## **Electronic Cigarettes**

The Committee recognizes that the increased use of electronic cigarettes and similar devices pose possible threats to public health, particularly for teenagers and young adults. While these devices are often promoted as safe alternatives to tobacco, studies suggest they may still contain chemicals that pose health risks to the user. The Committee urges NIH to expand research on the oral health consequences of e-cigarettes, and to consider interdisciplinary collaboration between schools of dentistry and traditional cancer researchers.

## Action taken or to be taken:

Electronic cigarettes (e-cigs) are often thought of as a safer alternative to conventional cigarettes. This unsupported view has contributed to increasing popularity amongst high schoolers, including never smokers, and has become a public health crisis. The National Institute of Dental and Craniofacial Research (NIDCR) was an early leader in supporting e-cig research, and in 2016 launched an initiative to understand the biological and physiological effects of e-cigs on cells, tissues and organs of the oral cavity.<sup>28</sup> Due in part to this early research, evidence of the harmful effect of e-cigs is quickly accumulating.

NIDCR-supported researchers uncovered molecular clues demonstrating chronic e-cig use likely contributes to oral cancer. By comparing oral cells from the mouths of e-cig users and non-users they found that over 60 percent of the abnormally expressed genes from e-cig users' oral cells were associated with cancer.<sup>29</sup> Another group of scientists tested the effects of aerosolized e-cig liquids in the craniofacial frog model *Xenopus laevis*. They found that e-cig exposure during embryonic development induces a variety of craniofacial defects.<sup>30</sup> Future research on this topic will address whether e-cig use by pregnant women increases the risk of having a child with craniofacial defects. Several other NIDCR-supported researchers are focused on the effects of e-cig use on the oral microbiome – the collection of bacteria, fungi, and viruses in the mouth crucial to oral health and disease. One group is investigating specific microbial and oral host defense changes, like salivary gland and immune cell function caused by e-cigs, in young adults,<sup>31</sup> another is working to identify biological markers of e-cig exposure,<sup>32</sup> and a third is focused on the link between e-cigs and oral cancer.<sup>33</sup>

NIDCR continues to support research and foster interdisciplinary collaborations to understand how e-cigarettes contribute to oral diseases and to develop novel strategies to reduce their use, especially among young adults and pregnant women. This includes the Institute's commitment to supporting dentist researchers and promoting interdisciplinary collaborations between dental researchers and other scientists and clinicians. For example, NIDCR supports collaborative supplements to bring together ideas, theories, methods, and approaches from different scientific

<sup>&</sup>lt;sup>28</sup> www.grants.nih.gov/grants/guide/rfa-files/RFA-DE-16-005.html; www.grants.nih.gov/grants/guide/rfa-files/RFA-DE-16-004.html

<sup>&</sup>lt;sup>29</sup> www.ncbi.nlm.nih.gov/pubmed/30744164

<sup>30</sup> www.ncbi.nlm.nih.gov/pubmed/28957438

<sup>31</sup> www.projectreporter.nih.gov/project info description.cfm?aid=9665257&icde=46827893

<sup>32</sup> www.projectreporter.nih.gov/project info description.cfm?aid=9833771&icde=46827800

<sup>33</sup> www.projectreporter.nih.gov/project info description.cfm?aid=9665258&icde=46827837

and clinical disciplines to advance oral health research.<sup>34</sup> Further, over 70% of NIH research support to dental schools is from NIDCR,<sup>35</sup> and many of the e-cig research projects NIDCR supports are conducted at dental schools. NIDCR is currently collaborating with NCI and other ICs and Offices on Funding Opportunity Announcements to support basic research on e-cigs<sup>36</sup> and research to examine population-based prevention of disease, including potential risks, benefits, and impacts on e-cig use behavior among different populations.<sup>37</sup>

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<sup>&</sup>lt;sup>34</sup> https://www.nidcr.nih.gov/grants-funding/reissuance-administrative-supplement-collaborative-science-ascs

<sup>35</sup> https://www.ncbi.nlm.nih.gov/pubmed/28033063

<sup>&</sup>lt;sup>36</sup> www.grants.nih.gov/grants/guide/pa-files/PAR-17-475.html; www.grants.nih.gov/grants/guide/pa-files/PAR-17-476.html; www.grants.nih.gov/grants/guide/pa-files/PAR-18-846.html; www.grants.nih.gov/grants/guide/pa-files/PAR-18-845.html <sup>37</sup> www.grants.nih.gov/grants/guide/pa-files/PAR-17-472.html; www.grants.nih.gov/grants/guide/pa-files/PAR-17-473.html; www.grants.nih.gov/grants/guide/pa-files/PAR-18-611.html; www.grants.nih.gov/grants/guide/pa-files/PAR-18-612.html; www.grants.nih.gov/grants/guide/pa-files/PAR-18-848.html; www.grants.nih.gov/grants/guide/pa-files/PAR-18-847.html

## Temporomandibular Disorders [TMD]

The Committee commends NIDCR for its work with the Office of the Director and the National Academies of Sciences, Engineering, and Medicine in the comprehensive project, Temporomandibular Disorders: From Research Discoveries to Clinical Treatment. It also appreciates NIDCR's participation in the TMJ Patient-Led RoundTable to advance collaboration to work toward the common end of providing safe and effective treatments that improve patients' quality of life. The Committee encourages continued collaboration with governmental agencies and other stakeholders in the project. The Committee continues to be concerned that over 36,000,000 people, primarily women in their childbearing years, are affected physically, financially, and emotionally by TMD. The Committee is aware that TMD are primarily a multisystem disorder with overlapping conditions influenced by multiple biological and environmental factors rather than solely an orofacial pain condition. The Committee is cognizant that NIDCR's budget on TMD is a small percent of its overall budget despite the burden of this condition on individuals and society at large. The Committee urges NIDCR to increase funding that will expand the science base and enable increasing multidisciplinary research to advance this field. The Committee requests an update on TMD funding and the preliminary recommendations that came forth from the multiple TMJ public- private scientific meetings supported by NIH and NIDCR in the fiscal year 2021 CJ.

## Action taken or to be taken:

Fostering collaborations is key to tackling the challenges posed by Temporomandibular Disorders. NIDCR is a lead participant in the TMJ Patient RoundTable to advance partnerships to work toward the common goal of providing safe and effective treatments that improve patients' quality of life. Over the past year, NIDCR has continued its participation in the monthly RoundTable meetings, which are producing documents aimed at advancing TMD research and disseminating research results.<sup>260</sup> For example, to characterize the current state of TMD treatments and the strength of supporting data, the group identified and published abstracts of 94 meta-analyses and systematic review articles.<sup>261</sup>

In addition, NIDCR and the NIH Office of the Director are supporting a National Academies of Sciences, Engineering, and Medicine (NASEM) consensus study titled "Temporomandibular Disorders: From Research Discoveries to Clinical Treatment." This project began in fall 2018, convening an expert committee to review and address the current state of knowledge regarding TMD research, education and training, safety and efficacy of clinical treatments of TMD, and burden and costs associated with these disorders. The committee held five meetings throughout 2019. It also held a two-day public workshop and two additional webinars that covered the following TMD-related topics: scope and definitions, public health burden, basic and clinical research, current state of care, provider perspectives on patient care, and clinical education. Importantly, the voice of patient advocates was prominent at the workshop, and all participants expressed a sincere appreciation for the patient point of view. The committee will release its final report in March 2020. NIDCR will carefully consider the study findings and

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<sup>260</sup> http://www.tmj.org/Page/450/48

<sup>261</sup> http://mdepinet.org/wp-content/uploads/TMD-Treatment-MA-and-SRs\_Final.pdf

<sup>262</sup> www.nationalacademies.org/hmd/Activities/PublicHealth/TemporomandibularDisorders.aspx

plans to use the report, in partnership with stakeholders, to inform approaches to advance fundamental, translational, and clinical TMD research and help guide the development of policies related to evidence-based treatment and clinical management of TMD patients.

NIH has increased investments in pain research through the Helping to End Addiction Long-term (HEAL) Initiative. In FY19, NIH published over 40 funding opportunity announcements as part of HEAL. Further, NIDCR is collaborating with many other NIH ICs to support efforts to promote the discovery of robust candidate biomarkers and endpoints for pain conditions, including TMD, that can be used to facilitate the development of non-opioid therapeutics. For example, researchers are determining whether non-invasive methods that modulate the nervous system, such as direct current stimulation of specific brain regions, can reduce pain in TMD patients. Another HEAL project is investigating the role of neuronal ion channels – proteins responsible for transmitting nerve signals – in mediating TMD pain, with the hope that these proteins can be drug-targeted as a non-opioid pain treatment. These increased investments in TMD pain research will allow scientists working on TMD to leverage findings from related pain research to advance the field and accelerate the development of evidence-based strategies to prevent, diagnose, and treat TMD. The ultimate goal is to improve the lives of those affected physically, financially, and emotionally by these disorders.

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