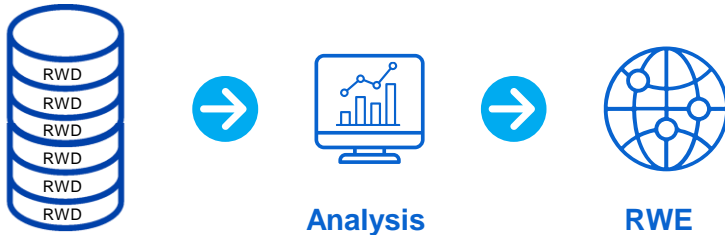# The Role of Real-World Data in Understanding Influenza Disease Burden
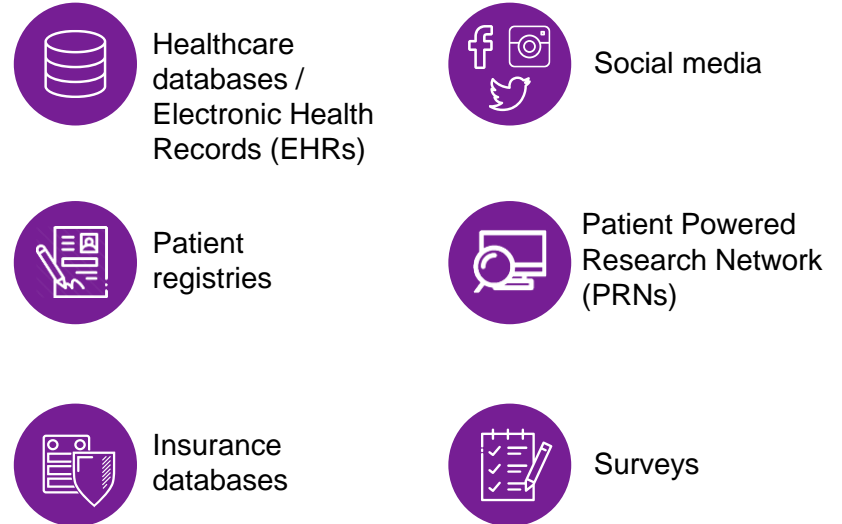
Background on Real World Data (RWD)

RWD provides Real World Evidence (RWE)

- **RWD** denotes data relating to patient or public health, which may be collected actively or passively through routine healthcare practice, surveys, digital monitoring, etc.

- This is in contrast to data generated through conventional clinical trials in dedicated research settings

Insights derived from RWD can be referred to as **RWE**

RWD
RWD
RWD
RWD
RWD
RWD

→ →

Analysis   **RWE**

There are a vast range of sources of RWD

Healthcare databases / Electronic Health Records (EHRs)

Social media

Patient registries

Patient Powered Research Network (PRNs)

Insurance databases

Surveys

There are advantages and limitations to RWD

Advantages

Improved efficiency
- Faster and cheaper vs clinical trials
- Less burden on patient

Deeper insights
- Allows research on high-risk groups
- Detection of less frequent side effects

Rapid access
- Rapid access to information and data
- Accelerated access to healthcare products and services

Insights into real-world patient experience
- Provides data on how treatments are administered in real-world setting as compared to a controlled trial scenario

Limitations

Variables to consider
- No randomization or screening so large number of variables to consider

Data quality, analysis and interpretation
- Data not always fit for purpose and not necessarily measured for research purposes
- Many clinically relevant outcomes not collected/available
- Experienced experts are needed to detect and interpret trends
- Extrapolating findings to other populations can be challenging

Data availability
- Often a lag in data availability (1+ years after event)

Confidentiality and data protection
- Access may be restricted

Seasonal Influenza Has a Significant Clinical and Economic Burden

Clinical Burden of Illness

- Annually, influenza infections occur in **5–20% of the population** in the US[1]
- From 2010–2019, the CDC estimates that the **annual** clinical burden of seasonal influenza ranges from[2]:

9.3–45.0 million
illnesses

4.3–23.0 million
HCP visits

140,000–810,000
hospitalizations

12,000–61,000
deaths*

Economic Burden of Illness

- As a result of influenza infection, there are an annual estimated:

17 million missed work days[3]

38 million missed school days[4,†]

- Influenza epidemics are estimated to cost the US economy

$87 billion/year

in illness (but not medically attended), outpatient visits, hospitalizations, mortality, and time lost from work or premature death[5,‡]
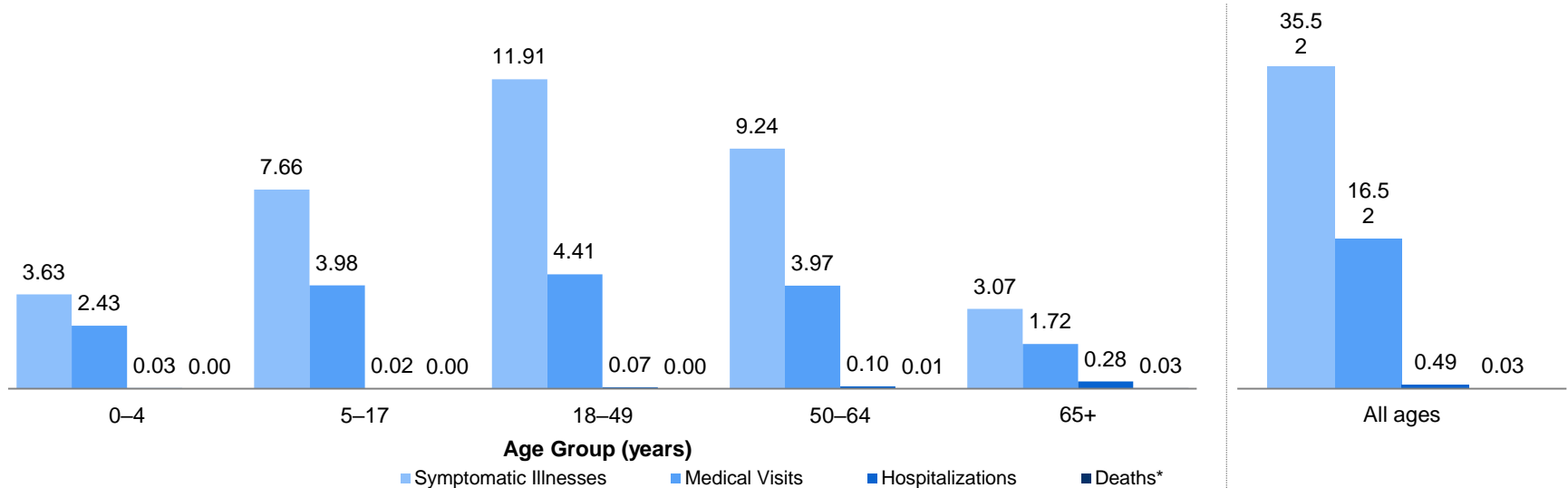
High Burden of Illness During the 2018–2019 Influenza Season

2018–2019 Influenza Severity

- Influenza A viruses were the predominant circulating viruses.
  - Influenza A (H1N1pdm09) viruses predominated from October 2018 – mid February 2019
  - Influenza A(H3N2) viruses more commonly reported starting in late February 2019.
- Moderate severity season based levels of outpatient influenza-like illness, hospitalizations rates, and proportions of pneumonia and influenza-associated deaths

Estimated Influenza Disease Burden by Age Group in the US, *Millions*

Age Group (years)	Symptomatic Illnesses	Medical Visits	Hospitalizations	Deaths*
0–4	3.63	2.43	0.03	0.00
5–17	7.66	3.98	0.02	0.00
18–49	11.91	4.41	0.07	0.00
50–64	9.24	3.97	0.10	0.01
65+	3.07	1.72	0.28	0.03
All ages	35.52	16.52	0.49	0.03

■ Symptomatic Illnesses   ■ Medical Visits   ■ Hospitalizations   ■ Deaths*

*Model uses the frequency of influenza-associated deaths that have cause of death related to pneumonia or influenza, other respiratory or cardiovascular, or other nonrespiratory, noncardiovascular.
https://www.cdc.gov/flu/about/burden/estimates.htm. Accessed May 22, 2020.

5

High-risk Patients Are Most Likely to Develop Influenza-related Complications

High-Risk Patients[1]

- Young children (<5 years, but especially aged <2 years)
- Adults aged ≥65 years
- Individuals residing in nursing homes or other long-term care facilities
- Pregnant women, including up to 2-weeks postpartum
- Individuals with chronic medical* and immunosuppressive conditions
- American Indians and Alaska Natives

Influenza-Related Complications[1,2]

Complications can arise from primary influenza or secondary bacterial infections

Moderate complications

- Sinus infection
- Ear infection
- Bronchitis

Severe complications

- Pneumonia
- Worsening of chronic medical conditions
- Myocarditis

- Encephalitis
- Myositis/rhabdomyolysis
- Multi-organ failure
- Sepsis

*Includes patients with asthma, neurological and neurodevelopmental conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle), chronic lung disease, heart disease, blood disorders, endocrine disorders, kidney disorders, liver disorders, metabolic disorders, people aged <19 years receiving long-term aspirin therapy, and people with extreme obesity (BMI ≥40 kg/m2). BMI=body mass index.
1. https://www.cdc.gov/flu/about/disease/high_risk.htm. Accessed May 22, 2020; 2. https://www.cdc.gov/flu/about/disease/complications.htm. Accessed May 22, 2020.

Diabetic patients with influenza have higher health resource needs

Compared to non-flu controls over the first 3 months after infection, diabetic patients with influenza had:

| Higher medical expenditure | More hospitalizations | More acute complications |

Requirements for higher medical expenditure and more hospitalizations remained in these patients at the end of the year

Compared to non-flu controls over the following year, more diabetic patients in the flu cohort had
- Been newly diagnosed with a cardiovascular complication
- Increased Diabetes Complications Severity Index (DCSI) score

Influenza could have a sustained negative impact on both health resource utilization as well as worsening of diabetes-related chronic complications

Database *US commercial claims data from the 2016–17 flu season, comparing the HRU and incidence of complications among T2DM patients (flu vs. non-flu)*

Lewing, et al. AMCP 2020 Short-and Long-Term Impact of influenza Infection on Health Resource Utilization and Diabetes Complications of Type 2 Diabetes Patients

AMCP- Academy of Managed Care Pharmacy; DCSI-Diabetes Complications Severity Index; HRU-health resource utilization; T2DM-Type 2 diabetes mellitus

COPD patients with flu have worse outcomes and increased use of healthcare resources

- COPD patients with influenza have **more emergency department visits** and **more long-term inpatient visits** over the following year, compared with those without influenza

- Influenza significantly increased the number of **COPD exacerbations, COPD-related ED visits** and inpatient visits up to a year after infection, compared with those without influenza

These findings suggest an influenza-induced, long-term, sustained deterioration of respiratory-related health in patients with underlying COPD, and highlight a significant unmet need in this high-risk population

Database *Truven MarketScan® Commercial Claims and Encounters Database and the MarketScan® Medicare Supplemental and Coordination of Benefits Database (IBM Watson Health, Cambridge, MA)*

Wallick, et al. ISIRV-AVG 2018 Impact of Influenza on the Short-and Long-Term Health of Patients with Chronic Obstructive Pulmonary Disease

COPD-chronic obstructive pulmonary disease

Patients with pneumonia co-infected with influenza have worse outcomes and increased healthcare needs

Compared to those without co-infection, hospitalized influenza patients who also contracted bacterial pneumonia spent longer:

In hospital

In intensive care

On a ventilator

These patients also had poorer performance on an ordinal endpoint scale than the overall flu cohort

Co-infection with bacterial pneumonia leads to poor outcomes and increased burden on healthcare resources in hospitalized influenza patients

Database *Premier healthcare database from October 2009 – May 2018 in hospitals with continuous enrollment of more than one patient per year with microbiology data*

Keebler, et al. OPTIONS X 2019 Pneumonia among Patients Hospitalized with Influenza in the United States, 2009–2018