Analysis and Management of Computable Operational Definition (CODef) Concept Variation Based on a Large Real-World Studies Library

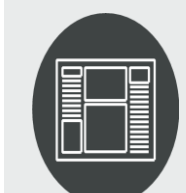Michael Buck[1], Craig G. Parker[1], Leanne Larson[2], Aaron W C Kamauu[3]

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Objective:

Regulatory agencies are requiring life sciences companies to submit more-rigorously developed study protocols including computable operational definitions (CODefs).

To date, large-scale CODef concept libraries have not been profiled or reported on, nor have maintenance requirements been delineated.

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Methods:
Using a newly created CODef library currently leveraged by a few life-science companies, we profiled the subset of value sets used to support their studies. We aggregated the results at three levels: 1) counting discrete concepts from related value-set groups together; 2) counting related value-set groups for each code system that share an 80% or more code overlap; and 3) counting each unique value-set variation. For example, the discrete concept of "Cerebrovascular Disease Diagnoses" has seven related value-set groups containing 19 unique value-set variations with similar provenance, but slightly different code lists used by multiple studies.

1 Discrete Concept
Cerebrovascular Disease (CCI) Diagnoses

7 Related Value Set Groups

- Cerebrovascular Disease (CCI) Diagnoses (ICD-10-CM)
- Cerebrovascular Disease (CCI) Diagnoses (ICD-10-WHO)
- Cerebrovascular Disease (CCI) Diagnoses (ICD-9-CM)
- Cerebrovascular Disease (CCI) Diagnoses (Aurum MedCodeID)
- Cerebrovascular Disease (CCI) Diagnoses (READ2)
- Cerebrovascular Disease (CCI) Diagnoses (SNOMED CT UK)
- Cerebrovascular Disease (CCI) Diagnoses (SNOMED CT US)

Value Set Group	Variations
ICD-10-CM	4
ICD-10-WHO	4
ICD-9-CM	3
Aurum MedCodeID	2
READ2	2
SNOMED CT UK	2
SNOMED CT US	2
Total	19

Results:
As of January 2025, this new CODef library contains 912 discrete concepts defined by 2,586 related value-set groups comprising 27 different code systems (e.g. ICD-10-CM, SNOMED CT, CPT, ATC, LOINC, CVX, etc.) with 2,813 unique value-set variations overall; and growing. Details by both US and international terminologies are presented. One interesting finding shows there are 98 discrete concepts with 227 value sets that are slight variations of the same code list. For example, the related value-set group "Cerebrovascular Disease (CCI) Diagnoses (ICD-10-CM)" contains three unique value-set variations for different studies (one with 100% overlap with the original literature review list and two with 96% overlap after dropping 23 of 528 codes).
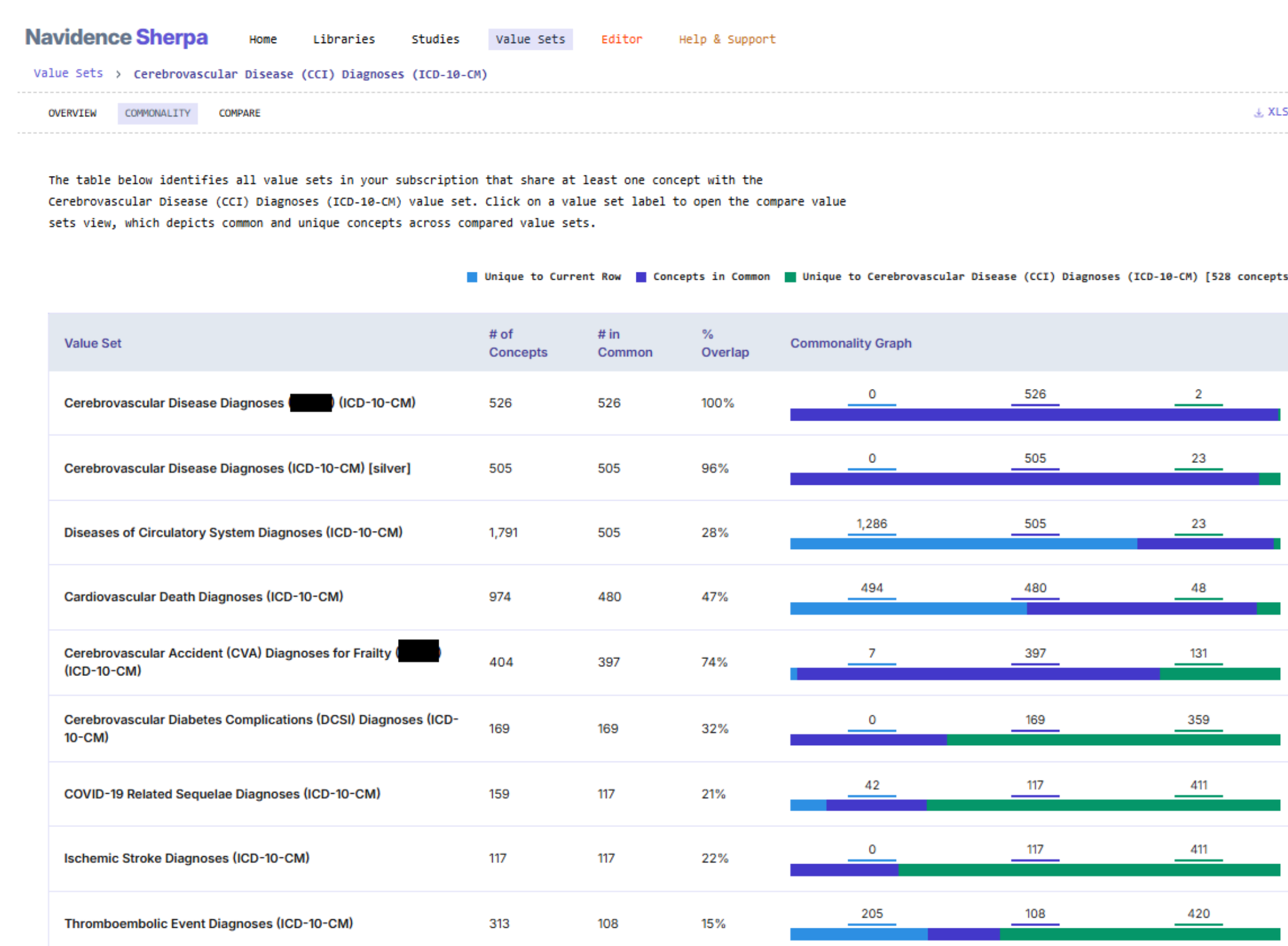
Figure 1: Comparison Reports

Table 1: CODef Library Sample

Discrete Concept Label	Related_Value Sets Group Label	Code System	Variation Count
Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses	Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses (ICD-9-CM)	ICD-9-CM	8
Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses	Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses (ICD-10-CM)	ICD-10-CM	7
Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses	Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses (SNOMED CT US)	SNOMED CT US	5
Cerebrovascular Disease (CCI) Diagnoses	Cerebrovascular Disease (CCI) Diagnoses (ICD-10-CM)	ICD-10-CM	4
Cerebrovascular Disease (CCI) Diagnoses	Cerebrovascular Disease (CCI) Diagnoses (ICD-10-WHO)	ICD-10-WHO	4
Chronic Kidney Disease (CKD) Related Procedures	Chronic Kidney Disease (CKD) Related Procedures (HCPCS)	HCPCS	4
Chronic Kidney Disease (CKD) Related Procedures	Chronic Kidney Disease (CKD) Related Procedures (ICD-10-PCS)	ICD-10-PCS	4
Myocardial Infarction (CCI) Diagnoses	Myocardial Infarction (CCI) Diagnoses (ICD-10-CM)	ICD-10-CM	4
Myocardial Infarction (CCI) Diagnoses	Myocardial Infarction (CCI) Diagnoses (ICD-9-CM)	ICD-9-CM	4
AIDS/HIV (CCI) Diagnoses	AIDS/HIV (CCI) Diagnoses (ICD-10-WHO)	ICD-10-WHO	3
Bone Marrow Procedures	Bone Marrow Procedures (ICD-9-CM)	ICD-9-CM	3
Bone Marrow Transplant Diagnoses	Bone Marrow Transplant Diagnoses (ICD-10-WHO)	ICD-10-WHO	3
Cardiac Failure Diagnoses	Cardiac Failure Diagnoses (ICD-10-CM)	ICD-10-CM	3
Cardiovascular Disease Diagnoses	Cardiovascular Disease Diagnoses (ICD-10-CM)	ICD-10-CM	3
Cardiovascular Disease Diagnoses	Cardiovascular Disease Diagnoses (ICD-10-WHO)	ICD-10-WHO	3
Cardiovascular Disease Diagnoses	Cardiovascular Disease Diagnoses (ICD-9-CM)	ICD-9-CM	3
Cerebrovascular Disease (CCI) Diagnoses	Cerebrovascular Disease (CCI) Diagnoses (ICD-9-CM)	ICD-9-CM	3
Congestive Heart Failure (CCI) Diagnoses	Congestive Heart Failure (CCI) Diagnoses (ICD-10-CM)	ICD-10-CM	3
Congestive Heart Failure (CCI) Diagnoses	Congestive Heart Failure (CCI) Diagnoses (ICD-9-CM)	ICD-9-CM	3
Coronary Artery Disease (CAD) Diagnoses for Frailty (Customer2)	Coronary Artery Disease (CAD) Diagnoses for Frailty (Customer2) (ICD-10-CM)	ICD-10-CM	3
Diabetes Mellitus Diagnosis Codes (Customer1)	Diabetes Mellitus Diagnosis Codes (Customer1) (ICD-9-CM)	ICD-9-CM	3
Diabetes Mellitus, Any Type (Broad) Diagnoses	Diabetes Mellitus, Any Type (Broad) Diagnoses (ICD-10-WHO)	ICD-10-WHO	3
Dialysis Procedures	Dialysis Procedures (CPT)	CPT	3
Hepatic Encephalopathy Diagnoses	Hepatic Encephalopathy Diagnoses (ICD-10-CM)	ICD-10-CM	3
Peripheral Vascular Disease (CCI) Diagnoses	Peripheral Vascular Disease (CCI) Diagnoses (ICD-10-CM)	ICD-10-CM	3
AIDS/HIV (CCI) Diagnoses	AIDS/HIV (CCI) Diagnoses (ICD-10-CM)	ICD-10-CM	2
AIDS/HIV Diagnoses (Customer1, Kidney Transplant, Study1)	AIDS/HIV Diagnoses (Customer1) (ICD-9-CM)	ICD-9-CM	2
Acute Kidney Injury Diagnoses	Acute Kidney Injury Diagnoses (ICD-10-CM)	ICD-10-CM	2
Acute Kidney Injury Diagnoses	Acute Kidney Injury Diagnoses (ICD-9-CM)	ICD-9-CM	2
Alcohol Dependence Diagnoses (Customer1)	Alcohol Dependence Diagnoses (Customer1) (ICD-10-CM)	ICD-10-CM	2
All-Cause Pneumonia Diagnoses (Customer1)	All-Cause Pneumonia Diagnoses (Customer1) (ICD-10-CM)	ICD-10-CM	2
All-Cause Pneumonia Diagnoses (Customer1)	All-Cause Pneumonia Diagnoses (Customer1) (ICD-9-CM)	ICD-9-CM	2
Anti-lymphocyte receptor antibodies (ALA) Therapies	Anti-lymphocyte receptor antibodies (ALA) Therapy Procedures (HCPCS)	HCPCS	2
Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses	Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses (Aurum MedCodeID)	Aurum MedCodeID	2
Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses	Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses (SNOMED CT UK)	SNOMED CT UK	2
Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses	Any Malignancy, except malignant neoplasm of skin (CCI) Diagnoses (SNOMED CT US)	SNOMED CT US	2
Asthma Diagnoses	Asthma Diagnoses (ICD-10-CM)	ICD-10-CM	2
Asthma Diagnoses	Asthma Diagnoses (ICD-10-WHO)	ICD-10-WHO	2
Asthma Diagnoses	Asthma Diagnoses (ICD-9-CM)	ICD-9-CM	2
Multiple Myeloma Diagnoses			
BCG Procedures	BCG Procedures (CPT)	CPT	2
Body Height Vital Signs	Body Height Vital Signs (Aurum MedCodeID)	Aurum MedCodeID	2
Body Height Vital Signs	Body Height Vital Signs (SNOMED CT UK)	SNOMED CT UK	2
Bone Marrow Transplant Procedures	Bone Marrow Transplant Procedures (ICD-9-CM)	ICD-9-CM	2
Brain Natriuretic Peptide Lab Tests	Brain Natriuretic Peptide Lab Tests (CPT)	CPT	2
CAR-T Therapy Procedure Codes (Study2)	CAR-T Therapy Procedure Codes (Study2) (ICD-10-PCS)	ICD-10-PCS	2
COVID-19 Related Procedures	COVID-19 Related Procedures (CPT)	CPT	2
COVID-19 Related Procedures	COVID-19 Related Procedures (HCPCS)	HCPCS	2
COVID-19 Related Procedures	COVID-19 Related Procedures (ICD-10-PCS)	ICD-10-PCS	2
COVID-19 Vaccination	COVID-19 Vaccination (Name)	Name	2
Carcinoma In Situ Diagnoses	Carcinoma In Situ Diagnoses (ICD-10-CM)	ICD-10-CM	2
Carcinoma In Situ Diagnoses	Carcinoma In Situ Diagnoses (SNOMED CT US)	SNOMED CT US	2
Cerebrovascular Disease (CCI) Diagnoses	Cerebrovascular Disease (CCI) Diagnoses (Aurum MedCodeID)	Aurum MedCodeID	2
Cerebrovascular Disease (CCI) Diagnoses	Cerebrovascular Disease (CCI) Diagnoses (READ2)	READ2	2
Cerebrovascular Disease (CCI) Diagnoses	Cerebrovascular Disease (CCI) Diagnoses (SNOMED CT UK)	SNOMED CT UK	2
Cerebrovascular Disease (CCI) Diagnoses	Cerebrovascular Disease (CCI) Diagnoses (SNOMED CT US)	SNOMED CT US	2
Chronic Ischemic Heart Disease Diagnoses	Chronic Ischemic Heart Disease Diagnoses (ICD-9-CM)	ICD-9-CM	2
Chronic Ischemic Heart Disease Diagnoses (Customer1)	Chronic Ischemic Heart Disease Diagnoses (Customer1) (READ2)	READ2	2
Chronic Ischemic Heart Disease Diagnoses (Customer1)	Chronic Ischemic Heart Disease Diagnoses (Customer1) (SNOMED CT US)	SNOMED CT US	2
Chronic Kidney Disease (CKD) Narrow Diagnoses	Chronic Kidney Disease (CKD) Narrow Diagnoses (Aurum MedCodeID)	Aurum MedCodeID	2
Chronic Kidney Disease (CKD) Stage IV Diagnoses	Chronic Kidney Disease (CKD) Stage IV Diagnoses (Aurum MedCodeID)	Aurum MedCodeID	2
Chronic Kidney Disease (CKD) Stage IV Diagnoses	Chronic Kidney Disease (CKD) Stage IV Diagnoses (ICD-10-WHO)	ICD-10-WHO	2
Chronic Kidney Disease (CKD) Stage V Diagnoses	Chronic Kidney Disease (CKD) Stage V Diagnoses (ICD-10-WHO)	ICD-10-WHO	2
Chronic Pulmonary Disease (CCI) Diagnoses	Chronic Pulmonary Disease (CCI) Diagnoses (ICD-10-CM)	ICD-10-CM	2
Chronic Pulmonary Disease (CCI) Diagnoses	Chronic Pulmonary Disease (CCI) Diagnoses (ICD-10-WHO)	ICD-10-WHO	2
Chronic Pulmonary Disease (CCI) Diagnoses	Chronic Pulmonary Disease (CCI) Diagnoses (ICD-9-CM)	ICD-9-CM	2

Table 2: Duplicate Discrete Concepts Only

Code System	Related Groups	Variation Count	Difference
Not Specified	3	7	4
ATC	4	8	4
Aurum MedCodeID	14	28	14
Aurum ProdCodeID	1	2	1
CPT	6	13	7
HCPCS	9	20	11
ICD-10-CM	39	93	54
ICD-10-PCS	4	10	6
ICD-10-WHO	26	59	33
ICD-9-CM	36	85	49
Name	6	12	6
NDC	1	2	1
READ2	8	16	8
RxNorm	3	6	3
SNOMED CT UK	12	24	12
SNOMED CT US	11	25	14
Grand Total	183	410	227

Conclusion: As organizations strive to adhere to regulatory requirements for CODefs, managing the complex representations of CODefs can quickly become challenging when moving from the discrete concept to related groups for each code system, to unique variations used in real-world research.