

Toward Patient – Centric Evidence Generation and Synthesis in TMD/TMJ: Patient Round Table and Beyond

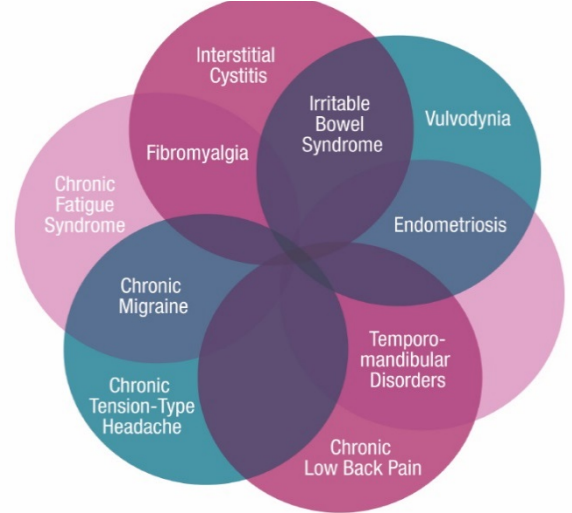
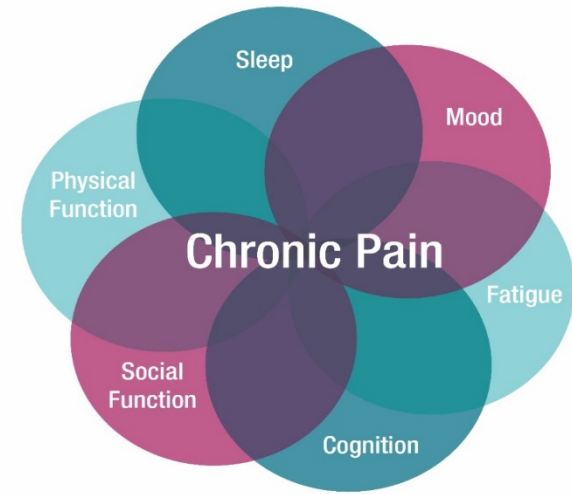
**Danica Marinac-Dabic, MD, PhD, FISPE
Director, Division of Epidemiology,
CDRH/FDA**

Outline

- TMD/TMJ - as a public health issue
- Context: Ongoing and evolving initiatives
 - MDEpiNet
 - CRNs
 - NEST
- Patient-Led Round Table -Progress to Date
- Key Gaps
- Promising Efforts and Opportunities

TMD

- Affects 35 million people (12%)
- Prevalence greater in women
- Complex disorder
- Gaps in evidence
- Need for interdisciplinary approach



Narrowing the Gap Between Currently Available and Urgently Needed



- Enhanced susceptibility and modifying factors (*e.g.*, sex):
 - Variability in clinical manifestation and disease severity
 - Variability in treatment responses and outcomes

- The need for diagnostic and prognostic biomarkers:
 - Intention-to-Treat population with degenerative and ankylotic TMD conditions to be treated with TMJ replacement
 - Predictive assessment of real-world device performance
 - Prevention and diagnostic/therapeutic management of adverse events

- *In silico* research and evidence integration for developing TMD-related Precision/Stratified Medicine applications

Assessment of Temp Dysfunc in Patie

Author links open overlay panelÖmerDurs
<https://doi.org/10.1016/j.jstrokecerebrovas>

Goal

The aim of this study was to assess [tempor](#)

Materials and Methods

Total of 100 participants, 50 healthy and 50 stroke patients. Digital caliper and algometer were used to [masticatory muscle](#) pressure pain threshold the assessment of facial paralysis severity. temporomandibular joint dysfunction asses [mastication](#) shift was measured by the que mastication side.

Findings

In intergroup comparison, significant decre motion parameters in favor of stroke group difference was found between groups for tl middle part of the left temporalis muscle, v result of intergroup examination of labial c it was found that labial commissure angle : group ($P < .05$). Intragroup examination of mastication side shift was seen in patients v

Conclusion

[It was concluded that, temporomandibular group compared with healthy group and us dysfunction treatment would be beneficial.](#)

Case Report Chronic Skull Joint Disease Lactic Acidosis

Mark A. Dobson
Victor M. Ro

¹Anesthesiology Res

²Assistant Professor

Thomas Jefferson U

³Assistant Professor

Philadelphia, PA,

⁴Medical Student, S

⁵Assistant Professor

⁶Assistant Professor

Thomas Jefferson U

⁷Resident, Departm

⁸Professor and Exec

Thomas Jefferson U

Correspondence sh

Received 4 July 20

Academic Editor: A

Copyright © 2018

which permits un

This report display acidosis is broad a due to chronic sku the setting of lacta stems from global unable to match g increased cellular e generalized tonic-c

Association Between Symptoms of Posttraumatic Stress Disorder and Signs of Temporomandibular Disorders in the General Population

Stefan Kindler, MD, DDS/Christian Schwahn, PhD/Olaf Bernhardt, DDS/Andreas Söhnel, DDS/Maria Mksoud, DDS/Reiner Biffar, DDS/Georg Meyer, DDS/Henry Völzke, MD/Hans Robert Metelmann, MD, DDS/Hans Jörgen Grabe

DOI: 10.11607/ofph.1905

Aims: To estimate the association between signs of temporomandibular disorders (TMD) and symptoms of posttraumatic stress disorder (PTSD) in a representative sample from the general population of northeastern Germany. **Methods:** Signs of TMD were assessed with a clinical functional analysis that included palpation of the temporomandibular joints (TMJs) and masticatory muscles. PTSD was assessed with the PTSD module of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, ed 4. The change-in-estimate method for binary logistic regression models was used to determine the final model and control for confounders. **Results:** After the exclusion of subjects without prior traumatic events, the sample for joint pain consisted of 1,673 participants with a median age of 58.9 years (interquartile range 24.8), and the sample for muscle pain consisted of 1,689 participants with a median age of 59.1 years (interquartile range 24.8). Of these samples, 84 participants had pain on palpation of the TMJ, and 42 participants had pain on palpation of the masticatory muscles. Subjects having clinical PTSD ($n = 62$) had a 2.56-fold increase in joint pain (odds ratio [OR] = 2.56; 95% confidence interval [CI]: 1.14 to 5.71, $P = .022$) and a 3.86-fold increase (OR = 3.86; 95% CI: 1.51 to 9.85, $P = .005$) in muscle pain compared to subjects having no clinical PTSD. **Conclusion:** These results should encourage general practitioners and dentists to acknowledge the role of PTSD and traumatic events in the diagnosis and therapy of TMD, especially in a period of international migration and military foreign assignments.

Systemic disease painful condition temporomandibular and migraine

Edwin Fernando Ruiz CONTRERAS^(a)
Giovana FERNANDES^(b)
Paula Cristina Jordani ONGARO^(b)
Leticia Bueno CAMPI^(b)
Daniela Aparecida Godoi
GONÇALVES^(b)

^(a)Universidade Estadual de Londrina – UEL,
Department of Restorative Dentistry,
Londrina, PR, Brazil.

^(b)Universidade Estadual Paulista – UNESP,
Araraquara Dental School, Department
of Dental Materials and Prosthodontics,
Araraquara, SP, Brazil.

Declaration of Interests: The authors
certify that they have no commercial or
associative interest that represents a conflict
of interest in connection with the manuscript.

Corresponding Author:
Edwin Fernando Ruiz Contreras
E-mail: edwinfr@igmail.com

Abstract: Temporomandibular
painful musculoskeletal con-
ditions and are frequently associated
with M with other painful ce-
rvicephalgia, body pain (BP), e-
ndometriosis, diabetes, cardiopul-
monary. **Methods:** This was a cross-
sectional study of 352 individuals. Partici-
pants were selected according to the presence of
free of TMD and any head/neck
TMD, but free of any HA; and
M. TMD was classified according
for Temporomandibular Disor-
ders physical symptoms (NPS) w-
ith International Classification of
Dental Disorders, were applied to iden-
tify painful conditions and system-
ic self-report. The prevalence of
TMD+M group. Multiple regres-
sion was associated with the TM
($p < 0.05$), cervicgia ($p < 0.05$)
significantly associated with
that individuals with a comorbid
more severe condition than the

Keywords: Migraine Disorder
Neck Pain; Headache; Comorbid

Research Paper

Orofacial Man- disorders of S Study

Vito Crincoli^(a), Mariaseve-
ra Limongelli^(a), Angela Tempe-
stini^(a)

1. Interdisciplinary Department of Me-
dical Sciences
2. Department of Basic Medical Science
3. Department of Emergency and Organ

^(a) Corresponding author: Prof. Vito Crin-
coli. E-mail: vito.crincoli@univ.it

© IvySpring International Publisher. This
work is licensed under the Creative Commons
Attribution License (CC BY).

Received: 2017.09.27; Accepted: 2017.10.10

Abstract

AIMS: Sjögren's syn-
drome, tooth decay, gingiv-
itis, term referred to as
of this study was disor-
ders (TMD) in
METHODS: The
the American-Euro-
pean patients, matched
symptoms was bas-
ed on Disorders (RDC/TMD)
RESULTS: SS pa-
tients, dysphagia, dysphagi-
a, chewing, difficulty in
patients and by 84.7%
at least one oral si-
gnificant by muscular contra-
cture (0.05). Furthermore
 $p = 0.020$.

CONCLUSIONS

Key words: Sjögren's

Original Article

Relationship between Expanded Disability Status Scale scores and the presence of temporomandibular disorders in patients with multiple sclerosis

Lucas Senra Corrêa Carvalho¹, Osvaldo José Moreira Nascimento¹,
Luciane Lacerda Franco Rocha Rodrigues², Andre Palma Da Cunha Matta¹

¹Department Of Neurology, University Federal
Fluminense, Niterói, Brazil,
²Department Of Graduate Program In
Temporomandibular Disorder, São Leopoldo Mandic,
Campinas, Brazil

Correspondence: Dr. Lucas Senra Corrêa Carvalho
Email: lucas.sccarvalho@bol.com.br

ABSTRACT

Objectives: The objectives of this study were to assess the prevalence of temporomandibular disorders (TMDs) in patients with relapsing-remitting multiple sclerosis (MS) and to investigate whether an association exists between the presence of TMD symptoms and the degree of MS-related disability. **Materials and Methods:** In all, 120 individuals were evaluated: 60 patients with a diagnosis of relapsing-remitting MS and 60 age- and sex-matched controls without neurological impairments. A questionnaire recommended by the European Academy of Craniomandibular Disorders for the assessment of TMD symptoms was administered. For those who answered affirmatively to at least one of the questions, the RDC/TMD Axis I instrument was used for a possible classification of TMD subtypes. The Expanded Disability Status Scale (EDSS) was the measure of the degree of MS-related disability. **Statistical Analysis Used:** Fisher's exact test was used to analyze the data. ANOVA was used to detect significant differences between means and to assess whether the factors influenced any of the dependent variables by comparing means from the different groups. **Results:** The prevalence of TMD symptoms in patients with MS was 61.7% versus 18.3% in the control group (CG). A diagnosis of TMD was established for 36.7% in the MS group and 3.3% in the CG ($P = 0.0001$). There were statistically significant differences between degrees of MS-related disability and the prevalence of TMD ($P = 0.0288$). **Conclusions:** The prevalence of both TMD and TMD symptoms was significantly greater in the MS group. EDSS scores and TMD prevalence rates were inversely related.

Key words: Multiple sclerosis, orofacial pain, temporomandibular disorder

Temporomandibular Disorder Patients: An Observation

Massimo Corsalini¹, Daniela Di Venere², France:

1. MD, DMD Assistant professor, Dental School University of Bari
2. DDS, PhD, PG Orth Assistant professor, Dental School Univr
3. DDS, Assistant professor, Dental School University of Bari, S
4. DDS, Assistant professor, Dental School University of Milan
5. DDS, PhD, PG Oral Surg. Assistant professor, Dental School

✉ Corresponding author: Prof. Massimo Corsalini. Clinica odon
Tel. +39 0805478729. Fax. +39 080 5478743. massimo.corsalini@un

© Ivyspring International Publisher. This is an open-access article distribut
licenses/by-nc-nd/3.0/). Reproduction is permitted for personal, noncom

Received: 2013.03.25; Accepted: 2013.10.07; Published: 2013.11

Abstract

BACKGROUND: Burning Mouth Syndrom of any lesions and burning of the oral mucos alterations. The purpose of our study is to Disorders (TMD) in patients with BMS an between BMS and TMD.

MATERIALS AND METHODS: Forty-established according to the classification of the protocol of the European Academy of Cr RDC/TMD criteria. The data were compare existence of an association between BMS an

RESULTS: 65.9% the BMS patients showed TMD according to RDC / TMD crite The chi-square test revealed a statistically s TMD.

CONCLUSION: The data suggest that th between BMS and TMD, may be for neurop engaged in TMD pathogenesis.

Association Between Chronic Tension-Type Headache Coexistent with Chronic Temporomandibular Disorder Pain and Limitations in Physical and Emotional Functioning: A Case-Control Study

Rüdiger Emshoff, MD, DMD

Associate Professor

Department of Oral and Maxillofacial Surgery
Medical University of Innsbruck
Innsbruck, Austria

Felix Bertram

Dental Student

Department of Prosthodontics
Philipps University
Marburg, Germany

Dagmar Schnabl, MD, DMD

Consultant

Department of Restorative and Prosthetic Dentistry
Medical University of Innsbruck
Innsbruck, Austria

Iris Emshoff, MD

Resident

Department of Anaesthesia and Intensive Care Medicine
Medical University of Innsbruck
Innsbruck, Austria

Correspondence to:

Dr Rüdiger Emshoff
University Clinic of Oral and Maxillofacial Surgery
Medical University of Innsbruck
Anichstraße 35
A-6020 Innsbruck, Austria
Phone: +43 512 516 1504

Aims: To assess the association between chronic tension-type headache coexistent with chronic temporomandibular disorder (TMD) pain and severe limitations in physical and emotional functioning. **Methods:** Sample size estimation was used to determine that this case-control study should include 126 subjects. Subjects suffering from chronic TMD who were aged between 18 and 68 were recruited in routine clinical practice. Of the 126 included subjects, 63 had TMD pain associated with chronic tension-type headache (cases) and 63 had TMD pain without a history of tension-type headache (controls). Clinical diagnosis of TMD was made according to the Research Diagnostic Criteria for TMD (RDC/TMD) Axis I criteria, and clinical diagnosis of headache was made according to the International Classification of Headache (ICHD-II). RDC/TMD Axis II criteria were applied to record the scores from the Graded Chronic Pain Scale (GCPS) and the Symptoms Checklist-90-Revised Depression (SCL-DEP) and Somatization (SCL-SOM) scales. A logistic regression analysis was used to assess the relationship between TMD pain with chronic tension-type headache and high levels of depression and somatization severity as scored on the SCL-DEP and SCL-SOM scales, respectively, and high pain-related disability (GCPS grade III or IV). Data were adjusted to take into account age, gender, time since TMD pain onset, chronic TMD pain intensity, and characteristic pain intensity.

Results: The presence of chronic tension-type headache was significantly associated with severe SCL-DEP (odds ratio [OR] = 7.2; $P < .001$), severe SCL-SOM (OR = 13.8; $P < .001$), and high pain-related disability (OR = 9.7; $P < .001$).

Conclusion: This study provides evidence of associations between the clinical diagnosis of chronic tension-type headache coexistent with chronic TMD pain and key aspects of physical and emotional functioning reflected in severe depression, severe somatization, and high pain-related disability. *J Oral Facial Pain Headache* 2017;31:55–60. doi: 10.11607/ofph.1654

RESEARCH ARTICLE

Association between temporomandibular disorders, chronic diseases, and ophthalmologic and otolaryngologic disorders in Korean adults: A

Hyun-Seop Song¹, Joon-Shik Shin¹, Heung Cho², Koh-Woon Kim², Yeon-Seoyoun Kim³, Mia Kim⁴, In-Hyuk Ha⁵

1 Jaseng Spine and Joint Research Institute, **2** Department of Korean Rehabilitation Medicine, Republic of Korea, **3** Department of Acupuncture and Moxibustion, Gangdong, Seoul, Republic of Korea, **4** College of Medicine, United States of America, **5** VIAplus, Siheung-si, Seoul, Republic of Korea, **7** D Center, College of Korean Medicine, Kyung

* hanihata@gmail.com



Submit a Manuscript: <http://www.wjgnet.com/esps/>
Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
DOI: 10.3748/wjg.v23.i1.103

World J Gastroenterol 2017 January 7; 23(1): 103-109
ISSN 1007-9327 (print) ISSN 2219-2840 (online)
© 2017 Baishideng Publishing Group Inc. All rights reserved.

ORIGINAL ARTICLE

Case Control Study

High risk of temporomandibular disorder in irritable bowel syndrome: Is there a correlation with greater illness severity?

Serena Gallotta, Vincenzo Bruno, Santo Catapano, Nicola Mobilio, Carolina Ciacci, Paola Iovino

CONCLUSION

IBS patients had a more than three times greater risk of TMD compared to HC. The risk of having TMD

that also fulfilled criteria for TMD seem to share along with chronic facial and abdominal pain a significant co-occurrence with psychiatric disorders and female preponderance.

Conclusions

These findings imply that TMDs, chronic diseases, and ophthalmologic and otolaryngologic disorders hold various correlations, suggesting the need for multitarget approaches to effectively address this phenomenon.

Original Article

Impact in oral health temporomandibular Parkinson's disease

PAULA FERNANDA DA COSTA SILVA^{1)*}, D...
LARA JANSISKI MOTTA¹⁾, SORAIA MICAEL...
KRISTIANNE PORTA SANTOS FERNANDES¹⁾

¹⁾ Nove de Julho University: Rua Vergueiro

Abstract. [Purpose] The aims of this study were to evaluate the prevalence of temporomandibular disorder (TMD) in a group of patients with Parkinson's disease, and the severity of the disease. [Methods] The criteria for Temporomandibular Disorders were based on the Research Diagnostic Criteria for Temporomandibular Disorders. The unpaired Student's t-test was used to compare the groups. The results were calculated to determine correlations. Fisher's exact test was used to test the hypothesis. [Results] Fifty-nine individuals with PD were included in the study. No significant associations were found between TMD and PD. A statistically significant difference between the groups was found (p=0.003). No significant correlation was found between the groups. [Conclusion] The prevalence of TMD was significantly different between groups with PD and without PD. **Key words:** Parkinson's disease, Craniomandibular disorders.

BEHAVIORAL SCIENCES

Association Between Disorders and Depression in the Northern Finland

Kirsi Sipilä , D.D.S., Juha Veijola, M.D., Ph.D.,
Aune M. Raustia, D.D.S., Ph.D. & ...show all
Pages 183-187 | Received 24 Aug 2000, Accepted 14 Mar 2001

 Download citation  <https://doi.org/10.1080/00007010008839500>

 References  Citations  Metrics

ABSTRACT

Facial pain and other symptoms of temporomandibular disorder (TMD) are common in the population. According to clinical studies, the maintenance of these symptoms. On the other hand, the prevalence of TMD in the study was to evaluate the association between TMD and depression in a sample of young adults. The study was a cohort consisting of 12,058 live births from the Finnish Twin Cohort. Information about reported depression (diagnosed by the DSM-IV criteria) was collected from a subsample of the cohort. The prevalence of TMD (SCN-25 DS) of the TMD symptoms, those with depression. In both genders, the proportion of TMD was higher in subjects with pain-related symptoms ("pain on jaw movement"), compared with subjects without pain. The prevalence of recognized depression was significantly higher in subjects with TMD (p<0.05), except when adjusting for marital status, education, and age. The results suggest that depression has an association with TMD.

Original articles

Pain threshold, sleep quality and anxiety levels in individuals with temporomandibular disorders

Carla Raquel de Melo Daher⁽¹⁾
Larissa Fernandes da Cunha⁽¹⁾
Ana Paula de Lima Ferreira⁽¹⁾
Ana Izabela Sobral de Oliveira Souza⁽¹⁾
Tiago Albuquerque Maranhão Rêgo⁽¹⁾
Maria das Graças Rodrigues de Araújo⁽¹⁾
Hilton Justino da Silva⁽¹⁾

ABSTRACT

Purpose: to evaluate the pressure pain threshold, sleep quality and anxiety levels of individuals with different types of chronic temporomandibular disorders (TMD).

Methods: a controlled, observational and cross-sectional study. TMD diagnosis followed the Research Diagnostic Criteria and the volunteers were divided into three groups: A-Muscular Disorder (n = 15), B- Articular Disorder (n = 10) and C- Control Group (n = 15). Evaluation was performed using the Pittsburg Sleep Quality Index, Visual Analog Scale, Algometry and Hospital Anxiety and Depression Scale. The significance level for all tests was 5%.

Results: lower threshold of pain was seen in the masticatory and cervical musculature within groups A and B. However, when TMD groups were compared to the control group, only a statistically significant difference in the pain threshold of the masticatory muscle and the trapezius muscle was found. Groups A and B presented poor sleep quality, showing a statistical difference when compared to the control group. Additionally, it was observed that patients in the groups with TMD presented anxiety, while those in the control group, did not present it.

Conclusion: individuals presented with TMD show lower levels of pain threshold, sleep quality and anxiety, as compared to healthy subjects. These results do not depend on the type of disorder presented.

Keywords: Temporomandibular Joint Disorder; Pain; Sleep; Anxiety

⁽¹⁾ Universidade Federal de Pernambuco, Centro de Ciências da Saúde, Recife, Pernambuco, Brasil.

Study performed at the Laboratório de Motricidade Oral do Departamento de Fonoaudiologia and at the Laboratório de Cinesioterapia e Recursos Terapêuticos Manuais (LACIRTEM) do Departamento de Fisioterapia da Universidade Federal de Pernambuco, Brasil.

Research support source: Program of Scientific Initiation Scholarships of Universidade Federal de Pernambuco - PIBIC / UFPE / CNPq.

Conflict of interests: Nonexistent



Prevalence of temporomandibular disorders in patients with Hashimoto thyroiditis

Authors

Authors and affiliations

Alina Grozdinska , Elisabeth Hofmann, Matthias Schmid, Ursula Hirschfelder

Original Article

First Online: 17 May 2018



Downloads

Abstract

Objectives

Autoimmune thyroid disease (AITD), also known as Hashimoto thyroiditis (HT), is a degenerative inflammatory disease with high prevalence among women and has been associated with fibromyalgia and widespread chronic pain. The goal was to determine the frequency of temporomandibular disorders (TMD) in patients with HT.

Results

The two groups did not differ in terms of demographic parameters or mandibular jaw mobility. Significantly higher levels of anti-TPO and anti-Tg were attested in all subjects of the HT group. Markedly elevated prevalence of TMD was found in the HT group. Muscle pain and stiffness were found in 45 (86.5%) subjects of the HT group ($p < 0.001$), of whom 33 (63.4%) also had disc displacement with reposition ($p < 0.001$). Whereas 50% of the control group showed no TMD symptoms, all subjects in the HT group had symptoms.

Conclusions

A significantly elevated prevalence of TMD was found in patients with HT. **Thus, patients with TMD who do not respond to therapy should be referred for thyroid diagnostic workup.**

Review

Tinnitus as a comorbidity to temporomandibular disorders – a systematic review

Caroline Skog, Jesper Fjellner, EwaCarin Ekberg, Birgitta Häggman-Henrikson 

First published: 20 August 2018 | <https://doi.org/10.1111/joor.12710>

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/joor.12710



PDF



TOOLS

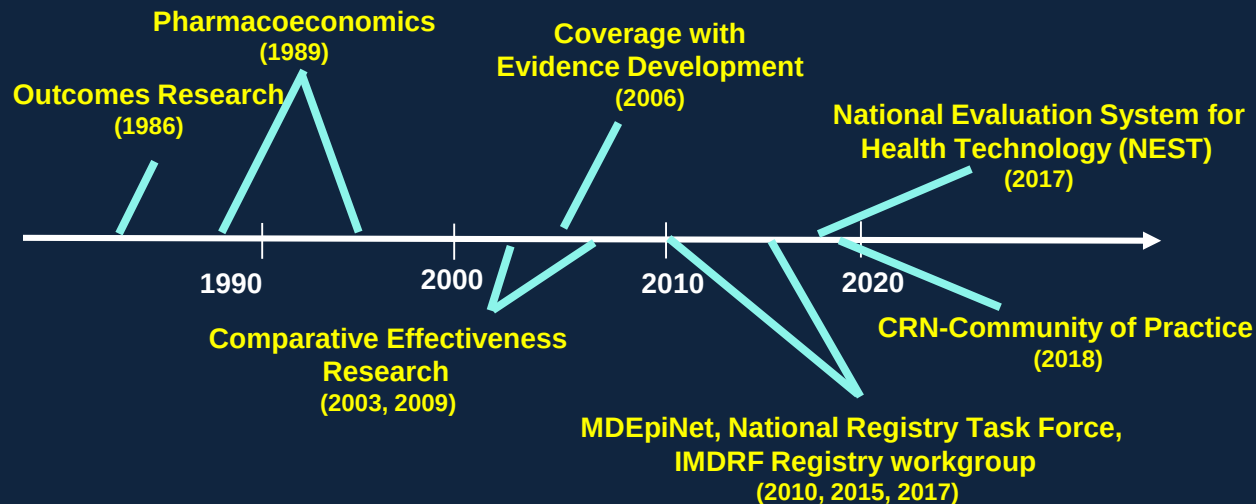


SHARE

Abstract

The aim of this systematic review was to evaluate the prevalence of tinnitus in patients with temporomandibular disorders (TMD) and the possible effects of TMD treatment on tinnitus symptoms. A search of the PubMed, Web of Science, and Cochrane databases from inception of each database up to January 2017 found 222 articles. After independent screening of abstracts by two of the authors, we assessed 46 articles in full text. The inclusion and exclusion criteria reduced these to 25 articles of which 22 studies reported prevalence based on 13,358 patients and 33,876 controls, and eight studies reported effect of TMD treatment on tinnitus based on 536 patients and 18 controls. The prevalence of tinnitus in patients with TMD varied from 3.7% to 70% (median 42.3%) whereas the prevalence in control groups without TMD varied between 1.7% and 26% (median 12%). The eight treatment studies, indicated that treatment of TMD symptoms may have a beneficial effect on severity of tinnitus. However, only one treatment study included a control group, meaning that the overall level of evidence is low. **The finding that tinnitus is more common in patients with TMD means that it can be regarded as a comorbidity to TMD.** However, in view of the lack of evidence currently available, further well-designed and randomized studies with control groups are needed to investigate whether possible mechanisms common to tinnitus and TMD do exist and whether TMD treatment can be justified to try to alleviate tinnitus in patients with TMD and comorbidity of tinnitus.

Grounded in Epidemiology, Evidence Based Medicine and Health Services Research



Building Global Real World Evidence Collaboratives for Health Technologies

The Medical Device Epidemiology Network (MDEpiNet) is a global public-private partnership that seeks to advance the collection and use of real-world data to improve patient outcomes. MDEpiNet brings together stakeholders from across the health ecosystem to develop and improve real-world data infrastructure, and carry out studies to better understand how devices perform in the real-world.

MDEpiNet has taken a lead on the development of Coordinated Registry Networks (CRNs) as set out in the National Registry Taskforce (read JAMA Perspective below). The list of the currently developing CRN is listed in the box on this page below...





MDEpiNet
Launch

International
Consortia
(e.g. ICOR, ICCR)

**THE VISION FOR
NATIONAL SYSTEM
LAUNCHED**
FDA 4- day Public
Meeting
Day 1. Launch of
FDA strategy
Day 2. MDEpiNet
Annual
Days 3-4. Registries

Reports:

- Planning Board
- MDEpiNet Registry Task Force
- IMDRF



NEST Data
Partners
Network



Develop and test
drive novel methods
and scientific
infrastructure for
device evidence
generation
synthesis and
appraisal nationally
and internationally

MDEpiNet
Methodology
Center at
Harvard

MDEpiNet Science
and
Infrastructure
Center at Cornell



CRN Community
of Practice



International Medical Device Regulators Forum

Title: Principles of International System of Registries Linked to Other Data Sources and Tools

Authoring Group: IMDRF Patient Registries Working Group

Date: 30 September 2016



Title: Methodological Principles in the Use of International Medical Device Registry Data

Authoring Group: IMDRF Patient Registries Working Group

Date: 16 March 2017



Tools for assessing the
Usability
of Registries for
Regulatory Decision
Making , March 2018

MDEpiNet: Intersections with FDA Strategic Initiatives and NEST

MDRTF Recommendations to FDA for NEST

Recommendations for a National Medical Device Evaluation System

Strategically Coordinated Registry Networks to Bridge Clinical Care and Research

A Report from the Medical Device Registry Task Force & The Medical Devices Epidemiology Network



BRIDGING UNMET CLINICAL CARE AND CLINICAL RESEARCH NEEDS WITH STRATEGICALLY COORDINATED REGISTRY NETWORKS

Report from the National Medical Device Registry Task Force & The Medical Devices Epidemiology Network

Mitchell W. Krucoff, Sharon Lise Normand, Fred Edwards, Theodore Lystig, Eve Ross, Elise Berliner, Kristi Mitchell, James Tchong, David Blaser, Ralph Brindis, Jack Cronenwett, Pamela Gavin, Linda Harrington, Amy Helwin, Kevin Larsen, William

VIEWPOINT

Bridging Unmet Medical Device Ecosystem Needs With Strategically Coordinated Registries Networks

Mitchell W. Krucoff, MD
Division of Cardiology,
Department of
Medicine, Duke
University Medical
Center, Durham,
North Carolina.

Art Sedrakyan, MD, PhD
MDEpiNet Science and
Infrastructure Center,
Weill Cornell Medical
College, New York,
New York.

In June 2014, the Medical Device Epidemiology Network (MDEpiNet) Public Private Partnership,¹ on behalf of the US Food and Drug Administration Center for Devices and Radiologic Health (CDRH), convened the Medical Device Registries Task Force (MDRTF) (see eAppendix in the Supplement). The task force was launched to address the CDRH's commitments²⁻³ to strengthen the medical device postmarket surveillance system using existing resources and under current authorities and to develop an integrated system that efficiently and effectively achieves its basic functions, from timely identification of postmarket signals to facilitating premarket device clearance and approval.

The MDRTF included broad stakeholder representation and was mandated to examine the objectives and lo-

The MDRTF recognized that most existing registries, electronic health records (EHRs), and data sources do not contain all the elements necessary for device evaluations, including device and procedural details, patient descriptors, or long-term outcomes. However, the MDRTF recognized that such limitations could be mitigated through interoperability solutions that strategically link complementary registries and data sources to produce networks for which the data composite could support robust device evaluation. The MDRTF termed this structure the strategically coordinated registries network, or CRN—with the recognition that many key elements in such networks (such as EHRs, administrative claims data, or mobile device outputs) are not registries per se. The MDRTF recommends strategic CRNs as the

natural construct for the national system for registry development and unique implementation rather than replace them. This structure could provide novel, immediate national system. Creation of CRNs is a "dual-purpose" leveraging of existing administrative data resources, and existing linked-registry models such as the

Strategically Coordinated Registry Networks (CRN) Principles:

- Link complementary sustainable registries/e-repositories (Professional society registries, EHRs, Claims data, PCORI- CDRNs)
- TPLC approach as a true continuum leveraging “real world” evidence
- “Dual purpose” existing national, regional or other large scale efforts

TMJ Patient-Led Round Table: Objectives

- Develop standardized data infrastructure : TMJ - CRN
- Affect a change in clinical trial practices to incorporate patient preference data and RWE experiences
- Develop a roadmap for the development of predictive analytics algorithms
- Develop evidence-based protocols and best practices for inclusion into health care
- Promote the development of collaborative multi-disciplinary research

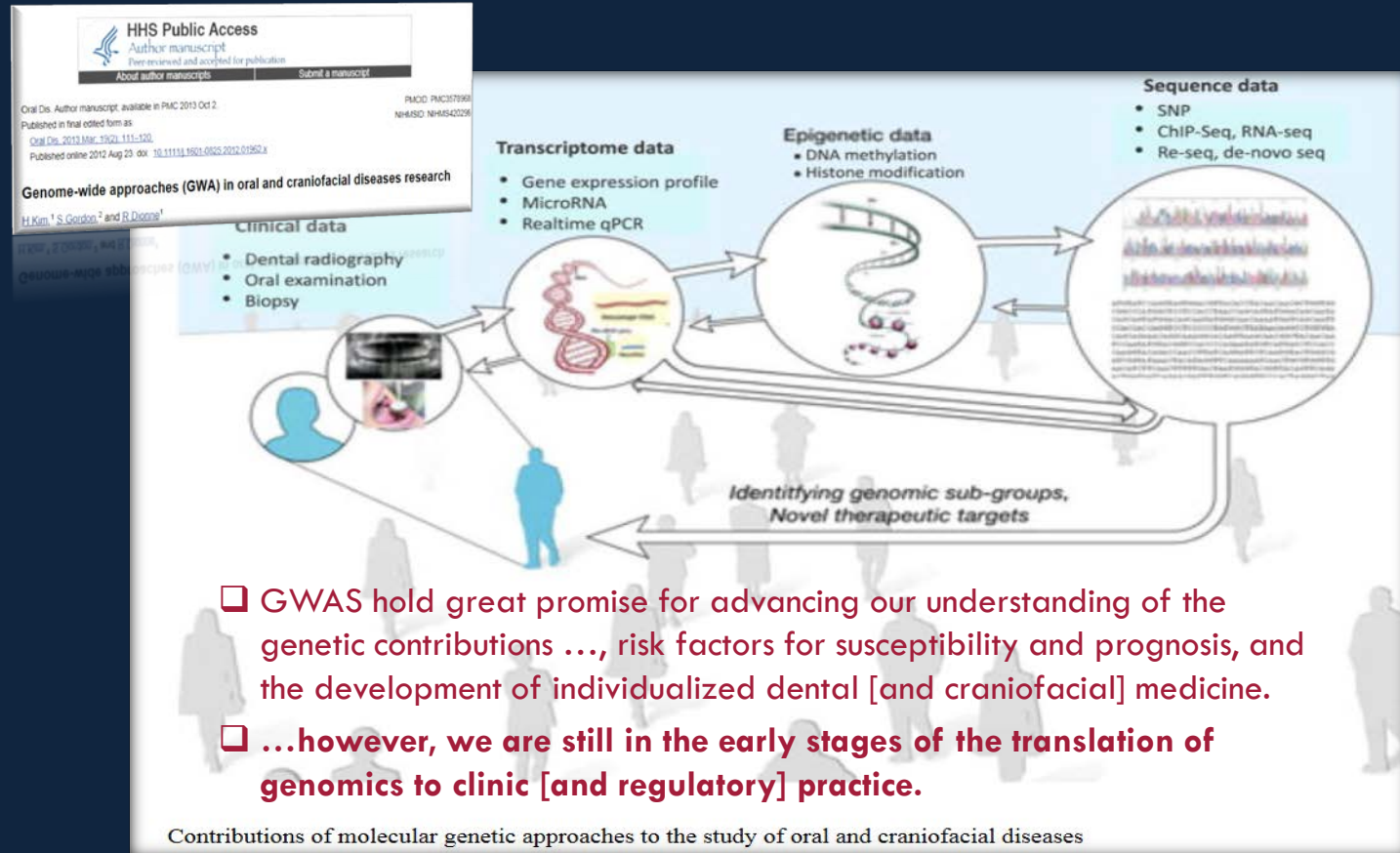
TMJ Patient-Led Round Table Working Groups

- WG1. Natural History and Assessment of Biomarkers Associated with Outcomes in TMJ Implant Patients
- WG2. Patient Reported Outcomes Evaluation
- WG3. Physician and Patient Education, Patient-Centered Treatment
- WG4. Data Collection and Analysis

National TMD/TMJ Research Plan Domains

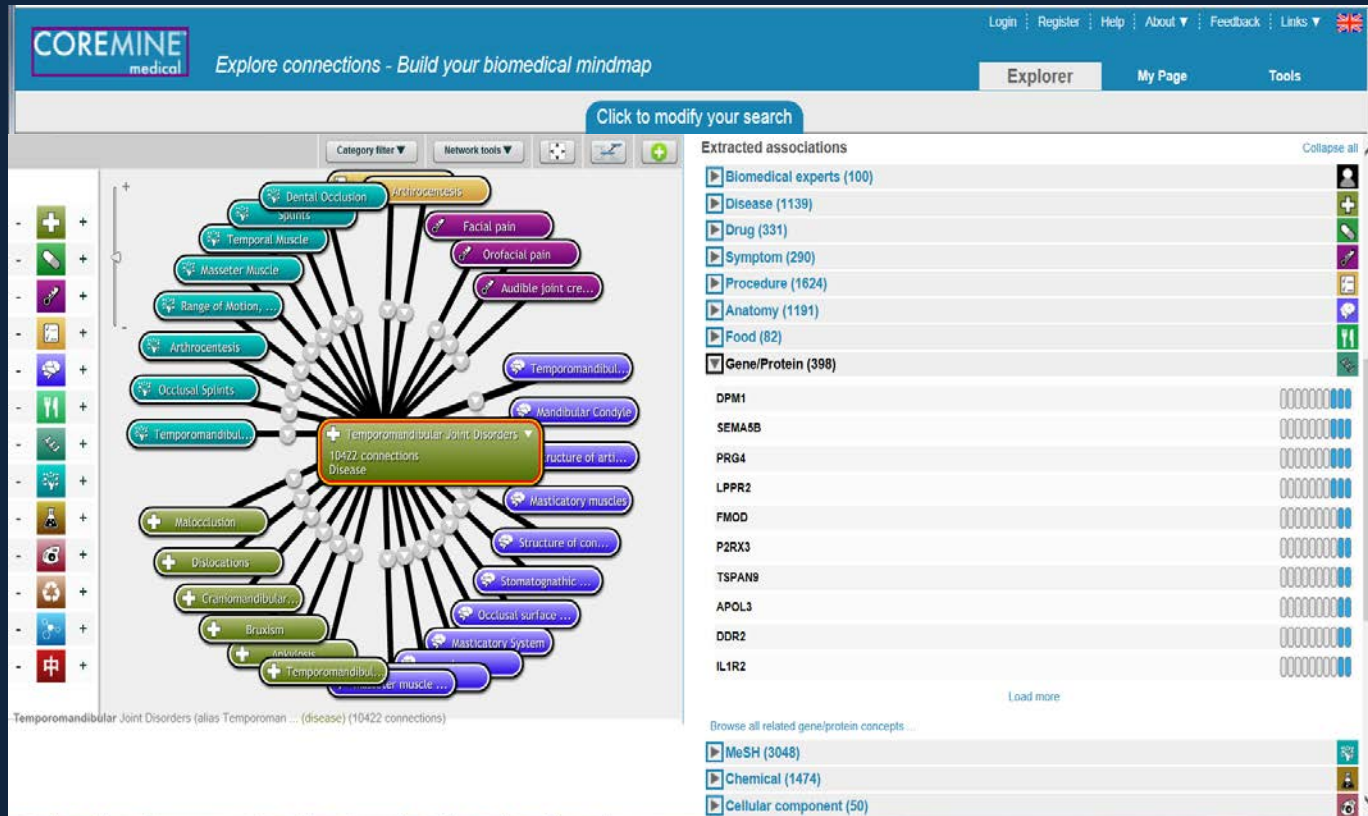
- Population/Epidemiologic Science
- Human Studies /Clinical Studies
- Basic Biological Science
- Data Science/Informatics
 - Example: In silico-approaches

Promise of 'Omic Research for elucidating the causes for susceptibility and inter-individual variability



- ❑ GWAS hold great promise for advancing our understanding of the genetic contributions ..., risk factors for susceptibility and prognosis, and the development of individualized dental [and craniofacial] medicine.
- ❑ ...however, we are still in the early stages of the translation of genomics to clinic [and regulatory] practice.

TMD in Coremine knowledgebase: >10,400 connections, including ~400 genes/proteins



Example of potential **sex/race**-related variability in utility of TMD biomarkers (Xiao et al 2015; 1000 Genomes)



20:35,437,703-35,438,703 Variant: rs143383

rs143383 SNP

Original source

Alleles

Location

Co-located variant

Most severe consequence

Evidence status

Clinical significance

HGVS names

Synonyms

Genotyping chips

About this variant

Description from SNPedia

Variants

G/A

Chromos

HGMD

5 prime

3 prime

RefSeq

This var

This var

This var

This var

rs143384 SNP

Original source

Alleles

Location

Most severe consequence

Evidence status

HGVS names

Synonyms

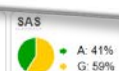
Genotyping chips

About this variant

Description from SNPedia

Population genetics

1000 Genomes Project Phase 3 allele frequencies



This var

This var

This var

This var

This var

This var

This var

This var

This var

This var

This var

This var

This var

This var

This var

This var

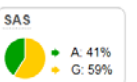
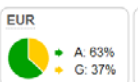
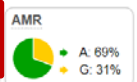
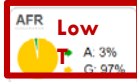
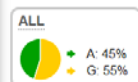
Association of GDF5, SMAD3 and RUNX2 polymorphisms with temporomandibular joint osteoarthritis in female Han Chinese.

Table 2. Genotype distribution and allele frequencies of polymorphisms in GDF5, SMAD3, RUNX2, TGFB1 and CYP11B1 genes in patients with TMJOA (n = 114) and healthy controls (n = 126)

Polymorphism	TMJOA patients (%)	Controls (%)	OR [95%CI]	P value
GDF5-rs143383				
CC	114	126	1.00	
CT	5 (4.4)	19 (15.1)	3.31 [1.15-9.55]	0.012 [†]
TT	47 (41.2)	54 (42.9)	4.45 [1.55-12.72]	0.027
	62 (54.4)	53 (42.1)	3.87 [1.40-10.74]	0.005
Dominant model (TT + CT vs. CC)			1.64 [0.99-2.74]	0.009
Recessive model (TT vs. CT + CC)			1.00	0.057
C allele	57 (25)	92 (36.5)		

Population genetics

1000 Genomes Project Phase 3 allele frequencies



Sub-populations

Sub-populations

Sub-populations

Sub-populations

Sub-populations

Example of a TMD biomarker limited to one racial subgroup (Smith et al 2013; 1000 Genomes)



J Pain. 2013 December ; 14(12 0): . doi:10.1016/j.jpain.2013.09.004.

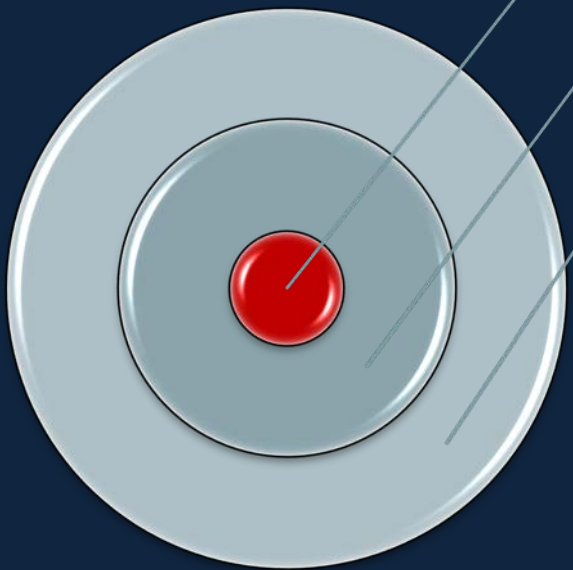
Genetic variants associated with development of TMD and its intermediate phenotypes: the genetic architecture of TMD in the OPPERA prospective cohort study

Shad B. Smith¹, Ellen Mir^{1,2}, Eric Bair^{1,2}, Gary D. Slade^{1,3,4}, Ron Dubner⁵, Roger B. Fillingim⁶, Joel D. Greenspan⁵, Richard Ohrbach⁷, Charles Knott⁸, Bruce Weir⁹, William Maixner^{1,10}, and Luda Diatchenko^{1,11}

Population	T Allele (%)	C Allele (%)
ALL	91%	9%
AFR (High C)	69%	31%
AMR	97%	3%
EAS	100%	0%
EUR	99%	1%
SAS	100%	0%

- “A SNP in *PTGS1* (*rs3842803*) showed the strongest association with global psychological symptoms. However, as this SNP is very rare in Caucasians/Europeans, but fairly common in African populations, the SNP remained strongly associated only in African-Americans.”

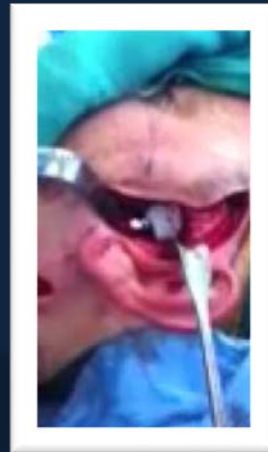
TMD complexity complicating treatment choices



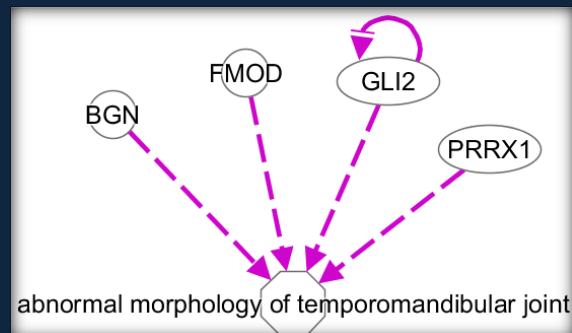
**Degenerative
and ankylotic
TMDs as
indications for
TMJ
REPLACEMENT
TMJ OA**

TMDs

(eg, chronic pain –
nociceptive,
neuropathic, etc.)



Ingenuity Knowledgebase (1): Genes involved in abnormal TMJ morphology



Provide Feedback | Support Dr. Torosyan Close IPA

Genes and Chemicals Diseases and Functions Pathways and Tox Lists

temporomandibular SEARCH Advanced Search

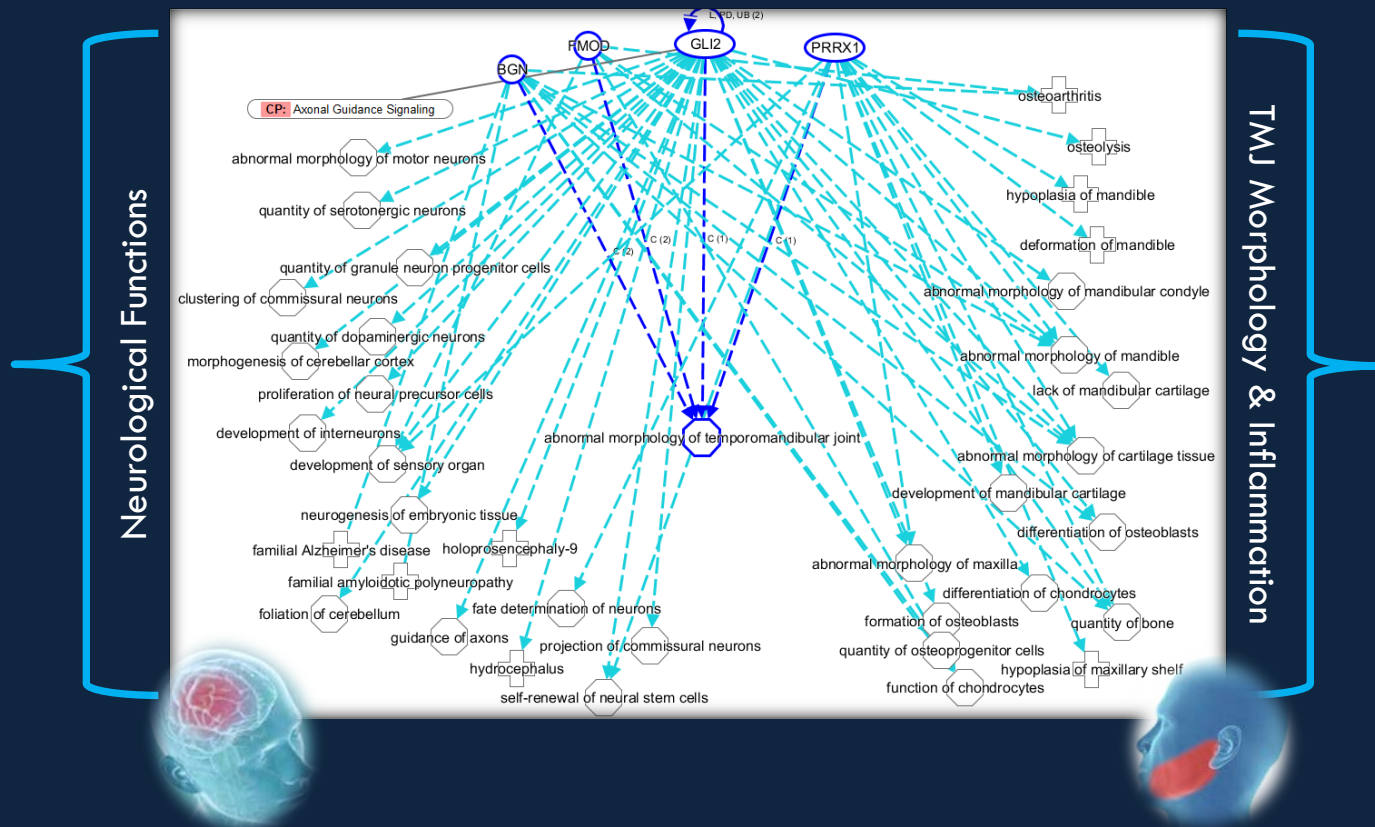
Search

ADD TO MY PATHWAY ADD TO MY LIST ANNOTATIONS SHOW FINDINGS EFFECT ON FUNCTION SHOW FUNCTIONS EXPAND FUNCTIONS BIOPROFILER

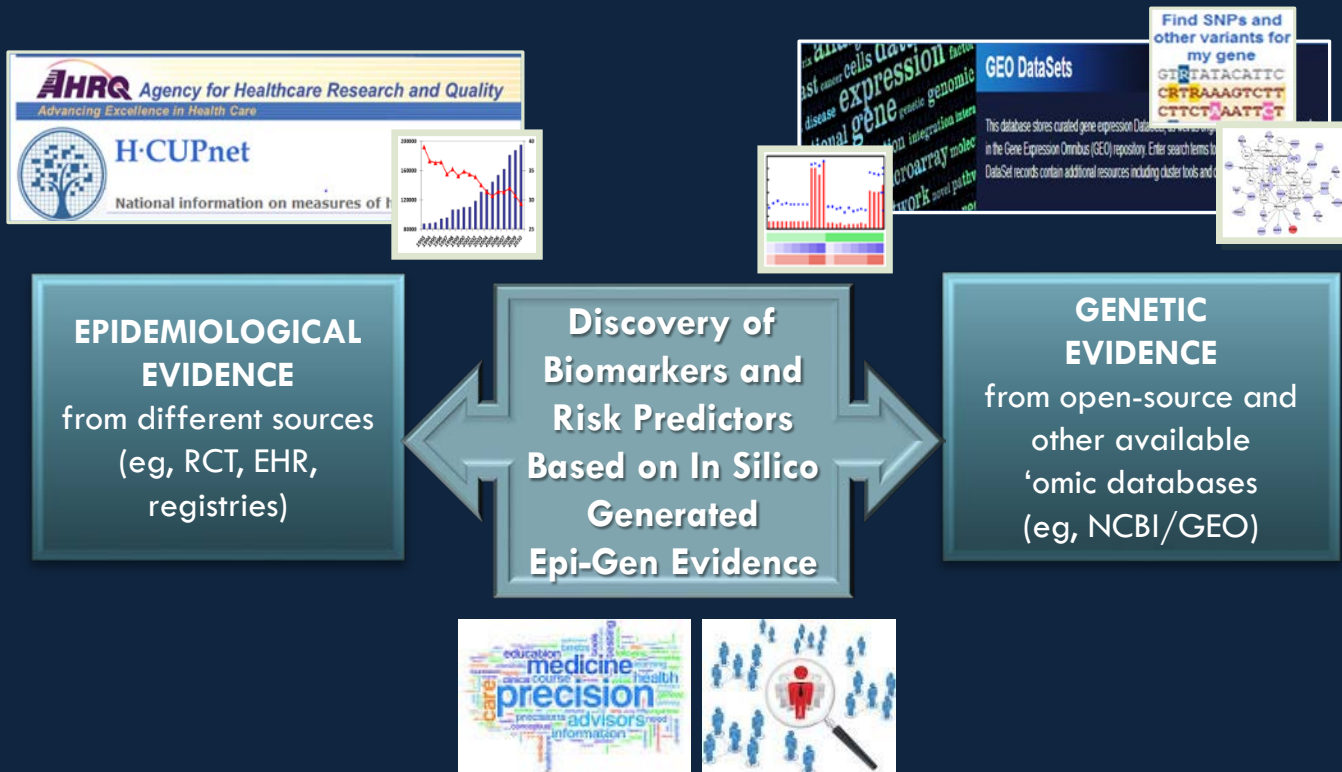
The search for temporomandibular matched 1 diseases and functions.

Diseases & Functions	Associated Molecule
☐ Matching Diseases & Functions	4
☐ Skeletal and Muscular System Development and Function	4
☐ abnormal morphology	4
☐ abnormal morphology of temporomandibular joint [abnormal morphology of temporomandibular articulation, abnormal morphology of articulation temporomandibularis]	4
BGN, FMOD, GLI2, PRRX1	

Ingenuity Knowledgebase (2): genes that are associated with Abnormal TMJ Morphology and Osteoarthritis can be also involved in Neurological Functions



In silico Framework: for Integrating Epidemiological and Genetic Evidence



In silico research: going beyond conventional evidence integration

- Apply *Systems Biology/Medicine* approach
- Integrate *multidisciplinary* evidence
- Extract new information by reanalyzing *raw pre-existing* data
- Integrate amassed device/biomaterial-related knowledge (eg, *biomedical, clinical, epidemiological, population genetics*, etc)
- Promote translational research by incorporating *pre-clinical* findings
- Data analysis and interpretation using *computer modeling and simulation*:
 - Elicit and test new hypotheses
 - Cross-validate the results from different sources

**Data repurposing and
reutilization:
the gift that keeps on giving**



What can be expected from *in silico* evidentiary approaches to the TMD area

- ✓ **Biological and clinical plausibility of TMD study endpoints and biomarkers based on:**
 - ✓ Better understanding of molecular/mechanistic underpinnings
 - ✓ Improved pre-selection for further qualification, validation and implementation steps
- ✓ **Clinical and regulatory relevance :**
 - ✓ New targets for different types of TMDs
 - ✓ Well-categorized TMD biomarkers (eg, diagnostic, monitoring, predictive, prognostic, etc)
 - ✓ Well-defined target subpopulations (eg, ITT for TMJ Replacement)
 - ✓ *Proactive* surveillance using new study endpoints (eg, biomarkers) for early detection and monitoring of adverse (clinical and subclinical) events in TMD/TMJ arthroplasty
 - ✓ Less burdensome and more ethical - *in vitro* and *ex vivo* – TMJ device/biomaterial testing
- ✓ Cost/time-efficient solutions for TMD-related Precision Medicine applications



- Acknowledgments:
 - Terrie Cowley, TMA
 - Yelisaveta (Lisa) Torosyan, FDA/CDRH

THANK YOU!

danica.marinac-dabic@fda.hhs.gov