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Market Structure for Naloxone

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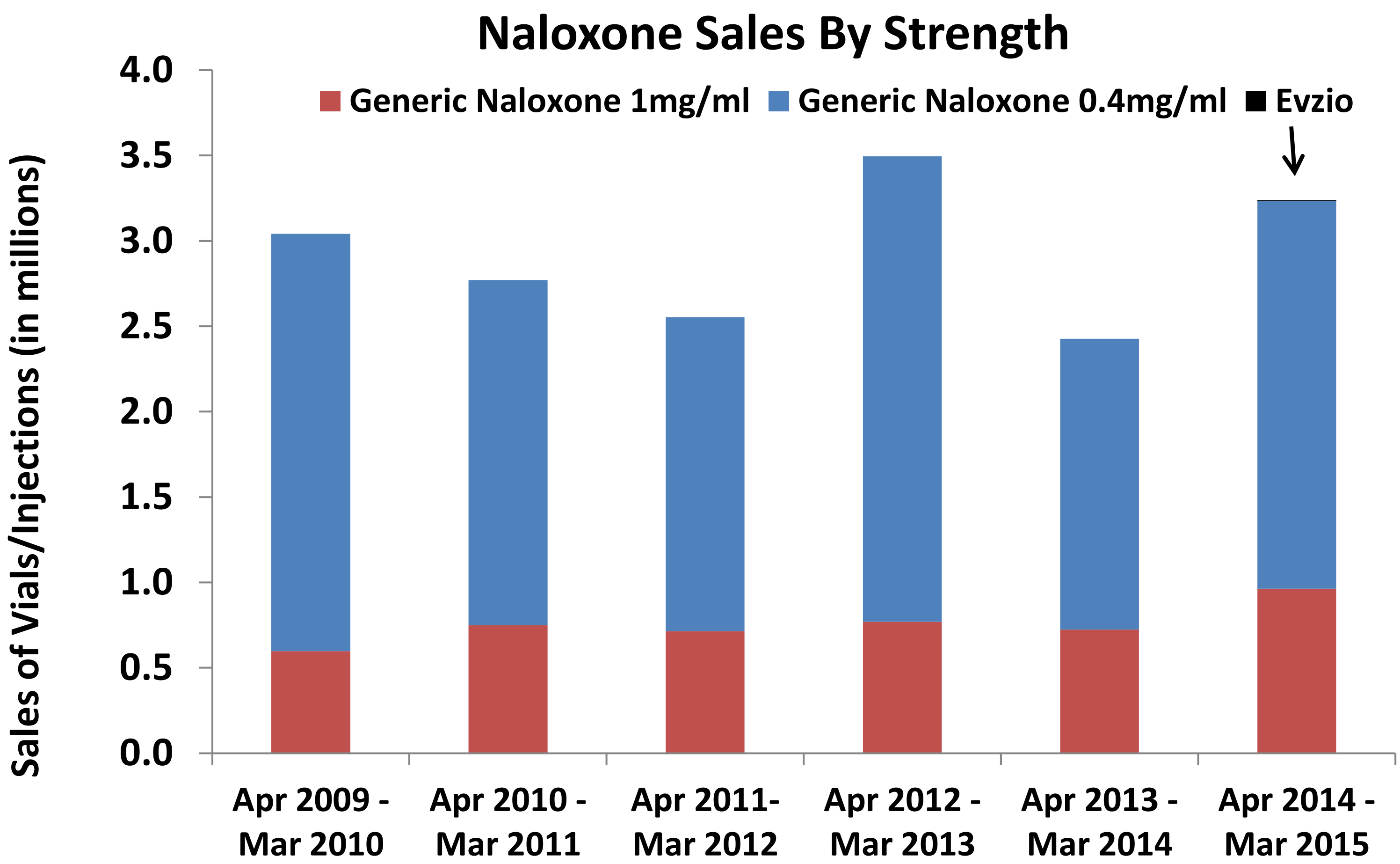
Sales Distribution Data

We use sales data to examine trends in the distribution of naloxone

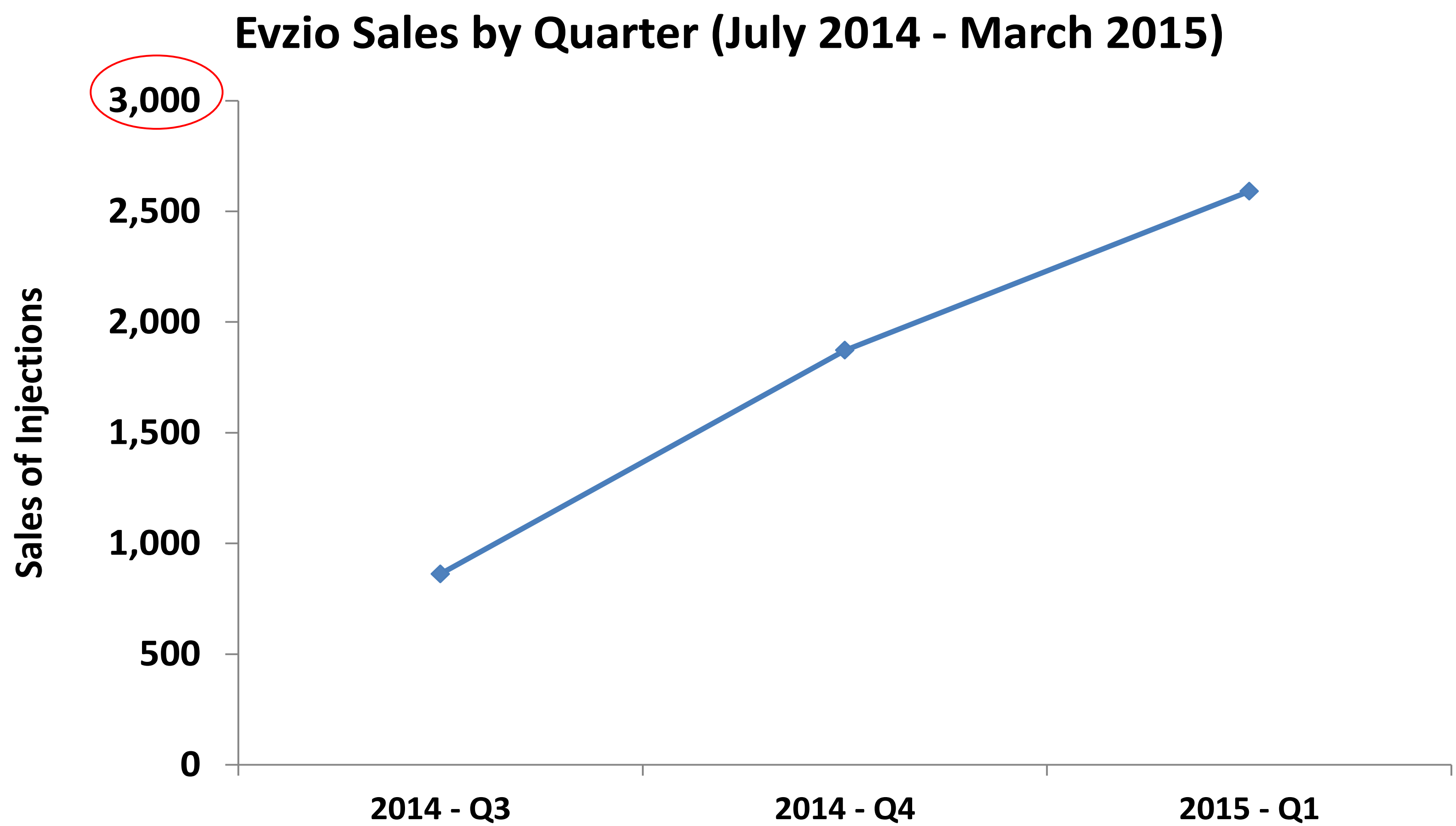
- **IMS Health, IMS National Sales Perspective™**
  - Nationally estimated sales distribution data from wholesalers on volume of drug sold from manufacturers to retail and non-retail markets
  - Captures number of vials/injections sold and total revenue for those sales
  - Nationally projected based on ~85% of the total market
  - **Direct sales, internet sales, and other sales outside of the wholesale pharmacy distribution process are not captured**

Majority of the vials/injections sold of naloxone are for the 0.4 mg/mL strength



Nationally Estimated Number of Vials/Injections of Naloxone, by Strength, Sold to All Settings of Care
Source: IMS Health, IMS National Sales Perspective (NSP)™, April 2009-March 2015. Extracted May 2015.

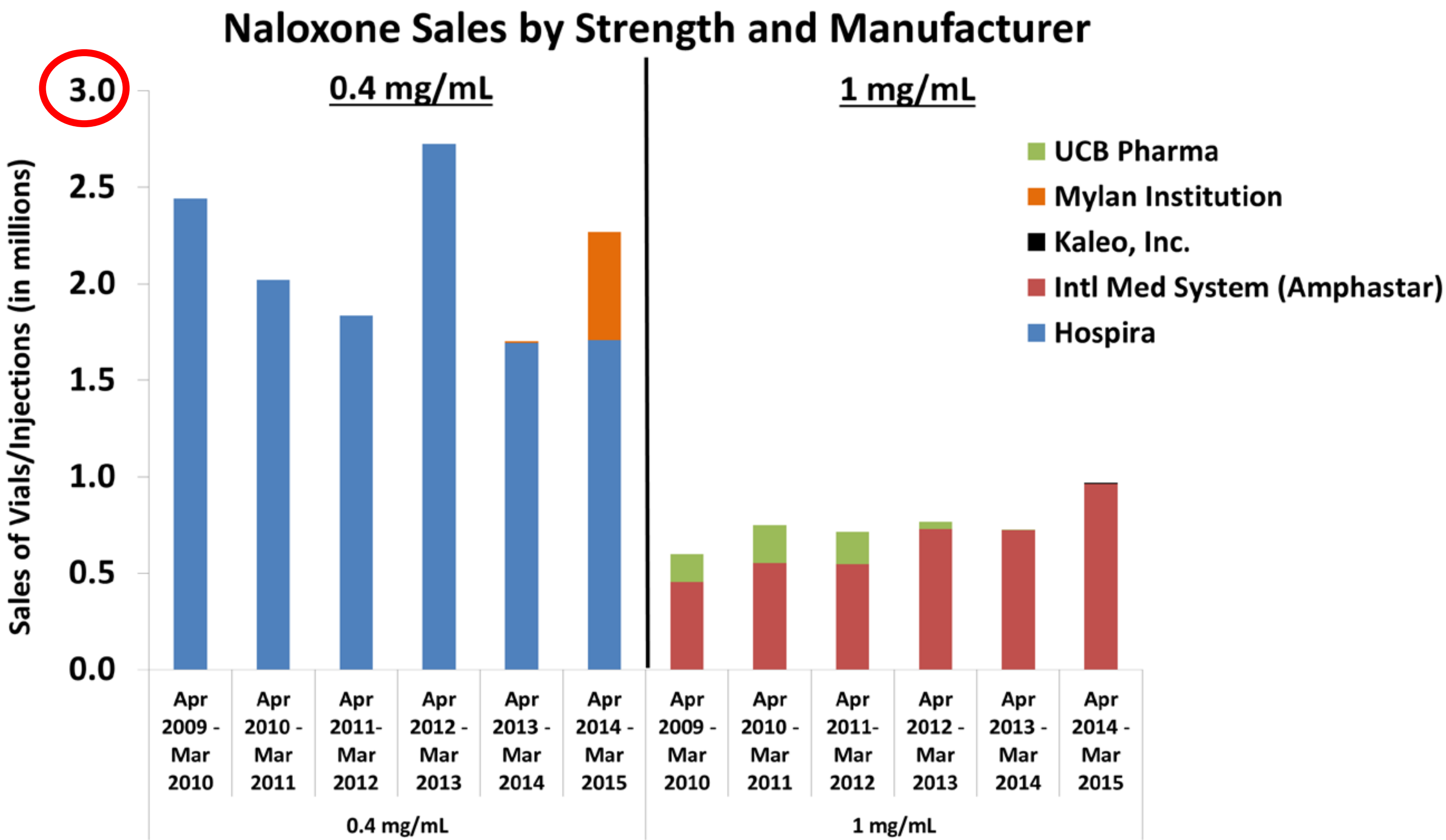
Evzio sales have increased since introduction but are still well below other formulations



Nationally Estimated Number of Vials/Injections of Evzio, Sold to All Settings of Care

Source: IMS Health, IMS National Sales Perspective (NSP)™, April 2009-March 2015. Extracted May 2015.

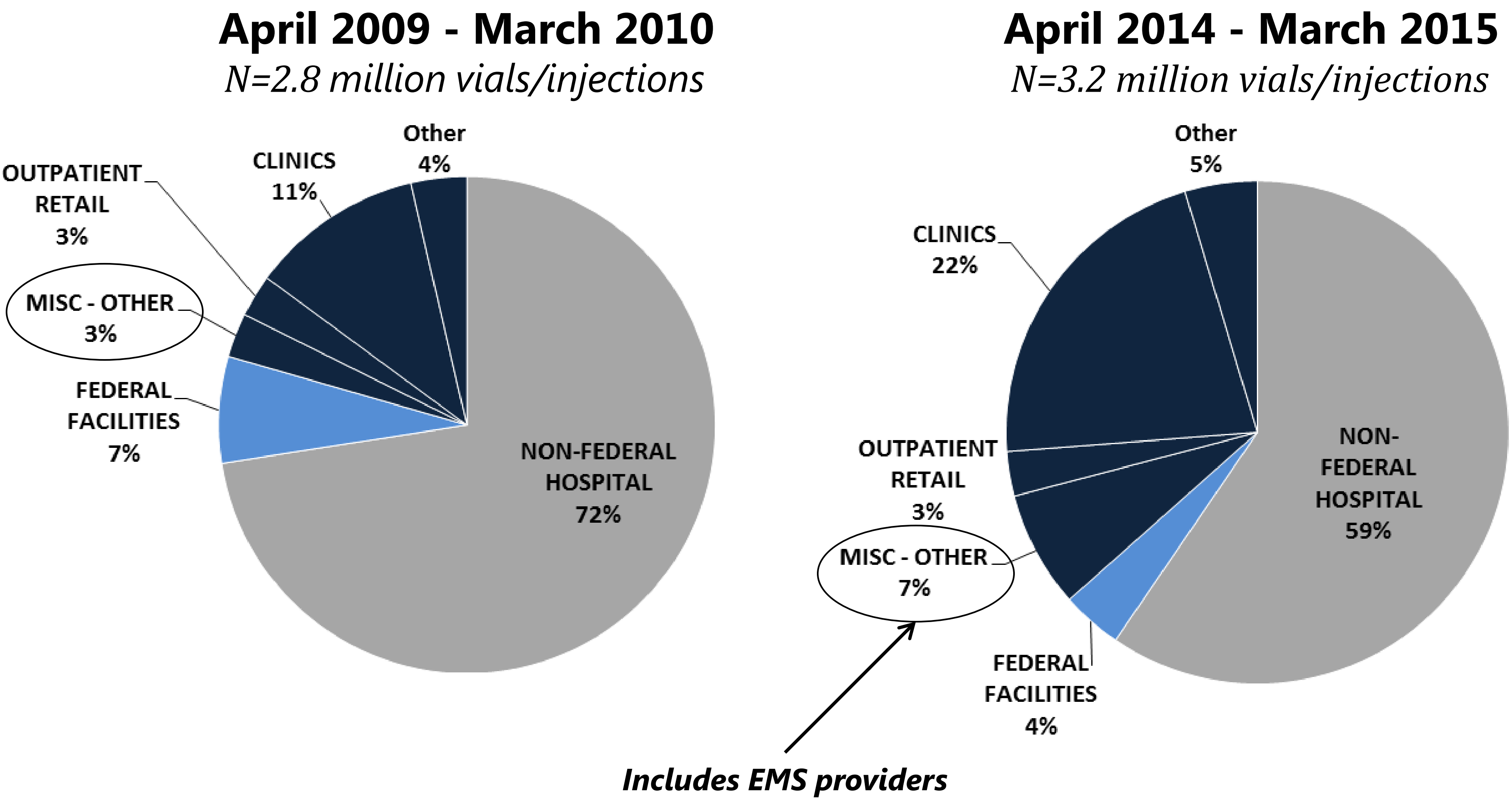
Each strength is sold primarily by one company



Nationally Estimated Number of Vials/Injections of Naloxone, by Strength and Manufacturer, Sold to All Settings of Care

Source: IMS Health, IMS National Sales Perspective (NSP)™, April 2009-March 2015. Extracted May 2015.

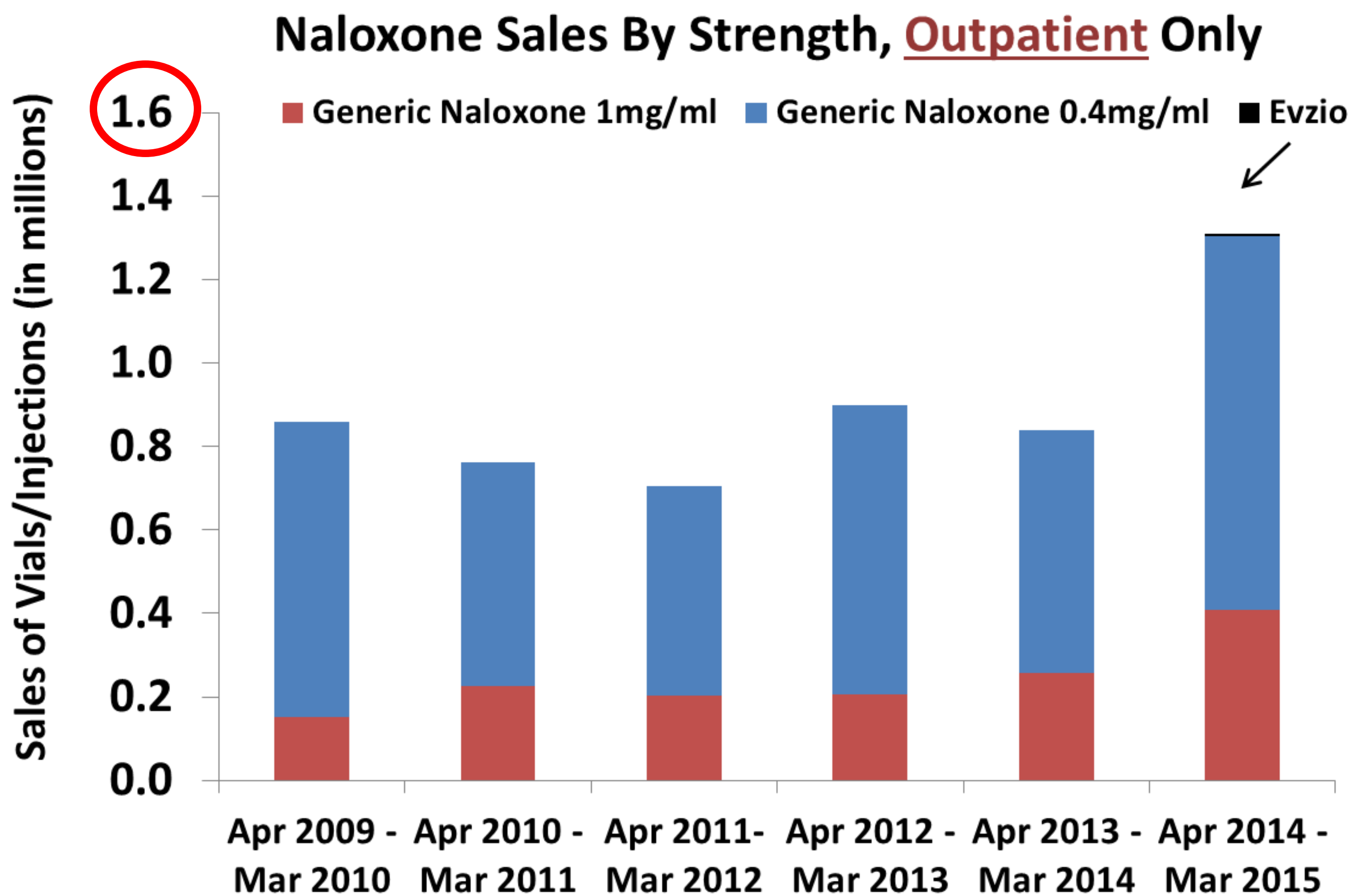
In the last 5 years, sales to outpatient settings have increased by 72%



Nationally Estimated Number of Vials/Injections of Naloxone Sold by Setting of Care

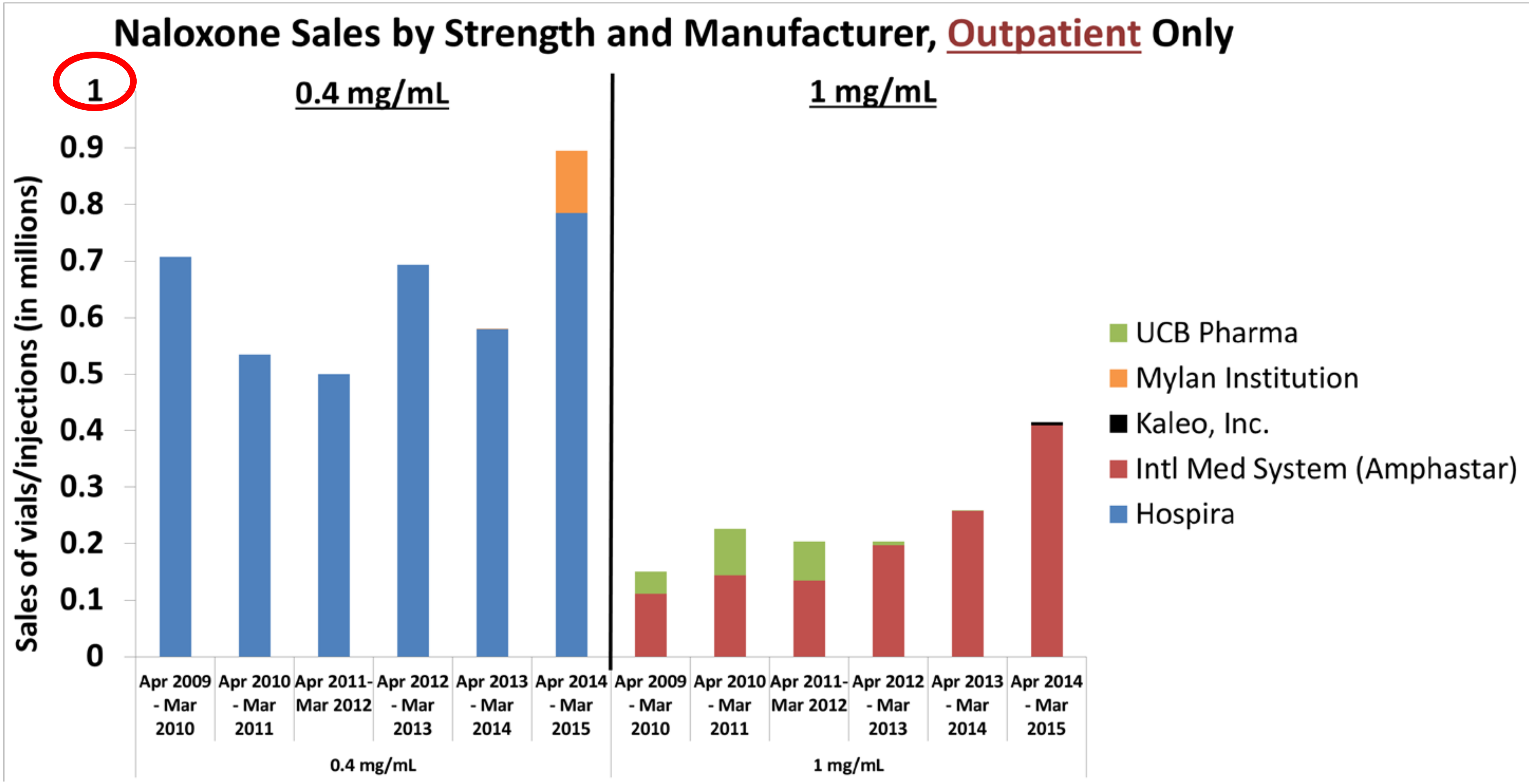
Source: IMS Health, IMS National Sales Perspective (NSP)™, April 2009-March 2015. Extracted May 2015.

Most of these additional outpatient sales occurred in 2014-2015



Nationally Estimated Number of Vials/Injections of Naloxone, by Strength, Excluding Non-Federal Hospitals
Source: IMS Health, IMS National Sales Perspective (NSP)™, April 2009-March 2015. Extracted May 2015.

Sales to outpatient settings also occur from a small number of companies



Nationally Estimated Number of Vials/Injections of Naloxone, by Strength and Manufacturer, Excluding Non-Federal Hospitals
Source: IMS Health, IMS National Sales Perspective (NSP)™, April 2009-March 2015. Extracted May 2015.

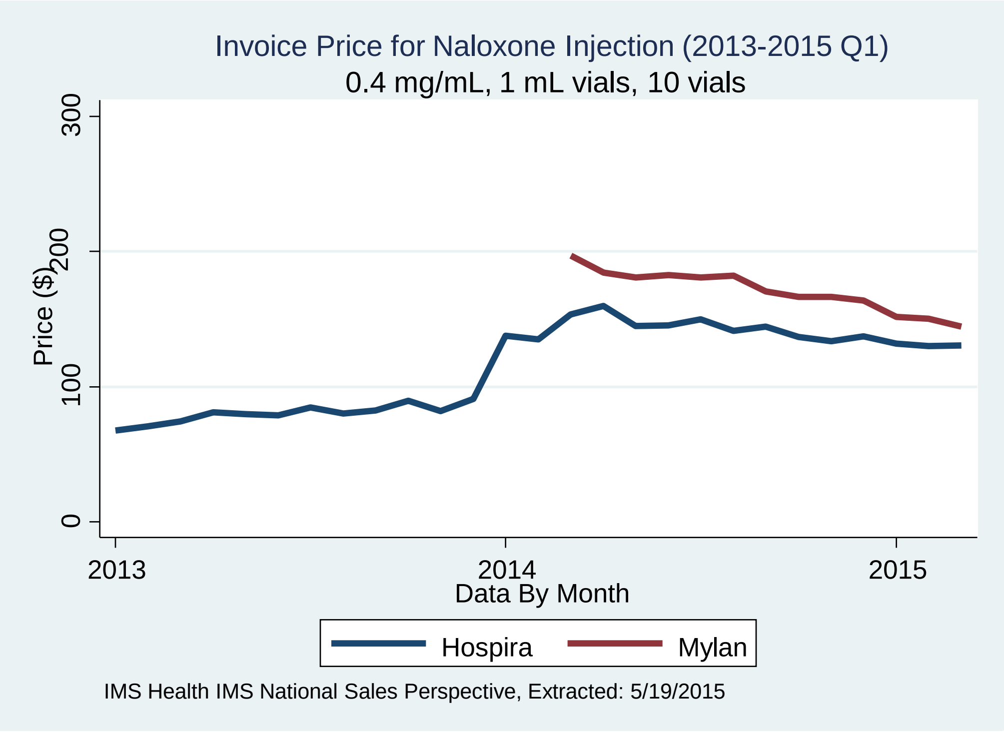
Pricing Data

We use the same data source to analyze trends in naloxone's price

- **Reminder: Data may not fully capture community use if direct sales are occurring from manufacturers to EMS providers**
- Captures **invoice price**:
  - Average price paid by pharmacies or hospitals to wholesalers
  - Includes any discounts that occur at the point of sale
- For this analysis, we continue to display only distribution to outpatient settings of care (excludes non-federal hospitals)
- We limit our analysis to the highest revenue formulation for a company and molecule in CY 2014

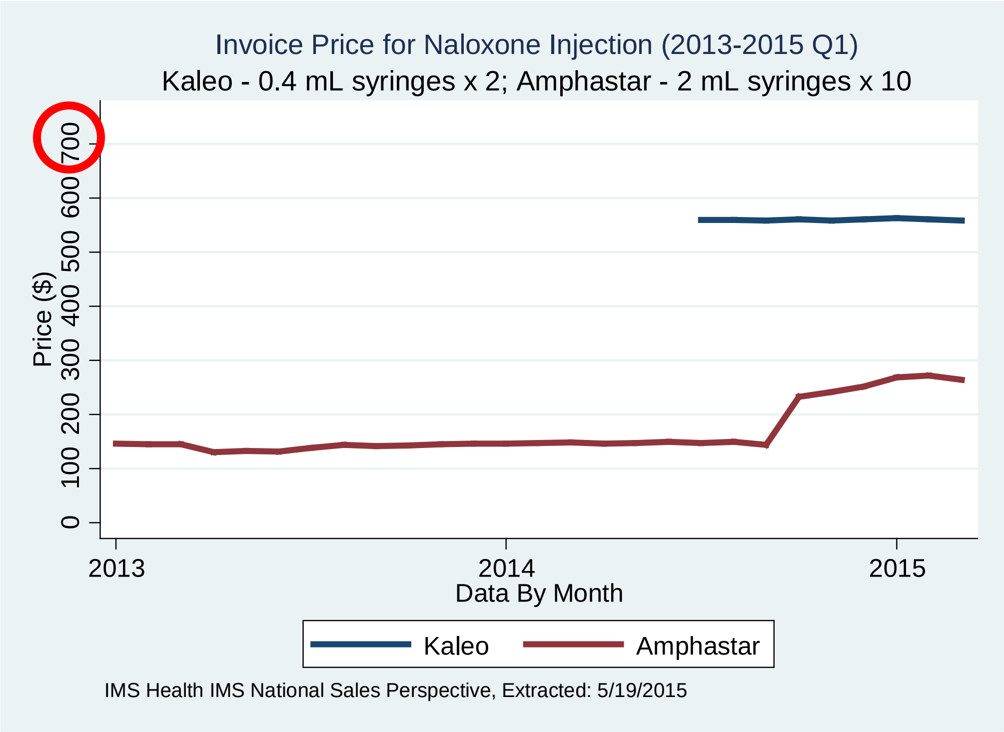
Price for the 0.4 mg/mL strength increased in January 2014

- Hospira's product increased in price by about 50% in January 2014
- Mylan introduced its product in March 2014 and has followed a similar pricing trend to Hospira



Price for the 1 mg/mL strength increased in September 2014

- Kaleo's auto-injector was introduced in July 2014 and was priced at about 4 times as much as the Amphastar product
- Amphastar's price increased by about 60% in September 2014

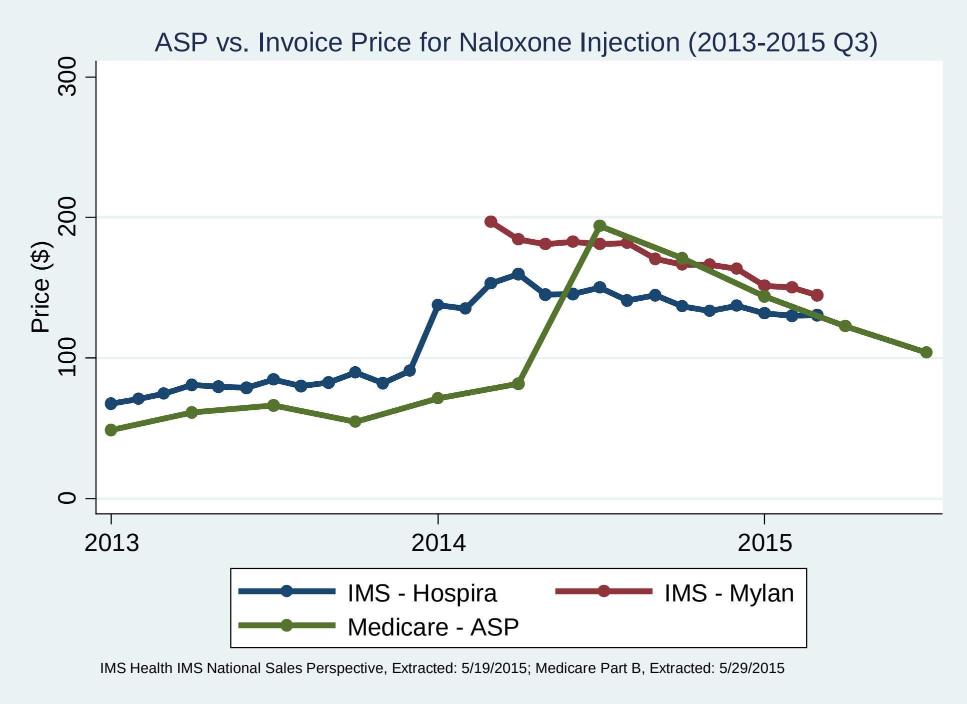


These price increases are part of a recent trend in generic injectable drugs

- We conduct the same analysis for all generic injectable drugs in the dataset, and end up with 1,109 formulations across 354 molecules in CY 2014
- We calculate percent changes in invoice price for each formulation on a month to month basis in CY 2014
- We find that **24.6%** of molecules had at least one billing unit in CY 2014 with a monthly price increase larger than 60% (Amphastar's price increase)
- **9.6%** of formulations had a monthly price increase larger than 60%

Medicare pricing data show a similar trend to the 0.4 mg/mL strength

- **Average Sales Price (ASP) – Medicare Part B**
  - Captures a volume-weighted average price (net of discounts) for all covered drugs that are subject to Medicaid rebates
  - Does not distinguish between strengths, and is **lagged by 2 quarters**



We are limited in our ability to analyze naloxone's market by the available data

- **Direct sales from manufacturers to EMS providers or other organizations are not captured in our sales distribution data**
- Sales distribution data do not directly measure drug utilization
  - Provide an estimate of purchases by channels of distribution (supply)
  - May proxy for utilization if facilities purchase drugs in quantities reflective of patient use
- Cannot determine which indication, clinical uses, or types of organizations within each distribution channel are driving the observed changes

Summary

- Sales of naloxone to outpatient settings increased by 72% in the last 5 years, while sales to inpatient/ER settings declined by 12%
- Each of the 0.4 mg/mL and 1 mg/mL strengths are primarily sold by one company
- Price increases occurred in January 2014 for the 0.4 mg/mL strength and in September 2014 for the 1 mg/mL strength. Since then, prices have remained elevated.
- 25% of generic injectable molecules had a monthly price increase at least as large as the 1 mg/mL strength in CY 2014

Future research is needed to expand upon this talk

- Understanding the novel ways in which naloxone is being distributed/prescribed
- Identifying additional data sources for:
  - Capturing sales that occur outside of the wholesale distribution process (e.g. direct sales)
  - Breaking down sales by state and other demographic variables
  - Measuring use of the drug (e.g. prescriptions/dispensing)