"USE CASE SELECTION - PROJECT SPRINT 1"

"THE FIBRILLIN GENiES"

Team Members -

Hemanth Sai Kumar Gaddam

Puja Mishra

Priyanka Reddy Kuta

Sanjana Rajan

Department of Informatics and Computing, Indiana University

INFO-B-581: Health Informatics Standards and Terminology

Professor Saptarshi Purkayastha

February 06, 2024

GROUP NAME: THE FIBRILLIN GENiES

Presented Use Case:

"A 34-year-old male patient with a history of rib cage defect (*Pectus excavatum*), long fingers, flat feet, and "double-jointedness" seeks a diagnosis. The clinician orders genetic testing on multiple Fibrillin-1 (FBN1) gene variants (mutations). A genetic testing laboratory receives the order and performs detailed testing, which shows that the "FBN1 c.7039_7040del (p.Met2347fs)" variant is positive, with all other tested FBN1 variants negative. The result is sent back to the clinician, who makes a diagnosis".

Standards and terminologies:

1. **Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT)**

SNOMED CT has been used widely across systems and healthcare institutes for research and information exchange. SNOMED CT has an extensive vocabulary covering almost 311,000 concepts related to various medical conditions (Wagholikar et al., 2011).

2. **International Classification of Diseases, 10th Revision (ICD-10)**

It is a globally recognized system for classifying diseases and medical conditions for various healthcare and statistical purposes (World Health Organization, 2019).

3. **Human Phenotype Ontology (HPO)**

This ontology's specificity and its ongoing updates to reflect new genetic insights make it a robust tool for capturing the nuanced phenotypic presentations associated with genetic variations (Köhler et al., 2019).

4. Logical Observation Identifiers Names and Codes (LOINC)

It is a comprehensive standard terminology for identifying health measurements, observations, and documents. LOINC codes facilitate effective electronic exchange and aggregation of clinical data from many sources to enable secondary analysis and semantic interoperability across healthcare settings (LOINC from Regenstrief, n.d.).

Clinical Elements Identified:

a.) Medical History

b.) Genetic Testing - Laboratory

c.) Diagnosis

CONCEPT TYPE	TERMINOLOGIES AND LINKS		

Table 1

MEDICAL HISTORY	SNOMED CT	ICD 10	Human Phenotype Ontology
Rib Cage Defect	Pectus Excavatum code:391987005 **SNOMED CT link**	Pectus Excavatum code:Q67.6 **ICD 10 code**	HPO term: Pectus excavatum (HP:0000767) **HPO link**
Long Fingers	Arachnodactyly (Long Fingers) Code: 62250003 **SNOMED CT Link**	Congenital contractural arachnodactyly under Marfan syndrome, unspecified code:Q87.40 **ICD 10 Link**	HPO Term: Arachnodactyly (HP:0001166). **HPO link**
Flat Feet	Pes Planus (Flat Feet):203534009	Pes Planus (Flat Feet) code: M21.42	HPO Term: Pes planus (HP:0001763)

	SNOMED CT link	ICD 10 code	HPO link
Double Jointedness	**Joint laxity:298203008** **SNOMED CT link**	**Joint Hypermobility code: M35.7** **ICD 10 Link**	○ **HPO Term: Joint hypermobility (HP:0001382)** **HPO link**

Table 2

GENETIC TESTING	LOINC	SNOMED CT
Fibrillin - 1 Gene Mutation	**LOINC CODE 49735-4** https://loinc.org/49735-4/ **LOINC CODE 40471-5** https://loinc.org/40471-5/	**SCTID: 773644000** https://browser.ihtsdotools.org/?perspective=full&conceptId1=773644000&edition=MAIN/2024-02-01&release=&languages=en

LOINC CODE 77114-7 https://loinc.org/77114-7/ **LOINC CODE 69484-4** https://loinc.org/69484-4/		

Table 3

DIAGNOSIS	ICD - 10	SNOMED - CT
	CODE: Q87.4LINK **CODE: Q87.41**LINK **CODE: Q87.410**LINK **CODE: Q87.418**LINK **CODE: Q87.42**LINK **CODE: Q87.43**LINK	**CODE: 19346006** **LINK**

CONCEPT - MEDICAL HISTORY

The 34-year-old male patient presented in the use case has a history of *Pectus excavatum*, long

fingers, flat feet, and double jointedness. The codes for these from various terminologies are

noted in **Table 1**.

Choice of Standard:

SNOMED CT is the choice of standards as it is said to have the possible terms required to record patient and other biomedical information. It has well-defined semantics and can be used to build new terms and group these terms (Bousquet et al., 2019).

Specific codes and term descriptions:

Pectus Excavatum

SNOMED CT Code: 39198700

Term description: This code identifies the condition of a sunken chest wall, which can have implications on cardiac and respiratory functions (Sharma & Carter, 2023).

Arachnodactyly (Long Fingers):

SNOMED CT Code: 30284900

Term description: Arachnodactyly, characterized by unusually long and slender fingers, is a sign that can suggest connective tissue disorders like Marfan Syndrome. The SNOMED CT code ensures that this phenotypic feature is accurately recorded, supporting the diagnostic process and subsequent management strategies (Find-A-Code, n.d.).

Pes Planus (Flat Feet):

SNOMED CT Code: 20353400

Term description: Documenting flat feet with this specific code helps in distinguishing between physiological variations and those that may indicate broader systemic issues, such as connective tissue disorders. The use of a standardized code aids in the assessment and potential referral for genetic evaluation when seen in a syndromic pattern (Find-A-Code, n.d.).

Joint Hypermobility:

SNOMED CT Code: 298203008

Term description: This code is used to document an increased range of joint movement, which can be a feature of various hereditary connective tissue disorders. Standardized documentation using SNOMED CT facilitates multidisciplinary care by clearly communicating patient needs across various specialties (Find-A-Code, n.d.).

Justification:

Multiple associations within SNOMED CT allow us to establish connections between various codes and concepts. Using clinical results and a patient's history of coronary heart disease, Mues et al. (2018) explain how SNOMED CT can be used to identify familial hypercholesterolemia (FH), a rare genetic metabolic condition. Until 2016, there was no code for recording this genetic condition in the ICD-10, which is mostly used for diagnostics.

It is because of its genetic roots, the case that was just presented to us can be compared to this one. Muse et al. (2018) discovered that when SNOMED CT was utilized, a significant

percentage of individuals had FH. In addition, they observed very good sensitivity and specificity, and the system reportedly has codes corresponding to the kind of mutation (homozygous or heterozygous). Physicians are further assisted by the links between the ICD-10 codes for the disorders. The reason for the missed diagnosis in this instance was likely the experts' ignorance of all the potential symptoms of the illness; nevertheless, because of SNOMED CT, all the symptoms were accurately examined and recorded, allowing for the patient's identification.

According to Campbell et al. (2016), clinical and laboratory findings can be utilized to create a conceptual model with SNOMED CT and its extension. as information pertaining to the genetics of the human genome continues to expand. Anatomic and molecular pathology, among other observables, are described as having a variety of defining and non-defining correlations in the templates that their team created for a "candidate concept model for observables" (Campbell et al., 2016, p. 354). Additionally, they put forth a model in which the precise location of a given gene can be determined using these concept models. This feature and flexibility strengthen the argument for why we choose SNOMED CT for this idea type.

CONCEPT TYPE: GENETIC TESTING - LABORATORY

In the given Use Case, considering the patient's medical history, signs, and symptoms the Clinician orders for genetic testing of Fibrillin-1 (FBN1) and its multiple variants suspecting a genetic mutation termed Marfan Syndrome.

The FBN1 gene encodes fibrillin-1, a crucial microfibril component vital for connective tissue integrity (Sakai et al., 2016). Pathogenic FBN1 variants lead to Marfan syndrome, affecting cardiovascular, ocular, and skeletal systems. These mutations also link to various connective tissue disorders and thoracic aortic aneurysms. Understanding molecular genetics aids in

correlating genotypes with phenotypes, informing precision medicine through genetic testing for enhanced diagnosis, risk assessment, and patient management (Sakai et al., 2016).

Choice of Standard:

As discussed in **Table 2,** LOINC's recent expansion to incorporate genetics terminologies significantly enhances its existing comprehensive coverage of clinical terminology. With LOINC codes already widely adopted in clinical reporting and health information exchange, leveraging this existing infrastructure for genetic coding avoids challenges associated with introducing entirely novel standards. A key benefit provided by LOINC is structured interoperability of codes with other clinical terminologies; genetic codes can map to sequence ontology terms, enabling valuable integration across heterogeneous data sources (Deckard et al., 2015).

Terms Description (Search LOINC FBN1 Gene Mutation, n.d.) **:**

After conducting a thorough research on suitable terminologies available in LOINC, the following related terms were identified:

a.) LOINC CODE 49735-4

This code standardizes the genetic analysis that focuses on ordering molecular tests, such as sequencing, PCR, or other nucleic acid approaches, to identify specific mutations in the FBN1 gene. The purpose is to precisely investigate known or suspected pathogenic variants related to fibrillin-1 protein defects, aiding in the diagnosis and evaluation of connective tissue disorders like Marfan syndrome (*LOINC 49735-4 FBN1 Gene targeted mutation analysis in blood or tissue by molecular genetics method*, n.d.).

b.) LOINC CODE 40471-5

This code involves the reporting of FBN1 gene mutations identified. The test results include a unique variant identifier, like "c.7039_7040del," facilitating the communication of precise mutation details for diagnosing fibrillinopathies such as Marfan syndrome. It enables comprehensive documentation of the genotype for correlation with disease-causing effects (*LOINC 40471-5 FBN1 Gene mutations found [identifier] in blood or tissue by molecular genetics method nominal*, n.d.).

c.) LOINC CODE 77114-7

This code establishes a standardized protocol for requesting extensive genetic testing of the FBN1 gene through sequencing methods on blood or tissue specimens. This comprehensive approach aims to detect all mutation types across the entire gene, as opposed to a targeted subset. The increased gene coverage enhances diagnostic accuracy, identifying disease-related mutations that may be missed by selective tests (*LOINC 77114-7 FBN1 Gene full mutation analysis in blood or tissue by sequencing*, n.d.).

d.) LOINC CODE 69484-4

This code gives a standardized procedure for requesting targeted testing of specific familial FBN1 gene mutations using molecular genetics methods on blood or tissue samples. This targeted testing is crucial for evaluating heritable connective tissue disorders, particularly within affected lineages such as Marfan syndrome (*LOINC 69484-4 FBN1 Gene Mutation Analysis Limited to Known Familial Mutations in Blood or Tissue by Molecular Genetics Method*, n.d.).

Supporting Evidence:

Deckard et al. (2015) highlight the historical challenge of inconsistent genetic terminology hindering clinical integration. With the increasing use of genetic testing, standardizing data is crucial. The LOINC system uniquely identifies genetic test elements, enabling a common vocabulary for reporting tests, variants, interpretations, and diagnoses. The authors illustrate LOINC's application in genetic testing scenarios, emphasizing its role in fostering understandable and actionable precision medicine. They conclude that structured vocabularies are essential for widespread interoperability, facilitating reliable data exchange for informed clinical care.

CONCEPT TYPE: Diagnosis

Standards That can be used: SNOMED CT

ICD- 10

Choice Of Standard: ICD-10

ICD-10 has been widely used as the standard of choice for Diagnosis.

TERM DESCRIPTION- ICD-10 CODE: Q87.4:

In the realm of medical diagnostics, the International Classification of Diseases, 10th Revision (ICD-10), emerges as a pivotal tool for encapsulating the vast spectrum of genetic anomalies and conditions manifesting in patients. Notably, the ICD-10 code Q87.4 is designated for encounters aimed at screening genetic and chromosomal irregularities, underscoring the framework's capacity to accommodate the nuanced domain of genetic testing (AAPC, n.d.). This classification facilitates the delineation of patient encounters specifically

oriented towards genetic screening, thereby providing a standardized approach to documenting such medical evaluations.

SUPPORTING EVIDENCE:

The International Classification of Diseases, 10th Revision (ICD-10) is considered the premier standard for diagnosing and coding medical conditions due to its comprehensive and detailed system. The granularity and specificity of ICD-10 surpass that of its predecessor, ICD-9, enabling a more precise depiction of patient diagnoses which is essential for accurate patient care and research (World Health Organization, 2019). Its global adoption facilitates international data exchange, enhancing the comparability of health information across borders (Centers for Disease Control and Prevention, 2015). ICD-10's detailed coding system improves data quality and patient care by reducing miscoding and misinterpretations, thus contributing to more effective treatment plans and health outcomes monitoring (American Health Information Management Association, 2015). Moreover, ICD-10 is designed to accommodate advances in medicine, allowing for the inclusion of new codes as diseases evolve and new treatments are developed, ensuring the system's relevance in modern healthcare (World Health Organization, 2019).

These aspects collectively underscore the significance of ICD-10 in enhancing the accuracy of health data, supporting healthcare advancements, and improving patient and public health outcomes.

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