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BMJ 2019 Aug 12; 366:l4673

Vitamin D Supplementation Didn't Lower Short-Term All-Cause Mortality

However, vitamin D₃ supplementation was associated with lower risk for cancer-related death.

Several meta-analyses have suggested that vitamin D supplementation lowers short-term mortality, especially in elders. In this new meta-analysis, researchers included recently published trials and addressed some limitations of previous analyses.

Fifty-two trials with >75,000 participants (median age, 74; ≈71% women; median follow-up, 1.2 years) were included. In most trials, vitamin D supplementation was compared with placebo or no treatment. When other agents were given (e.g.,

calcium), they were given at the same dosage to all groups. Vitamin D supplementation did not prevent early all-cause death; cardiovascular-related death; or non-cancer-related, non-cardiovascular-related death. **However, vitamin D supplementation significantly lowered risk for cancer-related death (risk ratio, 0.84; absolute difference, ≈4 fewer deaths/1000 people); this benefit was observed only in participants who received vitamin D₃ (not vitamin D₂) supplementation. A nearly significant difference for all-cause death was noted in the vitamin D₃ subanalysis.**

COMMENT: In this systematic review, vitamin D supplementation did not lower short-term risk for all-cause death; cardiovascular-related death; or non-cancer-related, non-cardiovascular-related death. However, risk for cancer-related death was significantly lowered by vitamin D₃ supplementation. The authors call for longer trials of vitamin D₃ supplementation. Note, however, that in the recently published VITAL trial (the longest-duration and largest trial of vitamin D₃ to date, with ≈26,000 participants who were followed for a median 5.3 years), no significant difference was noted in all-cause mortality, cancer-specific mortality, or incidence of invasive cancer (NEJM JW Gen Med Dec 15 2018 and *N Engl J Med* 2019; 380:33); VITAL was included in the current meta-analysis.

CITATION(S): Zhang Y et al. Association between vitamin D supplementation and mortality: Systematic review and meta-analysis. *BMJ* 2019 Aug 12; 366:14673. (<https://doi.org/10.1136/bmj.14673>)

JAMA Netw Open 2019 Aug 2; 2:e1910373

Opioids Are More Often Prescribed Later in the Day

In this study of primary care visits, opioid prescribing rates were also higher if the physician was running behind schedule.

Identifying and limiting the underlying contributing factors to unnecessary opioid prescriptions may help curb the ongoing opioid crisis. To explore the association between the time of day of primary care appointments and opioid prescribing, researchers queried a large electronic healthcare database for primary care appointments that recorded a new painful diagnosis. Patients with cancer or any opioid prescription within the previous year were excluded. Only established patients with scheduled visits seen on a day with at least 10 appointments on the clinician's schedule were included.

The analysis included roughly 678,000 adult patient visits with 5,600 primary care physicians during 2017. Physicians rarely had more than 21 appointments in a day. The overall opioid prescription rate was 4.7%. After adjustment for patient characteristics, opioids were 33% more likely to be prescribed in the last three visits of the day (visits 19–21) than in the first three visits (5.3% vs. 4.0%). Prescribing also increased with delays in appointment start time (4.4% if on time, 5.2% if ≥60 minutes late). These associations held in multiple sensitivity analyses. The association found between opioid prescriptions and appointment timing was not seen for other prescriptions, including statins, antihypertensive agents, nonsteroidal anti-inflammatory agents, and physical therapy referrals.

COMMENT — EMERGENCY MEDICINE: *Benton Hunter, MD*

These results suggest that physicians may be more likely to prescribe “what the patient wants” — or at least what they think the patient wants — when fatigued or pressed for time. These were primary care physicians, but I suspect the finding applies to emergency physicians, as we may be more likely to take the path of least resistance at the end of a shift or when the waiting room is backed up. This study provides the first step in avoiding this potential pitfall: helping us know it's there.

COMMENT — PEDIATRICS AND ADOLESCENT MEDICINE *F. Bruder Stapleton, MD*

These findings have relevance for pediatric providers and emphasize how we need to standardize prescribing and clinical practices to avoid variation and errors during a long, busy day.

CITATION(S): Neprash HT and Barnett ML. Association of primary care clinic appointment time with opioid prescribing. *JAMA Netw Open* 2019 Aug 2; 2:e1910373. (<https://doi.org/10.1001/jamanetworkopen.2019.103>)

JAMA Pediatr 2019 Sep 3

Inflammation During Adolescence and Risk for Early Death

Elevated erythrocyte sedimentation rate during late adolescence was associated with premature mortality from cancer and cardiovascular disease in a study of Swedish men.

Many diseases are linked to underlying inflammation and these diseases may increase mortality risk. The implications of exposure to inflammation during adolescence are not understood.

Using the erythrocyte sedimentation rate (ESR) as a marker for inflammation, researchers evaluated the association between inflammation and mortality in a cohort of roughly 106,000 healthy Swedish men who were 16 to 20 years old at the time of military conscription. During a mean observation period of 35 years (up to a maximum age of 57), 4835 men died (including 1105 from cancer; 874 from cardiovascular disease [CVD]; and 1502 from suicide, traffic accidents, or falls). ESR was significantly associated with overall mortality, with an adjusted hazard ratio (HR) of 1.36 for a high ESR (≥ 15 mm/h) versus a low ESR (≤ 10 mm/h). A high ESR was also significantly associated with mortality from cancer (HR, 1.78) and CVD (HR, 1.54), including myocardial infarction (HR, 2.50). ESR was not associated with mortality from other causes.

COMMENT: This study makes me question whether there is more in a simple “sed rate” measurement than we may have thought! The finding that a nonspecific marker of inflammation, when elevated in adolescence, is associated with premature mortality from cancer and CVD is striking. However, this study identified associations, not causality, and the long-term significance of abnormal levels of these biomarkers in adolescents is not known. Until we know more, pediatricians should consider following up adolescents with elevated ESR or other inflammation biomarkers, as inflammation may signal a variety of conditions.

CITATION(S): Kantor ED et al. Association of blood marker of inflammation in late adolescence with premature mortality. *JAMA Pediatr* 2019 Sep 3; [e-pub]. (<https://doi.org/10.1001/jamapediatrics.2019.2835>)

BMJ 2019 Aug 7; 366:l4414

Better Cardiovascular Health Is Associated with Lower Risk for Dementia

Life's Simple 7 score at age 50 predicted risk for later dementia.

The American Heart Association's Life's Simple 7 cardiovascular (CV) score comprises four behavioral measures (smoking, diet, exercise, and body-mass index) and three biological measures (fasting glucose level, blood cholesterol level, and blood pressure), each coded as 0, 1, or 2. Higher total score predicts lower risks for diabetes, coronary heart disease, and stroke. In this prospective study, researchers determined the association between the Life's Simple 7 score and risk for dementia.

Participants were ≈ 8000 British civil servants (32% women) free from dementia who underwent assessment of the Life's Simple 7 score at age 50. Participants were categorized as having poor (score, ≤ 6), intermediate (score, 7–11), or optimal (score, 12–14) CV health. During median follow-up of 25 years, the incidence of dementia among participants with poor CV health was significantly higher than the incidences among those with intermediate and optimal CV health (3.2 vs. 1.8

and 1.5 per 1000 person-years). After adjustment for multiple variables, incidence of dementia remained significantly higher in the group with poor CV health. This association also was observed among participants who remained free of CV disease during follow-up.

COMMENT: In this study, better CV health was associated with lower risk for dementia. Targeting the components of the Life's Simple 7 score, all of which are modifiable, might prevent not only adverse CV outcomes but also dementia.

CITATION(S): Sabia S et al. Association of ideal cardiovascular health at age 50 with incidence of dementia: 25 year follow-up of Whitehall II cohort study. *BMJ* 2019 Aug 7; 366:l4414. (<https://doi.org/10.1136/bmj.l4414>)

Ann Neurol 2019 Sep; 86:407

Race and Inflammatory Biomarkers in Alzheimer Disease

How is race related to the molecular basis of AD?

African-Americans (AAs) have a higher risk for Alzheimer disease (AD) and have lower cerebrospinal fluid (CSF) tau biomarkers. Inflammation has been linked to the AD process and may be more prominent in AAs. Researchers have now investigated the molecular basis of AD in AA and in Caucasians. In their approach, they first determined whether there were racially related differences in baseline CSF tau and cytokine biomarkers in middle-aged, cognitively normal participants with family histories of AD and in older participants with normal cognition, mild cognitive impairment, and AD dementia. The researchers then used the data to further inform immunohistochemical and gene-expression profile analyses in two autopsy cohorts of middle-aged African American and Caucasian participants.

In the middle-aged cognitively normal cohort, AAs had lower CSF IL-7 and IL-9 levels than Caucasians. CSF IL-9 had a nonlinear relationship with tau levels in Caucasians, but not in AAs. In the older cohort, cognitively normal AAs had lower CSF IL-9 levels than cognitively normal Caucasians, and elevated CSF IL-9 levels were associated with AD diagnosis only in AAs, not Caucasians. In immunohistochemical analyses of autopsied brains, downstream effects of IL-9 function were seen in AAs with AD but not Caucasians with AD. The association of gene expression profiles with AD pathology also differed between the races.

COMMENT: These findings offer intriguing insights into the molecular basis of AD and support the idea that inflammatory processes may influence the AD process, particularly in African-Americans. How the results could change the approach to the prevention and treatment of AD between AAs and Caucasians need further study. Future clinical trials should consider potential racial differences as new treatments are developed. In addition, the findings suggest that studies of inflammation and immunomodulatory therapy in AD should look carefully for differences in outcomes according to biomarker profiles.

CITATION(S): Wharton W et al. Interleukin 9 alterations linked to alzheimer disease in african americans. *Ann Neurol* 2019 Sep; 86:407. (<https://doi.org/10.1002/ana.25543>)

Pediatrics 2019 Sep 6

Is Celiac Disease Autoimmunity Associated with Child Behavior?

Undiagnosed celiac disease was associated with very slight elevations in anxiety and oppositional defiant symptom scores.

Celiac disease autoimmunity (CDA) occurs in about 1% of children, but most cases are undiagnosed. Children with diagnosed CDA have elevated rates of psychiatric symptoms, possibly due to the stress of dietary restrictions or another physiological mechanism involving the brain-gut axis or micronutrient deficiencies. Gluten elimination helps psychiatric symptoms in children with CDA, but it is unclear whether undiagnosed or subclinical CDA contributes to behavioral issues.

To examine this issue, researchers used data from 3715 children in a large, population-based study in the Netherlands. At age 6 years, children's blood was tested for CDA (positive tissue transglutaminase autoantibody titers) and parents completed behavioral scales. Only children with no prior diagnosis of celiac disease were included. Fifty-one children had CDA. In regression analyses adjusting for family income, ethnicity, and other factors, CDA was associated with very small increases (about 1/3 of a point) in anxiety and oppositional defiant symptom scores but was not associated with changes in scores for other child behaviors (such as attention problems, aggression, and autism symptoms).

COMMENT: Some families of children with behavioral disorders are interested in trying gluten-free diets. However, these diets can be expensive or can reinforce restrictive eating behaviors, without much benefit to the child. The results of this study do not convince me that we should consider broad CDA testing in children presenting with behavioral issues. However, ordering CDA testing on a case-by-case basis is reasonable when: 1) patients with behavioral issues are of European descent and have growth or gastrointestinal symptoms, and/or; 2) parents want to pursue testing before trying a gluten elimination diet.

CITATION(S): Wahab RJ et al. Celiac disease autoimmunity and emotional and behavioral problems in childhood. *Pediatrics* 2019 Sep 6; [e-pub]. (<https://doi.org/10.1542/peds.2018-3933>)

JAMA Pediatr 2019 Jul 29

Physicians Recommending Fewer Cough and Cold Medications, More Antihistamines, for Young Children

After 2008, nonopioid and opioid cough and cold medication recommendations fell for children younger than 2 years but did not change for children 2 to 6 years old.

In 2008, the U.S. Food and Drug Administration advised against use of over-the-counter cough and cold medication (CCM) in children <2 years old; manufacturers responded by voluntarily removing products intended for this age group and relabeling other child-focused products with a warning against use in children <4 years old.

To assess the effect of these changes, researchers analyzed data from two national surveys of ambulatory care practices representing 3.1 billion visits by children (age <18 years) from 2002 to 2015. All visits with a recommendation for CCM (drugs containing antitussives, decongestants, or expectorants), CCM with opioid, or single-agent antihistamine associated with a respiratory diagnosis were included in the analysis.

From 2002–2008 to 2009–2015, nonopioid CCM recommendations decreased significantly for children younger than 2 years (26% vs. 12%; adjusted odds ratio, 0.3), and opioid recommendations fell for children <4 years (4% vs. 1%; aOR, 0.1). There were no significant decreases in other age groups. During the same period, single-agent antihistamine recommendations increased significantly in children aged <2 years (7% vs. 11%; aOR, 10.6), 2 to 3 years (17% vs. 20%; aOR, 10.3), and 6 to 11 years (12% vs. 14%; aOR, 11.1).

COMMENT: Although the fall in CCM recommendations by physicians for the youngest patients is encouraging, the continued use in this age group (in 12% of visits in 2015) and the lack of a decrease for children aged 2 to 6 years show that the FDA recommendations and manufacturer actions have not been sufficient. Single-agent antihistamines may have

replaced CCM in physician's recommendations for the treatment of respiratory symptoms. Increased compliance with the FDA advice by individual clinicians and further promotion of it by trusted professional groups is needed.

CITATION(S): Horton DB et al. Trends in cough and cold medicine recommendations for children in the United States, 2002–2015. *JAMA Pediatr* 2019 Jul 29; [e-pub]. (<https://doi.org/10.1001/jamapediatrics.2019.2252>)

J Pediatr 2019 Aug 30; S0022-3476(19)30956-4

Baseline Concussion Screening Results in Children with ADHD

Among uninjured middle-school athletes given preseason concussion assessment, those with ADHD reported more and more-severe symptoms compared with matched controls.

Do children with attention-deficit/hyperactivity disorder (ADHD) perform similarly to those without ADHD in baseline, preparticipation screening tests for sports-related concussion? To find out, researchers conducted a small nested case-control study in middle-school athletes aged 11 to 12 years. They compared results of the 21-symptom Child Sport Concussion Assessment Tool Fifth Edition (Child SCAT5), administered prior to the school sports season, in 27 children with ADHD and 27 carefully matched controls. The Child SCAT5 captures presence and severity of symptoms and includes cognitive and balance assessments. Results were as follows:

- Children with ADHD reported more total symptoms and greater severity of symptoms compared with controls.
- The largest between-group differences in reported symptoms were for having a hard time concentrating, feeling sick to the stomach, feeling dizzy, forgetting, getting confused, and having headaches (odds ratios for ADHD group vs. controls, 11.6–59.1).
- Children without ADHD also reported relatively high frequencies of being easily distracted (52%), forgetting things (44%), and having headaches (56%). Corresponding rates in the ADHD group were 82%, 85%, and 85%.
- Cognitive tests did not differ between the two groups.
- Children with ADHD performed worse on balance tests overall and significantly worse on the single leg stance.

COMMENT: This small study demonstrates the importance of preparticipation screening tests in kids playing sports in order to correctly interpret responses after a potential concussive blow. It is interesting that the middle-school athletes without ADHD frequently reported some of the symptoms commonly associated with ADHD.

CITATION(S): Cook NE et al. Children with attention-deficit/hyperactivity disorder perform differently on pediatric concussion assessment. *J Pediatr* 2019 Aug 30; S0022-3476(19)30956-4; [e-pub]. (<https://doi.org/10.1016/j.jpeds.2019.07.048>)

J Int Neuropsychol Soc 2019 Aug; 25:740

Methylphenidate Improves Cognitive Problems After Childhood TBI

This small study shows the drug should be considered effective after these injuries.

Stimulants improve impaired attention and processing speed in adults with traumatic brain injury (TBI). Children with TBI are certainly vulnerable to the same problems in addition to pre-injury attention-deficit/hyperactivity disorder (ADHD). In this double-blind, placebo-controlled, crossover trial of methylphenidate in 26 children with moderate-to-severe TBI and attentional complaints (age range, 6–17), researchers evaluated both lab-based and everyday measures of attention, speed of processing, and executive functioning.

The children had had a TBI 6 or more months previously and had screened positive for ADHD via a parent-rating scale. Participants underwent randomization to receive methylphenidate (MPH) or placebo for 4 weeks; they then immediately crossed over to the other treatment. Ratings of executive and cognitive function were obtained at the “optimal dose visit” (weeks 4 and 8). Doses were increased to optimal response (children <25 kg: low, medium, and high doses, 18, 27, and 36 mg; children >25 kg, 18, 36, and 54 mg, respectively).

Mean age was 6.3 years at injury and 11.5 years at the baseline visit (mean Glasgow Coma Scale score, 11.9). The mean optimal dose was 40.5 mg (1.00 mg/kg/day). MPH was associated with significant improvements in processing speed, sustained attention, and executive function. Children who received MPH first and then crossed to placebo had worse performance than those who received placebo first. No test difference was seen between preinjury and secondary ADHD.

COMMENT: MPH has efficacy for treating attentional problems resulting from TBI in children, whether or not there was preinjury ADHD. The “rebound” effect of worsening performance after MPH discontinuation suggests that “drug holidays” or days off medications could be detrimental. Stimulants should be considered potentially effective and safe after childhood TBI.

CITATION(S): LeBlond E et al. Influence of methylphenidate on long-term neuropsychological and everyday executive functioning after traumatic brain injury in children with secondary attention problems. *J Int Neuropsychol Soc* 2019 Aug; 25:740. (<https://doi.org/10.1017/S1355617719000444>)

Female Pediatricians Get Paid Less, Do More at Home Than Their Male Peers

By Amy Orciari Herman Edited by David G. Fairchild, MD, MPH

Female pediatricians earn less than male pediatricians and are less satisfied with their share of work around the home, according to two analyses from a study of early and mid-career pediatricians, both published in *Pediatrics*.

The first included nearly 1000 pediatricians who reported their annual salary for 2016. The average salary was roughly \$177,000 for women versus \$226,000 for men. After adjustment for labor force characteristics, such as specialty, women still earned about \$26,000 less. After further adjustment for physician-specific job characteristics (e.g., number of patients seen) and work-family characteristics (e.g., being a parent), women earned \$8000 less than men.

The second analysis focused on some 1300 pediatricians who completed a survey on household responsibilities. Women were more likely than men to report being primarily responsible for six of nine household responsibilities, like cooking and cleaning, as well as for seven of nine childcare responsibilities, like homework and transportation. Women were less likely than men to be satisfied with this breakdown.

A commentator writes, "We ... need to recognize, value, and pay women for their work at a level equal to their male counterparts." She also notes that "women's loss in salary to be with children occurs in parallel with men's loss of time to be with children, and we need equality in both spheres."

LINK(S): [Pediatrics article on earnings](#) (Free abstract)

[Pediatrics article on household responsibilities](#) (Free abstract)

[Background: Physician's First Watch coverage of racial differences in physician salaries](#) (Free)

Accelerometer-Measured Physical Activity Is Associated with 5-Year Mortality

A dose-response relation was noted for both total activity and intensity of activity.

Most evidence about associations between physical activity and health outcomes is based on self-reported sedentary time and physical activity. In this meta-analysis, researchers determined associations between accelerometry-measured activity and all-cause death in eight studies with individual-level data on 36,383 participants (mean age, 63; 73% women). Accelerometers measured intensity of activity in “counts per minute” and total physical activity and sedentary time as “minutes per day.”

During a median follow-up of 5.8 years, 2149 deaths occurred. In an analysis of total activity (adjusted for multiple variables), participants in the first quartile (least total activity) had highest risk for all-cause death; risk was significantly lower in the second (46% lower), third (59% lower) and fourth (66% lower) quartiles; similar results were obtained when data were stratified by intensity of activity. Obverse differences were noted for sedentary time.

COMMENT: In this study, any accelerometer-measured physical activity, regardless of intensity, was associated with lower risk for all-cause death. From a practical standpoint, the largest risk reduction occurred between the least and second-least active quartiles — a difference of only 60 minutes of light activity or 5 minutes of vigorous activity daily. The maximum risk reductions occurred at 375 minutes of light activity and 24 minutes of vigorous activity daily. However, some residual confounding (in which low levels of activity resulted in part from medical conditions that accelerate mortality) seems likely in this analysis, despite statistical adjustment for some comorbidities.

CITATION(S): Ekelund U et al. Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: Systematic review and harmonised meta-analysis. *BMJ* 2019 Aug 21; 366:14570. (<https://doi.org/10.1136/bmj.14570>)

Klenk J and Kerse N. Every step you take. Walk more and sit less: Even light exercise is linked to a lower risk of death. *BMJ* 2019 Aug 21; 366:15051. (<https://doi.org/10.1136/bmj.15051>)

Polyunsaturated Fatty Acids, Glucose Metabolism, and Diabetes

In a meta-analysis, increasing intake of PUFAs had no effect on glucose metabolism or risk for diabetes.

Evidence is mixed regarding the relation between polyunsaturated fatty acids (PUFAs), which commonly are found in fish and various plants, and glucose metabolism. In this meta-analysis of 83 randomized trials that involved 121,000 participants with and without diabetes, researchers sought to determine the effects of increasing intake of PUFAs (ω -3 fatty acids, ω -6 fatty acids, α -linolenic acid, and total PUFAs) on glucose metabolism and risk for type 2 diabetes.

Omega-3 fatty acids had no effect on measures of glucose metabolism (i.e., glycosylated hemoglobin, fasting serum insulin, fasting glucose, and insulin resistance) or risk for diabetes. Similar results were obtained for α -linolenic acid, ω -6 fatty acids, and total PUFAs; however, the evidence was of low quality.

COMMENT: In this meta-analysis of randomized trials, intake of PUFAs had no effect on glucose metabolism or risk for type 2 diabetes. Based on these results, increasing intake of PUFAs for preventing or treating diabetes is not recommended.

CITATION(S): Brown TJ et al. Omega-3, omega-6, and total dietary polyunsaturated fat for prevention and treatment of type 2 diabetes mellitus: Systematic review and meta-analysis of randomised controlled trials. *BMJ* 2019 Aug 21; 366:l4697. (<https://doi.org/10.1136/bmj.l4697>)

Lancet 2019 Aug 24; 394:663

How Should We Select Patients for Blood Pressure–Lowering Treatment?

A retrospective study suggests that we should look at overall cardiovascular risk, regardless of baseline BP.

Should treatment to lower blood pressure (BP) be initiated based on baseline BP, overall cardiovascular (CV) risk, or a combination of the two? In a retrospective study, researchers analyzed CV outcomes in a British cohort of 1.2 million primary care patients (age range, 30–79) without baseline CV disease. They calculated how CV outcomes would have changed with one of four selection strategies for BP-lowering treatment:

- BP >140/90 mm Hg alone
- BP >140/90 mm Hg plus either CV risk score >20% (on QRISK2) or known diabetes or renal disease; or BP >160/90 mm Hg alone
- BP >140/90 mm Hg plus CV risk score >10%
- CV risk score >10% alone

More patients were eligible for treatment based on high BP alone than with any of the other strategies (39% vs. 22%, 27%, and 29%). During average follow-up of 4.3 years, the CV risk–only strategy identified a larger proportion of patients who developed CV disease than did any of the other strategies (68% vs. 63%, 47%, and 56%). Assuming that BP-lowering treatment would lower CV risk by 20%, the number needed to treat to prevent 1 adverse CV outcome during 10 years would be slightly lower with the CV risk–only strategy than with the other strategies (27 vs. 38, 28, and 29).

COMMENT: These data suggest that treatment to lower BP is most efficient when it is targeted to patients with elevated CV risk, regardless of baseline BP. One caveat is that the study cohort included few patients with systolic BP <120 mm Hg; thus, the analysis does not address patients with high CV risk but low baseline BP (e.g., a 65-year-old male smoker with hyperlipidemia and BP of 110/60 mm Hg). Current guidelines that recommend using both BP and CV-risk criteria might merit re-evaluation.

CITATION(S): Herrett E et al. Eligibility and subsequent burden of cardiovascular disease of four strategies for blood pressure-lowering treatment: A retrospective cohort study. *Lancet* 2019 Aug 24; 394:663. ([https://doi.org/10.1016/S0140-6736\(19\)31359-5](https://doi.org/10.1016/S0140-6736(19)31359-5))

Kahan T. Strategies to identify patients for antihypertensive treatment. *Lancet* 2019 Aug 24; 394:615. ([https://doi.org/10.1016/S0140-6736\(19\)31665-4](https://doi.org/10.1016/S0140-6736(19)31665-4))

Excessive Alcohol Use and Cognitive Decline

Alcohol-use disorder is both preceded by and predictive of lower intelligence.

Most studies of the relationship between alcohol use and intelligence scores are cross-sectional, leaving the question of cause and effect unresolved. The short-term detrimental effects of excessive alcohol use on intellectual performance have long been documented, but the long-term consequences are unclear.

Now, researchers in Denmark have conducted a longitudinal study in which 2499 men in Danish health registries and the Lifestyle and Cognition Follow-up study 2015 were assessed for alcohol-related disorders and changes in intelligence test scores at two time points (mean ages, 20 and 62 years). A history of alcohol-related hospital diagnoses (ARHDs; psychiatric, somatic, or both) was used as a proxy for the diagnosis of alcohol-use disorder. Of the cohort, 167 had psychiatric ARHDs, 13 had somatic ARHDs, and 27 had both.

Men with versus without ARHDs had significantly lower IQ scores at baseline (mean difference, -5.0 points) and significantly greater declines in IQ scores from baseline to follow-up (mean difference, -3.7 points). Men with versus without somatic ARHDs had an even greater mean decline in IQ score (-7.6 points). Analyses adjusted for average units of alcohol consumed, psychiatric or medical comorbidity, and binge drinking showed that the effects were lower in magnitude but still significant. In several follow-up analyses, the effects were found not to be driven by recent alcohol problems. Thus, the effects of excessive alcohol use on cognitive function appear to be long-lasting.

COMMENT; Although this study does not provide definitive proof that problematic alcohol use causes long-term cognitive decline — as there may be unmeasured comorbidities that could predispose someone to both — the longitudinal data are more convincing than data from cross-sectional studies. These results can be used by providers to educate patients with problematic drinking that continued heavy alcohol consumption will accelerate cognitive decline.

CITATION(S): GrønkJaer M et al. Intelligence test scores before and after alcohol-related disorders — A longitudinal study of Danish male conscripts. *Alcohol Clin Exp Res* 2019 Aug 6; [e-pub]. (<https://doi.org/10.1111/acer.14174>)
