GULF WAR ILLNESS

No Updates this Week for Gulf War Illness or Chronic Multisymptom Illness.

CHRONIC FATIGUE SYNDROME

Defining the prevalence and symptom burden of those with self-reported severe chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a two-phase community pilot study in the North East of England.

Strassheim VJ[1], Sunnquist M[2], Jason LA[3], Newton JL[4].

BMJ Open. **2018 Sep 19**;8(9):e020775. doi: 10.1136/bmjopen-2017-020775. PMID: 30232103.

OBJECTIVES: To define the prevalence of severe chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and its clinical characteristics in a geographically defined area of Northern England. To understand the feasibility of a community-based research study in the severely affected CFS/ME group.

DESIGN: A two-phase clinical cohort study to pilot a series of investigations in participants own homes.

SETTING: Participants were community living from the area defined by the Northern clinical network of the UK.

PARTICIPANTS: Adults with either a medical or a self-reported diagnosis of CFS/ME. Phase 1 involved the creation of a database. Phase 2: five participants were selected from database, dependent on their proximity to Newcastle.

INTERVENTIONS: The De Paul fatigue questionnaire itemised symptoms of CFS/ME, the Barthel Functional Outcome Measure and demographic questions were collected via postal return. For phase 2, five participants were subsequently invited to participate in the pilot study.

RESULTS: 483 questionnaire packs were requested, 63 were returned in various stages of completion. 56 De Paul fatigue questionnaires were returned: all but 12 met one of the CFS/ME criteria, but 12 or 22% of individuals did not fulfil the Fukuda nor the Clinical Canadian Criteria CFS/ME diagnostic criteria but 6 of them indicated that their fatigue was related to other causes and they barely had any symptoms. The five pilot participants completed 60% of the planned visits.

CONCLUSIONS: Severely affected CFS/ME individuals are keen to participate in research, however, their symptom burden is great and quality of life is poor. These factors must be considered when planning research and methods of engaging with such a cohort.

Cardiopulmonary Exercise Test Methodology for Assessing Exertion Intolerance in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.

Stevens S[1], Snell C[1], Stevens J[1], Keller B[2], VanNess JM[1,3].

Front Pediatr. **2018 Sep 4**;6:242. doi: 10.3389/fped.2018.00242. PMCID: PMC6131594. PMID: 30234078. eCollection 2018.

Background: Concise methodological directions for administration of serial cardiopulmonary exercise testing (CPET) are needed for testing of patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). Maximal CPET is used to evaluate the coordinated metabolic, muscular, respiratory and cardiac contributions to energy production in patients with ME/CFS. In this patient population, CPET also elicits a robust post-exertional symptom flare (termed, post-exertional malaise); a cardinal symptom of the disease. CPET measures are highly reliable and reproducible in both healthy and diseased populations. However, evidence to date indicates that ME/CFS patients are uniquely unable to reproduce CPET measures during a second test, despite giving maximal effort during both tests, due to the effects of PEM on energy production.

Methodology: To document and assess functional impairment due to the effects of post-exertional malaise in ME/CFS, a 2 day CPET procedure (2-day CPET) has been used to first measure baseline functional capacity (CPET1) and provoke post-exertional malaise, then assess changes in CPET variables 24 h later with a second CPET to assess the effects of post-exertional malaise on functional capacity. The second CPET measures changes in energy production and physiological function, objectively documenting the effects of post-exertional malaise. Use of CPET as a standardized stressor to induce post-exertional malaise and quantify impairment associated with post-exertional malaise has been employed to examine ME/CFS pathology in several studies. This article discusses the results of those studies, as well as the standardized techniques and procedures for use of the 2-day CPET in ME/CFS patients, and potentially other fatiguing illnesses.

Conclusions: Basic concepts of CPET are summarized, and special considerations for performing CPET on ME/CFS patients are detailed to ensure a valid outcome. The 2-day CPET methodology is outlined, and the utility of the procedure is discussed for assessment of functional capacity and exertion intolerance in ME/CFS.

HEADACHE and MIGRAINE

Benefit-risk assessment of erenumab and current migraine prophylactic treatments using the likelihood of being helped or harmed.

Vo P[1], Wen S[2], Martel MJ[3], Mitsikostas D[4], Reuter U[5], Klatt J[1].

Cephalalgia. **2018 Sep 19**:333102418801579. doi: 10.1177/0333102418801579. PMID: 30231626. [Epub ahead of print]

Objective: This study evaluated the benefit-risk profile of erenumab relative to other therapies approved for migraine prophylaxis and available in the majority of European countries.

Methods: Trials were identified via a published systematic literature review updated to December 2017 using MEDLINE. Erenumab's pivotal trials study reports were also included (NCT02066415, NCT02456740). From these sources, ≥ 50% responder rates and discontinuations due to adverse events were extracted to generate numbers needed to treat and harm and likelihood of being helped or harmed, a quantitative benefit-risk measure.

Results: Eleven articles (nine randomized clinical trials) met the inclusion/exclusion criteria. Low numbers needed to treat (range: 4-13) were observed for most treatments, while numbers needed to harm showed substantial differences (erenumab's higher numbers needed to harm indicating better tolerability). In chronic and episodic migraine, likelihoods of being helped or harmed for erenumab 70 mg were 143 and 167, and 42 and 167 for erenumab 140 mg. Likelihoods of being helped or harmed in chronic migraine were 2 and 3 for topiramate (two studies) and 4 for onabotulinumtoxinA. In episodic migraine, likelihoods of being helped or harmed were 2 for topiramate and 2 for propranolol.

Conclusions: While all prophylactic treatments were more likely to help than harm (likelihood of being helped or harmed > 1), erenumab showed a likelihood of being helped or harmed of high magnitude, supporting its favorable benefit-risk profile across the entire migraine frequency spectrum, in contrast with other prophylactic treatments.

Sustained onabotulinumtoxinA therapeutic benefits in patients with chronic migraine over 3 years of treatment.

Vikelis M[1,2,3], Argyriou AA[4], Dermitzakis EV[5], Spingos KC[6], Makris N[4], Kararizou E[7].

J Headache Pain. **2018 Sep 17**;19(1):87. doi: 10.1186/s10194-018-0918-3. PMID: 30225735.

BACKGROUND: Evidence on whether the therapeutic effect and good safety profile of onabotulinumtoxinA (Botox®) in chronic migraine (CM) patients is maintained over long term treatment is still limited. We herein aimed at assessing whether there is a sustained benefit and good safety with repeated onabotulinumtoxinA sessions in CM over more than three years of treatment.

METHODS: We prospectively enrolled 65 CM patients, who were classified as responders after three sessions of onabotulinumtoxinA and were eligible to further continue treatment. Data documenting longitudinal changes from the trimester after the third onabotulinumtoxinA administration (T1) to the trimester after completing two years of treatment (T2) and eventually to the trimester after completing three years of treatment (T3) in (i) mean number of monthly headache days (ii) migraine severity as expressed by the mean number of days with peak headache intensity of > 4/10, and (iii) mean number of days with use of any acute headache medication, were prospectively collected from patients' headache diaries.

RESULTS: A total of 56 (86.1%) of 65 patients achieved to attain onabotulinumtoxinA over three years. At T3, a significant reduction in mean monthly headache days was evident, compared to T1 (3.4 ± 1.7 vs 7.2 ± 3.8; $P < 0.001$) with diminished mean number of monthly days with peak headache intensity of more than 4/10 and a significant change in days using acute headache medications per month between T1 and T3 (2.8 ± 1.3 vs 4.7 ± 3.2; $P < 0.001$). Significant changes were also noticed in all efficacy variables from T2 to T3. Therapy was safe and well tolerated with low rates of adverse events or drop-outs.

CONCLUSION: The long -term treatment with onabotulinumtoxinA proved effective, safe and well tolerated over three years. Our findings support the strategy to consistently deliver sessions of use of onabotulinumtoxinA over long time in CM patients (Trial registration NTC03606356, registered retrospectively, 28 July 2018).

HEADACHE and MIGRAINE (Continued)

Coexistence of Symptoms Associated with Trigeminal Pathways in Chronic and Episodic Migraine and the Effects on Quality of Life.

Ceylan M[1], Yalcin A[1].

Pain Med. **2018 Sep 14**. doi: 10.1093/pm/pny118. PMID: 30239907. [Epub ahead of print]

Objective: The functional impairment in migraine greatly depends on the chronicity of the disease. Patients with migraine suffer from sleep difficulties and concentration problems. Cranial autonomic symptoms, vertigo, dizziness, and cutaneous allodynia are also frequent in patients with migraine. In this paper, we aim to investigate the coexistence of these symptoms and their effects on the quality of life of patients with chronic and episodic migraine.

Methods: The study included 1,080 patients with migraine. The presence of cranial autonomic symptoms, vertigo/dizziness, cutaneous allodynia, concentration-related impairment in function, and abnormal sleep latency was sought in patients with questionnaires, and comparisons were made between episodic and chronic migraine groups.

Results: Abnormal sleep latency and concentration-related impairment in function were more frequent in patients with chronic migraine compared with those with the episodic form ($P < 0.001$ for both). Furthermore, these two symptoms were significantly more frequent in separate patient groups with cranial autonomic symptoms, vertigo/dizziness, and cutaneous allodynia than patients without ($P < 0.005$).

Conclusion: Abnormal sleep latency and concentration-related impairment in function were more frequent in patients with chronic migraine than those with the episodic form. Cranial autonomic symptoms, vertigo/dizziness, and cutaneous allodynia were significantly coexisting in migraine patients.

CHRONIC PAIN

Multimodal Treatment Options, Including Rotating to Buprenorphine, Within a Multidisciplinary Pain Clinic for Patients on Risky Opioid Regimens: A Quality Improvement Study.

Oldfield BJ[1,2,3], Edens EL[1,2], Agnoli A[4], Bone CW[1,2], Cervone DJ[1], Edmond SN[1,2], Manhapra A[2,5], Sellinger JJ[1,2], Becker WC[1,2].

Pain Med. **2018 Sep 1**;19(suppl_1):S38-S45. doi: 10.1093/pm/pny086. PMID: 30203007.

Objectives: We aimed to evaluate a novel clinical program designed to address unsafe use of opioids prescribed for pain-the Opioid Reassessment Clinic (ORC)-to inform practice and health system improvement.

Design: Controlled, retrospective cohort study.

Setting: The ORC is a multidisciplinary clinic in a primary care setting in a Veterans Health Administration hospital designed to perform longitudinal treatment of patients with unsafe use of opioids prescribed for pain, including tapering or rotating to the partial opioid agonist buprenorphine.

Subjects: We included patients referred to the ORC from March 1, 2016, to March 1, 2017, who had an intake appointment (intervention group) and who did not (control group).

Methods: We compared a priori-defined metrics at the patient, clinic process, and health system levels and compared metrics between groups.

Results: During the study period, 114 veterans were referred to the ORC, and 71 (62%) of these had an intake appointment. Those in the intervention group were more likely to trial buprenorphine ($N = 41$, 62% vs $N = 1$, 2%, $P < 0.01$) and had greater reductions in their full agonist morphine equivalent daily dose than those in the control group (30 mg [interquartile range {IQR} = 0-120] vs 0 mg [IQR = 0-20] decrease, $P < 0.01$). Of those engaging in the ORC, 20 (30%) had not transitioned chronic pain management back to their primary care providers (PCPs) by the end of follow-up. Only one patient transitioned the management of buprenorphine to the PCP.

Conclusions: Results suggest the ORC was effective in reducing total prescribed opioid doses and in transitioning patients to partial-agonist therapy, but PCP adoption strategies are needed.

CHRONIC PAIN (Continued)

Patient Experiences Navigating Chronic Pain Management in an Integrated Health Care System: A Qualitative Investigation of Women and Men.

Driscoll MA[1,2], Knobf MT[3], Higgins DM[4,5], Heapy A[1,2], Lee A[1,2], Haskell S[1,6].

Pain Med. **2018 Sep 1**;19(suppl_1):S19-S29. doi: 10.1093/pm/pny139. PMID: 30203009.

Background: Rates of pain among veterans are as high as 60%; rates approach 80% in women seeking Department of Veterans Affairs (VA) care. Prior studies examined experiences managing pain in community samples, with gender disparities observed. As the largest national integrated health care system in the country, the VA offers a unique environment to a) study perceptions of pain care among men and women and b) contrast experiences using an integrated health care setting with prior observations in the private sector.

Methods: A purposive sample of chronic pain patients was recruited to qualitatively describe perceptions of managing pain in an integrated health care system (VA) and to explore gender differences. A constant comparative approach with sequential analysis was used to reach thematic consensus.

Results: Ten focus groups (N = 48; six groups of women [N = 22]; four groups of men [N = 26]) revealed an overarching theme, "just keep plugging," which reflected pain as a constant struggle. Three subthemes emerged: "always a reacquaintance process" described frustration with the use of trainees in the medical center. The need to navigate "so many hoops" referred to frustrations with logistical barriers. "To medicate or not" reflected tensions around medication use. A distinct theme, "the challenges of being female," reflected women's perceptions of stigma and bias.

Conclusions: Most of the identified challenges were not unique to the integrated setting. Findings revealed advantages to receiving pain care in this setting. Tensions between patient expectations and guidelines governing provider behavior emerged. Improved patient education, provider communication and sensitivity to the unique needs of women may optimize care.

Bidirectionality of Pain Interference and PTSD Symptoms in Military Veterans: Does Injury Status Moderate Effects?

Lee SY[1], Finkelstein-Fox L[1], Park CL[1], Mazure CM[2,3], Huedo-Medina TB[4], Hoff R[2,3,5].

Pain Med. **2018 Jul 16**. doi: 10.1093/pm/pny133. PMID: 30016463. [Epub ahead of print]

Objective: Pain and post-traumatic stress disorder (PTSD) symptoms are strongly correlated in veteran populations. Arguments for which one condition predicts or worsens the other condition have gone in both directions. However, research addressing this issue has been primarily limited to cross-sectional studies rather than examinations of a potential bidirectional relationship between pain interference and PTSD symptoms over time. In addition, no studies have examined deployment injury status as potentially moderating this bidirectional effect in veterans. To address these gaps in the literature, the present longitudinal study examined whether there is a bidirectional relationship between pain interference and PTSD symptoms in a sample of male and female veterans returning from Operation Iraqi Freedom, Operation Enduring Freedom, or Operation New Dawn (N = 729) and whether deployment injury status moderates this relationship.

Methods: Participants completed phone interviews regarding pain interference and PTSD symptoms at three time points, each three months apart.

Results: Pain interference at Time 1 predicted worse PTSD symptoms at Time 2 for the subset of veterans who sustained injuries during deployment (n = 381) but not for veterans with pain interference who did not sustain injuries (n = 338). From Time 1 to Time 3, elevations in PTSD symptoms were mediated by pain interference for injured veterans; in contrast, PTSD symptoms did not appear to drive changes in pain interference in either group.

Conclusions: These results indicate that physical symptom management should be a crucial target of psychological intervention for returning veterans with PTSD symptoms and deployment-related injuries.

CHRONIC PAIN (Continued)

Health care utilization by veterans prescribed chronic opioids.

Kay C[1,2], Wozniak E[2], Ching A[1], Bernstein J[1].

J Pain Res. **2018 Sep 10**;11:1779-1787. doi: 10.2147/JPR.S167647. PMCID: PMC6137951. PMID: 30237732. eCollection 2018.

Purpose: Ambulatory resources such as telephone calls, secure messages, nurse visits, and telephone triage are vital to the management of patients on chronic opioid therapy (COT). They are also often overlooked as health care services and yet to be broadly studied. The aim of the present study was to describe the Veterans Affairs (VA) health care utilization by patients based on COT, type, and amount of opioids prescribed.

Patients and Methods: A retrospective chart review was done on 617 patients on COT at a VA primary care clinic. Instances of health care utilization (emergency department visits [EDVs], hospitalizations, clinic visits, telephone triage calls, telephone calls/secure messages/nurse visits) were obtained.

Results: Patients were likely to have more telephone calls, secure messages, or nurse visits if they were prescribed a schedule II opioid or if they were on more than one opioid. Model-based results found that patients on COT were more likely to have EDVs, telephone triage calls, and clinic contact compared to patients who were not on chronic opioids.

Conclusion: The results are despite having a Patient Aligned Care Team, which is the VA's patient-centered medical home. This suggests that reducing health care utilization for patients on COT may not be possible with just a primary care involvement.

The relationship of self-efficacy to catastrophizing and depressive symptoms in community-dwelling older adults with chronic pain: A moderated mediation model.

Cheng ST[1,2], Leung CMC[1], Chan KL[1], Chen PP[3], Chow YF[4], Chung JWY[1], Law ACB[5], Lee JSW[6], Leung EMF[7], Tam CWC[8].

PLoS One. **2018 Sep 18**;13(9):e0203964. doi: 10.1371/journal.pone.0203964. PMID: 30226892. eCollection 2018.

Self-efficacy has been consistently found to be a protective factor against psychological distress and disorders in the literature. However, little research is done on the moderating effect of self-efficacy on depressive symptoms in the context of chronic pain. This cross-sectional study aimed to examine if pain self-efficacy attenuated the direct relationship between pain intensity and depressive symptoms, as well as their indirect relationship through reducing the extent of catastrophizing when feeling pain (moderated mediation). 664 community-dwelling Chinese older adults aged 60-95 years who reported chronic pain for at least three months were recruited from social centers. They completed a battery of questionnaires on chronic pain, pain self-efficacy, catastrophizing, and depressive symptoms in individual face-to-face interviews. Controlling for age, gender, education, self-rated health, number of chronic diseases, pain disability, and pain self-efficacy, pain catastrophizing was found to partially mediate the connection between pain intensity and depressive symptoms. Furthermore, the relationship between pain intensity and depressive symptoms was moderated by pain self-efficacy. Self-efficacy was also found to moderate the relationship between pain intensity and catastrophizing and the moderated mediation effect was confirmed using bootstrap analysis. The results suggested that with increasing levels of self-efficacy, pain intensity's direct effect on depressive symptoms and its indirect effect on depressive symptoms via catastrophizing were both reduced in a dose-dependent manner. Our findings suggest that pain self-efficacy is a significant protective factor that contributes to psychological resilience in chronic pain patients by attenuating the relationship of pain intensity to both catastrophizing and depressive symptoms.

OTHER RESEARCH OF INTEREST

The Gulf War Era Cohort and Biorepository: A Longitudinal Research Resource of Veterans of the 1990-1991 Gulf War Era.

Khalil L[1], McNeil RB[1,2], Sims KJ[1], Felder KA[1], Hauser ER[1,3,4], Goldstein KM[5,6], Voils CI[7,8], Klimas NG[9,10], Brophy MT[1,11], Thomas CM[1], Whitley RL[1], Dursa EK[1,2,12], Helmer DA[1,3,4,13,14], Provenzale DT[1,5,15].

Am J Epidemiol. **2018 Jul 30**. doi: 10.1093/aje/kwy147. PMID: 30060060. [Epub ahead of print]

The United States Department of Veterans Affairs Gulf War Era Cohort and Biorepository (GWECB) is a nationally representative longitudinal cohort of United States Veterans who served during the 1990-1991 Gulf War era. The GWECB combines survey data, such as demographic, health behavior, and environmental exposure data; medical records; and a linked biorepository of blood specimens that can support a broad range of future research regarding health concerns unique to Veterans of this era. To build this resource, the Veterans Affairs Cooperative Studies Program initiated a pilot study (2014-2016) to establish the GWECB and evaluate the processes required to build and maintain the resource. Participants (n=1,275) consented to future sharing of their data and biospecimens for research purposes. We describe the pilot study, including recruitment and enrollment procedures, data collection and management, quality control, and challenges experienced. The GWECB data available to investigators under approved sharing mechanisms, and the procedures for accessing them, are extensively detailed. The study's consenting documents and a website link for the research survey are provided. Our hope is that new research drawing on the GWECB data and biospecimens will result in effective treatments and improved approaches to address the health concerns of Gulf War Era Veterans.

Signatures of T cell dysfunction and exclusion predict cancer immunotherapy response.

Jiang P[1,2], Gu S[3], Pan D[4,5], Fu J[6], Sahu A[1,2], Hu X[1,2], Li Z[6], Traugh N[3], Bu X[3], Li B[1,2,7], Liu J[8], Freeman GJ[3], Brown MA[3,9], Wucherpfennig KW[10,11], Liu XS[12,13,14,15].

Nat Med. **2018 Aug 20**. doi: 10.1038/s41591-018-0136-1. PMID: 30127393. [Epub ahead of print]

Cancer treatment by immune checkpoint blockade (ICB) can bring long-lasting clinical benefits, but only a fraction of patients respond to treatment. To predict ICB response, we developed TIDE, a computational method to model two primary mechanisms of tumor immune evasion: the induction of T cell dysfunction in tumors with high infiltration of cytotoxic T lymphocytes (CTL) and the prevention of T cell infiltration in tumors with low CTL level. We identified signatures of T cell dysfunction from large tumor cohorts by testing how the expression of each gene in tumors interacts with the CTL infiltration level to influence patient survival. We also modeled factors that exclude T cell infiltration into tumors using expression signatures from immunosuppressive cells. Using this framework and pre-treatment RNA-Seq or NanoString tumor expression profiles, TIDE predicted the outcome of melanoma patients treated with first-line anti-PD1 or anti-CTLA4 more accurately than other biomarkers such as PD-L1 level and mutation load. TIDE also revealed new candidate ICB resistance regulators, such as SERPINB9, demonstrating utility for immunotherapy research.

RAC-GWVI Note: This work represents one of the many studies underway in the breakthrough area of research on cancer immunotherapy and checkpoint inhibitors. The current paper follows from the work done by James P. Allison and Tasuku Honjo (neither directly involved in the current abstract) who were awarded earlier this week the 2018 Nobel Prize in Physiology or Medicine.

OTHER RESEARCH OF INTEREST (Continued)

A gut-brain neural circuit for nutrient sensory transduction.

Kaelberer MM[1], Buchanan KL[2], Klein ME[1], Barth BB[3], Montoya MM[3], Shen X[3], Bohórquez DV[4,5,6].

Science. **2018 Sep 21**;361(6408). pii: eaat5236. doi: 10.1126/science.aat5236. PMID: 30237325.

The brain is thought to sense gut stimuli only via the passive release of hormones. This is because no connection has been described between the vagus and the putative gut epithelial sensor cell-the enteroendocrine cell. However, these electrically excitable cells contain several features of epithelial transducers. Using a mouse model, we found that enteroendocrine cells synapse with vagal neurons to transduce gut luminal signals in milliseconds by using glutamate as a neurotransmitter. These synaptically connected enteroendocrine cells are referred to henceforth as neuropod cells. The neuroepithelial circuit they form connects the intestinal lumen to the brainstem in one synapse, opening a physical conduit for the brain to sense gut stimuli with the temporal precision and topographical resolution of a synapse.

A gut feeling.

Hoffman BU[1,2], Lumpkin EA[3,4].

Science. **2018 Sep 21**;361(6408). Pp. 1203-1204. doi: 10.1126/science.aau9973. PMID: 30237346

Perspective on the above Kaelberer et al. article: A gut-brain neural circuit for nutrient sensory transduction.

Summary (in journal Science):

The anatomist Friedrich S. Merkel predicted in 1880 that sensory systems are composed of epithelial cells and sensory nerves, which together transform environmental cues into neural signals that trigger our rich sensory experiences. We now know that this hypothesis mostly holds true for the canonical senses of vision, hearing, taste, and touch. Perhaps surprisingly, the peripheral outposts of these classical sensory systems (eyes, ears, tongue, and skin) are dwarfed by the human body's largest sensory organ—the gut. Enteroendocrine cells, which are rare epithelial cells that decorate the gut lining, have long been suspected to be sensory receptor cells that inform the brain about ingested nutrients. Since their description, these cells were assumed to play a role in metabolism and gut physiology by releasing slow-acting peptide hormones that stimulate neurons throughout the gut and in the brain. On page 1219 of this issue, Kaelberer *et al.* challenge this view by demonstrating that gut enteroendocrine cells locally excite sensory nerves through release of the neurotransmitter glutamate. A recent study of enterochromaffin cells, a subset of enteroendocrine cells, also found that gut signals are transmitted at epithelial-neural synapses through release of the neurotransmitter serotonin. Together, these findings overturn a decades-old dogma that enteroendocrine cells signal exclusively through hormones.

On the Prospects for a (Deep) Learning Health Care System.

Naylor CD[1].

JAMA. **2018 Aug 30**. doi: 10.1001/jama.2018.11103. PMID: 30178068. [Epub ahead of print]

In 1976, Maxmen[1] predicted that artificial intelligence (AI) in the 21st century would usher in “the post-physician era,” with health care provided by paramedics and computers. Today, the mass extinction of physicians remains unlikely. However, as outlined by Hinton[2] in a related Viewpoint, the emergence of a radically different approach to AI, called deep learning, has the potential to effect major changes in clinical medicine and health care delivery. This Viewpoint reviews some of the factors driving wide adoption of deep learning and other forms of machine learning in the health ecosystem.

[Link to full text of article in JAMA Viewpoint]

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