



# Reports of shoulder dysfunction following inactivated influenza vaccine in the Vaccine Adverse Event Reporting System (VAERS), 2010-2016

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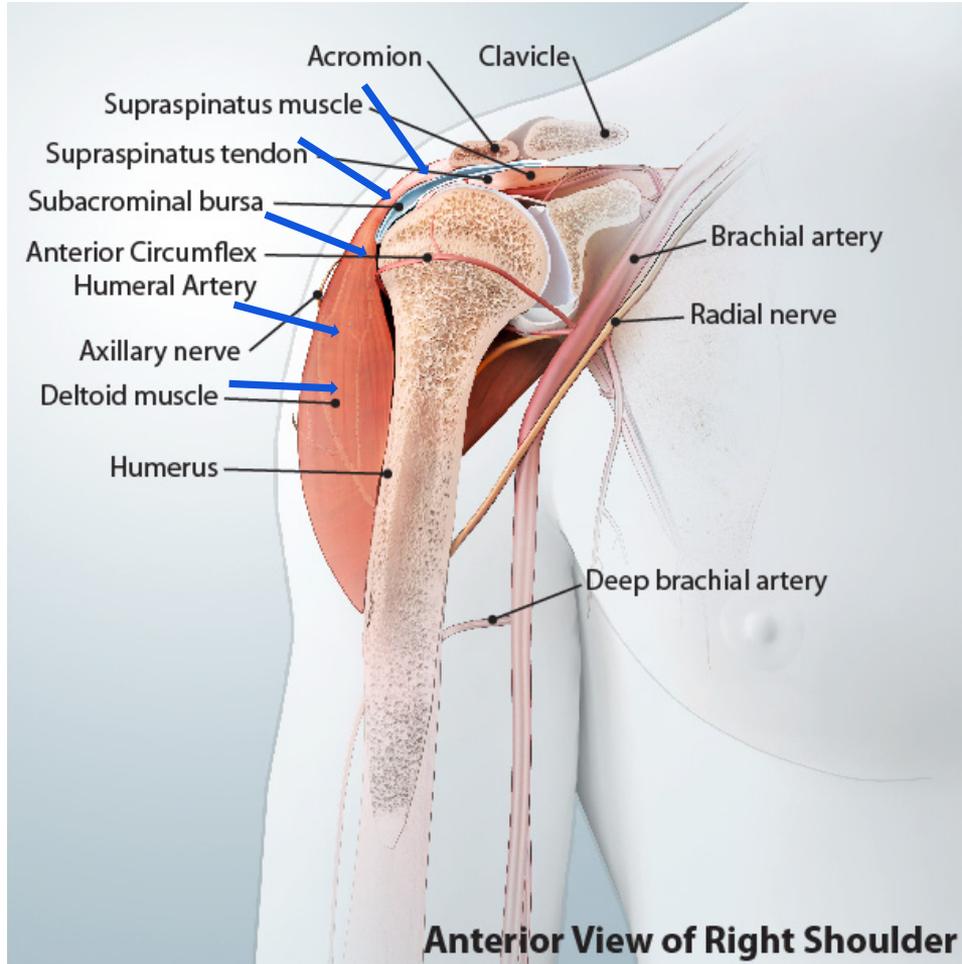
# Disclaimer

- The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of the CDC or FDA

# Anatomy of the upper arm



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# Background: shoulder injury following vaccination

- Atanasoff et al. (2010)<sup>1</sup>
  - Review of 13 claims in the National Vaccine Injury Compensation Program (VICP) between 2006-2010 involving limited and painful range of motion of the shoulder following vaccination
- Institute of Medicine (2012)<sup>2</sup>
  - Based on Atanasoff et al. paper and other case series and case reports:
    - Concluded that the evidence convincingly supports a causal relationship between the injection of a vaccine and deltoid bursitis
- In February 2017, shoulder injury related to vaccine administration (SIRVA) added to the VICP Vaccine Injury Table<sup>3</sup>

<sup>1</sup>Atanasoff et al. Shoulder injury related to vaccine administration (SIRVA). *Vaccine*. 2010;28(51):8049-52.

<sup>2</sup>IOM (Institute of Medicine). 2012. *Adverse effects of vaccines: Evidence and causality*. Washington, DC: The National Academies Press.

<sup>3</sup>National Vaccine Injury Compensation Program: Revisions to the Vaccine Injury Table. A Rule by the Health and Human Services Department. 82 FR 6294.

Effective date February 21, 2017. <https://www.federalregister.gov/documents/2017/01/19/2017-00701/national-vaccine-injury-compensation-program-revisions-to-the-vaccine-injury-table>

# Background: shoulder injury following vaccination<sup>1</sup>

- Shoulder injury related to vaccine administration (SIRVA) manifests as shoulder pain and limited range of motion occurring after the administration of a vaccine intended for intramuscular administration in the upper arm
- These symptoms are thought to occur as a result of unintended injection of vaccine antigen or trauma from the needle into and around the underlying bursa of the shoulder resulting in an inflammatory reaction
- **[By definition] SIRVA is caused by an injury to the musculoskeletal structures of the shoulder** (e.g. tendons, ligaments, bursae, etc.)
- **SIRVA is not a neurological injury** and abnormalities on neurological examination or nerve conduction studies (NCS) and/or electromyographic (EMG) studies would not support SIRVA as a diagnosis (even if the condition causing the neurological abnormality is not known)

# Objective

- Describe reports submitted to the Vaccine Adverse Event Reporting System (VAERS) of shoulder dysfunction<sup>1</sup> following inactivated influenza vaccine (IIV)

<sup>1</sup>VAERS is a passive reporting system and causality generally cannot be assessed using VAERS data alone. Shoulder dysfunction following immunization implies only a temporally associated adverse event of shoulder dysfunction, while shoulder injury related to vaccine administration (SIRVA) implies vaccination caused a shoulder injury.

# Vaccine Adverse Event Reporting System (VAERS)<sup>1</sup>

## Strengths

- National data
- Accepts reports from anyone
- Rapidly detects safety signals
- Can detect rare adverse events
- Data available to public

## Limitations

- Reporting bias
- Inconsistent data quality and completeness
- Lack of unvaccinated comparison group
- Generally cannot assess causality
- Coding practices can affect types and numbers of adverse events identified in reports

<sup>1</sup>Vaccine Adverse Event Reporting System: <http://vaers.hhs.gov>; jointly managed by CDC and FDA

# Methods: definition of shoulder dysfunction following IIV<sup>1</sup>

- Shoulder pain and restricted range of motion following injection of IIV into the upper arm
- Affected shoulder must be of same arm in which IIV was administered alone
- Exclude reports where more than one vaccination – in addition to IIV – was given in the arm with the affected shoulder (e.g., IIV and PPSV23, Tdap/Td, etc.)
- Onset <48 hours after IIV vaccination
- Exclude reports of neurological injuries (e.g., brachial neuritis, which is a separate VICP table injury)
- Symptoms last longer than one week (to differentiate from injection site reactions)<sup>2</sup>

<sup>1</sup>Adapted from the Vaccine Injury Compensation Program (VICP) definition for shoulder injury following vaccine administration (SIRVA) with modification

<sup>2</sup>Modified from VICP requirement of >6 months of residual effects due to limitations on follow-up in VAERS

# Methods: VAERS search strategy and case reviews

- Searched VAERS database for reports of shoulder dysfunction following IIV from July 2010 through June 2016
  - Used MedDRA<sup>1</sup> terms that potentially described shoulder dysfunction and selected vaccine administration error terms
  - And text string search of reports for “arm” or “shoulder”
- All reports identified in initial search were reviewed and classified into three categories: “Not a case,” “Indeterminate case,” or “Possible case”
- Key information from reports entered into an electronic database using a standardized extraction form in MS Access

<sup>1</sup>Medical Dictionary for Regulatory Activities (<https://www.meddra.org/>)

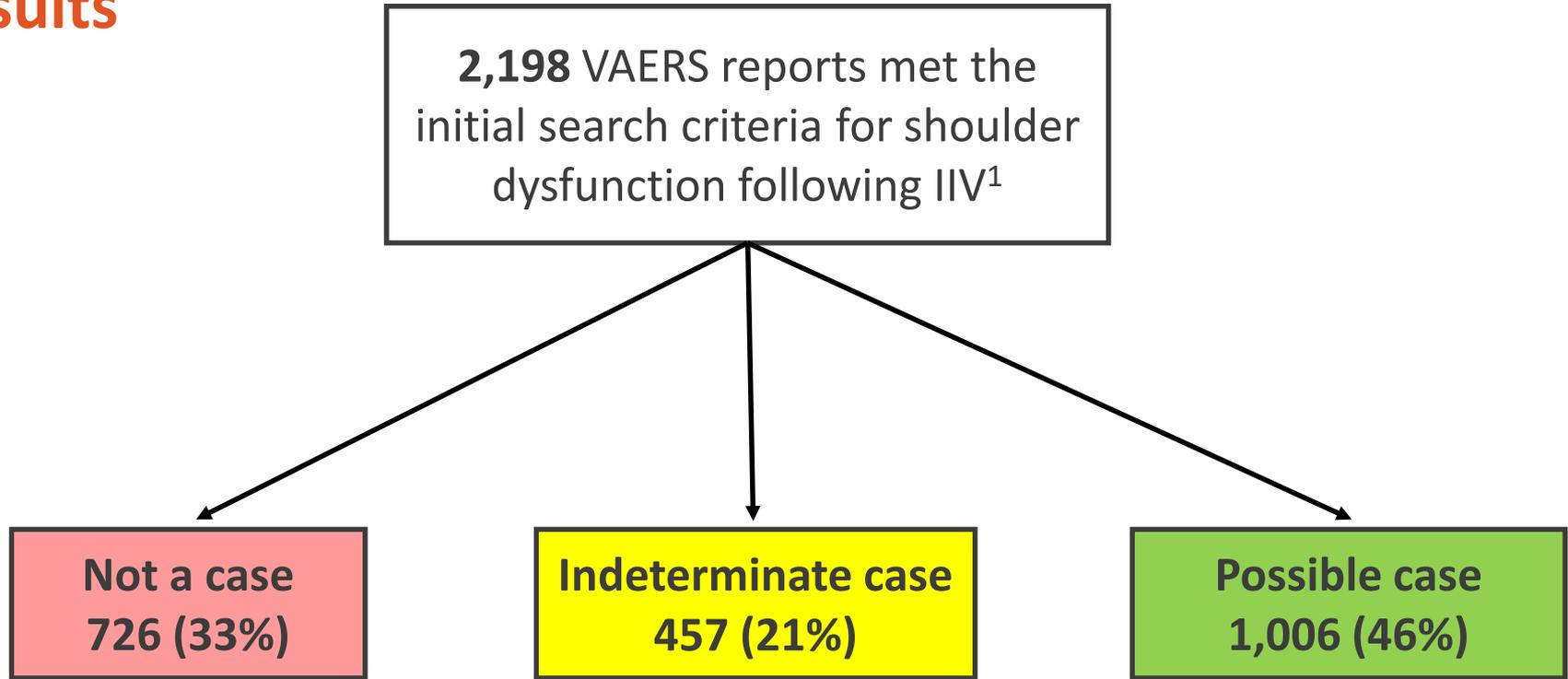
# MedDRA Terms used in search for shoulder dysfunction

Acute osteomyelitis involving shoulder region	Capsulitis of shoulder	Osteoarthritis, localised, primary, involving shoulder region
Acute synovitis	Cervicobrachalgia	Osteoarthritis, localised, secondary, involving shoulder region
Adhesive capsulitis of shoulder	Cervicobrachial syndrome	Osteoarthritis, localized, not specified whether primary or secondary, involving shoulder region
Administration site joint discomfort	drug administration error	Osteoarthritis, unspecified whether generalized or localized, involving shoulder region
Administration site joint effusion	Effusion of joint of shoulder region	Other affections of shoulder region, not elsewhere classified
Administration site joint erythema	Effusion of upper arm joint	Other and unspecified injury to shoulder and upper arm
Administration site joint infection	Injected limb mobility decreased	Other and unspecified superficial injury of shoulder and upper arm, infected
Administration site joint inflammation	Injection site joint discomfort	Other and unspecified superficial injury of shoulder and upper arm, without mention of infection
Administration site joint movement impairment	Injection site joint erythema	Other specified arthropathy involving shoulder region
Administration site joint pain	Injection site joint infection	Other specified arthropathy involving upper arm
Allergic arthritis involving shoulder region	Injection site joint inflammation	Other specified crystal arthropathies involving shoulder region
arthralgia	Injection site joint movement impairment	Other specified disorders of bursae and tendons in shoulder region
Arthropathy involving shoulder region	Injection site joint pain	Other specified disorders of joint of shoulder region
Arthropathy unspecified, involving upper arm	Injury to other specified nerve(s) of shoulder girdle and upper limb	Other symptoms referable to joint of shoulder region
Arthropathy, unspecified, involving shoulder region	Injury to peripheral nerve(s) of shoulder girdle and upper limb	Other symptoms referable to upper arm joint
Brachialgia	Joint injury	
Bursa calcification	Joint range of motion decreased	
Bursa disorder	Joint swelling inflammatory	
Bursa injury	Late effect of injury to peripheral nerve of shoulder girdle and upper limb	
Bursal fluid accumulation	Loose body in joint of shoulder region	
Bursal synovitis	Neck, shoulder and arm syndrome	
Bursitis		

# MedDRA Terms used in search for shoulder dysfunction (cont.)

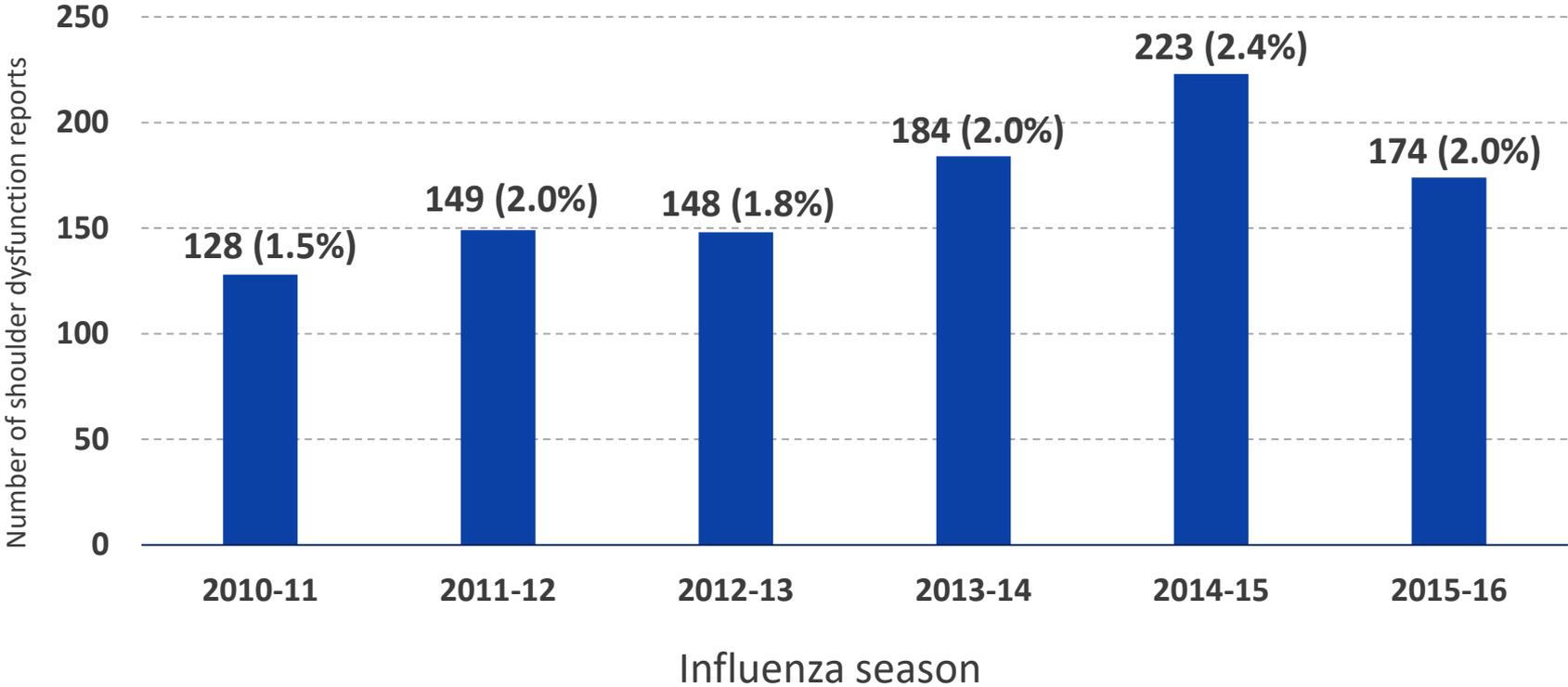
Pain in (l) shoulder	Shoulder osteoarthritis	Traumatic arthrosis
Pain in (r) shoulder	Shoulder pain	Unspecified disorder of joint of shoulder region
Pain in joint involving shoulder region	Shoulder pain (due joint disorder)	Unspecified disorder of upper arm joint
Pain in joint involving upper arm	Shoulder region stiffness of joint, not elsewhere classified, involving upper arm	Unspecified infective arthritis involving shoulder region
Pain in upper extremities	skeletal injury	Unspecified monoarthritis involving shoulder region
Palindromic rheumatism involving shoulder region	Stiffness shoulder	Unspecified monoarthritis involving upper arm
Periarthritis scapulohumeralis	Subacromial bursitis	Unspecified osteomyelitis involving shoulder region
Purulent synovitis	Synovial cyst	Unspecified polyarthropathy or polyarthritis involving shoulder region
Pyogenic arthritis involving shoulder region	Synovial disorder	Vaccination site joint discomfort
Rotator cuff syndrome	Synovial rupture	Vaccination site joint effusion
Rotator cuff syndrome of shoulder and allied disorders	Synovitis	Vaccination site joint erythema
Scapula pain	Synovitis of shoulder	Vaccination site joint infection
Shoulder bursitis	Tendon injury	Vaccination site joint inflammation
Shoulder discomfort	Tendon rupture	Vaccination site joint movement impairment
Shoulder dystocia	Transient arthropathy involving shoulder region	Vaccination site joint pain
Shoulder hand syndrome	Transient arthropathy involving upper arm	Vaccination site joint swelling
Shoulder joint pain associated with	Traumatic arthritis	Villonodular synovitis involving shoulder region
Shoulder ligament rupture	Traumatic arthropathy involving shoulder region	Villonodular synovitis involving upper arm
Shoulder muscle stiffness	Traumatic arthropathy involving upper arm	

# Results



- We included **possible cases** in the preliminary analysis

# Shoulder dysfunction reports following IIV, N (% among all IIV reports) by influenza season, 2010-2016



# Characteristics of shoulder dysfunction (SD) vs. non-shoulder dysfunction reports following IIV, July 2010-June 2016

	SD following IIV, n (%)	Non-SD following IIV, n (%)
<b>Total reports</b>	1,006	50,247
<b>Non-serious</b>	933 (93)	46,707 (93)
<b>Female</b>	829 (82)	34,421 (69)
<b>Median age in years</b>	51 (range 14-94 years)	50 (range 0-102 years)
<b>Age groups</b>		
0-18	3 (<1)	8,541 (17)
19-59	702 (70)	23,709 (47)
60+	289 (29)	16,934 (34)
Unknown	12 (1)	1063 (2)
<b>Type of reporter</b>		
Patient	528 (52)	10,999 (22)
Vaccine provider	273 (27)	23,416 (47)
Manufacturer	36 (4)	4,613 (9)
Other/unknown	169 (17)	11,219 (22)

# Characteristics of shoulder dysfunction reports following IIV, July 2010-June 2016

	n (%)
<b>Total reports</b>	<b>1,006</b>
<b>Median onset interval<sup>1</sup> (days)</b> Symptoms occurring on day of vaccination	day 0 755 (75)
<b>Pain had <u>not</u> resolved at time report was made to VAERS</b>	859 (85)
<b>Seen by healthcare provider for shoulder dysfunction</b>	496 (49)
<b>Referred to specialist<sup>2</sup></b>	176 (18)
Orthopedist	130
Surgeon (not specified)	18
Other specialist <sup>3</sup>	47

<sup>1</sup>By definition, onset interval for shoulder dysfunction is <48 hours following vaccination, day 0 = day of vaccination

<sup>2</sup>Not mutually exclusive

<sup>3</sup>Includes specialist such as rehabilitation medicine, chiropractor, neurologist, acupuncturist, and unspecified “other doctor”

# Characteristics of shoulder dysfunction reports following IIV, July 2010-June 2016

Most commonly reported shoulder dysfunction-related adverse events <sup>1</sup> (N=1,006 total reports)	n (%)
Shoulder pain	442 (44)
Injected limb mobility decreased	407 (41)
Joint range of motion decreased	191 (19)
Drug administered at inappropriate site	156 (16)
Bursitis	94 (9)
Arthralgia	92 (9)
Rotator cuff syndrome	90 (9)
Frozen shoulder	57 (6)
Shoulder bursitis	30 (3)

<sup>1</sup>Not mutually exclusive

# Reported impact on activities of daily living among shoulder dysfunction reports following IIV, July 2010-June 2016

Reported impact on activities of daily living (ADLs) (N=1,006 total reports)	n (%)
Noticeable but do not interfere with ADLs or result in absenteeism from work	4 (<1)
Interferes with ADLs, but unknown if it resulted in absenteeism from work	332 (33)
Interferes with ADLs and/or results in absenteeism from work	229 (23)
Unknown/not stated in report how symptoms affected ADLs and/or absenteeism from work	441 (44)

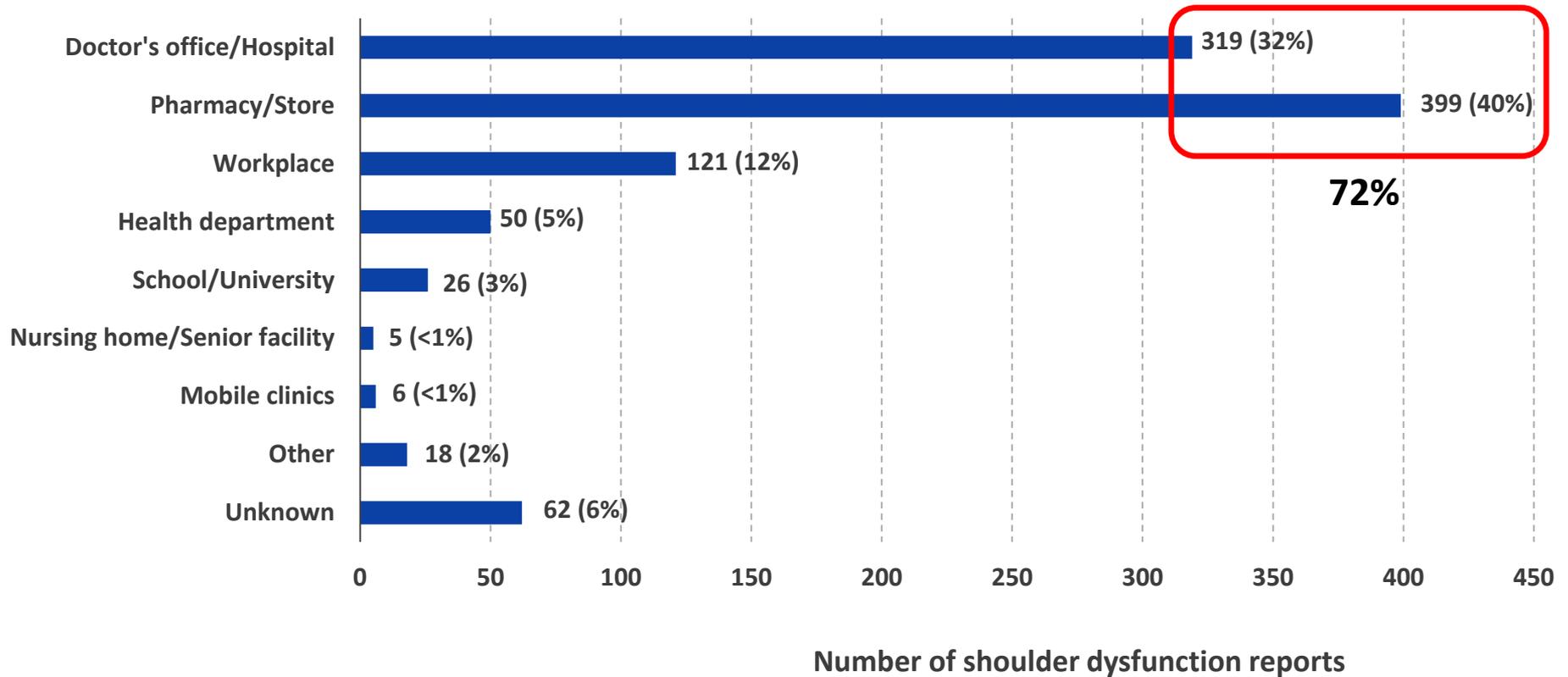
} 56%

# Shoulder dysfunction reports following IIV where a contributing factor was described (222 of 1,006 reports), July 2010-June 2016

Contributing factors <sup>1</sup> described in narrative (N=222 total reports)	n
Vaccination given too high on arm	177
Improper/poor administration technique	35
Uneven position between vaccinator and patient (vaccinator standing and patient sitting)	5
Other (needle “too long,” past history of shoulder pain, etc.)	22

<sup>1</sup>Not mutually exclusive

# Place of vaccination in shoulder dysfunction reports following IIV, July 2010-June 2016



# Summary

- Reports to VAERS of shoulder dysfunction following IIV ranged from 128-223 during the six influenza seasons from 2010-2011 to 2015-2016
  - During that period around 130 million doses of IIV were distributed each influenza season in the United States
- There was a higher percentage of reports of shoulder dysfunction following IIV among females when compared to non-shoulder dysfunction reports
- Most (70%) reports were in the age group 19-59 years; few were in individuals 0-18 years (<1%)
- When possible contributing factors were described, vaccination given too high on the arm was most commonly reported
- The most common place of vaccination documented in reports was in pharmacies/drug stores and doctor's offices/hospitals

# Conclusion

- Improperly placed IIV (or any injectable vaccination) has the potential to cause shoulder injury<sup>1</sup>; however
- Reports to VAERS of shoulder dysfunction following IIV appear rare, given the amount of IIV distributed in the United States each influenza season
- There does not appear to be an increase in shoulder dysfunction reports following IIV submitted to VAERS during recent seasons
  - Approximately 2% of all IIV reports during 2010-2011 through 2015-2016 seasons
- Proper administration technique is important



Image by Alissa Eckert, CDC Division of Communication Services

<sup>1</sup> IOM (Institute of Medicine). 2012. Adverse effects of vaccines: Evidence and causality. Washington, DC: The National Academies Press.

# Acknowledgements

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# Thank you

For more information, contact CDC  
1-800-CDC-INFO (232-4636)  
TTY: 1-888-232-6348 [www.cdc.gov](http://www.cdc.gov)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



# Extra slides

# Shoulder dysfunction reports following IIV classified as serious, July 2010-June 2016

- Serious (N=65)<sup>1</sup>
  - 55 (85%) resulted in permanent disability (per reporter)
  - 8 hospitalized (for shoulder related injury)
  - 2 considered as life threatening
- Sex: 45 female, 18 male, 2 unknown sex
- Median age (range): 53 years (24-92 years)<sup>2</sup>
- Seven patients reported requiring surgical treatment for management of shoulder dysfunction following IIV
- Diagnoses of hospitalized cases<sup>3</sup>:
  - Adhesive capsulitis (2)
  - Rotator cuff tear (2)
  - Shoulder pain (2)
  - Bursitis (1)
  - Impingement syndrome of right shoulder (1)

<sup>1</sup>Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization or permanent disability, eight did not meet serious criteria; <sup>2</sup>Age unknown in four reports; <sup>3</sup>Four were hospitalized and three had outpatient surgery

# Duration<sup>1</sup> of unresolved shoulder dysfunction in reports following IIV, June 2010-July 2016

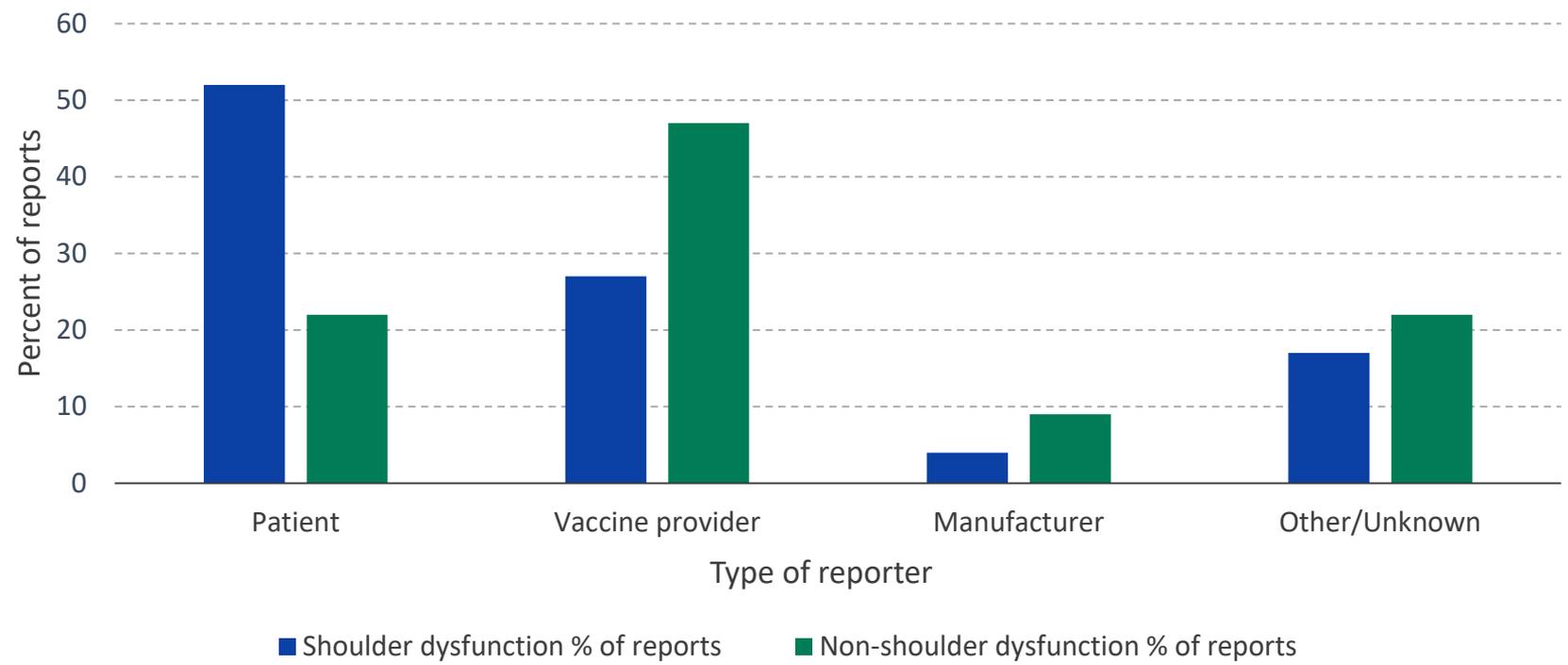
	n (%)
<b>Total reports<sup>2</sup></b>	<b>859</b>
7-30 days	299 (35)
31-90 days	234 (27)
91-180 days	99 (12)
181-365 days	110 (13)
365+ days	105 (12)
Missing <sup>3</sup>	12 (1)

<sup>1</sup>Duration is calculated by date of report – date of adverse event onset, if date of report was missing, receive date was used

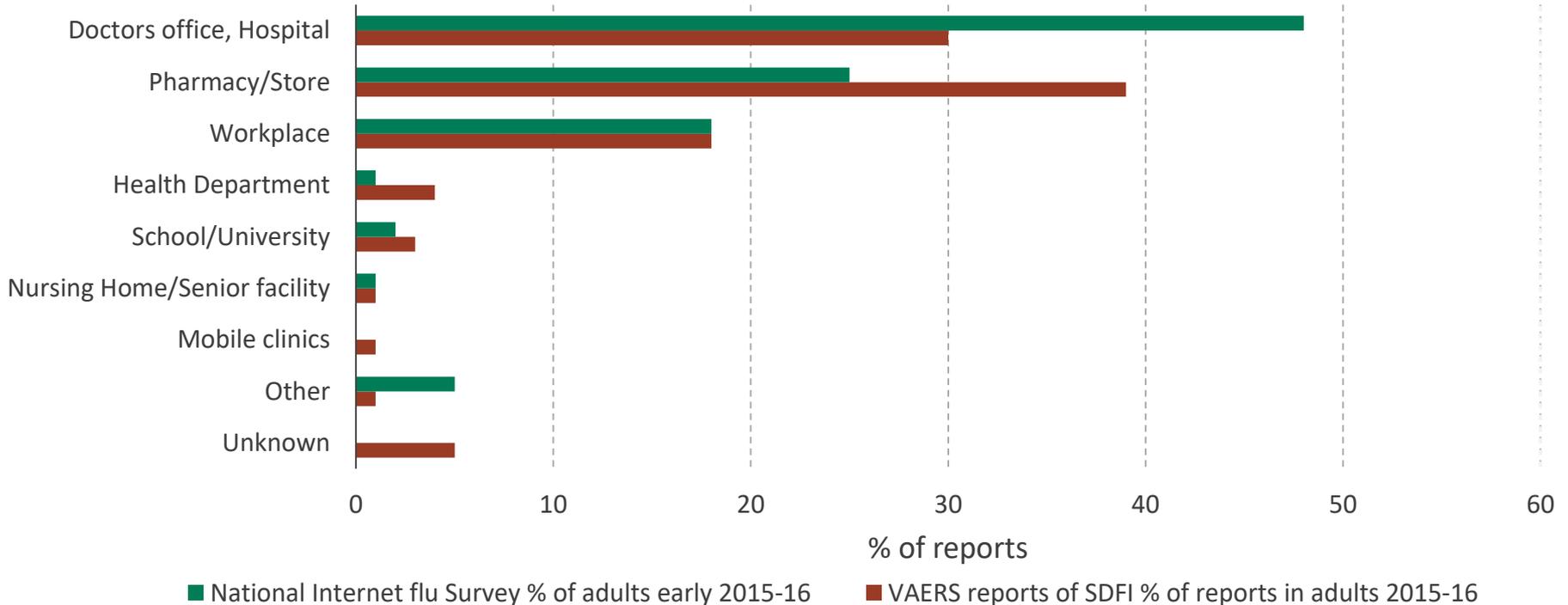
<sup>2</sup>Duration only calculated for those who had unresolved pain at time of report

<sup>3</sup>Duration could not be calculated for those who had missing onset date

# Reporter type among shoulder dysfunction reports following IIV compared to non-shoulder dysfunction reports, July 2010-June 2016



# Place of IIV vaccination for adults (%): National flu survey 2015-16<sup>1</sup> vs. VAERS reports of shoulder dysfunction following IIV in adults 2015-16



<sup>1</sup>Data for national flu survey for the 2015-16 influenza season from July through November