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Another Study of Cholesterol in Older Patients

High LDL cholesterol levels, measured after age 68, were not associated with higher mortality.

As our population ages, healthy older patients often ask whether they should be concerned about their cholesterol levels. In this analysis, researchers used data from the Women's Health Initiative studies to examine associations between lipids and longevity in older adults.

A subgroup of 3600 women who were born before 1926 — and thus would be age 90 or older by the year 2016 — were included in this cohort. Lipids were measured when participants were 68 to 81 years old; those with histories of cardiovascular disease or cancer were excluded. After adjustment for numerous potentially confounding medical and lifestyle variables, no association was found between HDL cholesterol levels (at ages 68–81) and survival to age 90. However, women whose LDL cholesterol levels were in the two highest quartiles (149–183 mg/dL and >183 mg/dL) had higher odds of survival to age 90 with intact mobility, compared with those whose LDL cholesterol levels were lower than 126 mg/dL (odds ratios, ≈1.4).

COMMENT: In another recent observational study of older men and women with no history of cardiovascular disease, higher LDL cholesterol levels in those who were 75 or older were not associated with risk for subsequent coronary events (NEJM JW Gen Med Jan 15 2020 and *J Am Geriatr Soc* 2019; 67:2560). In the current study, higher LDL cholesterol levels in relatively healthy older women actually were associated with longer survival. Until we have compelling evidence that cholesterol-lowering drugs improve clinical outcomes in such patients, we should emphasize healthy lifestyle and resist pharmacologic intervention.

CITATION(S): Maihofer AX et al. Associations between serum levels of cholesterol and survival to age 90 in postmenopausal women. *J Am Geriatr Soc* 2020 Feb; 68:288. (<https://doi.org/10.1111/jgs.16306>)

Neurology 2020 Jan 8

Acute Sleep Loss and Plasma Biomarkers of Brain Health

In young, healthy men, plasma levels of total tau but not amyloid were elevated after acute sleep loss.

Biomarkers in the cerebrospinal fluid (CSF) have shown changes after acute sleep loss, but data are limited on how acute sleep loss affects plasma levels. In this two-condition cross-over study, investigators obtained plasma cerebral biomarker levels in 15 young, healthy men (mean age, 22 years) after one night of acute sleep loss and one night of normal sleep in a controlled laboratory environment. The investigators measured participants' fasting plasma levels of amyloid beta-42 (A β 42), amyloid beta-40 (A β 40), total tau, neurofilament light protein, and glial fibrillary acidic protein (GFAP) at 19:30 and 7:30 hours. The participants either slept or stayed awake between 22:30 and 7:00 hours.

Compared with normal sleep, plasma total tau levels had a greater evening-to-morning increase after sleep loss. Between the two sleep conditions, no significant differences in evening-to-morning changes were apparent in plasma A β , neurofilament light protein, and GFAP. Significant evening-to-morning decreases in plasma A β 42 and GFAP were determined to be sleep-independent.

COMMENT: These results suggest that plasma total tau can increase after acute sleep loss in younger men, which is similar to studies showing increased CSF tau levels in older adults after acute sleep loss. Prior studies have shown that sleep loss affects diurnal patterns in CSF A β 42 levels, although a similar pattern was not seen with plasma A β 42 levels in this study. The National Sleep Foundation recommends 7 to 9 hours of sleep in adults aged 18 to 65 years and 7 to 8 hours of sleep in those aged >65 years (*Sleep Health* 2015; 1:233). How long-term effects of chronic sleep loss and insufficient sleep affect plasma levels of cerebral biomarkers requires further research.

CITATION(S): Benedict C et al. Effects of acute sleep loss on diurnal plasma dynamics of CNS health biomarkers in young men. *Neurology* 2020 Jan 8; [e-pub]. (<https://doi.org/10.1212/WNL.0000000000008866>)

BMJ 2020 Jan 8; 368:l6669. (<https://doi.org/10.1136/bmj.l6669>)

Just How Much of a Benefit Do We Get from a Healthful Lifestyle?

A long-term analysis suggests that adopting such a lifestyle at midlife might add as long as 10 years of disease-free life.

Virtually everyone knows that a healthful lifestyle — never smoking, normal body-mass index (BMI), moderate-to-vigorous physical activity, moderate alcohol intake, and a higher-quality diet — is good for their health. What very few people know is *just how much* benefit they get from achieving *all* these lifestyle goals.

A Harvard team examined data from about 111,000 people at age 50 and followed them prospectively for as long as 34 years. Healthful lifestyle factors were measured repeatedly and systematically, and development of various diseases and death were recorded. The primary endpoint was life expectancy free from diabetes, cardiovascular diseases, and cancer. Women who met all the healthful lifestyle measures had an additional 10.7 years of disease-free life compared with women who met no healthful lifestyle measures. For men, the number was 7.6 additional disease-free years.

COMMENT: Most of my patients know that a healthful lifestyle is good for them, but very few appreciate just how good — which negatively affects their desire to adopt one. This report might be helpful in that regard. You can say to your 50-year-old patient: “Adopting a healthful lifestyle (compared with not doing so) might allow you to live an additional 7 to 10 *disease-free* years.” For many, that would be an attractive and meaningful goal.

CITATION(S): Li Y et al. Healthy lifestyle and life expectancy free of cancer, cardiovascular disease, and type 2 diabetes: Prospective cohort study. *BMJ* 2020 Jan 8; 368:l6669. (<https://doi.org/10.1136/bmj.l6669>)

Lancet 2020 Feb 9

“Accelerated Surgery” for Hip Fractures Produces Modest Benefits

In a randomized trial, surgery within 6 hours of presentation resulted in a 1-day shorter hospital stay.

In high-income countries, about 95% of hip fractures are managed surgically. Observational studies have suggested that “accelerated surgery,” within a few hours of diagnosis, is associated with lower risks for major complications and short-term mortality than is standard care.

Researchers enrolled 2970 patients (mean age, 79) in 17 countries who presented during usual working hours with low-energy mechanism hip fractures that required surgery; patients were randomized to accelerated surgery (goal was to operate within 6 hours of diagnosis) or standard care. The median time to surgery in the accelerated-surgery group was 6 hours; in the standard-care group, it was 24 hours.

The primary outcomes, mortality and a composite of major complications (i.e., death, myocardial infarction, stroke, venous thromboembolism, sepsis, pneumonia, and major bleeding) within 90 days after surgery, were similar in both groups. However, compared with patients in the standard-care group, those randomized to accelerated surgery had significantly fewer strokes, infections without sepsis, urinary tract infections, and episodes of delirium. Accelerated-surgery patients were mobilized about 1 day earlier on average and were discharged from the hospital about 1 day sooner.

COMMENT: Accelerated surgery might prevent some complications by shortening the period of immobilization, pain, and urinary catheterization that typically precedes hip fracture surgery. Accelerated surgery also might shorten hospital stays, but it requires additional resources for rapid medical optimization and disrupts operating room schedules. These researchers are conducting an economic analysis to determine whether the costs of accelerated surgery are justified by its relatively modest benefits.

CITATION(S): The HIP ATTACK Investigators. Accelerated surgery versus standard care in hip fracture (HIP ATTACK): An international, randomised, controlled trial. *Lancet* 2020 Feb 9; [e-pub]. ([https://doi.org/10.1016/S0140-6736\(20\)30058-1](https://doi.org/10.1016/S0140-6736(20)30058-1))

Physical Therapy vs. Meniscectomy in Osteoarthritis Patients with Meniscal Tears

Outcomes at 5 years were not different.

In the previously published METEOR study ([NEJM JW Gen Med May 1 2013](#) and *N Engl J Med* 2013; 368:1675), researchers randomized 350 patients with meniscal tears and mild-to-moderate osteoarthritis (OA) to physical therapy (PT) alone or meniscectomy followed by PT. Intent-to-treat analyses showed that physical function and pain improved equally in the two groups at 6 and 12 months; however, 30% of PT-alone patients had crossed over to surgery by 6 months, and another 5% had crossed over at 12 months.

The METEOR researchers now report 5-year outcomes in the same patient population. Standardized OA pain scores (the primary outcome) improved in both groups during the first 24 months and were stable at 24 to 60 months. Twenty-five patients (7%) underwent total knee replacement (TKR; a secondary outcome) during the 5-year follow-up. In an intent-to-treat analysis, TKR risk in those randomized to partial meniscectomy or PT alone was not significantly different. However, in an as-treated analysis (combining patients initially randomized to meniscectomy plus those who crossed over to it), meniscectomy recipients were more likely to undergo TKR than were those who received PT alone (10% vs. 2%). This difference was significant after adjustment for baseline characteristics.

COMMENT: This 5-year follow-up reinforces the initial 1-year message — outcomes with PT alone and meniscectomy were the same at 60 months. Hence, PT should be the initial option for OA patients with meniscal tears, and surgery should be considered only if PT fails. Moreover, in the as-treated analysis, patients who underwent meniscectomy had a higher likelihood of requiring TKR; previous studies have suggested that partial meniscectomy might predispose patients to progression of OA.

CITATION(S): Katz JN et al. Five-year outcome of operative and nonoperative management of meniscal tear in persons older than forty-five years. *Arthritis Rheumatol* 2020 Feb; 72:273. (<https://doi.org/10.1002/art.41082>)

Eczema Is Correlated with Osteoporotic Fractures

Patients with severe eczema had doubled risk for spinal fractures, compared with the general population.

Some data suggest that atopic dermatitis is a risk factor for osteoporotic fractures. Researchers used the U.K. general practice health database to perform a matched cohort study of about 500,000 adults with atopic eczema and 2,500,000 controls.

During 5 years, patients with eczema had a small but statistically significant excess risk for hip, pelvic, spinal, and wrist fractures, compared with controls (hazard ratio, 1.1). For patients with severe eczema, risk for spinal fractures was twofold higher, and risk for hip or pelvic fracture was nearly twofold higher, than risks in controls.

COMMENT: I have never thought much about fracture risk in my eczema patients, but even after adjusting for oral corticosteroid use, a significant correlation still existed between eczema severity and osteoporotic fractures. Unfortunately, these researchers could not gather data on bone density. In addition, inflammation, dietary habits, vitamin D levels, topical steroid use, and other factors might contribute to excess risk. No matter the cause, these findings encourage us to minimize use of systemic corticosteroids in atopic dermatitis patients and to consider bone-density testing in patients with severe eczema.

CITATION(S): Lowe KE et al. Atopic eczema and fracture risk in adults: A population-based cohort study. *J Allergy Clin Immunol* 2020 Feb; 145:563. (<https://doi.org/10.1016/j.jaci.2019.09.015>)

Urology 2020 Feb; 136:212

Prostatic Artery Embolization to Treat Complications of BPH

This procedure shows promise for selected patients with benign prostatic hyperplasia.

Prostatic artery embolization (PAE), an outpatient procedure performed by interventional radiologists, is an option for managing urinary retention and severe hematuria caused by benign prostatic hyperplasia (BPH). Patients at high risk for complications from more invasive treatments and patients with extremely large prostate volume are especially suitable for PAE.

In this case series from Yale University, 75 patients (mean age, 78) underwent PAE for urinary retention, ongoing or severe gross hematuria, or both conditions. All patients were considered to be poor surgical candidates because of large gland size or medical comorbidities. Most patients had 6 to 12 months of follow-up. Among the 46 patients with urinary retention, about three quarters became catheter-free during follow-up. Among the 55 patients with gross hematuria (of whom 16 had required transfusions), hematuria resolved in nearly all cases. Procedure-related complications were infrequent.

COMMENT: Prostatic artery embolization appears to have a role in treating selected patients with complications from BPH. PAE currently is performed at a number of U.S. referral centers and will likely become more available during the near future.

CITATION(S): Ayyagari R et al. Prostatic artery embolization in nonindex benign prostatic hyperplasia patients: Single-center outcomes for urinary retention and gross prostatic hematuria. *Urology* 2020 Feb; 136:212. (<https://doi.org/10.1016/j.urology.2019.11.003>)

Korea. J Allergy Clin Immunol Pract 2020 Feb; 8:690

What Are the Most Common Causes of Stevens–Johnson Syndrome?

Antiglaucoma eye drops, allopurinol, and antiseizure medications topped the list in Korea.

Based on previous U.S. epidemiologic studies, drugs most commonly associated with Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) include allopurinol, anticonvulsants (e.g., lamotrigine, carbamazepine, phenytoin, phenobarbital), sulfamethoxazole, nevirapine, and oxicam nonsteroidal anti-inflammatory drugs. Using a South Korean health claims database, researchers determined the most common causes in Korea.

They determined that carbonic anhydrase inhibitors (used as antiglaucoma eye drops), allopurinol, carbamazepine, lamotrigine, fluoroquinolones, aminopenicillins, cephalosporins, and acetaminophen (in descending order) were the main causes of SJS/TEN. For carbamazepine and carbonic anhydrase inhibitors, the time to onset ranged from 4 to 28 days, with a peak incidence occurring at 16 days; whereas for allopurinol and lamotrigine, onset was at 21 to 44 days, with a peak incidence at 32 days.

COMMENT: Interestingly, carbonic anhydrase inhibitors were the most common cause of SJS/TEN in South Korea, and sulfonamide antibiotics did not crack the top 10. This could be due to genetic differences in the Korean population or

differences in prescribing habits between Korean and U.S. clinicians. A database review has many flaws, but my take home points from this study are to always consider eye drops as a cause of SJS/TEN, especially in Asian patients, and that onset of an adverse reaction can take weeks.

CITATION(S): Yang M-S et al. Searching for the culprit drugs for Stevens–Johnson syndrome and toxic epidermal necrolysis from a nationwide claim database in Korea. *J Allergy Clin Immunol Pract* 2020 Feb; 8:690. (<https://doi.org/10.1016/j.jaip.2019.09.032>)

Hepatology 2020 Feb 3; [e-pub]. (<https://doi.org/10.1002/hep.31158>)

The Impact of Physical Activity on Nonalcoholic Fatty Liver Disease

Physical activity, specifically during leisure time and travel-to-work time, is associated with lower prevalence of NAFLD.

Studies have demonstrated an inverse association between nonalcoholic fatty liver disease (NAFLD) and physical activity (PA). However, the impact on NAFLD by type, intensity, and duration of PA is poorly understood.

To address this issue, investigators conducted a serial, cross-sectional study of 24,588 adults (mean age, 47.4 years) included in the 2007–2016 U.S. National Health and Nutrition Examination Survey. Patients with NAFLD were identified using noninvasive panels. PA was defined, based on 2018 guidelines, as >150 minutes/week of moderate-intensity PA, >75 minutes/week of vigorous-intensity PA, or an equivalent combination of the two. All patients completed a validated questionnaire that assessed occupation-related PA, transportation-related PA, leisure-time PA, and sitting time.

PA was lower in individuals with NAFLD than in those without NAFLD, in an analysis adjusted for gender and ethnicity. Individuals with versus without adequate leisure-time PA had 40% lower odds of NAFLD, and those with versus without adequate transportation-related PA had 33% lower odds of NAFLD, in analyses adjusted for multiple confounders. Sitting time had an inverse dose-response relationship with NAFLD.

COMMENT: This study adds to the literature demonstrating an inverse association between PA and NAFLD. It further suggests advising patients that increasing PA during leisure time and travel-to-work time may protect against this disease.

Note to readers: At the time we reviewed this paper, its publisher noted that it was not in final form and that subsequent changes might be made.

CITATION(S): Kim D et al. Inadequate physical activity and sedentary behavior are independent predictors of nonalcoholic fatty liver disease. *Hepatology* 2020 Feb 3; [e-pub]. (<https://doi.org/10.1002/hep.31158>)

JAMA Netw Open 2020 Jan 3; 3:e1919615. (<https://doi.org/10.1001/jamanetworkopen.2019.19615>)

Parity, Breast-Feeding, and Menopause

Pregnancy and breast-feeding appeared to lower subsequent risk for early menopause.

Women are born with a limited supply of eggs, but ovarian suppression may slow the depletion of the ovarian follicle pool. To evaluate whether parity and breast-feeding affect risk for early menopause (i.e., before age 45), researchers analyzed data from a cohort of 108,887 premenopausal participants in the Nurses' Health Study.

In multivariable models adjusted for age, menarche, smoking, alcohol, diet, obesity, infertility, and oral contraceptive use, higher parity was associated with lower risk for early menopause. Among parous women, risk for early menopause was lowest among those who breast-fed for ≥ 6 months.

COMMENT: Early menopause has been associated with excess risk for cardiovascular disease, and several studies have suggested that breast-feeding reduces maternal risk for breast cancer, ovarian cancer, endometrial cancer, diabetes, hypertension, and heart disease. This study's finding that breast-feeding delays early menopause may have broad clinical relevance; still, many women continue to find it difficult to follow breast-feeding recommendations — a stark reminder of the importance of paid maternity leave in supporting long-term maternal health.

CITATION(S): Langton CR et al. Association of parity and breastfeeding with risk of early natural menopause. *JAMA Netw Open* 2020 Jan 3; 3:e1919615. (<https://doi.org/10.1001/jamanetworkopen.2019.19615>)

Obstet Gynecol 2020 Feb; 135:352. (<https://doi.org/10.1097/AOG.0000000000003648>)

Stress Incontinence Surgery Can Improve Sexual Function

Women reported improvement in some aspects of sexual function within 1 year of surgery regardless of which procedure was performed.

Urinary incontinence affects up to 55% of U.S. women and often causes sexual dysfunction. This secondary analysis of data from two studies of surgical procedures for stress incontinence examined whether surgical correction improved sexual function and whether any one procedure was best for this purpose. Sexual activity during the preceding 6 months was reported at baseline and the 12- and 24-month postoperative visits by 924 primarily white women who underwent transobturator sling surgery (mean age, 50.0), retropubic sling surgery (mean age, 50.6), Burch procedure (mean age, 49.6), or fascial sling surgery (mean age, 49.1). Women reporting sexual activity completed validated sexual function questionnaires at each visit.

At baseline, mean sexual function scores did not differ significantly among treatment groups. At 12 months, scores improved in all groups without significant differences among procedures. Improvement persisted without rising further at the 24-month evaluation. Outcomes included less pain and fear of incontinence during intercourse, reduced avoidance of intercourse due to “bulging in the vagina,” and attenuated negative emotional reactions (e.g., fear, disgust, shame, guilt) during intercourse. No improvements in desire, arousal, orgasm, or sexual satisfaction were reported.

COMMENT: Like many other studies of sexual function, this one narrowly defined sexual activity as penetrative intercourse rather than a full range of sexual expression. Additionally, participants were not racially/ethnically diverse. The questionnaires themselves highlight some of the issues that complicate sex for women with stress incontinence. Although there was no nonsurgical or untreated comparison group, all four groups reported sustained postsurgical improvement in sexual function, suggesting that any of these procedures improve at least some components of such function.

CITATION(S): Glass Clark SM et al. Effect of surgery for stress incontinence on female sexual function. *Obstet Gynecol* 2020 Feb; 135:352. (<https://doi.org/10.1097/AOG.0000000000003648>)

https://www.cdc.gov/mmwr/volumes/69/wr/mm6905a5.htm?s_cid=mm6905a5_w

CDC Issues Guidance on New Hexavalent Vaccine for Infants

The CDC has published guidance on administering a new hexavalent vaccine to prevent diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type b, and hepatitis B infection (DTaP-IPV-Hib-HepB). The three-dose Vaxelis vaccine was approved in 2018 but is not expected to be available in the U.S. until 2021.

The vaccine is indicated for use in infants at ages 2, 4, and 6 months and is licensed for use in children aged 6 weeks through 4 years.

It counts as the first three doses of the DTaP vaccine; it should not be given as the fourth or fifth dose. In addition, a fourth dose of IPV must be given separately to protect against polio, and a booster dose of Hib conjugate vaccine must also be given.

When needed, DTaP-IPV-Hib-HepB can be administered in a catch-up schedule for children under age 5 years.

Of note, the observed rate of fever was higher with this combination vaccine than with the DTaP-IPV/Hib pentavalent vaccine (roughly 47% vs. 34%).

eLife 2020 Jan 7; 9:e49555. (<https://doi.org/10.7554/eLife.49555>)

It's Time to Abandon 98.6°F (37°C)

Analysis of changing U.S. body temperature measurements over time found a progressive decline in average normal body temperature of 0.03°C per birth decade.

Every grade schooler can tell you that normal body temperature is 98.6°F (37°C), information drawn from Wunderlich's 1851 study of axillary temperature measurements in 25,000 German patients. However, more recent studies yield an average temperature of 97.9°F (36.6°C). To understand this difference, researchers analyzed 677,423 measurements from three data sets: Union Army veterans of the Civil War (UAVCW) 1862–1930, National Health and Nutrition Examination Survey I (NHANES I) respondents 1971–1975, and the Stanford Translational Research Integrated Database (STRIDE) cohort 2007–2017.

Temperature measurements progressively decreased from the UAVCW cohort to the NHANES I cohort and then to the STRIDE cohort. Across all three cohorts, temperature progressively decreased with increasing age (−0.003°C to −0.0043°C per year). Analysis of NHANES I and STRIDE data confirmed previously reported positive correlations between body-mass index (BMI) and body temperature and between later hour of the day and increased temperatures. Over the 197 birth-year span of the cohorts, temperature steadily decreased 0.03°C per decade in both men and women and in both black and white populations. Analysis of the impact of chronic infectious diseases on body temperature in the UAVCW cohort found that tuberculosis and pneumonia diagnoses were associated with increased body temperature in the absence of fever.

COMMENT: Although axillary temperature measurements are typically lower than oral temperatures, the authors propose that the observed temperature change is unlikely to be caused by measurement variables but rather by physiologic changes. Untreated chronic infections such as syphilis, periodontitis, and tuberculosis were common in Wunderlich's time, and modern heating and cooling systems have likely decreased the physiologic stress of adapting to differing ambient temperatures that could raise resting metabolism. Both factors have likely contributed to lower average body temperatures in today's population.

CITATION(S): Protsiv M et al. Decreasing human body temperature in the United States since the Industrial Revolution. *eLife* 2020 Jan 7; 9:e49555. (<https://doi.org/10.7554/eLife.49555>)