

Covid-19, Diagnostic History and Mortality from Medicare 1999-2021, In an All-Cause Mortality Approach

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Abstract

Introduction: SARS-CoV-2 infections co-occurred with other diverse pre-existing clinical conditions in mortality cases. We use encounter level health data to evaluate the impact of non-Covid-19 diagnostic events on all-cause mortality observed among Covid-19 positive cases billing Medicare. We further investigate prior diagnostic codes which occur in pre-pandemic study years among cases presenting to Medicare clinically with Covid-19 and cases with Covid-19 who experience all-cause mortality to inform patient population management.

Methods: We aggregated encounter level records sourced from all Medicare beneficiaries from 1999-2021. Odds ratios were constructed using diagnostic history, age decile, study year and survival status.

We used Generalized Linear Model (GLM) to predict the Decedent Observation Odds Ratio (DOOR) from study year, case observation odds ratio, age decile, non-covid conditions within counts of distinct covid-ever cases and their decedents. Odds ratios are relative to covid-never cases, or cases who did not present with Covid-19 clinically.

Results: High explanatory DOOR measures are observed for diagnostic codes commonly associated with inpatient Covid-19 mortality. High DOOR measures are also observed for individuals living with specific kinds of cancers, experiencing cardiac arrest or acute tubular necrosis.

Conclusion: Covid-ever mortality is influenced by primary infection itself and exacerbations of pre-existing conditions. Consequences of primary infection are observable in GLM, as well as meaningful prior clinical risk factors such as cancer, diabetes, cardiac and respiratory disease. Long-covid conditions require surviving Covid-19 clinical presentation and are predictable from GLM models.

Keywords: Covid-19; Mortality; Generalized Linear Model (GLM)

Introduction

Sars-Cov-2 (Covid-19) is a highly infectious pathogen with pandemic reach and high mortality [1,2]. Perhaps half of all residents of the United States (US) have experienced Covid-19 infection (at least once) as of this writing [3-5]. Reported attributable mortality for Covid-19 reached over one million dead in the US alone [6,7]. Despite a wealth of data, a robust analysis using real world data to understand the impact of clinical co-factors on pandemic mortality among patients with pre-existing conditions remains poorly characterized.

Further, the course of Covid-19 illness in pathophysiological terms and

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populations affected remain incompletely described. This is perhaps because of the diversity of the infected individuals, as well as the severity of preexisting conditions in the US [8-12]. In turn, parsing and segmenting Covid-19 infection and mortality effects from clinical experiences in the general population is natively difficult. Preexisting conditions can have high mortalities, further complicating the evaluation of the impact of Covid-19 [13]. It is difficult to say if a patient who experiences Covid-19 infection dies because of Covid-19 or their underlying morbidity or perhaps the interactions of both. Lastly, individuals who present with Covid-19 clinically may have documented prior conditions. The impact of these prior conditions to inform downstream mortality is under-considered when evaluating the impact of Covid-19 [14-18]. However, current data shows the association of high mortality rates among patients with pre-existing conditions.

To address the need for population level risk assessment, pathophysiology and to inform further and identify subjects for future research, this paper reviews the clinical diagnostic events of the Medicare population and considers the impact of their retrospective care from years 1999 to 2021. We compare the odds of dying from Covid-19 among Medicare beneficiaries to those who never contract Covid-19. This study uses machine learning methods to discover which non-covid conditions are statistically associated with variations in mortality within observed, historic non-covid clinical presentations. Study results may be useful to better identify indexes of concern for pandemic Covid-19 mortality and potentially inform care for individuals with preexisting conditions.

Methods

Data collection

We collected all identifiable claims records from Medicare from 1999 through 2021. Any claim which contained a diagnostic code ICD9-CM or ICD10-CM was considered. Data was acquired through the Virtual Research Data Center's Chronic Conditions Warehouse. Cases that billed for diagnostic code U07.1, (Emergency use of U07.1 | COVID-19) was considered Covid-19 positive.

Data transformation

We first mapped claim level diagnostic codes to SNOMED-CT. Study records are not aggregated within ICD10-CM or ICD9-CM but within the controlled diagnostic vocabulary of SNOMED-CT. To support interoperability the Observational Medical Outcomes Partnership's (OMOP) Athena vocabulary was used to transform ICD9-CM and ICD10-CM to SNOMED-CT.

Study index

The study dataset is an aggregated index of distinct case volumes. Case volumes are disaggregated by year of

observation, SNOMED-CT (diagnostic) code and 10-year age group membership at code utilization. This age-year-diagnostic unit, or AYD forms the basis of the study's count data models. The AYD units were disaggregated by study ever-survival status and covid-ever status. Cases were counted as ever-dead if they died (failed to survive) in the study period. Because the covid-ever population gains qualification in 2020, retrospective death should be understood as a public health opportunity. The final study dataset describes covid-ever and Medicare baseline (all) case volumes who died or survived from 1999 through 2021 by their age at diagnostic code utilization within a study year. This study produced 1,703,246 AYD units for the covid-ever Medicare population. Case AYD aggregates with fewer than 10 individuals were dropped from the study to preserve privacy and prevent individual care from conflating this population level analysis.

Data analysis

Four relative rates (risk panels) were used to calculate two odds ratios used in this study.

1. Baseline Observation Rate

The baseline observation rate was calculated as any Medicare case within AYD unit divided by any Medicare case within AY. This expresses the risk of being observed with an AYD unit for the baseline population with emphasis on inequality within diagnosis.

2. Covid-Ever Observation Rate

The covid-ever observation rate was calculated as any covid-ever case within AYD divided by any covid-ever case within AY. This expresses the risk of a covid-ever case being observed within an AYD unit with emphasis on inequality within diagnosis.

3. Case Observation Odds Ratio (COOR)

The case observation odds ratio was calculated by dividing baseline observation rate (1) by covid ever observation rate (2). The COOR describes the relative odds of a beneficiary contained within an AYD ever presenting clinically with Covid-19 versus beneficiaries never presenting clinically with Covid-19 within an AYD unit.

4. Baseline Survival Rate

The baseline survival rate was calculated as any Medicare case that did not survive the study within AYD unit divided by any Medicare case that did not survive the study within AY. This expresses the risk of observing a decedent within an AYD unit for the baseline population with emphasis on inequality within diagnosis.

5. Covid-Ever Survival Rate

The covid-ever survival rate was calculated as any covid-

ever case that did not survive the study within AYD unit divided by any covid-ever case that did not survive the study within AY. This expresses the risk of observing a covid-ever decedent within an AYD unit for the covid-ever population with emphasis on inequality within diagnosis.

6. Decedent Observation Odds Ratio (DOOR)

The decedent observation odds ratio was calculated by dividing baseline survival rate by covid-ever survival rate. The DOOR expresses the relative odds of an AYD containing a beneficiary that did not survive the study in the covid- ever group versus the covid-never group.

The above calculations return the risk of observing a covid-ever case or decedent, retrospectively, relative to a covid-never case or decedent. Note survival is ‘study survival status’ being attributed retrospectively. In this way cases can die in 2021 or 1999 and have their retrospective care qualified in the survived or decedent pool (within AYD). Decedent cases who die in 2020 would have their retrospective care classified as ‘decedent’ which would then be compared across covid-ever/covid-never groups and survived/ever-died.

Generalized Linear Model

This study evaluates the variance of the AYD odds ratios described above, and the attributable explanation of specific AYDs to specific ORs observed in the Medicare population. This variance is ranked as a coefficient above or below the intercept within H2o.AI models. The model ranked AYDs for their ability to explain variance in DOOR. In the model AYD was expressed as three features, not a combined term. The result of interest is the GLM covariate term for each diagnosis. Due to hardware constraints the model only considers AYD units that contained at least 500 cases. We do not report model summary statistics, because the goal of the model is not predictive; nor should it inform information technology products. Rather the model intends to segment DOOR from itself and order the results set.

Human Subjects Protections

This study was exempted from traditional Internal Review Board (IRB) review under exemption category four subsection two: "Exemption category four applies to secondary research of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met: (1) When the identifiable materials are publicly available or (2) when the data is recorded by the investigator in a de-identified manner (analysis dataset), ie. no identifiers are accessible to the research once the analysis begins. For example, the researcher conducts a retrospective medical chart review and records the necessary data in a datasheet for future analysis without any personal identifiers nor a code which would allow the investigator to link back to subjects."

The analysis dataset does not contain identifiable information. Because the study itself does not consider identifiable records we are exempt from review. Creating an aggregated dataset within year of birth with a large population and without race, gender or place identifiers may be a candidate method for making conclusions found in at-scale identifiable data available to researchers without compromising privacy or supporting reidentification.

Table 1 describes distinct individuals over study time. Covid-ever cases survived into 2020, unlike never-covid cases who did not present with Covid-19 clinically. Note: only 32 distinct individuals presented with Covid-19 clinically in 2019. In turn the death rates should be interpreted with care, as the Medicare beneficiaries with clinical covid died within the years of 2020 and 2021, while Medicare beneficiaries who never experienced covid could die at any time (1999-2021).

Table 2 shows the retrospective diagnostic breadth of covid-ever cases. Distinct diagnostic codes, (without patient volume) appear stable within age group over time for the covid-ever group.

By 2016, CMS transitioned to ICD10-CM codes, which are more verbose than ICD9-CM, with perhaps 10 times the volume of distinct codes available. While increases in distinct code volume are observed they are perhaps due to cases surviving to present with covid clinically (in 2019 and beyond). Because the sample is retrospective and case qualifying conditions occur in the end of the study period, diagnostic volumes should decrease retrospectively, as not all cases present in 2020 are enrolled in 1999. Diagnostic breadth decreases in some age groups from 2021 to 2020, perhaps because of mortality among the covid-ever cases.

Towards clinical demography, cases who survive past two standard deviations of median survival within birth cohort tend to avoid presenting with high mortality chronic diseases because they avoid cancer, heart disease, diabetes and exposure deaths (HIV, opioids, tobacco, homicide). In turn, very old adults (90+) may have smaller diagnostic breadths.

Fig 1 displays distinct covid-ever cases (x axis) by deaths if observed (y axis) by retrospective diagnostic code (points) and age group (color). Retrospective variation by decedent volume and case volume are detected when axis variation is considered. Note that AYD units should have larger volumes towards the end of the study, which contains the terms of

Table 1: Cases, decedents and covid-ever cases

1999-2020	Cases	Deaths	Rate
Medicare Beneficiaries Never-Covid	11,40,82,395	4,88,66,264	42.83%
Medicare Beneficiaries Ever-Covid	42,34,351	7,58,105	17.90%

Table 2: Distinct diagnostic code utilization within age group and year for covid-ever cases, 1999-2021

	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-99	100-109
1999		16	40	39	187	167			
2000		16	47	52	214	222	3		
2001		16	53	60	252	275	10		
2002		21	56	76	299	324	22		
2003		20	68	86	338	376	40		
2004	1	23	71	106	360	425	65		
2005	1	24	79	137	387	475	102		
2006	1	23	83	148	425	524	143		
2007	1	30	87	162	463	566	192		
2008	1	32	97	183	503	606	236		
2009	1	35	106	205	538	649	294	2	
2010	2	42	121	230	581	692	360	4	
2011	5	47	139	258	631	757	432	18	
2012	6	54	145	283	677	808	507	33	
2013	6	57	158	308	724	877	574	60	
2014	6	61	161	333	791	936	641	108	
2015	5	65	174	405	961	1,170	812	163	
2016	6	61	173	416	960	1,171	825	210	
2017	7	64	188	443	1,051	1,296	920	304	
2018	8	71	199	478	1,129	1,419	1,024	408	
2019	9	78	220	507	1,223	1,548	1,145	519	4
2020	12	90	232	549	1,324	1,662	1,268	649	17
2021	12	92	227	526	1,312	1,693	1,262	617	22

enrollment (covid-ever). Cases did not need to die in a given study year to be observed and counted as retrospectively deceased.

Fig 2 shows distinct covid-ever cases within AYD units by their COOR. This figure caps COOR at 50, to avoid outliers distorting the distribution. Said outliers are not counterfactual, they simply represent AYD units where AYD members had extreme shares of covid-ever versus covid-never cases. Study year 2005 presents with high retrospective COOR, suggesting acute events within past years may provide positive predictive value of individuals presenting with Covid-19 clinically. Prior influenza seasons and outbreaks of infectious diseases in nursing homes are

candidate explanations. AYD units above a COOR of 1, or no difference are detected in all study years. Study years 2020 and 2021 show AYD units that have high COOR and population counts; this is perhaps because those AYD units are related to Covid-19 clinical episodes.

Fig 3 describes DOOR by distinct covid cases within AYD units. DOOR is relatively small, ranging from 0 to 2 until 2013. 2020 and 2021, covid pandemic years see DOOR for specific AYD units expand to 8 and 10, respectively. DOOR can parse AYD units to highlight which AYD are overrepresented among mortality cases with a given segmentation, in this case covid-ever versus. covid-never retrospective study.

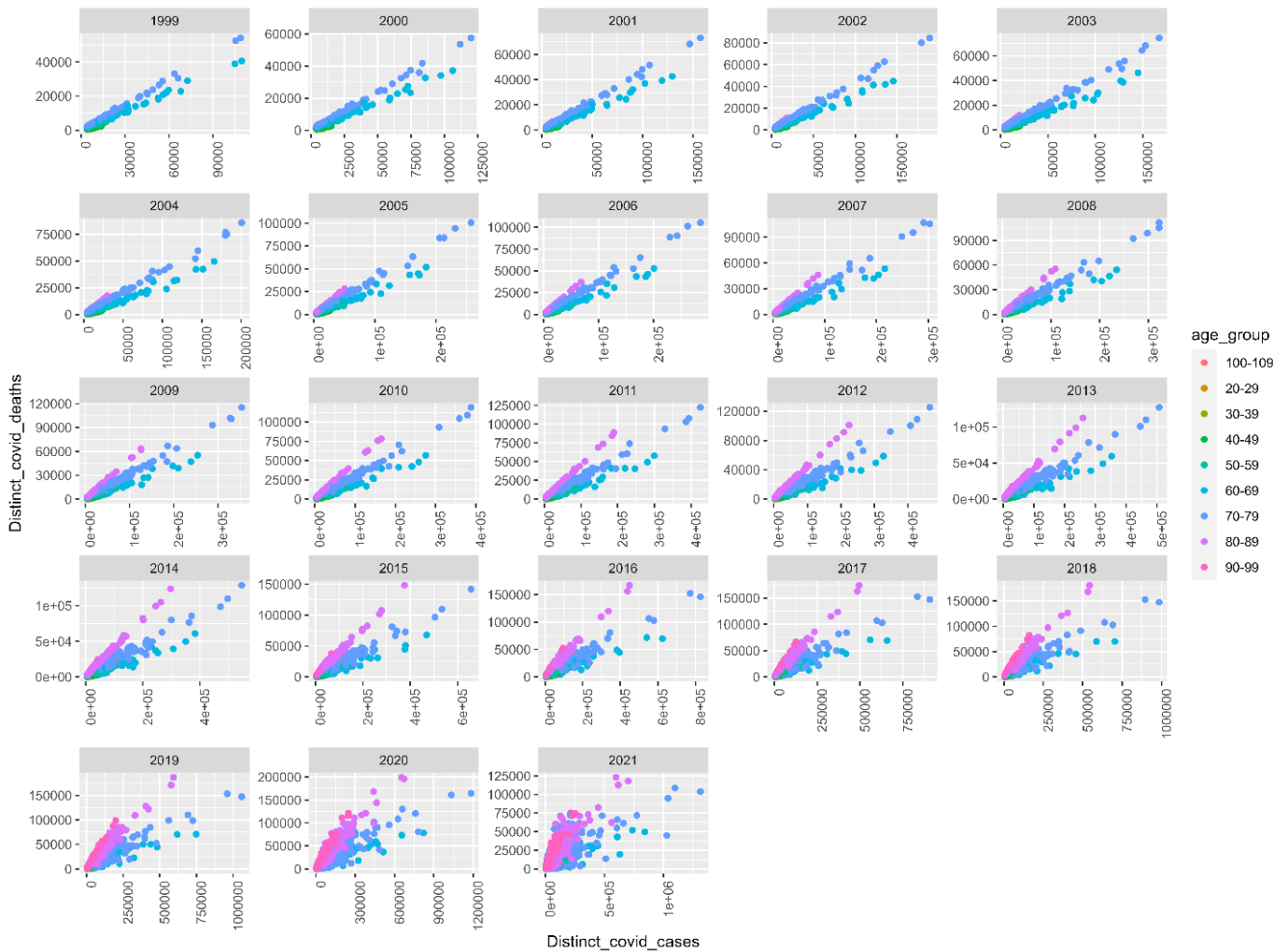


Fig 1: Scatterplot matrix of distinct covid-ever cases (x axis) and deaths (y axis) within year, age group and diagnostic code

Fig 4 shows the relationships between DOOR and COOR within AYD units. As above, COOR is capped at 50. DOOR ranges from 0-5 until 2020, where even higher values are observed. COOR decreases in 2016, perhaps because of the added specificity of ICD10-CM code utilization. Study years 2016 through 2019 show retrospective predictive value of all-cause mortality relative to patients who did not present with Covid-19. Thin bands observed prior to study year 2016 indicate that although cases were not radically more likely to present with Covid-19 within diagnostic and age group, they were more likely to die if ever described within AYD relative to patients who did not present with Covid-19. AYD units depart from the trend in 2005, and outliers are observed in all years prior to 2016.

Table 3 shows AYD units with high odds ratios. Highest DOOR AYD units are, given the study years perhaps Covid-19 cases experiencing Covid-19 related mortality. Highly ranked COOR values indicate conditions common in old age, institutionalized populations (nursing homes with

infectious disease outbreaks prior to Covid-19 pandemic era). Conditions common to adults already old (70+) in 2005 provide predictive value, where 15 years later they succumb to respiratory disease (at 85+). Very high COOR and DOOR values indicate that covid-ever cases are experiencing observation and mortality risks above the AYD Medicare baselines.

Table 4 shows the highest ranked DOOR diagnoses; which are ranked by their ability to explain variance in DOOR learned from AYD units. While conditions associated with Covid-19 mortality are present, liver cancer, lung cancer, bacterial pneumonia, upper body thrombosis and MERSA sepsis (perhaps due to being hospitalized with Covid-19) all feature in the top 20 conditions.

Table 5 shows the least explanatory AYD units when considering DOOR. Though counter intuitive, clinical diagnosis that was not explanatory of DOOR variance can yield clinically meaningful results. To experience long-covid, cases must have Covid-19 and survive to present with long-

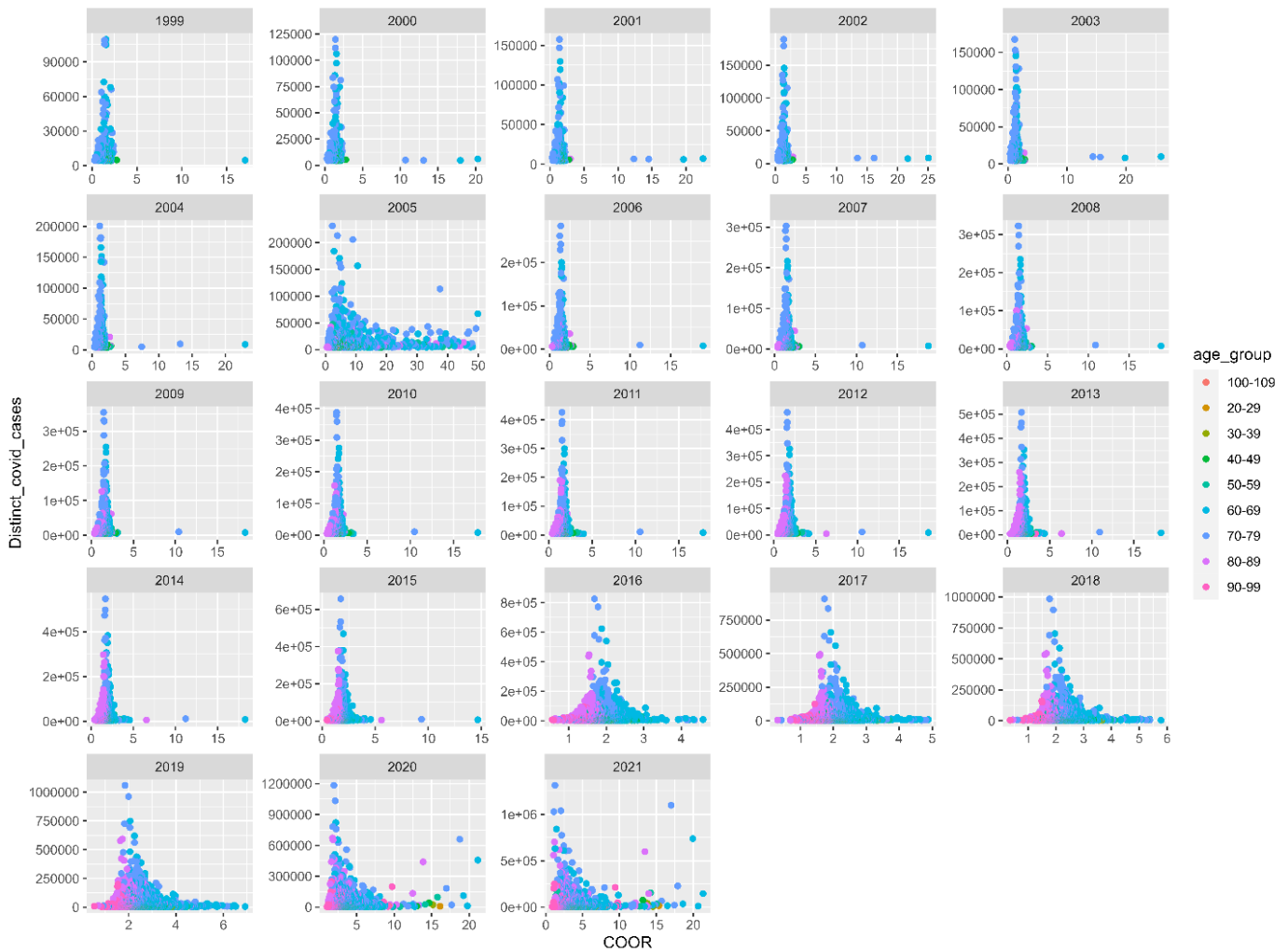


Fig 2: Scatterplot matrix of distinct covid-ever beneficiaries (y axis) by COOR (x axis) within year, age group and diagnostic code

covid. These individuals would have a low DOOR score and their AYD units would not explain variance in DOOR. Said presentations are observed with clinical diagnosis, ‘loss of sense of smell’ and ‘chronic cough’. They populate at the bottom of the model features when ordered by DOOR coefficients at row 2179 out of 2183 rows.

Limitations

This method, though robust, should not be used for the evaluation of nested sub-populations unless they are specifically controlled for in the baseline extract. This model should only be used to evaluate covid-ever cases versus their AYD baselines. This study only considered covid-ever case status within the subset. Interactions within the subset should not be assumed or assigned greater meaning other than ‘more or less likely than baseline’. Coinfection cases (for example, HIV and Covid-19) could be evaluated if the subset model and baseline model considered coinfection negative cases. This generalist model is useful, however for identifying candidates

for further research both at the benchtop and bedside.

This model only considered Medicare claims data. While robust and spanning multiple study years and treatment sites, this model should not be used to interpret outcomes from other patient populations. Note the Medicare population here is any individual who billed Medicare from 1999 through 2021. This population include recipients of Social Security Disability Insurance, individuals over the age of 65, patients experiencing end stage renal disease, organ transplant recipients and spouse survivors of Medicare beneficiaries and may include undocumented individuals living in the United States. Hospice, nursing home, long term care and Part-B, Part-C and Part-D beneficiaries were not excluded or disambiguated. The findings presented here are true of the Medicare population in all its complexity.

Discussion

Machine vision for clinical research is traditionally thought of in machine learning for image analysis [19-21].

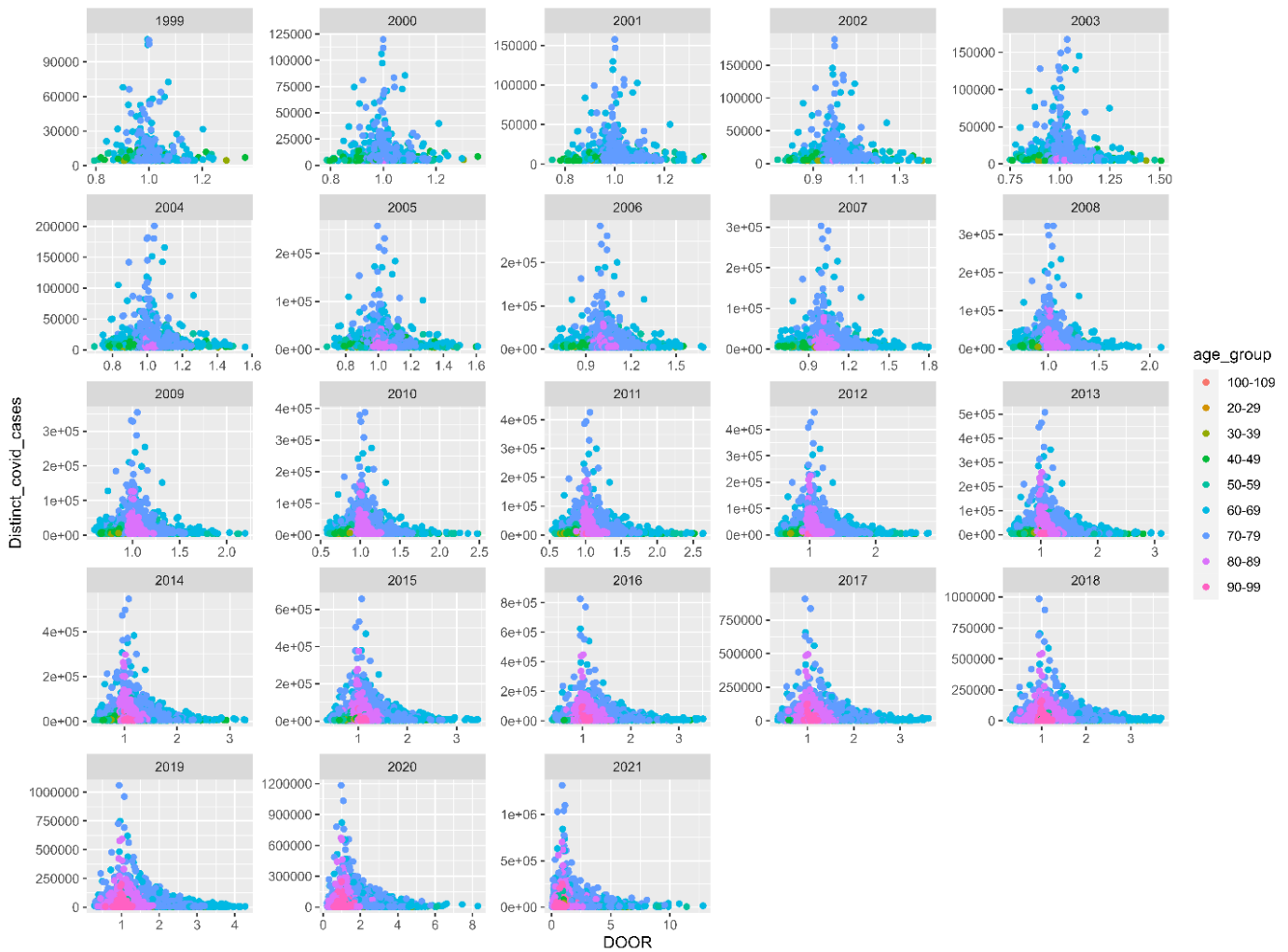


Fig 3: Scatterplot matrix of distinct covid-ever cases (x axis) and DOOR (y axis) within year, age group and diagnostic code

Here, machine vision for human pathology via machine learning is attempted using tabulated real-world data. The goal of the model is perhaps unusual, depending on the level of mathematics training of the audience [22,23]. The model is not attempting to predict the future, but rather segment AYD units and patient volumes to learn which AYD units are related to covid-ever and survival status over study time [17].

A method for classifying retrospective care to inform the specificity of a clinical condition is sorely lacking. Here, we demonstrate that such a method is well within reach (generalized linear models are not new) and can achieve both known-knowns (ventilators) all too familiar to providers caring for dying Covid-19 patients and perhaps some known-unknowns, like higher mortality in Covid-19 cancer and cardiac arrest cases which warrants further investigation [14,24-27]. Cardiac arrest often results from serious conditions (acute or pre-existing) that may be responsible for this event. How Covid-19 impacts patients whose life courses are already intersecting with environmental exposures to causal agents of chronic conditions can be informed by the

study dataset. Further, how Covid-19 recurses through human communities (especially nursing homes) as one of many infectious agents should demonstrate the need to better understand the environments which produce Covid-19 exposure, including clinical settings [28]. Many of these patients are immunocompromised which may explain the dire consequences seen in this patient population.

Covid-19 is unlikely to be the last emerging infectious disease to impact the Medicare population. In turn, the lessons that can be learned and deployed are high value to limit mortality and improve quality of care. Table 1 demonstrates that the Medicare population is ‘high mortality’ and is perhaps not ‘just another health insurance program’. Rather, Medicare insures individuals at the end of their lives, regardless of how old they are when their lives end. Table 2 demonstrates the diagnostic breath within the covid-ever population. While some conditions may be synonyms for each other, this study used SNOMED-CT mappings and counted distinct cases within AYD units to improve clinical accounting. The covid-ever population is diagnostically diverse, when retrospective



Fig 4: Distinct covid-ever cases within diagnostic code by COOR (x axis) and DOOR (y axis), disaggregated by study year and age group

Table 3: Highest ranked COOR and DOOR values by AYD with ever-cases and ever-decedents

OR Rank	Diagnosis	Year	Age Group	COOR	DOOR	Covid Cases	Covid Dead
DOOR 1	Cardiac arrest	2021	60-69	5.621116	12.7996	14,517	11,728
DOOR 2	Cardiac arrest	2021	50-59	4.443997	11.4116	4,532	3,514
DOOR 3	Palliative care	2021	60-69	5.572379	10.787	35,764	24,350
DOOR 4	Mediastinal emphysema	2021	60-69	9.570231	9.8766	5,037	3,140
DOOR 5	Not for resuscitation	2021	60-69	6.34527	9.86593	41,817	26,040
DOOR 6	Septic shock	2021	60-69	8.073529	9.80267	27,114	16,776
DOOR 7	Cardiac arrest	2021	70-79	4.511979	9.54759	22,335	18,689
DOOR 8	Shock	2021	60-69	6.894183	9.49667	13,143	7,878
DOOR 9	Dependence on respirator	2021	60-69	8.126317	9.26419	17,384	10,165
DOOR 10	Anoxic encephalopathy	2021	60-69	6.383796	9.16421	4,412	2,552
DOOR 11	Palliative care	2021	50-59	4.20244	9.00703	8,255	5,052
DOOR 12	Cardiogenic shock	2021	60-69	4.710182	8.92264	4,812	2,710
DOOR 13	Acute respiratory distress syndrome	2021	60-69	14.46835	8.85802	21,964	12,280
DOOR 14	Not for resuscitation	2021	50-59	4.831182	8.8497	8,751	5,262

DOOR 15	Mechanical failure of instrument or apparatus during procedure	2021	60-69	7.818232	8.82151	7,008	3,902
DOOR 16	Mixed acid-base balance disorder	2021	60-69	7.818232	8.82151	7,008	3,902
DOOR 17	Cardiac arrest	2020	60-69	3.750514	8.28268	10,680	8,380
DOOR 18	Palliative care	2021	70-79	4.679915	8.0542	75,737	53,461
DOOR 19	Acute tubular necrosis	2021	60-69	6.880515	7.91728	17,818	8,904
DOOR 20	Pneumothorax	2021	60-69	5.792531	7.91375	9,934	4,962
COOR 1	Infection due to Group A Shigella	2011	70-79	12199.88	1.25434	5,744	1,950
COOR 2	Infection due to Group A Shigella	2012	60-69	5024.259	1.54	4,494	1,073
COOR 3	Late effects of central nervous system tuberculosis	2003	70-79	3250.723	1.03057	7,973	3,533
COOR 4	Late effects of central nervous system tuberculosis	2001	70-79	1969.732	1.05506	6,139	3,010
COOR 5	Late effects of central nervous system tuberculosis	1999	70-79	1866.427	1.00972	4,303	2,165
COOR 6	Amebic ulcer of skin	2006	60-69	1731.046	1.2367	4,651	1,367
COOR 7	Amebic ulcer of skin	2006	70-79	1515.433	1.14381	5,670	2,410
COOR 8	Late effects of central nervous system tuberculosis	2002	70-79	1475.157	1.02186	7,168	3,276
COOR 9	Late effects of central nervous system tuberculosis	2000	70-79	1445.705	1.01437	5,095	2,485
COOR 10	Amebic ulcer of skin	2008	70-79	1181.716	1.15818	5,367	2,049
COOR 11	Amebic ulcer of skin	2007	70-79	1149.49	1.14039	5,114	2,045
COOR 12	Blepharoconjunctivitis	2005	60-69	1093.759	1.20108	7,348	2,249
COOR 13	Amebic ulcer of skin	2009	70-79	844.551	1.1305	5,045	1,765
COOR 14	Amebic ulcer of skin	2011	70-79	749.9762	1.18576	5,104	1,638
COOR 15	Amebic ulcer of skin	2010	70-79	711.1185	1.18202	5,109	1,750
COOR 16	Blepharoconjunctivitis	2005	70-79	619.4802	1.10596	8,662	3,758
COOR 17	Amebic ulcer of skin	2014	70-79	546.5532	1.35909	4,720	1,391
COOR 18	Somatic dysfunction of lumbar region	2005	70-79	538.5339	0.90879	32,791	11,690
COOR 19	Cervical somatic dysfunction	2005	70-79	535.2009	0.8902	24,610	8,594
COOR 20	Somatic dysfunction of lumbar region	2005	60-69	514.2503	0.83224	27,999	5,938

Table 4: Highest ranked coefficients when predicting DOOR from AYD values

COEF Rank	Diagnosis	COEF	Standard Error	Z Value	P Value
1	Anoxic encephalopathy	6.747676	0.23155	29.14134	2.65E-185
2	Cardiac arrest	5.717084	0.127645	44.78893	0
3	Mediastinal emphysema	5.578207	0.192414	28.99065	1.99E-183
4	Cardiogenic shock	4.37418	0.169499	25.8065	5.41E-146
5	Secondary malignant neoplasm of liver	4.082191	0.192413	21.21578	1.69E-99
6	Shock	4.07086	0.142956	28.47627	4.29E-177
7	Mechanical failure of instrument or apparatus during procedure	3.765781	0.14295	26.34327	5.23E-152
8	Mixed acid-base balance disorder	3.765781	0.14295	26.34327	5.23E-152
9	Dependence on respirator	3.627979	0.117473	30.88341	1.13E-207
10	Pressure ulcer of hip	3.594287	0.321513	11.1793	5.53E-29
11	Acute respiratory distress syndrome	3.526631	0.122105	28.88199	4.43E-182
12	Sepsis due to methicillin resistant Staphylococcus aureus	3.407956	0.169496	20.10641	1.35E-89
13	Hepatic failure	3.229828	0.1344	24.03138	5.79E-127
14	Tracheostomy present	3.15557	0.169496	18.61739	3.98E-77
15	Acute thrombosis of superficial vein of upper extremity	3.097249	0.321513	9.633369	6.01E-22
16	Finding of urine output	3.040841	0.231536	13.13337	2.43E-39
17	Pneumonia due to Gram negative bacteria	3.029736	0.231535	13.08542	4.55E-39

18	Hypovolemic shock	3.016566	0.231536	13.02852	9.59E-39
19	Pain due to neoplastic disease	2.859936	0.154118	18.55683	1.22E-76
20	Secondary malignant neoplasm of lung	2.780388	0.231535	12.00848	3.52E-33

Table 5: Lowest ranked coefficients when predicting DOOR from AYD variances

COEF Rank	Diagnosis	COEF	Standard Error	Z Value	P Value
2169	Snapping thumb syndrome	-1.1783	0.16949	-6.9523	3.63E-12
2170	Chalazion of lower eyelid	-1.1875	0.19241	-6.1718	6.80E-10
2171	Lateral epicondylitis	-1.1898	0.16949	-7.0202	2.24E-12
2172	Contact dermatitis due to plants, except food	-1.1994	0.1344	-8.9241	4.63E-19
2173	Acute disease	-1.1994	0.19242	-6.2331	4.61E-10
2174	Iliotibial band friction syndrome	-1.2013	0.23153	-5.1885	2.13E-07
2175	Disorder of knee	-1.2104	0.32151	-3.7646	1.67E-04
2176	Keratoconjunctivitis sicca, in gren's syndrome	-1.2296	0.32151	-3.8244	1.31E-04
2177	Lichen sclerosus et atrophicus	-1.2436	0.19241	-6.4635	1.03E-10
2178	Human papilloma virus screening	-1.2507	0.13439	-9.3068	1.36E-20
2179	Loss of sense of smell	-1.2867	0.19241	-6.6873	2.29E-11
2180	Chronic cough	-1.2879	0.19242	-6.6928	2.21E-11
2181	Horseshoe retinal tear without detachment	-1.3215	0.32151	-4.1104	3.96E-05
2182	Telogen effluvium	-1.4681	0.32151	-4.5664	4.97E-06
2183	Vertebrogenic pain syndrome	-1.5276	0.23155	-6.5976	4.22E-11

years are considered. Care might be improved by taking a broader, retrospective patient history (decades) instead of a ‘chief complaint’ as this study does [29-31].

Figure 1 demonstrates the shifting burden of care within the covid-ever population; which is to be expected as Figure 1 is uncontrolled for enrollment or ageing. Prior events (prior to Covid-19 diagnosis) appear robust, as expected in this large population study. Figures two and three demonstrate that retrospective case events are determining, in some cases, down stream risk of being observed with Covid-19 clinically or dying in the study period. In this study, positive predictive value is detected, though not assessed; as the goal of this study is to understand statistically attributable explanations of AYD variance of the DOOR statistic. Figure 4 highlights the study risk panels over time, and indicates that prior risk (especially in 2005) impacts the risk of presenting with Covid-19 clinically and dying in the study period.

Table 3 highlights high COOR and DOOR AYD units. Prior to model segmentation, AYD rankings for COOR and DOOR can be informative. Table 4 details the highest ranked DOOR covariates from the GLM model. While inpatient mortality diagnoses associated with covid-ever cases are observed, cardiac arrest, cancer and diabetes related diagnosis is predominant. This means that the variance of DOOR across AYD units is best explained by these diagnoses. There is substantial clinical research indicating that cardiac, cancer and diabetes outcomes are influenced by Covid-19 infection,

and vice-versa [24,26,27,32]. Table 5 suggests that cases that survive Covid-19 are eligible for long-covid syndromes [33-35]. While long covid syndromes are still being described, Medicare cases may provide case evidence to support benchtop or bedside conclusions.

Conclusion

Machine vision for pathology segmentation is readily available with at-scale real world data. The Medicare population has taken the brunt of Covid-19 and presents a natural experiment to understand the interrelatedness of pathology emergency and vulnerability. Prior clinical conditions may impact Covid-19 mortality and inform caregivers of patients presenting clinically with Covid-19.

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References

1. Hiscott J, Alexandridi M, Muscolini M, et al. The global impact of the coronavirus pandemic. Cytokine Growth Factor Rev 53 (2020): 1-9.
2. Noor AU, Maqbool F, Bhatti ZA, et al. Epidemiology

- of CoViD-19 Pandemic: Recovery and mortality ratio around the globe. *Pak J Med Sci* 36 (2020): S79–84.
3. Clarke KEN. Seroprevalence of Infection-Induced SARS-CoV-2 Antibodies — United States, September 2021–February 2022. *MMWR Morb Mortal Wkly Rep* [Internet]. 2022 [cited 2023 Mar 7]; 71.
 4. Ahmad FB. Provisional Mortality Data — United States, 2021. *MMWR Morb Mortal Wkly Rep* [Internet]. 2022 [cited 2023 Mar 7]; 71.
 5. Akinbami LJ. SARS-CoV-2 Serology and Self-Reported Infection Among Adults — National Health and Nutrition Examination Survey, United States, August 2021–May 2022. *MMWR Morb Mortal Wkly Rep* [Internet]. 2022 [cited 2023 Mar 7]; 71.
 6. COVID-19 Provisional Counts - Weekly Updates by Select Demographic and Geographic Characteristics [Internet]. 2023 [cited 2023 Mar 7].
 7. Excess Deaths Associated with COVID-19 [Internet]. 2023 [cited 2023 Mar 7].
 8. Djaharuddin I, Munawwarah S, Nurulita A, et al. Comorbidities and mortality in COVID-19 patients. *Gac Sanit* 35 (2021): S530-532.
 9. Greenwald SD, Chamoun NG, Manberg PJ, et al. Covid-19 and excess mortality in medicare beneficiaries. *PloS One* 17 (2022): e0262264.
 10. Tarazi WW, Finegold K, Sheingold SH, et al. COVID-19-Related Deaths And Excess Deaths Among Medicare Fee-For-Service Beneficiaries. *Health Aff Proj Hope* 40 (2021): 879-885.
 11. Dessie ZG, Zewotir T. Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients. *BMC Infect Dis* 21 (2021): 855.
 12. Alimohamadi Y, Tola HH, Abbasi-Ghahramanloo A, et al. Case fatality rate of COVID-19: a systematic review and meta-analysis. *J Prev Med Hyg* 62 (2021): E311-320.
 13. McKenna MT, Zohrabian A. U.S. burden of disease--past, present and future. *Ann Epidemiol*. 2009 Mar;19(3):212-219.
 14. Zhang JJ, Dong X, Liu GH, et al. Risk and Protective Factors for COVID-19 Morbidity, Severity, and Mortality. *Clin Rev Allergy Immunol* 64 (2023): 90-107.
 15. Rea IM, Alexander HD. Triple jeopardy in ageing: COVID-19, co-morbidities and inflamm-ageing. *Ageing Res Rev* 73 (2022): 101494.
 16. Gallo Marin B, Aghagoli G, Lavine K, et al. Predictors of COVID-19 severity: A literature review. *Rev Med Virol* 31(2021): 1-10.
 17. Gasmi A, Peana M, Pivina L, et al. Interrelations between COVID-19 and other disorders. *Clin Immunol Orlando Fla* 224 (2021): 108651.
 18. Ejaz H, Alsrhani A, Zafar A, et al. COVID-19 and comorbidities: Deleterious impact on infected patients. *J Infect Public Health* 13 (2020): 1833-1839.
 19. Madabhushi A, Lee G. Image analysis and machine learning in digital pathology: Challenges and opportunities. *Med Image Anal* 33 (2016): 170-175.
 20. McAlpine ED, Michelow P, Celik T. The Utility of Unsupervised Machine Learning in Anatomic Pathology. *Am J Clin Pathol* 157 (2022): 5-14.
 21. Roohi A, Faust K, Djuric U, et al. Unsupervised Machine Learning in Pathology: The Next Frontier. *Surg Pathol Clin* 13 (2020): 349-358.
 22. Kushner RF, Sorensen KW. Lifestyle medicine: the future of chronic disease management. *Curr Opin Endocrinol Diabetes Obes* 20 (2013): 389-395.
 23. Saleem F, Al-Ghamdi ASAM, Alassafi MO, et al. Machine Learning, Deep Learning, and Mathematical Models to Analyze Forecasting and Epidemiology of COVID-19: A Systematic Literature Review. *Int J Environ Res Public Health* 19 (2022): 5099.
 24. Williams N. Prehospital Cardiac Arrest should be considered when evaluating Covid-19 mortality in the United States. *Methods Inf Med* (2023).
 25. Smulowitz PB, O'Malley AJ, Khidir H, et al. National Trends In ED Visits, Hospital Admissions, And Mortality For Medicare Patients During The COVID-19 Pandemic. *Health Aff Proj Hope* 40 (2021): 1457-1464.
 26. Langerbeins P, Hallek M. COVID-19 in patients with hematologic malignancy *Blood* 140 (2022): 236-252.
 27. Marjot T, Webb GJ, Barritt AS, et al. COVID-19 and liver disease: mechanistic and clinical perspectives. *Nat Rev Gastroenterol Hepatol* 18 (2021): 348-364.
 28. Carnahan JL, Lieb KM, Albert L, et al. COVID-19 disease trajectories among nursing home residents. *J Am Geriatr Soc* 69 (2021): 2412-2418.
 29. Alwin DF. Integrating Varieties of Life Course Concepts. *J Gerontol B Psychol Sci Soc Sci* 67 (2012): 206–220.
 30. Jones NL, Gilman SE, Cheng TL, et al. Life Course Approaches to the Causes of Health Disparities. *Am J Public Health* 109 (2019): S48–55.
 31. Settersten RA, Bernardi L, Härkönen J, et al. Understanding

- the effects of Covid-19 through a life course lens. *Curr Perspect Aging Life Cycle* 45 (2020): 100360.
32. Chang MH, Moonesinghe R, Truman BI. COVID-19 Hospitalization by Race and Ethnicity: Association with Chronic Conditions Among Medicare Beneficiaries, *J Racial Ethn Health Disparities* 9 (2020): 325-334.
 33. Salerno S, Messana JM, Gremel GW, et al. COVID-19 Risk Factors and Mortality Outcomes Among Medicare Patients Receiving Long-term Dialysis. *JAMA Netw Open* 4 (2021): e2135379.
 34. Kamal M, Abo Omirah M, Hussein A, et al. Assessment and characterisation of post-COVID-19 manifestations. *Int J Clin Pract* 75 (2021): e13746.
 35. Duggal P, Penson T, Manley HN, et al. Post-sequelae symptoms and comorbidities after COVID-19. *J Med Virol* 94 (2022): 2060–2066.