MEDICAL BITS FROM YOUR DOCTOR

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"You become strong by defying defeat and by turning loss and failure, into success".

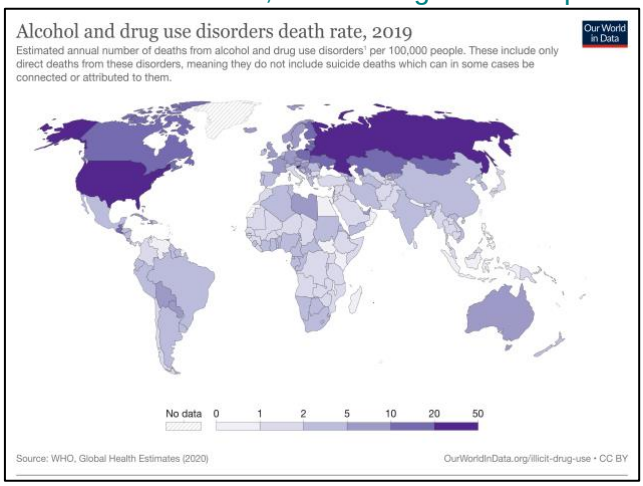
Napoleon Bonaparte

"The fool has one great advantage over the man of sense: He is always satisfied with himself."

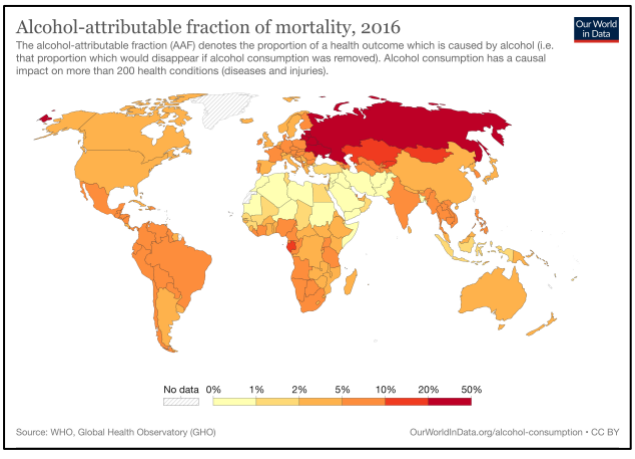
Napoleon Bonaparte

Alcohol-Associated Disease

Globally, excess consumption of alcohol is the most prevalent of all substance use disorders worldwide, with a single annual prevalence of over 100 million, leading to almost 3 million premature deaths (5.3% of global deaths). In the US, almost 70% of adults consume beverages containing ethanol and acute intoxication is associated with several acute medical and social complications, such as domestic violence, homicide, suicide and accidents. Yet, most humans recognize that moderate consumption can be pleasurable and has an important role in social engaging and bonding.

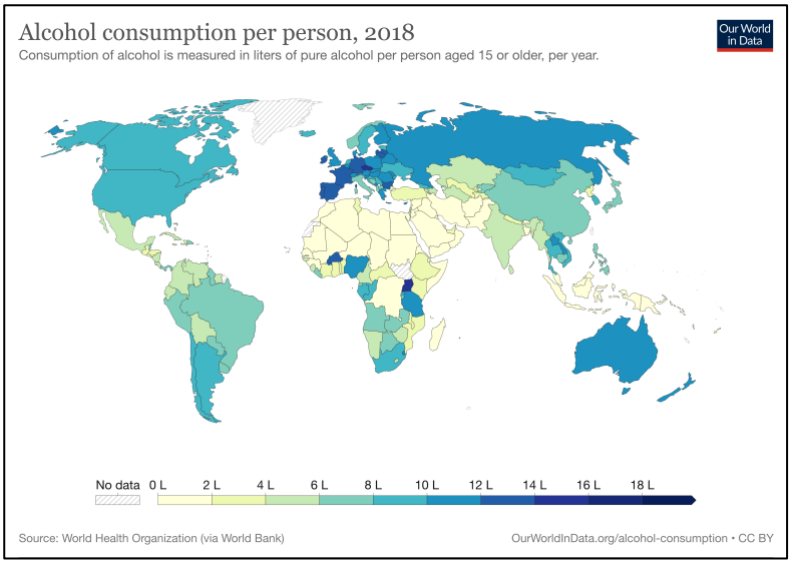


Surprisingly, whereas more than half of patients with depression take anti-depressants and almost a ¼ of patients with opioid-addiction take prescription drugs, less than 3% of alcoholics are offered medications to mitigate their excessive use.



Almost 30 million Americans suffer from it and 140,000 of them die from alcohol-related causes annually. It is the fourth highest cause of preventable death and except for tobacco, alcohol is responsible for a higher burden of disease than any other drug and consumption increased with the first pandemic of XXI century.

Thus, we decided to review this important topic and answer some basic questions.



A brief history of alcoholic beverages

Like most histories, that of alcohol is a fascinating journey that accompanies humanity from the very beginning of primitive societies and spans thousands of years. All primates are able to metabolize alcohol, and the first exposures were likely due to fermenting fruit. The archeological record is very sparse, but the oldest verifiable brewery dating back 13,000 years, was found in a burial site near Haifa. Residues of a wheat and barley-based alcohol (likely "beer") were found in mortars carved into a cave floor. Probably our ancestors honoring the dead in ritual feasts (or Israelis and Palestinians toasting to "eternal peace").

Evidence dating to 7,000 BC has also been found in Northern China in the Henan province with analysis confirming a fermented drink made of grapes, berries, honey and rice. At the same time, barley beer and grape wine making was developed in the Middle East. Some researchers think that "booze" predated the Neolithic and agriculture and some have proposed that the desire for the "Magic" of alcohol may have been an important incentive for agriculture.

Evidence of alcoholic beverages production can be found in all continents, with firm records dating back to between 5,000-2,000 BC. The medicinal use of alcohol was already mentioned in the oldest Sumerian and Egyptian texts from 2,100 BC. Testimony of alcoholic drinks has been found dating to 5,500 BC in Persia, 3,400 BC in Egypt, 2,000 BC in pre-Hispanic Mexico and 1,500 BC in Sudan. The Irish/Celtic peoples were not far behind, making different types of alcoholic ciders and beers around 3,000 BC. The ruins of Hierakonpolis, Egypt, from 3,400 BC has remains of the oldest brewery, capable of making more than 300 gallons of beer daily!

The art of wine making reached the Greek peninsula by 2,000 BC, and by the days of Homer (700 BC), wine consumption was so important that it was considered an intrinsic part of their culture and those who did not drink were felt to be "barbarians". Plato praised moderate wine consumption as important to health and happiness, but admonished against drunkenness and excess.
Hippocrates identified "medicinal properties" and later Aristotle and Zeno admonished against excessive consumption.

Bacchus, enlivened Roman banquets. Dionysus, Greek Symposia! Both have been busy, "blessing" the libations of Civilization for Millenia. The Roman belief that wine was a daily necessity for all strata of society, incentivized its production in every corner of the Roman Empire, but it appears that Romans diluted their wine (4:1 or sometimes 2:1 before drinking), moderating alcoholic consumption.

The process of distillation was discovered by the Arabs, in their Golden Age (8th century) reaching Salerno in the 12th century and paving the way for stronger spirits. In Medieval Europe, with poor sanitation, the consumption of alcoholic drinks helped avoid water-borne diseases, such as cholera and other entero-bacteria. Medieval monasteries helped preserve and advance Western culture through the replication of classical manuscripts from antiquity and disseminate new ethical and scientific ideas. In their "free time", European monks refined brewing techniques and developed various types of beer, wine and spirits. It seems that the monastic and spiritual life allowed for some "earthly pleasures".

For protestant leaders from Martin Luther to John Calvin to Anglicans, and even Puritans, alcohol was a gift of God to be used in moderation for pleasure and health. But despite the ideal of limited consumption, records indicate that most Europeans consumed up to 10 times the current libation levels.

In the Exploration age, ships carried more beer than water, as it was safer to drink beer or diluted wine than the polluted water of those days. The Mayflower was no exception and within a few years, the Colonists were engaged in making hard apple cider, which remained the beverage of choice until the mid-1800's.

The solution to the constant problem of spoilage of foods and beverages was found by no other than Louis Pasteur in the mid 19th century. It is difficult to overstate the importance of his restless scientific journey. Despite suffering a right cerebral hemorrhage at the prime of his career at the age of 45, leaving him with residual left-sided hemiplegia, most of his important contributions to science were completed by a hemiplegic Pasteur. Appropriately, Louis Pasteur and Albert Einstein have been the most celebrated scientists of human history.

Pasteur hypothesized that the spoilage of wine and milk was due to the presence of bacteria and yeast in the fluid. He heated the wine to a temperature just below its boiling point and then allowed it to cool. The process killed the harmful microbes without altering the wine. He later refined the process using different temperatures and times of heating leading to the Pasteurization, which revolutionized the food and all beverage industries at the outset of the industrial revolution, which brought about mass production.

After the age of Prohibition in the early part of the 20th century, governments worldwide stepped in to ascertain quality and alcoholic concentration, but also regulate and (mostly) tax the production and sale of alcoholic beverages.
From simple, natural and fermented concoctions, alcoholic beverages have evolved and diversified alongside humanity and continue to play a significant role in our cultural and social interactions.

Bottomline: The systematic analysis from the Global Burden of Diseases, injuries and risk factors study (GBD) is the most comprehensive estimate of the global impact of alcohol and was conducted over 26 years in 195 nations. There is no amount of alcohol consumption that is "healthy". It accounts for 2.2% of female deaths and 6.8% of male deaths and it is the leading cause of disability adjusted life-years (DALYs) among those 15-49 years-old.

In conclusion, the level of alcohol intake that minimizes your health risks is ZERO, even after consideration of the estimated positive effects on ischemic heart disease and diabetes.

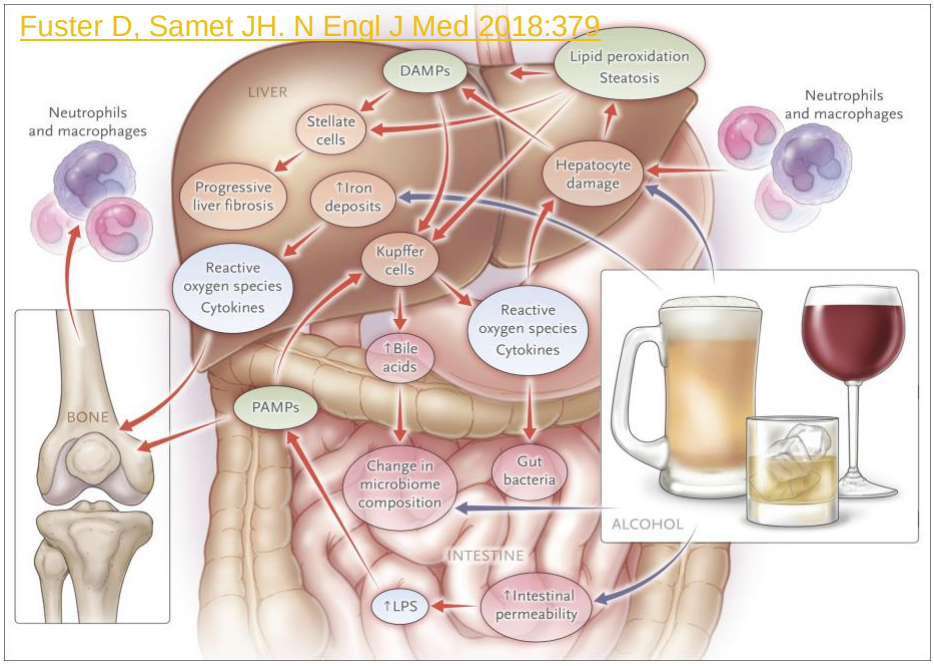
ALCOHOL-ASSOCIATED DISEASE

Upon ingestion, ethanol readily crosses cell membranes with 20% absorbed by the stomach and 80% by the proximal small bowel, with levels reaching peak blood concentration within an hour (with an empty stomach). The enzyme alcohol dehydrogenase is primarily responsible for breaking down ethanol, and its concentration is known to be less prevalent in the stomach and liver of women and Asian populations, which may place them at increased risk of complications.

Alcoholic liver disease comes in different "flavors", from simple "fatty liver" (steatosis) to alcoholic steatohepatitis (increased liver enzymes and evidence of liver inflammation) to progressive liver fibrosis which can lead to cirrhosis and also liver cancer. Once inflammation (elevated liver enzymes) has become established, abstinence may not totally reverse the damage. Acute alcoholic hepatitis is a severe complication, is associated with acute liver failure and has a mortality as high as 40%!

At-risk drinking

Our liver is able to metabolize 20-30 grams of pure alcohol daily without consequences. A standard drink (12 oz of beer, 5 oz of wine, 1.5 oz of liquor) contains 14 g of alcohol. People who drink consistently more than 4 drinks daily will develop fatty liver within 2 years, reversible with abstinence. More alcohol results in further damage and daily drinking is more deleterious than intermittent intake.

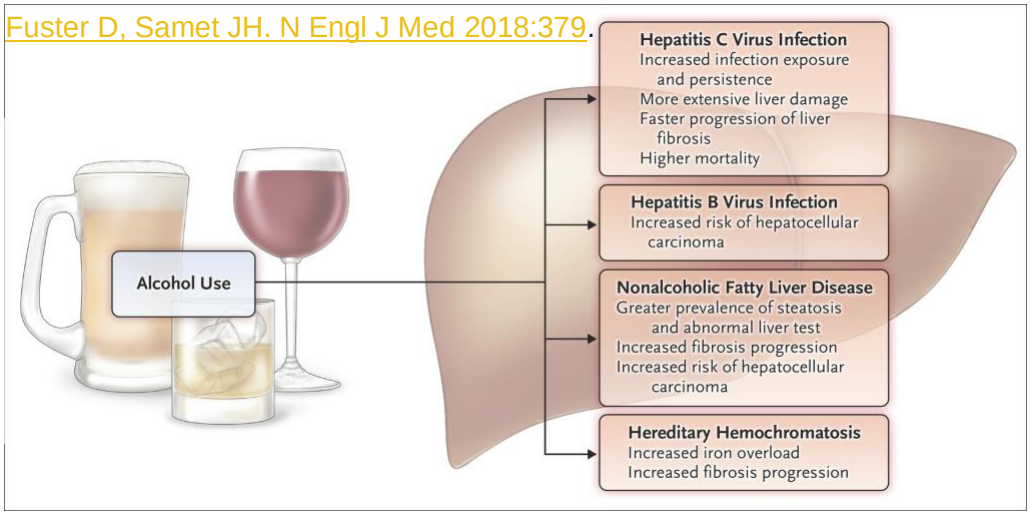


How much is too much:

- > 14 drinks weekly or 4 drinks on an occasion for healthy men.
- > 7 drinks weekly or 3 drinks on an occasion for nonpregnant healthy women.
- "Binge" drinking: heavy episodic drinking > 5 drinks for men or > 4 for women in one sitting. Associated with injuries, psychosocial problems and other poor outcomes.

The causal association between intake and liver disease is well documented, but cirrhosis develops in only 10-20% of heavy drinkers. Other conditions, such as obesity, type II diabetes, the metabolic syndrome and hepatitis C infection, increase the risk and accelerate the progression of liver fibrosis.

Alcohol appears to increase Hepatitis C and Hepatitis B replication and accelerates hepatic damage. No amount of intake is safe for those with underlying hepatitis B or hepatitis C infection. The same may apply to those with underlying hemochromatosis (iron overload).



Fuster D, Samet JH. N Engl J Med 2018:379.

There are several questionnaires developed to identify alcohol-use disorder, such as the AUDIT and AUDIT-C tools, but a single question developed by the NIH – NIAAA is simple and accurate:

"How many times in the past year did you have 5 (4 for women) or more drinks in a day?" > 0 is +.

Treatment of alcohol-withdrawal

Sudden abstinence or significant decrease in heavy alcohol intake, can precipitate an alcohol withdrawal syndrome, which is mitigated by benzodiazepines. In patients with decreased liver function, they can precipitate confusion and sleepiness (hepatic encephalopathy) and other drugs such as baclofen, clonidine, gabapentin and topiramate can be helpful.

Table 1. Summary of Pharmacologic Treatment Recommendations for Patients with the Alcohol Withdrawal Syndrome and Liver Disease.

Drug	Dosage	Use in Patients with Liver Disease
Diazepam	10–20 mg orally every 1–2 hr as needed until symptoms are minimal*	Yes, but avoid use in patients with poor synthetic function, decompensated cirrhosis, or both
Chlordiazepoxide	50 mg orally every 1–2 hr as needed until symptoms are minimal*	Yes, but avoid use in patients with poor synthetic function, decompensated cirrhosis, or both
Lorazepam†	2 mg orally every 1–2 hr as needed until symptoms are minimal*	Yes
Oxazepam†	30 mg orally every 1–2 hr as needed until symptoms are minimal*	Yes

Fuster D, Samet JH. N Engl J Med 2018:379

Promotion of Abstinence

There are several strategies for prevention of relapse that can be implemented in primary care settings, such as a supportive Pt-Dr relationship, regular follow-up visits, mobilizing family and friend support, engaging in 12-step programs and facilitating positive lifestyle changes as well as having a plan for early recognition and management of relapses.

Treatment Goals:

- Abstinence and/or reduction of intake
- Participation in counseling / mutual help groups
- Promote pleasant and sober activities.
- Restoration of self-esteem
- Resolution of alcohol-associated social problems.
- Improved overall physical health and fitness.

Interventions:

- Motivational Interviewing
- Cognitive Behavioral Therapy
- Residential treatment
- Mutual help groups
- Contingency management
- Combined behavioral intervention
- Medical management

Pharmacologic treatments to promote abstinence

There are several medications approved by the FDA for treatment of alcohol-use disorders, but some should be used with caution in patients with abnormal liver function.

Treatment should be offered for at least 3 months and frequently for longer than a year.

Disulfiram blocks acetaldehyde dehydrogenase, triggering nausea, vomiting and flushing when alcohol is consumed and was approved in 1951.

Table 2. Summary of Pharmacologic Treatment Recommendations for Patients with Alcohol-Use Disorder and Liver Disease.

Drug	Dosage	FDA-Approved for Treatment of Alcohol-Use Disorder*	Use in Patients with Liver Disease
Naltrexone	50 mg orally once a day or 380 mg intramuscularly monthly for ≥4 mo	Yes	Yes, but use with caution in patients with acute hepatitis and decompensated cirrhosis
Disulfiram	250–500 mg once a day for ≥3 mo	Yes	No
Acamprosate	666 mg three times a day†	Yes	Yes
Baclofen	10 mg three times a day; ≤80 mg once a day	No	Yes‡
Gabapentin	900–1800 mg once a day	No	Data are limited§
Ondansetron	1–16 μg per kg of body weight twice a day	No	Data are limited¶
Topiramate	300 mg once a day	No	Data are limited‖
Varenicline	2 mg once a day	No	

Fuster D, Samet JH. N Engl J Med 2018:379

Naltrexone is an opioid receptor blocker, that reduces the alcohol-induced dopamine release in the brain pleasure centers, decreasing the motivation to drink and is more effective in males with family history of alcoholism and high levels of craving. Acamprosate, Nalmefene, Gabapentin and Baclofen also have benefits and can be very helpful in the right setting.

Semaglutide (Ozempid and Wegovy) and similar drugs may also be effective to curb drinking and reduce alcohol cravings. There are ongoing NIH supported randomized clinical trials to determine if semaglutide is effective for alcoholism. We already know it is effective for fatty-liver and steatohepatitis.

Neurologic complications of alcohol

Chronic and steady excessive alcohol consumption can lead to acute and chronic neurologic complications.

Wernicke Encephalopathy, is a common acute disorder manifested by confusion, oculomotor dysfunction and ataxia (imbalance) related to thiamine (Vitamin B1) deficiency and it requires immediate thiamine replenishment to prevent death or development of Korsakoff syndrome.

Korsakoff Syndrome is a late neuropsychiatric manifestation of Wernicke encephalopathy with selective anterograde and retrograde amnesia due to damage of the medial temporal brain lobes oftentimes associated with confabulation and patients rarely recover.

Ventricular Enlargement and Cognitive Dysfunction occurs in 50-70% of individuals with long-term alcohol use disorder and has been blamed on ethanol neurotoxicity with selective neuronal density loss in the superior frontal cortex of the frontal lobes. MRIs completed before and after 3 months of abstinence show an increase in white matter volume suggesting that a component of white matter injury is reversible.

Alcoholic Cerebellar Degeneration develops in some alcoholics due to the degeneration of large neurons in the cerebellar cortex and is exacerbated by malnutrition (frequent in alcoholics), presenting with weakness, unsteadiness, leg incoordination and progressing to tremors, diplopia, dysarthria and occasionally blurred vision.

Peripheral Neuropathy occurs frequently in alcoholics and it is usually a symmetric polyneuropathy occasionally with autonomic involvement.
Myopathy or muscle loss is underrecognized but very common as well.

Non-Alcoholic fatty liver disease (NAFLD)

Since we are briefly alluding to liver disease, it's impossible to sidestep a brief description and warning on NAFLD, which is now the most common chronic liver disease worldwide with a prevalence of almost 30%! Obesity is an inflammatory condition and we now have better treatment and management tools. Remember that more than 100 million Americans suffer from obesity. Major risk factors are central obesity, diabetes, elevated cholesterol and the metabolic syndrome.

There are several new medications for management of obesity and many others in development which are very promising!

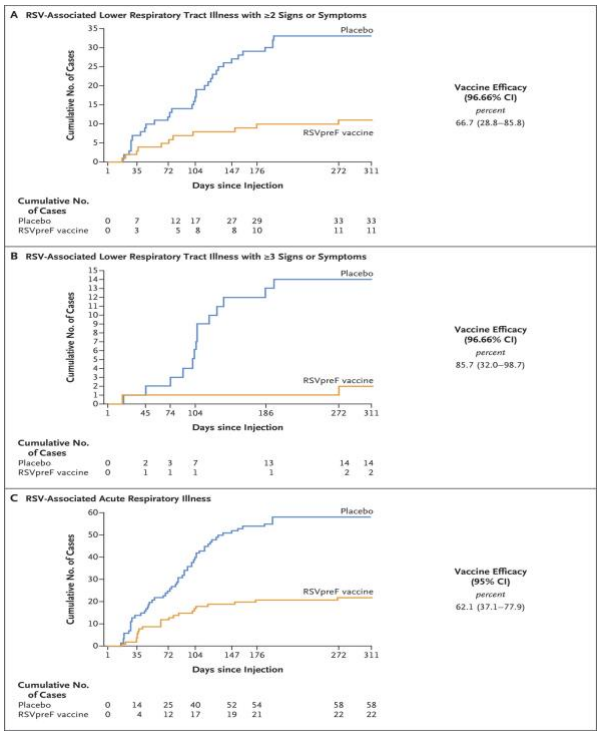
- Glucacon-like peptide-1 agonists (GLP-1) – Injectable weekly:
  - Dulaglutide, Exenatide, Liraglutide, Lixisenatide, Semaglutide
- GLP-1 – glucose-dependent insulinotropic polypeptide – Injectable weekly:
  - Tirzepatide
- Daily oral GLP-1 agonists:
  - Semaglutide and orforglipron.
- Glucose-dependent insulinotropic, glucose-like peptide 1 and glucagon receptor agonist:
  - Retatrutide.

NEW VACCINES

COVID Monovalent 2023-24 booster.

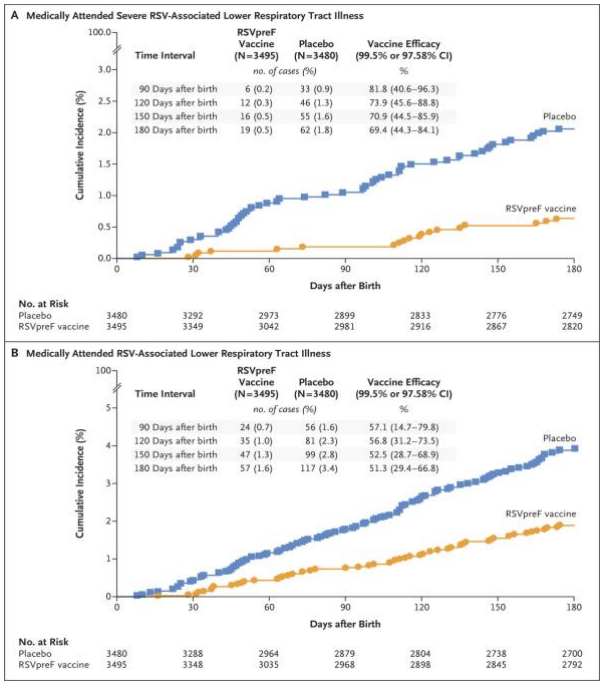
As you are all aware, two new mRNA monovalent vaccines are now available, based on the new circulating XBB.1.5 strain of coronavirus. It is anticipated to be safe and more effective than the older vaccines. As the virus continues to mutate and adapt, we must update our immunity. You have already acquired natural and vaccine-induced immunity, making vaccination optional but in my opinion, still a good idea for most of you.

Respiratory Syncytial Virus (RSV) vaccine



RSV is an important cause of lower respiratory tract disease in older adults and as anticipated earlier this year, two recombinant RSV vaccines have now been approved for individuals > 60 yo. Both are subunit vaccines based on the prefusion RSV F glycoprotein with efficacy over 80% compared to placebo and were approved by the FDA in May 2023 and recommended by the Adult Committee on Immunization Practices.

Vaccine efficacy with respect to a first episode of RSV-associated lower respiratory tract illness for the evaluable efficacy population (16,306 participants in the RSV preF vaccine group and 16,308 participants in the placebo group).



Other recent studies have also demonstrated adequate safety and efficacy.

Another phase 3 clinical trial evaluated efficacy and safety in almost 8000 pregnant women at 24 through 36 weeks' gestation, randomized to a single IM injection of 120 ucg of bivalent RSV prefusion F protein-based vaccine or placebo demonstrated safety and efficacy.

DEBUNKING MYTHS: Q & A

Vitamins are organic molecules that are essential in SMALL AMOUNTS for normal metabolism. They cannot be synthesized by our body and therefore must be ingested to prevent disease. Minerals are also essential micronutrients. This does not mean that large doses or “pharmacologic doses” of vitamins are beneficial to our health. Numerous population-based studies have been completed, with equivocal results. In conclusion: Take a multivitamin daily and if at risk for osteopenia or osteoporosis, at least 1000-2000 IU of Vitamin D3 and... be happy! More is not best and certainly not better!

Other Myths:

I have an egg-allergy. I can’t get the influenza vaccine. Myth! You can get the vaccine without any concerns. Even patients with history of egg-induced anaphylaxis have been safely immunized with influenza vaccine since it is highly purified and not contraindicated.

I have a history of GBS (Guillain-Barre Syndrome) or CIDP (Chronic inflammatory Demyelinating Polyneuropathy) and can’t receive any vaccines. Myth! In studies, no patients developed recurrent GBS or CIDP after immunization. The GBS Foundation recommends avoidance of the vaccine suspected to have caused disease if administered within 6 weeks of disease onset.

I have Pernicious Anemia and require B12 shots. Myth! Oral intake of 500-1000 ucg B12 daily is safe, cheaper and equally effective for most patients! The higher dose ensures adequate amounts become absorbed by the intestine, even in cases of Pernicious Anemia or distal small bowel resection (where B12 / Intrinsic factor complex is incorporated. Of course, there are some few exceptions to this “rule”.

HAPPY AUTUMN !!!

Dearest patient and friend Mary Hatziyannis won the MUG contest!

If you have 10 minutes, enjoy this time-lapse of the Entire Universe.
If you have another 10 minutes, read Dr. Fauci's reflections.

If you have 6 more minutes, the massive expanse of our Universe and the magnificent insignificance of humanity will delight you.
You will not be able to watch these two videos without smiling.

If you have 7 minutes daily, you can start to improve your fitness right now with the Scientific 7- Minute Workout. Get the app on your phone!
11 more minutes will get you in shape!
For core strength, try this 9-minute routine!
Can you pass this 10-second BALANCE TEST?

AND START EXPLORING AND PRACTICING MINDFULNESS! It will also help you lower your blood pressure and levels of stress. It will raise pain threshold and your overall sense of well-being.
THERE ARE MULTIPLE RESOURCES ON THE WEB.

Let's all remember that the only certainty in life, is death and the only fountains of youth proven by science and experience are love, exercise, laughter, humor and a positive attitude!

OFFICE UPDATES

- Olivia Dragovits (oliviad@chevychasepulmonary.com) is my assistant, always ready to help with her wonderful demeanor and multi-tasking abilities, as she works towards her Medical School acceptance.
- Emily Swearingen, Moghaddaseh Hosseini and Lauren Roling joined us this summer and along with Nicole Loy and Jonathan Sir are always ready to help with your office needs as they continue to work towards their Medical School acceptance.
- Our former assistants continue to make progress towards their Medical degree. Patty Zhao is now a 4th year student at UVa. Emily Ferguson is a 3rd year student at Jefferson University in PA. Simran Singh is now a second-year Med School student at University of Buffalo.
- Samantha Morales is now at University of South Carolina School of Medicine. Andrew Fookes is at Georgetown University School of Medicine nearby and Nicholes Rhinesmith moved to Nashville to attend Physician Assistant School at Vanderbilt University.

Wishing you a Happy and Healthy Autumn!

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