

# Assessment of prior opioid tolerance among new users of fentanyl transdermal system in FDA's Sentinel System

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# Disclosure statement

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# Background

- Some extended-release and long-acting (ER/LA) opioid analgesic formulations and dosages are intended only for patients with prior opioid tolerance
  - Extended-release hydromorphone – all doses
  - Extended-release oxycodone (single dose >40 mg or daily dose >80 mg)
  - **Fentanyl transdermal system (FTS) – all doses**

# REMS for ER/LA opioid analgesics

- FDA approved a Risk Evaluation & Mitigation Strategy (REMS) for ER/LA opioid analgesics in July 2012
- Requires ER/LA opioid analgesic sponsors to fund provider education on safe prescribing
- “Blueprint” developed by FDA includes
  - Assessing patients for treatment
  - Initiating, modifying, and discontinuing therapy
  - Monitoring ongoing therapy
  - Counseling patients about safe use
  - Being familiar with product-specific drug information

# Evaluating REMS Impact

Candidate metrics for monitoring ER/LA opioid analgesic REMS impact have been proposed

- A metric to identify opioid tolerance in patients prescribed select ER/LA opioid analgesics was developed and applied to the US Medicare population (Willy et al 2014)

# Objective

- To identify the proportion of new FTS users <65 years who had evidence of prior opioid tolerance, stratified by product strength and tolerance definition

# Sentinel Initiative

- Launched in 2008 by FDA to leverage electronic data sources (largely claims) for medical product safety surveillance
  
- Sentinel utilizes a distributed database with data partners throughout the US
  - Currently 17 Data Partners - primarily commercial insurers
  - >200 million unique members

# Methods

- 13 Data Partners
- Retrospective cohort
- Jan 1, 2009 - Dec 31, 2013
- Inclusion criteria:
  - <65 years of age
  - First incident dispensing of FTS / user, 183 day washout
  - Medical and pharmacy enrollment during washout period
- Exclusion criteria:
  - Medical claim for opioid poisoning during washout period
  - Inpatient stay 30 days prior to dispensing

# Tolerance definitions

	Per day for 7 <u>consecutive</u> days immediately prior to new opioid-tolerant-only dose index date	Per day for <u>any</u> 7 days in 30 days prior to new opioid-tolerant-only dose index date
≥ 30 mg oxycodone equivalents	<b>Primary Definition</b>	Secondary Definition
> 0 mg oxycodone equivalents	Tertiary Definition	Quaternary Definition

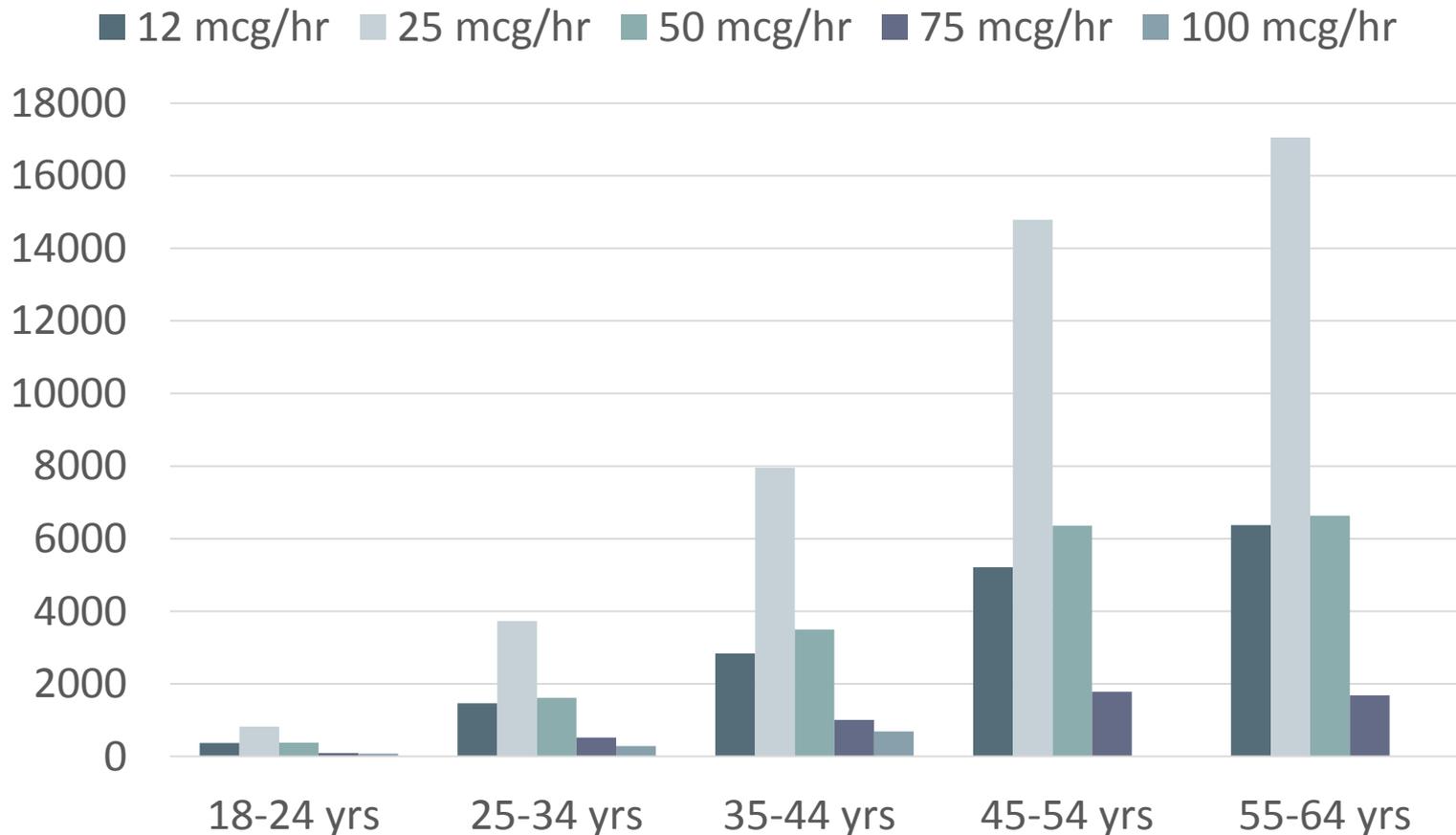
# Analysis

- Stratified by tolerance definition, sex, age category, year, and strength
  - 12, 25, 75, 100 mcg/hr + non-manufacturer strengths (multiple dispensings occurring on the same day were summed)

## Number of fentanyl patch episodes by strength, 2009-2013

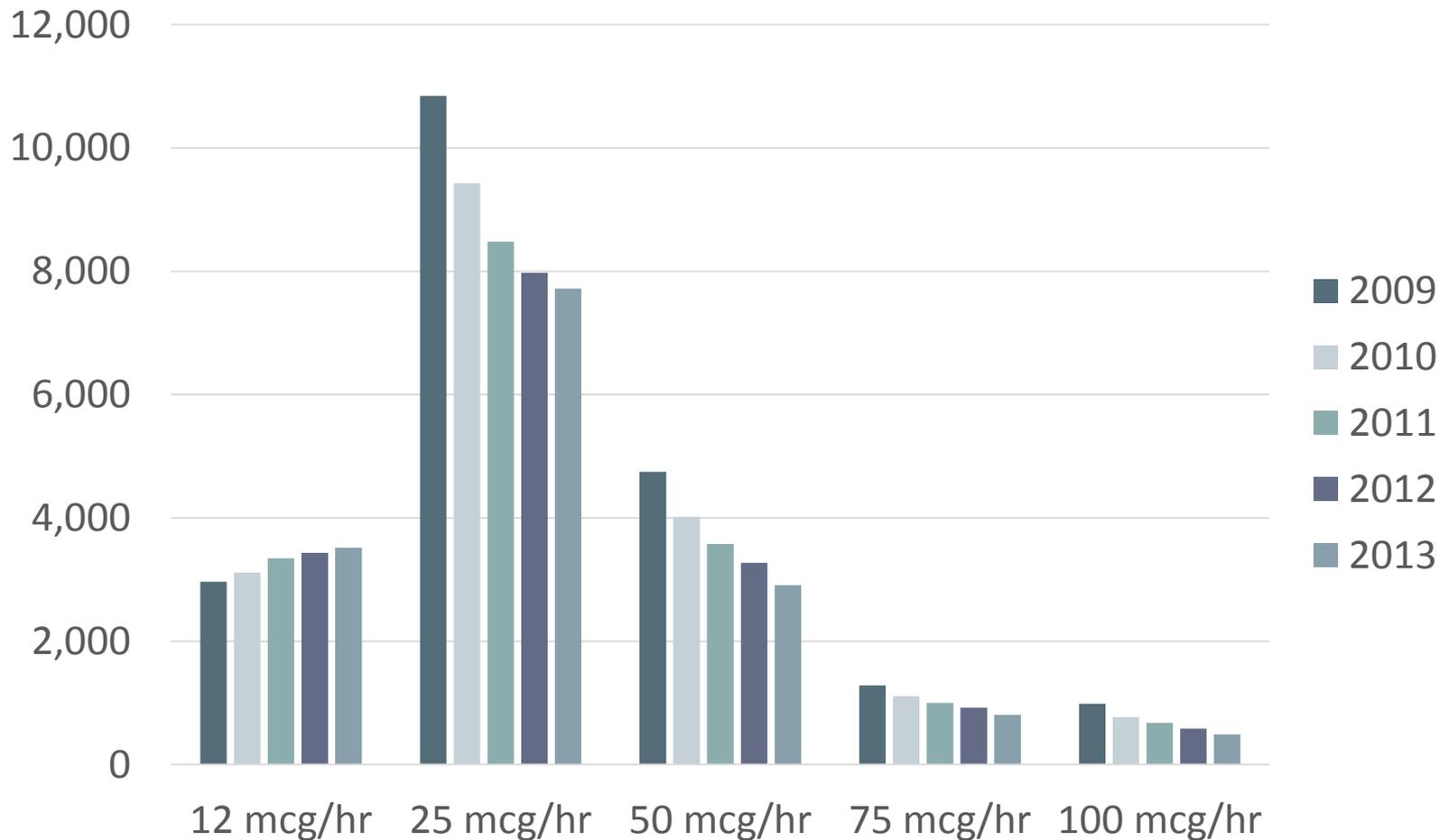
	12 mcg/hr	25 mcg/hr	50 mcg/hr	75 mcg/hr	100 mcg/hr
<b>Episodes</b>	16,379	44,450	18,527	5,118	3,507
<b>Age (yrs)</b>					
0 – 11	32	23	7	2	4
12 - 17	75	79	32	11	8
18 - 24	375	827	380	99	77
25 - 34	1,464	3,731	1,614	523	290
35 - 44	2,841	7,954	3,502	1,011	686
45 - 54	5,214	14,785	6,358	1,785	12,76
55 - 64	6,378	17,051	6,634	1,687	11,66
<b>Sex</b>					
Male	5,124	18,327	8,727	2,510	1,839
Female	11,255	26,123	9,800	2,608	1,668

# Number of fentanyl patch episodes by strength and age, 2009-2013

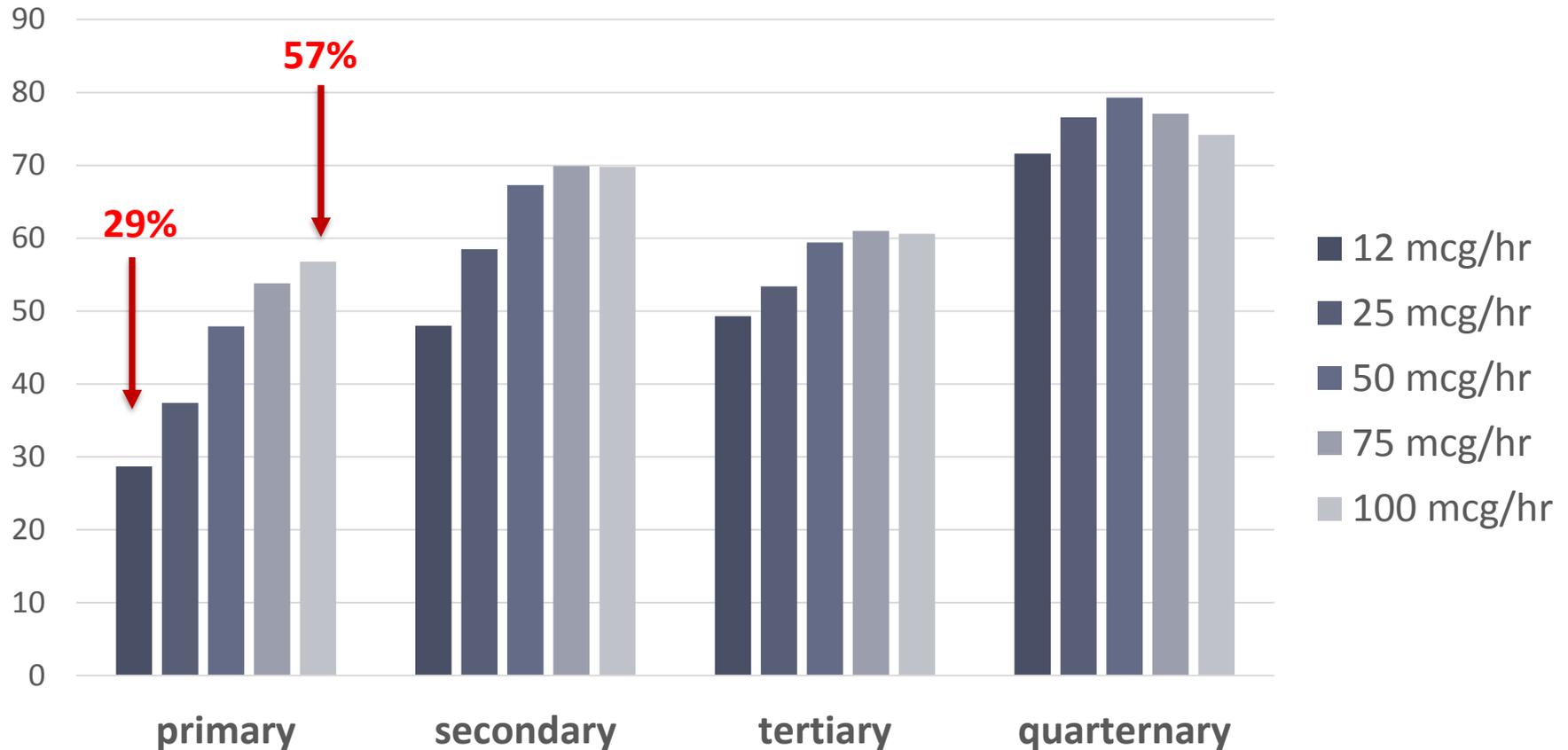


Members <18 yrs have age had <100 episodes per strength

# Number of fentanyl patch episodes by strength and year, 2009-2013



## Fentanyl patch episodes with evidence of prior tolerance by strength & tolerance definition, 2009-2013



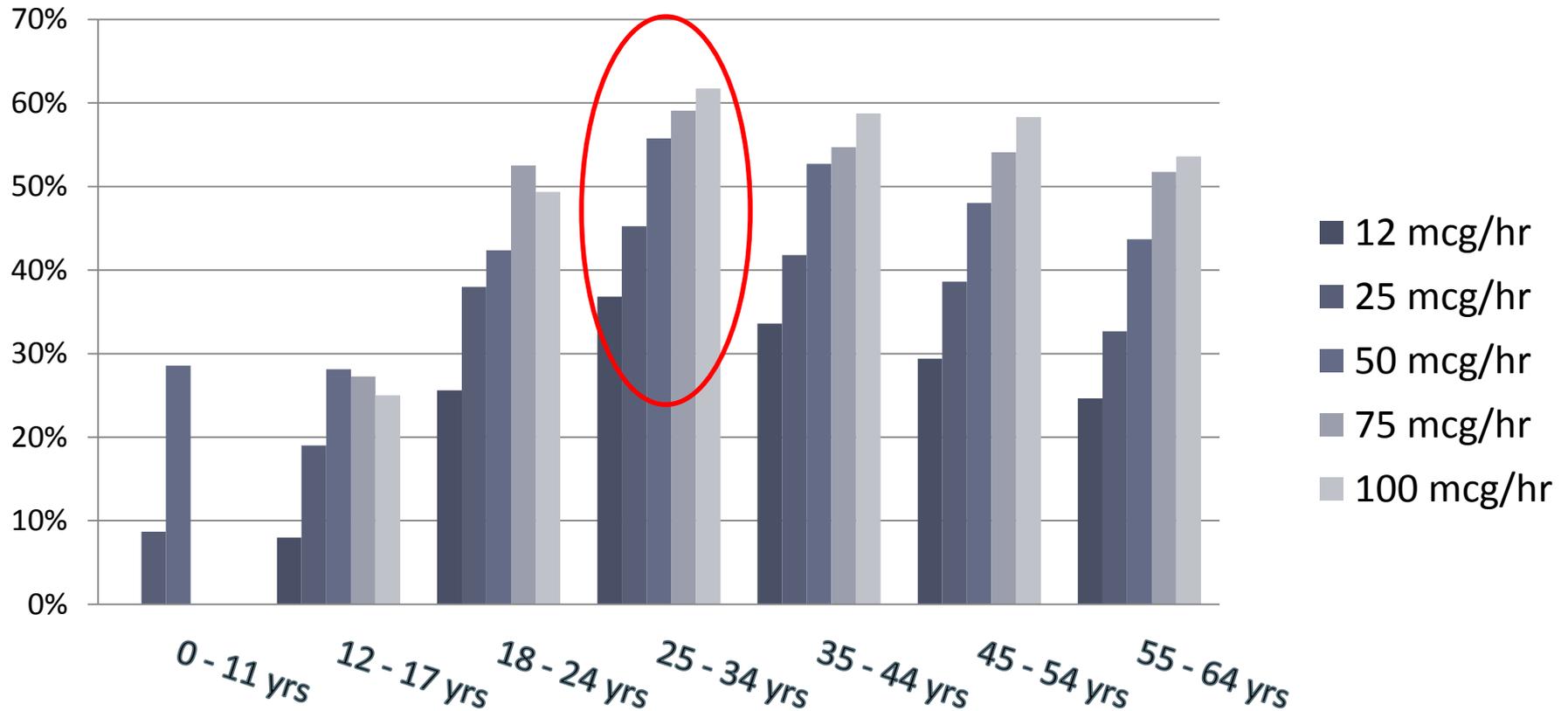
**Primary**  $\geq 30$  mg / d in prior 7 consecutive days

**Tertiary**  $> 0$  mg / d in prior 7 consecutive days

**Secondary**  $\geq 30$  mg / d for 7 d in 30 d prior

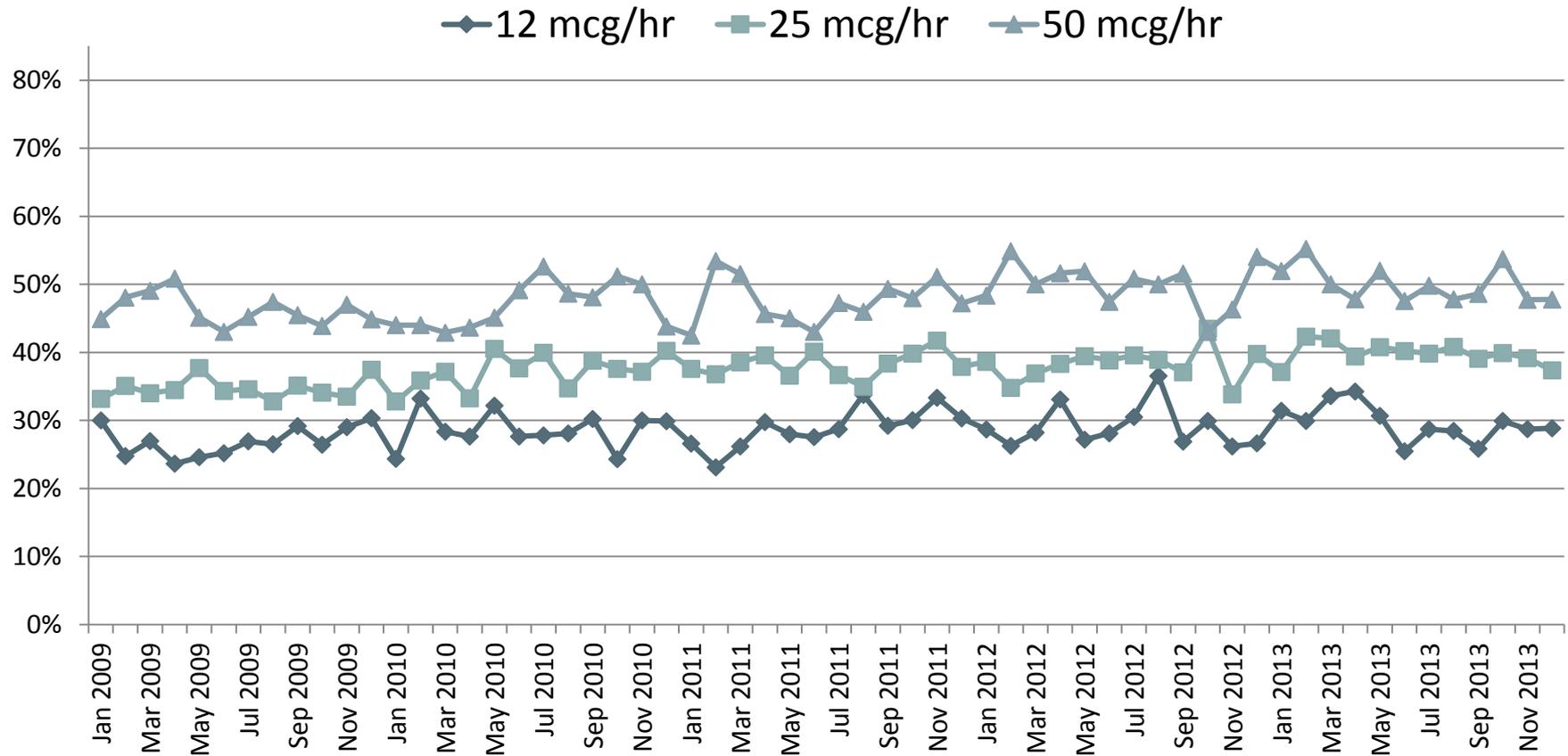
**Quaternary**  $> 0$  mg / d for 7 d in 30 d prior

## Fentanyl patch episodes with evidence of prior tolerance by strength & age, primary definition, 2009-2013



Primary def:  $\geq 30$  mg / d in prior 7 consecutive days

# Fentanyl patch episodes with evidence of prior tolerance by strength & time, primary definition, 2009-2013



Primary def:  $\geq 30$  mg / d in prior 7 consecutive days

# Large proportion of FTS episodes lack evidence of tolerance

- Proportion with prior tolerance especially low among patients receiving lower strength fentanyl patches
- Nearly half (43%) of those with highest strength product do not have evidence of tolerance by the primary definition
- REMS-affiliated provider training started March 2013; thus, these data do not provide sufficient opportunity to evaluate the impact of training on safe prescribing practices

# Strengths and limitations

- Size of Sentinel distributed data network
- Limitations:
  - Algorithm for determining opioid tolerance has not been validated
  - Predominantly commercially insured
  - Opioid dispensings incomplete if members bypass insurance and pay out-of-pocket
  - Prior opioids may have been provided in setting not captured in data (e.g. rehab)

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# Questions?

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