THE UNIVERSITY OF BRITISH COLUMBIA
Faculty of Dentistry

ENGAGING DENTISTS IN EARLY DETECTION OF RARE

Daniel Graf

CRANIOFACIAL, ORAL, DENTAL DISORDERS (CODED) CLUSTER –DENTISTRY, UBC

Outline of Presentation

- Dentistry and Rare
- Early Diagnosis – Craniofacial and Oral imaging
- Integration and Treatment – D-CARE network initiative
- Understanding Rare – involvement of craniofacial/oral/dental research
- Dentistry and Health in Canada - NOHRS
- CODED – a UBC-led dedicated (research) cluster dedicated to Rare

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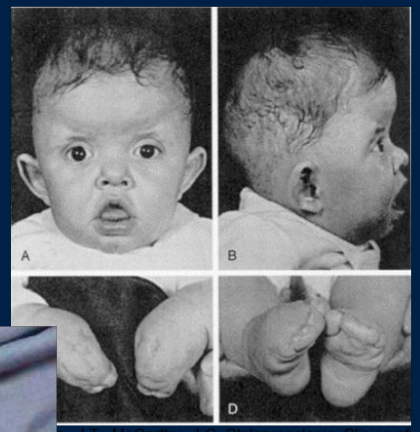
Importance of Dentistry for congenital malformations

Syndromes



, J.T., McCarthy, J.G. Otolaryngologic Clinics of America 33:1257 - 1284

Cleft Lip / Palate

Mineralization Defects

- 70% of congenital disorders have craniofacial involvement and many syndromes have dental findings
- Specialist clinics provide care for craniofacial syndromes, cleft/lip palate.
- For many rare disorders, children do not receive specialist dental assessment.
- Reporting of dental findings is often incidental or lacking. Specific recommendations for dental care are often lacking.

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Dental Disorders of Developmental Origins

ICD-10-CM (International Classification of Diseases, Tenth Revision, Clinical Modification)

Diseases of oral cavity and salivary glands (K00-K14)

K00 Disorders of tooth development and eruption

- **K00.0 Anodontia**
- **K00.1 Supernumerary teeth**
- **K00.2 Abnormalities of size and form of teeth**
- **K00.3 Mottled teeth**
- **K00.4 Disturbances in tooth formation**
- **K00.5 Hereditary disturbances in tooth structure, not elsewhere classified**
- **K00.6 Disturbances in tooth eruption**
- **K00.7 Teething syndrome**
- **K00.8 Other disorders of tooth development**
- **K00.9 Disorder of tooth development, unspecified**

OMIM and literature terms go beyond ICD-10-CM

~90% genes also annotated for non-dental presentations (syndromes)

Not considered here are anomalies of the
- Oral cavity (high arched palate, narrow palate)
- Periodontium (gums)

K00.0	**ANODONTIA**	HYPODONTIA OLIGODONTIA
K00.1	**SUPERNUMERARY TEETH**	DISTOMOLAR FOURTH MOLAR MESIODENS PARAMOLAR SUPPLEMENTARY TEETH
K00.2	**ABNORMALITIES OF SIZE AND FORM OF TEETH**	CONCRESCENCE FUSION GEMINATION DENS IN DENTE DENS EVAGINATUS DENS INVAGINATUS ENAMEL PEARLS MACRODONTIA MICRODONTIA PEG-SHAPED TEETH (CONICAL TEETH) SUPERNUMERARY ROOTS TAURODONTISM TUBERCULUM PARAMOLARE
K00.3	**MOTTLED TEETH**	DENTAL FLUOROSIS MOTTLING NON-FLUORIDE ENAMEL OPACITIES
K00.4	**DISTURBANCES IN TOOTH FORMATION**	APLASIA/HYPOPLASIA OF CEMENTUM DILACERATION ENAMEL HYPOPLASIA REGIONAL ODONTODYSPLASIA TURNER'S TOOTH
K00.5	**HEREDITARY DISTURBANCES IN TOTTH STRUCTURE, NOT ELSEWHERE CLASSIFIED**	AMELOGENESIS IMPERFECTA ODONTOGENESIS IMPERFECTA DENTINOGENESIS IMPERFECTA DENTINAL DYSPLASIA SHELL TEETH
K03.4	**HYPERCEMENTOSIS**	CEMENTUM HYPERPLASIA

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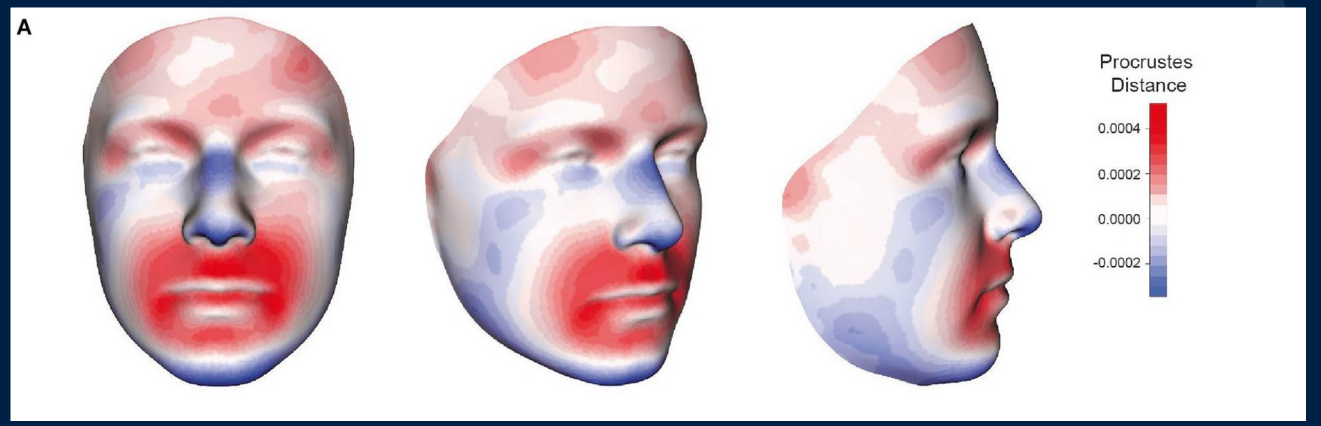
Craniofacial shape analysis

3D craniofacial shape analysis has documented predictive power for syndrome diagnosis

Low et al, Am J Med Genet A. 2016 Nov;170(11):2835-2846



Roth et al 2021 FCDB 645386

Inclusion of craniofacial/oral/dental assessments as part of existing genetics assessment to improve diagnostic yield of genomic screening.

Dentists are trained to take pictures

Untapped potential to include 3D photography as part of pediatric oral health assessment

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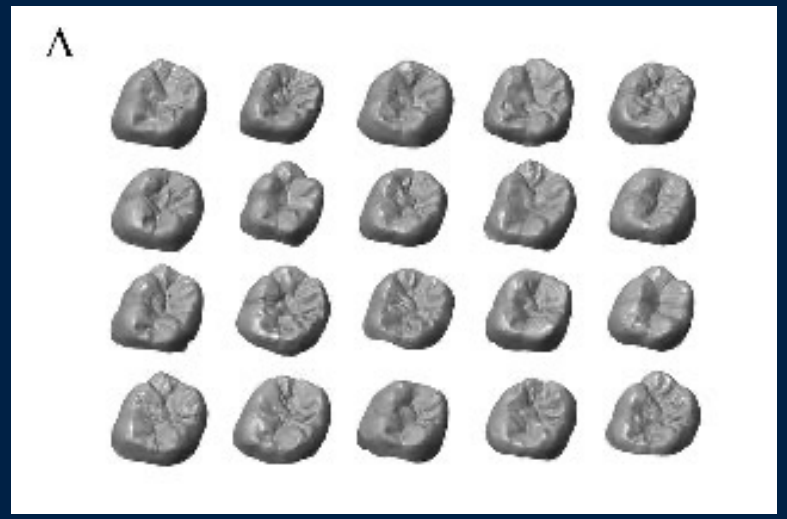
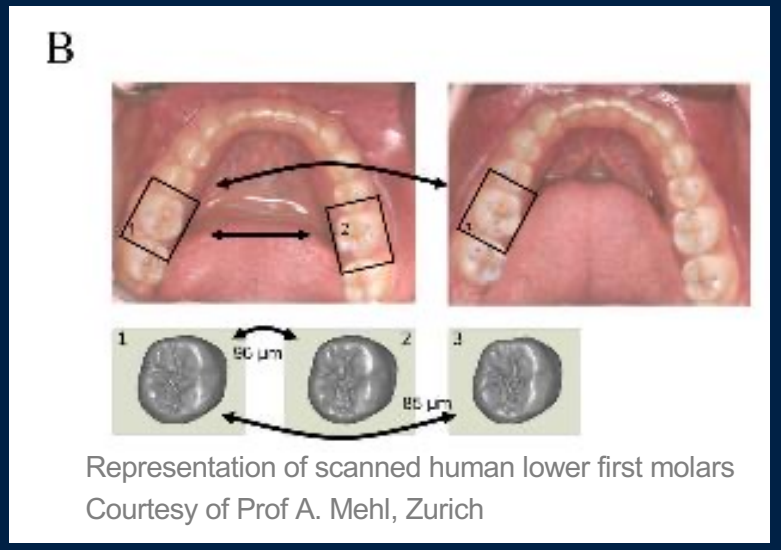
Tooth/oral cavity shape analysis to aid diagnosis of rare disorders





Representation of scanned human lower first molars
Courtesy of Prof A. Mehl, Zurich

A plethora of **tooth shape variations** exists in humans.

These differences reflect small variations in tooth development during development

Provide fingerprints of small (genetic) differences during pre-mineralization stages of tooth development.

Oral cavity size/shape differences similarly provide information of developmental differences, e.g. high arched, narrow palate

Both can be documented using intraoral scanners (3D images)

Untapped potential to include 3D intraoral imaging as part of pediatric oral health assessment

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D-CARE Network

Rare often presents with distinctive oral manifestations that can serve as indicators for diagnosis and management.

Early diagnosis can point to other manifestations or help prevent/manage complications often occurring later in life.

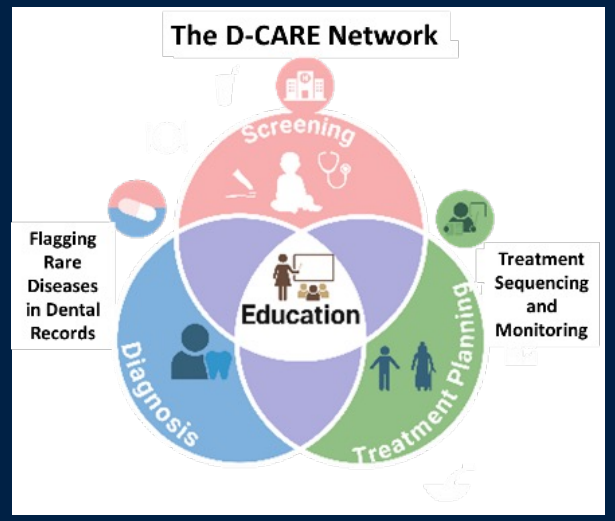
- Tooth agenesis as part of a syndrome with a high risk of colorectal cancer (#608615 - Oligodontia-Colorectal Cancer Syndrome; ODCRCS);
- Dental/oral phenotypes associated with Loeys-Dietz syndrome phenotypic series (PS609192)
- Disorders affecting bone remodeling predisposing to fractures often show distinct facial features (Osteogenesis Imperfecta Phenotypic Series - PS166200).

Unaddressed oral health challenges often escalate with age, particularly in undiagnosed cases, compounding their already complex care needs.

However, without adequate knowledge and training, treatment errors may occur, leading to significant psychological, economic, and social consequences.

The D-CARE network aims to establish a foundation for Dentistry - Comprehensive Access to Rare Expertise.

D-CARE Network



Canadian collaboration involving:

UBC
(D. Graf, S. Vora, M. MacDougall, J. Richman)

Dalhousie University
(A. Bagirath, V. D'Zouza, T. Cook)

University of Saskatchewan
(Szabo-Rogers)

The D-CARE network as a transformative, first-in-kind initiative in Canada, addresses critical gaps in oral health care for individuals with rare diseases.

It aligns with priorities outlined in the National Oral Health Research Strategy Framework (NOHRS) and CIHR strategic priorities (Advance Research Excellence in All its Diversity; Pursue Health Equity through Research; Integrate Evidence in Health Decisions)

It aims to tackle leading issues such as access and inequities in oral health care, the integration of emerging diagnostic and treatment methods, and advancing knowledge mobilization and implementation science.

Topics to be addressed through a series of meetings / workshops
1) Rare and Their Impact on Oral Health:
2) Research Needs and Opportunities in Rare and Oral Health:
3) Oral Health Provider Perspectives on Rare:
4) Educational Perspectives on Rare and Dentistry:
5) Patient and Caregiver Perspectives on Rare and Oral Health:
6) Synthesis of Opportunities and Challenges: Defining the Path Forward.

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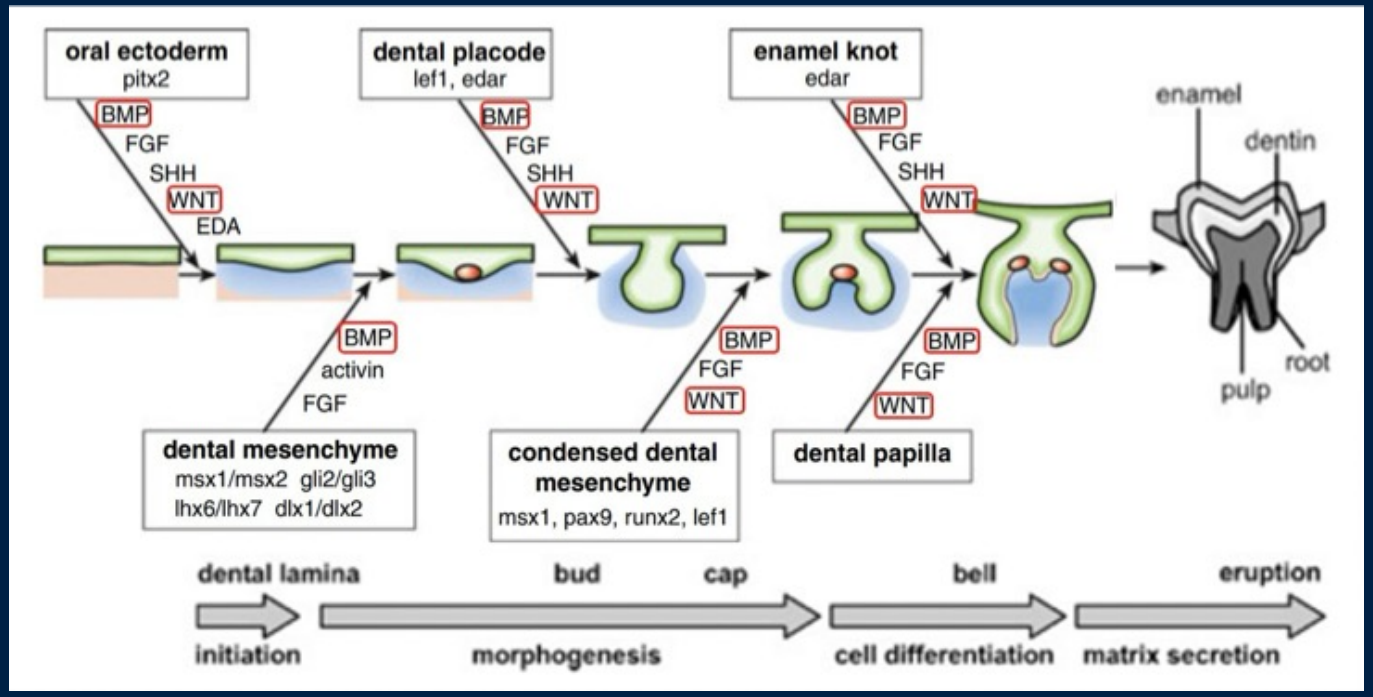
The tooth as model to study rare diseases

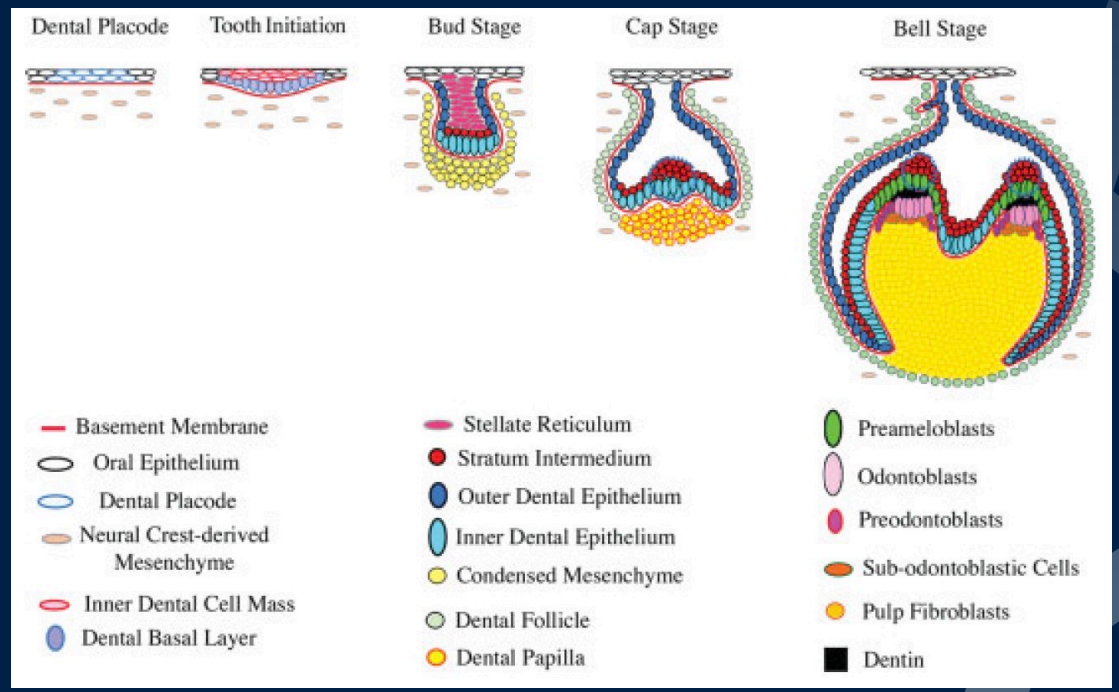
Tooth development offers a well-defined developmental system to study gene variants contributing to rare disorders.

- Well-defined developmental stages and fate map of cells
- Ability to assess many phenotypic variations: tooth shape, mineralization, root formation, accessory/succession teeth

Translational Craniofacial Genomics (TCG) hub for clinicians, geneticists and researchers will facilitate the first-step experiments to establish pathogenicity of newly identified gene variants. The hub is modelled on the Rare Disease Discovery Hub (BCCH Research Institute).



Thesleff 2006 AJMG, 2014 ADJ



Mitsiadis 2009, Birth Defects Res C Embryo Today

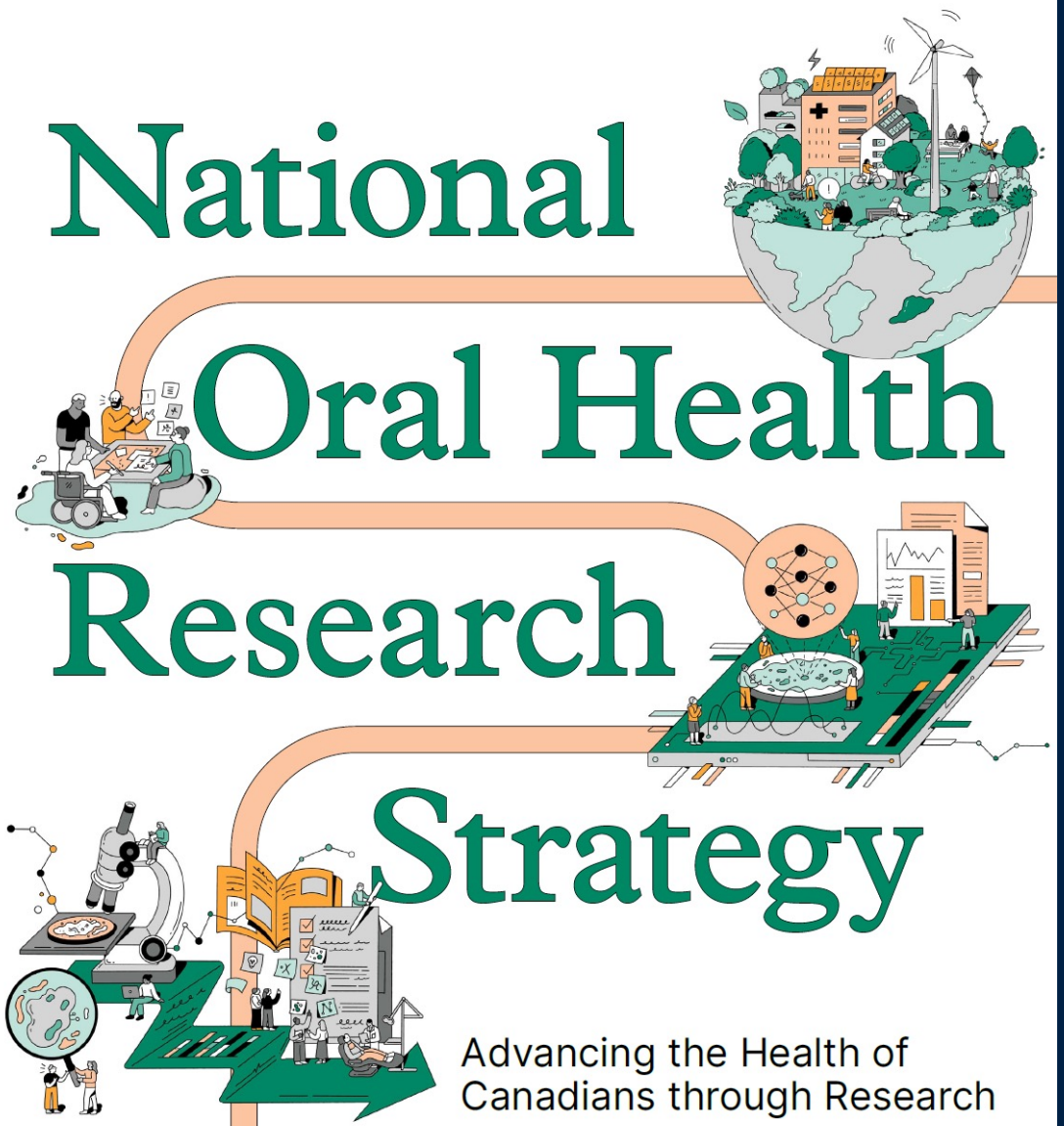
Time to Engage Dentistry in Early Detection and Diagnosis of Rare

- Canadian Health Measures Survey Cycle 7
- Canadian Dental Care Plan
- Stats Canada

- The Lancet Commission on Oral Health will publish its report
- The WHO recently published its Global Strategy and Action Plan on Oral Health

- The world of science and the challenges facing society are advancing rapidly
- The Canadian National Oral Health Research Strategy (NOHRS) is one of the few national oral health research strategies worldwide.
- Available on: https://cihr-irsc.gc.ca/e/52773.html

National Oral Health Research Strategy



Advancing the Health of Canadians through Research

2024 — 2030

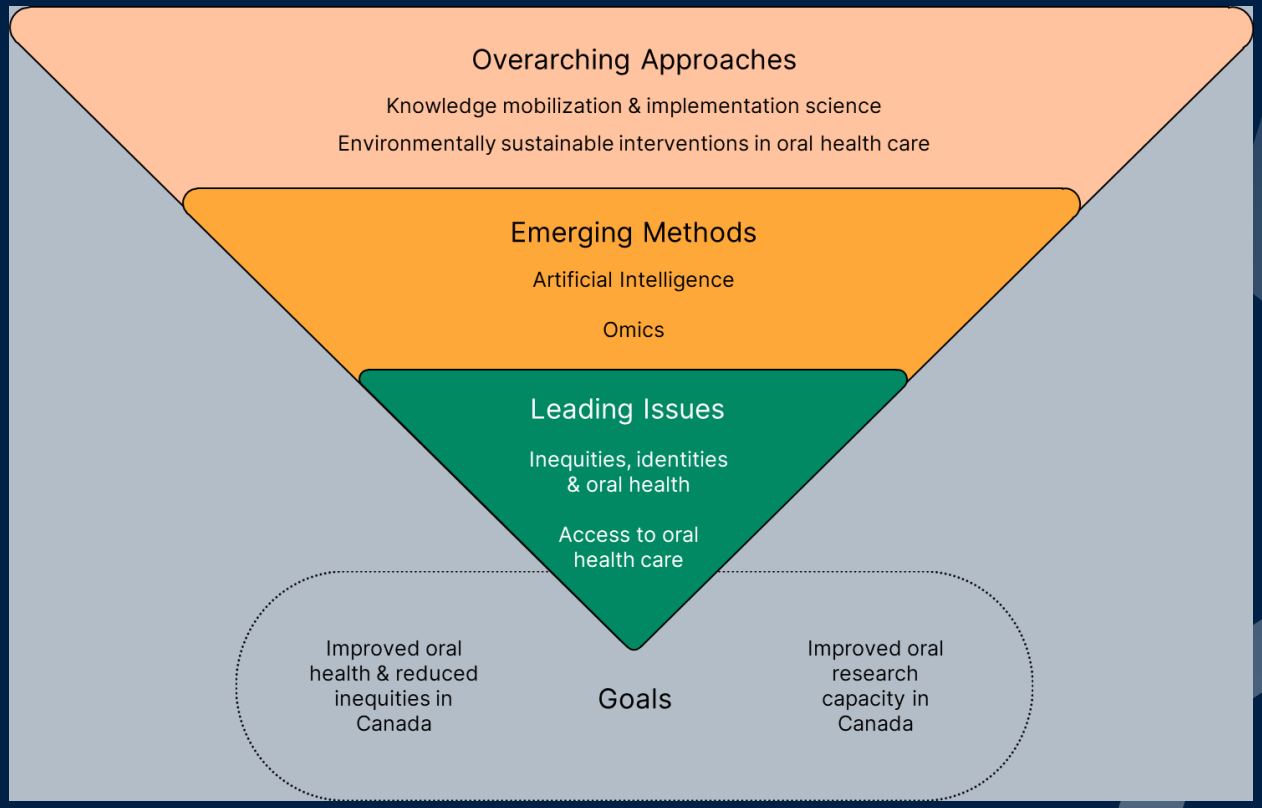
Canada

CIHR IRSC Institute of Musculoskeletal Health and Arthritis / Institut de l'appareil locomoteur et de l'arthrite

Dentistry and Health in Canada

NOHRS is a collaborative initiative led by the Canadian Institutes of Health Research's (CIHR) Institute of Musculoskeletal Health and Arthritis (IMHA) in partnership with various Canadian oral health professional organizations and research/academic institutions

Research Priorities



CODED

- CODED is the first of its kind core in Canada specifically focusing on craniofacial/oral/dental malformations.
- CODED aims to provide comprehensive access to Rare expertise in oral health and to facilitate research in the etiology of genetic disorders associated with orofacial structures.
- CODED involves a diverse group of researchers, clinicians, geneticists, and genetic counsellors from UBC, other Canadian universities, and patient organizations.
- CODED's goal is to help improve differential diagnosis and treatment for Rare to benefit patients and care specialists.

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