

A National Interagency Temporomandibular Disorder Research Plan

This research plan was developed through the [MDEpiNet TMJ Patient Led RoundTable](#) – an interagency, multi-stakeholder initiative. The research priorities included in this plan are those identified as most important to patients and other stakeholder groups at the May 11, 2018 RoundTable meeting, as well as those extracted from a Briefing Report prepared by the four RoundTable Working Groups. (The briefing report summarizing the overall RoundTable initiative can be viewed [online](#).) The outcomes of these research recommendations will provide answers to the needs of patients communicated at the RoundTable meetings, though the advancement of scientific understanding of the biopsychosocial underpinnings of temporomandibular disorders (TMD) and the implementation of accurate, precise treatment options for patients – ultimately resulting in improved quality of life for TMD patients.

Research priorities contained in this plan focus on two aspects of TMD:

1. Studies gathering information to assess the quality, safety and reliability of temporomandibular joint (TMJ) replacement implants, and studies to predict those at greatest risk of harm from TMJ implant devices (e.g., mechanical failures, tissue reactions)
2. Studies collecting data on TMD patients *without* implanted devices to determine the progression of pain, dysfunction, changes in quality of life, and the development of other co-morbidities stratified as:
 - a. TMD patients with no invasive or non-invasive procedures to the joints
 - b. TMD patients with non-surgical procedures to manipulate or realign the joints (e.g., stabilization splints, bite guards, etc.)
 - c. TMD patients with invasive procedures, such as arthrocentesis, arthroscopy, condylotomy arthroplasty, reconstructive surgery, Botox injections, steroid treatments, etc.

A Priority Listing of Recommendations to Advance Research on Temporomandibular Disorders (TMD)

Note: Please see page 5 for an acronym key of federal agencies listed in the table below.

Research Type	Studies	Responsible Federal Agencies
Population/Epidemiological Science		NIH, CDC, FDA, DoD, VA
	<u>Cross Sectional Study Design</u>	
	1. TMD patients with implants vs. TMD patients with implants vs. control group with no TMD	NIDCR, FDA
	2. Chronic TMD vs. Control	NIDCR
	3. Efficacy and harms of TMD treatments (TMD patients with implants, TMD patients without implants receiving all other TMD treatments)	NIDCR, NIAMS, NINDS
	<u>Longitudinal Study Design</u>	
	1. Chronic TMD patients followed for 5 years	NIDCR, FDA

	<p>2. Implant patients characterized at baseline and followed for 5+ years</p> <p>TMD and comorbidities (both pain and non-pain disorders), their development, risk factors</p> <p>Studies of disease progression, resilience and reversal</p> <p>Incidence, prevalence and risk factors for TMD</p> <p>Individual, economic, and societal costs of TMD</p> <p>Nutritional impact on oral disability</p> <p>Efficacy of physical therapy in all stages of TMD</p> <p>Palliative care of TMD patients</p> <p>Meta-analyses (multiple small cohorts exist)</p>	<p>NIDCR, FDA</p> <p>NIDCR, NINDS, NINR, NIAMS, NIDA, NICHD, NCCIH, NIMH, NIDDK, NHLBI, NHGRI, NIDCD</p> <p>In addition to above: CDC</p> <p>In addition to above: CDC, HRSA, CMS</p> <p>In addition to above: NIH CC</p> <p>In addition to above: FDA, AHRQ</p>
<p>Human/Clinical Studies</p>	<p>Clinical Treatment Trials (efficacy, pragmatic)</p> <p>Patient Centered Outcomes Trials</p> <ol style="list-style-type: none"> 1. Develop treatment guidelines 2. Develop best practices 3. Patient-reported outcomes 4. Predictors of treatment outcomes (success, failure) – individual, subgroups <p>Neurological and psychological systems trials</p> <ol style="list-style-type: none"> 1. Identify mechanisms by which psychosocial variables contribute to acute and chronic TMD and responses to implants and other TMJ treatments 2. Biopsychosocial factors impacting TMD patients and their loved ones/caregivers 3. Influence of psychological risk factors in TMD patients undergoing both successful and failed treatments 4. Biobehavioral approaches to treat psychological comorbidities (depression, anxiety, etc.) 	<p>NIH, FDA, PCORI</p> <p>In addition to above: AHRQ</p> <p>In addition to above: AHRQ</p> <p>In addition to above: AHRQ, HRSA</p>

	<p>Sex differences</p> <ol style="list-style-type: none"> 1. Effects of sex hormones upon disease initiation, progression and responses to drug treatments, surgical interventions and implants <p>Neuro-endocrine system interactions</p> <ol style="list-style-type: none"> 1. Stress-induced mechanisms as causes of TMD progression (PTSD, social isolation, etc.) <p>Immune/Inflammatory mechanisms</p> <ol style="list-style-type: none"> 1. Role of the innate and adaptive immune system in the onset and progression of TMD and responses to surgical procedures and implant devices 2. Response to foreign substances including metals and plastics 3. Role of cytokines in disease onset, progression, regression and resilience <p>TM joint tissues and mechanisms</p> <ol style="list-style-type: none"> 1. Development biology of the TM joint and related tissues 2. Unique characteristics of TM joint tissues and mechanics that distinguish them from other joints of the body 3. Unique characteristics of TM joint tissues and mechanics that distinguish them from other biological structures (e.g., arteries, heart valves, and in conditions such as Ehlers-Danlos syndrome, Marfans syndrome) 4. Cellular models of TM joint tissues and TM muscles <p>Tissue engineering of TM joint and disk replacements</p> <ol style="list-style-type: none"> 1. Novel materials 2. Regenerative medicine approaches 	<p>Emphasis on: ORWH, NIDCR, NICHD</p> <p>Emphasis on: NINDS, NIMH</p> <p>Emphasis on: NIAID, NIBIB</p> <p>Emphasis on: NIEHS</p> <p>Emphasis on: NIDCR, NIAMS</p> <p>Emphasis on: NIDCR, NIAMS, NIBIB</p>
<p>TMD & Data Science/ Biomedical Informatics</p>	<p>Advanced data analysis, artificial intelligence, machine learning, deep learning, novel clustering methods applied to TMD research at all levels</p> <ol style="list-style-type: none"> 1. eQTL analyses 2. Polygenic approaches 3. Pathway analyses 	<p>All NIH Institutes, NLM, NIH Data Science Office, FDA, DoD, VA, AHRQ</p>

	4. Development of high-risk/high-reward innovative approaches to data analysis for precise identification of TMD subjects, disease risk, positive therapeutic effectiveness and outcomes	In addition: NIH Common Fund
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Federal Agency Acronym Key

Acronym	Full Agency Name	Web site
AHRQ	Agency for Healthcare Research and Quality	www.ahrq.gov/
CC	NIH Clinical Center (a Center of the NIH)	https://clinicalcenter.nih.gov/
CDC	U.S. Centers for Disease Control and Prevention	www.cdc.gov/
CMS	Centers for Medicare & Medicaid Services	www.cms.gov/
DoD	U.S. Department of Defense	www.defense.gov/
FDA	U.S. Food and Drug Administration	www.fda.gov/
HRSA	Health Resource & Services Administration	www.hrsa.gov/
NHGRI	National Human Genome Research Institute (an Institute of the NIH)	www.nhgri.nih.gov/
NHLBI	National Heart, Lung, and Blood Institute (an Institute of the NIH)	www.nhlbi.nih.gov/
NIAID	National Institute of Allergy and Infectious Diseases (an Institute of the NIH)	www.niaid.nih.gov/
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases (an Institute of the NIH)	www.niams.nih.gov/
NIBIB	National Institute of Biomedical Imaging and Bioengineering (an Institute of the NIH)	www.nibib.nih.gov/
NICHHD	Eunice Kennedy Shriver National Institute of Child Health and Human Development (an Institute of the NIH)	www.nichd.nih.gov/
NIDA	National Institute of Drug Abuse (an Institute of the NIH)	www.nida.nih.gov/
NIDCD	National Institute on Deafness and Other Communication Disorders (an Institute of the NIH)	www.nidcd.nih.gov/
NIDCR	National Institute of Dental and Craniofacial Research (an Institute of the NIH)	www.nidcr.nih.gov/
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases (an Institute of the NIH)	www.niddk.nih.gov/
NIEHS	National Institute of Environmental Health Sciences (an Institute of the NIH)	www.niehs.nih.gov/
NIMH	National Institutes of Mental Health (an Institute of the NIH)	www.nimh.nih.gov/
NINDS	National Institute of Neurological Disorders and Stroke (an Institute of the NIH)	www.ninds.nih.gov/
NINR	National Institute of Nursing Research (an Institute of the NIH)	www.ninr.nih.gov/
NIH	National Institutes of Health	www.nih.gov/
NCCIH	National Center for Complementary and Integrative Medicine (a Center of the NIH)	www.nccih.nih.gov/
NLM	National Library of Medicine	www.nlm.nih.gov/
ORWH	Office of Research on Women's Health (an Office of the NIH)	www.orwh.nih.gov/
PCORI*	Patient-Centered Outcomes Research Institute	www.pcori.org/
VA	U.S. Department of Veterans Affairs	https://www.va.gov/

* not a federal agency, but independent non-profit organization