

Changes in incidence rates of outcomes of interest in vaccine safety studies during the COVID-19 pandemic

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Outline

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Introduction

The COVID-19 pandemic caused an abrupt drop in in-person health care (inpatient, Emergency Department, outpatient) and a sudden increase in telehealth visits

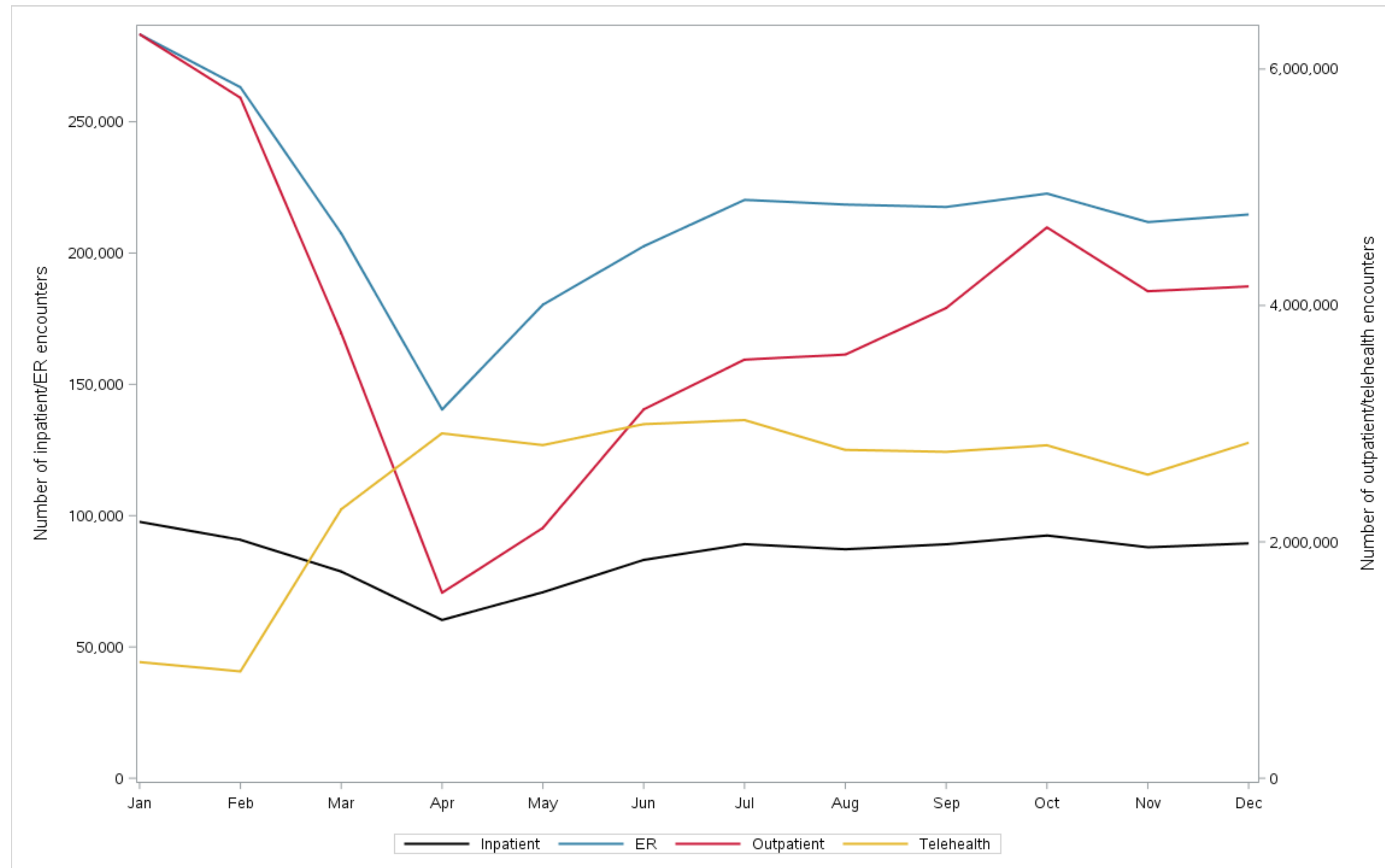


Figure. Healthcare utilization (encounters) in VSD sites before the pandemic and after the start of the pandemic, 2020

Introduction

- Vaccine Safety Datalink (VSD), a collaboration between the Centers for Disease Control and Prevention (CDC) and 8 integrated health systems, conducts vaccine safety studies using large electronic health record databases
- The changes in health care utilization pose significant challenges in ongoing and future vaccine safety studies that identify outcomes of interest using information captured during in-person health care encounters

Objective

To examine the changes in incidence rates of selected outcomes of interest in vaccine safety studies during the COVID-19 pandemic

Outcomes of interest

Acute disseminated encephalomyelitis (ADEM)

Acute myocardial infarction (AMI)

Acute respiratory distress syndrome

Anaphylaxis

Appendicitis

Bell's palsy

Convulsion/seizure

Disseminated intravascular coagulation

Encephalitis/myelitis/encephalomyelitis (EMEM)

Guillain-Barre syndrome (GBS)

Immune thrombocytopenia (ITP)

Kawasaki disease

Myocarditis/pericarditis

Narcolepsy and cataplexy

Pulmonary embolism

Stroke, hemorrhagic

Stroke, ischemic

Thrombocytopenia

Thrombotic thrombocytopenic purpura (TTP)

Transverse myelitis (TM)

Venous thromboembolism (VTE)

Methods

- The study included members from 8 VSD sites from January 1, 2017 through December 31, 2020
- Using ICD-10 diagnosis codes or laboratory criteria, we identified 21 incident outcomes in traditional in-person settings and all settings including telehealth visits
- Defined 4 periods in 2020 and corresponding periods in each year during 2017–2019:
 - January-February (pre-pandemic)
 - April-June (early pandemic)
 - July-September (middle pandemic)
 - October-December (late pandemic)
- Calculated incidence rates of outcomes in each period
- Conducted difference-in-difference analyses and reported ratios of incidence rate ratios (RRR) to examine changes in rates from pre-pandemic to early, middle, and late pandemic in 2020, after adjusting for changes (seasonality) across similar periods in 2017–2019

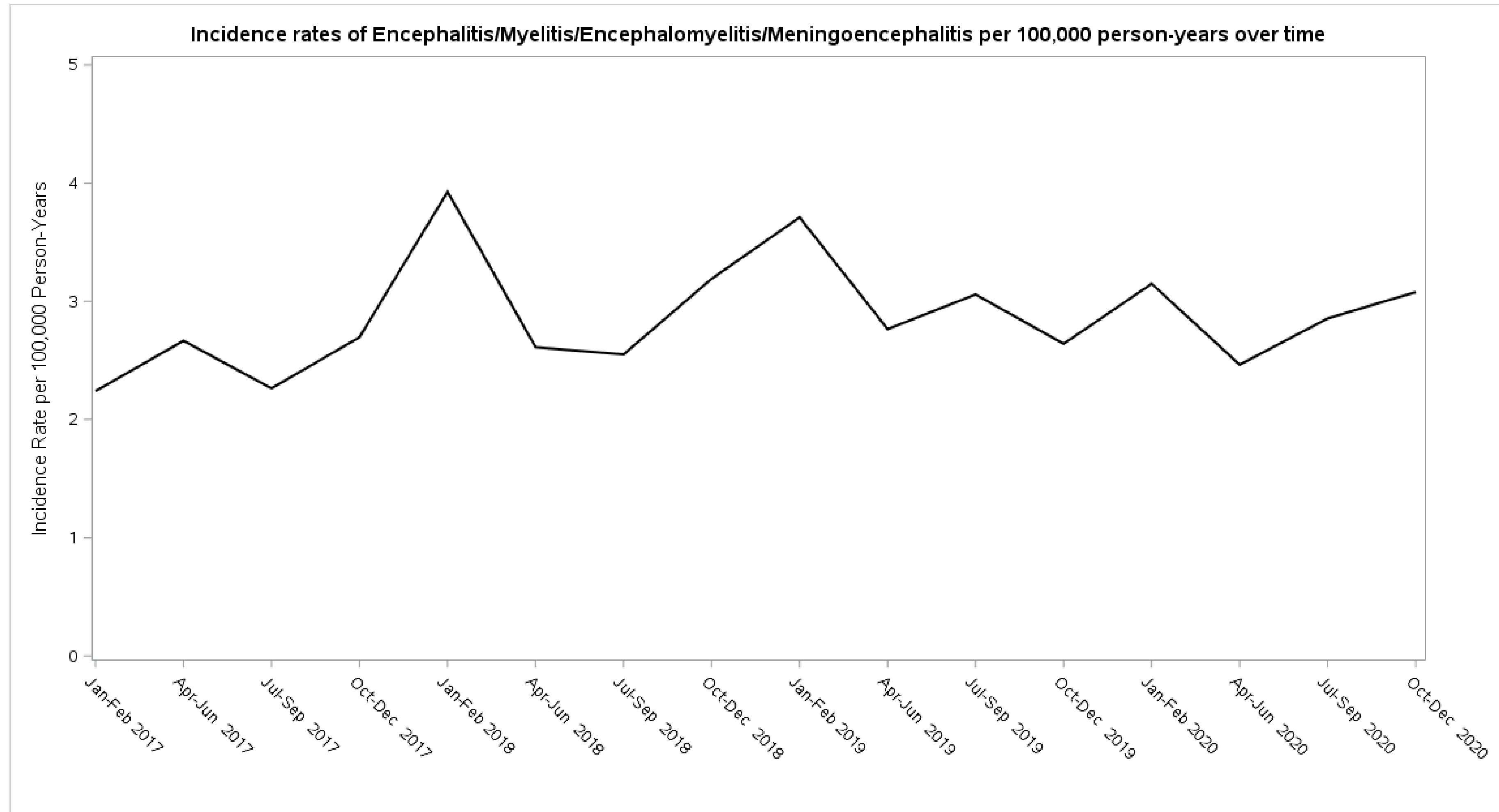
Outcomes without significant changes

Incidence rates of acute disseminated encephalomyelitis (ADEM), encephalitis/myelitis/encephalomyelitis/meningoencephalitis (EMEM), and thrombotic thrombocytopenic purpura (TTP) did not change significantly during the COVID-19 pandemic.

Outcomes	Settings*	Apr-Jun		Jul-Sep		Oct-Dec	
		RRR (95% CI)	p-value	RRR (95% CI)	p-value	RRR (95% CI)	p-value
ADEM	ED, IP	0.74 (0.14, 4.07)	0.73	1.44 (0.32, 6.56)	0.63	0.80 (0.17, 3.69)	0.78
EMEM	ED, IP	0.93 (0.62, 1.39)	0.73	1.11 (0.75, 1.65)	0.59	1.10 (0.75, 1.62)	0.62
TTP	ED, IP	0.58 (0.32, 1.04)	0.07	0.82 (0.47, 1.43)	0.48	0.75 (0.43, 1.32)	0.32

* IP=inpatient, ED=Emergency Department, OP=outpatient

Incidence rates of EMEM



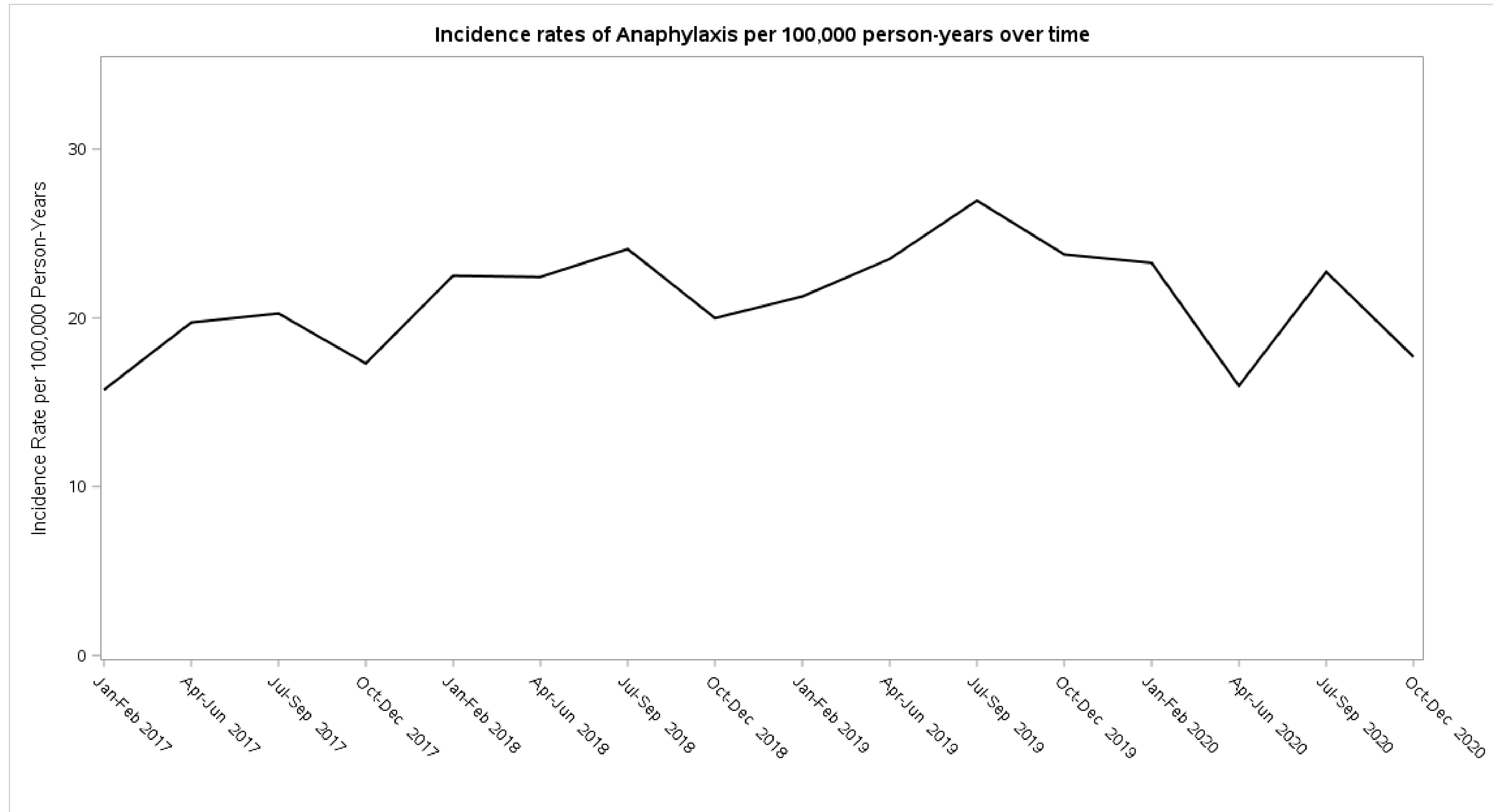
Outcomes with rate reduction

Rate reductions were observed at least during the early pandemic period in 2020 for acute myocardial infarction (AMI), anaphylaxis, appendicitis, Bell's palsy, convulsion/seizure, Guillain-Barre syndrome (GBS), immune thrombocytopenia (ITP), narcolepsy/cataplexy, hemorrhagic stroke, ischemic stroke, and venous thromboembolism (VTE).

Outcomes	Settings*	Apr-Jun		Jul-Sep		Oct-Dec	
		RRR (95% CI)	p-value	RRR (95% CI)	p-value	RRR (95% CI)	p-value
AMI	ED, IP	0.88 (0.82, 0.95)	0.002	1.07 (0.99, 1.15)	0.09	1.10 (1.02, 1.18)	0.02
Anaphylaxis	ED, IP	0.62 (0.53, 0.72)	<.001	0.81 (0.70, 0.94)	0.004	0.74 (0.64, 0.86)	<.001
Appendicitis	ED, IP	0.88 (0.82, 0.93)	<.001	0.97 (0.92, 1.03)	0.36	0.99 (0.93, 1.05)	0.78
Bell's palsy	ED, IP, OP	0.76 (0.71, 0.82)	<.001	0.87 (0.81, 0.93)	<.001	0.88 (0.82, 0.95)	<.001
Convulsion/seizure	ED, IP	0.79 (0.75, 0.84)	<.001	0.88 (0.83, 0.93)	<.001	0.86 (0.81, 0.91)	<.001
GBS	ED, IP	0.64 (0.46, 0.88)	0.006	0.90 (0.66, 1.22)	0.48	0.77 (0.57, 1.05)	0.10
ITP	ED, IP, OP	0.41 (0.35, 0.49)	<.001	0.69 (0.60, 0.80)	<.001	0.74 (0.64, 0.86)	<.001
Narcolepsy/cataplexy	ED, IP, OP	0.29 (0.23, 0.36)	<.001	0.50 (0.41, 0.61)	<.001	0.62 (0.51, 0.76)	<.001
Hemorrhagic stroke	ED, IP	0.86 (0.79, 0.95)	0.003	1.04 (0.95, 1.14)	0.42	1.03 (0.94, 1.13)	0.49
Ischemic stroke	ED, IP	0.81 (0.77, 0.85)	<.001	0.96 (0.91, 1.00)	0.06	0.97 (0.92, 1.01)	0.17
VTE	ED, IP, OP	0.70 (0.66, 0.75)	<.001	0.92 (0.86, 0.97)	0.003	0.97 (0.92, 1.03)	0.31

* IP=inpatient, ED=Emergency Department, OP=outpatient

Incidence rates of Anaphylaxis



Outcomes with significant differences between in-person and all settings

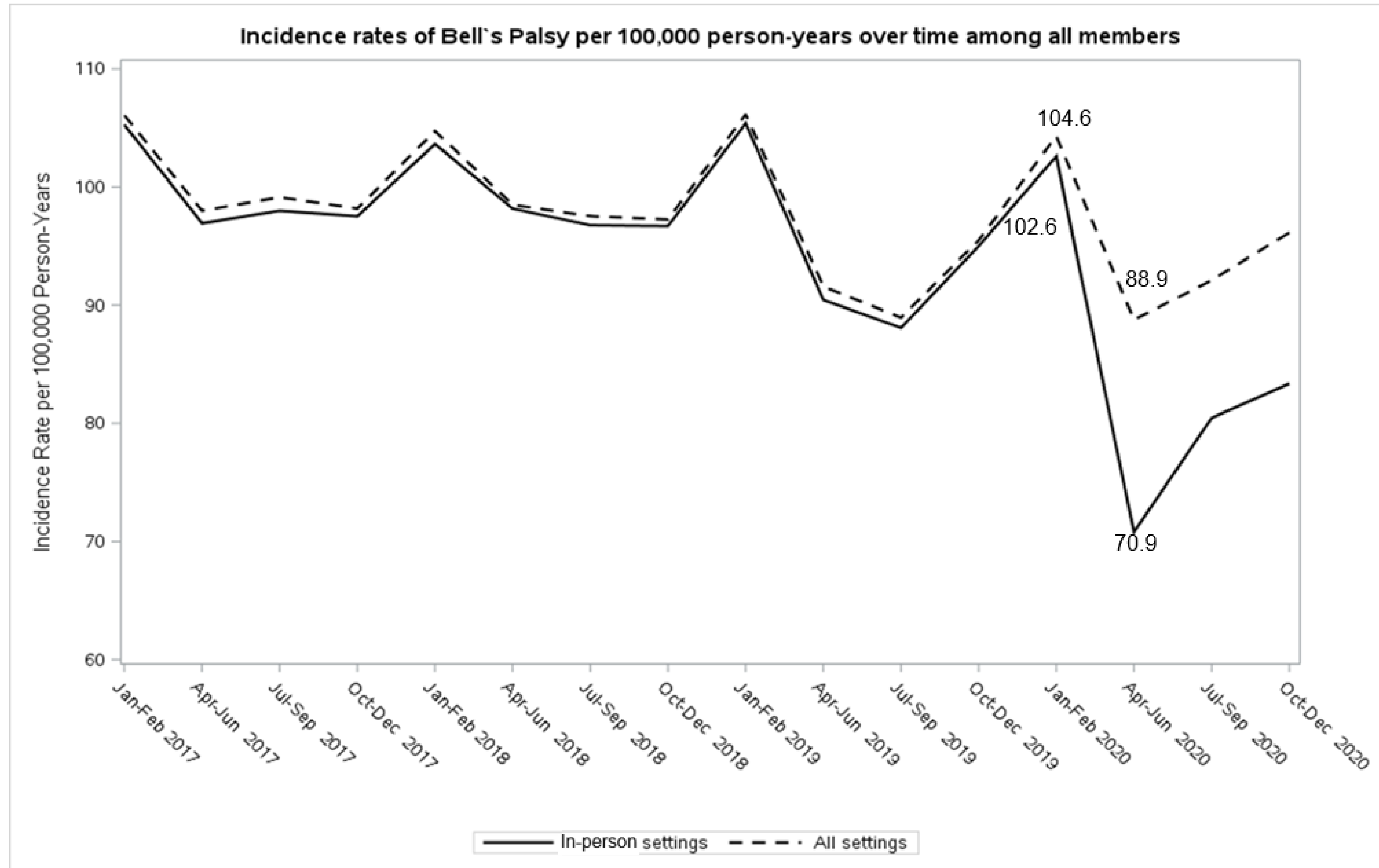
- Incidence rates of Bell's palsy, ITP and narcolepsy/cataplexy were significantly higher in all settings (including telehealth) than in in-person settings during the pandemic.
- Identification of incident cases included the outpatient setting
- Incidence rates in the late pandemic period from all settings returned to the pre-pandemic level

Outcomes	Settings*	Apr-Jun		Jul-Sep		Oct-Dec	
		RRR (95% CI)	p-value	RRR (95% CI)	p-value	RRR (95% CI)	p-value
Bell's palsy	ED, IP, OP	0.76 (0.71, 0.82)	<.001	0.87 (0.81, 0.93)	<.001	0.88 (0.82, 0.95)	<.001
ITP	ED, IP, OP	0.41 (0.35, 0.49)	<.001	0.69 (0.60, 0.80)	<.001	0.74 (0.64, 0.86)	<.001
Narcolepsy/cataplexy	ED, IP, OP	0.29 (0.23, 0.36)	<.001	0.50 (0.41, 0.61)	<.0001	0.62 (0.51, 0.76)	<.001

Outcomes	Settings*	Apr-Jun		Jul-Sep		Oct-Dec	
		RRR (95% CI)	p-value	RRR (95% CI)	p-value	RRR (95% CI)	p-value
Bell's palsy	ED, IP, OP, TH	0.94 (0.88, 1.00)	0.07	0.98 (0.92, 1.05)	0.57	1.00 (0.94, 1.07)	0.89
ITP	ED, IP, OP, TH	0.70 (0.61, 0.81)	<.001	0.89 (0.78, 1.02)	0.10	0.93 (0.81, 1.07)	0.30
Narcolepsy/cataplexy	ED, IP, OP, TH	0.73 (0.61, 0.88)	<.001	0.81 (0.68, 0.97)	0.02	0.96 (0.80, 1.14)	0.62

* IP=inpatient, ED=Emergency Department, OP=outpatient, TH=telehealth

Incidence rates of Bell's Palsy



Conclusions

- Incidence rates of some outcomes of interest changed during the pandemic. When vaccine safety studies are conducted for these outcomes, the use of a historical comparison period during the pandemic should be avoided
- Inclusion of telehealth visits should be considered for vaccine safety outcomes involving the outpatient setting such as Bell's palsy, ITP, and narcolepsy/cataplexy
- Further monitoring of outcomes may be needed to better understand the impact of the COVID-19 pandemic

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