# Predicting Neurological Comorbidities of HIV with Supervised Machine Learning: Analysis of a Large Healthcare Database in Low Memory Conditions

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# ABSTRACT

With the success of highly active antiretroviral therapy (HAART / ART), an unfortunate, painful death from AIDS is no longer the inevitable future for persons living with HIV (PLWH). However, since ART only reduces – but does not eliminate – viral load, the infection can still have long-term effects on their host. Some long-term cardiovascular and neurological complications are only now being discovered. I analyzed inpatient records of 3,123 PLWH and 1,717,774 uninfected individuals from the MarketScan Commercial and Medicare database for the year 2013 for comorbidity rates with a variety of cardiovascular and neurological conditions, and found that PLWH were at elevated risk for many conditions that had been so far overlooked in the literature. To highlight some of the conclusions from my analysis, I found that PLWH were 5.26 times more likely to be diagnosed with peripheral neuropathy and 79.17 times more likely to develop disorders of the choroid. The findings can be critical towards further exploration of related disease processes of HIV-infection, perhaps even to discover interplay with other fields of biological science such as genetics that have been thus far under-emphasized and unwittingly placed PLWH at risk.

Further, with the aging of the HIV population and the increased need to optimize healthcare resources as the global population burgeons and ages, accurately identifying PLWH at risk of neurological complications for early intervention is imperative. Using supervised machine learning techniques, I was able to create a neural net taking in a patient's cardiovascular disease profile plus minimal demographic parameters (age, gender, and state of residence) that was predictive of neurological complications to an accuracy level of >97% across all models. In

particular, the inclusion of demographic variables did not improve predictive accuracy. Development of this method into a widespread predictive mechanism to aid clinical decisionmaking could be financially beneficial to providers while increasing the quality of care to patients, as resources and interventions can be redirected to high risk groups.

## INTRODUCTION

The discovery and rise in affordability of antiretroviral therapy since 1980 has increased the life expectancy of people living in HIV. Today, an estimated 1.1 million individuals in the United States are considered PLWH (Anon, 2020), and their average life expectancy has increased 11.8 years as a result of ART (Gueler et al., 2017). While this is encouraging news for public health, the recent discourse around value-based care has cast doubt upon the long-held belief that a longer life is always a better life.

As PLWH live to older age, clinicians have been more likely to encounter PLWH with longerterm cardiovascular and neurological complications, including cardiomyopathy, hypertension, endocarditis, and meningitis (Barbaro, 2002). However, many key questions that are crucial to clinical decision-making and care planning remain unanswered. Is it possible to determine, before onset, the point at which the effects of a disease become irreversible? Additionally, what sort of complications could the patient face, and how debilitating are they? Last but not least, what future complications are expected based on the patient's current state?

Large-scale bioinformatics analysis can help to answer these questions by identifying populations at the greatest risk of developing complications for early clinical and therapeutic intervention. It could also help to redirect research resources towards investigating the most lethal or highest risk complications, which may not necessarily be the most prevalent. Lastly, advances in computer science and statistical modelling have made possible the prediction of a patient's unique trajectory, that, if accurate, could reduce the level of uncertainty and invasive testing that patients have to endure, improve the quality of care physicians can provide, as well as better optimize limited healthcare resources over the patient population.

The first stage of HIV infection is often referred to as acute HIV infection and manifests in the form of flu-like symptoms, caused by the assault of the virus on CD4 cells in the blood. As a

result of this mechanism's direct linkage to the most important organ in the cardiovascular system, the heart, there exists ample research into the cardiovascular complications of HIV infection, particularly in the immediate and short term (Glesby, 2017). As the population of PLWH has grown older, research efforts in recent years have focused on the increased risk of PLWH for long-term cardiovascular complications, and initial findings have pointed to strong associations between infection and heart failure, stroke, and myocardial infarctions (Alonso et al., 2019). A more detailed, comprehensive scan of PLWH's risk of cardiovascular complications as a whole remains absent, however, which this study aims to fill in through a breadth-first analysis of cardiovascular condition buckets before homing in on certain categories that pose as a relatively higher risk for PLWH compared to non-infected counterparts.

In contrast, the biological mechanism between HIV infection and the nervous system is not as well understood. Because the brain is a relatively immune privileged site, the central nervous system serves as an ideal reservoir for the virus, which is able to infect long-lived cells with minimal cytopathology, such as resident macrophages, microglia, and astrocytes (Churchill and Nath, 2013). Clinically debilitating central nervous system symptoms continue to be observed in more than 50% of patients receiving combination antiretroviral therapy, comparable to the pre-antiretroviral era rates (Clifford, 2008). Primary disorders resulting from the direct effects of the virus are more well-researched, and include HIV-associated neurocognitive disorders, vacuolar myelopathy, and distal symmetric polyneuropathy, to name a few. Research on secondary disorders, which result from marked immunosuppression and opportunistic infections, is only in its nascency (Bilgrami and O'keefe, 2014). A common example is cryptococcal meningitis (Kalinoski et al., 2020). This study aims to unveil a holistic understanding of the neurological complications that pose as greater risks for PLWH, which is imperative for the purposes of improving current treatments, discover new ones, deliver better preventative care to PLWH, and prevent future transmission. Compared to an sweep of comorbid cardiovascular conditions, for

which the community has a more detailed understanding, a neurological analysis is perhaps even more crucial.

To achieve the above goals, this pilot study aims to explore two key questions: On a national level, what neurological complications pose the greatest risk to PLWH relative to uninfected persons? Secondly, can common cardiovascular endpoints be used to predict potential comorbidities for individual PLWH medical profiles? Importantly, the approach used in this study will yield correlation not causation between PLWH and analyzed conditions, and the findings present a starting, not an ending point, for understanding comorbidities with HIV infection from a more granular perspective than has been done in previous literature.

# METHODS

## Population Data

Data from the Truven Health MarketScan Medicare Supplemental and Coordination of Benefits Database (Truven Health Analytics, Ann Arbor, Michigan) for the period of January 1, 2013 through December 31, 2013 was analyzed. This database includes healthcare claims for inpatient and outpatient services for individuals enrolled in private health plans or employersponsored Medicare plans from across the United States; individuals are tracked via a unique enrollee identifier that is constructed by encrypting information provided by data contributors. Granularity of the information reaches all levels of care, pharmacy claims, and relevant demographic and enrollment information. The database population is widely distributed across all regions of the United States and is generally representative of the commercially insured population. This study was reviewed and approved by the Institutional Review Board of the University of Chicago, and a waiver of the informed consent was obtained. Licensing restrictions prevent me from making data and study materials available to other investigators for purposes of reproducing the results, but interested parties could obtain and license the data by contacting Truven Health Analytics Inc.

#### Definition of HIV and Uninfected Groups

The "HIV" group was defined as all patients in the MarketScan database with an HIV diagnosis without restrictions on age, gender or state of residence. An HIV infection was defined using the presence of the 042 (HIV Disease) code per the International Classification of Diseases, Ninth Revision-Clinical Modification (ICD-9-CM) designation. The "Uninfected" group was defined as all other enrollees that presented an inpatient claim that year.

#### Outcome Definition

I defined cardiovascular and neurological endpoints by applying validated algorithms to diagnostic codes from inpatient claims. Regarding cardiovascular endpoints, all conditions listed under "Diseases of the Circulatory System" under the ICD-9-CM designation were examined down to the 3-digit level, which includes codes in 390-450. Regarding neurological endpoints, all conditions listed under "Diseases of the Nervous System and Sense Organs" under the ICD-9-CM designation were examined down to the 3-digit level, which includes to the 3-digit level, which includes codes in 390-450. Regarding neurological endpoints, all conditions listed under "Diseases of the Nervous System and Sense Organs" under the ICD-9-CM designation were examined down to the 3-digit level, which includes codes in 320-389. A full list of codes examined is included in Table X.

#### Statistical Analysis

Comorbidity rates were calculated as the number of diagnoses as a percentage of the group size. Relative risk of a condition for infected group compared to the uninfected group was evaluated by dividing the comorbidity rate for the infected group over the uninfected group to attain a risk ratio. This can be interpreted as the number of times by which an infected individual is more likely to be diagnosed with the condition compared to an uninfected individual.

# Model Design and Evaluation

Neural networks were built using the TensorFlow module in Python 3.7.0. Separate models were built to predict comorbidities of 5 different sets of neurological conditions. All models were constructed with the following architecture (Table 1):

Layer	Input	Output	Activation Function
1	Array of boolean variables of a patient's cardiovascular end points, and associated one-hot encoded demographic data (if applicable)	Array of 64 numerical values	Linear
2	Activated output of layer 1	Array of 32 numerical values	Sigmoidal
3	Activated output of layer 2	Array of numbers ranging from 0 to 1, one for each neurological end point	Rectified Linear Unit (ReLU)

#### Table 1 | Model Structure

Models were constructed in TensorFlow v2.1.0 using Python 3.7.0. All layers are of "Dense" structure. Adam optimizer was used and measure of error was taken as mean squared error.

All models were evaluated and trained using the metric of mean squared error, and optimized using Adam (Diederik P. Kingma, 2015). This optimizer was preferred for two reasons: Firstly, it computes adaptive learning rates for individual parameters, which is beneficial in this case as the predictive power of each condition and demographic variable is unclear. Secondly, it increases the speed of training relative to many other older optimizers such as RMSprop and SGD, which is useful in my case as the training dataset was large to begin with and a singular run through would already be very time-consuming.

In addition to testing evaluation during training, a small set of enrollee identifiers were also chosen at random from the test set to conduct manual accuracy tests of the final models for each label, which could be a condition or a bucket of conditions, depending on the model framework. Model output for each label was rounded off to 0 or 1, and then compared with the actual data. Accuracies, false negatives (Model = 0, Actual = 1) and false positives (Model = 1, Actual = 0) were tabulated and taken as percentages for each label.

# Large Dataset Machine Learning Protocol Design for Low Memory Environments

Due to limitations in computational space with the result that the entire year's data was too large to fit in the RAM of the available computer, the following unconventional training protocol was designed using multiprocessing in Python 3.7.0 and Sqlite3.



#### Figure 1 | Training Protocol

1A) Shows a typical model training protocol. A script is loaded into RAM, which makes a query to a database or other file in the disk that holds the dataset. The entire dataset is then loaded into Random Access Memory (RAM), and then fed into the model, which is constructed in RAM. Utilizing this method for this study would have required ~ 800MB - 99CB of RAM for the dataset, plus ~ 4 GB RAM for maintaining the model by the OS.
1B) Shows the protocol that was developed for this study. The script is loaded into RAM, which makes queries to the Sqlite3 database that holds the dataset. Small chunks of the dataset, per the query instructions, are loaded onto a queue that is located in shared memory in RAM with the model process. The model training process pops chunks of data off of the queue for training and testing until a termination signal is sent by the data collection process.

Cleaned and coded patient records were stored in a series of indexed tables in a Sqlite3 database, which was preferred as, of the database software available, it provided all the necessary features in the simplest package. During training and testing, two processes ran in parallel – data selection from the database, and training or evaluation through the model.

Enrollee identifiers were previously assigned into a 70%:30% training and testing set, as is common practice in machine learning. This meant that ~1.2 million patient records were designated for training, and 0.8 million patient records were designated for testing. In normal circumstances, the entirety of the training or test records would be loaded into RAM and then processed by the model, which is also constructed and refined in RAM. With a large dataset to the order of GBs, and eventually perhaps TBs, this would have been infeasible, not to mention disrespectful to other users of the same central server. Alternatively, a supercomputer would have been required.

Hence, the batched protocol (Figure 1) was devised. Prior to model construction, the lists of identifiers were segmented into 10,000-length chunks to be accessed one at a time from the database, which meant that the requirement for RAM per batch was reduced to approximately 6MB. Pulled records were then one-hot encoded for demographic data, if applicable, and added to a shared memory queue of Numpy arrays. The model process would then pop the latest chunk of data from the queue to be fed through the model for testing or training. At any given point in time, the RAM requirement was thus reduced greatly to the chunks held by the length of the queue, plus space for OS maintenance (~4GB).

Importantly, the process of retrieving data from disk is much more time-consuming compared to the training process. The protocol was optimized by running the same batch of data through the model for 3 epochs of training, such that the training time took up roughly the same time as the data retrieval process.

3 epochs should not cause overfitting, as evidenced by the fact that testing error never rises. Moreover, new data is shown after the 3 epochs elapse, and thus any overfitted weight would have been corrected by the next batch of data. Further mathematical proof and insight into black box neural nets is needed to rigorously ascertain the validity of overfitting as a concern.

# FINDINGS

For the year 2013, the MarketScan inpatient records included 3,123 PLWH and 1,717,774 uninfected individuals. In sum, 2,113,883 inpatient encounters were analyzed. This excludes 4,959 encounters which did not have a unique enrollment identifier.

# **Comorbidity Analysis**

Comorbidity rates for key cardiovascular and neurological conditions were calculated. The risk ratio represents the increased likelihood of diagnosis for the listed condition for the infected group compared to the uninfected group.

Cardiovascular and Neurological Conditions Overview

	PL	WH	Uninf	ected	Risk
Cardiovascular and Neurological Conditions	Cases	Comorb	Cases	Comorb	Ratio
HIV	3,123	100.00%	0	0.00%	
Cardiovascular Conditions					
Acute Rheumatic Fever	0	0.00%	182	0.01%	0.00x
Chronic Rheumatic Heart Disease	35	1.12%	10,279	0.60%	1.87x
Hypertensive Disease	1,023	32.76%	346,410	20.17%	1.62x
Ischemic Heart Disease	292	9.35%	102,890	5.99%	1.56x
Diseases Of Pulmonary Circulation	132	4.23%	30,522	1.78%	2.38x
Heart Disease, Other	751	24.05%	200,520	11.67%	2.06x
Cerebrovascular Disease	214	6.85%	58,961	3.43%	2.00x
Arteries, Arterioles, Capillaries	117	3.75%	34,276	2.00%	1.88x
Veins, Lymphatics, And Other Circulatory	421	13.48%	89,729	5.22%	2.58x
Neurological Conditions					
Inflammatory CNS And Sense Organs	153	4.90%	7,827	0.46%	10.65x
Organic Sleep Disorders	62	1.99%	46,337	2.70%	0.74x
Hereditary And Degenerative Diseases Of CNS	82	2.63%	24,427	1.42%	1.85x
Pain	192	6.15%	132,937	7.74%	0.79x
Headache Syndromes	6	0.19%	2,076	0.12%	1.58x
CNS, Other	417	13.35%	110,788	6.45%	2.07x
Peripheral Nervous System	172	5.51%	33,148	1.93%	2.85x
Eye And Adnexa	118	3.78%	30,219	1.76%	2.15x
Ear And Mastoid	52	1.67%	17,305	1.01%	1.65x

#### Table 2 | Cardiovascular and Neurological Conditions Overview Comorbidity Rates

Group comorbidity rates for key cardiovascular and neurological condition categories, MarketScan 2013. Categories highlighted in red text were earmarked for further analysis.

At first glance, HIV infection is associated with around 1.5x the risk of ischemic heart disease compared to the uninfected group, which is in line with official reports (American Heart Association News, 2019). HIV infection is associated with double the risk for cardiovascular conditions falling into the categories of "Heart Disease, Other" and "Veins, Lymphatics and Other Circulatory". It is also associated with 10 times the risk for neurological conditions falling into the category of "Inflammatory CNS and Sense Organs".

A deeper dive was done into the cardiovascular condition categories with the highest comorbidity rates for the infected population, which are highlighted in red (Table 2). I will now proceed to detail findings for each of these buckets.

Cardiovascular Conditions: Hypertensive Disease

	PL	WH	Uninf	ected	Risk
Hypertensive Disease Conditions	Cases	Comorb	Cases	Comorb	Ratio
Essential Hypertension	912	29.20%	329,158	19.16%	1.52x
Hypertensive Heart Disease	37	1.18%	7,776	0.45%	2.62x
Hypertensive Chronic Kidney Disease	191	6.12%	26,498	1.54%	3.96x
Hypertensive Heart And Chronic Kidney Disease	11	0.35%	2,471	0.14%	2.45x
Secondary Hypertension	3	0.10%	1,064	0.06%	1.55x

#### Table 3 | Hypertensive Disease Comorbidity Rates

Group comorbidity rates for hypertensive disease categories, MarketScan 2013. Condition with the highest risk ratio is highlighted in red.

PLWH are 1.62 times more likely to contract hypertensive disease conditions as a whole compared to noninfected persons (Figure 2). A closer look shows that HIV infection is associated with higher risk – risk ratio > 1 – of contracting all subcategories of hypertensive disease. In particular, they are at higher risk of contracting hypertensive heart disease than hypertensive chronic kidney disease, and also of contracting them simultaneously (Table 3). Both the prevalence and mechanisms for these two complications have been documented in the literature (Gopal et al., 2009; Wyatt, 2017). Research on the immunological pathway between HIV infection and essential hypertension is more nascent, but existent (Masenga et al., 2019).

	PL	.WH	Unin	fected	Risk
Other Forms of Heart Disease Conditions	Cases	Comorb	Cases	Comorb	Ratio
Acute Pericarditis	18	0.58%	2,703	0.16%	3.66x
Acute And Subacute Endocarditis	21	0.67%	1,932	0.11%	5.98x
Acute Myocarditis	4	0.13%	631	0.04%	3.49x
Other Diseases Of Pericardium	58	1.86%	8,394	0.49%	3.80x
Other Diseases Of Endocardium	175	5.60%	43,897	2.56%	2.19x
Cardiomyopathy	104	3.33%	22,802	1.33%	2.51x
Conduction Disorders	66	2.11%	19,470	1.13%	1.86x
Cardiac Disrhythmias	383	12.26%	119,488	6.96%	1.76x
Heart Failure	205	6.56%	48,836	2.84%	2.31x
III-Defined Descriptions, Complications Of Heart Disease	135	4.32%	32,560	1.90%	2.28x

## Cardiovascular Conditions: Other Forms of Heart Disease

#### Table 4 | Other Forms of Heart Disease Comorbidity Rates

Group comorbidity rates for hypertensive disease categories, MarketScan 2013. Condition with the highest risk ratio is highlighted in red.

PLWH are 2.06 times more likely to contract other heart disease conditions as a whole compared to noninfected persons (Figure 2). At first glance, most of the listed heart disease complications are fairly niche, with fewer than 100,000 incidences per year. HIV infection is associated with elevated risk of at least 2 times that of uninfected patients for all conditions except for conduction disorders and cardiac dysrhythmias.

HIV infection is associated with highest risk of endocarditis, which is unsurprising given that intravenous drug use, a common HIV vector, is also associated with increased rates of infective endocarditis, which is supported by the literature (Cecchi et al., 2007). Complications related to first the pericardium, both acute and other, posed the second highest risk for the infected group. However, recent literature has focused more on conditions related to the myocardium such as myocarditis and cardiomyopathy, as there has been suspicion that HAART may be a cause of myocardial dysfunction (Nelson et al., 2014). Lastly, in line with the literature, HIV infection is associated with approximately 2x greater risk of heart failure compared to the uninfected group (Butt et al., 2011); (Remick et al., 2014).

#### Cardiovascular Conditions: Veins, Lymphatics and Other Circulatory

	PL	.WH	Unin	fected	Risk
Veins, Lymphatics, And Other Circulatory	Cases	Comorb	Cases	Comorb	Ratio
Phlebitis And Thrombophlebitis	31	0.99%	6,240	0.36%	2.73x
Portal Vein Thrombosis	14	0.45%	1,368	0.08%	5.63x
Other Venous Embolism And Thrombosis	108	3.46%	25,278	1.47%	2.35x
Varicose Veins of Lower Extremities	6	0.19%	1,802	0.10%	1.83x
Hemorrhoids	44	1.41%	8,418	0.49%	2.87x
Varicose Veins of Other Sites	47	1.50%	4,180	0.24%	6.18x
Noninfectious Disorders of Lymphatic Channels	16	0.51%	3,121	0.18%	2.82x
Hypotension	188	6.02%	39,877	2.32%	2.59x
Other Disorders of Circulatory System	38	1.22%	11,439	0.67%	1.83x

 Table 5 | Veins, Lymphatics, And Other Circulatory Conditions Comorbidity Rates

 Group comorbidity rates for other forms of heart disease categories, MarketScan 2013.

 Condition with the highest risk ratio is highlighted in red.

PLWH are 2.58 times more likely to contract veins, lymphatic, and other circulatory conditions as a whole compared to noninfected persons (Figure 2). Infection is associated with the highest relative risk for varicose veins in sites other than lower extremities, and portal vein thrombosis (PVT). It is important to note that all of these complications are fairly niche, with prevalence rates lower than 2% except for hypotension. Research of vein-related HIV complications is sparse, but a handful of clinical cases and reviews on the linkage between infection and PVT exist (Sullivan et al., 2000; Ramanampamonjy et al., 2005). To this day, the biological mechanism between HIV infection and thrombosis is not clear.

Next, a deeper dive was done into the neurological condition categories that posed as the greatest additional risk to PLWH, which are highlighted in red (Table 2).

Neurological Conditions: Inflammatory Diseases of the Central Nervous System Comorbidity Rates

	PL	.WH	Unin	Risk	
Inflammatory CNS and Sense Organs Conditions	Cases	Comorb	Cases	Comorb	Ratio
Bacterial Meningitis	20	0.64%	1,201	0.07%	9.16x
Meningitis Due To Other Organisms	36	1.15%	208	0.01%	95.20x
Meningitis Of Unspecified Cause	62	1.99%	3,768	0.22%	9.05x
Encephalitis, Myelitis, And Encephalomyelitis	50	1.60%	1,951	0.11%	14.10x
Intracranial And Intraspinal Abscess	14	0.45%	1,450	0.08%	5.31x
Phlebitis Intracranial Sinus	0	0.00%	550	0.03%	0.00x
Late effects of intracranial abscess or pyogenic infection	1	0.03%	103	0.01%	5.34x

#### Table 6 | Inflammatory CNS and Sense Organs Conditions Comorbidity Rates

Group comorbidity rates for inflammatory CNS and sense organ condition categories, MarketScan 2013. Condition with the highest risk ratio is highlighted in red.

PLWH are 10.65 times more likely to contract inflammatory CNS conditions as a whole compared to noninfected persons (Figure 2). HIV infection is associated with elevated risk of at least 2 times that of uninfected patients for all inflammatory CNS conditions except for intracranial sinus phlebitis, which is an incredibly rare condition. Infected persons were associated with the highest relative risk of suffering from meningitis, a comorbidity that has been thoroughly researched within the literature, in particular cryptococcal meningitis (Jarvis and Harrison, 2007; Park et al., 2009).

Neurological Conditions: Other Conditions of the Central Nervous System Comorbidity Rates

	PL	.WH	Unin	fected	Risk
Other Conditions of the CNS Conditions	Cases	Comorb	Cases	Comorb	Ratio
Multiple Sclerosis	9	0.29%	6,106	0.36%	0.80x
Other Demyelinating Diseases	3	0.10%	1,010	0.06%	1.60x
Hemiplegia And Hemiparesis	43	1.38%	8,336	0.49%	2.81x
Infantile Cerebral Palsy	2	0.06%	3,054	0.18%	0.36x
Other Paralytic Syndromes	21	0.67%	6,309	0.37%	1.82x
Epilepsy And Recurrent Seizures	87	2.79%	27,471	1.60%	1.74x
Migraine	59	1.89%	32,325	1.88%	1.00x
Cataplexy And Narcolepsy	0	0.00%	579	0.03%	0.00x
Other Conditions Of Brain	247	7.91%	37,904	2.21%	3.58x
Other And Unspecified Disorders	51	1.63%	10,345	0.60%	2.72x

#### Table 7 | Other Conditions of the CNS Comorbidity Rates

Group comorbidity rates for other central nervous system condition categories, MarketScan 2013. Condition with specificity that has the highest risk ratio is highlighted in red.

PLWH are 2.07 times more likely to contract other CNS conditions as a whole compared to

noninfected persons (Figure 2). In terms of specifically delineated complications, infected

persons were associated with the highest relative risk of being diagnosed with hemiplegia and hemiparesis. While disparate cases of hemiplegia have been reported in the literature for both perinatal transmissions and adults, and some hypotheses exist relating opportunistic and untreated central nervous system aspergillosis to this condition, this is not representative of all cases (Kugler et al., 1991; Park et al., 2009). More commonly, but to a lower risk, infected persons were also diagnosed with epilepsy and recurrent seizures at higher rates compared to uninfected persons. This is in line with the literature, where HIV-infected individuals who experience seizures tend to develop epilepsy later on, but the pathology remains unclear (Kellinghaus et al., 2008).

Importantly, infected persons were at the highest risk of being diagnosed with other conditions of brain or unspecified disorders. They were not at higher risk of being diagnosed with multiple sclerosis, migraines and cataplexy and narcolepsy. Logically, and as observed, HIV-infection did not put individuals at higher probabilities of being diagnosed with infantile cerebral palsy.

Neurological	Conditions:	Peripheral	Nervous S	vstem	Comorbidit	/ Rates
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	PL	.WH	Unin	fected	Risk
Peripheral Nervous System Conditions Conditions	Cases	Comorb	Cases	Comorb	Ratio
Trigeminal Nerve Disorders	3	0.10%	1,214	0.07%	1.36x
Facial Nerve Disorders	11	0.35%	2,075	0.12%	2.92x
Disorders Of Other Cranial Nerves	1	0.03%	460	0.03%	1.20x
Nerve Root And Plexus Disorders	4	0.13%	1,514	0.09%	1.45x
Mononeuritis Of Upper Limb And Mononeuritis Multiplex	4	0.13%	2,456	0.14%	0.90x
Mononeuritis Of Lower Limb And Unspecified Site	47	1.50%	6,220	0.36%	4.16x
Hereditary And Idiopathic Peripheral Neuropathy	62	1.99%	6,479	0.38%	5.26x
Inflammatory And Toxic Neuropathy	45	1.44%	12,098	0.70%	2.05x
Myoneural Disorders	3	0.10%	1,441	0.08%	1.15x
Muscular Dystrophies And Other Myopathies	22	0.70%	2,748	0.16%	4.40x

 Table 8 | Peripheral Nervous System Conditions Comorbidity Rates

Group comorbidity rates for peripheral nervous systems condition categories, MarketScan 2013. Condition with the highest risk ratio is highlighted in red.

PLWH are 2.85 times more likely to contract peripheral nervous system (PNS) conditions as a

whole compared to noninfected persons (Figure 2). PNS complications have very low

comorbidity rates of mostly below 1% for both infected and uninfected groups, suggesting a

level of nicheness that may be indicative of why limited research has been done regarding their biological mechanism. That being said, infected persons were associated with the highest relative risk of being diagnosed with peripheral neuropathy, muscular dystrophies and other myopathies. Variability in HIV-infection associated risk of diagnosis was high for disorders of different PNS regions, with lower risk associated with facial nerve and nerve root disorders, and low or no elevated risk of diagnosis for trigeminal nerve, oher cranial nerves, myoneural disorders. PNS neuropathies have been reported to occur in a third of AIDS patients and now also in chronic HIV infection or neurotoxic ART cases, though the exact pathogenesis is unknown (Schifitto G, n.d.; Wang et al., 2014).

# Neurological Conditions: Eye & Adnexa Conditions Comorbidity Rates

	PL	WH	Unin	fected	Risk
Eye and Adnexa Conditions Conditions	Cases	Comorb	Cases	Comorb	Ratio
Disorders Of The Globe	2	0.06%	283	0.02%	3.89x
Retinal Detachments And Defects	2	0.06%	235	0.01%	4.68x
Other Retinal Disorders	10	0.32%	5,526	0.32%	1.00x
Chorioretinal Inflammations, Scars, Other Disorders Of Choroid	19	0.61%	132	0.01%	79.17x
Disorders Of Iris And Ciliary Body	5	0.16%	397	0.02%	6.93x
Glaucoma	9	0.29%	3,240	0.19%	1.53x
Cataract	1	0.03%	668	0.04%	0.82x
Disorders Of Refraction And Accommodation	0	0.00%	472	0.03%	0.00x
Visual Disturbances	40	1.28%	9,581	0.56%	2.30x
Blindness And Low Vision	15	0.48%	2,910	0.17%	2.84x
Keratitis	3	0.10%	253	0.01%	6.52x
Corneal Opacity And Other Disorders Of Cornea	0	0.00%	194	0.01%	0.00x
Disorders Of Conjunctiva	10	0.32%	2,147	0.12%	2.56x
Inflammation Of Eyelids	4	0.13%	1,059	0.06%	2.08x
Other Disorders Of Eyelids	2	0.06%	865	0.05%	1.27x
Disorders Of Lacrimal System	3	0.10%	746	0.04%	2.21x
Disorders Of The Orbit	8	0.26%	1,776	0.10%	2.48x
Disorders Of Optic Nerve And Visual Pathways	6	0.19%	1,747	0.10%	1.89x
Strabismus And Other Disorders Of Binocular Eye Movements	6	0.19%	1,616	0.09%	2.04x
Other Disorders Of Eye	18	0.58%	3,130	0.18%	3.16x

Table 9 | Eye and Adnexa Conditions Comorbidity Rates

Group comorbidity rates for eye and adnexa condition categories, MarketScan 2013. Condition with the highest risk ratio is highlighted in red.

PLWH are 2.15 times more likely to contract eye and adnexa conditions as a whole compared to noninfected persons (Figure 2). Like PNS complications, eye and adnexa conditions have generally very low comorbidity rates of below 1%, except for visual disturbances. That aside, the

infected group is associated with overwhelming higher comorbidity rates for chorioretinal inflammations, in line with the literature, which are usually due to opportunistic infections that cannot be prevented (Saini et al., 2019). Disorders of iris and ciliary bodies as well as keratitis are also higher for the infected group, but to a much smaller magnitude. Overall, the infected group is associated with double or higher the comorbidity rates of uninfected controls.

## Models

Moving on to the machine learning portion of this study, separate models were trained to predict comorbidities for the 5 sets of neurological conditions investigated above: 1) general buckets of neurological conditions, 2) inflammatory diseases of the central nervous system, 3) other conditions of the central nervous system, 4) peripheral nervous system conditions, 5) eye and adnexa conditions.

In general, models' training speed was fairly quick, with error plateauing by around batch epoch 26, which is around batch 8. This means that models only required 80,000 individual patient profiles to train. Overfitting was not observed, as training and testing error remained low throughout the rest of the dataset, which was trained on anyway to be safe; no uptick in testing error was noted.

# Training and Testing Error



#### Figure 2 | Training and Testing Error for Models with Demographics

Models take in an array of Boolean variables for diagnosis of cardiovascular indications and HIV infection, plus demographic variables of age, gender, state of residence. Each line represents one model. Models differ with respect to the array of neurological end points it is trained to predict.

- CNSI Inflammatory CNS and sense organ conditions
- CNSO Other conditions of the CNS
- Eye Conditions of the eye and adnexa
- PNS Conditions of the Peripheral Nervous System
- All Buckets of Neurological Conditions in Table 2
- A) Training error calculated as mean squared error, plotted against epochs.

B) Testing error calculated as mean squared error, plotted against batches. 1 batch is run through the model 3 times for training, so error is evaluated every 3 epochs. The first evaluation occurs after the first batch of data is trained on the model, explaining why most curves begin with error below 0.5, i.e. better than random chance.

On average, all models attained a very low training error rate, and all final training error rates fell

below 5%. The model predicting complications within broad neurological buckets performed the

worst, with a still impressive training error rate of 3%.

#### Models including All Demographic Variables

			Casas			Potos	
			False	False		False	False
А	All Neurological	Accurate	Positive	Negative	Accuracy	Positive	Negative
	Inflammatory CNS And Sense Organs	994	0	5	99.50%	0.00%	0.50%
	Urganic Sleep Disorders Hereditary And Degenerative Diseases Of CNS	979	0	20	98.00% 97.50%	0.00%	2.00%
	Pain	907	õ	92	90.79%	0.00%	9.21%
	Headache Syndromes	997	0	2	99.80%	0.00%	0.20%
	CNS, Other	907	0	92	90.79%	0.00%	9.21%
	Peripheral Nervous System	974	0	25	97.50%	0.00%	2.50%
	Ear And Mastoid	993	0	6	99.40%	0.00%	0.60%
	Average				96.89%	0.00%	3.11%
	Inflammatory CNS and Sense Organs Conditions		Cases	Falso		False	Falso
С	Conditions	Accurate	Positive	Negative	Accuracy	Positive	Negative
	Bacterial Meningitis	998	0	1	99.90%	0.00%	0.10%
	Meningitis Due To Other Organisms	999	0	0	100.00%	0.00%	0.00%
	Meningitis Of Unspecified Cause	995	0	4	99.60%	0.00%	0.40%
	Intracranial And Intraspinal Abscess	996	0	3	99.70%	0.00%	0.30%
	Phlebitis Intracranial Sinus	999	0	0	100.00%	0.00%	0.00%
	Late effects of intracranial abscess or pyogenic infection	999	0	0	100.00%	0.00%	0.00%
	Average				99.89%	0.00%	0.11%
			Cases			Rates	
F	Other Conditions of the CNS Conditions	Accurate	False	False	Accuracy	False	False
-		Accurate	Positive	Negative	Accuracy	Positive	Negative
	Multiple Scierosis Other Demyelinating Diseases	992	0	7	99.30%	0.00%	0.70%
	Hemiplegia And Hemiparesis	989	0	10	99.00%	0.00%	1.00%
	Infantile Cerebral Palsy	996	0	3	99.70%	0.00%	0.30%
	Other Paralytic Syndromes	992	0	7	99.30%	0.00%	0.70%
	Epilepsy And Recurrent Seizures	977	0	22	97.80%	0.00%	2.20%
	Cataplexy And Narcoleosy	909	0	0	100.00%	0.00%	0.00%
	Other Conditions Of Brain	951	ŏ	48	95.20%	0.00%	4.80%
	Other And Unspecified Disorders	986	0	13	98.70%	0.00%	1.30%
	Average				98.80%	0.00%	1.20%
			Cases			Rates	
G	Peripheral Nervous System Conditions Conditions	Accurate	Cases False	False	Accuracy	Rates False	False
G	Peripheral Nervous System Conditions Conditions	Accurate	Cases False Positive	False Negative	Accuracy	Rates False Positive	False Negative
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders	Accurate	Cases False Positive	False Negative	Accuracy 99.70%	Rates False Positive 0.00%	False Negative 0.30% 0.00%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves	Accurate 996 999 999	Cases False Positive 0 0 0	False Negative 3 0 0	Accuracy 99.70% 100.00% 100.00%	Rates           False           Positive           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.00%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders	Accurate 996 999 999 999	Cases False Positive 0 0 0 0	False Negative 3 0 0 3	Accuracy 99.70% 100.00% 100.00% 99.70%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.00% 0.30%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Rock And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex	Accurate 996 999 999 996 997	Cases False Positive 0 0 0 0 0	False Negative 3 0 0 3 2 2	Accuracy 99.70% 100.00% 100.00% 99.70% 99.80% 00.70%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.30% 0.30% 0.20%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Rock And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Unspecified Site Hereditary And Idionastic Periphera Neuronathy	Accurate 996 999 999 999 996 997 996 993	Cases False Positive 0 0 0 0 0 0 0 0	False Negative 3 0 0 3 2 3 6	Accuracy 99.70% 100.00% 99.70% 99.80% 99.70% 99.40%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.30% 0.30% 0.30% 0.60%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxio Neuropathy	Accurate 996 999 999 996 997 996 993 993	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0	False Negative 3 0 0 3 2 3 6 6 6	Accuracy 99.70% 100.00% 99.70% 99.80% 99.70% 99.40% 99.40%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.20%           0.30%           0.60%           0.60%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders	Accurate 996 999 999 996 997 996 993 993 993 993	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False Negative 3 0 0 3 2 3 6 6 6 2	Accuracy 99.70% 100.00% 99.70% 99.80% 99.40% 99.40% 99.40% 99.80%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.20%           0.30%           0.60%           0.60%           0.20%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders Muscular Dystrophies And Other Myopathies	Accurate 996 999 996 997 996 993 993 993 997 996	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False Negative 3 0 0 3 2 2 3 6 6 6 2 3	Accuracy 99.70% 100.00% 99.70% 99.80% 99.70% 99.40% 99.40% 99.80% 99.70%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.30% 0.20% 0.30% 0.60% 0.60% 0.20% 0.20% 0.30%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders Muscular Dystrophies And Other Myopathies Average	Accurate 996 999 999 996 997 996 993 993 993 997 996	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           2           3           6           6           2           3	Accuracy 99.70% 100.00% 99.70% 99.80% 99.70% 99.40% 99.40% 99.80% 99.70% <b>99.72%</b>	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.20%           0.30%           0.60%           0.60%           0.20%           0.30%           0.60%           0.20%           0.30%           0.60%           0.20%           0.30%           0.20%           0.30%           0.20%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Rock And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders Muscular Dystrophies And Other Myopathies Average	Accurate 996 999 996 997 996 993 993 993 997 996	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           2           3           6           2           3	Accuracy 99.70% 100.00% 99.70% 99.80% 99.70% 99.40% 99.40% 99.80% 99.70% <b>99.72%</b>	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.20%           0.60%           0.60%           0.30%           0.40%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Unspecified Site Hereditary And Toxic Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders Muscular Dystrophies And Other Myopathies Average Eye and Adnexa Conditions Conditions	Accurate 996 999 996 997 996 993 993 993 997 996	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           2           3           6           2           3           False	Accuracy 99.70% 100.00% 99.70% 99.70% 99.40% 99.40% 99.40% 99.80% 99.70% <b>99.72%</b>	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.30%           0.30%           0.60%           0.60%           0.20%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.30%           0.28%
G	Peripheral Nervous System Conditions Conditions         Trigeminal Nerve Disorders         Facial Nerve Disorders Other Cranial Nerves         Nerve Root And Plexus Disorders Mononeuritis Multiplex         Mononeuritis Of Upper Limb And Mononeuritis Multiplex         Mononeuritis Of Lower Limb And Unspecified Site         Hereditary And Idiopathic Peripheral Neuropathy         Inflammatory And Toxic Neuropathy         Wyoneural Disorders         Muscular Dystrophies And Other Myopathies         Average         Eye and Adnexa Conditions Conditions         Disorders Of The Globe	Accurate 996 999 996 997 996 993 993 993 997 996	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False Negative 3 0 0 3 2 3 6 6 6 2 3 3 8 False Negative	Accuracy 99.70% 100.00% 99.70% 99.70% 99.40% 99.40% 99.40% 99.40% 99.80% 99.72%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.30%           0.30%           0.60%           0.30%           0.60%           0.30%           0.60%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.00%
G	Peripheral Nervous System Conditions Conditions           Trigeminal Nerve Disorders           Facial Nerve Disorders           Disorders Of Other Cranial Nerves           Nerve Root And Plexus Disorders           Mononeuritis Of Upper Limb And Mononeuritis Multiplex           Mononeuritis Of Lower Limb And Unspecified Site           Hereditary And Idiopathic Peripheral Neuropathy           Inflammatory And Toxic Neuropathy           Myoneural Disorders           Muscular Dystrophies And Other Myopathies           Average           Eye and Adnexa Conditions Conditions           Disorders Of The Globe           Reinal Detachments And Defects	Accurate 996 999 996 997 996 993 993 993 996 996 <b>Accurate</b> 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           6           6           2           3           6           9           9           9           9           9           9           9           9           9           9           9           9	Accuracy 99.70% 100.00% 99.70% 99.70% 99.40% 99.40% 99.80% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	Faise           Negative           0.30%           0.00%           0.30%           0.20%           0.30%           0.60%           0.60%           0.20%           0.30%           0.60%           0.20%           0.30%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Upper Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders Muscular Dystrophies And Other Myopathies Average Eye and Adnexa Conditions Conditions Disorders Of The Globe Retinal Disorders Other Retinal Disorders	Accurate 996 999 997 996 993 997 996 993 997 996 <b>Accurate</b> 999 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           6           2           3           6           2           3	Accuracy 99.70% 100.00% 99.70% 99.70% 99.40% 99.40% 99.40% 99.40% 99.70% 99.70% 99.70% 99.70% 99.70%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           D.00%           D.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	Faise           Negative           0.30%           0.00%           0.30%           0.30%           0.30%           0.60%           0.60%           0.20%           0.30%           0.20%           0.30%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.00%           0.20%
G	Peripheral Nervous System Conditions Conditions           Trigeminal Nerve Disorders           Facial Nerve Disorders Other Cranial Nerves           Disorders Other Cranial Nerves           Mononeuritis Of Upper Limb And Mononeuritis Multiplex           Mononeuritis Of Lower Limb And Unspecified Site           Hereditary And Toxic Neuropathy           Inflammatory And Toxic Neuropathy           Myoneural Disorders           Muscular Dystrophies And Other Myopathies           Average           Eye and Adnexa Conditions Conditions           Disorders Of The Globe           Retinal Detachments And Defects           Other Retinal Disorders           Disorders Of The Globe           Reting Loss And Defects           Other Retinal Disorders	Accurate 996 999 997 996 993 997 996 993 997 996 Accurate 999 999 997 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           6           2           3           6           2           3	Accuracy 99.70% 100.00% 99.70% 99.80% 99.40% 99.40% 99.40% 99.80% 99.72% Accuracy 100.00% 100.00% 100.00%	Rates           Paise           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.00%           0.30%           0.20%           0.60%           0.60%           0.60%           0.30%           0.20%           0.30%           0.40%           0.00%           0.00%           0.00%           0.20%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Other Cranial Nerves Nerve Root And Plexus Disorders Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders Muscular Dystrophies And Other Myopathies Average Ege and Adnexa Conditions Conditions Disorders Of The Globe Retinal Detachments And Defects Other Retinal Disorders Other Gliary Model Disorders Of Ins And Cliary Body Glaucoma	Accurate 996 999 996 997 996 993 993 993 997 996 Accurate 999 999 999 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False Negative 3 0 0 3 2 2 3 6 6 6 2 3 3 6 6 6 2 3 3 8 Negative Negative 0 0 0 2 0 0 0 3 3	Accuracy 99.70% 100.00% 99.70% 99.80% 99.40% 99.40% 99.40% 99.80% 99.72% Accuracy 100.00% 99.72%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.00%           0.30%           0.30%           0.30%           0.30%           0.30%           0.30%           0.30%           0.60%           0.20%           0.30%           0.20%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Upper Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders Muscular Dystrophies And Other Myopathies Average Eye and Adnexa Conditions Conditions Disorders Of The Globe Retinal Detachments And Defects Other Retinal Disorders Other Getinan Disorders Conformation Inflammations, Scars, Other Disorders Of Choroid Disorders Of Iris And Ciliary Body Glaucoma Cataract	Accurate 996 999 997 996 997 996 993 997 996 999 999 999 999 999 999 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           0           3           6           6           2           3           6           6           2           3	Accuracy 99.70% 100.00% 99.70% 99.70% 99.40% 99.40% 99.70% 99.70% 99.72% Accuracy 100.00% 100.00% 100.00% 99.70%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.00%           0.30%           0.00%           0.30%           0.60%           0.20%           0.30%           0.00%           0.30%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions           Trigeminal Nerve Disorders           Facial Nerve Disorders           Disorders Of Other Cranial Nerves           Nerve Root And Plexus Disorders           Mononeuritis Of Upper Limb And Mononeuritis Multiplex           Mononeuritis Of Upper Limb And Unspecified Site           Hereditary And Idiopathic Peripheral Neuropathy           Inflammatory And Toxic Neuropathy           Myoneural Disorders           Muscular Dystrophies And Other Myopathies           Average           Eye and Adnexa Conditions Conditions           Disorders Of The Globe           Retinal Disorders           Other Retinal Disorders           Other Retinal Disorders Of Ires And Defects           Other Retinal Disorders Of Ires And Cliary Body           Glaucoma           Cataract           Disorders Of Refraction And Accommodation	Accurate 996 999 996 997 996 993 993 993 993 997 996 Accurate 999 999 997 999 999 997 999 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           2           3           6           6           2           3           7           8           9           9           9           9           0           2           0           2           0           2           0           2           0           3           0           3	Accuracy 99.70% 100.00% 99.70% 99.40% 99.40% 99.40% 99.70% 99.80% 99.72% Accuracy 100.00% 100.00% 99.80% 100.00%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.30% 0.20% 0.60% 0.20% 0.20% 0.20% 0.20% 0.20% 0.00% 0.00% 0.00% 0.00% 0.00%
G	Peripheral Nervous System Conditions Conditions         Trigeminal Nerve Disorders         Facial Nerve Disorders Of Other Cranial Nerves         Nerve Root And Plexus Disorders O         Mononeuritis Of Upper Limb And Mononeuritis Multiplex         Mononeuritis Of Upper Limb And Unspecified Site         Hereditary And Idiopathic Peripheral Neuropathy         Inflammatory And Toxic Neuropathy         Myoneural Disorders         Muscular Dystrophies And Other Myopathies         Average         Eye and Adnexa Conditions Conditions         Disorders Of The Globe         Retinal Detachments And Defects         Other Retinal Disorders         Chorioretinal Inflammations, Scars, Other Disorders Of Choroid         Disorders Of Iris And Ciliary Body         Glaucoma         Catarat         Disorders Of Refraction And Accommodation         Visuad Disturbances	Accurate 996 999 996 997 996 993 997 996 999 999 999 999 999 999 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False Negative 3 0 3 2 3 6 6 6 6 2 3 3 8 8 8 9 8 9 8 9 8 9 8 9 9 0 0 0 0 0 0 0	Accuracy 99.70% 100.00% 99.70% 99.80% 99.40% 99.40% 99.40% 99.80% 99.70% 99.72% 100.00% 100.00% 100.00% 100.00% 99.80%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.20%           0.30%           0.20%           0.30%           0.20%           0.00%           0.00%           0.00%           0.30%           0.00%           0.30%           0.00%           0.30%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions         Trigeminal Nerve Disorders         Facial Nerve Disorders Other Cranial Nerves         Nerve Root And Plexus Disorders Other Cornial Nerves         Nonneuritis Of Upper Limb And Mononeuritis Multiplex         Mononeuritis Of Lower Limb And Unspecified Site         Hereditary And Idiopathic Peripheral Neuropathy         Inflammatory And Toxic Neuropathy         Myoneural Disorders         Muscular Dystrophies And Other Myopathies         Average         Ege and Adnexa Conditions Conditions         Disorders Of The Globe         Retinal Detachments And Defects         Other Retinal Disorders         Otherders Of Iris And Ciliary Body         Glaucoma         Cataract         Disorders Of Refraction And Accommodation         Visual Disturbances         Blindness And Low Vision	Accurate 996 999 996 997 996 993 997 996 997 996 999 999 999 999 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           2           3           6           2           3           6           2           3           6           2           3           6           2           3           6           10           2           0           2           0           2           0           2           0           10           10           10           10           10           10           10           10           10           10           10           10           10           10           10           10	Accuracy 99.70% 100.00% 99.70% 99.70% 99.70% 99.40% 99.70% 99.70% 99.72% Accuracy 100.00% 99.80% 100.00% 100.00% 100.00% 100.00%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.00%           0.30%           0.20%           0.30%           0.60%           0.30%           0.60%           0.60%           0.60%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Nononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Upper Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders Muscular Dystrophies And Other Myopathies Average Eye and Adnexa Conditions Conditions Disorders Of The Globe Retinal Detachments And Defects Other Retinal Disorders Cohoriential Inflammations, Scars, Other Disorders Of Choroie Disorders Of Iris And Ciliary Body Glaucoma Cataract Disorders Of Refraction And Accommodation Visual Disturbances Blindness And Low Vision Keratiis Corneal Opacity And Other Disorders Of Cornea	Accurate 996 999 997 996 993 996 993 996 997 996 999 999 999 999 999 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           6           6           2           3           6           2           3           6           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0	Accuracy 99.70% 100.00% 99.70% 99.70% 99.40% 99.40% 99.70% 99.70% 99.72% Accuracy 100.00% 99.72% 100.00% 100.00% 100.00% 100.00% 100.00%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.00%           0.30%           0.00%           0.30%           0.60%           0.20%           0.30%           0.60%           0.20%           0.30%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions         Trigeminal Nerve Disorders         Disorders Of Other Cranial Nerves         Nerve Root And Plexus Disorders         Mononeuritis Of Upper Limb And Mononeuritis Multiplex         Mononeuritis Of Lower Limb And Unspecified Site         Hereditary And Toxic Neuropathy         Inflammatory And Toxic Neuropathy         Wonceuril Disorders         Muscular Dystrophies And Other Myopathies         Average         Eye and Adnexa Conditions Conditions         Disorders Of The Globe         Retinal Detachments And Defects         Other Retinal Disorders         Disorders Of The Globe         Retail Detachments And Defects         Other Retinal Disorders         Disorders Of Refraction And Accommodation         Visual Disturbances         Blindness And Low Vision         Kerattiis         Conjunctiva	Accurate 996 999 996 997 996 997 996 Accurate 999 997 999 999 997 999 999 999 999 99	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           2           3           6           6           2           3           7           8           9           0           2           3           6           6           2           3           0           2           0           2           0           2           0           2           0           2           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0      0	Accuracy 99.70% 100.00% 99.70% 99.40% 99.40% 99.40% 99.70% 99.70% 99.77% 99.72% Accuracy 100.00% 99.80% 100.00% 99.80% 100.00% 99.50% 100.00% 99.50%	Rates           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.20%           0.30%           0.20%           0.30%           0.60%           0.60%           0.60%           0.20%           0.30%           0.20%           0.30%           0.20%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions         Trigeminal Nerve Disorders         Facial Nerve Disorders         Disorders Of Other Cranial Nerves         Nerve Root And Plexus Disorders         Mononeuritis Of Upper Limb And Mononeuritis Multiplex         Mononeuritis Of Lower Limb And Unspecified Site         Hereditary And Toxic Neuropathy         Myoneural Disorders         Muscular Dystrophies And Other Myopathies         Average         Eye and Adnexa Conditions Conditions         Disorders Of The Globe         Retinal Detachments And Defects         Other Retinal Disorders         Chorioretinal Inflammations, Scars, Other Disorders Of Choroid         Disorders Of Iris And Ciliary Body         Glaucoma         Catarat         Disorders Of Refraction And Accommodation         Visual Disturbances         Blindness And Low Vision         Kerattitis         Conjunctiva         Inflammation Of Eyelids	Accurate 996 999 996 997 996 993 997 996 999 999 999 999 999 999 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           0           3           6           6           2           3           6           2           3           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0	Accuracy 99.70% 100.00% 99.70% 99.70% 99.40% 99.70% 99.40% 99.70% 99.70% 99.72% Accuracy 100.00% 100.00% 100.00% 100.00% 100.00% 100.00%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.20%           0.30%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions         Trigeminal Nerve Disorders         Facial Nerve Disorders Other Cranial Nerves         Nerve Root And Plexus Disorders Other Cornial Nerves         Nonneuritis Of Upper Limb And Mononeuritis Multiplex         Mononeuritis Of Lower Limb And Unspecified Site         Hereditary And Idiopathic Peripheral Neuropathy         Inflammatory And Toxic Neuropathy         Myoneural Disorders         Muscular Dystrophies And Other Myopathies         Average         Ege and Adnexa Conditions Conditions         Disorders Of The Globe         Retinal Detachments And Defects         Other Retinal Disorders         Otherders Of Refraction And Accommodation         Visual Disturbances         Blindness And Low Vision         Keratitis         Corneal Opacity And Other Disorders Of Cornea         Disorders Of The Slobe         Retratitis         Corneal Opacity And Other Disorders Of Cornea         Disorders Of Refraction And Accommodation         Visual Disturbances         Blindness And Low Vision         Keratitis         Corneal Opacity And Other Disorders Of Cornea         Disorders Of Evplids         Other Placeders Of Lowing Contention	Accurate 996 999 996 997 996 993 997 996 997 999 999 999 999 999 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           6           2           3           6           2           3           6           2           3           6           2           3           6           2           3           6           10           2           0           2           0           2           0           0           2           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           <	Accuracy 99.70% 100.00% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.72% Accuracy 100.00% 99.80% 100.00% 100.00% 99.80% 100.00% 99.80%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.07%           0.07%           0.30%           0.20%           0.30%           0.60%           0.30%           0.60%           0.60%           0.60%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Nononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Upper Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders Muscular Dystrophies And Other Myopathies Average Eye and Adnexa Conditions Conditions Disorders Of The Globe Retinal Detachments And Defects Other Beinal Disorders Control Class Inflammations, Scars, Other Disorders Of Choroic Disorders Of Iris And Ciliary Body Glaucoma Cataract Disorders Of Refraction And Accommodation Visual Distrumences Blindness And Low Vision Keratitis Corneal Opacity And Other Disorders Of Cornea Disorders Of Eyelids Disorders Of Eyelids Disorders Of Eyelids Disorders Of Deglids Disorders Of Conjunctiva Inflammation Of Eyelids Disorders Of Deglids Disorders Of Deglids Disorders Of Deglids Disorders Of Deglids Disorders Of Conjunctiva Inflammation Of Eyelids Disorders Of Deglids Disorders Of Disorders Disorders Of Deglids	Accurate 996 999 997 996 997 996 997 996 997 996 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           6           6           2           3           6           2           3           6           2           3           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0	Accuracy 99.70% 100.00% 99.70% 99.70% 99.40% 99.40% 99.70% 99.70% 99.72% Accuracy 100.00% 100.00% 100.00% 100.00% 100.00% 100.00% 99.50% 100.00% 100.00% 99.80%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.00%           0.30%           0.60%           0.30%           0.60%           0.30%           0.60%           0.30%           0.60%           0.20%           0.30%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions           Trigeminal Nerve Disorders           Facial Nerve Disorders           Disorders Of Other Cranial Nerves           Nerve Root And Plexus Disorders           Mononeuritis Of Upper Limb And Mononeuritis Multiplex           Mononeuritis Of Lower Limb And Unspecified Site           Hereditary And Toxic Neuropathy           Myoneurial Disorders           Muscular Dystrophies And Other Myopathies           Average           Eye and Adnexa Conditions Conditions           Disorders Of The Globe           Retental Detachments And Defects           Other Retinal Disorders           Disorders Of The Globe           Retail Detachments And Defects           Other Retinal Disorders           Disorders Of Refraction And Accommodation           Visual Disturbances           Blindness And Low Vision           Kerattitis           Conjunctiva           Inflammation of Eyelids           Other Solid Sciences Of Conjunctiva           Inflammation Of Eyelids           Others Solid Conjunctiva           Disorders Of Lacrimal System           Disorders Of Conjunctiva           Inflammation Of Eyelids           Others Disorders Of Lacrimal System           Disorders	Accurate 996 999 996 997 996 997 996 997 996 997 996 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           6           2           3           6           2           3           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0	Accuracy 99.70% 100.00% 99.70% 99.80% 99.70% 99.40% 99.70% 99.70% 99.70% 99.70% 99.70% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00%	Rates           Faise           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions           Trigeminal Nerve Disorders           Facial Nerve Disorders Of Other Cranial Nerves           Nerve Root And Plexus Disorders O           Mononeuritis Of Upper Limb And Mononeuritis Multiplex           Mononeuritis Of Lower Limb And Unspecified Site           Hereditary And Idiopathic Peripheral Neuropathy           Inflammatory And Toxic Neuropathy           Myoneural Disorders           Muscular Dystrophies And Other Myopathies           Average           Eye and Adnexa Conditions Conditions           Disorders Of The Globe           Retinal Detachments And Defects           Other Retinal Disorders           Chorioretinal Inflammations, Scars, Other Disorders Of Choroic           Disorders Of Iris And Cliary Body           Glaucoma           Catarat           Disorders Of Refraction And Accommodation           Visual Disturbances           Blindness And Low Vision           Keratitis           Conjunctiva           Inflarmation of Eyelids           Other Sort Disorders Of The Globe           Inflarmation of Type           Biondress And Low Vision           Keratitis           Coreal Opacity And Other Disorders Of Corea           Disorders Of Lawring System	Accurate 996 999 996 997 996 993 997 996 999 999 999 999 999 999 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           6           6           2           3           6           2           3           6           2           3           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0 <t< td=""><td>Accuracy 99.70% 100.00% 99.70% 99.80% 99.70% 99.40% 99.70% 99.80% 99.70% 99.70% 99.70% 99.72% 100.00% 100.00% 100.00% 100.00% 100.00% 99.50% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00%</td><td>Rates           Faise           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%</td><td>False           Negative           0.30%           0.00%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%</td></t<>	Accuracy 99.70% 100.00% 99.70% 99.80% 99.70% 99.40% 99.70% 99.80% 99.70% 99.70% 99.70% 99.72% 100.00% 100.00% 100.00% 100.00% 100.00% 99.50% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00%	Rates           Faise           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.20%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%
G	Peripheral Nervous System Conditions Conditions           Trigeminal Nerve Disorders           Facial Nerve Disorders Other Cranial Nerves           Nerve Root And Plexus Disorders Other Cranial Nerves           Nerve Root And Plexus Disorders Mononeuritis Multiplex           Mononeuritis Of Upper Limb And Mononeuritis Multiplex           Mononeuritis Of Lower Limb And Unspecified Site           Hereditary And Idiopathic Peripheral Neuropathy           Inflammatory And Toxic Neuropathy           Myoneural Disorders           Muscular Dystrophies And Other Myopathies           Average           Ege and Adnexa Conditions Conditions           Disorders Of The Globe           Retinal Detachments And Defects           Other Retinal Disorders           Other Glaucoma           Glaucoma           Glaucoma           Blindness And Low Vision           Keratitis           Corneal Opacity And Other Disorders Of Cornea           Disorders Of Conjunctiva           Inflammation Of Eyelids           Other Retinal Disorders Of System           Disorders Of The Orbit           Disorders Of The Orbit </td <td>Accurate 996 997 996 997 996 993 997 996 997 999 999 999 999 999 999 999</td> <td>Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0</td> <td>False           Negative           3           0           3           6           2           3           6           2           3           6           2           3           6           2           3           6           2           3           6           7           7           8           9           0           2           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0</td> <td>Accuracy 99.70% 100.00% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00%</td> <td>Rates           Faise           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%</td> <td>False           Negative           0.30%           0.07%           0.07%           0.30%           0.20%           0.30%           0.60%           0.30%           0.60%           0.60%           0.60%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%</td>	Accurate 996 997 996 997 996 993 997 996 997 999 999 999 999 999 999 999	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           6           2           3           6           2           3           6           2           3           6           2           3           6           2           3           6           7           7           8           9           0           2           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0           0	Accuracy 99.70% 100.00% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 99.70% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00% 100.00%	Rates           Faise           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.07%           0.07%           0.30%           0.20%           0.30%           0.60%           0.30%           0.60%           0.60%           0.60%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%

#### Models with No Demographic Variables

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		Cases			Rates	
All Neurological	Accurate	False	False	Accuracy	False	False
Inflammatory CNIS And Sansa Organs	004	Positive	Negative	00.50%	0.00%	0 50%
Organic Sleep Disorders	994	0	20	99.50%	0.00%	2.00%
Hereditary And Degenerative Diseases Of CNS	974	ő	25	97.50%	0.00%	2.50%
Pain	907	0	92	90.79%	0.00%	9.21%
Headache Syndromes	997	0	2	99.80%	0.00%	0.20%
CNS, Other	907	0	92	90.79%	0.00%	9.21%
Peripheral Nervous System	974	0	25	97.50%	0.00%	2.50%
Eye And Adnexa	986	0	13	98.70%	0.00%	1.30%
Ear And Mastoid	993	0	6	99.40%	0.00%	0.60%
Average				96.89%	0.00%	3.11%
		Cases			Rates	
Inflammatory CNS and Sense Organs Conditions Conditions	Accurate	False Positive	False Negative	Accuracy	False Positive	False Negative
Bacterial Meningitis	998	0	1	99.90%	0.00%	0.10%
Meningitis Due To Other Organisms	999	0	0	100.00%	0.00%	0.00%
Meningitis Of Unspecified Cause	995	0	4	99.60%	0.00%	0.40%
Encephalitis, Myelitis, And Encephalomyelitis	999	0	0	100.00%	0.00%	0.00%
Intracranial And Intraspinal Abscess	996	0	3	99.70%	0.00%	0.30%
Phlebitis Intracranial Sinus	999	0	0	100.00%	0.00%	0.00%
Late effects of intracranial abscess or pyogenic infection	999	0	0	100.00%	0.00%	0.00%
nverage				33.03 /6	0.00 /8	0.11%
		Cases	Falsa		Rates	Falsa
Other Conditions of the CNS Conditions	Accurate	Positive	Negative	Accuracy	Positive	Negative
Multiple Sclerosis	992	0	7	99.30%	0.00%	0.70%
Other Demyelinating Diseases	999	0	0	100.00%	0.00%	0.00%
Hemiplegia And Hemiparesis	989	0	10	99.00%	0.00%	1.00%
Infantile Cerebral Palsy	996	0	3	99.70%	0.00%	0.30%
Other Paralytic Syndromes	992	0	7	99.30%	0.00%	0.70%
Epilepsy And Recurrent Seizures	977	0	22	97.80%	0.00%	2.20%
Migraine	989	0	10	99.00%	0.00%	1.00%
Cataplexy And Narcolepsy	999	0	0	100.00%	0.00%	0.00%
Other Conditions Of Brain	951	0	48	95.20%	0.00%	4.80%
Other And Unspecified Disorders	986	0	13	98.70%	0.00%	1.30%
Averaue				30.00 /0	0.00 /6	1.20 /6
		Cases	Falsa		Rates	Falsa
Peripheral Nervous System Conditions Conditions	Accurate	Cases False Positive	False Negative	Accuracy	Rates False Positive	False Negative
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders	Accurate 996	Cases False Positive	False Negative 3	Accuracy 99.70%	Rates False Positive 0.00%	False Negative
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders	Accurate 996 999	Cases False Positive 0 0	False Negative 3 0	Accuracy 99.70% 100.00%	Rates False Positive 0.00% 0.00%	False Negative 0.30% 0.00%
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves	Accurate 996 999 999	Cases False Positive 0 0 0	False Negative 3 0 0	Accuracy 99.70% 100.00% 100.00%	Rates False Positive 0.00% 0.00% 0.00%	False Negative 0.30% 0.00% 0.00%
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders	Accurate 996 999 999 999	Cases False Positive 0 0 0 0	False Negative 3 0 0 3	Accuracy 99.70% 100.00% 100.00% 99.70%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.00% 0.30%
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex	Accurate 996 999 999 999 996 997	Cases False Positive 0 0 0 0 0 0	False Negative	Accuracy 99.70% 100.00% 100.00% 99.70% 99.80%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.00% 0.30% 0.20%
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Unspecified Site	Accurate 996 999 999 999 996 997 996	Cases False Positive 0 0 0 0 0 0 0 0 0	False Negative 3 0 0 3 2 3	Accuracy 99.70% 100.00% 100.00% 99.70% 99.80% 99.70%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.00% 0.30% 0.20% 0.30%
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy	Accurate 996 999 999 996 997 996 993	Cases False Positive 0 0 0 0 0 0 0 0 0 0	False Negative 3 0 0 3 2 3 6	Accuracy 99.70% 100.00% 100.00% 99.70% 99.80% 99.70% 99.40%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.30% 0.30% 0.20% 0.30% 0.60%
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Piexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy	Accurate 996 999 999 996 997 996 997 996 993 993	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0	False Negative 3 0 0 3 2 3 6 6 6	Accuracy 99.70% 100.00% 100.00% 99.70% 99.80% 99.70% 99.40%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.30% 0.30% 0.20% 0.30% 0.60%
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders	Accurate 996 999 999 996 997 996 993 993 993 993	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False Negative 3 0 0 3 2 3 6 6 6 2	Accuracy 99.70% 100.00% 100.00% 99.70% 99.80% 99.70% 99.40% 99.40% 99.80%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.30% 0.30% 0.30% 0.30% 0.60% 0.60% 0.20%
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Wyoneural Disorders Muscular Dystrophies And Other Myopathies	Accurate 996 999 996 997 996 993 993 993 997 996	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False Negative 3 0 0 3 2 3 6 6 6 2 3 3	Accuracy 99.70% 100.00% 100.00% 99.70% 99.80% 99.40% 99.40% 99.80% 99.80% 99.70%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.30% 0.20% 0.30% 0.60% 0.60% 0.20% 0.20%
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders Muscular Dystrophies And Other Myopathies Average	Accurate 996 999 999 996 997 996 993 993 993 997 996	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           2           3           6           6           2           3	Accuracy 99.70% 100.00% 99.70% 99.70% 99.40% 99.40% 99.40% 99.40% 99.70% <b>99.72%</b>	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False           Negative           0.30%           0.00%           0.30%           0.30%           0.30%           0.30%           0.60%           0.20%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%           0.30%           0.20%
Peripheral Nervous System Conditions Conditions Trigeminal Nerve Disorders Facial Nerve Disorders Disorders Of Other Cranial Nerves Nerve Root And Plexus Disorders Mononeuritis Of Upper Limb And Unspecified Site Hereditary And Idiopathic Peripheral Neuropathy Inflammatory And Toxic Neuropathy Myoneural Disorders Muscular Dystrophies And Other Myopathies Average	Accurate 996 999 999 996 997 996 993 993 993 993 997 996	Cases False Positive 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	False           Negative           3           0           3           2           3           6           2           3	Accuracy 99.70% 100.00% 99.70% 99.80% 99.70% 99.40% 99.40% 99.40% 99.40% 99.9.70%	Rates           False           Positive           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%           0.00%	False Negative 0.30% 0.00% 0.20% 0.30% 0.60% 0.60% 0.20% 0.20% 0.20% 0.28%
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Table 10 | Manual Test Accuracy Rates For All Conditions A, C, E, G, I) Manual model accuracy rates for models developed with demographic variables (age, gender, state of residence). The manual test set was a randomly chosen set of 1000 patient IDs from the machine learning test set. Predicted values were rounded off to 0 or 1 and then compared to the labelled dataset record. Accuracy, false positive (Model = 1, Label = 0) and false negative (Model = 0, Label = 0) rates were calculated for each labelled condition. Models are generally very accurate, and where inaccurate tend to false negatives and not false positives. Error rates >2% are highlighted in red. Highest error rates were for neurological buckets, and second for other conditions of CNS. B, D, F, H, J) Manual model accuracy rates for models developed without demographic variables. Differences in performance with the models that included demographics variables would have been filled with yellow. No difference in model performance were observed for all conditions, whether for accurate cases, false positives or negatives.

#### Manual Testing Accuracy and Performance

Since each model is predicting comorbidity rates with an array of diseases, model accuracy must also be evaluated for each specific condition. The models were highly accurate for all conditions, attaining accuracy rates >95% overall (Table 10). In the cases where the model was not fully accurate, they tended towards outputting false positives instead of false negatives.

Conditions with the high false positive rates tend to be of two types. They may be hereditary or inborn – such as for the bucket of "Hereditary and Degenerative Diseases of CNS" and "Epilepsy and recurrent seizures". For the latter bucket, while epilepsy can be developed at older ages, up to 30-40% of epileptic patients are born with the condition (Anon, n.d.). The high rates of inborn patients which could pose a difficulty in classification, as there is a mix of HIV-caused epilepsy and inborn errors.

The second type of label with higher false positives are highly nonspecific, such as "Other conditions of Brain", and the buckets "Pain" and "Other conditions of the CNS". Since the conditions making up these labels may have very heterogeneous phenotypes and underlying biological causes, the inconsistency across patient profiles may pose difficulty in classification learning.

#### Predictiveness of Demographic Variables

In this pilot study, only three demographic variables were used – age, gender and state of residence. Inclusion of demographic variables – whether just age and gender, or further inclusion of state of residence – did not markedly increase model accuracy in training or testing for all label combinations, though it did marginally increase training speed (Figure 3).

This conclusion is further supported by the manual tests, in which models that included all demographic variables came up with the exact same number of accurate cases, false positives and false negatives for every analyzed label as those models without demographics (Table 10).



#### Figure 3 | Training and Testing Error for Models with Varying Demographic Variables

Models take in an array of Boolean variables for diagnosis of cardiovascular indications and HIV infection, plus demographic variables of age, gender, state of residence. The inclusion of demographic data points was varied.

A, C, E) Training error calculated as mean squared error, plotted against epochs.

B, D, F) The first evaluation of testing error occurs after the first batch of data is trained on the model, explaining why most curves begin with error below 0.5, so error is evaluated every 3 epochs. The first evaluation of testing error occurs after the first batch of data is trained on the model,

explaining why most curves begin with error below 0.5, i.e. better than random chance.

A, B) Averaged training and testing error for the three types of models. Models with no demographic variables learn the slowest, with the gentlest slope. Overall, the models seem to attain the same level of accuracy.

C, D) Training and testing error for models with no demographic variables. PNS and "All" (referring to neurological buckets) models take the longest to train. All models train to roughly the same accuracy, with the "All" model plateauing at a slightly higher error rate.

Each line represents one model. Models differ with respect to the array of neurological end points it is trained to predict.

CNSI - Inflammatory CNS and sense organ conditions

CNSO - Other conditions of the CNS

Eye - Conditions of the eye and adnexa

PNS - Conditions of the Peripheral Nervous System

All - Buckets of Neurological Conditions in Table 2

E, F) Training and testing error for models with only age and gender demographic variables. Compared to C, D, models train faster and plateau at epoch 20. Similar patterns on eventual model accuracy hold - the "All" model plateaus at a slightly higher error rate, and the others train to roughly the same accuracy.

## DISCUSSION

A large health insurance dataset was successfully analyzed to show a comprehensive map of HIV infections to neurological complications. Further, machine learning methods were successfully deployed to predict patients' neurological comorbidities using their cardiovascular diagnostic profiles.

#### Multiprocessing Protocol for Low-Memory Environments

The greatest contribution of this research to the medical community lies in the unconventional multiprocessing protocol, which is well suited for environments such as distributed hospital networks that have large disk storage for their patient data, but low processing space as the facilities were not built for heavy data analytics work. As hospitals begin to adopt predictive analytics for both staffing and patient care, this protocol could prove valuable (Wong, n.d.; Bresnick, 2015).

Batch training for deep learning is a widely used method in the field of machine learning to cope with low memory environments (Muellerklein, n.d.). A sweep of the relevant literature shows two key shortcomings in using existing batch training protocols for large data analysis of patient information: Firstly, existing protocols load the batch of data into memory, then conduct a randomized training-testing split, which therefore does not keep a record of entries used in training and testing for replicability purposes. The protocol developed for this study solves for this by pre-determining two randomized sets of enrollee identifiers to be used for training and testing to be stored separately, which the script will load directly from the file when needed (Brownlee, 2019). In this study's case, this would have created undue work when I attempted to create multiple models for the same patients, with slightly varying predictors (e.g. the inclusion of demographic variables) and labels (e.g. different sets of neurological complications). While it is possible to

automate the batch file creation process, this would have also increased the hard disk space requirement by 1.5x, which would be unideal if this pilot were to scale up to encompass the entirety of the outpatient records consuming on the order of terabytes. The protocol developed for this study solves for this by storing the patient records in a Sqlite3 database with tables of Boolean variables indicating existence of diagnosis for conditions to be selected as examples or labels as needed.

## Comorbidity of Neurological and Cardiovascular Complications

Prior to this study, little to no work had been done to characterize the full landscape of neurological complications that plagued PLWH. Without analysis of large, representative databases of medical records, the literature has so far focused on clinical cases and community studies, which are valuable but insufficient in elucidating the nuances for even the most common comorbidities such as meningitis and peripheral neuropathies. This study was uniquely able to point out the distribution of risks of disorders in the nervous system. For example, in the PNS, facial nerve and lower limb neuritis are more prevalent than myoneural and nerve root disorders. Understanding the distribution in risk of specific regions of the CNS may guide therapeutic research towards neuroprotection for infected individuals.

Most of these neurological complications are very niche, with comorbidity rates below 2%. This study was also able to uncover neurological conditions that have similar comorbidities for PLWH in terms of diagnostic probabilities relative to uninfected persons, hitherto overlooked in the literature. An example is hemiplegia, which has prevalence rates (~ 1.5% for PLWH) comparable to meningitis and peripheral neuropathies, and similar risk ratios (~2x) to a lot of eye and adnexa conditions. A holistic mapping of neurological complication risks for PLWH may bring the community closer towards cracking the pathophysiology of HIV-nervous system interactions at low viral loads.

Since many neurological complications are charted to opportunistic infections, early detection and aggressive treatment is critical. For example, choroid inflammations and infections must be treated early to prevent blindness. Accurate and early identification of PLWH who are most likely to develop such complications would be very valuable (Testi et al., 2020). Opportunistic infections occur for a variety of reasons, and an understanding of how residual viral loads of HIV lead to common weaknesses in the nervous system can pave the way towards improving targeting of future treatments for regions at higher risk of complications, or barring prevention, aid the development of treatments that effectively manage these complications once arisen.

Since previous literature on the implications of HIV on cardiovascular endpoints is quite extensive, I will briefly highlight just a few notable findings. Of all the subcategories analyzed, hypertensive complications were the most prevalent at 32.76% of the infected group, and other heart disease complications came in second at 24.05% of the infected group. The findings were generally in line with the literature, though there seems to be more existing research for conditions with higher prevalence rates, such as hypertensive chronic kidney disease and cardiomyopathy (>3%). Relative to uninfected persons, these conditions' risk ratios were comparable to those of pericarditis and varicose veins conditions, where the latter conditions are of relatively lower prevalence (<2%).

#### Cardiovascular diagnostic profile is predictive of neurological complications

The medical community has made great strides towards optimizing patient care with machine learning techniques, such as using medical records to predict emergency room admissions and drug effects (Tatonetti et al., 2012; Lucini et al., 2017). However, limited success has been attained in the prediction of future disease onset. In this study, prediction of only a small scope of conditions was attempted, and it was found that a supervised machine learning protocol was able to predict, with very high accuracy (>95%), a patient's neurological diagnostic profile based on their cardiovascular diagnostic profile. Importantly, only 80,000 records were needed for

model error to plateau, which is only 0.2% of the United States population. A good-sized hospital network would easily see that number of unique patients each year. This analysis shows that good predictive tools are perhaps not so far out of reach.

Importantly, though the error rates are low for the constructed models, errors tend towards false positives instead of false negatives. In the context of treatment, false negatives – i.e. overlooking a condition – are viewed as more costly, but it is equally important to distinguish those who need treatment from those who do not, so that valuable medical resources are appropriately spared for those who need them. Hence, until these false positives can be decreased, these predictive models should not be taken as gospel truth, or even as an autonomous diagnostic tool – they are better for use in supplementing physician examination or to flag a patient for closer monitoring.

#### Limited Predictive Power of Demographic Variables

Within the limited existing literature, unsupervised machine learning models have leaned heavily on the predictive power of demographic and enrollment variables for comorbidity predictions (Miotto et al., 2016). For the models constructed in this study, demographic variables actually contributed limited predictive power for comorbidity predictions. This suggests that neurological complications of HIV may not be dependent on age or gender, or the level of care provided by a person's geographical location.

A key next step would be to expand the current protocol to use a patient's past cardiovascular disease profile to predict their future neurological diagnostic profile. I expect that age and gender variables may be more contributive to model accuracy if models are built for the same patients over a few years' time frame, e.g. predicting if they will be diagnosed for a certain condition over the next 5 years.

# Limitations and Further Research

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The comorbidity conclusions could be made more statistically robust by constructing the uninfected group through age-, gender- and location-matching with members of the infected group. Currently, rates are calculated on the entirety of the population. That, combined with the fact that the size of the infected group is markedly smaller than the uninfected group, meant t-tests and general statistical measures of significance were unusable. The conclusions and the risk ratios remain important as they represent a measurement of relative likelihood, but adjusting the risk ratios through controlling for other characteristics of the groups would be clinically helpful in addition to being more statistically robust.

Further research will validate the conclusions and the models constructed on outpatient claims. Outpatient visits tend to be more common, and would provide valuable data points for the models to train on. Moreover, a model trained on only inpatient claims may present a form of selection bias when used to predict diagnoses based on outpatient diagnostic profiles, as inpatient cases tend to reflect more severe illnesses.

The health trajectory of a PLWH can be rife with uncertainty and with overlooked complications, undue pain and financial stress for both patients and medical systems. This work sets the groundwork towards two important goals to alleviate some of the above: Firstly, to point out ignored neurological comorbidities whose biological mechanisms may shed more light on the pathogenesis of HIV in the nervous system. Secondly, to use a patient's past medical record to more confidently understand their future medical risks. For the medical profession and community, this work represents an important stride towards precision medicine and value-based care.

# APPENDIX

Condition	ICD-9-CM Codes
HIV-1 Infection	042
Cardiovascular Conditions	200, 201, 202
Chronic Rheumatic Heart Disease	393, 394, 395, 396, 397, 398
Hypertensive Disease	401, 402, 403, 404, 405
Essential Hypertension	401
Hypertensive Heart Disease	402
Hypertensive Chronic Kidney Disease	403
Secondary Hypertension	405
Ischemic Heart Disease	411, 412, 413, 414
Diseases Of Pulmonary Circulation	415, 416, 417
Acute Pericarditis	420, 421, 422, 423, 424, 423, 420, 427, 420, 423
Acute And Subacute Endocarditis	421
Acute Myocarditis	422
Other Diseases Of Endocardium	423
Cardiomyopathy	425
Conduction Disorders	426
Cardiac Disrhythmias	427
III-Defined Descriptions, Complications Of Heart Disease	428
Cerebrovascular Disease	430, 431, 432, 433, 434, 435, 436, 437, 438
Arteries, Arterioles, Capillaries	440, 441, 442, 443, 444, 445, 446, 447, 448, 449
Veins, Lymphatics, And Other Circulatory	451, 452, 453, 454, 455, 456, 457, 458, 459
Portal Vein Thrombosis	452
Other Venous Embolism And Thrombosis	453
Varicose Veins of Lower Extremities	454
Hemorrholds	455
Noninfectious Disorders of Lymphatic Channels	457
Hypotension	458
Other Disorders of Circulatory System	459
Inflammatory CNS And Sense Organs	320 321 322 323 324 325 326
Bacterial Meningitis	320
Meningitis Due To Other Organisms	321
Meningitis Of Unspecified Cause	322
Intracranial And Intraspinal Abscess	323
Phlebitis Intracranial Sinus	325
Late effects of intracranial abscess or pyogenic infection	326
Organic Sleep Disorders	327
Pain	330, 331, 332, 333, 334, 335, 336, 337 338
Headache Syndromes	339
CNS, Other	340, 341, 342, 343, 344, 345, 346, 347, 348, 349
Multiple Sclerosis Other Demuclipating Diseases	340
Hemiplegia And Hemiparesis	342
Infantile Cerebral Palsy	343
Other Paralytic Syndromes	344
Epilepsy And Recurrent Seizures	345
Cataplexy And Narcolepsy	347
Other Conditions Of Brain	348
Other And Unspecified Disorders	349
Trigeminal Nerve Disorders	350, 351, 352, 353, 354, 355, 356, 357, 358, 359
Facial Nerve Disorders	350
Disorders Of Other Cranial Nerves	352
Nerve Root And Plexus Disorders	353
Mononeuritis Or Upper Limb And Mononeuritis Multiplex Mononeuritis Of Lower Limb And Upspecified Site	355
Hereditary And Idiopathic Peripheral Neuropathy	356
Inflammatory And Toxic Neuropathy	357
Myoneural Disorders Muscular Dystrophics And Other Myonathics	358
Fue And Adams	360, 361, 362, 363, 364, 365, 366, 367, 368. 369.
Eye Anu Adrexa	370, 371, 372, 373, 374, 375, 376, 377, 378, 379
Disorders Of The Globe Retinal Detachments And Defects	360
Other Retinal Disorders	362
Chorioretinal Inflammations, Scars, Other Disorders Of	
Choroid Disorders Of Iris And Ciliany Both	363
Glaucoma	365
Cataract	366
Disorders Of Refraction And Accommodation	367
Visual Disturbances Blindness And Low Vision	368
Keratitis	370
Corneal Opacity And Other Disorders Of Cornea	371
Disorders Of Conjunctiva	372
Inflammation Ut Eyelids Other Disorders Of Evelids	373
Disorders Of Lacrimal System	375
Disorders Of The Orbit	376
Disorders Of Optic Nerve And Visual Pathways Strabismus And Other Disorders Of Dimocular Eye	377
Other Disorders Of Eve	379
Ear And Masteid	380 381 382 383 384 385 386 387 388 389

 Table S1 | ICD-9-CM Code Dictionary for Analyzed Conditions

 Mapping of ICD-9-CM codes for all analyzed cardiovascular, neurological endpoints and HIV infection.

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