A Role for Large Data Sources in Assessing Efforts to Improve Opioid Prescribing

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Competing interests

Alec Walker …

- prepared a white paper sponsored by the Opioid Analgesic REMS Program Companies (RPC) on the topic of this talk.
- is coordinating a study of overdose over extended follow-up in long-term opioid users (PMR 3033-2) sponsored by the Opioid Postmarketing Consortium (OPC).
- assessed and published on “doctor/pharmacy shopping” under contract with OPC (PMR 3033-8)
- advised Purdue Pharma on the interpretation of its postmarketing studies (PMR 3051-1, -2, -3, -4) and presented this interpretation at an FDA Advisory Committee meeting on September 10, 2020.
- has received no compensation in relation to today’s presentation and has no related financial interests.

Walker AM, et al. Possible opioid shopping and its correlates. Clin J Pain. 2017 Nov;33(11):976-982
Walker AM et al. Information on doctor and pharmacy shopping for opioids adds little to the identification of presumptive opioid abuse disorders in health insurance claims data. Subst Abuse Rehabil. 2019;10:47-55

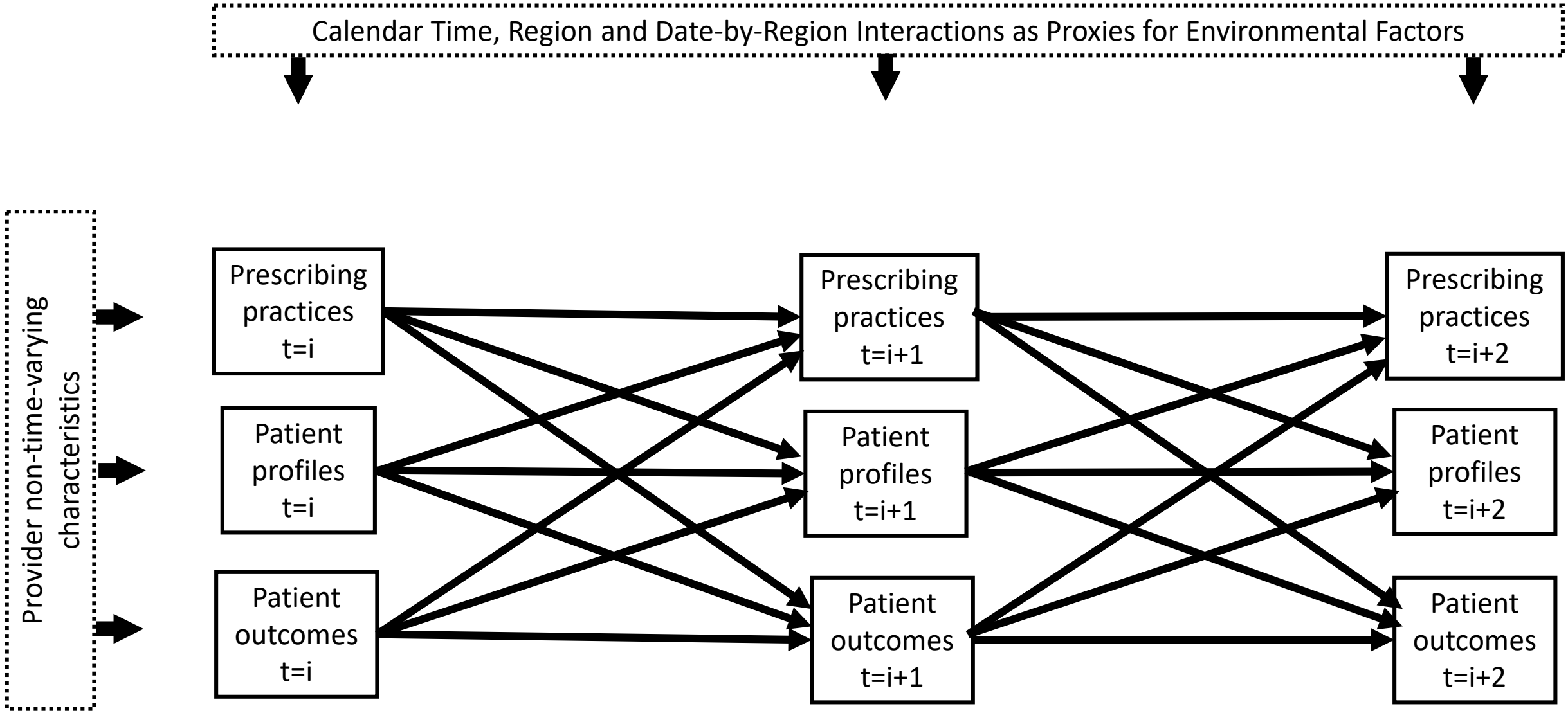
An empirical goal – bring prescribing into line with guidance

- To whom
  - Severity
  - Acuteness
  - Likely duration
  - Comorbidities
- With what
  - Substance
  - Strength
  - Form
  - Duration
- Under what circumstances
  - Concomitant therapy
  - Monitoring

So many determinants of prescribing

- Prescribers' Environment
  - Regulation
  - Promotion
  - Professional and public media
  - Colleagues
- Prescriber
  - Training
  - Experience of patient satisfaction
  - Experience of prior adverse outcomes for pateints
- Patients
  - Pain level
  - Sense of health empowerment
  - Direct and indirect experience of other patients' outcomes

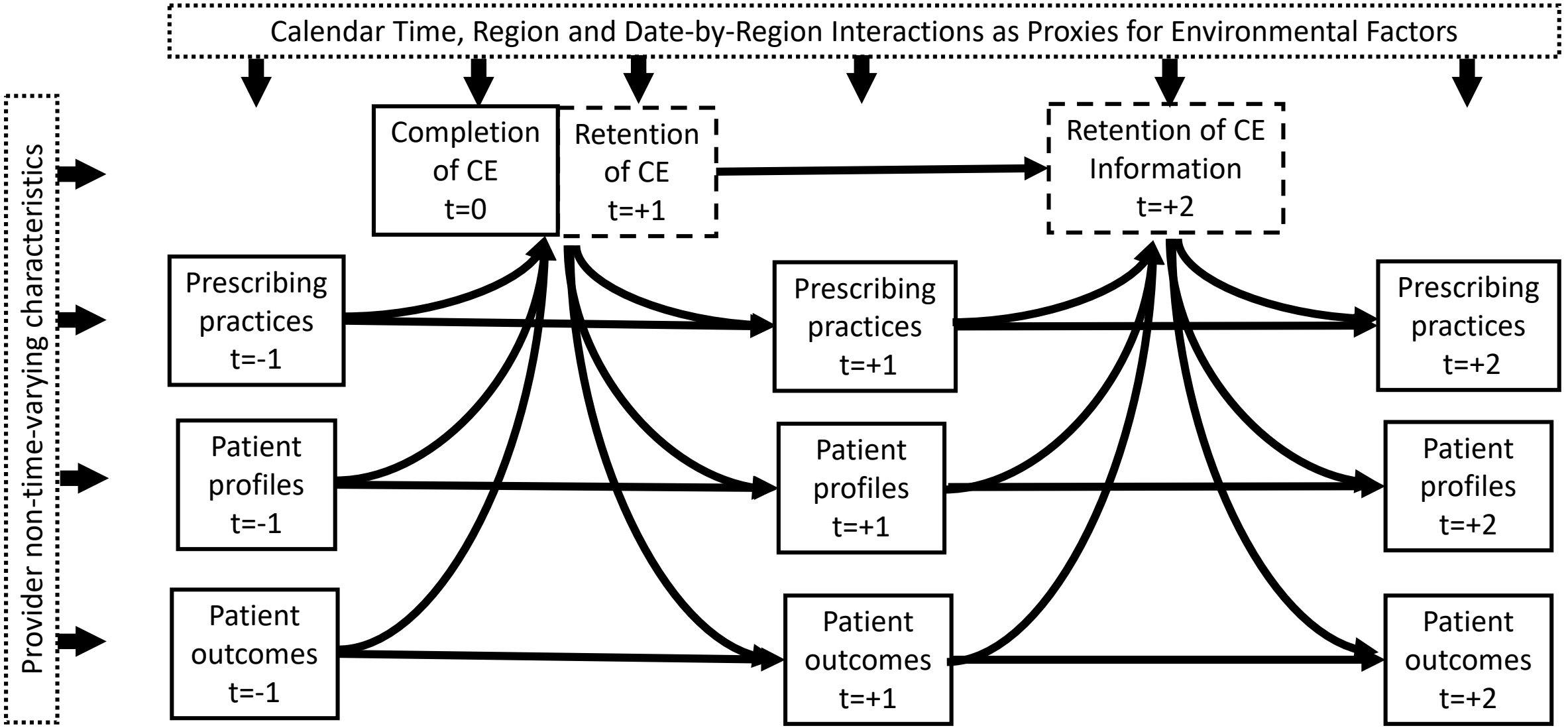
All of these affecting one another, and leading to **turbulence**, not equilibrium.


Calendar Time, Region and Date-by-Region Interactions as Proxies for Environmental Factors
Provider non-time-varying characteristics
Prescribing practices t=i
Patient profiles t=i
Patient outcomes t=i
Prescribing practices t=i+1
Patient profiles t=i+1
Patient outcomes t=i+1
Prescribing practices t=i+2
Patient profiles t=i+2
Patient outcomes t=i+2

Challenges

- “… 527 federal and state opioid-related policies … were approved … 2016–2018... 170 specifically imposed limits on opioid prescribing and an additional 35 specifically referred to, or incorporated, the Centers for Disease Control and Prevention opioid prescribing guideline ...
- “… Assessing the impact of these changes is difficult, at best, but will be necessary if interventions are to be refined to increase their effectiveness.”

Duensing K et al. An Examination of State and Federal Opioid Analgesic and Continuing Education Policies: J Pain Res 2020:13 2431–2442


Calendar Time, Region and Date-by-Region Interactions as Proxies for Environmental Factors
Provider non-time-varying characteristics
Completion of CE t=0
Retention of CE t=+1
Retention of CE Information t=+2
Prescribing practices t=-1
Patient profiles t=-1
Patient outcomes t=-1
Prescribing practices t=+1
Patient profiles t=+1
Patient outcomes t=+1
Prescribing practices t=+2
Patient profiles t=+2
Patient outcomes t=+2

What's in some large data resources

- National dispensing data (~90%) of all dispensings, all time-stamped
  - Prescriber ID and Encrypted recipient ID

  →Any characteristic definable by longitudinal dispensing patterns is calculable (drug dose and form, drug sequencing, total dose, etc.) – both as an outcome and a predictor of later outcomes

  →Prescribers can be characterized according to the kinds of patients they see and patients likewise by the kinds of prescribers they see

  →Patient-prescriber networks can be empirically defined
  - Many practice characteristics, including location and imputed specialty can be attached to prescriber nodes
- Insurers and ACO's have a view of many of the same dispensings and patients, plus
  - Much detailed data on pt from insurance claims histories

Some previous activities to assess patterns of opioid use

- Geographic variation and temporal trends in dispensing
  - Clusters (*post hoc* geo-temporal) and their demographic characteristics
- Derive user characteristics from dispensing data
  - Concurrent use of multiple prescribers and outlets (“shopping”)
- Work backwards from opioid deaths
  - General prescribers per 100,000 population
  - State PDMP characteristics

Basak A et al. Detection of spatiotemporal prescription opioid hot spots with network scan statistics: Multistate analysis. JMIR Public Health Surveill. 2019 Jun 17;5(2):e12110
Cerdá M et al. measuring relationships between proactive reporting state-level prescription drug monitoring programs and county-level fatal prescription opioid overdoses. Epidemiology. 2020 Jan;31(1):32-42
Jones CW et al. Comparison between buprenorphine provider availability and opioid deaths among US counties. J Subst Abuse Treat. 2018 Oct;93:19-25
McDonald DC et al. Geographic variation in opioid prescribing in the U.S. J Pain. 2012 Oct;13(10):988-96
Piper BJ et al. Trends in medical use of opioids in the U.S., 2006-2016. Am J Prev Med. 2018 May;54(5):652-660
Walker AM et al. Information on doctor and pharmacy shopping for opioids adds little to the identification of presumptive opioid abuse disorders in health insurance claims data. Subst Abuse Rehabil. 2019;10:47-55

Many of the CDC's recommended Quality Improvement Measures for opioid prescribing can also be defined and assessed in relation to place and time using dispensing and claims data.

Many more can be assessed when there are electronic health records.

Centers for Disease Control and Prevention. *Quality Improvement and Care Coordination: Implementing the CDC Guideline for Prescribing Opioids for Chronic Pain.* 2018. National Center for Injury Prevention and Control, Division of Unintentional Injury Prevention, Atlanta, GA.

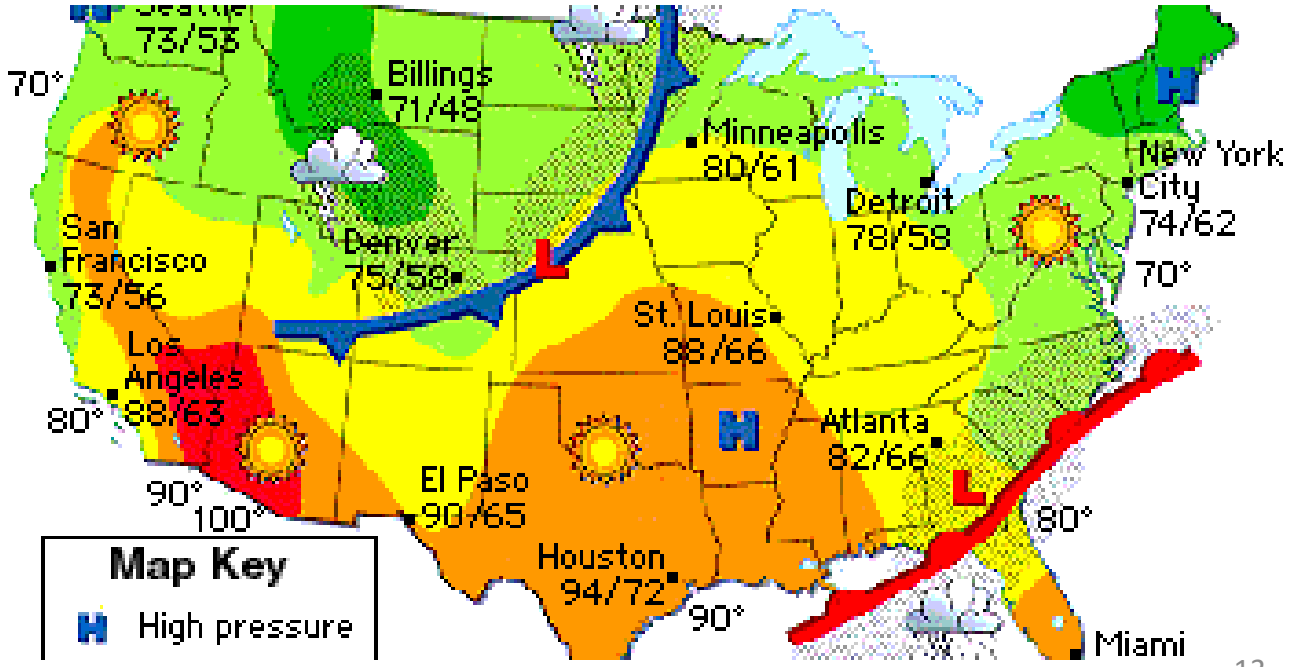
Measures to assess CDC Guidelines		
Feasible for testing in a claims or EHR environment -- ♠ Feasible for testing with dispensing-only data -- ♠		
Short-term opioid therapy		
1.	The percentage of patients with a **new opioid prescription for an immediate-release opioid.**	♠♠
2.	The percentage of patients with a new opioid prescription for chronic pain with documentation that a **PDMP was checked** prior to prescribing.	
3.	… with documentation that a **urine drug test** was performed prior to prescribing.	♠
4.	… **with a follow-up visit within four weeks …**	♠
5.	The percentage of patients with a new opioid prescription for acute pain for a **three days' supply or less.**	♠♠
Long-term opioid therapy		
6.	The percentage of **patients on long-term opioid therapy who are taking 50 MMEs or more per day.**	♠♠
7.	… who are taking **90 MMEs or more per day.**	♠♠
8.	… who **received a prescription for a benzodiazepine.**	♠♠
9.	… who had a **follow-up visit at least quarterly**.	♠
10.	… who had **at least quarterly pain and functional assessments**.	♠
11.	… who had documentation **that a PDMP was checked at least quarterly**.	
12.	… who the clinician **counseled on the risks and benefits of opioids at least annually**.	
13.	… with documentation that a **urine drug test was performed at least annually.**	♠
14.	… who **had at least one referral or visit for nonpharmacologic therapy** as a treatment for pain.	♠
15.	… who were **counseled on the purpose and use of naloxone, and either prescribed or referred to obtain naloxone**.	
16.	The percentage of **patients with an opioid use disorder (OUD) who were referred to or prescribed medication-assisted treatment (MAT)**.	♠

Proposal – A national "weather map" of opioid prescribing

- From dispensing data
  - Choose key outcomes
  - Chunk provider-time into short-term blocks, each characterized by
    - Region, calendar time ← Jointly a proxy for many environmental factors
    - Current patient panel, current patient outcomes, current dispensing
    - Provider-historical prescribing patterns, patient panels
    - Regional-historical prescribing patterns, patient panels
  - Fit regressions to estimate relations
  - Assess short-term forecasting
- Link continuing education recipients to the model using parallel encryption of NPI numbers
- Use forecast behavior for individuals as the counter-factual for assessing CE impact on actual behavior

Uses of the weather map

- Impact of regional efforts
- Areas of high and low compliance
- Areas suitable for PE program evaluation
  - Temporal stability
  - Small regional gradients
- Dynamics and covariates
  - Prescribing patterns
  - Patient profiles
  - Doctor profiles



Direct evaluation of CE with large data – Preliminaries

- Clarity on legal status of use of provider linkage to dispensing data
  - Individual prescribers need to be identifiable and their data usable
  - Any evaluable CE (i.e. REMS-compliant) should have linkage as part of the up-front course agreement of both participants and CE provider
  - Permissions to perform analyses of non-CE interventions
    - Granted in advance, or
    - Present by law or regulation
- Identification of practical regional research environments
  - Demonstrably low or predictable impact of environmental factors on prescribing
  - High prevalence of practices out of line with guidance

Direct evaluation of CE with large data – RCT

- Classic RCT – impact of CE in those who want it
  - Volunteer pool limited to regular prescribers
  - Overweighted for “needs-improvement” patterns
  - Some chosen at random for CE (practice group clusters)
  - Measure trajectory of prescribing before to after in CE trained and not-trained
  - Compared specific CE’s and CE to “usual care”
- Randomized consent – separates out effect of willingness to join
  - At-risk pool of ”needs-improvement” prescribers
  - Investigators approach a randomized subset of practice-group clusters for CE
  - Comparisons
    - Reference group – those not approached
    - Intervention group – those approached
    - Secondary analyses involve subsets according to intervention acceptors and acceptor-like persons in the reference group

Zelen M. A new design for randomized clinical trials. N Engl J Med. 1979;300:1242–1245.
Zelen M. Randomized consent designs for clinical trials: An update. Stats in Med. 1990;9:645–656.

Direct evaluation of CE with large data – Observational designs with individuals

- Single-arm trials
  - Measure trajectory of prescribing before to after CE
  - Highly suspect
    - Self-selection into CE not representative of CE impact
    - Environmental changes over time
- Comparator cohorts, as for RCT except that
  - Volunteers all receive CE
  - Comparators matched on historical trajectory of prescribing
- For both, *post hoc* assessment of a stable research environment
  - Continued relative stability or gradual change in the comparison group

Direct evaluation of CE with large data – Observational designs with groups

- Intervention – *offering* specific CE programs
- Unit of observation – natural groupings of association of prescribers
  - Clinic
  - Care organization
  - Region
- Analysis
  - Unit's treatment allocation is an "instrument" for CE
  - To be analyzed directly (the impact of offering training)
  - Or as a path to program evaluation, with further assumptions
- Comparisons as before

What should be ahead?

- Weather maps
  - The data and methods are available already
  - Results are easy to communicate
  - Public policy can be national without being homogenized
  - **Identify candidate research venues**
- Assessment
  - Existing data are powerful and complete
  - Must have an unimpeded data-use framework
  - Choose venues judiciously
    - Winds of change may not be gale-force in every place
  - Standard research designs apply

Thank you

Thanks also to FDA staff and to Jack Cordes at Harvard TH Chan for useful comments on earlier drafts.

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