DOES OLIVE OIL HELP YOU LIVE LONGER?

Interviewed by Hilary Farmer

Dr Marta Guasch-Ferre and colleagues recently published a paper on the major health benefits of consuming olive oil. As their paper attracted widespread media attention, NutriNews asked Dr Guasch-Ferre to discuss her study results with our readers. Marta is a Senior Research Scientist in the Department of Nutrition at the Harvard T.H. Chan School of Public Health and Instructor in Medicine at Harvard Medical School and Brigham and Women’s Hospital. She holds a PhD in Nutritional Epidemiology, and her research interests include the role of the Mediterranean diet on type 2 diabetes and cardiovascular disease. She is currently working on Dietary Interventions, metabolomics, type 2 diabetes and cardiovascular disease in the context of the PREDIMED Study (a randomized clinical trial for primary
Dr Guasch-Feré’s research is also focused on evaluating the effect of olive oil, nuts and other dietary fats on type 2 diabetes and cardiovascular disease in Mediterranean populations (the PREDIMED Study) but also in non-Mediterranean large cohorts (Nurses’ Health Study I and II and Health Professionals Follow-up Study).

**NN:** Dr Guasch-Ferre, you just had a paper published in Journal of the American College of Cardiology, which attracted quite a bit of media attention. According to your findings, people in the highest category of olive oil consumption had the lowest risk of CVD, cancer, neurodegenerative and respiratory mortality compared to those who rarely or never used olive oil. Would you like to comment on these findings?

**MGF:** In two large cohort studies (The Nurses’ Health Study and the Health Professionals Follow-up Study) with up to 30 years of follow-up, people who ate higher amounts of olive oil showed 19 percent lower risk of total and cardiovascular disease mortality, 17 percent lower risk of cancer mortality, 29 percent lower risk of neurodegenerative mortality, and 18 percent lower risk of respiratory mortality, compared with those who never or rarely consumed olive oil. Also, we observed that replacing 10 g of margarine, butter, mayonnaise or dairy fat with the same amount of olive oil was associated with 8-34% lower risk of total and cause-specific mortality. Something important to add here is that while olive oil was better than animal fat, it was not superior to other plant oils (including canola, corn, and safflower oil). Therefore, consumption of other plant oils could also be a healthy alternative when compared to animal fat, especially because they tend to be more affordable in the US compared to olive oil. However, further research is needed to confirm the effects of plant oils on health outcomes.

This is the first long-term study on olive oil and mortality, which includes more than 90,000 participants followed for up to 30 years, that has been conducted in the American population. Previous studies were conducted in Mediterranean and European populations where the consumption of olive oil tends to be higher. In recent years, olive oil has become more popular in the US and its consumption has increased.

**NN:** Might this lower risk factor also be attributable to the fact that most people who follow healthier diets such as the Mediterranean Diet also, in general, have overall healthier lifestyles?
MGF: This is a good point and it is certainly important to focus on a healthy diet and lifestyle, and not just on a single dietary factor. However, the models were adjusted for multiple confounders including dietary factors, lifestyle factors, history of diseases as well as socioeconomic status factor, and the associations were significant, even after adjusting for BMI. Several previous studies, including the large PREDIMED trial, have shown the beneficial effects of olive oil consumption on health. I think it is especially important to consider olive oil as a good substitute for other, unhealthier fats.

NN: I found it very interesting that higher olive oil consumption is also associated with a 29% lower risk of neurodegenerative mortality. Can you offer some kind of explanation for this?

MGF: This was probably one of the most novel results of the study. The evidence on olive oil and cardiovascular health is quite strong, however, research on neurodegenerative diseases is lacking. That said, because much of dementia is due to vascular disease, the strong evidence that higher olive oil intake can reduce risk of cardiovascular disease provides additional support for a reduction in the risk of cognitive decline and dementia. Mechanistic evidence is accruing in support of the hypothesis that olive oil, particularly the virgin variety rich in bioactive polyphenols, also reduces the underlying pathology of Alzheimer's disease and other neurodegenerative diseases. There has also been some evidence on the benefits of the Mediterranean diet on the risk of cognitive decline.

NN: This is the first long-term observational study on olive oil consumption and mortality in the US. How do your findings compare with previous studies conducted elsewhere?

MGF: What is important about this study is that even low amounts of olive oil can offer some benefit on reducing the risk of premature death, especially when substituting other types of fats for olive oil. It is a combination of both reducing the amount of unhealthier fats while adding healthy fats such as olive oil. The main difference with previous studies, for example the PREDIMED Study and other studies conducted in Spain or Mediterranean regions, is that the consumption of olive oil in the US is much lower. For example, the mean intake in the analyzed populations was 10 g per day while in the PREDIMED Study it was 40 g per day even before starting the trial, but we have still observed its beneficial associations with health outcomes. Importantly, the analyzed cohorts (NHS and HPFS) are one of the cohorts worldwide with better repeated measurements of diet throughout the years (starting in the 1980s and until today). We have used updated dietary data every 4 years and other factors every 2 years; we have used several statistical methods to capture the diet throughout the follow-up period (cumulative average of olive oil during follow-up) to minimize the potential bias of using a single measurement.

NN: Your findings also suggest that consuming olive oil vs butter, margarine, and other animal fats is also associated with lowers risk of CVD, cancer, and other chronic diseases. What would you suggest people try do to gradually replace these unhealthy fats in their diet with olive oil?

MGF: The first step would be to try using olive oil for salads or bread. Then gradually, people can start using olive oil for cooking instead of butter or other animal fats. Some people believe that olive oil can't be used for frying, but it is a misconception because it can be used for frying. In addition, it can also be used for baking. Another nice idea is to cook ‘sofrito’ which is a traditional Mediterranean sauce made with tomatoes, onion, peppers, garlic, bay leaves, and species cooked in olive oil. That pairs well with rice and pasta.

I was born and raised in Barcelona, and traditionally we use olive oil as the main source of fat and almost for everything. Olive oil is very accessible and commonly used in Spain. My grandfather and also my husband’s grandfather had a lot of olive trees; even now our family gets cold pressed extra virgin olive oil from our family trees. We try to bring olive oil when we go home for vacation and use it here in Boston.
**NN:** What made you decide to undertake this study in the first place?

**MGF:** I have always been interested in the health effects of olive oil, nuts, and the Mediterranean diet. Indeed, my thesis work was conducted in the PREDIMED Study looking at the associations of key components of the Mediterranean Diet, olive oil and nuts, on cardiovascular disease and mortality. When I started my postdoctoral training at the Department (almost 7 years ago!) I thought it would be very interesting to replicate the findings of my thesis on US cohorts where the intake of olive oil is lower but is becoming more popular. Since then, we have published several papers on olive oil, including the associations with type 2 diabetes, CVD, and now mortality. I think looking at all-cause and specific-mortality is interesting because not much research has been done in large cohort studies and the repeated measurements of diet in the cohorts are very interesting data to explore.

**NN:** Does the type of olive oil (virgin, extra virgin, light) matter?

**MGF:** Yes, this is a really good question. The extra-virgin olive oil is just cold pressed olive juice that is almost unprocessed; that is why the extra-virgin and olive oil varieties have higher amounts of polyphenols, vitamins and other bioactive components that have been associated with better blood lipid profiles and lower inflammation. However, regular olive oil still has a good fatty acid profile (mostly monounsaturated fat) that confers various health benefits. In our study, we couldn’t differentiate among the types of olive oil, which is a limitation of the study, but even so we found that olive oil consumption, no matter what the type, is associated with lower risk of death. In one of our previous studies in the PREDIMED, the EVOO variety was the one to exert the most benefits for CVD in a Mediterranean population at high CVD risk.

**NN:** What are your main take-away points?

**MGF:** My suggestion would be to use olive oil for dressing, frying, baking, and in bread when possible. In Spain and other Mediterranean countries, a high amount (3-4 tablespoon per day or 40 g) has been recommended, but the recommended amount for US population can be moderated especially if other plant oils are also used. The key is to replace saturated fat and animal fat with unsaturated plant oils, including olive oil, for chronic disease prevention and improving longevity.

**NN:** Do you plan to expand on this research in the future?

**MGF:** Yes, this is one of my favorite lines of research, and our next work will be to look at the relationship between olive oil and weight change in the same US cohorts. There is still a myth that because olive oil contains high amounts of fat, it may lead to weight gain and obesity. However, no scientific evidence supports this notion.


NEWS IN THE DEPARTMENT

GRANTS

Josiemer Mattei, PhD, MPH, Donald and Sue Pritzker Associate Professor of Nutrition, received funding from Triple S Foundation to implement La Cajita Mutua, a program aiming to increase intake of fruit and vegetables, alleviate food insecurity, and strengthen social connections by distributing fresh locally-sourced produce to underserved communities in Puerto Rico. Abrania Marrero (doctoral candidate) and Dr Mattei are co-principal investigators.

PUBLICATIONS

Dr Mattei and her team also published the following paper:

Chronic Diseases and Associated Risk Factors Among Adults in Puerto Rico After Hurricane Maria
Josiemer Mattei, Martha Tamez, June O’Neill, Sebastien Haneuse, Sigrid Mendoza, Jonathan Orozco, Andrea Lopez-Cepero, Carlos F. Ríos-Bedoya, Luis M. Falcón, Katherine L. Tucker, José F. Rodríguez-Orengo
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2787979

Albert Salas-Huetos, PhD, Postdoctoral Research Fellow, recently published a paper in Fertility and Sterility. In this large, prospective analysis conducted among participants of the EARTH study over 14 years, the researchers found that men’s adherence to eight commonly used a priori defined healthy dietary pattern scores was unrelated to infertility treatment outcomes and semen quality parameters among couples undergoing ART. To our knowledge, this is the first study to date examining the relationship between men’s adherence to several a priori dietary patterns and couples’ ART outcomes and male semen parameters in the same cohort.

Paternal adherence to healthy dietary patterns in relation to sperm parameters and outcomes of assisted reproductive technologies. Fertility and Sterility, In Press. DOI: 10.1016/j.fertnstert.2021.10.021

Drs Jeremy Furtado and Frank Sacks along with colleagues from Pfizer and Eli Lilly have published the following paper that examines the paradox of pharmaceutical CETP inhibitors torcetrapib and evacetrapib, drugs that greatly increase HDL cholesterol levels but did not reduce cardiovascular events in phase 3 trials. HDL cholesterol, widely known as "the good cholesterol", is familiar to many of us as a marker of heart health measured by physicians as part of our primary care regimen. However, the reputation of HDL has been tarnished by recent Mendelian randomization studies and the failure of drugs of this class to reduce cardiovascular disease. Recent studies indicate that the key to understanding HDL is through the study of its many heterogeneous subspecies, each of which may have a unique function and association with disease, rather than the cholesterol content of HDL. This latest paper finds that while the drugs increased HDL overall, the increases were predominantly in dysfunctional subspecies that are not protective against heart disease. This explains, in part, the lack of clinical benefit of these treatments and highlights the need for additional research in HDL subspeciation. One burning question to which these findings logically lead... do behavioral changes that both increase HDL and reduce heart disease risk such as exercise and improving diet quality (reducing saturated fats and refined carbs while increasing unsaturated fats) increase the beneficial HDLs and reduce the dysfunctional ones? Stay tuned!

Furtado JD, Ruotolo G, Nicholls SJ, Dullea R, Carvajal-Gonzalez S, Sacks FM. Pharmacological Inhibition of CETP (Cholesteryl Ester Transfer Protein) Increases HDL (High-Density Lipoprotein) That Contains ApoC3 and Other HDL Subspecies Associated
OTHER NEWS

Healthy Living Guide 2021/2022
A Digest on Healthy Eating and Healthy Living

Once again the Department of Nutrition has published its guide for happier and healthier living. The Healthy Living Guide 2021/2022 features a mix of new and updated content from The Nutrition Source, with a focus on tips and strategies for developing healthy habits. You can also take a test on the level of your healthy living knowledge!

As we all continue to navigate the twists and turns of this ongoing pandemic and try to adjust to the “new normal”, we once again encourage you to do what you can to incorporate healthy behaviors into your daily life. This year’s edition of the Healthy Living Guide revisits the core themes of eating well, being active, and getting enough sleep with selected research highlights, as well as a closer look at some popular nutrition and lifestyle topics.

The editorial team for the Guide includes Frank Hu, MD, PhD, Chair; Fredrick J. Stare Professor of Nutrition and Epidemiology; Lilian Cheung, ScD, RD, Lecturer; Director of Health Promotion and Communication; Brett Otis, ALM, Nutrition Communications Project Manager; and Nancy Oliveira, MS, RD, Science Writer.
Download a copy of the Healthy Living Guide (PDF) featuring printable tip sheets and summaries, or access many of the full online articles if you want to explore some topics further.

https://www.hsph.harvard.edu/nutritionsource/2022/01/06/healthy-living-guide-2021-2022/

New Faculty Appointments

The following faculty have received reappointments in the Department of Nutrition:

Emily Oken, MD has been reappointed as Professor in the Department of Nutrition (secondary).

Vasanti Malik, ScD has been reappointed as Adjunct Assistant Professor of Nutrition.

Changzheng Yuan, ScD has been reappointed Adjunct Assistant Professor of Nutrition.

MONDAY NUTRITION SEMINARS

The Department of Nutrition holds its weekly Monday Nutrition Seminar Series every Monday throughout the academic year. The talks are varied, but they highlight the many different aspects of cutting-edge research that is currently being conducted in the fields of nutrition and global public health. These seminars are held from 1:00-1:50 pm and are free and open to the public. Because of COVID-19, the seminars have been presented via Zoom since March of 2020, and this zoom format will continue for now. A zoom link for viewing will be available one week prior to each seminar.

The following speakers will present in February 2022:

Feb 7  Dr Linda Adair, Professor, Department of Nutrition, University of North Carolina/Chapel Hill  
– Early Life Influences on Adult Health & Wellbeing: Comparative Studies from Low and Middle Income Countries in the COHORTS Collaboration – NGHP

Feb 14 Dr Thomas R Frieden, President and CEO, Resolve to Save - TBD

Feb 21 PRESIDENTS DAY

Feb 28 Dr William A. Masters, Professor of Food Economics and Policy, Friedman School of Nutrition, Tufts University - TBD
NEW FACES IN THE DEPARTMENT

Dr Andrea Glenn
Postdoctoral Research Fellow

Hi everyone, my name is Andrea and I am excited to be joining the Nutrition Department! I’m originally from Nova Scotia, Canada and I recently completed a PhD in Nutritional Sciences at the University of Toronto. I am also a Registered Dietitian. My previous research experience includes the role of plant-based dietary patterns and the glycemic index in the prevention and management of type 2 diabetes and cardiovascular disease. I am working under the mentorship of Dr Frank Hu, and my postdoctoral research will involve investigating the metabolomic signature of the Portfolio diet and its relationship with cardiometabolic diseases.

In my free time, I enjoy running, trying out new restaurants and recipes, and I also occasionally foster rescue dogs until they find their forever homes.

New study suggests that Epstein-Barr virus may be leading cause of multiple sclerosis

By Marianna Cortese and Kjetil Bjornevik

According to a study led by Alberto Ascherio, Professor of Epidemiology and Nutrition, and senior author of the study, and his team, multiple sclerosis (MS), which is a progressive disease that affects 2.8 million people worldwide and for which there is no definitive cure, is likely caused by infection with the Epstein-Barr virus (EBV). Their findings were published online in Science on January 13, 2022.

Ascherio states that “The hypothesis that EBV causes MS has been investigated by our group and others for several years, but this is the first study providing compelling evidence of causality. This is a big step because it suggests that most MS cases could be prevented by stopping EBV infection, and that targeting EBV could lead to the discovery of a cure for MS.”
To determine the connection between EBV and MS, the researchers conducted a study among more than 10 million young adults on active duty in the U.S. military. 955 individuals were diagnosed with MS during their period of service. Ascherio’s team analyzed serum samples taken biennially by the military and determined the soldiers’ EBV status at time of first sample and the relationship between EBV infection and MS onset during the period of active duty. After infection with EBV, the risk of MS increased 32-fold after infection but was unchanged after infection with other viruses. Serum levels of neurofilament light chain, a biomarker of the nerve degeneration typical in MS, increased only after EBV infection. Their findings cannot be explained by any known risk factor for MS and suggest EBV as the leading cause of MS.

“Currently there is no way to effectively prevent or treat EBV infection, but an EBV vaccine or targeting the virus with EBV-specific antiviral drugs could ultimately prevent or cure MS,” said Ascherio.

Dr Marianna Cortese, Research Scientist, and Dr Kjetil Bjornevik, Research Scientist, who are co-first authors of these study, further add that “EBV has long been a top suspect etiologic factor for MS and has been investigated by our group, as well as others worldwide for many years. The proof of causality has, however remained elusive. The high seroprevalence of EBV - about 95% are infected in the adult population - in combination with the fact that MS is a relatively rare disease has been a huge obstacle in demonstrating a causal link. This is exactly the obstacle that our team was able to overcome in this study. This story started 20 years ago when Drs Alberto Ascherio and Kassandra L. Munger, Senior Research Scientist, started collaborating with the US military to access the unique data of military personnel on active duty who had blood samples stored in the Department of Defense Serum Repository. This is a unique cohort with repeated blood samples collected in young adulthood, in the years leading up to when MS incidence starts to increase. Researchers analyzed a cohort of ~10 million individuals with ~60 million stored blood samples, and the confirmation of 955 individuals who developed MS during their military service, and identified 35 individuals who were EBV-negative in young adulthood and then went on to develop MS. We could show that all but one of these individuals seroconverted before they developed first symptoms of MS, and that the risk of developing MS was 32-fold increased with seroconversion vs. persistent seronegativity.

In contrast, similar analyses revealed no association between infection with cytomegalovirus (a common herpes virus with a mode of transmission similar to EBV) and MS risk. This strong link cannot be explained by other known risk factors and provides compelling evidence that EBV is the leading cause of MS. We also addressed common concerns regarding the possibility of reverse causation, i.e., that MS may increase the risk of being infected with EBV: Serum concentrations of serum neurofilament light chain, a sensitive marker of neuroaxonal injury that can increase years before the first neurological symptoms and are therefore an early marker of the disease, were increased only after EBV infection. Further, the serological response to all known human pathogenic viruses as assessed by VirScan, a high throughput technology that enables a simultaneous peptide-based antibody profiling, was similar among
cases and controls in both pre- and post-MS onset samples, apart from the serological response to EBV, indicating that MS is not associated with an immune dysregulation that increases the risk of acquiring EBV and underlining the specificity of the EBV-MS link. The findings from this study may accelerate the development of better MS treatments and an EBV vaccine.”

The article has received a considerable amount of interest from both the MS community as well as the media (Altmetric score: https://science.altmetric.com/details/120824398), and the response has been exceedingly positive.

Drs. Ascherio and Munger are shared last authors and Drs. Bjornevik and Cortese are shared first authors of the paper.


MORE RESEARCH NEWS

Does calorie labeling prompt healthier restaurant meals?

According to new research led by first author Anna Grummon, a Research Fellow in Nutrition, restaurant offerings introduced after calorie labeling went into effect in 2018 contained an average of 25% fewer calories than items introduced earlier. This is because The Affordable Care Act contains a provision that requires restaurant chains with 20 or more US locations to post calorie counts.

Grummon states that “The nationwide rollout of these calorie labels appeared to prompt restaurants to introduce lower-calorie items to their menus”. The calories of more than 35,300 menu items offered by 59 large restaurant chains in the US were analyzed by the researchers between 2012 and 2019. “These labels are giving consumers information about foods they might want to order that was not easy to access before the law,” Grummon continues. “Folks can decide how they want to use that information to meet their health goals.”
The Role of Sugar-Sweetened Beverages in the Global Epidemics of Obesity and Chronic Diseases

Dr Vasanti Malik, Adjunct Assistant Professor of Nutrition, and Dr Frank Hu, Professor and Chair of Dept. of Nutrition, recently published an invited review paper on the role of sugar-sweetened beverages (SSBs) in the global epidemics of obesity and chronic diseases in *Nature Reviews Endocrinology* [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8778490/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8778490/)

SSBs continue to be a major source of added sugar in the diet and an accumulating body of evidence has linked habitual intake with weight gain and a higher risk of type 2 diabetes (T2D), cardiovascular diseases and some cancers. For these reasons, SSBs have become a clear target for policy and regulatory action. With new evidence emerging, it is important to have updated evidence summaries that can inform dietary recommendations and policies. Our review provides a comprehensive update on the evidence linking SSBs to obesity, cardiometabolic outcomes and related cancers. We consider methods to grade the strength of nutritional research and discuss the biological mechanisms of constituent sugars. We also examine global trends in intake, including updated figures and maps using Global Dietary Database data, and discuss alternative beverages, including artificially sweetened beverages, and policy strategies targeting SSBs that have been implemented in different settings. Overall, we found that strong evidence from cohort studies and clinical trials on risk factors supports an etiologic role of SSBs in relation to weight gain and cardiometabolic diseases. Considering the high levels of consumption in many populations, including in low- and middle-income countries that are underlying rapid urbanization, we suggest that policy efforts across different levels of jurisdiction are needed to help reduce intake of SSBs.
Welcome to the fourth of our monthly updates regarding Diversity, inclusion and Belonging within the Department of Nutrition! This column will provide updates regarding NUT-DIB committee efforts along with departmental wide updates for newest developments, changes, and initiatives. While we are currently establishing useful forms of communication to/from the committee, please feel free to submit anonymously via our Qualtrics form https://harvard.az1.qualtrics.com/jfe/form/SV_8D642fDG6wcRNUG

The Nutrition DIB Committee is happy to announce our official ODI Training dates! These trainings will be hosted by our Office for Diversity, Inclusion, and Belonging. Please be sure to be on the lookout for departmental announcements regarding zoom details. We have been exploring new innovative ways that allow all to share topics for discussion along with remote social events that can allow all to gather together safely. Please feel free to reach out to a committee member if you have any feedback or would like a specific topic discussed reviewed. Stay Warm!