Duke Clinical Research Institute

Case Study #3: Sentinel Initiative

October 19, 2016

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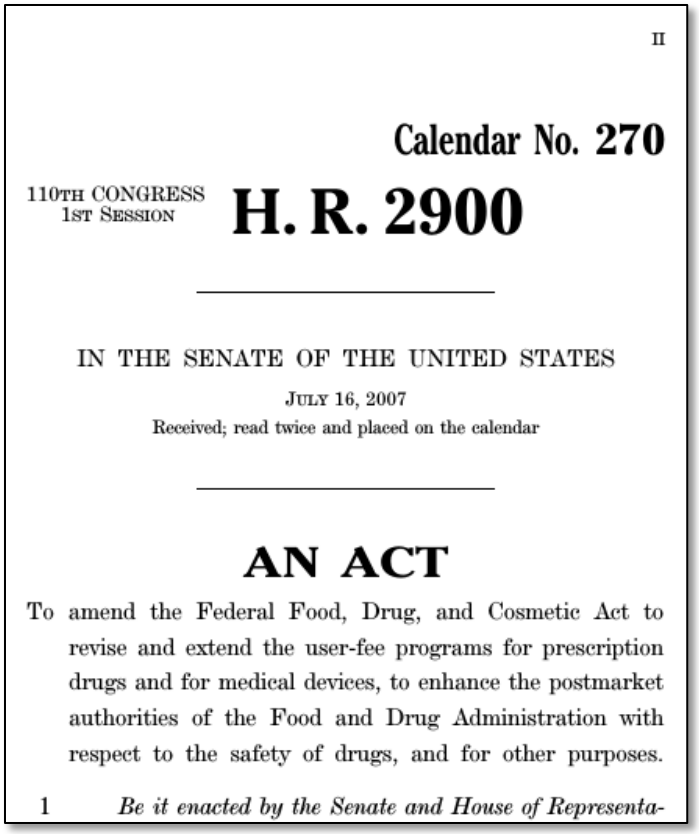
Duke University

Sentinel Initiative

- Response to 2007 FDA Amendments Act mandate to create an active surveillance system
- Mini-Sentinel pilot
- Continuous access to electronic healthcare databases
  - Access data from 25m individuals by July 2010
  - Access data from 100m individuals by July 2012



II

Calendar No. 270

110TH CONGRESS
1ST SESSION

H. R. 2900

IN THE SENATE OF THE UNITED STATES

JULY 16, 2007

Received; read twice and placed on the calendar

AN ACT

To amend the Federal Food, Drug, and Cosmetic Act to revise and extend the user-fee programs for prescription drugs and for medical devices, to enhance the postmarket authorities of the Food and Drug Administration with respect to the safety of drugs, and for other purposes.

Be it enacted by the Senate and House of Representa-

Not-so-secret ingredients

- Engaged partners
- Attention to data quality
- Reusable tools

Sentinel Partner Organizations

Lead – HPHC Institute

Data and scientific partners

Scientific partners

Bringing engaged partners together

- Centralized vs distributed systems
- Distributed data system is preferred because
  - Data sits behind data partner's firewall
  - Data remains under local control
  - Only minimally necessary info is shared in a given analysis
  - Patient privacy and proprietary interests are preserved

Not-so-secret ingredients

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- Attention to data quality
- Reusable tools

Sentinel Common Data Model

Administrative

Enrollment	Demographic	Dispensing	Encounter	Diagnosis	Procedure
Person ID	**Person ID**	**Person ID**	**Person ID**	**Person ID**	**Person ID**
Enrollment start & end dates	Birth date	Dispensing date	Service date(s)	Service date(s)	Service date(s)
Drug coverage	Sex	National drug code (NDC)	Encounter ID	Encounter ID	Encounter ID
Medical coverage	ZIP code	Days supply	Encounter type & provider	Encounter type & provider	Encounter type & provider
Medical record availability	Etc.	Amount dispensed	Facility	Diagnosis code & type	Procedure code & type
			Etc.	Principal discharge diagnosis	Etc.

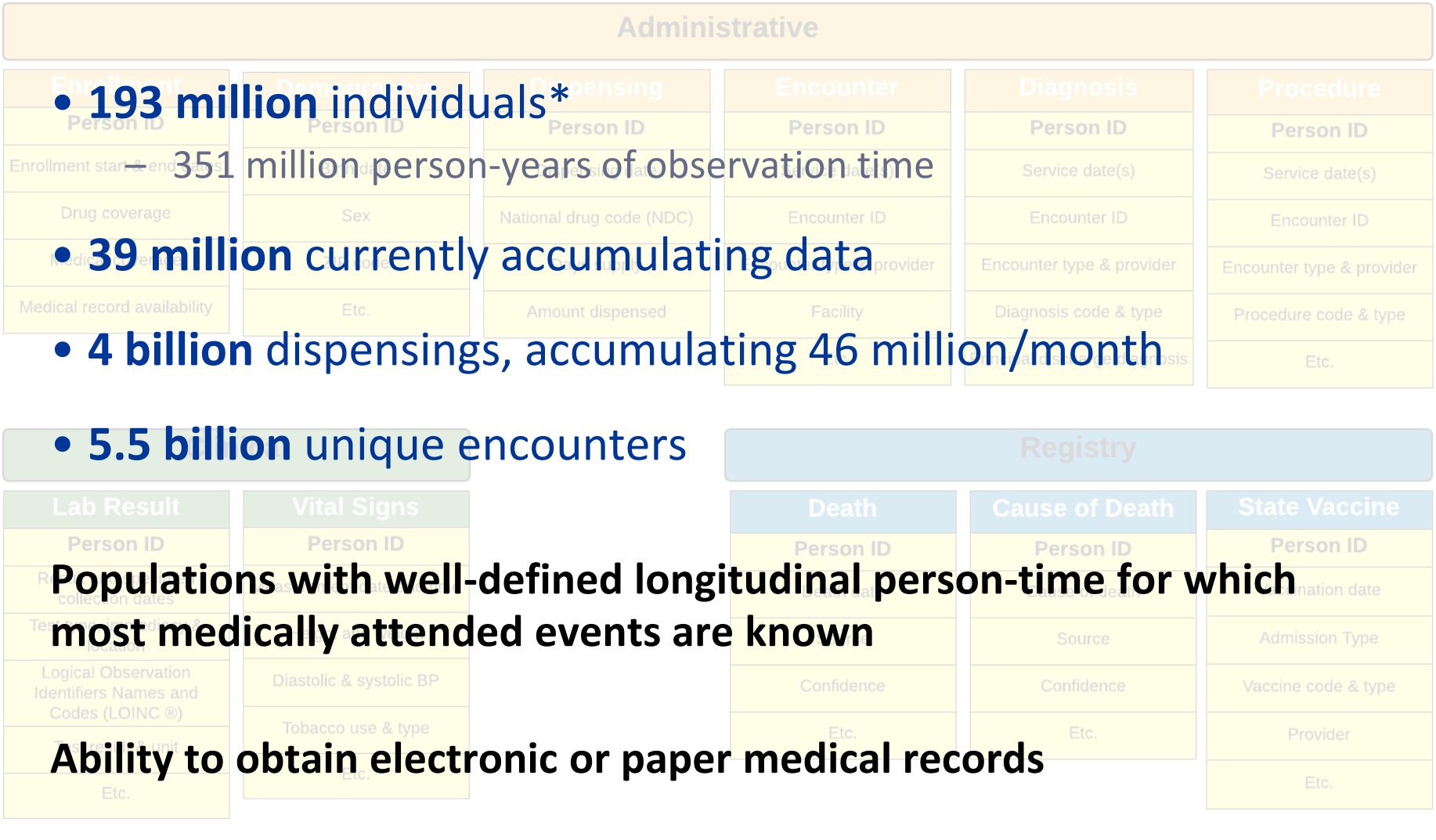
Clinical

Lab Result	Vital Signs
Person ID	**Person ID**
Result and specimen collection dates	Measurement date and time
Test type, immediacy & location	Height and weight
Logical Observation Identifiers Names and Codes (LOINC ®)	Diastolic & systolic BP
Test result & unit	Tobacco use & type
Etc.	Etc.

Registry

Death	Cause of Death	State Vaccine
Person ID	**Person ID**	**Person ID**
Death date	Cause of death	Vaccination date
Source	Source	Admission Type
Confidence	Confidence	Vaccine code & type
Etc.	Etc.	Provider
		Etc.

Sentinel Common Data Model



- **193 million** individuals*
  - 351 million person-years of observation time
- **39 million** currently accumulating data
- **4 billion** dispensings, accumulating 46 million/month
- **5.5 billion** unique encounters

Populations with well-defined longitudinal person-time for which most medically attended events are known

Ability to obtain electronic or paper medical records

Rigorous data checking and characterization

- ~1500 data checks with each refresh

Obs	ENCTYPE	ADATE	COUNT	PERCENT
1	AV	2000	7030952	5.1370
2	AV	2001	7454699	5.4466
3	AV	2002	8014346	5.8555
4	AV	2003	8261199	6.0358
5	AV	2004	8251011	6.0284
6	AV	2005	8857635	6.4716
7	AV	2006	9576674	6.9969
8	AV	2007	10240959	7.4823
9	AV	2008	11831682	8.6445
10	AV	2009	13785025	10.0716
11	AV	2010	14499322	10.5935
12	AV	2011	14988289	10.9508
13	ED	2000	193108	0.1411
14	ED	2001	213180	0.1558
15	ED	2002	231296	0.1690
16	ED	2003	232122	0.1696
17	ED	2004	230756	0.1686
18	ED	2005	266406	0.1946
19	ED	2006	291381	0.2129
20	ED	2007	314060	0.2295
21	ED	2008	343936	0.2513
22	ED	2009	400500	0.2926
23	ED	2010	414312	0.3027
24	ED	2011	451881	0.3302
25	IP	2000	432504	0.3
26	IP	2001	477466	0.3
27	IP	2002	517710	0.3
28	IP	2003	543660	0.3
29	IP	2004	543692	0.3
30	IP	2005	587863	0.4

Obs	RXDATE	N
1	2000JAN	75816
2	2000FEB	68872
3	2000MAR	240058
4	2000APR	248527
5	2000MAY	261254
6	2000JUN	258289
7	2000JUL	241145
8	2000AUG	260316
9	2000SEP	252799
10	2000OCT	260813
11	2000NOV	254161
12	2000DEC	259611
13	2001JAN	275314
14	2001FEB	242270
15	2001MAR	278558
16	2001APR	260591
17	2001MAY	268647
18	2001JUN	267520
19	2001JUL	257699
20	2001AUG	279320
21	2001SEP	251170

Obs	Age_group	COUNT	PERCENT
1	0.1 0-1 Yrs	602059	1.4996
2	02. 2-4 Yrs	1376997	3.4298
3	03. 5-9 Yrs	2553188	6.3595
4	04. 10-14 Yrs	2638462	6.5719
5	05. 15-18 Yrs	2135457	5.3190
6	06. 19-21 Yrs	1670742	4.1615
7	07. 22-44 Yrs	14770481	36.7906
8	08. 45-64 Yrs	11221814	27.9515
9	09. 65-74 Yrs	1854092	4.6182
10	10. 75+ Yrs	1324163	3.2982

Obs	px_codetype	enctype	COUNT	PERCENT
1	09	AV	3891384	0.2061
2	09	ED	940211	0.0498
3	09	IP	7716848	0.4088
4	09	IS	168596	0.0089
5	09	OA	510196	0.0270
6	C2	AV	4906255	0.2599
7	C2	ED	325738	0.0173
8	C2	IP	392155	0.0208
9	C2	IS	18219	0.0010
10	C2	OA	222605	0.0118
11	C3	AV	212648	0.0113
12	C3	ED	5276	0.0003
13	C3	IP	7755	0.0004
14	C3	IS	269	0.0000
15	C3	OA	2030	0.0001
16	C4	AV	1364119936	72.2580
17	C4	ED	95271865	5.0466
18	C4	IP	50242438	2.6614
19	C4	IS	3914519	0.2074
20	C4	OA	27959691	1.4810
21	HC	AV	252901204	13.3963
22	HC	ED	14811325	0.7846
23	HC	IP	8125355	0.4304
24	HC	IS	1600478	0.0848
	HC	OA	31067795	1.6457
	ND	AV	16692216	0.8842
	ND	ED	639229	0.0339
	ND	IP	147970	0.0078
	ND	IS	12924	0.0007
	ND	OA	819916	0.0434
	OT	AV	194765	0.0103
	OT	ED	374	0.0000
	OT	IP	2607	0.0001
	OT	IS	1367	0.0001
	OT	OA	348	0.0000

Why check after every refresh?

- Underlying data sources are dynamic
- Verify compliance with the common data model
- Identify changes in Data Partners' data sources or transformation processes
- Identify problems and/or differences in Data Partners' data transformation methods

Not-so-secret ingredients

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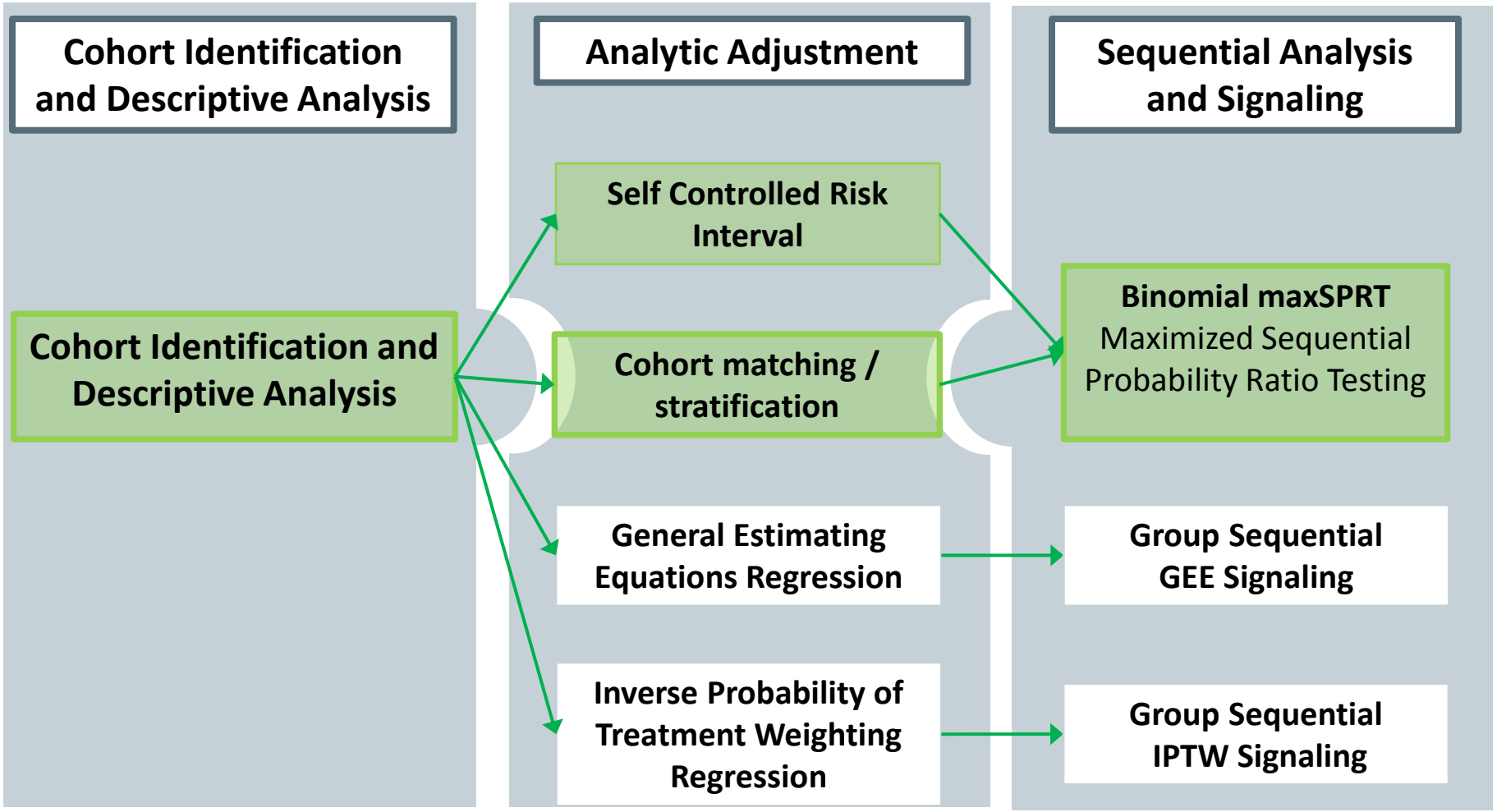
- Reusable tools

Reusable Rapid Query Tools



PERSPECTIVE

DABIGATRAN AND POSTMARKETING REPORTS OF BLEEDING

Dabigatran and Postmarketing Reports of Bleeding

Mary Ross Southworth, Pharm.D., Marsha E. Reichman, Ph.D., and Ellis F. Unger, M.D.

N ENGL J MED 368;14 NEJM.ORG APRIL 4, 2013

Intracranial and Gastrointestinal Bleeding Events in New Users of Dabigatran and Warfarin from the Mini-Sentinel Distributed Database, October 2010 thr

Analysis		Dabigatran	
	No. of Patients	No. of Events	no. 100,0
Gastrointestinal hemorrhage			
Analysis with required diagnosis of atrial fibrillation	10,599	16	
Sensitivity analysis without required diagnosis of atrial fibrillation	12,195	19	
Intracranial hemorrhage			
Analysis with required diagnosis of atrial fibrillation	10,587	8	
Sensitivity analysis without required diagnosis of atrial fibrillation	12,182	10	

* Patients were included in the cohorts if, in the 183 days before the inc rolled in plans for drug and medical coverage and had been given a d were excluded from the cohorts if, in the 183 days before the index di inpatient or emergency department setting or a claim for dispensing drug exposure, from inpatient or emergency department settings only

No increased risk

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 6, 2014 VOL. 370 NO. 6

Intussusception Risk after Rotavirus Vaccination in U.S. Infants

W. Katherine Yih, Ph.D., M.P.H., Tracy A. Lieu, M.D., M.P.H., Martin Kulldorff, Ph.D., David Martin, M.D., M.P.H., Cheryl N. McMahill-Walraven, M.S.W., Ph.D., Richard Platt, M.D., Nandini Selvam, Ph.D., M.P.H., Mano Selvan, Ph.D., Grace M. Lee, M.D., M.P.H., and Michael Nguyen, M.D.

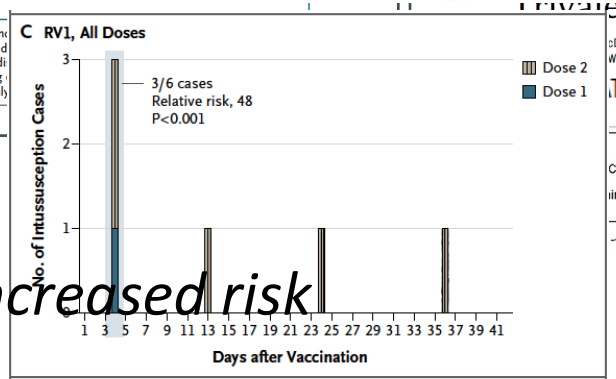


Figure 2. Distribution of Intussusception Cases According to Day of Symptom Onset after Vaccination.

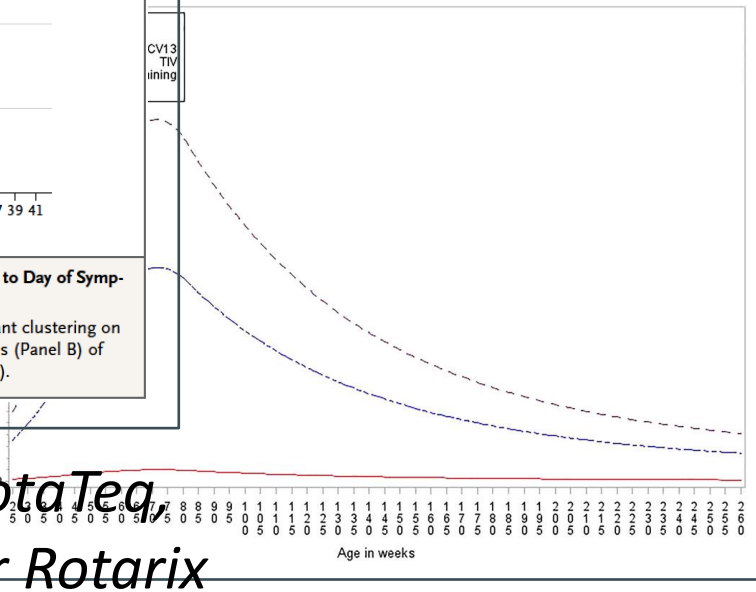
The age-adjusted temporal scan statistic showed significant clustering on days 3 to 7 after the first dose (Panel A) and after all doses (Panel B) of RV5 and on day 4 after all doses of Rotarix (RV1) (Panel C).

No increased risk

Seizures After 2010–2011
nt Inactivated Influenza Vaccine

cD[a], David Martin, MD, MPH[b], Martin Kulldorff, PhD[a], Lingling Li, PhD[a], David V. Cole, BM[a], Walraven, MSW, PhD[c], Nandini Selvam, PhD[d], Mano S. Selvan, PhD[a], Grace M. Lee, MD, MPH[e,f]

TRICS Volume 136, number 4, October 2015



Label change for RotaTeq

No label change for Rotarix

Impact / Dissemination

- 4 FDA drug safety communications
- 48 Methods reports / white papers
- 70 Peer-reviewed articles
- 137 Assessments of products, conditions, product-outcome pairs

Thank you