Pharmaceutical Industry Marketing, Physician Prescribing, and Stimulant Misuse

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Disclosures / Funding Source

- **Conflict of interest statement:**
  - I have no commercial relationships to disclose
  - I will not be discussing any unapproved uses of pharmaceuticals or devices

- **Funding Sources:**
  - National Institute on Drug Abuse K23DA045085, K23DA045085-S1, L40DA042434, UM1DA049412, R01DA047975, R01DA046527-S1
  - American Heart Association ENACT: End Nicotine Addiction in Children and Teens grant
  - Thrasher Research Fund Early Career Award
  - Academic Pediatric Association Young Investigator Award
By the end of 20 minutes, learners will:

1. Review the potential causal pathways leading from pharmaceutical company marketing to prescribing and overdose

2. Assess the evidence linking marketing and opioid-related outcomes

3. Identify gaps in the evidence linking marketing and stimulant-related outcomes
Four Waves of the Overdose Crisis

- Drug Company Marketing
- Increased Prescribing
- Increased Use / Misuse
- Overdose

Image adapted from CDC/NCHS National Vitality Statistics System, Mortality; CDC, 2020
Part 1: Opioids
Drug Company Opioid Marketing

- Physician Payments Sunshine Act of 2010 required documentation of all marketing of value ≥$10 (effective August 2013)
- Retrospective analysis of all marketing for opioids
- Between Aug 2013 and Dec 2015:
  - 375,266 marketing interactions (non-research) totaling $46,158,388
  - 68,177 physicians (1 in 12 overall; 1 in 5 family medicine physicians)
  - Most frequent marketing was meals (94%, median value $14)
  - Most costly marketing was speaking fees (63%, median value $2,010)

Retrospective study of $n=369,139$ physicians prescribing opioids in Medicare Part D in 2015

Linked prescribing with Open Payments data on opioid marketing received the previous year (2014)

Overall, total opioid dispensing decreased from 2014 to 2015, but increased in physicians who received opioid marketing

After adjusting for prior opioid claims and changes in total drug claims, physicians receiving marketing had 9.3% (95% CI, 8.7-9.9%) more opioid claims

Opioid Marketing & Prescribing

- Drug Company Marketing
- Increased Prescribing
- Increased Use/Misuse
- Overdose

Hadland SE et al. JAMA Intern Med, 2018;178(6):861-863
Opioid Marketing & Overdose

- Retrospective study of 2014-2016 county-level opioid mortality linked to previous year’s opioid marketing
- 70% of counties received marketing
- For a typical county of 10,000 people...
  - 4 additional payments (=1 SD) were associated with 18% more deaths involving prescription opioid
  - 1 additional physician receiving marketing (=1 SD) associated with 12% more deaths
- This association was mediated by county prescribing rates

Opioid Marketing & Overdose

Drug Company Marketing

Increased Prescribing

Increased Use / Misuse

Overdose

A Word on Causality

- Studies are observational and we cannot exclude reverse causality; however, we…
  - Lagged outcomes from exposures
  - Adjusted for previous opioid prescribing

- In truth, there likely is reverse causality—that is, drug companies target doctors who already prescribe at high levels
  - This is a known marketing strategy

- Drug companies unlikely to invest millions in marketing if it did not result in profits

- Marketing often targeted counties hard hit by overdose—how can this be justified?

**Drug Company Marketing**

**Increased Prescribing**

**Increased Use / Misuse**

**Overdose**
Part 2: Stimulants
Stimulant Overdoses

Drug Company Marketing → Increased Prescribing → Increased Use / Misuse → Overdose

Ahmad FB, et al. National Center for Health Statistics, 2021
Stimulant Overdoses in Youth 13-25 Years

Drug Company Marketing

Increased Prescribing

Increased Use / Misuse

Overdose

Trends in substance involvement among opioid overdose deaths

Stimulant Prescribing, Use & Misuse

Increased Prescribing
- Amphetamine dispensing increased 2.5-fold from 2006 to 2016

Increased Use / Misuse
- Per DEA, most commonly used (and misused) prescription stimulant is amphetamine (e.g., Adderall)
- In Monitoring the Future, 1 in 14 college students reports past-year amphetamine use

Monitoring the Future, University of Michigan, 2020
Stimulant Marketing

- Analysis of stimulant marketing between 2014-2018
- 98% of marketing interactions were meals
- Vyvanse most heavily marketed (nearly half of all interactions)
- 1 in 18 US physicians received marketing during study period
  - 1 in 5 pediatricians
  - 1 in 6 psychiatrists
  - 1 in 8 family physicians

My Worries:

Poor Understanding of Causal Pathways:
Pathways from prescription stimulant misuse to illicit stimulant use remain poorly understood

New Marketing Strategies:
To date, marketing has focused on newer, brand-name stimulants (high cost, low volume)
A major manufacturer could instead focus on generic stimulants (low cost, high volume)
This could precipitate a new prescription drug crisis by escalating demand (akin to 1st wave of opioid overdose crisis)

Adulteration:
Counterfeit prescription stimulants containing methamphetamine are appearing in the Northeast
Overdose risk on prescription stimulants relatively low, but contamination with illicit methamphetamine high risk (akin to 3rd wave of opioid overdose crisis)
Take-Home Points:

Conclusions:
1. Opioid marketing is strongly associated with subsequent prescribing
2. Opioid marketing is also linked to county overdose mortality
3. Stimulant marketing, like opioid marketing, is widespread, particularly meals

Implications:
Marketing may be a counterforce in national efforts to reduce prescribing of controlled substances and overdose mortality
Manufacturers should consider voluntarily ceasing stimulant marketing, and policies should limit the number (not only the dollar value) of industry interactions
Thank you!

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