

Identification of ordinal endpoints indicating influenza complications: A feasibility analysis relevant to the study of medical countermeasures

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Background

- Medical countermeasures (MCMs) are FDA-regulated products (biologics, drugs, devices) that may be used in the event of a potential public health emergency
- “Ordinal endpoints” (categorical outcomes evaluated on an ordered scale of increasing severity) of influenza complications may be useful in evaluating the utilization, safety, and/or effectiveness of influenza-related MCMs
- Influenza is a test case and serves as a proxy for other public health emergency events
- FDA’s Sentinel System is an active surveillance system that uses routine querying tools and pre-existing electronic healthcare data from multiple Data Partners to monitor the safety of regulated medical products

Objectives

- To determine whether ordinal endpoints can be identified for patients with evidence of influenza and influenza-related conditions in the Sentinel System
- To describe underlying conditions and influenza testing patterns of patients with influenza-related endpoints

Results

Table 1. Number of patients per cohort, by influenza season

Cohort	July 2014 – June 2015	July 2015 – June 2016	July 2016 – June 2017
ILI	1,078,978	570,290	988,101
P&I	3,614,409	3,125,995	3,608,933
MAARI	12,727,154	11,688,443	12,623,014

Figure 1. Baseline characteristics per cohort, July 2016 – June 2017

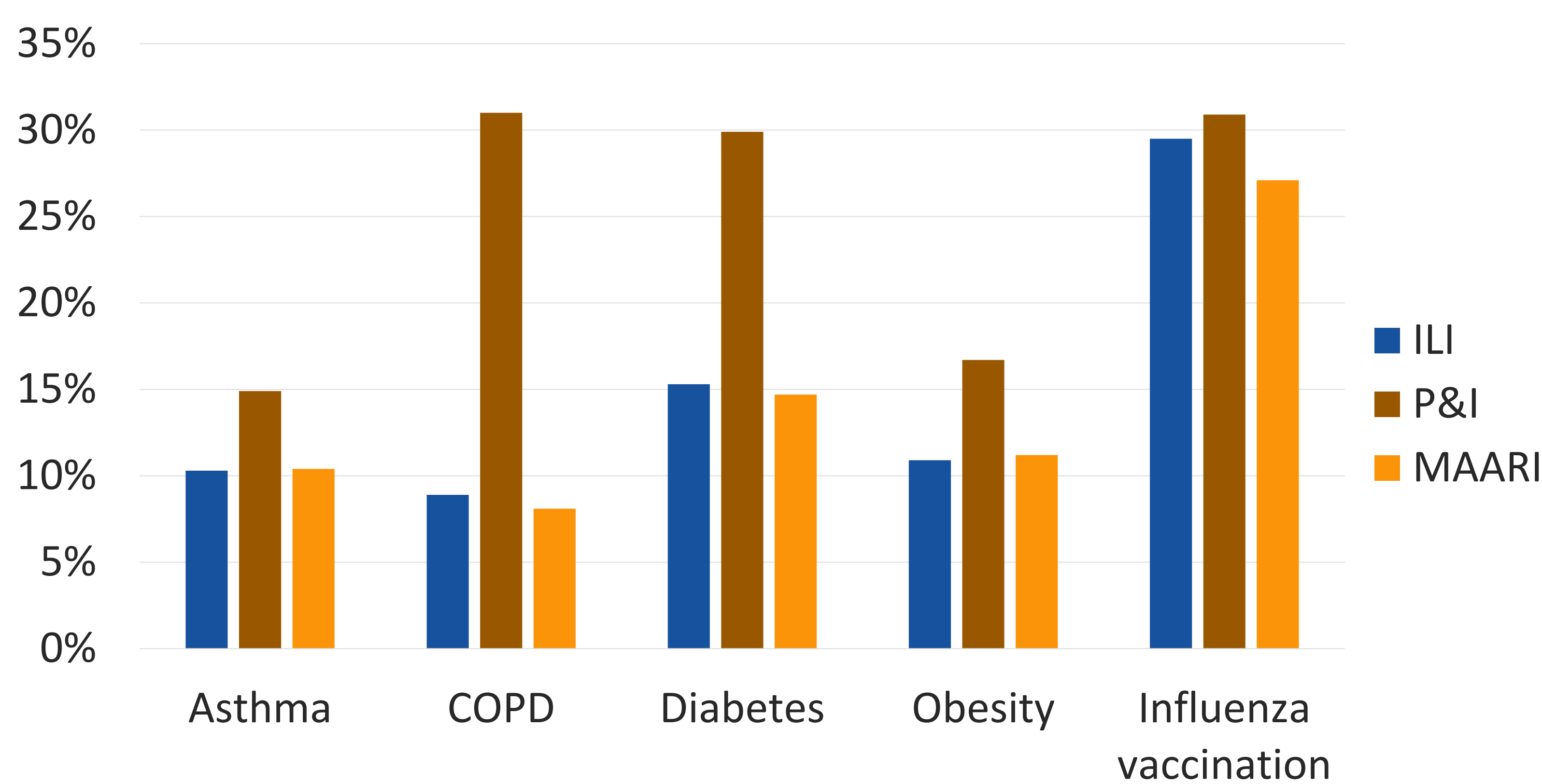


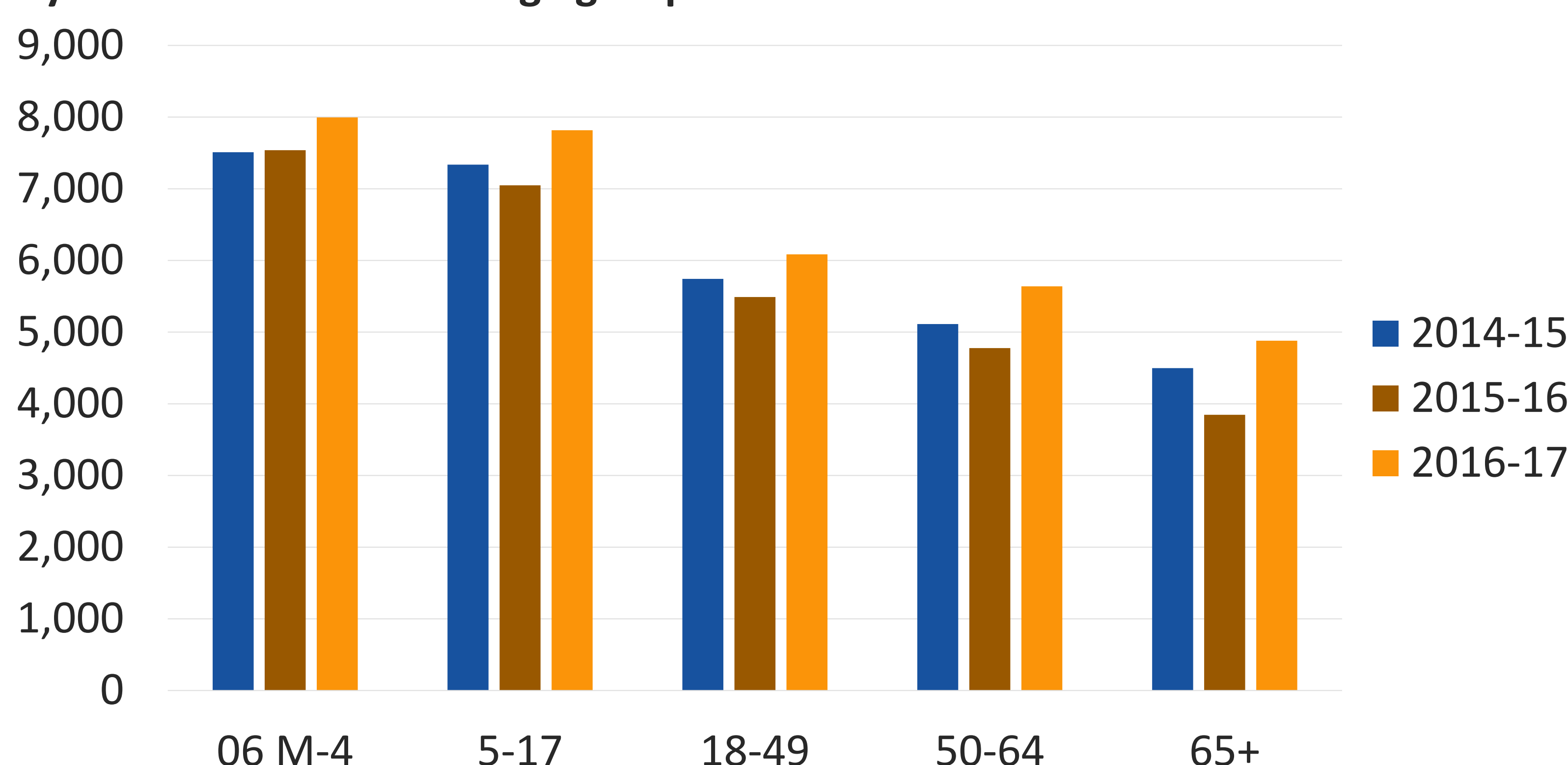
Table 2. Proportion of patients with an influenza vaccination prior to cohort entry, by influenza season

Cohort	July 2014 – June 2015	July 2015 – June 2016	July 2016 – June 2017
ILI	35%	23%	30%
P&I	32%	29%	31%
MAARI	28%	26%	27%

Table 3. Proportion of patients tested for influenza in the 30 days after cohort entry, by influenza season

Cohort	July 2014 – June 2015	July 2015 – June 2016	July 2016 – June 2017
ILI	57%	54%	62%
P&I	20%	13%	20%
MAARI	11%	8%	11%

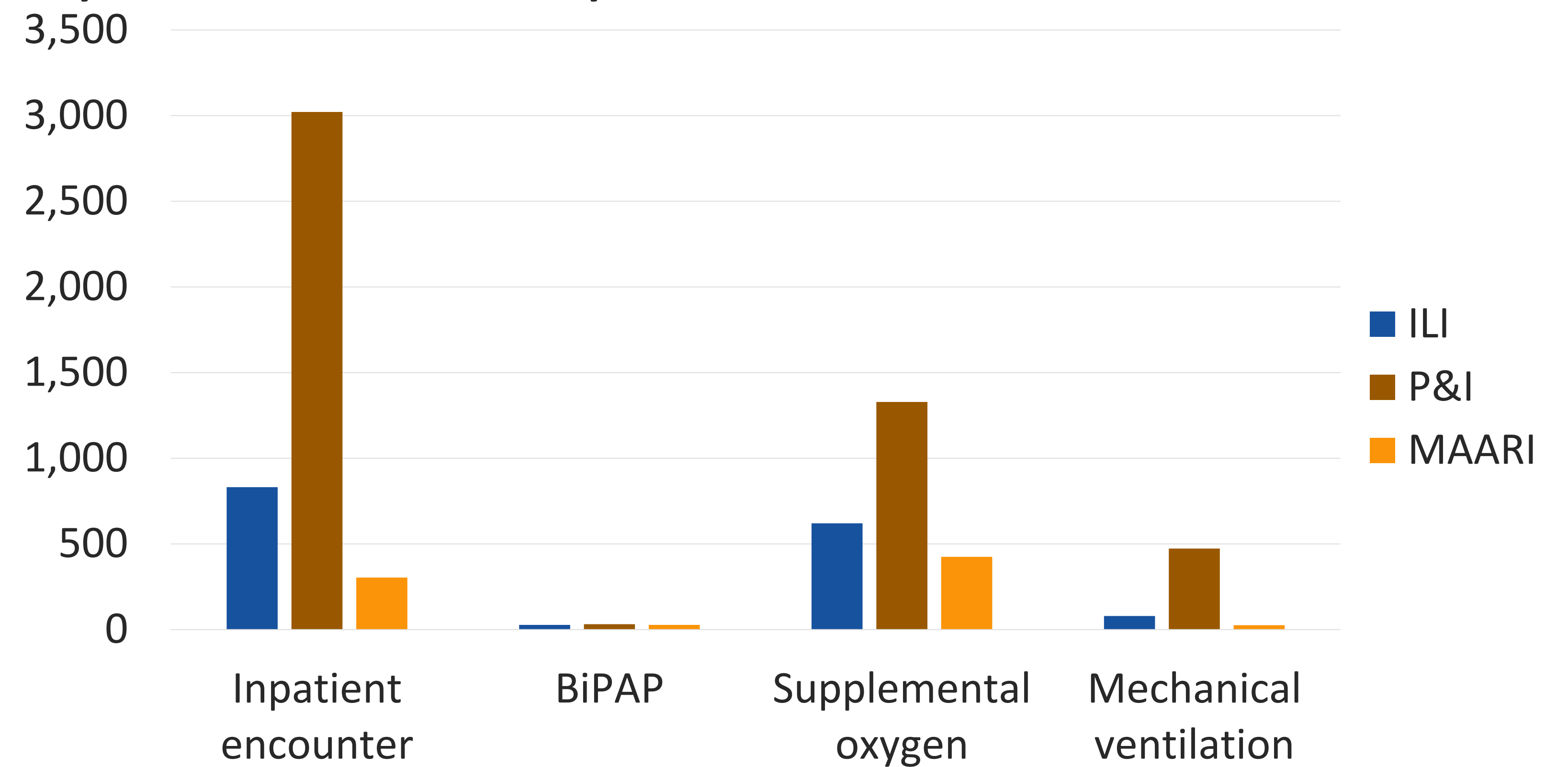
Figure 2. Rates of influenza testing in the 30 days after ILI cohort entry / 10,000, by influenza season and age group



Methods

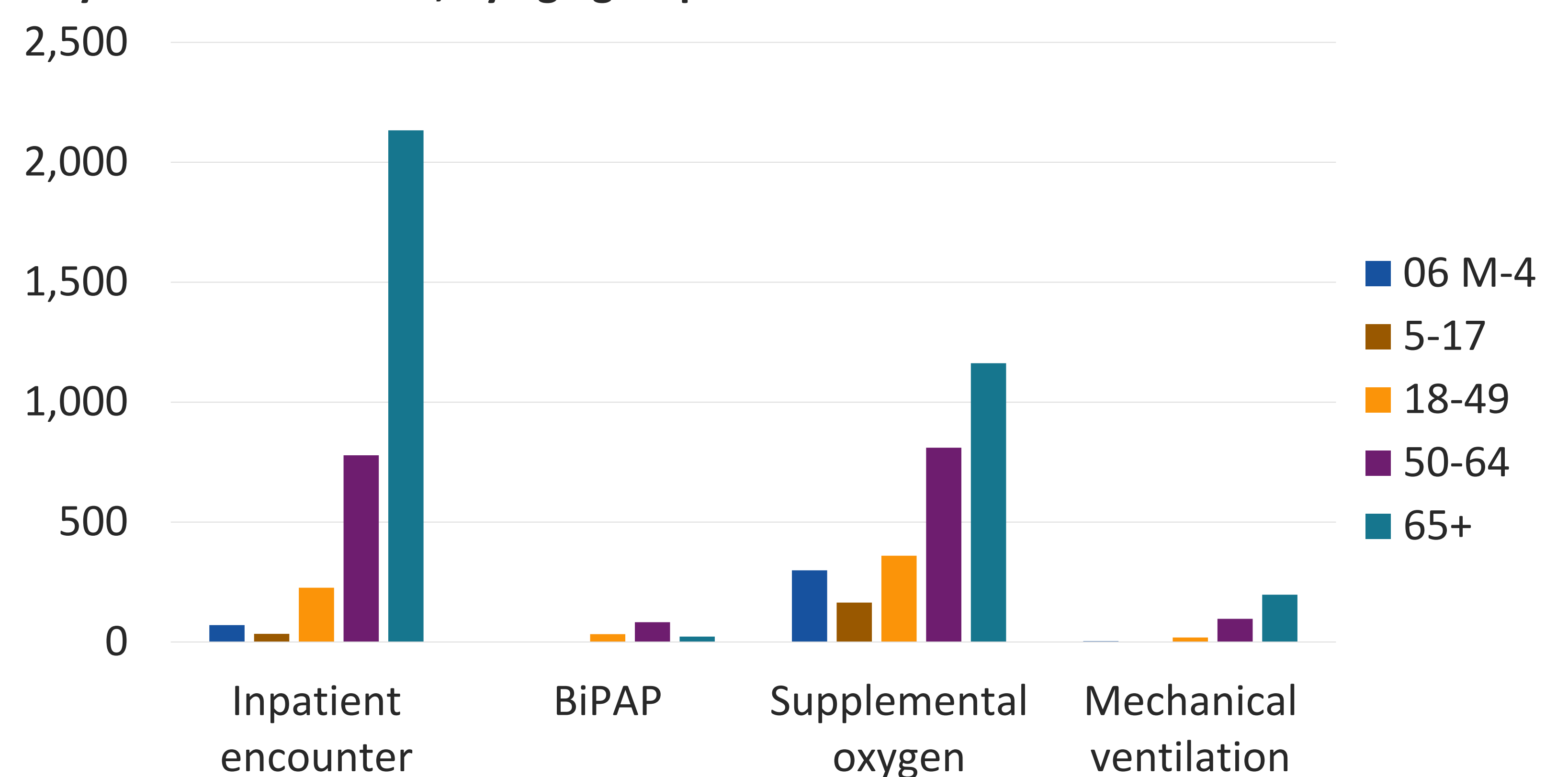
- Members aged ≥ 6 months of age with at least 183 days of continuous enrollment in medical and drug coverage
- Cohort entry diagnosis of incident A) influenza-like illness¹ (ILI), B) pneumonia and influenza² (P&I), or C) medically attended acute respiratory illness³ (MAARI) in the outpatient and emergency department care settings; incidence assessed with respect to a washout of 30 days
- Identified influenza testing in the outpatient and emergency department care settings within 30 days after cohort entry
- Identified ordinal endpoints within 30 days after cohort entry, including: 1) inpatient encounters; administration of 2) biphasic positive airway pressure (BiPAP), 3) supplemental oxygen, and 4) mechanical ventilation; and 5) extracorporeal membrane oxygenation (ECMO)
- Evaluated underlying conditions in the 183 days prior to cohort entry diagnosis
- Three influenza seasons: July 1, 2014 – June 30, 2015; July 1, 2015 – June 30, 2016; July 1, 2016 – June 30, 2017
- Data from 14 participating Data Partners contributing to the Sentinel System

Figure 3. Rates of ordinal endpoints in the 30 days after cohort entry / 10,000, July 1, 2016 – June 30 2017, by cohort



*Rate of ECMO after ILI, P&I, and MAARI cohort entry < 2 / 10,000

Figure 4. Rates of ordinal endpoints in the 30 days after ILI cohort entry / 10,000, July 2016 – June 2017, by age group



Conclusions and Discussion

- Differences in cohort sizes across seasons were expected, as 2014-15 was a moderate influenza season with a poor vaccination match, 2015-16 was mild with a good match, and 2016-17 was moderate with a decent match
- The ILI cohort had the highest rate of influenza testing, with the youngest age groups tested most frequently
- The P&I cohort had the highest proportion of all underlying conditions at baseline and the largest capture of ordinal endpoints
- Ordinal endpoints relevant to MCMs are identifiable in administrative claims data
- Limitation: cohorts were defined by ICD-9/10-CM diagnoses and were not confirmed by laboratory tests
- Limitation: BiPAP rates were lower than expected, likely due to billing practices

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¹Eick-Cost et al. Assessment of ICD-9-based Case Definitions for Influenza-like Illness Surveillance. *MSSMR* 2015; 22(9):2-7.

²Matias et al. Estimates of hospitalization attributable to influenza and RSV in the US during 1997–2009, by age and risk status. *BMC Public Health* 2017; 17(1):271.

³Omer et al. Impact of Statins on Influenza Vaccine Effectiveness Against Medically Attended Acute Respiratory Illness. *JID* 2016; 213(8):1216-23.