Addressing the Challenge of Sample Size in Rare Disease: Expanding the Use of Health Plan Claims in Patients with Only Medical Coverage, Lacking Corresponding Prescription Insurance Coverage

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Introduction

- Health plan claims databases can contain substantial number of patients with only medical coverage, that is, without corresponding prescription drug coverage. This may occur when prescription coverage is not purchased, or such coverage is acquired from another source such as with Medicare Part D programs. Health outcomes research on these patients in health plan claims data is severely limited without prescription utilization information
- The PharMetrics Plus database is a heavily industry-utilized and well-differentiated database used in a variety of life sciences and commercial effectiveness studies. The database has more than 210 million unique enrollees and is representative of the US commercially insured claims marketplace. Over 250 peer reviewed publications have used PharMetrics Plus data
- It was recently observed (internal analysis) that in the PharMetrics Plus database, up to 40% of patients with continuous medical eligibility in a given year may not have accompanying continuous eligibility for prescription drug coverage. This may occur due to a lack of purchasing concomitant prescription drug coverage, or coverage through an alternate payer such as may occur with Medicare Part D
- Neuroendocrine tumors (NETs) are neoplasms of specialized cells of the body's neuroendocrine system. These cells have traits of both hormone-producing endocrine cells and nerve cells. They are found throughout the body's organs and help control many of the body's functions. Most NETs take years to develop and grow slowly, although some NETs are fast-growing. Common areas for NETs to develop include the gastrointestinal tract and pancreas[1]
- NETs are rare, with about 12,000 people diagnosed with the disease annually in the US[2]. Being a rare disease, sample size can be challenging in conducting real-world studies in claims databases

Objectives

- This study examines the ability to expand the utility of the PharMetrics Plus database through adding prescription claims data to patients in the database who lack continuous eligibility for prescription drug coverage during the study period. The goal would be to expand the available sample size and demonstrate that research can be conducted on such patients by linking their medical claims to an open-source prescription claims database
- This study will explore if the characteristics of patients with METs having continuous medical and pharmacy eligibility are similar to those having only continuous medical eligibility that can be linked to prescription claims data

Methods

Database

IQVIA PharMetrics® Plus

- IQVIA PharMetrics® Plus is a health plan claims database comprised of fully adjudicated medical and pharmacy claims for more than 190 million unique enrollees since 2006. Data contributors to the database are largely commercial health plans. It is representative of the commercially insured US national population for patients under 65 years of age. It contains a longitudinal view of inpatient and outpatient services, prescription and office/outpatient administered drugs, costs, and detailed enrollment information. All data are compliant to the Health Insurance Portability and Accountability Act (HIPAA) to protect patient privacy

Longitudinal Prescription Data (LRx)

- IQVIA receives nearly 4 billion prescription claims per year with history from January 2004 with coverage up to 92% for the retail channel, 62% for traditional and specialty mail order, and 76% for long-term care. The longitudinal prescription data (LRx) is derived from electronic information received from pharmacies, payers, software providers and transactional clearinghouses. This information represents activities that take place during the prescription transaction and contains information regarding the product, provider, payer and geography. LRx data is longitudinally linked back to an anonymous patient token and can be linked to events within the dataset itself and across other patient data assets, including PharMetrics Plus

Medical Claims Data (Dx)

- Approximately 1 billion professional fee claims per year submitted, representing over 870,000 practitioners per month. Records are available from September 1999, with approximately 95% of claims available for analyses within 3 weeks of the service date. Over time, there is representation from approximately 236 physician specialties (e.g., American Medical Association (AMA) classifications such as Family Medicine, Pediatrician, Radiologist, Urologist, etc.) as well as representation of non-physician practitioners (e.g., Nurse Practitioners and Physicians Assistants). The data includes patient demographics, physician demographics, diagnoses, procedures, and in-office administered drugs

Population Selection

- Index Period: 1/1/2013 – 11/30/2020
- Study Period: 1/1/2012 – 12/31/2020 (Figure 1)
- Patients with ≥ 2 non-ancillary medical claims containing a diagnostic code for GI or pancreatic neuroendocrine tumors were selected
- Additional inclusion-exclusion criteria are shown on Table 1, study timelines in Figure 1
- There are 2 populations compared in this study:
  - **Original population:** Patients with 12 months pre and 1-month post-index eligibility for both medical and pharmacy benefits
  - **Expanded population:** Patients with 12 months pre and 1-month post-index eligibility for medical benefits AND can be linked to LRx/Dx database
- The relationship between the original and expanded populations can be seen in Figure 2

Figure 1: Study Timeframe

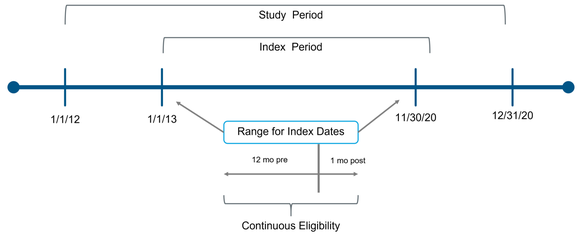

Figure 2 – Overlap Between Study Populations

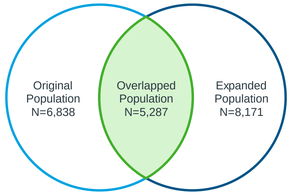

Table 1 – Attrition Table

Step #	Attrition Reason	Patients Remaining	
		Original	Expanded
1	Patients with ≥2 qualifying outpatient claims at least 30 days apart where at least one is specific for GI-NET or P-NET or ≥1 inpatient claim with a diagnosis code specific to GI-NET or P-NET during the index period. The date for the first claim with a diagnosis code specific to GI-NET or P-NET in the index period will serve as the index date	61,488	61,488
2	Patients ≥18 years of age as of the index date	61,212	61,212
3	Patients with ≥12 months of continuous health plan enrollment with medical benefits prior to their index date	43,383	43,383
4	Patients with ≥1 months of continuous health plan enrollment with medical benefits following their index date	41,905	41,905
5	Exclude patients with multiple primary tumor types, except GI-NET, P-NET, or non-malignant skin cancer	14,242	14,242
6	Apply standard IQVIA data cleaning processes to remove patients with data quality issues	10,210	10,210
	Original: Patients with ≥12 months of continuous Rx enrollment prior to their index date and ≥1 months of continuous Rx enrollment following their index date; Expanded: With Linkable ID	6,838	8,177
	Final Study Population		
	GI-NET	2,177	2,623
	P-NET	4,661	5,554

Results

- Of the 10,210 patients that met the basic criteria for a diagnosis of MET, 6838 met the continuous eligibility requirement for medical and pharmacy eligibility, while 8,177 met the criteria for medical eligibility only and had a linkable ID to the LRx/Dx database, increasing the potential cohort by 19.6%
- The demographic characteristics of the original and expanded populations are shown in Table 2. The median age, gender and geographic distribution of the two groups were quite similar, with the expanded population slightly younger and less female
- The clinical characteristics are shown in Table 4. Five co-morbidities showed a decrease of 10% or more in the expanded population: Cardiac arrythmia, Dementia/Alzheimer's, Epilepsy/Seizure, HIV/AIDS, and peripheral vascular disease. Only one co-morbidity showed an increase of 10% or more in the expanded population: Renal failure/dialysis. The other 18 co-morbidities showed less than a 10% difference from the original to the expanded population
- Treatment characteristics of the populations are shown in Table 3. There was very little difference noted in the proportion of patients that were observed with 1st, 2nd and 3rd line-of-therapy (LOT). A 10% or greater treatment exposure difference was noted between the populations for Bevacizumab, Capcecitabine+temozolomide, carboplatin, cisplatin, everolimus, lanterotide, and lutetium LU 177 dotatate
- The HCRU and cost characteristics of the two population is shown in Table 5. The original and expanded populations were quite similar, with a less than 3% difference in the portion of patients with a hospitalization or emergency room visit, as well as all-cause per-member-per-month (PPPM) cost

Table 2 – Demographic Characteristics

Demographic Characteristics	Original N=6,838		Expanded N=8,177	
Age				
Mean	56.9		56.5	
SD	11.2		10.7	
Median	58		58.0	
Age Group: (n, %)				
18-34 y	276	4.0%	321	3.9 %
35-44 y	499	7.3%	591	7.2 %
45-54 y	1,585	23.2%	1,911	23.4 %
55-64 y	3,680	53.8%	4,619	56.5 %
> 65 y	798	11.7%	735	9.0 %
Gender (n,%)				
Male	3,346	48.9%	4,089	50.0%
Female	3,492	51.1%	4,088	50.0%
Geographic Region (n,%):				
Northeast	1,415	20.7%	1,508	18.4%
Midwest	1,870	27.3%	2,548	31.2%
South	2,536	37.1%	3,168	38.7%
West	1,017	14.9%	953	11.7%

Table 3 – Treatment Characteristics

Observed Therapy		Original N=6,838		Expanded N=8,177	
		N	%	N	%
Patients with Line of Therapy (LOT)	1L	3,237	47.3%	3,897	47.7%
	2L	1,277	18.7%	1,548	18.9%
	3L	400	5.8%	494	6.0%
Patients with Treatment in 1L	BEVACIZUMAB	16	0.5%	14	0.4%
	CAPECITABINE + TEMOZOLOMIDE	261	8.1%	212	5.4%
	CARBOPLATIN	27	0.8%	25	0.6%
	CISPLATIN	27	0.8%	38	1.0%
	ETOPOSIDE	38	1.2%	43	1.1%
	EVEROLIMUS	47	1.5%	34	0.9%
	FLUOROURACIL	1,428	44.1%	1,801	46.2%
	GEMCITABINE HCL	1,012	31.3%	1,216	31.2%
	IRINOTECAN HCL	1,309	40.4%	1,707	43.8%
	LANREOTIDE ACETATE	172	5.3%	229	5.9%
	LUTETIUM LU 177 DOTATATE	3	0.1%	11	0.3%
	OCTREOTIDE ACETATE	431	13.3%	495	12.7%
	OXALIPLATIN	1,371	42.4%	1,758	45.1%
	PACLITAXEL	674	20.8%	831	21.3%
	SUNITINIB MALATE	13	0.4%	11	0.3%

Footnotes: 1. Highlighted are >=10% change up or down from the original population
2. Therapy counts are derived from the PharMetrics Plus database only

Table 4 – Clinical Characteristics

Clinical Characteristic		Original N=6,838		Expanded N=8,177	
		N	%	N	%
NCI comorbidity index	0	4,164	60.9%	5,201	63.6%
	>0 - <1	0	0.0%	0	0.0%
	1 - <2	1,545	22.6%	1,687	20.6%
	2 - <3	447	6.5%	525	6.4%
	3+	682	10.0%	764	9.3%
Comorbid Conditions	Alcohol/drug abuse	1,015	14.8%	1,231	15.1%
	Asthma	497	7.3%	575	7.0%
	Cardiac arrythmia	942	13.8%	1,010	12.4%
	Cardiac valvular disease	382	5.6%	411	5.0%
	Cerebrovascular disease	290	4.2%	314	3.8%
	Chronic kidney disease (excluding end stage renal failure/dialysis)	246	3.6%	292	3.6%
	Chronic pain/fibromyalgia	1,045	15.3%	1,180	14.4%
	Congestive heart failure	264	3.9%	284	3.5%
	COPD	477	7.0%	518	6.3%
	Dementia/Alzheimer's	65	1.0%	67	0.8%
	Depression	964	14.1%	1,071	13.1%
	Diabetes	1,938	28.3%	2,186	26.7%
	Dyslipidemia	3,053	44.6%	3,466	42.4%
	Epilepsy/seizure disorder	82	1.2%	87	1.1%
	Hepatitis	268	3.9%	299	3.7%
	HIV/aids	28	0.4%	28	0.3%
	Hypertension	3,473	50.8%	3,963	48.5%
	Liver disease/gallbladder/pancreas	3,988	58.3%	4,512	55.2%
	Myocardial infarction/CAD	757	11.1%	823	10.1%
	Osteoarthritis	2,677	39.1%	3,056	37.4%
	Paralysis/hemiplegia/paraplegia	51	0.7%	55	0.7%
	Peptic ulcer disease	269	3.9%	296	3.6%
	Peripheral vascular disease	569	8.3%	597	7.3%
	Renal failure/dialysis	57	0.8%	76	0.9%
	Rheumatologic disease (SLE, RA, AS, PSA)	374	5.5%	460	5.6%
	Schizophrenia	16	0.2%	20	0.2%
	Sleep disorders	1,090	15.9%	1,293	15.8%
	Smoking or history of smoking	1,038	15.2%	1,162	14.2%
	Thyroid disease	897	13.1%	1,028	12.6%

Footnote: Highlighted are >=10% change up or down from the original population

Table 5 – HCRU and Cost

HCRU/Cost factors	Original N=6,838		Expanded N=8,177	
	N	%	N	%
Patients with ≥1 hospital admission	4,277	62.5%	5,128	62.7 %
Patients with ≥1 ER visit	3,105	45.4%	3,811	46.6 %
All-cause costs¤, PPPM	$13,288		$12,918	

Summary and Conclusions

- This study demonstrated that in the PharMetrics Plus database, there were a substantial number of patients with NETs that would have qualified for all study criteria with the exception of having concomitant continuous pharmacy coverage eligibility in the specified pre and post-index periods
- When patients with only medical eligibility were considered and having a linkable ID to the LRx/Dx database, the potential study population increased by almost 20%
- The demographic, clinical, treatment and HCRU/cost characteristics of the original and expanded populations were found to be very similar. These results are encouraging toward utilizing patients in a health plan claims database such as PharMetrics Plus that have medical but not pharmacy benefit coverage, especially in the case of rare diseases where sample size can be a limiting issue

References

1. https://www.cancer.net/cancer-types/neuroendocrine-tumors/introduction (accessed April 7, 2022)
2. https://www.cancer.net/cancer-types/neuroendocrine-tumors/statistics (accessed April 7, 2022)

Disclosure

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