CDC AFM Update

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Measles, Mumps, Rubella, Herpesvirus, and Polio Domestic Epidemiology Team
Division of Viral Diseases
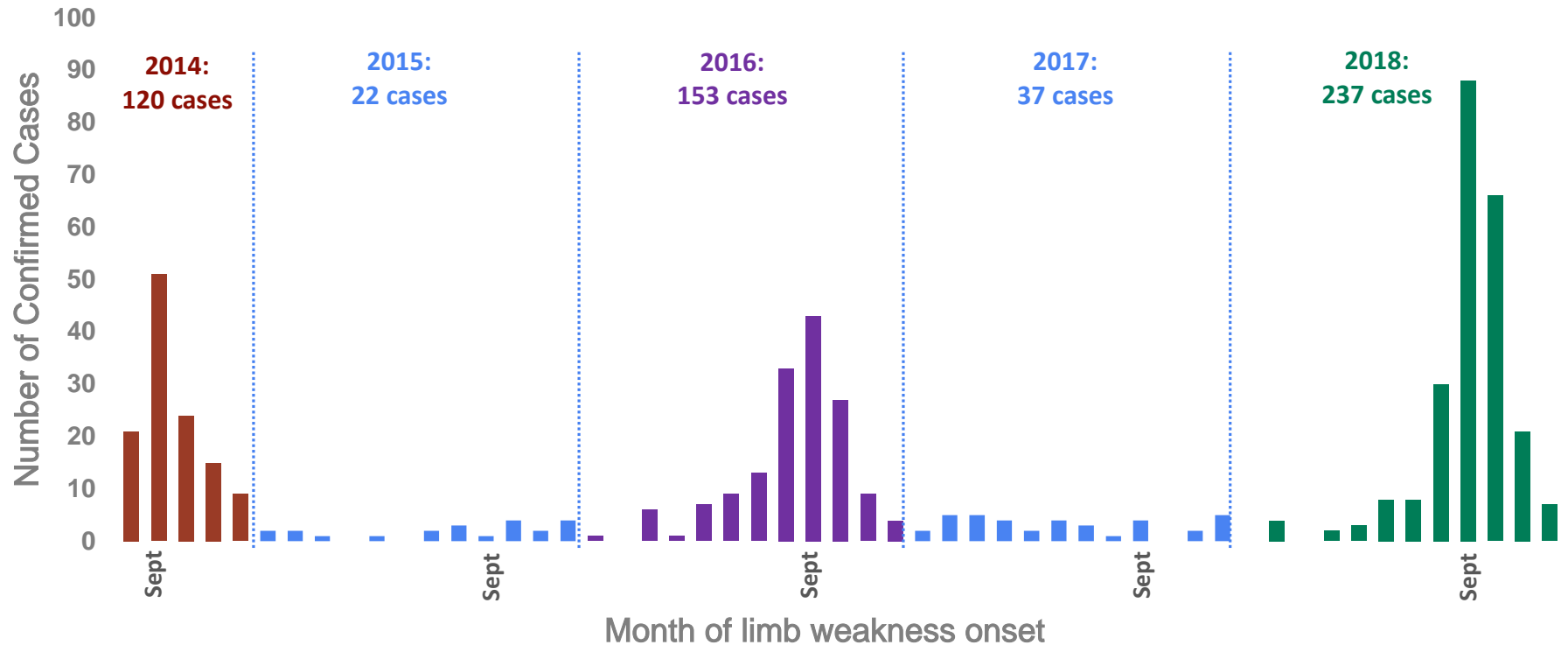**National Center for Immunization and Respiratory Diseases**

Board of Scientific Counselors Meeting

December 5, 2019

Background

National increase in AFM cases every 2 years since 2014

Number of confirmed reported AFM cases, Aug 2014 – December 2018 (n=569)

2014:
120 cases

2015:
22 cases

2016:
153 cases

2017:
37 cases

2018:
237 cases

Number of Confirmed Cases

Month of limb weakness onset

Sept

https://www.cdc.gov/acute-flaccid-myelitis/cases-in-us.html

AFM presents with rapid onset of limb weakness and spinal cord grey matter lesions
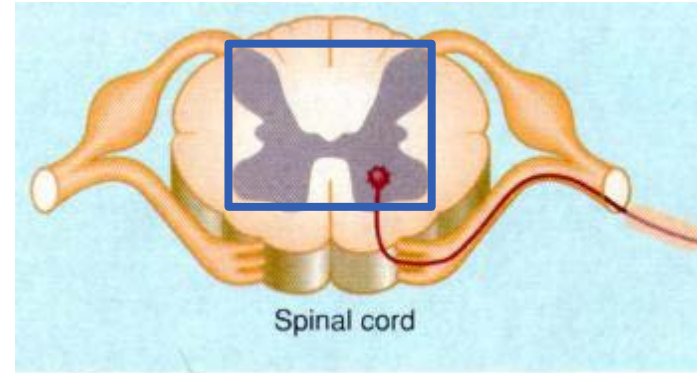
Sudden limb weakness

Difficulty with swallowing or speaking
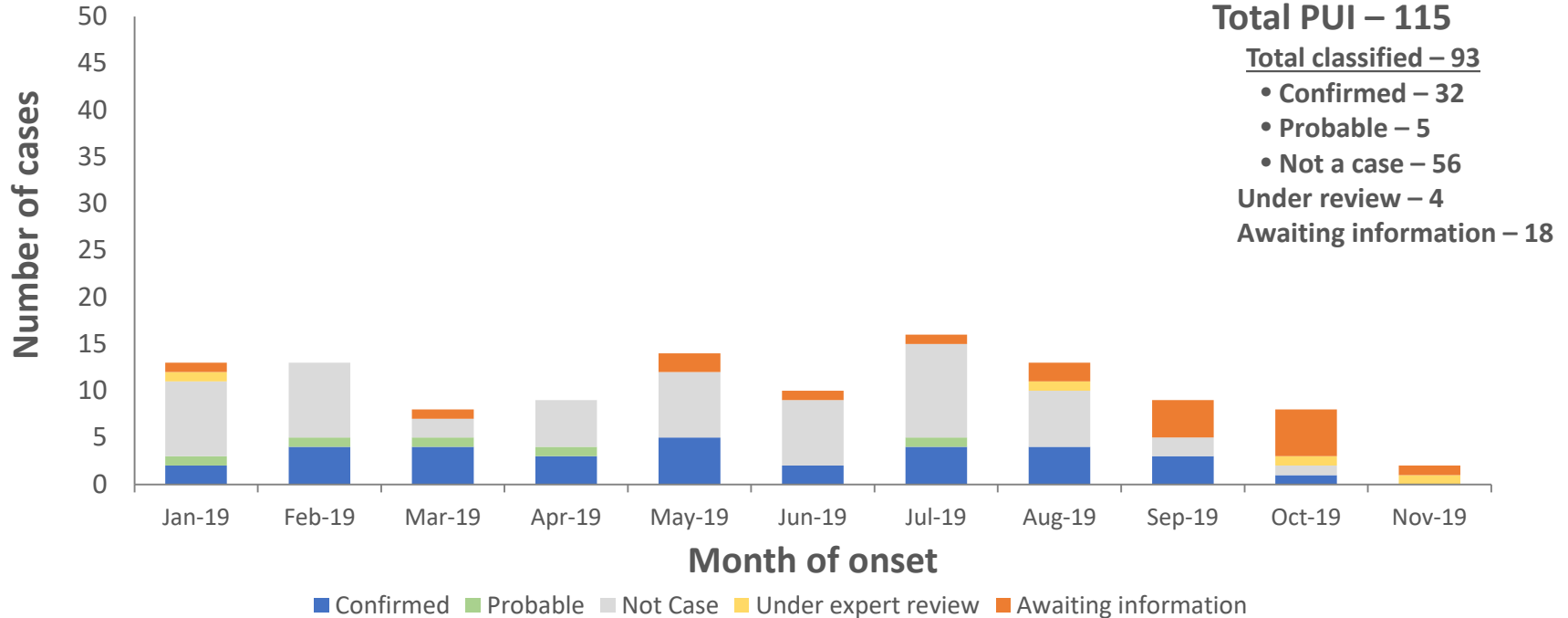
Facial droop or weakness

Ptosis

Spinal cord

- Lesions in spinal grey matter, particularly anterior horn cell distribution
- Cervical spinal cord most affected

2019 AFM epidemiology

2019 looks like another non-peak year for AFM activity

Number of U.S. AFM patients under investigation reported to CDC by case status and month of onset, Jan-Nov 26, 2019

Total PUI – 115
Total classified – 93
• Confirmed – 32
• Probable – 5
• Not a case – 56
Under review – 4
Awaiting information – 18

Lack of geographic clustering of 2019 AFM cases

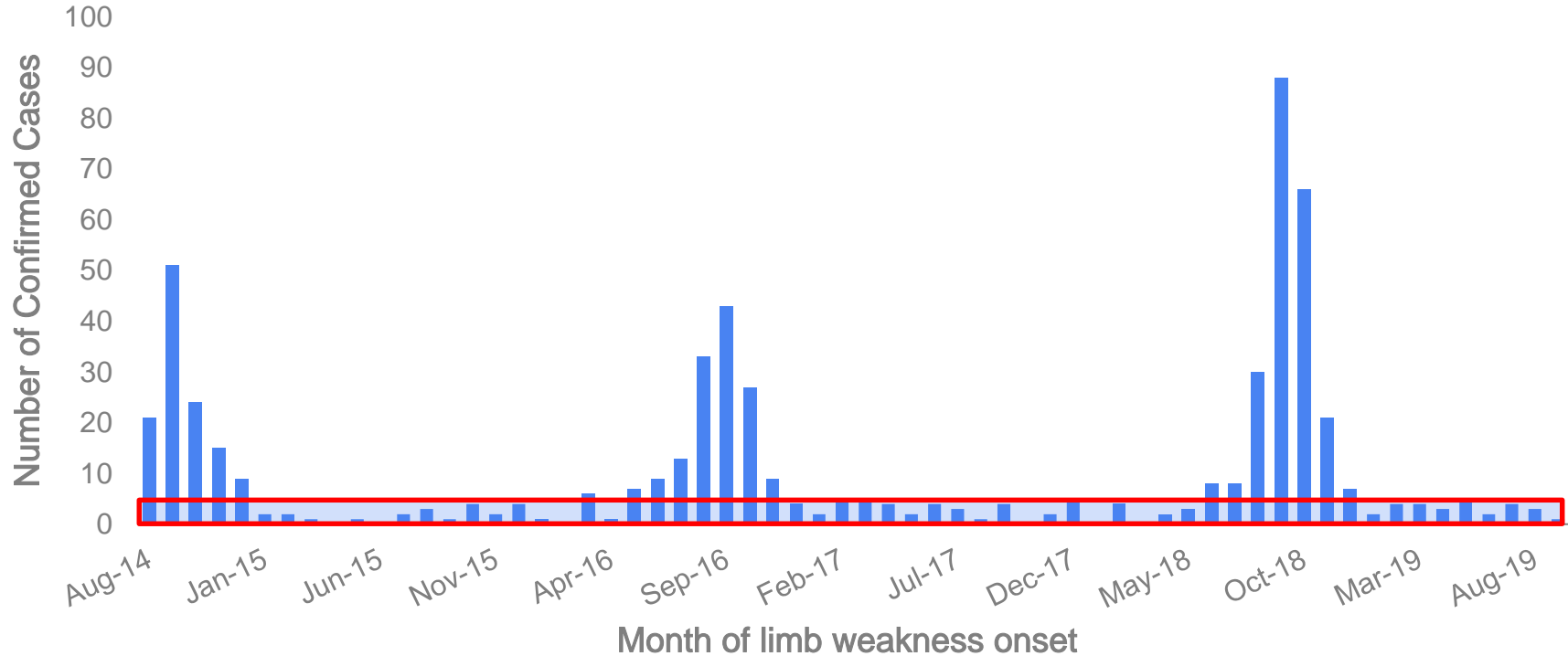## 2019 confirmed cases of acute flaccid myelitis (AFM) by state (N=32)
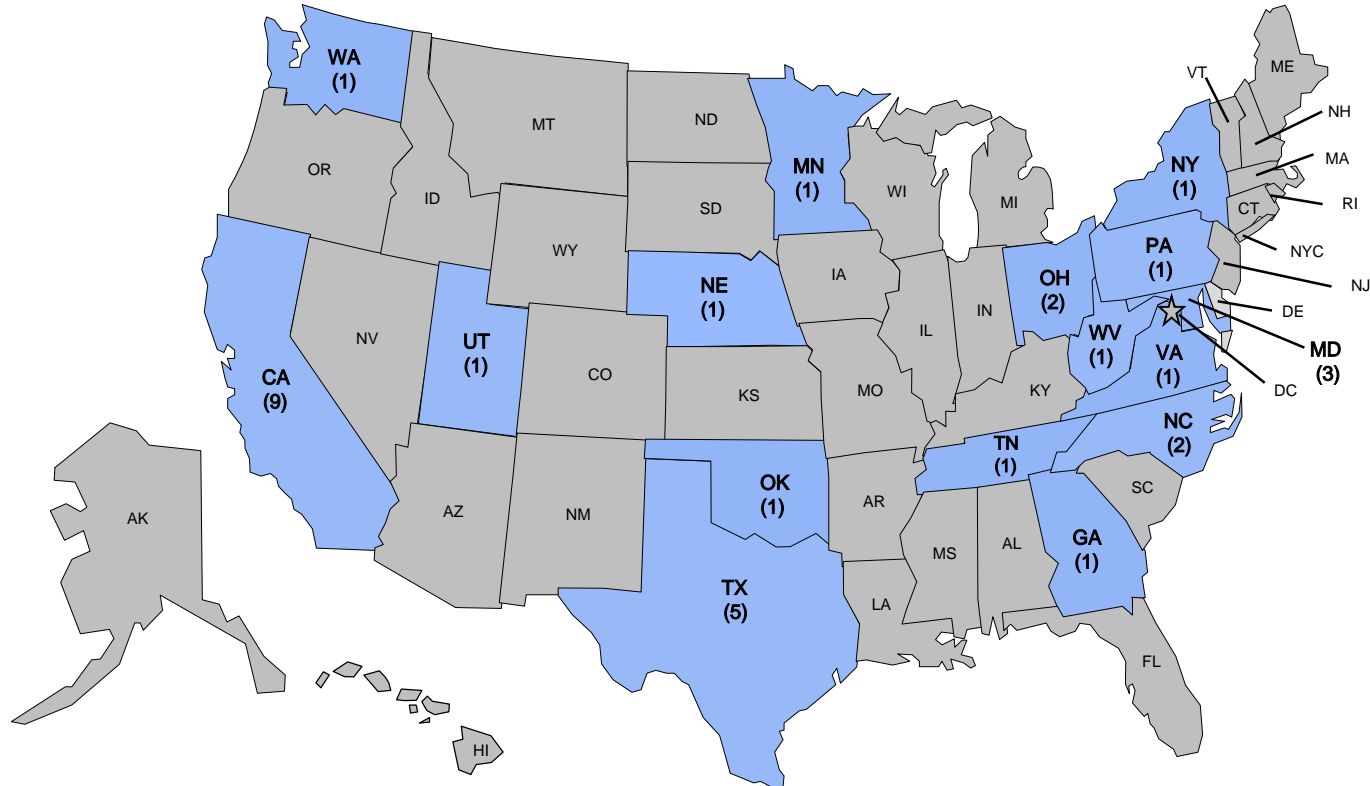
*Confirmed AFM cases as of Nov. 26, 2019. Patients under investigation are still being classified, and the case counts are subject to change.
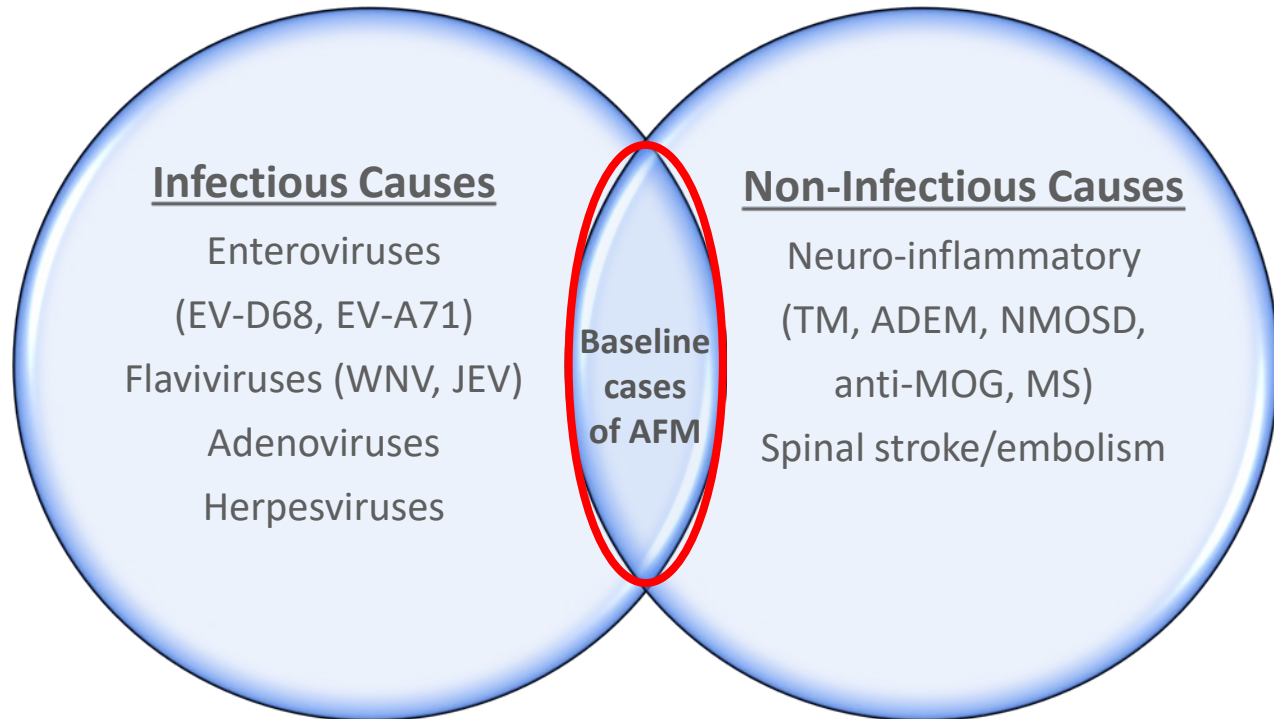
Evidence for a viral etiology

U.S. surveillance shows a consistent baseline rate of AFM

Number of confirmed reported AFM cases, Aug 2014 – Sept 2019 (n=597)

https://www.cdc.gov/acute-flaccid-myelitis/cases-in-us.html

Baseline cases of AFM have multiple causes

Infectious Causes

Enteroviruses

(EV-D68, EV-A71)

Flaviviruses (WNV, JEV)

Adenoviruses

Herpesviruses

Baseline cases of AFM

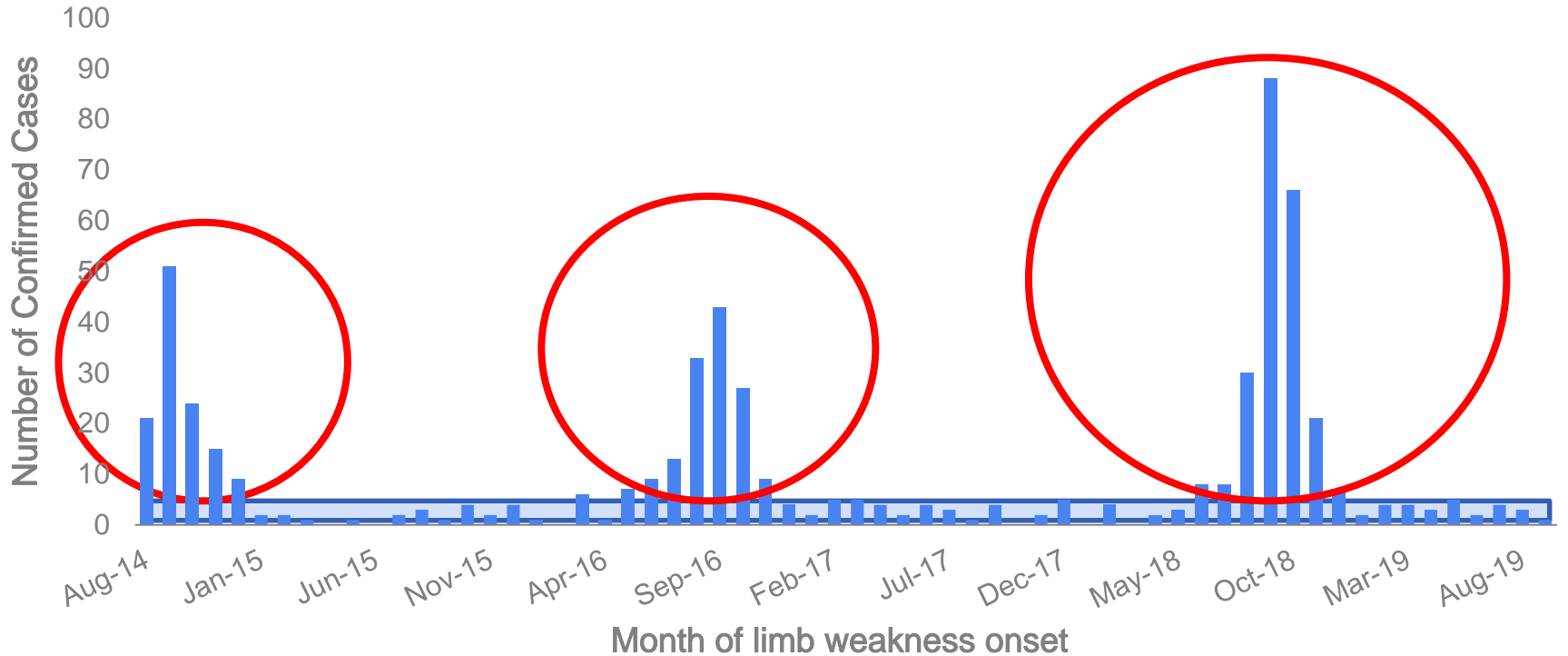**Non-Infectious Causes**

Neuro-inflammatory

(TM, ADEM, NMOSD,
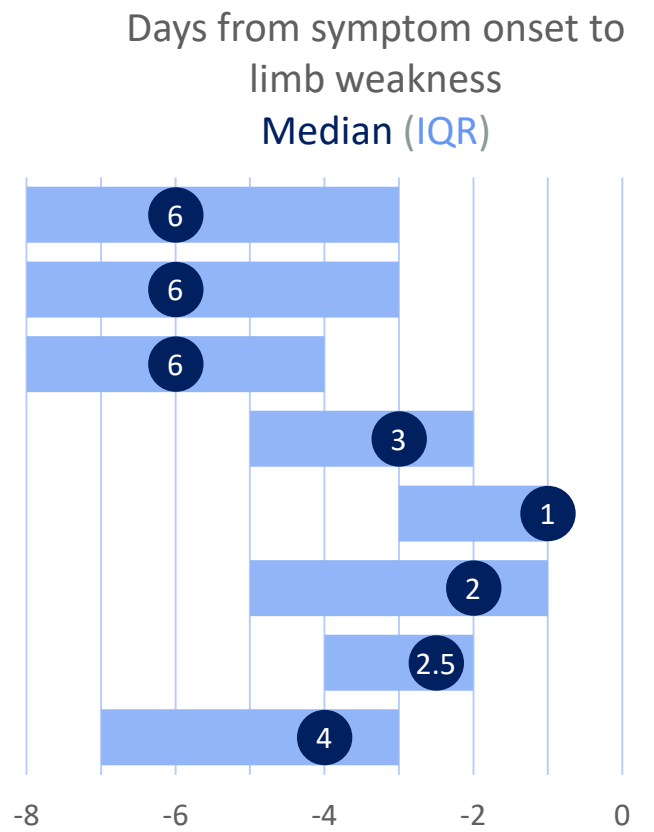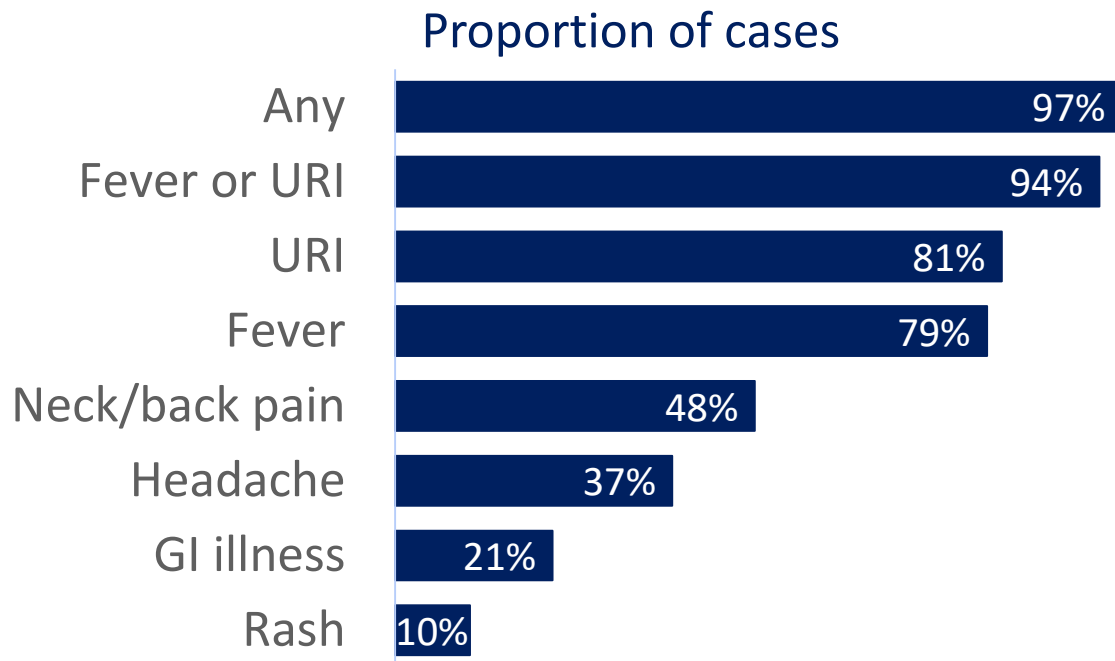
anti-MOG, MS)

Spinal stroke/embolism

What is causing the biennial peaks in AFM?

Number of confirmed reported AFM cases, Aug 2014 – Sept 2019 (n=597)

97% of AFM cases have symptoms of a viral illness

Among 228 confirmed AFM cases with onset in 2018

Days from symptom onset to limb weakness
Median (IQR)

Proportion of cases

Symptom	Proportion	Days (Median)
Any	97%	6
Fever or URI	94%	6
URI	81%	6
Fever	79%	3
Neck/back pain	48%	1
Headache	37%	2
GI illness	21%	2.5
Rash	10%	4

-8   -6   -4   -2   0

Kidd, et al. CDC preliminary data

AFM diagnostic testing remains low yield

CDC testing results, 2018
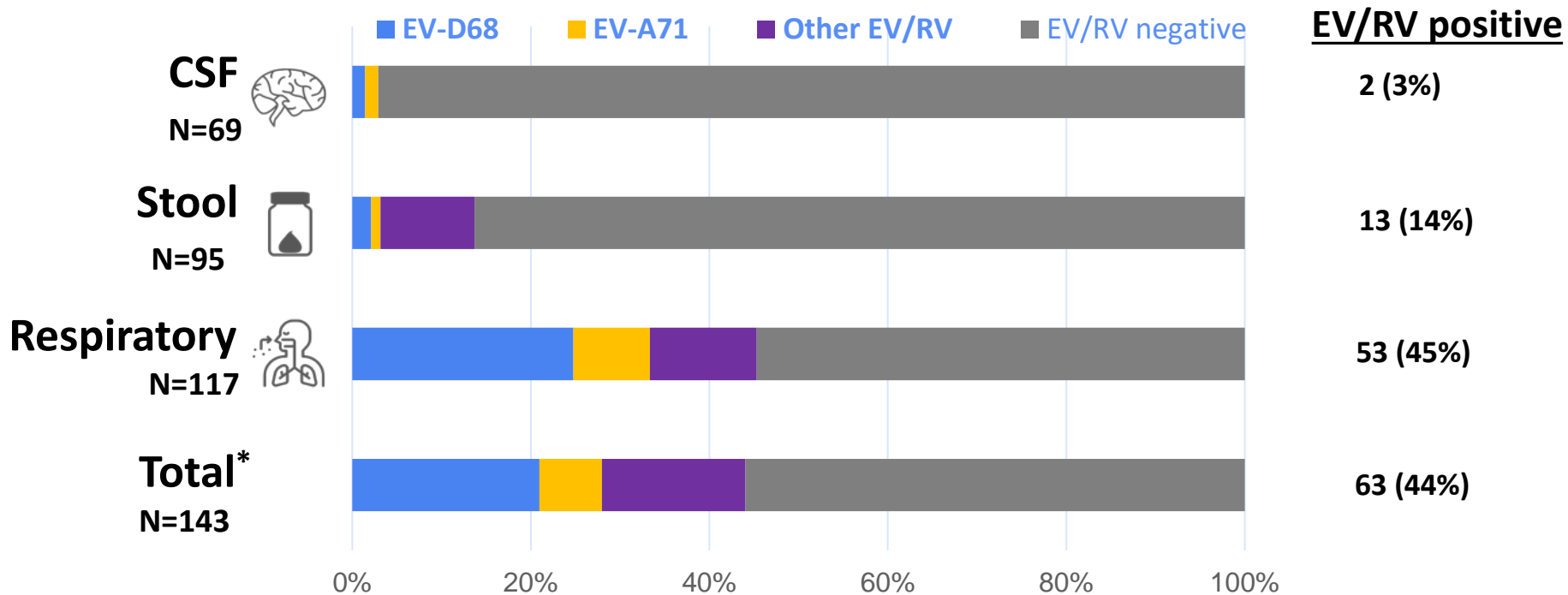
*Some patients had multiple positive specimens

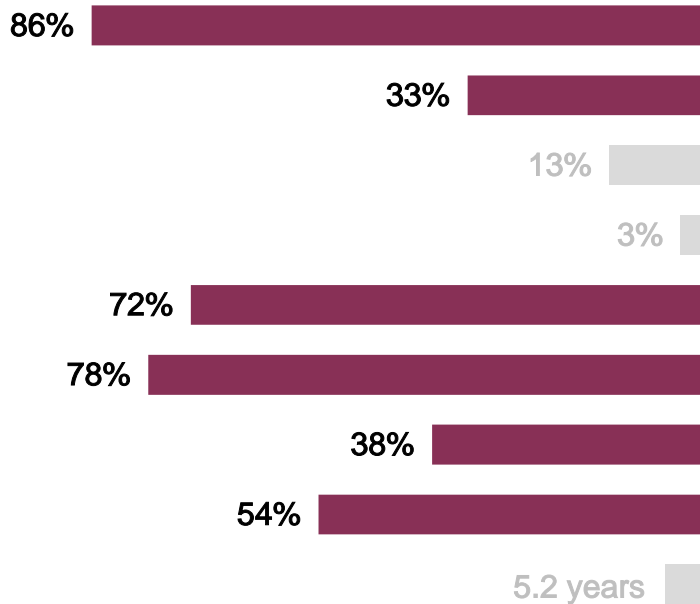Lopez, et al. Vital Signs: Surveillance for Acute Flaccid Myelitis – US, 2018, MMWR 2019
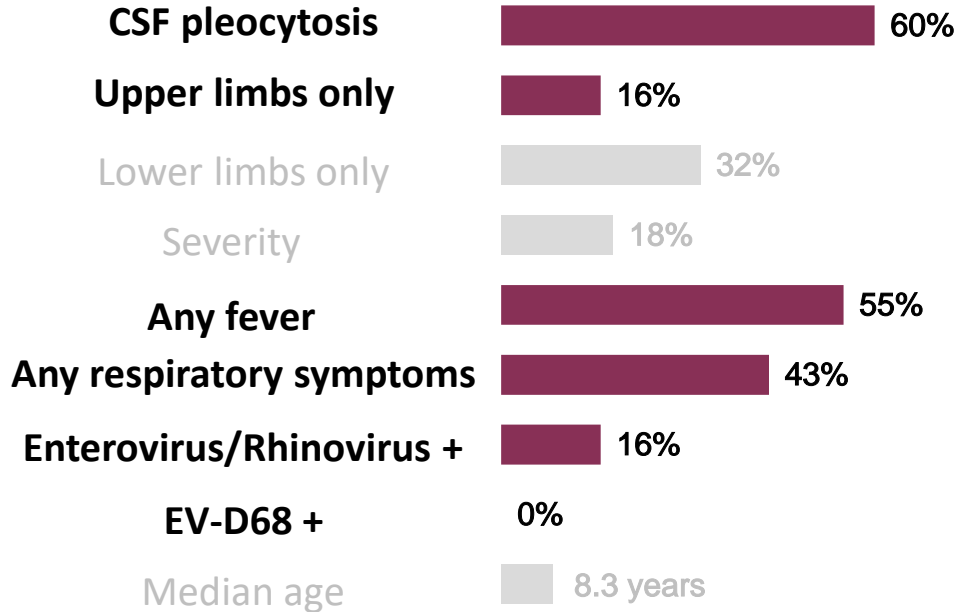
AFM cases in peak years are different from non-peak years

– **More pleocytosis, upper extremity weakness, preceding illness, EV/RV and EV-D68 +**

2016 and 2018

2015 and 2017

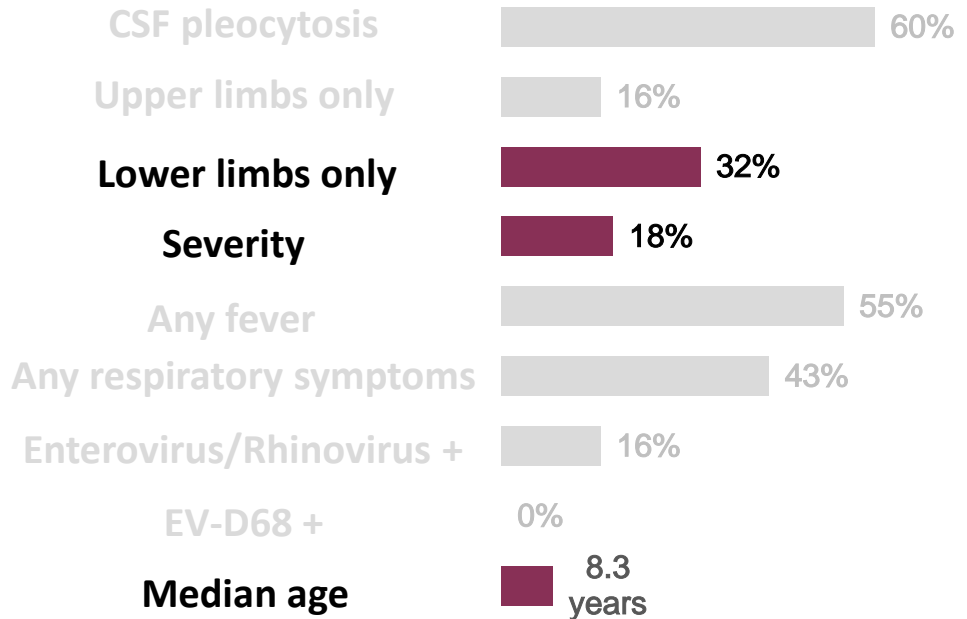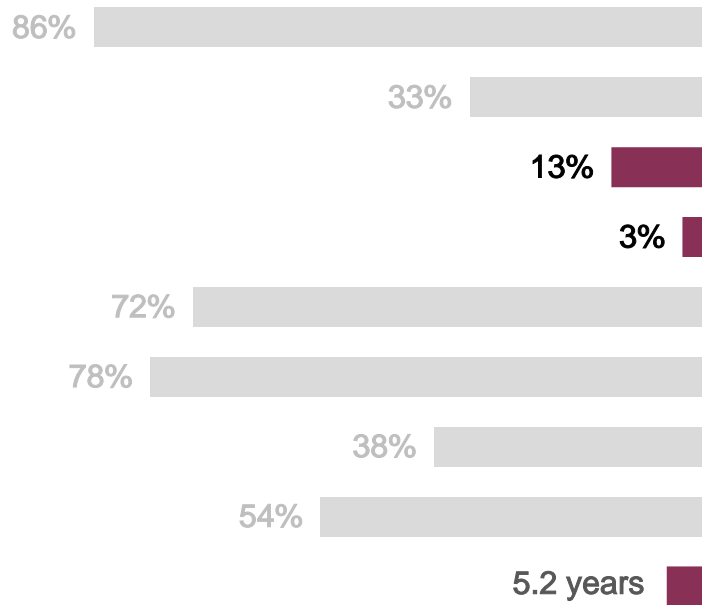| 2016 and 2018		2015 and 2017
86%	**CSF pleocytosis**	60%
33%	**Upper limbs only**	16%
13%	Lower limbs only	32%
3%	Severity	18%
72%	**Any fever**	55%
78%	**Any respiratory symptoms**	43%
38%	**Enterovirus/Rhinovirus +**	16%
54%	**EV-D68 +**	0%
5.2 years	Median age	8.3 years

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AFM cases in non-peak years have more lower extremity weakness, are more severe and older

2016 and 2018

2015 and 2017

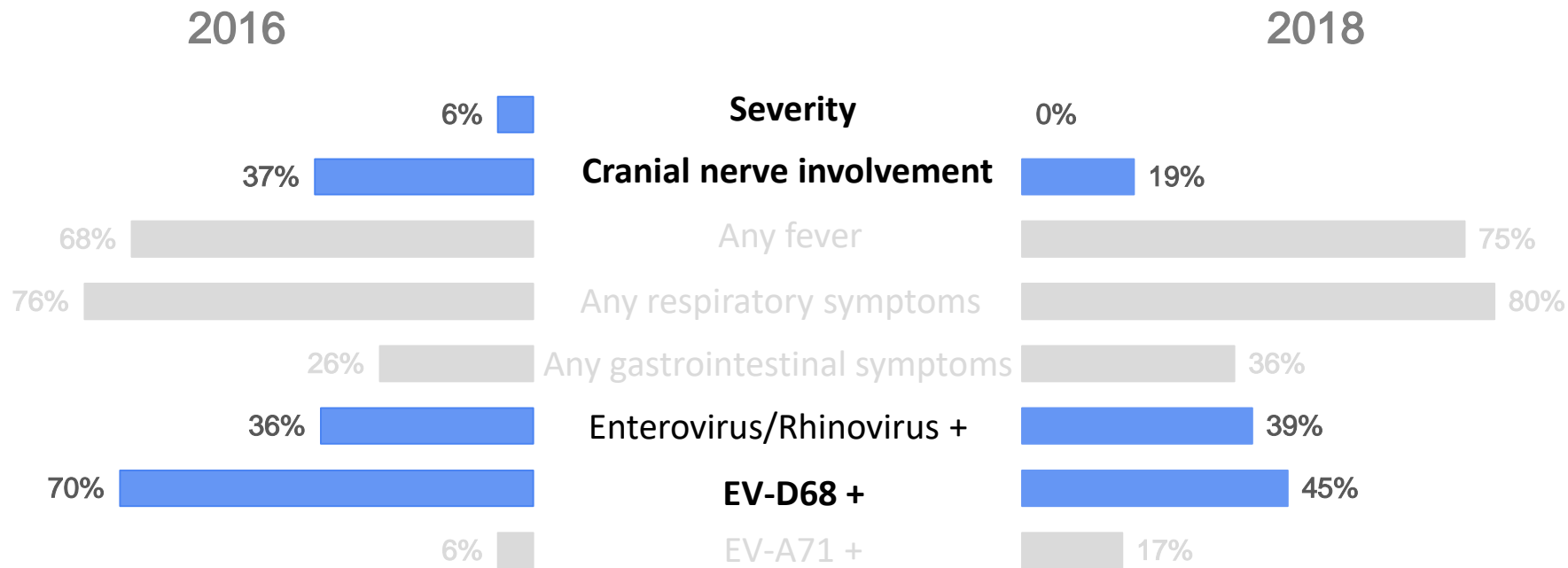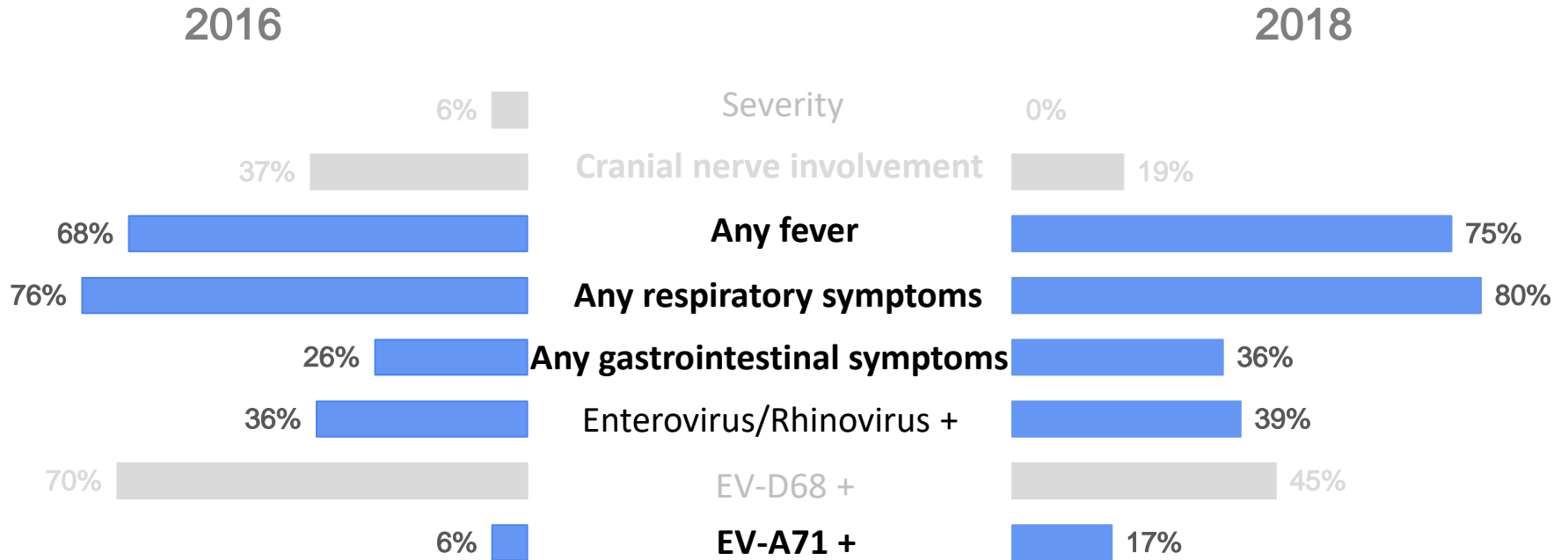| 2016 and 2018		2015 and 2017
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5.2 years	**Median age**	8.3 years

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AFM cases during peak years also have differences

– 2016 cases had more severity, cranial nerve involvement and EV-D68 +

2016		2018
6%	**Severity**	0%
37%	**Cranial nerve involvement**	19%
68%	Any fever	75%
76%	Any respiratory symptoms	80%
26%	Any gastrointestinal symptoms	36%
36%	Enterovirus/Rhinovirus +	39%
70%	**EV-D68 +**	45%
6%	EV-A71 +	17%

Preceding illness and EV-A71 detections greater in 2018 cases

2016   **2018**

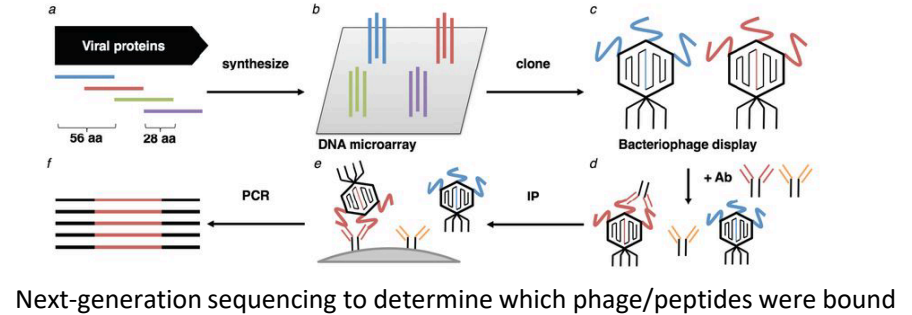| 2016	Category	2018
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68%	**Any fever**	75%
76%	**Any respiratory symptoms**	80%
26%	**Any gastrointestinal symptoms**	36%
36%	Enterovirus/Rhinovirus +	39%
70%	EV-D68 +	45%
6%	**EV-A71 +**	17%

Enterovirus-binding antibodies in CSF of AFM patients

- **SeroChip (peptide microarray)**

1. Block and add serum/plasma sample
2. Wash and add detecting antibody
3. Wash, dry and scan
4. Data Analysis

- Proteins
- Antibodies in serum/plasma (primary)
- Florescence anti-antibody (detecting secondary)

- **VirScan (phage display)**

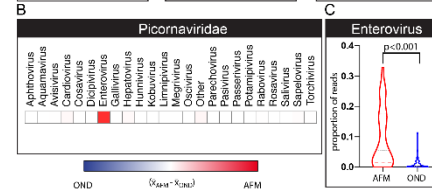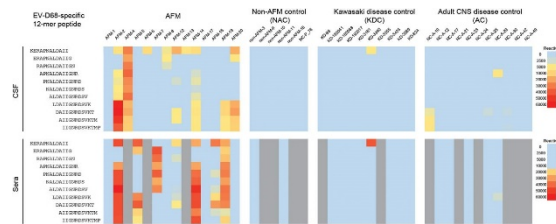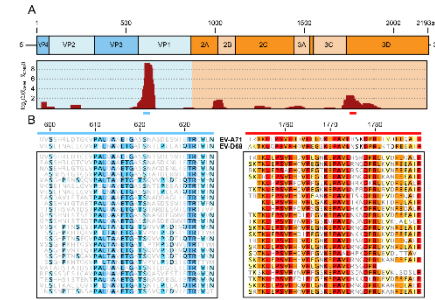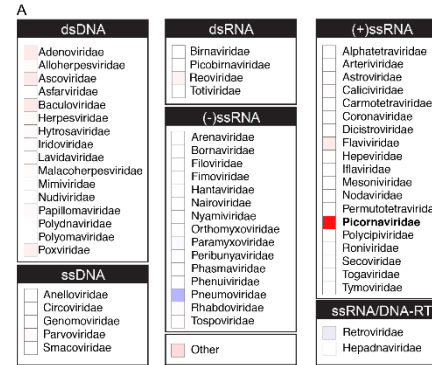Next-generation sequencing to determine which phage/peptides were bound
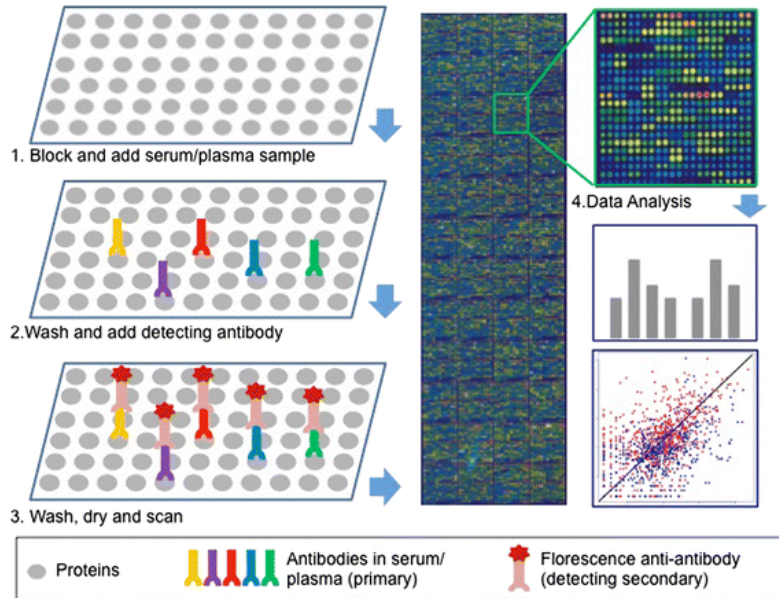
- Tested 14 paired CSF and serum samples from AFM patients in both assays
- VirScanstudy tested CSF from additional cases
- Limitation: Control patients were not ideal

SeroChip method: Tokarz et al., Sci Rep 2018;8:3158; **VirScan method:** Xu at al., Science 2015;348:aaa0698

Enterovirus-binding antibodies in CSF of AFM patients

- **SeroChip (160,000, 12-aa)**

- **VirScan (482,000, 62-aa)**

Mishra et al., mBio 2019;10:e01903-19; Schubert et al., Nature Med 2019;In Press, https://www.biorxiv.org/content/10.1101/666230v2
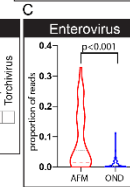
Preparations for AFM Response, 2020

Research activities in preparation for 2020

Enhance surveillance for AFM
- New Vaccine Surveillance Network (NVSN) AFM surveillance
- Pilot studies to improve case finding and decrease reporting lag
- Epidemiology and Laboratory Capacity (ELC) funding to health departments for increased AFM surveillance, outreach, and education

Characterize the etiologies causing AFM
- Enhanced viral surveillance to characterize EV/RV types (Emerging Infections Program [EIP], NVSN)
- EV-D68 national sero-survey (1999-2018)
- EV-D68 viral shedding study
- Examine enterovirus biology in neuronal and respiratory disease models

Understand AFM pathophysiology
- Characterize clinical spectrum using AFM medical chart abstraction data
- NIH natural history study
- Long-term follow-up data collection
- Update clinical guidance document

Increase outreach and communications
- Market research with health care providers to improve AFM communication strategies
- Development of new AFM content and products for HCPs, parents and the public
- Continue AFM parent engagement

Preparedness and response activities for 2020

Monitor and Prepare
- Prepare COCA call
- Develop templates for rapid alerts – Epi-X, Health Alert Notifications (HANs)
- Develop communication messages
- Set laboratory testing algorithm

Activate
- Establish AFM team response structure
- Alert health jurisdiction partners
- Alert health care providers through medical society/social media outreach
- COCA call for health care providers
- Sitrep for CDC leadership/HHS

Respond
- Track suspect case notifications
- Classify cases
- Conduct diagnostic laboratory testing
- Continue medical outreach efforts
- Active website updates to inform public
- Public/parent inquiry response

Demobilize and Evaluate
- After action report
- 2020 surveillance data analysis and publications

Acknowledgments

CDC

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Thank you