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**NOAC Reversal Agent Think Tank Follow-Up:  
Post Approval Safety & Effectiveness**  
*Pharmacoepidemiologic Approaches and Big Data*

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FDA  
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### Likely scenarios

- Patients prescribed NOAC by PCP for maintenance, most likely for A-fib, then present to the ER for a fall, car accident or other trauma.
  - › Operationally, a study would have to recruit these patients in the ER and follow them through any surgeries as well as post-op recovery.
- Patients prescribed NOAC by PCP present to clinic or PCP with pain (e.g., hip pain, etc.) and require surgery .
  - › Operationally, a study could assess whether these patients underwent any treatment changes, i.e. coming off a NOAC and starting traditional anticoagulant therapy to prep for surgery.

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## Assumptions

- NOACs are prescribed in the out-patient setting.
- Most if not all NOAC reversal agents will be administered in a hospital settings.
  - › ER, ICU, OR
- Bleeding events are likely to occur closely in time to administration of NOAC reversal agent
- Longer term follow-up, if required, will likely come from the out-patient setting.

## Big Data for Studying the Safety of NOAC Reversal Agents

- Health Insurance Claims Data
- Pharmacy claims – outpatient & inpatient
- Electronic Health Records
  
- *Who are covered in these data?*
- *Will you know if NOAC users have had a bleeding event, and if so, which reversal agent was used?*
- *How will you get those data?*



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## Big Data for NOAC Reversal Agent Safety Study

- Health Insurance Claims Data
  - Good source for NOAC Prescription that are filled
  - Hospital details are “bundled” for payment; little detail on treatments and events
- Pharmacy Claims – outpatient & inpatient
  - Good source for NOAC Prescription that are filled **but only if filled at hospital or health plan pharmacy**
  - Bad source for in-hospital drugs administered unless \$\$\$\$
- Electronic Health Records
  - Good data on patient characteristics, risk factors & prescriptions that are written
  - Bleeding event will be recorded but no detail from ER, ICU or OR

## The Challenge for NOAC Reversal Agents

The Potential for Drug Safety Studies  
Through Integrated Delivery Systems

An example

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## COMPASS Network

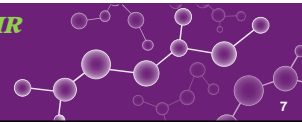
*COMparative effectiveness and PATient Safety & Surveillance*

Quintiles' COMPASS Research network is a distributed data network comprised of **integrated healthcare delivery networks** and **clinical and claims data warehouses**

- > Representing diverse geographies (8 of 9 U.S. Census Divisions)
- > Including diverse practice settings (urban and rural)
- > Covering 13M+ lives

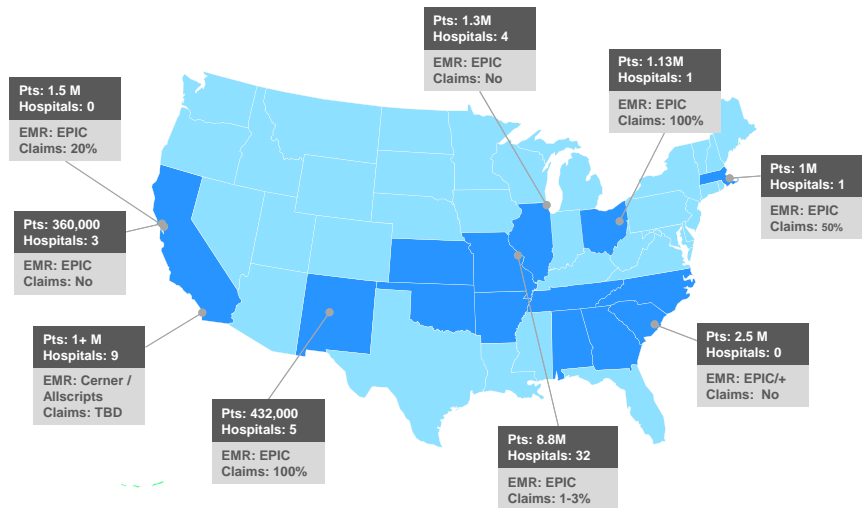


*Integrated delivery networks capture patients' EMR data across the continuum of care, linking de-identified ambulatory, inpatient, surgical, labs & some claims/billing data*



## Quintiles' COMPASS Research Network\*

*Site detail as of Q4 2014*



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**Desired Details of a bleeding event in the EMR**

Examples	Structured Field	Manual Chart Review
• Was NOAC reversal agent used, e.g., pre-op for urgent surgery?	Meds, surgery dates	
• Was there bleeding?	✓	
• Intracranial? Other life-threatening bleed?		Severity and other info may be in progress notes
• Post-op bleeding?		Descriptors may be in progress notes
• Trauma related?		Descriptors may be in progress notes
• Occurred with in-hospital procedure?	✓	

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**Desired Details of a bleeding event in the EMR**

Examples	Structured Field	Manual Chart Review
• Assoc. with medical device?		Progress/surgical notes
• Assoc w other drugs which can augment blood levels of the NOAC?	Con meds	association will be noted by the MD in the notes

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### Counts from 1 Integrated Delivery Network

IDN Size (~M)		Pradaxa (dabigatran)	Xarelto (rivaroxaban)	Eliquis (apixaban)
	<b>Approval date</b>	10/19/2010	7/1/2011	12/12/12
<b>8.0</b>	All patients prescribed NOAC in data warehouse	8,861	22,533	4,387
	Patients prescribed in 2014*	2,540	10,460	2,957
	First order date in 2014	1138	8165	2550

### Count from 2 Integrated Delivery Networks

IDN Size (~M)		Pradaxa (dabigatran)	Xarelto (rivaroxaban)	Eliquis (apixaban)
	<b>Approval date</b>	10/19/2010	7/1/2011	12/12/12
<b>8.0</b>	All patients prescribed NOAC in data warehouse	8,861	22,533	4,387
	Patients prescribed in 2014*	2,540	10,460	2,957
	First order date in 2014	1138	8165	2550
<b>1.3</b>	Total NOAC patients	902	796	256
	Patients prescribed in 2014*	275	503	209
	First order date in 2014	902	796	256

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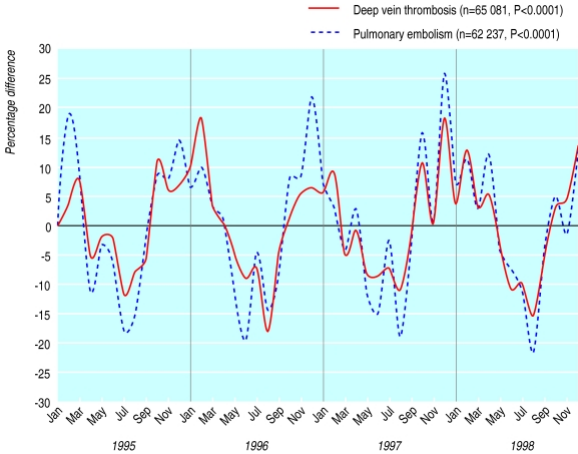


## Other challenges to keep in mind



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## Natural variability in outcomes of interest (e.g., DVT, PE in France, 1995-98)

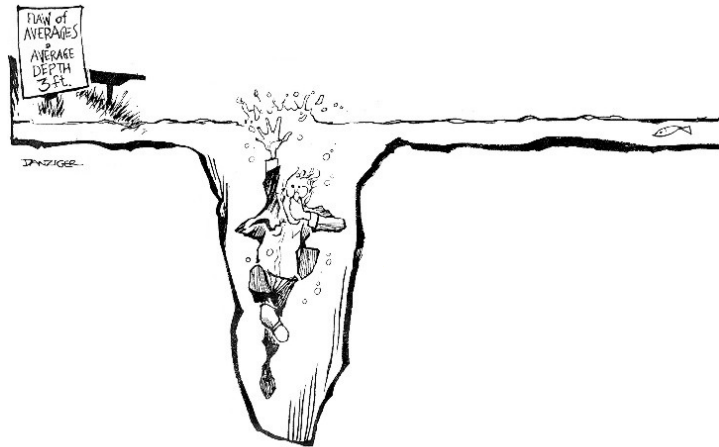


Boulay F et al. Seasonal variations in hospital admission for deep vein thrombosis and pulmonary embolism: analysis of discharge data *BMJ* [323\(7313\); 2001 Sep 15](#)

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## Treatment heterogeneity



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**Understanding drug safety  
from big data is not as simple as a  
push of a button**



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