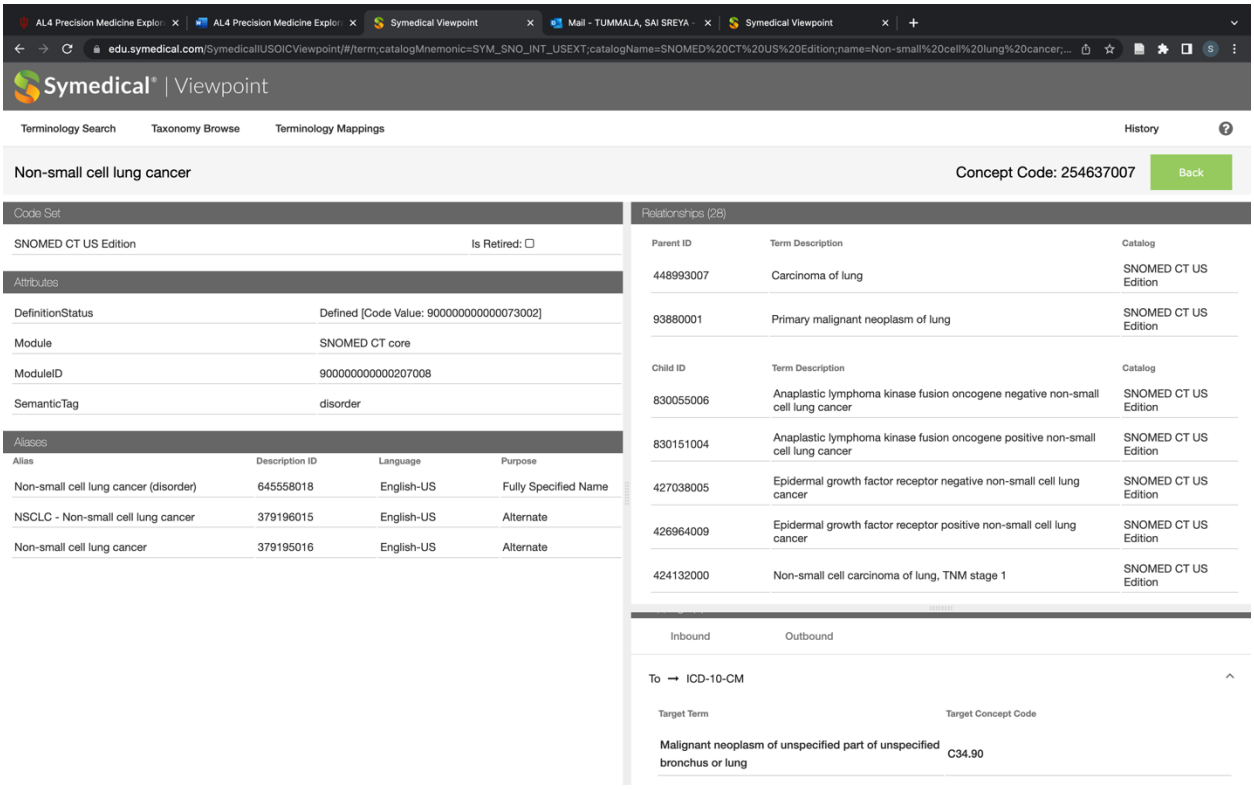
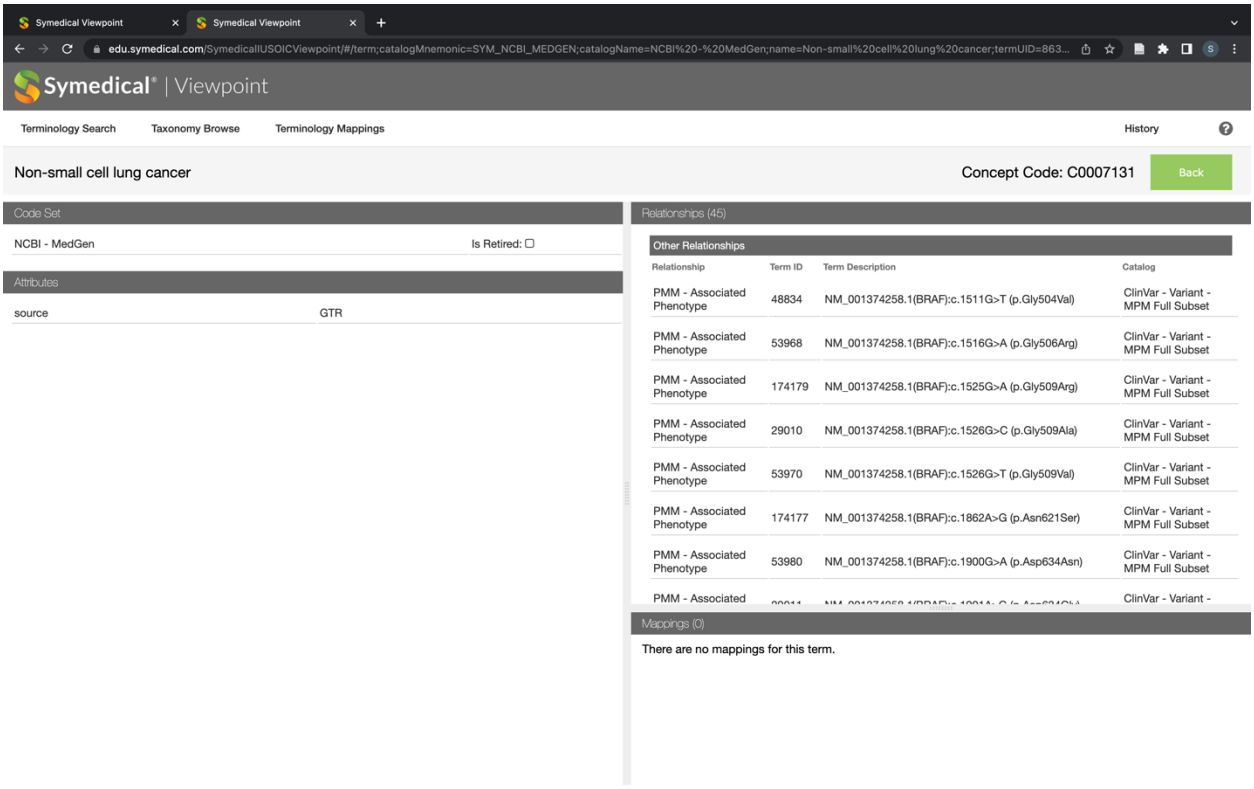
PART-A

4. Screen shot of Non-small cell lung cancer relationships and mapping in SNOMEDT-CT

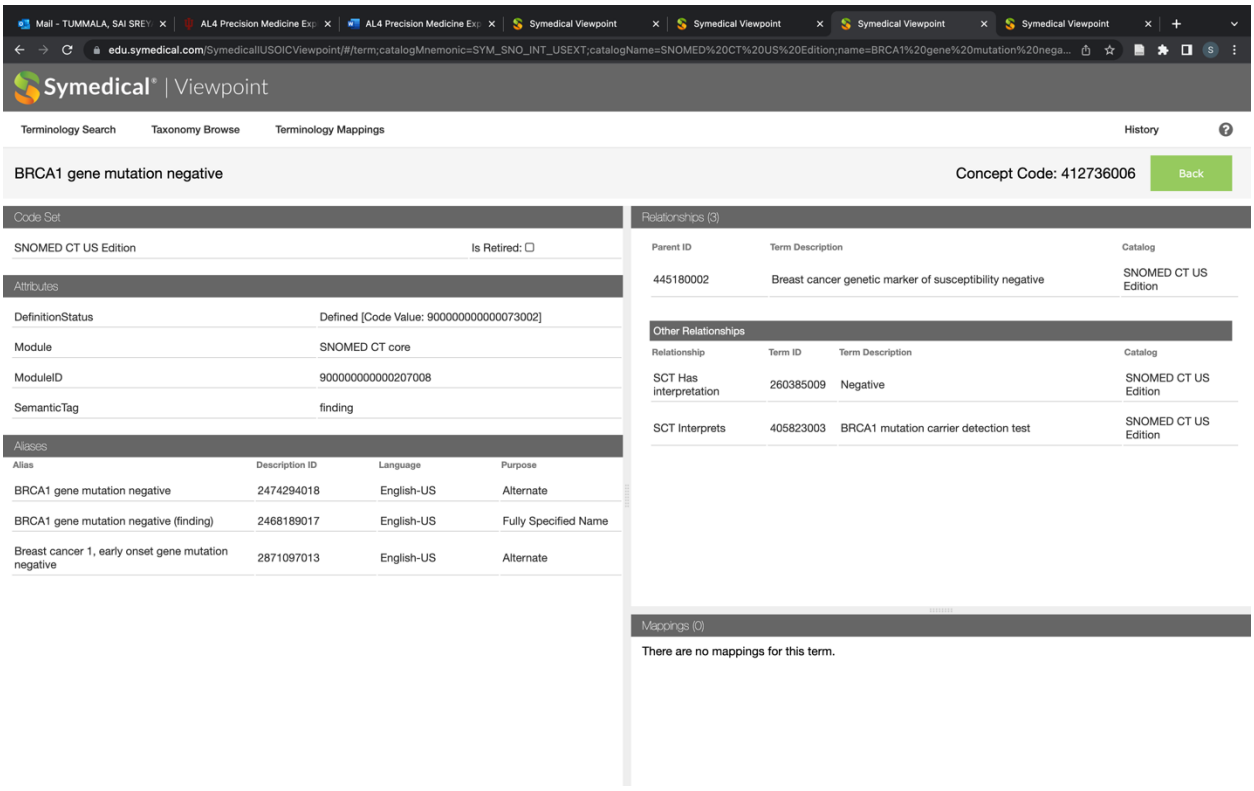


Screen shot of Non-small cell lung cancer relationships in NCBI-MedGen

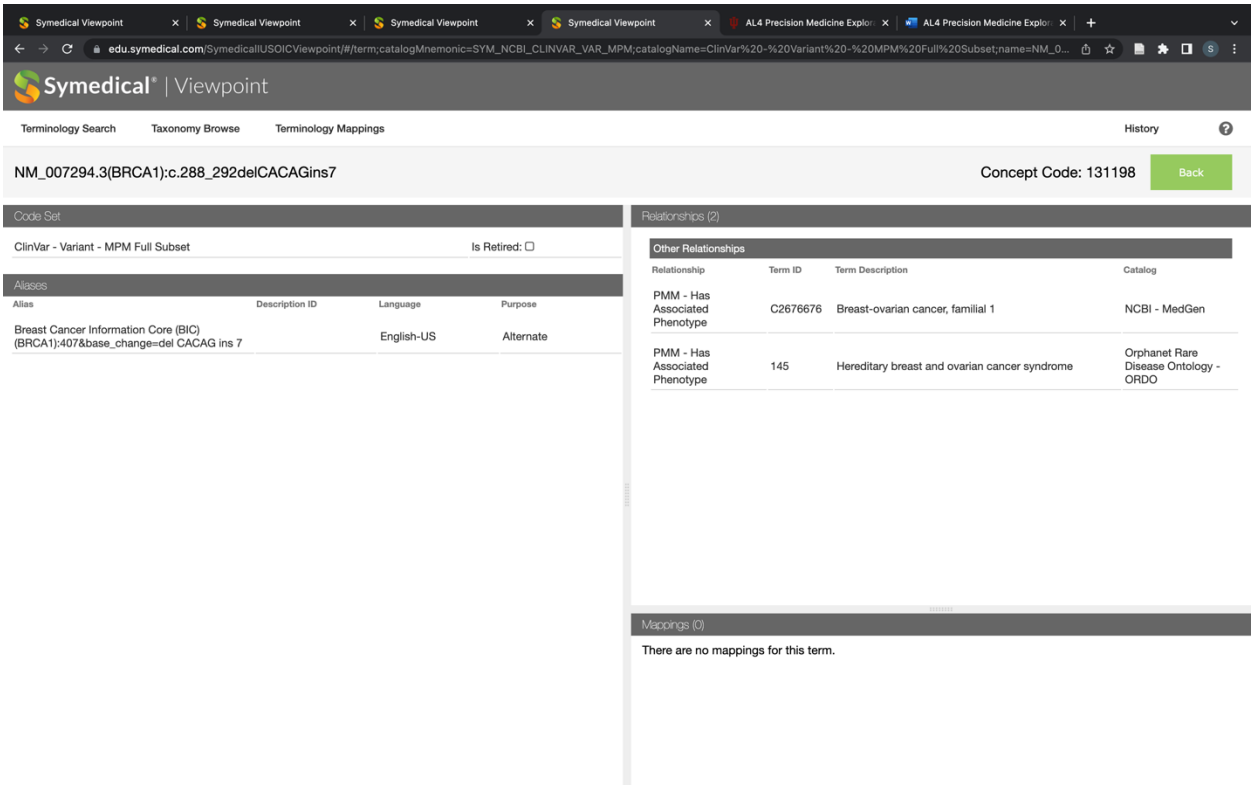


PART-B

4. Screen shot of BRCA1 gene mutation negative relationships in SNOMED-CT:



Screen shot of BRCA1 gene mutation negative precise variant in ClinVar code set:



PART-C:

2a.

Relationships provide a formal method to represent the semantic flow. These help us to tract the connections among various clinical conditions and play a key role in interoperability.

In SNOMED-CT the term ‘Non-small cell lung cancer’ has 28 relationships which include, parent, child, and other relations. The parent relations contain information on a broader aspect detailing the location of cancer. The child relations contain added detail of the type of cancer. Other relations specify the relation of given term with other clinical terms and conditions. On the other hand, when the same term ‘Non-small cell lung cancer’ is searched in code set NCBI-MedGen, there appears to be only other relationships associated with the given term. The term descriptions in other relationships root to the genetic variants tangled to the given term. These genetic variants are derived from ClinVar - Variant - MPM Full Subset. The total number of relationships found with this term are 45 which is in contrast with that found in SNOMED-CT. The catalog for the term in SNOMED-CT is SNOMED-CT which contrasts with the catalog found in NCBI MedGen that is ClinVar - Variant - MPM Full Subset. Defining these relationships is vital in research as they can be detected by NLP based algorithms. Example of one such algorithm is DIRECT which proved to be efficient in detecting oncology concepts and attribute relationships (Kersloot et al., 2019). These relationships can therefore be used to encode clinical narratives reducing the manual work thus saving the time for clinicians.

2b.

The term ‘Non-small cell lung cancer’ when searched in SNOMED-CT contained much more information when compared to NCBI-MedGen code set. In terms of patient perspective, there isn’t comprehensive description and clear picture in the code set to know the details of the given condition. When such insufficient information is used by the clinician to form diagnosis or prescribe medication, there is a lot of scope for medical errors. Paper written by McDonald et al., (2013) states that, evaluations of interventions can prevent the diagnostic errors. When the required data concerning condition is not available, it becomes difficult for the clinician to derive at interventions. The vast amount of data representing genetic variants provided by ClinVar - Variant - MPM Full Subset is valuable in identifying the genetic causes of the given condition and relationship with other genes. All of the above-described reasons can result in altered diagnosis compromising the patient safety. Added to this, when the information concerning a condition is restricted or unavailable, the scope for the patient to understand and communicate about the problem is hampered. Above all, insufficient data regarding a condition is seen a major obstacle to data sharing across the clinical information systems. This results in failure of semantic interoperability.

3. Term description: BRCA1 gene mutation negative

SNOMED-CT code: 412736006

4a.

In the code set NCBI-MedGen the genetic term ‘BRCA1 gene mutation negative’ is associated with a parent and two other relationships. The terms here are used to describe the lack of BRCA1

gene mutations in the person. These relationships markdown to the SNOMED-CT catalogue. Other relationships specify the conditions which are associated of not having the BRCA1 gene mutation. On the other hand, when the genetic variant of BRCA1 gene mutation negative is search in ClinVar - Variant - MPM Full Subset, most of the displayed variants did not have any relationships. One variant which contained other relationships describe the presence of similar phenotype associated with given term in other clinical conditions. There are two catalogs associated with ClinVar - Variant - MPM Full Subset which are MedGen and Orphanet Rare Disease Ontology – ORDO. According to Plakhins et al., (2011) there exists a great amount of genotypic-phenotypic correlation among BRCA1 genes.

4b.

Information pertaining to the clinical variants of a given condition is paramount as it determines the diagnosis and aid in the modality of treatment. Such information plays a key role in understanding the hereditarian relationships and interlinked clinical conditions. These variants also provide insights about other affected areas involving the same gene mutations. So, such information is need for prognosis as well. But for the given term, most of the variants in the ClinVar - Variant - MPM Full Subset failed to provide the possible relationships. This can be seen with other clinical conditions as well. In such situations, clinical interpretation of the condition and management of the genetic variants becomes impossible to control (Marian, 2020). The scope for precision medicine declines when such type of relationships is not defined. Genetic variants are determinants to susceptibility of a disease and outcomes of a treatment (Marian, 2020). It is always a good practice to search for relationships of the genetic variants to

possibly identify the associated conditions caused by those variants. This helps to improve the patient safety and outcomes.

References:

Kersloot, M. G., Lau, F., Abu-Hanna, A., Arts, D. L., & Cornet, R. (2019). Automated Snomed CT concept and attribute relationship detection through a web-based implementation of Ctakes. *Journal of Biomedical Semantics*, *10*(1), 14. https://doi.org/10.1186/s13326-019-0207-3

Marian, A. J. (2020). Clinical interpretation and management of genetic variants. *JACC: Basic to Translational Science*, *5*(10), 1029–1042. https://doi.org/10.1016/j.jacbts.2020.05.013

McDonald, K. M., Matesic, B., Contopoulos-Ioannidis, D. G., Lonhart, J., Schmidt, E., Pineda, N., & Ioannidis, J. P. (2013). Patient safety strategies targeted at diagnostic errors: A systematic review. *Annals of Internal Medicine*, *158*(5 Pt 2), 381–389. https://doi-org.proxy.ulib.uits.iu.edu/10.7326/0003-4819-158-5-201303051-00004

Plakhins, G., Irmejs, A., Gardovskis, A., Subatniece, S., Rozite, S., Bitina, M., Keire, G., Purkalne, G., Teibe, U., Trofimovics, G., Miklasevics, E., & Gardovskis, J. (2011). Genotype-phenotype correlations among brca14153dela and 5382INSC mutation carriers from Latvia. *BMC Medical Genetics*, *12*(1), 147. https://doi.org/10.1186/1471-2350-12-147