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Might Team Sports Protect Against Effects of Adverse Childhood Experiences?

Longitudinal data show lower odds of depression and anxiety in those adults exposed to ACEs who played team sports as adolescents.

Team sports participation in childhood and adolescence has been linked with better mental health. Now, researchers have examined its long-term mental health benefits in people with adverse childhood experiences (ACEs).

In a longitudinal study of health from adolescence to adulthood, investigators assessed emergence of depression, anxiety, and depressive symptoms in adulthood (self-reported at ages 24 to 32 years) by ACE status (any vs. none) among 9668 participants. Among those reporting ACEs, mental health outcomes were evaluated based on self-reported participation in team sports during grades 7 to 12. Covariates included demographics, parental education, family structure, lack of health insurance, and school characteristics.

Just under 50% of participants reported one or more ACE, with 21% reporting two or more. Individuals with any ACEs had significantly higher unadjusted rates of adult mental health problems than those reporting no ACEs (depression, 19% vs. 13%; anxiety, 14% vs. 12%; depressive symptoms, 24% vs. 15%). In adjusted models, sports participation during adolescence was associated with lower odds of adult diagnosis of depression (adjusted odds ratio, 0.76 [95% CI, 0.59–0.97]) and anxiety (aOR, 0.70 [95% CI, 0.56–0.89]) among those reporting ACEs. Sex-stratified analysis showed that participating in sports conferred significantly lower odds of all three mental health outcomes in adulthood for boys, but only one for girls (anxiety). School connectedness, self-esteem, and feeling socially accepted mediated between 16% and 35% of the relationship between sports participation and mental health outcomes.

COMMENT; The possibility that adolescent team sports participation might mitigate some of the increased risk for adult mental health problems among those exposed to ACEs gives clinicians yet another reason (on top of physical activity, socialization, and learning team dynamics, among others) to recommend that children and youth take part in team sports and other activities that can increase feelings of connectedness, self-esteem, and social acceptance.

CITATION(S): Easterlin MC et al. Association of team sports participation with long-term mental health outcomes among individuals exposed to adverse childhood experiences. *JAMA Pediatr* 2019 May 28; [e-pub]. (<https://doi.org/10.1001/jamapediatrics.2019.1212>)

BMJ 2019 Jun 12; 365:l2110

Effects of Increasing or Decreasing Red Meat Intake

Changes in red meat consumption directly affected 25-year all-cause mortality.

High consumption of red meat is associated with excess risks for cardiovascular disease (CVD), cancer, and death. In this analysis, researchers used data from the Nurses' Health Study (54,000 women; age range, 30–55 at study entry) and the Health Professionals Study (28,000 men; age range, 40–75 at study entry) to examine health effects of changing red meat consumption over time.

Participants were free of CVD and cancer at baseline. Data were collected from 1986 through 2010; diet and lifestyle factors were measured every 4 years. More than 14,000 deaths occurred during the studies. Adjusted for numerous potential confounders, increasing red meat consumption by 3.5 servings weekly during an 8-year period was associated with significantly higher risk for all-cause death (10% higher) compared with no change in red meat consumption. Reducing red meat intake and replacing it with other sources of protein, whole grains, or vegetables was associated with significantly lower relative risks (range, 5% to 26% lower).

COMMENT: Although residual confounding is conceivable, this study affirms what has long been suspected: Higher red meat consumption is associated with higher relative risk for death; lowering red meat consumption and replacing it with healthier foods is associated with lower risk.

CITATION(S): Zheng Y et al. Association of changes in red meat consumption with total and cause specific mortality among US women and men: Two prospective cohort studies. *BMJ* 2019 Jun 12; 365:l2110. (<https://doi.org/10.1136/bmj.l2110>)

Circulation 2019 Jun 10

Three Easy Ways to Save Almost 100 Million Lives Worldwide

Expanding blood pressure treatment, reducing dietary sodium, and eliminating trans fats could dramatically decrease mortality.

Noncommunicable diseases (NCDs) are the leading cause of death worldwide and are largely preventable through changes in modifiable risk factors. Researchers quantified the global impact of three public health interventions on NCD mortality: increasing the coverage of hypertension treatment to 70%, reducing dietary sodium by 30%, and eliminating trans fats.

Using data from a myriad of sources, including population health surveys and WHO Global Health Estimates, the investigators predicted changes in mortality between 2015 and 2040. According to the analysis, the three interventions could delay 94.3 million deaths during 25 years (39.4 million from boosting hypertension treatment, 40.0 million from reducing sodium intake, and 14.8 million from eliminating trans fats). The effects were greater for men than women and for older (age ≥ 70) than younger people. The largest number of projected delayed deaths occurred in East Asia and the Pacific, followed by South Asia, a region encompassing Central/Eastern Europe and Central Asia, and Sub-Saharan Africa.

COMMENT; This epidemiological analysis suggests that three simple population-level interventions could dramatically decrease the global burden of NCDs. To achieve this goal, low- and middle-income countries in particular need public health resources and infrastructure to increase access to pharmacotherapy for hypertension, the leading modifiable risk factor for early cardiovascular disease. As the authors point out in the discussion, the interventions are not only feasible but extremely cost-effective. The lowest-hanging fruit might be eliminating trans fats through national legislation, as has been done in some high-income countries, like the U.S. What is clear from this and other similar analyses is that to substantially move the needle in cardiovascular disease prevention, interventions must move beyond the level of individual patients.

CITATION(S): Kontis V et al. Three public health interventions could save 94 million lives in 25 years: Global impact assessment analysis. *Circulation* 2019 Jun 10; [e-pub]. (<https://doi.org/10.1161/CIRCULATIONAHA.118.038160>)

Amazon's PillPack Pharmacy Accused of Violating Customer Privacy

PillPack, the online pharmacy acquired by Amazon last year, has been accused of violating customer privacy in separate lawsuits within the last year. The lawsuits accuse the online pharmacy of violating privacy by calling or texting consumers to solicit business. In the lawsuits, customers claim unwanted marketing calls have invaded their privacy. Mary Alice Lawless, a managing director at health research consulting firm EverythingHealth, said Pillpack's alleged actions could make it challenging to win the trust of customers.

<https://www.beckershospitalreview.com/pharmacy/amazon-s-pillpack-pharmacy-accused-of-violating-customer-privacy.html>

Drug Makers Sue to Block Requirement for Listing Prices in TV Ads

The rule, set to take effect July 9, is one of the most visible efforts by the administration to try to address high drug prices. Johnson & Johnson has begun disclosing its list price in TV ads, but three other drug manufacturers (Merck, Eli Lilly, Amgen) are suing the government to avoid such disclosures. They are trying to block a rule that would force them to put the price of their drugs in television advertisements beginning this summer on the list price of any drug that costs more than \$35 a month. Alex M. Azar II, the secretary of HHS, announced the new rule in May, contending that forcing pharmaceutical companies to disclose their prices could push companies to lower them. He was a top executive at Lilly before joining the Trump administration in January 2018.

<https://www.nytimes.com/2019/06/14/health/drug-prices-tv-ads.html>

Waning Effectiveness of the Acellular Pertussis Vaccine

Children fully vaccinated against pertussis are still at risk, which increases with time since immunization.

The original pertussis vaccine, derived from the cellular components of *Bordetella pertussis* in the 1940s, was highly effective but caused adverse side effects (fever, febrile seizures). In the 1990s, it was replaced with a less reactogenic acellular pertussis vaccine. Five doses of the vaccine by age 4 to 6 years and a booster between 11 and 12 years are currently recommended. Despite high rates of vaccination, we continue to see large pertussis outbreaks.

To determine risk for pertussis by vaccination status and time since vaccination, researchers followed 470,000 children born between 1999 and 2016 from age 3 months to 11 years. During the monitoring period, they identified 738 cases of pertussis, 603 in fully vaccinated children. Compared with fully vaccinated children, pertussis risk was 13 times higher in unvaccinated children and doubled in undervaccinated children. Pertussis immunity waned over time; in fully vaccinated children aged 19 to <84 months, pertussis risk was 5 times greater at ≥ 3 years since vaccination versus <1 year, and in those aged 84 to 132 months, risk was doubled at ≥ 6 years since vaccination versus <3 years.

COMMENT: This study adds significantly to our understanding of how immunity provided by the acellular pertussis vaccine wanes over time. More than four out of five pertussis cases in this cohort were among fully vaccinated children, indicating that immunity provided by the current acellular pertussis vaccine is suboptimal. This fact makes it all the more important to adhere to the vaccination schedule. The whole-cell pertussis vaccine, though more reactogenic, seems to have been more effective.

CITATION(S): Zerbo O et al. Acellular pertussis vaccine effectiveness over time. *Pediatrics* 2019 Jun 10; [e-pub]. (<https://doi.org/10.1542/peds.2018-3466>)

Recovery from Mild Traumatic Brain Injury

A natural-history study shows the importance of the evaluation and follow-up of patients with mild brain injury.

Mild traumatic brain injury (mTBI) accounts for 80% to 90% of all cases of traumatic brain injury (TBI) worldwide. Recovery often occurs in weeks to months without special therapy, but a subgroup of patients experience persistent post-traumatic complaints such as forgetfulness, irritability, and problems with concentration.

To characterize the history of recovery of patients with mTBI, investigators enrolled 1154 mTBI patients and 299 patients with peripheral orthopedic traumatic injury (controls; OTCs) and followed them to 12 months after injury. The investigators used computed tomography (CT) to determine the presence or not of acute intracranial findings and measured its association with outcomes. The primary outcome measure was the Glasgow Outcome Scale Extended (GOSE) score, which is based on patient or proxy report of injury-related dependence or difficulties in major functional domains of daily life such as activities of daily living, work, social/leisure activities, and relationships.

At admission, mTBI participants had Glasgow Coma Scale (GCS) scores of 13 to 15. Many of the participants with either mTBI or OT had functional limitations at 2 weeks postinjury. At 12 months, more mTBI patients than OTCs had functional limitations (53% vs. 38%). Among patients with mTBI, more of those with than without a positive CT scan reported impairment (61% vs. 49%). Regardless of CT findings, mTBI patients had more impairment than OTCs did.

COMMENT: Patients with mTBI must be followed closely to prevent chronic problems. As other research has shown, preinjury mental health problems, education, and age are also important predictors for recovery. In this study, rates of dysfunction were highest for complex tasks, such as work and social/leisure activities, and such difficulties persisted even to 12 months postinjury for more than half of patients.

CITATION(S): Nelson LD et al. Recovery after mild traumatic brain injury in patients presenting to US level I trauma centers: A Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) study. *JAMA Neurol* 2019 Jun 3; [e-pub]. (<https://doi.org/10.1001/jamaneurol.2019.1313>)

PLoS One 2019 Jun 7; 14:e0218112

Activities of Daily Living Are Linked to Cognitive Function

Subtle declines in various activities of daily living are associated with cognitive impairment.

Clinicians often screen at-risk patients for impaired executive functioning and inquire about their abilities to perform activities of daily living (ADLs), but little has been published tying specific cognitive deficits to impairments in ADLs. Investigators in Taiwan studied mental status and ADLs in 102 people aged ≥ 65 (55 women) — 31 with Alzheimer or vascular dementia (subgrouped into mild, moderate, and severe dementia), 36 with mild cognitive impairment (MCI), and 35 normal controls. Three standardized tests assessed mental status, and other scales measured basic ADLs (e.g., bathing, dressing, controlling bladder and bowels, climbing stairs) and instrumental ADLs (e.g., telephone use, finance handling, food preparation).

Patients with depression or other dementia types were excluded. When necessary, legal guardians reported patients' ADLs. Impaired food preparation and medication responsibility separated MCI patients from normal controls. Patients with mild dementia were considerably better than those with severe dementia on a broad range of basic and instrumental ADLs and better than those with moderate dementia at financial handling and food preparation. Impaired cognitive function on two scales were highly associated with decline in instrumental ADLs in older participants (age, ≥ 81).

COMMENT: Although this study is small, its findings reinforce clinical impressions that subtle declines in ADLs, often initially detected by family members, are tied to progressive declines in cognition. Families' impressions of ADL functioning, particularly for patients beyond age 80, should be routinely obtained. This study highlights both how little we know about the implications of declining cognitive function per se for deteriorating ADLs and the need for research to better delineate points at which specific patterns of cognitive deficits augur significant risks for vehicular driving, independent living, and other practical matters.

CITATION(S): Lee MT et al. How do impairments in cognitive functions affect activities of daily living functions in older adults? *PLoS One* 2019 Jun 7; 14:e0218112. (<https://doi.org/10.1371/journal.pone.0218112>)

Pediatr Emerg Care 2019 Jun 6

Buzzy Device Versus EMLA for Pain Control in Pediatric IV Placement

Although the Buzzy device was less effective for pain control than an EMLA patch, it works much faster, so don't throw the "buzzy" out with the bathwater.

Researchers compared pain scores during IV placement and venipuncture between children randomized to treatment with an EMLA patch (lidocaine 2.5%, prilocaine 2.5%) or external cold/vibration pain distraction via a Buzzy device

(<https://buzzyhelps.com/>). Roughly 300 children aged 18 months to 6 years were enrolled in each treatment arm at a Canadian pediatric emergency department (ED). Pain was measured using the Children's Hospital of Eastern Ontario Pain Scale (score ranges from 4 [no pain] to 13). A score >8 was considered pain severe enough to need analgesia.

More children in the EMLA group than the Buzzy group had a pain score ≤8 (62% vs. 37%). Mean pain scores were 7.2 in the EMLA group versus 8.5 in the Buzzy group. Parents preferred EMLA to Buzzy; 94% wanted to use the treatment again (versus 81%). Success with IV placement and venipuncture was similar between groups.

COMMENT: Although the Buzzy device appears less effective than an EMLA patch for pain control during pediatric venipuncture or IV placement, I think the device still has an important place in the ED. It is quick, easy, cost effective, and doesn't require any preparation or pharmacy orders to provide at least some pain control and distraction, especially since waiting up to an hour for EMLA to take effect is unrealistic for most ED IV placements.

CITATION(S): Bourdier S et al. Cold vibration (Buzzy) versus anesthetic patch (EMLA) for pain prevention during cannulation in children: A randomized trial. *Pediatr Emerg Care* 2019 Jun 6; [e-pub]. (<https://doi.org/10.1097/PEC.0000000000001867>)

Scand J Gastroenterol 2019 Jun 10; 1

Risk Factors for Recurrence of Pancreatic Cancer After Surgery

Some of the most common features of the disease portend a worse prognosis.

Despite advances in imaging, chemotherapy, and surgery, pancreatic ductal adenocarcinoma (PDAC) still conveys a poor prognosis in most cases, with true clinical cure being uncommon. In a recent study from Japan, investigators analyzed which clinicopathological factors were most likely to predict disease recurrence after surgery.

Among 359 patients who underwent surgery without neoadjuvant therapy, almost three quarters developed recurrent disease at a median time of just over 1 year. On multivariate analysis, risk factors for shorter recurrence-free survival included an elevated serum carbohydrate antigen 19-9 (CA 19-9; >37 U/mL), tumor size >2.6 cm, not undergoing adjuvant treatment, presence of malignant adenopathy, lack of an R0 resection margin, and grade 3 tumor pathology. Of these, only tumor size >2.6 cm and elevated serum CA 19-9 level are evaluable before surgery. In patients with both of these risk factors, 5-year recurrence was 92% and median time to survival was 1.7 years, compared with 61% and 7.2 years in those with neither risk factor.

COMMENT: This study is most notable for the fact that none of the patients received neoadjuvant therapy, which in some parts of the world is standard of care. Based on these data, the authors advocate neoadjuvant therapy for patients with both of the identified preoperative risk factors for recurrence and poor prognosis. Distressingly, this will include many patients; most pancreatic cancers are diagnosed at sizes above the cutoff of 2.6 cm, and serum CA 19-9 is elevated in approximately 70% of patients with PDAC. Further efforts are urgently needed to enable identification of these tumors at a more treatable stage.

CITATION(S): Izumo W et al. Evaluation of preoperative prognostic factors in patients with resectable pancreatic ductal adenocarcinoma. *Scand J Gastroenterol* 2019 Jun 10; 1; [e-pub]. (<https://doi.org/10.1080/00365521.2019.1624816>)

Stool Processing Method Might Be Important for Efficacy in Fecal Transplantation Protocols

Odds of short-term remission in ulcerative colitis were higher using anaerobically prepared pooled donor stool versus standard autologous stool.

Treatment for ongoing mild-to-moderate ulcerative colitis in the face of active therapy remains problematic. Fecal microbiota transplantation (FMT) has been suggested as a safe alternative to more-aggressive immunosuppression for controlling inflammation.

In the current trial, researchers at three Australian centers randomized 73 patients with mild-to-moderate ulcerative colitis to undergo FMT with pooled donor stool processed in anaerobic conditions or autologous stool processed in standard fashion. FMT was administered via colonoscopy followed by two enemas within 7 days.

The primary endpoint of steroid-free remission at week 8 was met by 32% of the pooled donor stool group versus 9% of the autologous stool group (odds ratio, 5.0, 95% confidence interval, 1.2–20.1). Clinical response and endoscopic healing rates were also higher in the pooled donor group. Serious adverse events occurred in three patients in the pooled group and two in the standard group. Treatment acceptability was high overall (95%).

COMMENT: FMT is considered investigational by the FDA for treating refractory *Clostridium difficile* infection and is under study for treating other chronic conditions. The data for ulcerative colitis are mixed. A main driver of success seems to be the nature of the stool itself; i.e., certain microbiome patterns are associated with better outcomes. Other variables are the delivery system and stool processing regimen. This current study used a novel approach of colonoscopy-delivered stool with additional topical applications. At this time, FMT should be considered experimental for the treatment of ulcerative colitis, and patients should be treated in the context of a clinical trial, as we have a long way to go before understanding how this intervention can and should be used.

CITATION(S): Costello SP et al. Effect of fecal microbiota transplantation on 8-week remission in patients with ulcerative colitis: A randomized clinical trial. *JAMA* 2019 Jan 15; 321:156. (<https://doi.org/10.1001/jama.2018.20046>)

Kelly CR and Ananthakrishnan AN. Manipulating the microbiome with fecal transplantation to treat ulcerative colitis. *JAMA* 2019 Jan 15; 321:151.
