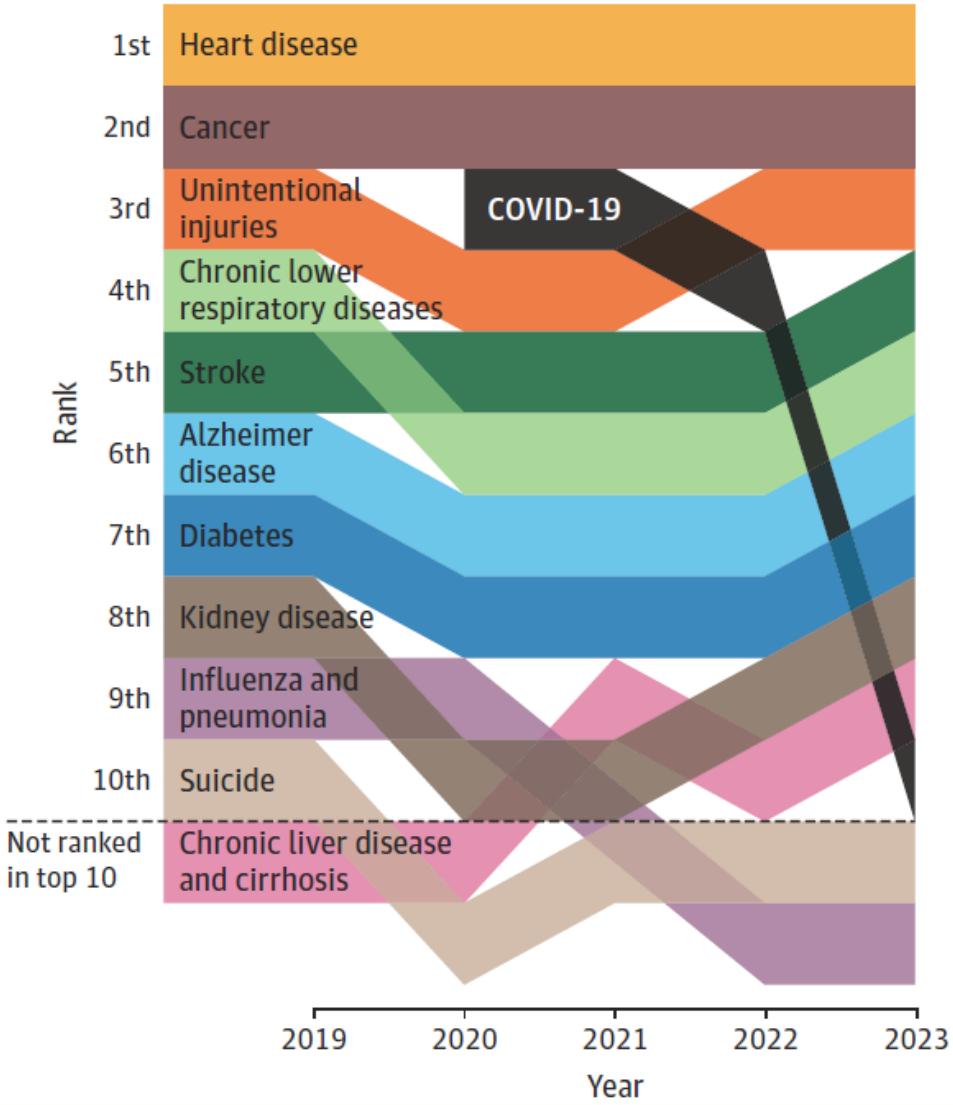
Observations and insights about the future of laboratory testing and data solutions

Why care?

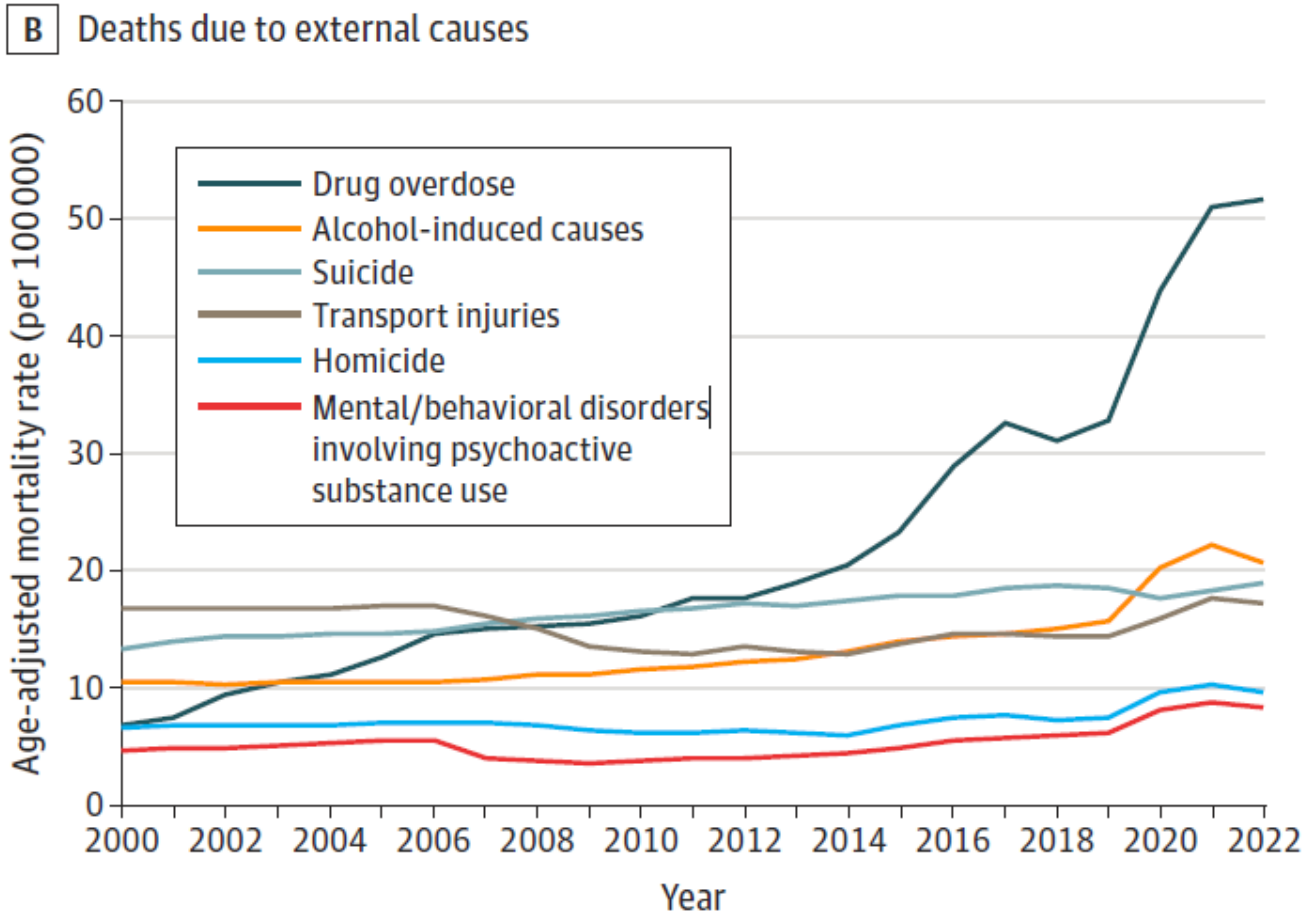
- Deaths from drug & alcohol use soared post-pandemic
- Deaths from chronic liver disease & cirrhosis, likewise, climbed

Figure. Trends in the Ranking of Leading Causes of Death—US, 2019-2023



JAMA. 2024;332(12):957-958. doi:10.1001/jama.2024.15563

A steady, but lethal climb



- Deaths from drug overdose more than tripled
- Alcohol-related **mortality increased 51.6%** from 2000-2019 & doubled from 2019-2021

Woolf SH. Increasing Mortality Rates in the US, but Not From COVID-19. *JAMA.* 2024;332(12):959–960. doi:10.1001/jama.2024.13626

Alcohol and alcohol-related deaths

- Alcohol is the most commonly used substance among those 12+ in the U.S.
- Excessive alcohol use, the leading preventable cause of death, kills ~ 178,000 each year

https://www.cdc.gov/alcohol/facts-stats/index.html

Mortality risk depends on pattern of use

- ~67% of alcohol-related deaths (117,000) were from chronic conditions, which develop from drinking alcohol over time
  - Cancer, heart disease, liver disease, and mental health conditions
- ~33% of alcohol-related deaths (61,000) were from binge drinking or drinking to excess on 1 occasion
  - Motor vehicle crashes, alcohol-associated drug overdoses, alcohol poisonings, and suicide

https://www.cdc.gov/alcohol/facts-stats/index.html

How to assess risk?

Self-reporting is hit or miss…

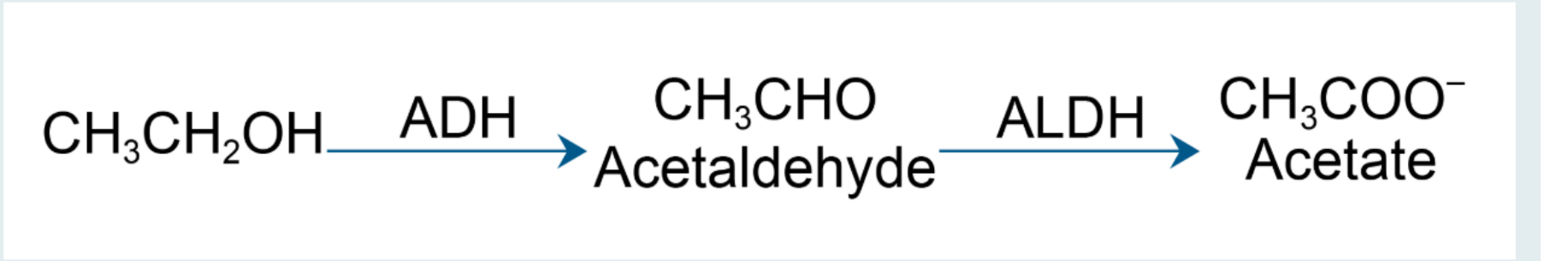
- Self-reports underestimate the prevalence of substance use among youths by 30%-60% compared to laboratory tests[1]
- When confidentiality is ensured, studies suggest self-reports of alcohol and substance use are valid[2]
- Even with an accurate drink count, differences in the alcohol content of drinks, rate of drinking, as well as individual differences in pharmacokinetics make accurately gauging the level of use & risk difficult[2]

1. J Am Acad Child Adolesc Psychiatry 2023;62(7):791-804.
2. Addict Behav. 2015 Jun 25;50:205–212.

The lab can help

"You're fired, Jack. The lab results just came back, and you tested positive for **Coke**."

Alcohol metabolizes rapidly

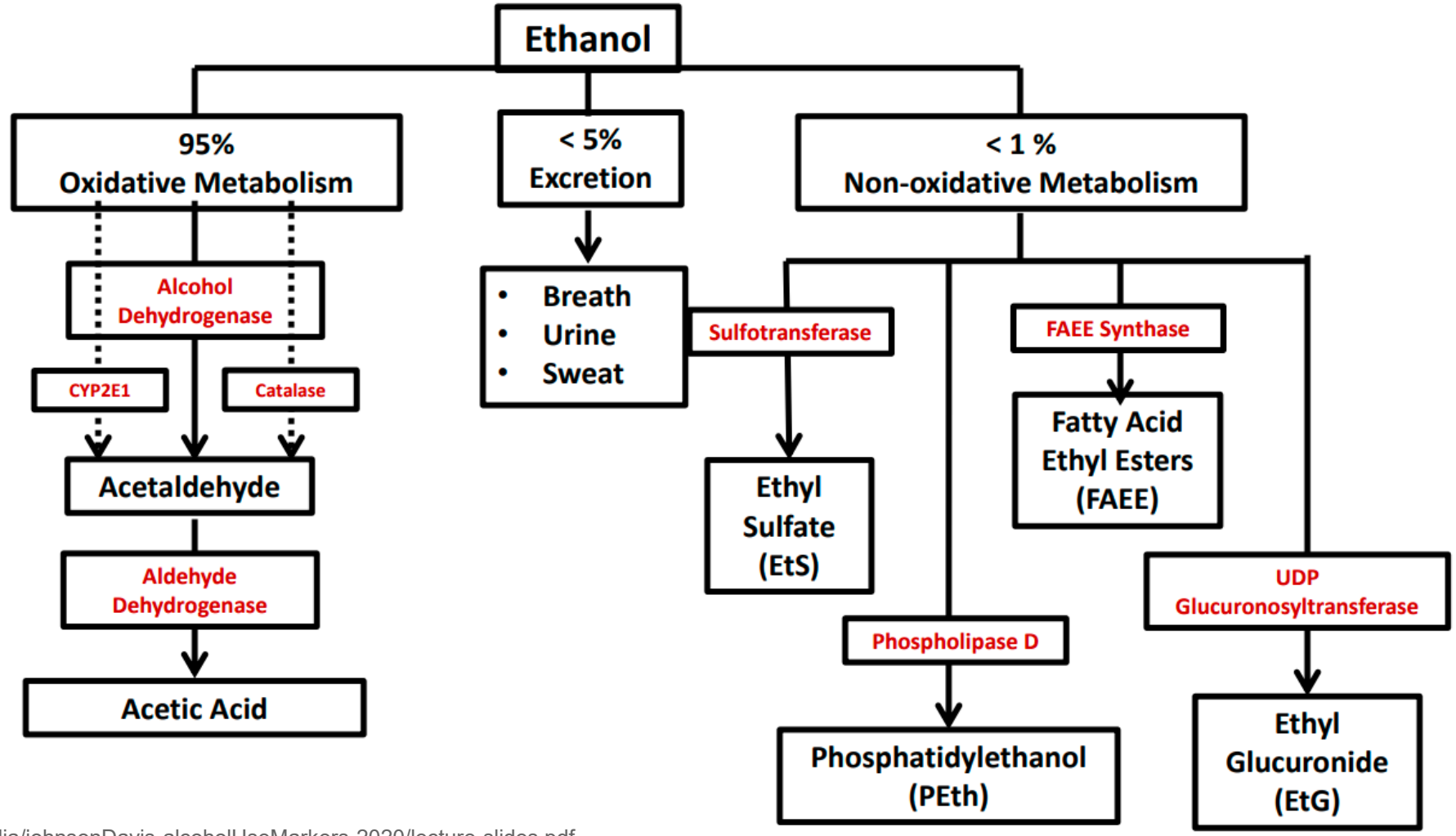


The chemical name for alcohol is ethanol (CH3CH2OH). The body processes and eliminates ethanol in separate steps. Chemicals called enzymes help to break apart the ethanol molecule into other compounds (or metabolites), which can be processed more easily by the body. Some of these intermediate metabolites can have harmful effects on the body.

Most of the ethanol in the body is broken down in the liver by an enzyme called alcohol dehydrogenase (ADH), which transforms ethanol into a toxic compound called acetaldehyde (CH3CHO), a known carcinogen. However, acetaldehyde is generally short-lived; it is quickly broken down to a less toxic compound called acetate (CH3COO-) by another enzyme called aldehyde dehydrogenase (ALDH). Acetate then is broken down to carbon dioxide and water, mainly in tissues other than the liver.

National Institute on Alcohol Abuse & Alcoholism
https://www.niaaa.nih.gov/publications/alcohol-metabolism

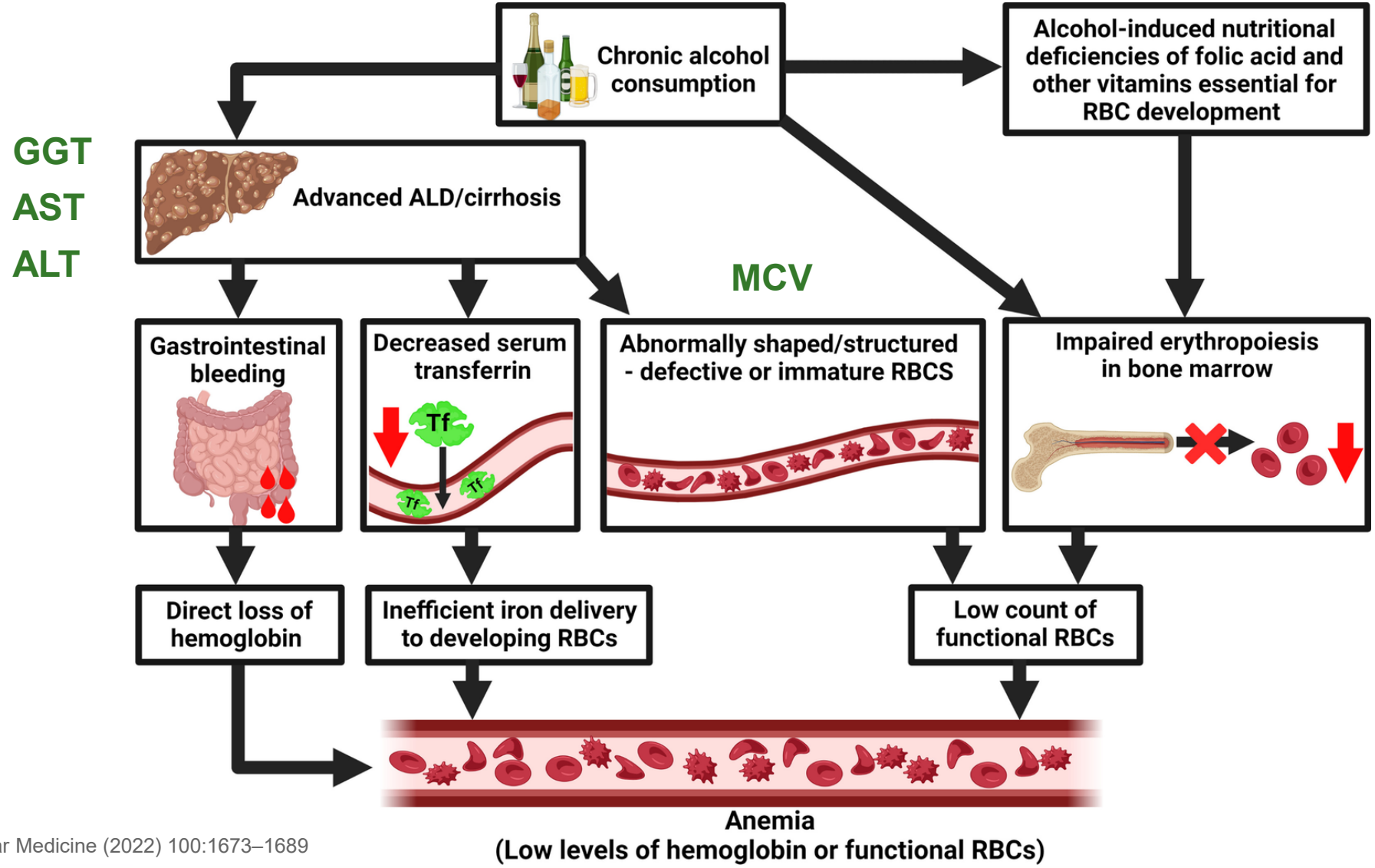
…and only a small amount can be detected



https://arup.utah.edu/media/johnsonDavis-alcoholUseMarkers-2020/lecture-slides.pdf

Direct and indirect alcohol biomarkers

Direct Markers	Indirect Markers
Ethanol	Carbohydrate deficient transferrin (CDT)
Ethanol Metabolites (EtG + EtS)	Gamma glutamyl transferase (GGT)
Phosphatidylethanol (PEth)	Mean corpuscular Volume (MCV)
	Aspartate amino transferase (AST)
	Alanine amino transferase (ALT)



Journal of Molecular Medicine (2022) 100:1673–1689

Exhibit 1. Characteristics of Several Alcohol Biomarkers[6,7,8,9,10,11]

Biomarker	Type of Drinking Characterized	Sensitivity/ Specificity	Examples of Possible Sources of False Positives	General Comments
Aspartate Amino Transferase (AST), Alanine Amino Transferase (ALT)	Unknown, but heavy and lasting for several weeks	Moderate/Moderate (somewhat lower sensitivity than GGT as screen for heavy drinking)	See GGT. Excessive coffee consumption can lower values.	Primarily reflects liver damage that is often related to alcohol. ALT seems less sensitive than AST. Ratios of AST to ALT greater than 2 may suggest liver damage that is alcohol related. Performs best in adults ages 30 to 60 years.
Gamma Glutamyl Transferase (GGT)	Probably at least 5 drinks/ day for several weeks	Moderate/Moderate (as screen for heavy drinking)	Liver and biliary disease, smoking, obesity, diabetes, and medications inducing microsomal enzymes.	Most commonly used traditional biomarker. Primarily reflects liver damage that is often related to alcohol consumption. Performs best in adults ages 30 to 60 years.
Mean Corpuscular Volume (MCV)	Unknown, but heavy and lasting up to several months	Moderate/Moderate (sensitivity somewhat below GGT as screen for heavy drinking)	Hemolysis, bleeding disorders, anemia, folate deficiency, hypothyroidism, hyperglycemia, and medications reducing folate.	Poor biomarker for relapse because of sluggish response to drinking. Higher sensitivity in women than men. Performs best in adults ages 30 to 60 years.

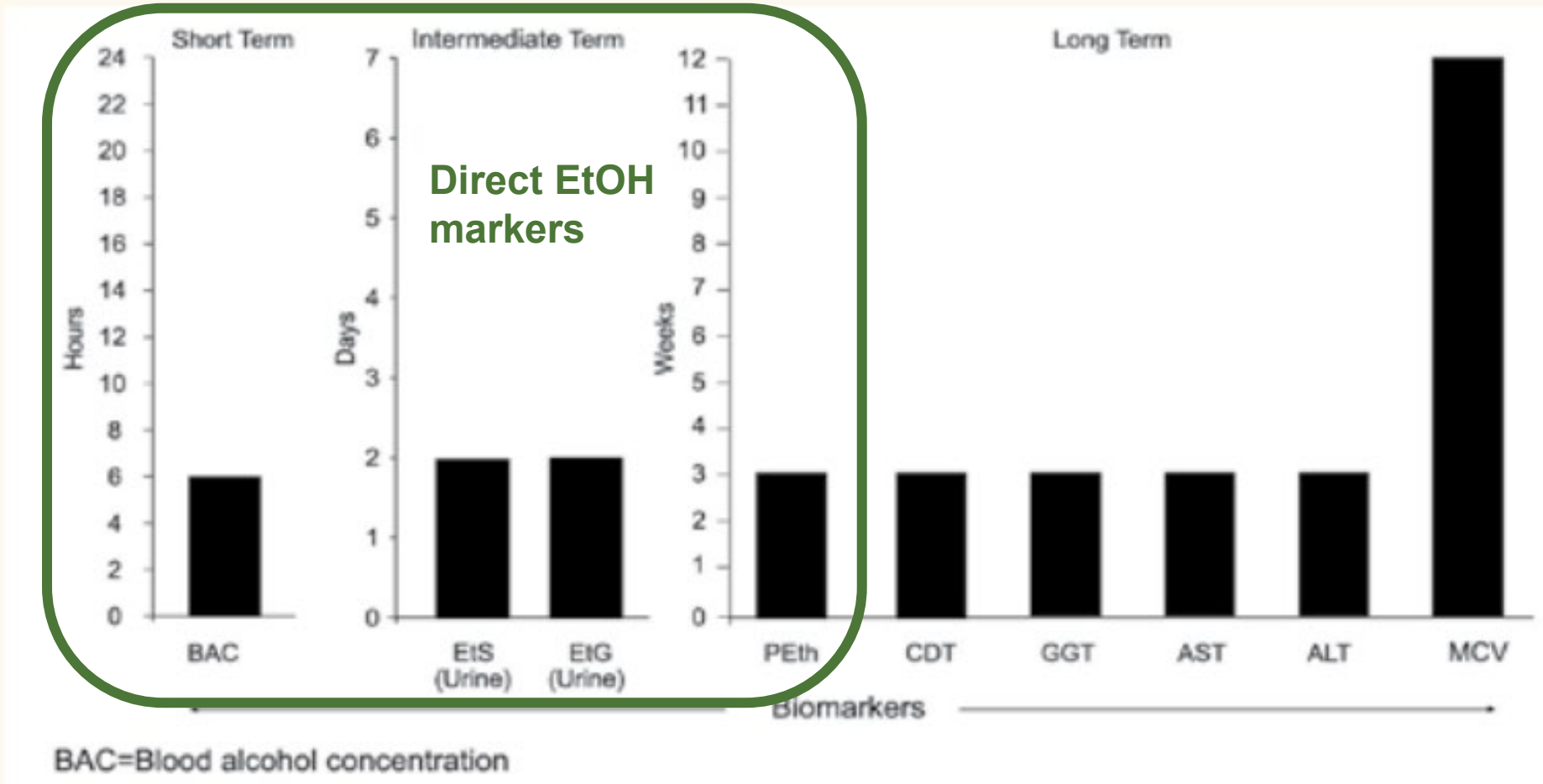
SAMHSA Advisory The Role of Biomarkers in the Treatment of Alcohol Use Disorders, 2012 Revision Spring 2012, Volume 11, Issue 2

Exhibit 1. Characteristics of Several Alcohol Biomarkers[6,7,8,9,10,11]

Biomarker	Type of Drinking Characterized	Sensitivity/ Specificity	Examples of Possible Sources of False Positives	General Comments
Carbohydrate-Deficient Transferrin (CDT)	Probably at least 5 drinks/day for approximately 2 weeks	Moderate/High (as screen for alcohol dependence)	Rare genetic transferring variant, primary biliary cirrhosis, chronic end-stage liver disease, fulminant hepatitis C. Values are also altered due to smoking or obesity.	Equal to, or possibly slightly better than, GGT, but much more specific. Biomarker of relapse to heavy drinking following a period of abstinence. Likely less sensitive for women and younger people.
Ethyl Glucuronide (EtG), Ethyl Sulfate (EtS)	Perhaps as little as a single drink	High/High (as indicator of relapse)	Extraneous alcohol exposure, such as alcohol in medications, hygiene products, cosmetics, foods, etc., can elevate values of biomarkers.	As direct analytes of nonoxidative breakdown of alcohol, highly sensitive. Probably little gender, age, or ethnicity effect. New, but promising biomarkers; more research is warranted.
Phosphatidyl Ethanol (PEth)	Possibly 3 or 4 drinks/day for several days	High/High (additional research is needed)	None likely but still unknown due to paucity of research.	Probably little gender, age, or ethnicity effect. Linear dose–response relationship with recent drinking levels. A new but promising biomarker; more research is warranted.

SAMHSA Advisory The Role of Biomarkers in the Treatment of Alcohol Use Disorders, 2012 Revision Spring 2012, Volume 11, Issue 2

Exhibit 2. Window of Assessment for Various Alcohol Biomarkers[6, 11]



SAMHSA Advisory The Role of Biomarkers in the Treatment of Alcohol Use Disorders, 2012 Revision Spring 2012, Volume 11, Issue 2

Biomarker utility in risk assessment

Binge Drinkers	Chronic Drinkers
Blood Alcohol Concentration (BAC)	Carbohydrate deficient transferrin (CDT)
Alcohol metabolites (EtG, EtS)	Alcohol metabolites (EtG, EtS)
	Mean corpuscular Volume (MCV)
	AST, ALT, & GGT
	Phosphatidylethanol (PEth)

Ethanol measurement

- Ethanol can be measured on breath, blood, and urine[1]
- Detection is limited to presence of ethanol in the specimen[1]
- Half life (t1/2) of ethanol in blood is 2-14 hours & in urine is < 24 hours[2]
- Ethanol is a volatile compound and may evaporate from the specimen[2,3]
- Mouthwash, hand sanitizer, vaping oils, kombucha, liquid cough syrups, etc. contain ethanol

1. Biomolecules. 2015 Jun 29;5(3):1339–1385
2. Nanau RM, Neuman MG. Biomolecules and biomarkers used in diagnosis of alcohol drinking and in monitoring therapeutic interventions. Published 2015 Jun 29.
3. https://arup.utah.edu/media/johnsonDavis-alcoholUseMarkers-2020/lecture-slides.pdf

Carbohydrate Deficient Transferrin (CDT)

- Transferrins are iron transport molecules with carbohydrate chains[1]
- Liver damage from excessive alcohol exposure induces transferrin isoforms with reduced (or deficient) carbohydrate chains[1]
- CDT is reported as a proportion relative to total transferrin[1]
- CDT can detect (~2 week) chronic, heavy drinking, M>F[2]
- CDT has high specificity for EtOH-associated liver damage but has been associated with hepatitis & cirrhosis[1]
- CDT may be affected by smoking, medications, and abstinence from drinking[1,2]

1. Biomolecules. 2015 Jun 29;5(3):1339–1385
2. Golka K, Wiese A. Carbohydrate-deficient transferrin (CDT)--a biomarker for long-term alcohol consumption. J Toxicol Environ Health B Crit Rev. 2004

Urine alcohol metabolites (EtG + EtS)

Alcohol Metabolites - Urine

- The presence of Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) can reveal alcohol exposure up to 80 hours post-exposure.
- EtS and EtG are both minor metabolites of alcohol and can be used to identify behaviors that might be consistent with alcohol consumption.
- The presence of EtS and EtG does not definitively mean that an alcoholic beverage was consumed

Walsham NE, Sherwood RA. Ethyl glucuronide and ethyl sulfate. Adv Clin Chem. 2014;67:47-71.

Urine alcohol metabolites (EtG + EtS)

Alcohol Metabolites - Urine

Ethyl Sulfate

- Metabolite of ethanol
- Stable in urine (not prone to synthesis or degradation)
- It's presence in urine can detect recent alcohol exposure
- Cutoff: 100 ng/mL

Ethyl Glucuronide

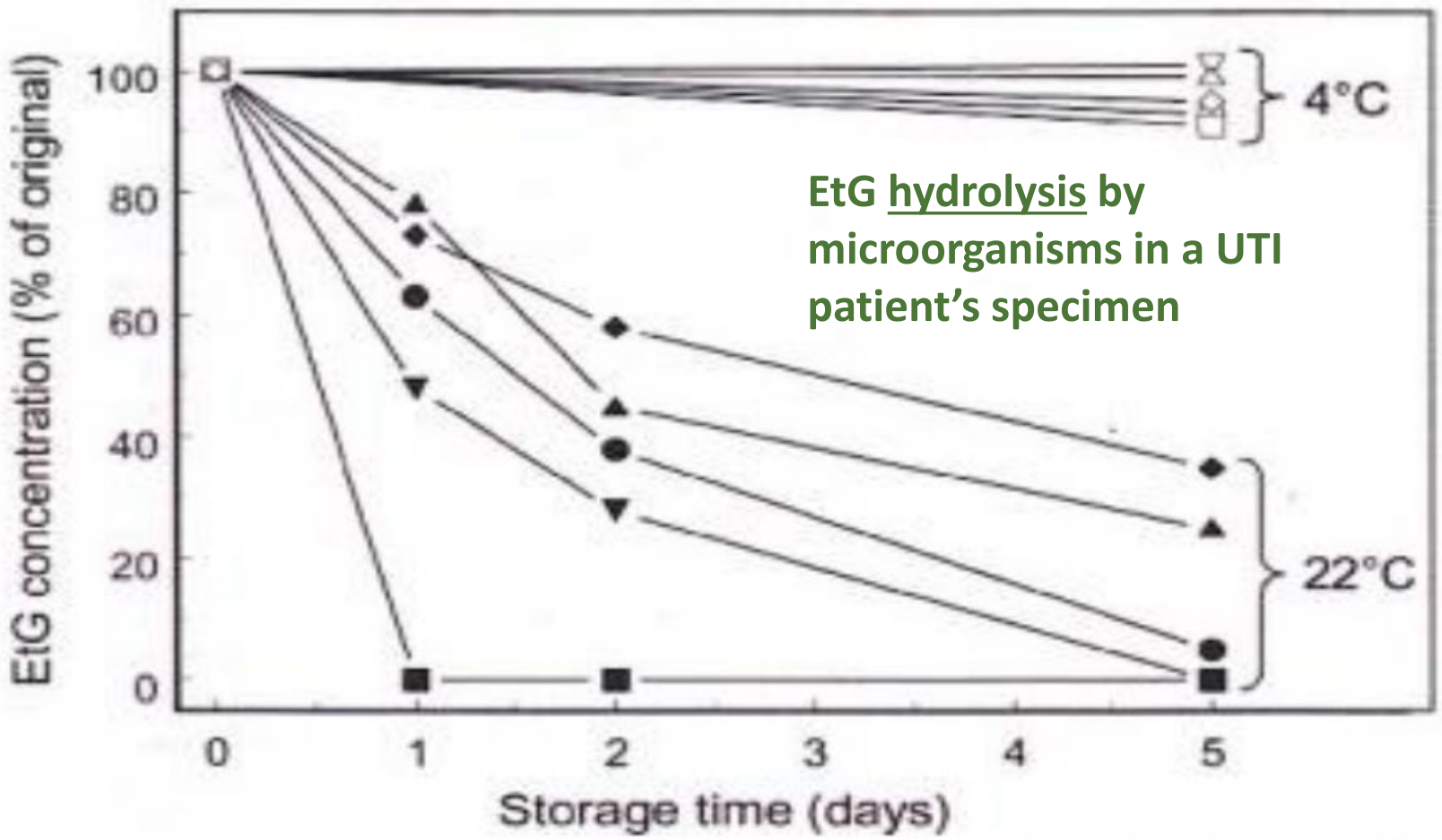
- Metabolite of ethanol
- Subject to degradation from certain bacteria (i.e., E.coli)
- Subject to synthesis from bacteria (E. coli) with yeast (Candida sp.)
- Cutoff: 500 ng/mL

Understanding EtG/EtS

- When a patient is exposed to ethanol or ethyl alcohol they metabolize it into many byproducts including acetaldehyde, ethyl sulfate and ethyl glucuronide.
- Incidental exposure to ethyl alcohol from sources such hand sanitizers, mouth wash, certain medications and some beverage sources (i.e., Kombucha) can result in low concentrations of EtS and EtG.
- Cutoffs for EtS and EtG are based on recommendations of SAMHSA.

Walsham NE, Sherwood RA. Ethyl glucuronide and ethyl sulfate. Adv Clin Chem. 2014;67:47-71.

EtG is affected in vitro by bacteria



EtG <u>hydrolysis</u> by microorganisms in a UTI patient's specimen

EtG <u>production</u> by microorganisms in a diabetic patient's specimen

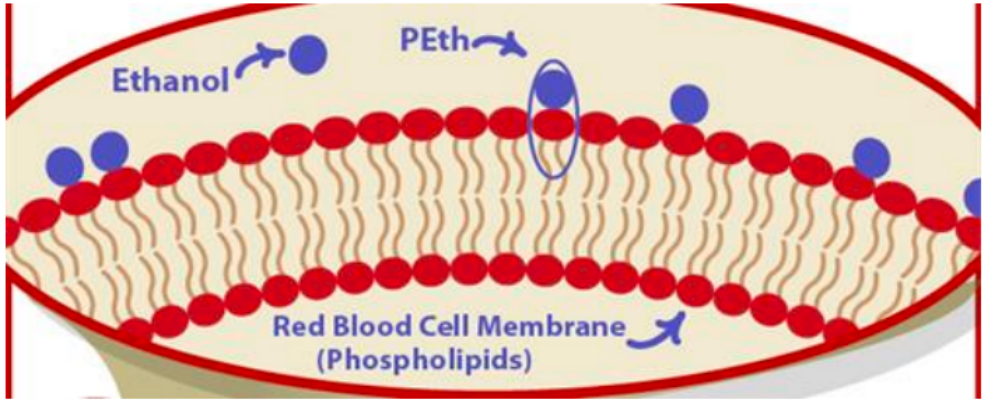
Clin Chem 2005 Sep;51(9):1728-30.

Rules of thumb-alcohol metabolites

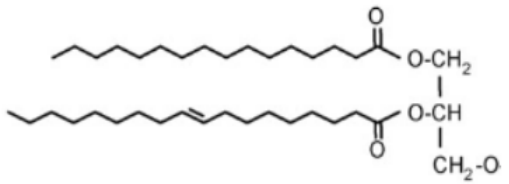
- If EtS is positive, it's POSITIVE
- Alcohol metabolites are most useful when paired

Phosphatidylethanol (PEth)

- Long-term direct biomarker of alcohol use
- Formed in the presence of ethanol
- PEths are incorporated into the membrane of erythrocytes
- PEth half-life of 4±0.7 days
- Specificity: ~100%

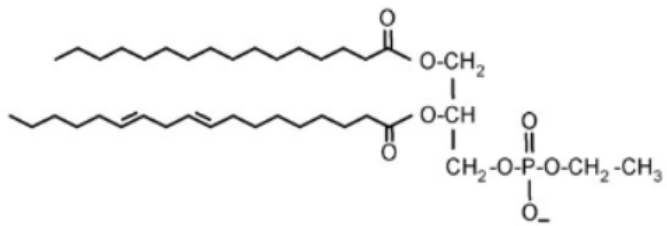


www.usdtl.com



PEth-16:0/18:1*

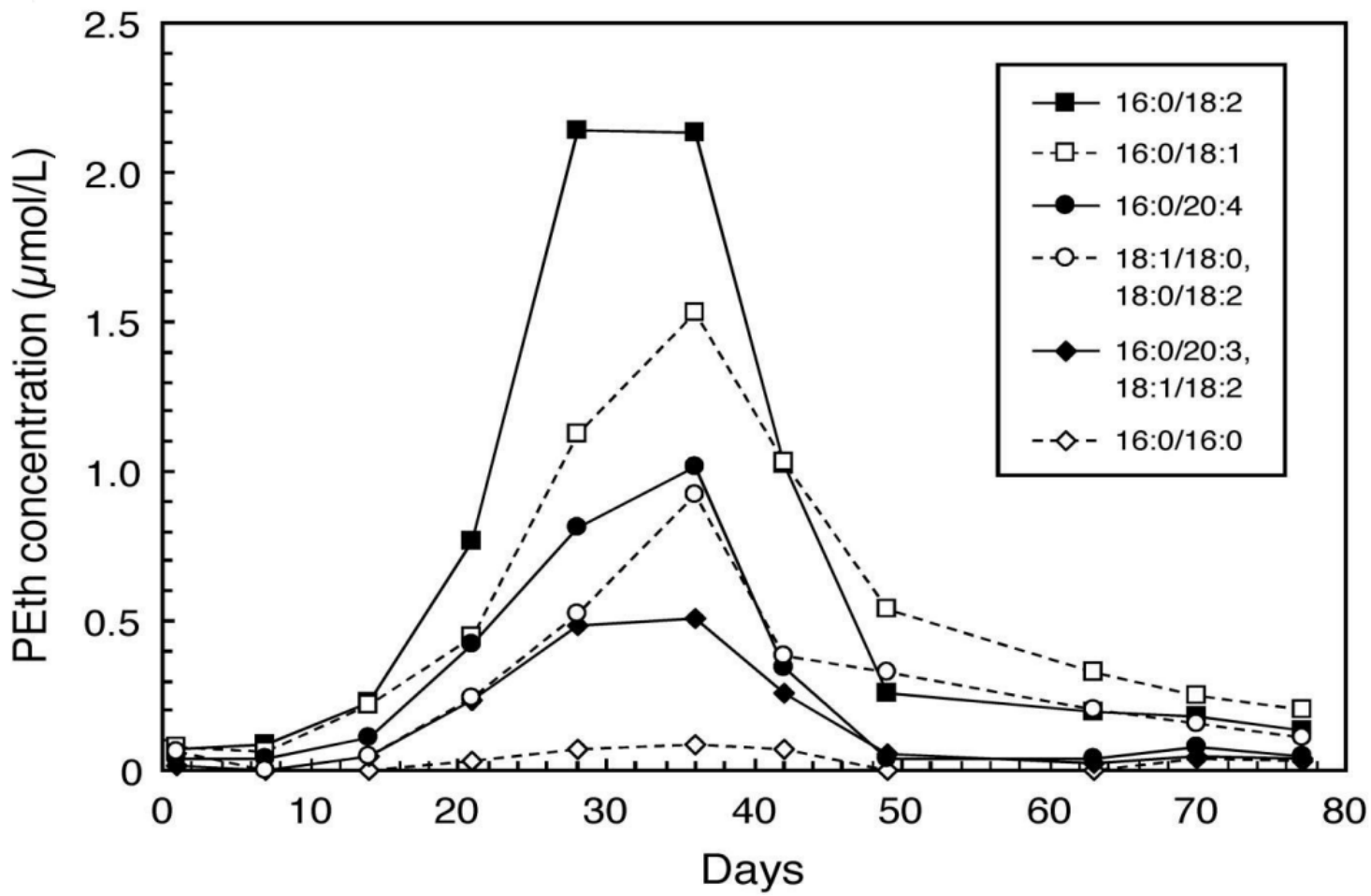
1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoethanol (POPEth)



PEth-16:0/18:2

1-palmitoyl-2-linoleoyl-sn-glycero-3-phosphoethanol (PLPEth)

Detection windows for PEth homologues



https://arup.utah.edu/media/johnsonDavis-alcoholUseMarkers-2020/lecture-slides.pdf

PEth

- PEth is blood-based and offers a long window of detection (1-2 weeks)[1]
- May be detectable for ~4 weeks in chronic, excessive drinkers[1,2]
- It is not subject to interference by incidental exposures (eg sanitizers)
- Higher alcohol consumption leads to higher PEth levels in the blood
- A PEth test may not detect a single drink or casual drinking. A positive result may indicate chronic drinking (multiple drinks/day)[1]

1. J Forensic Sci. 2018;63(6):1634-1640
2. Int J Legal Med. 2016;130(6):1527-1533

PEth – What do results mean?

- The PEth test results include 2 components that may indicate probable abstinence or probable chronic drinking and confirm the presence of PEth:

  - **16:0/18:1 (POPEth)**

    <20 ng/mL: probable abstinence[1]

    >200 ng/mL: probable chronic drinking[1]

  - **16:0/18:2 (PLPEth)***

    Confirms presence of PEth

    *Does not have established reference ranges[1]; subject to change as more data become available

1. *J Forensic Sci*. 2018;63(6):1634-1640

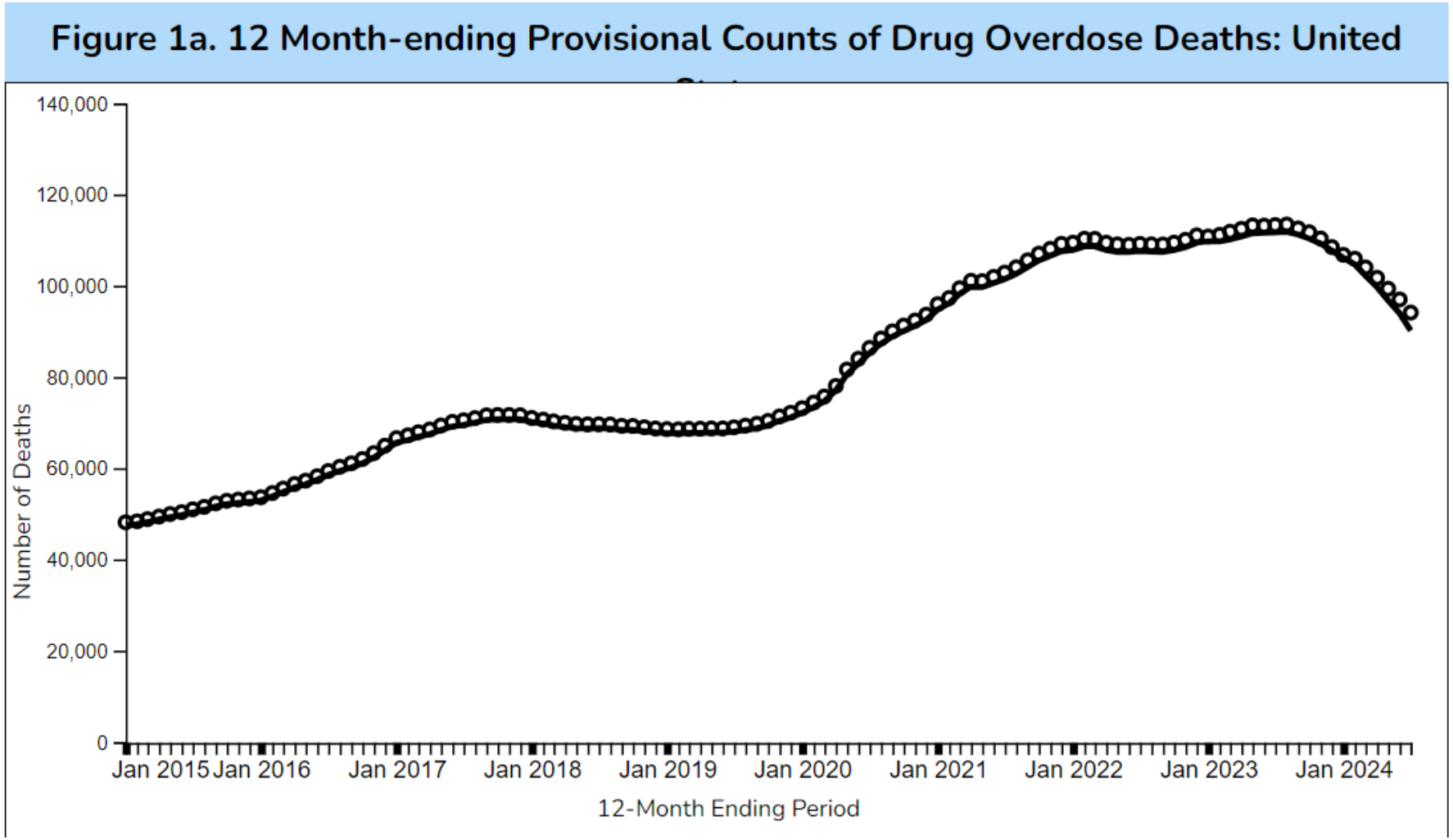
Summary

- Risks from drug and alcohol use depend on many factors- type, frequency, and amount
- Alcohol is easily accessible and represents the most used/abused substance among Americans
- Alcohol-related deaths are generally due to excessive “binges” and chronic use
- Incorporating laboratory measures can optimize catching high-risk drinkers

Biomarker utility in risk assessment

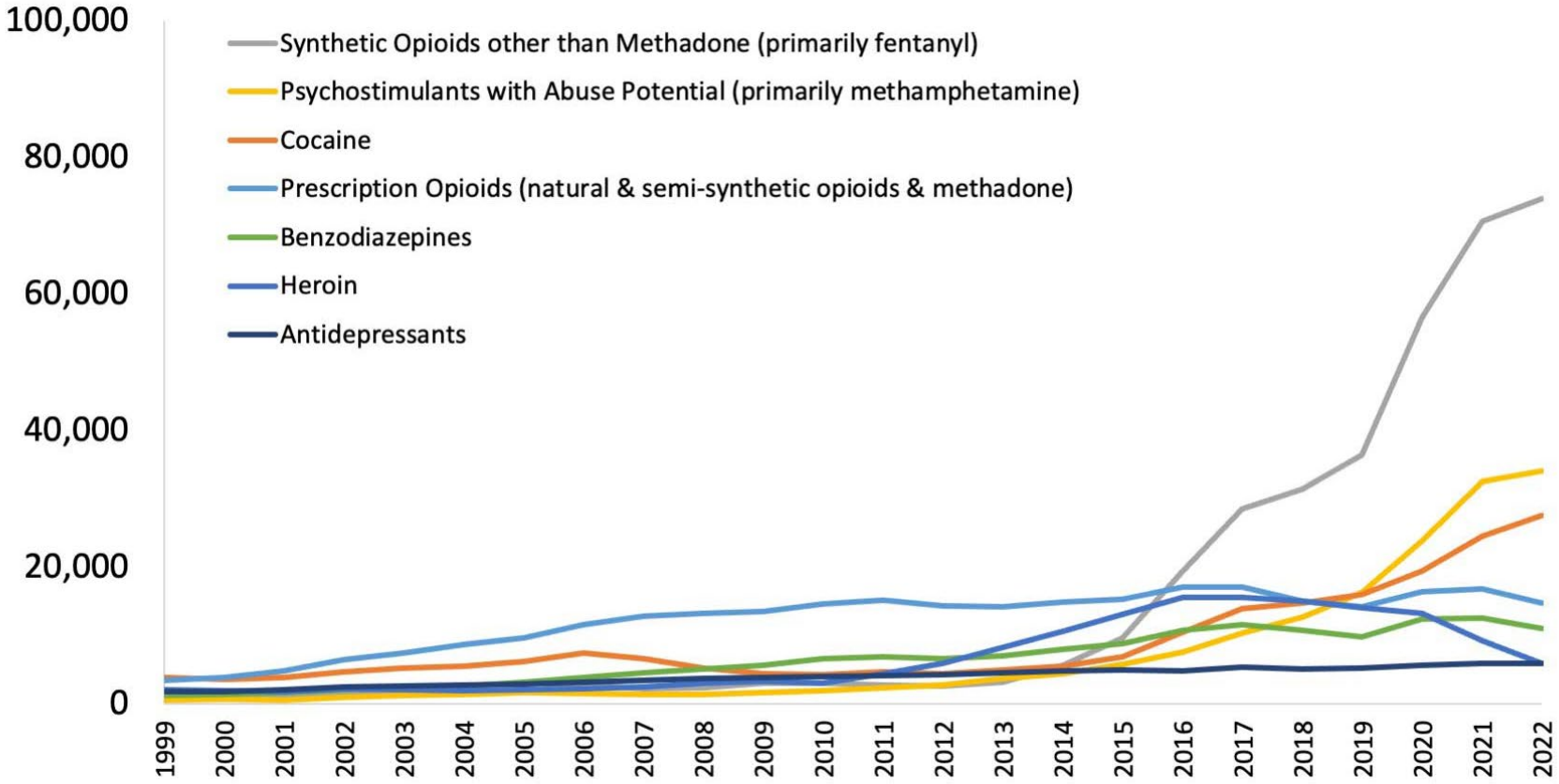
Binge Drinkers	Chronic Drinkers
Blood Alcohol Concentration (BAC)	Carbohydrate deficient transferrin (CDT)
Alcohol metabolites (EtG, EtS)	Alcohol metabolites (EtG, EtS)
	Mean corpuscular Volume (MCV)
	AST, ALT, & GGT
	Phosphatidylethanol (PEth)

Good news on the horizon?



NCHS, National Vital Statistics System. Estimates for 2023 and 2024 are based on provisional data. Estimates for 2015-2022 are based on final data (available from: https://www.cdc.gov/nchs/nvss/mortality_public_use_data.htm). Accessed Jan. 13, 2025.

Yet evaders remain…



*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024.

NIDA. 2024, August 21. Drug Overdose Deaths: Facts and Figures . Retrieved from https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates on 2025, January 9

https://theconversation.com/carfentanil-is-100-times-more-potent-than-fentanyl-and-its-killing-people-245492

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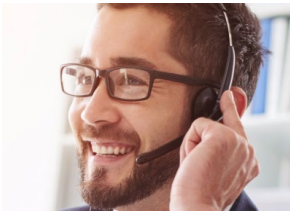
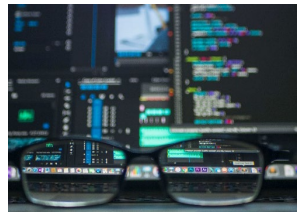


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- Attending Physician Statements
- Data products
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Leading provider
of individual health risk assessment services for life insurers in North America

Emerging leader
for collection and data services for clinical trials and academic human-subject research

4-5K
mobile phlebotomists in our national network

85%
US Population within 25 miles of Phlebotomy network

30%
Life insurance eligible exams collected in a Quest PSC

18K
Added weekly appointments at PSCs in summer of 2023

2 Day
Improvement in exam turnaround time in 2023

100+
US regional branch offices & 9 Canadian branch offices

1,500
PSCs performing life insurance exams

National call center

1.1M
phone-based medical history interviews annually

~70%
US Population Health Data

224M
Unique individuals

98B
Laboratory tests available in LabPiQture

5.8B
diagnoses

92% CSAT
score with consumers

33 NPS
score with clients

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Based on ExamOne internal reporting and metrics

JAMA. 2024;332(12):957-958. doi:10.1001/jama.2024.15563

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Thank you!