Case Studies Beware!

Rx and Labs return minor improvements in HIV prevalence capture for Medicare Parts D and B for 2012 to 2016

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Introduction

Retrospective observational data reuse research requires a case definition that minimizes False Negative(FN) and False Positive(FP) patients while still returning True Positive(TP) and True Negative (TN) Cases. HIV disease is very complicated to study because:

a. FN cases are a consequence of TP only case definitions (FP avoidance).

b. HIV disease uses different kinds of clinical data at different points of etiology; Labs and Rx in early years, INPT Dx and OUTPT Dx in late years and Death_CT as endpoint. Where you draw your inclusion criteria codes **from** gets different stages of HIV disease.

The patients we think we have enrolled has a lot to do with how sensitive we are with inclusion and exclusion criteria.

METHODS

1. We used a maximum sensitivity definition (no FP; INPT and OUTPT Dx only) to identify HIV disease cases among Medicare Enrollees. TP = 299,272.
2. We then searched the remaining beneficiaries for 'FN' signs in labs and Rx claims.
3. We retained 'HIV-maybe' cases who could not be HIV TP but could be HIV FN's. Labs_FN = 8,880, Rx_FN = 23,826 .

RESULTS

Looking for FN cases reveals possibly an additional 7.9 % and 12.9% case volume. These FN patients most likely have poly payer dynamics masking INPT and OUTPT HIV care from Medicare. They also could be 'etiology early' and on some level clinically uninteresting. They could also be pre, post exposure prophylaxis cases, HEP-B cases or off label users of HIV meds.

There are 299,272 distinct HIV+ patients on Medicare from 2012-2016.

HIV Labs and HIV Rx provides at least an additional 7.9% and 12.9% HIV+ Medicare patients

(if you don't mind False Positives in an HIV outcomes study).

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Abstract: In preparation for submitting a formal OHDSI Network study of HIV+ patients we are evaluating methods for defining an HIV cohort. Here we use a 100% Sample of CMS beneficiary claims from Medicare and Medicaid to discover the recall of HIV case definitions using formal ICD-9 or ICD-10 diagnosis, labs for viral load tests on Part-B and HIV medications on Part-D. We find that additional prevalence recall is comparatively small; but the large volume of Medicare Part-D only HIV+ patients should give Part-D data-reuse researchers pause.

Background: In preparation to submitting a formal OHDSI Network study of HIV+ patients we are evaluating methods for defining and HIV+ cohort. Research on OHDSI network data often requires the definition of a cohort of patients based on consistent and clear criteria to ensure that data generated from different data sources are truly comparable. Ideally, these definitions should be tested and validated in multiple, independent data sources before launching a network study. We are considering SNOMED CT and LOINC for our case definition but before we finalize our definitions, we have tested some elements of the candidate definitions on Centers for Medicare and Medicaid Services claims.

The Centers for Medicare and Medicaid Services (CMS) makes every claim from 1999-onward available to inform researchers working to enhance the quality and improve the outcomes of CMS beneficiaries via the Chronic Conditions Warehouse (CCW). CCW allows for unparalleled access to patient level claims data which describes the healthcare of Americans to data-reuse researchers. HIV research requires complex enrollment cohort definitions to maintain case cohesion. Without cohesion, survival times, placebo effects or treatment effects attributed to HIV+ patients might actually be being learned from HIV- patients.

The difficulty in finding a quality HIV case definition is compounded by the ways in which HIV disease has been defined by providers over time (AIDS, ELISA and now PNAT), the abundance of survival influential co-infections these patients experience (TB, HCV, CMV, Meningococcal Neisseria) and the lack of certainty between infection date, diagnosis date and the observation period under consideration in the proposed study. Pre and Post Exposure Prophylaxis, Hepatitis B treatment and 'off label use' are not uncommon with HIV medications, further confounding Rx based approaches.

Methods: We used a CCW case definition for HIV Disease composed of ICD-9 and ICD-10 diagnostic codes for HIV disease to generate a case index of HIV 'certainty' CMS beneficiaries who billed CMS for qualifying care from 2000 to 2016. We used a list of CPT-4 and HCPCS codes supplied by ATHENA to identify HIV 'Labs_Maybe' beneficiaries receiving qualifying Lab outpatient services in Medicare Part-B claims from 2012-2016 to serve as our Labs subset. Our Rx subset of HIV 'Rx_Maybe' beneficiaries was learned by searching Medicare Part-D for National Drug Codes (NDC) supplied by the State of Florida's Medicaid program HIV algorithm for anti-retroviral drugs (577 NDCs) for data years 2012-2016. Though the true number of HIV anti-retroviral NDCs is unknown; using an active case definition from the State of Florida allows us to test our method in real world terms.

Results: Any beneficiary with a CCW HIV flag (ICD-9 or 10) on any inpatient or outpatient claim who sought services from 2000 to 2016 was eligible to be counted as HIV certain if they were observed in 2012-2016. Over the five year observation period CCW flagged 299,272 distinct HIV+ beneficiaries who claimed services. This number is observation period inclusive and does not control for annualized variation of claims, services, mortality, continuity of coverage within the observation period or HIV+ flagged cases who only sought services outside the observation period or who died before the observation period began.

To be a Labs_Maybe case, beneficiaries needed to lack a CCW diagnosis flag for HIV and have at least one genotype, phenotype, drug resistance or quantification CPT4\HCPCS code for HIV virus on a Medicare Part-B claim. 111,989 HIV distinct certainty cases had at least one HIV lab event over the observation period. An additional 8,880 distinct beneficiaries had at least one HIV lab who also did not qualify under the CCW definition or an additional 7.93% over certainty cases.
To be an Rx_Maybe case, beneficiaries needed to lack a CCW diagnosis flag for HIV and have at least one NDC code used by the State of Florida in their HIV case definition algorithm for Medicaid beneficiaries.

184,691 distinct HIV certainty cases had at least one Rx event over the observation period. An additional 23,826 beneficiaries had at least one HIV Rx who did not qualify under the CCW definition or an additional 12.9% over certainty cases.

Discussion: The risk of using medication or labs as enrollment criteria most likely outweighs the benefits of using formal diagnosis codes for HIV research. Medication and lab indexes will most likely improve recall; however the amount that could be won is most likely less than 12.9% of additional prevalence assuming 100% of added prevalence is true positive (highly unlikely given non-HIV indications for common HIV Rx) and Medicare Part-D is representative. Additionally, the underlying patchwork of payers in HIV care may lead HIV cases to not being fully accounted for under single payer records systems. Alternative payers like VA and Ryan White as well as medication specialty programs like ADAP and Medicaid may account for an additional fraction of HIV labs, inpatient, outpatient and Rx care that this special population receives. Finally, the lack of a formal index of HIV NDCs creates challenges in estimating the ceiling of additional Rx-Maybe cases.

Conclusion: Labs and Rx may add additional cases to our cohort but the diverse sources of medication claims may confound using medication as a case definition in claims data sets.

Notes:

CDC Changed the HIV case definition to make viral load tests a valid confirmatory test in HIV screening! Viral load tests do not equal a HIV+ PT.

Truvada has on label non-HIV care uses including Pre & Post exposure and HEP-B care. Many 'stronger' HIV drugs including combination drugs are post exposure on label too. HIV Meds do not equal a HIV+ PT.

HRSA provides HIV medication, treatment and an assortment of services for 250k HIV+ Americans every year. These bills do not go to CMS. HIV+ cases have private insurance and no insurance. Insurance claims do not a complete epidemiology make.

There are 4,558,314 dispensations to 324,400 HIV-TP pts on Part-D, and 18,202,434 dispensations on Medicaid to 258,249 HIV-TP Medicare pts from 2006 to 2016. This means 80% of Rx from HIV TP is on Medicaid, not Medicare Part-D among HIV TP Medicare cases. There could be more Rx-FP Medicare cases with Maybe_Rx on Medicaid.

The AIDS case definition has changed several times. Calling a case definition from AIDS conditions is only as useful and accurate as the era the provider coded the cases in and assumes the provider knew the definition changed.

HIV is not like other diseases for complex reasons (susceptibility, screening, acuity, onset, duration, severity and outcomes are all random, repeated, episodic, unstable and under-described). Informatics can save you from some of these effects but don't blame informatics for not saving you from all of them.

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