

TTS in RWD: challenges and opportunities

EMA TTS Workshop
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AGENDA

- Challenges
- Learnings (i) - Background rates
- Learnings (ii) – Historical (O/E) comparisons

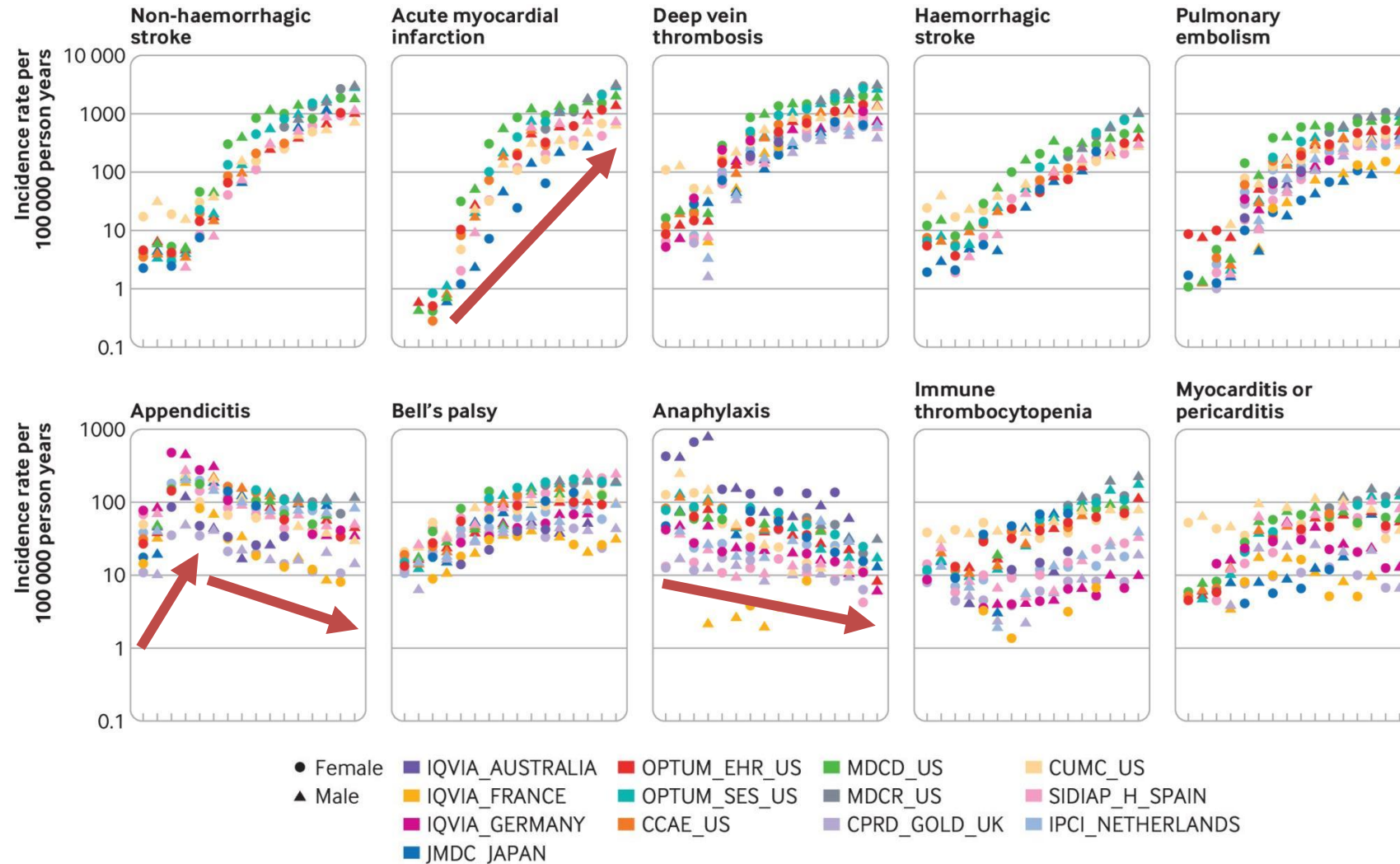
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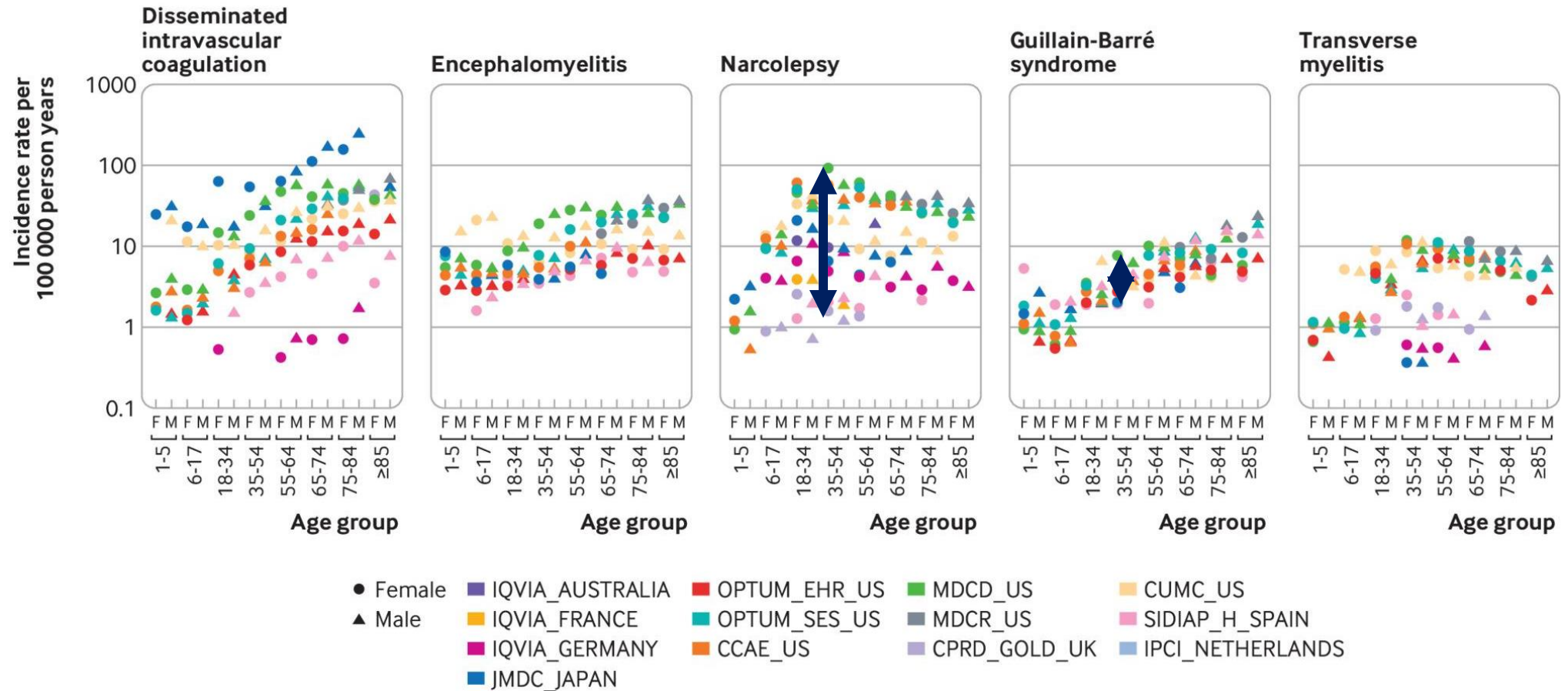
Challenges in the characterisation of background rates in general:

Heterogeneity

Age and sex stratified incidence rates for 15 AESI



Age and sex stratified incidence rates for 15 AESI



Choices

- Great heterogeneity depending on choices e.g. anchoring vs random vs fixed date (eg 1st Jan)
- This affects more for shorter time rate estimation eg 28-day rates

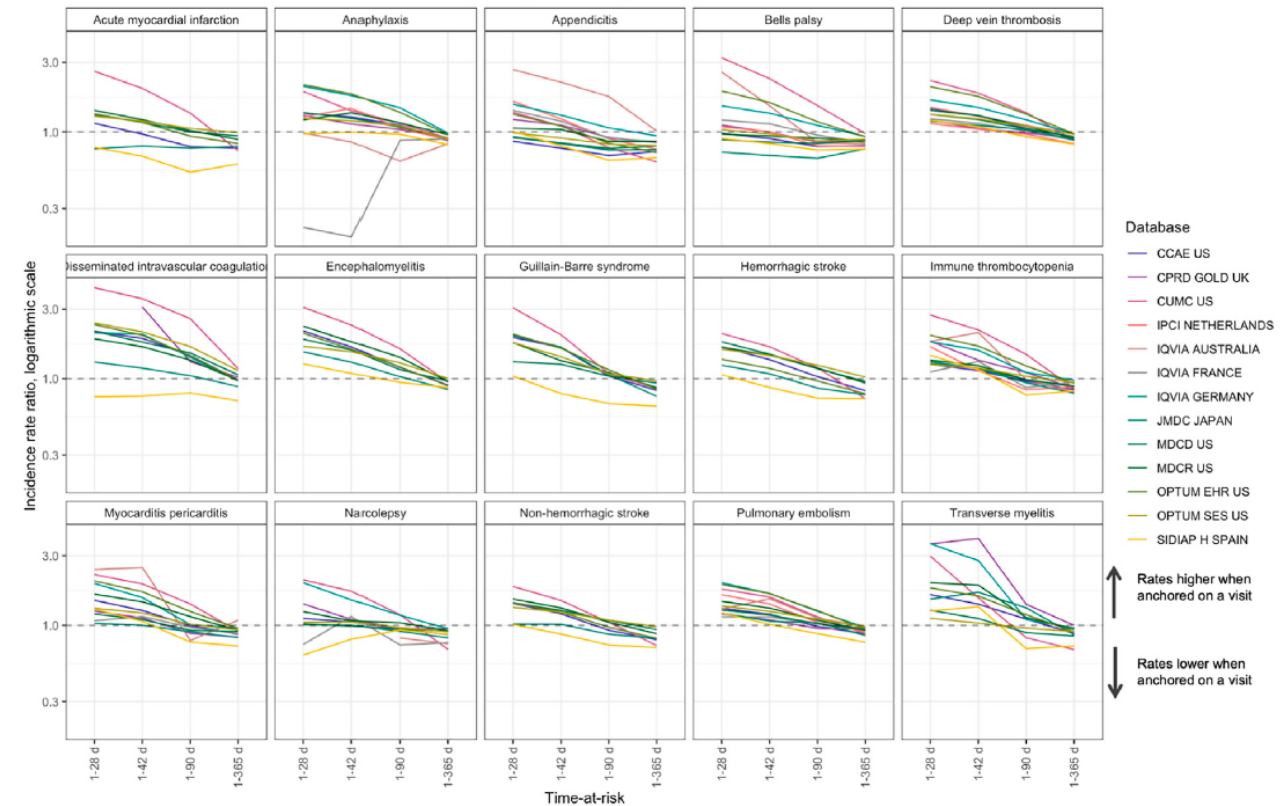


FIGURE 4 | Comparison of anchoring on a random visit versus anchoring on January 1st in patients with a visit in the next year for time-at-risk 1–28, 1–42, 1–90 and 1–365 days, incidence rate ratio.

CONCLUSIONS

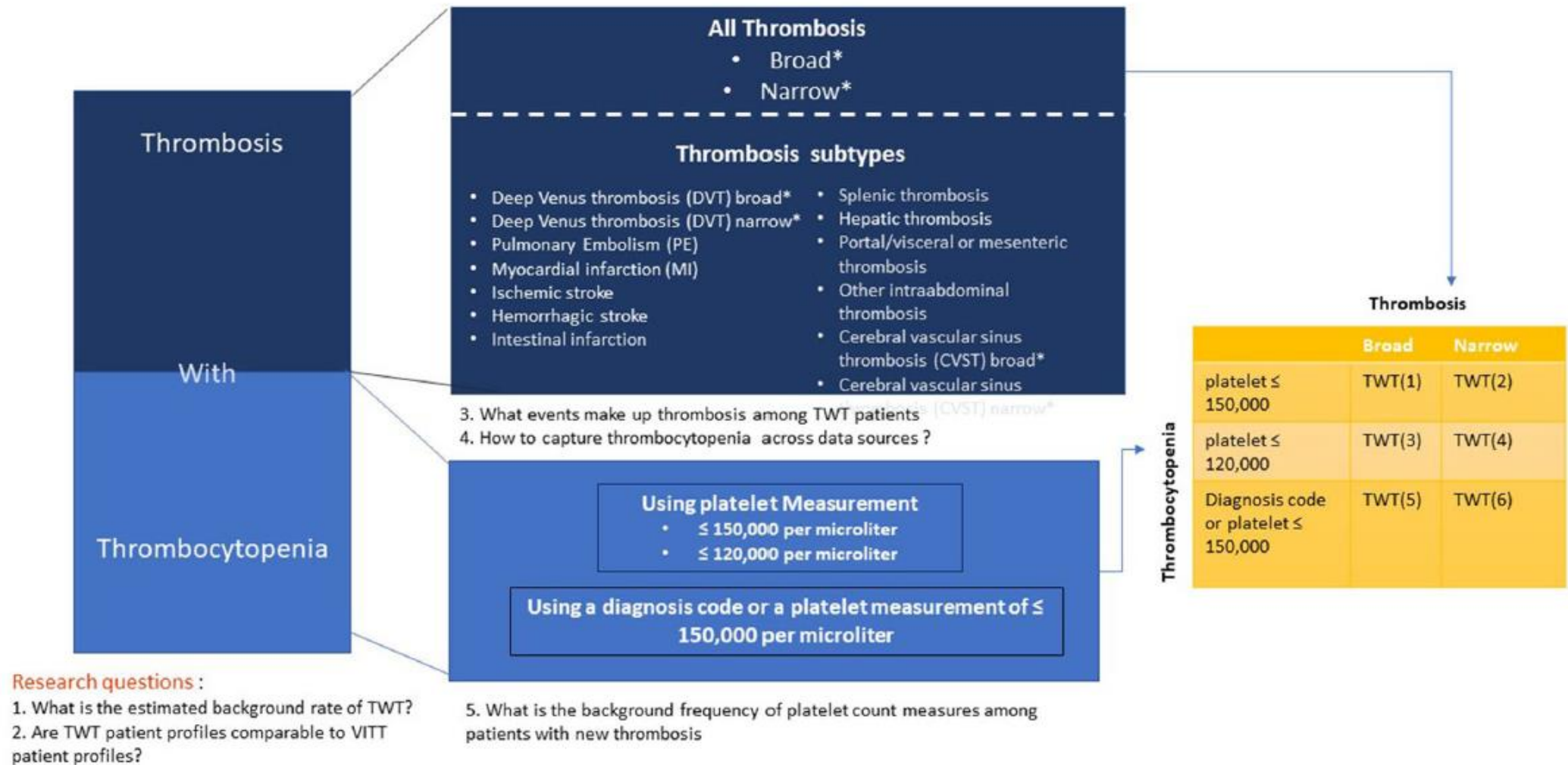
- Background rates are not “one number” ...
- If “one number” is really needed, we need to adjust/standardize by age & sex
- Must use the same data for obs & exp rates (next sections)
- Bear in mind the impact of “anchoring” e.g. post-vaxx

Challenges in the characterisation of background rates of TTS:

Measurements + Diagnoses

There's no code for TwT/VITT ...

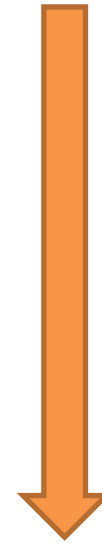
Phenotype Algorithms for the Identification and Characterization of Vaccine-Induced Thrombotic Thrombocytopenia



Diagnosis + Measurements availability...

Table 3 Incidence proportion of platelet measures among patients with thrombotic events and the frequency of a platelet measurement $\leq 150,000$ per microliter among those with a platelet measure

Data source	Thrombosis events <i>N</i>	Any platelet measure <i>N</i>	Proportion of plate- let measures (%)	Platelet < 150,000/ μ l <i>N</i>	Proportion of platelet < 150,000/ among any platelet measure (%)
FIMIM-IMASIS	27,841	24,545	88.16	4787	19.50
HIC	64,231	49,851	77.61	5464	10.96
CUMC	234,584	134,499	57.34	31,439	23.37
Optum_EHR	3,684,392	1,781,677	48.36	322,018	18.07
CC_Serbia	19,236	5079	26.40	1179	23.21
IQVIA_Australia	18,272	3523	19.28	133	3.78
SIDIAP	414,458	79,106	19.09	10,625	13.43
IQVIA_Germany	395,295	28,072	7.10	1553	5.53
CPRD	412,313	27,621	6.70	1401	5.07
Biobank_UK	39,305	2182	5.55	53	2.43



- + many RWD assets (e.g. most health claims) DO NOT HAVE any measurement data
- + no RWD asset that I know of has data on anti-PF4 (or similar) measurements

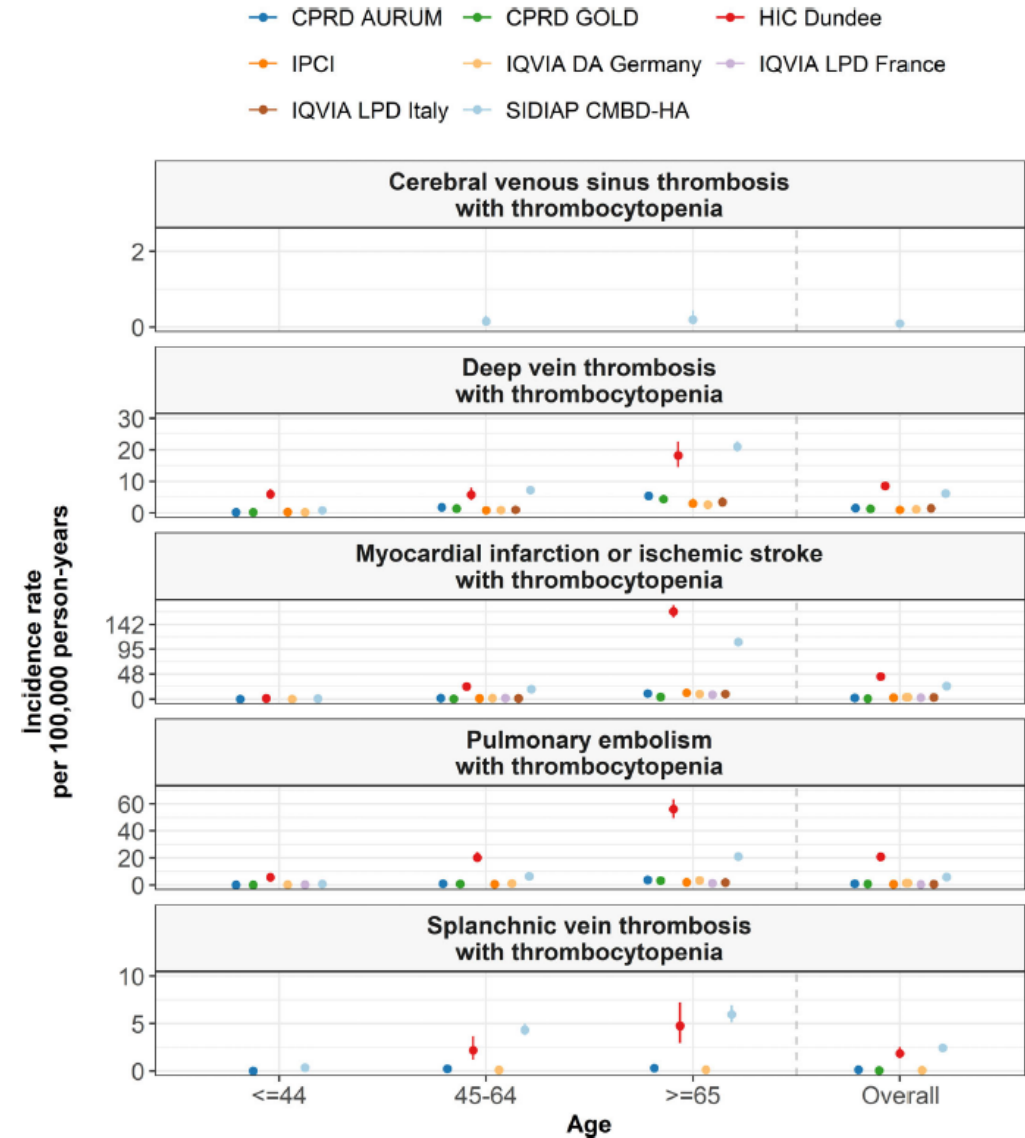
CONCLUSIONS (2)

- TwT is a new syndrome, with no bespoke SNOMED/ICD code
- Identification in RWD depends on the presence of diagnostic codes + lab data
- % of lab measurement/s presence will determine % TwT
- No PF4 or similar antibody measurements readily available

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Background rates of TwT in 8 European datasets



Expected N of events per 10 million person-months in general population

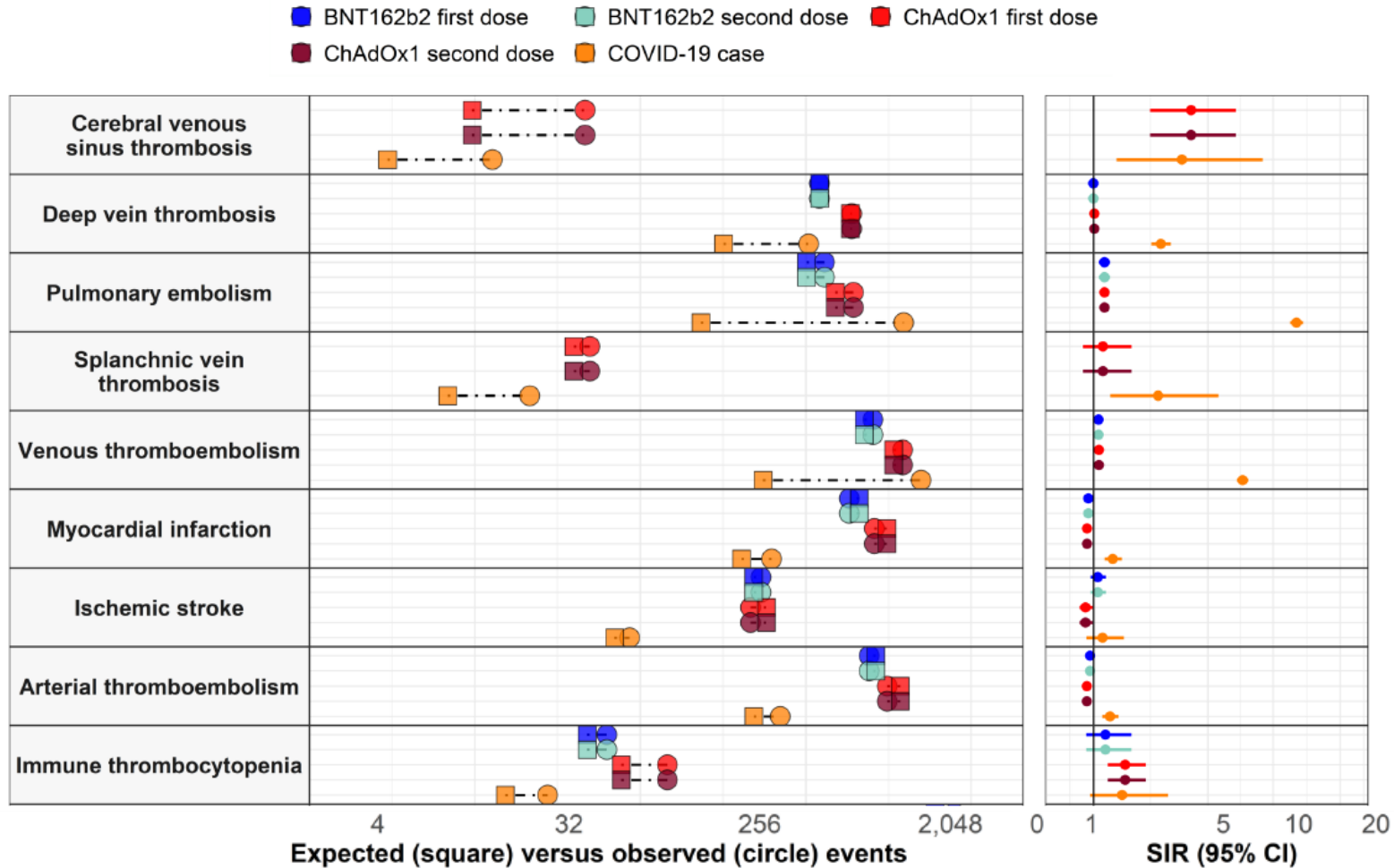
	Age <=44	Age 45-64	Age >=65	Overall	
Cerebral venous sinus thrombosis with thrombocytopenia		2 (1 to 3)	2 (1 to 4)	1 (1 to 2)	SIDIAP CMBD-HA
Deep vein thrombosis with thrombocytopenia	2 (1 to 3)	18 (15 to 21)	53 (48 to 59)	15 (14 to 16)	CPRD AURUM
	2 (1 to 4)	14 (10 to 19)	43 (34 to 54)	13 (11 to 15)	CPRD GOLD
	59 (45 to 75)	58 (40 to 79)	179 (143 to 222)	84 (72 to 97)	HIC Dundee
	3 (1 to 7)	9 (4 to 16)	30 (18 to 46)	10 (7 to 14)	IPCI
	2 (1 to 3)	9 (7 to 12)	26 (22 to 31)	11 (10 to 13)	IQVIA DA Germany
Myocardial infarction or ischemic stroke with thrombocytopenia	10 (4 to 18)	34 (23 to 49)	14 (10 to 20)	14 (10 to 20)	IQVIA LPD Italy
	8 (7 to 10)	72 (64 to 80)	207 (191 to 224)	61 (57 to 65)	SIDIAP CMBD-HA
	1 (0 to 1)	20 (17 to 23)	105 (97 to 114)	24 (22 to 25)	CPRD AURUM
Pulmonary embolism with thrombocytopenia	5 (3 to 9)	43 (34 to 54)	10 (8 to 12)	10 (8 to 12)	CPRD GOLD
	14 (8 to 23)	238 (202 to 279)	1,641 (1,527 to 1,762)	428 (401 to 456)	HIC Dundee
	13 (7 to 21)	118 (94 to 147)	28 (22 to 34)	28 (22 to 34)	IPCI
	2 (1 to 3)	20 (16 to 23)	98 (90 to 106)	35 (33 to 38)	IQVIA DA Germany
	19 (14 to 25)	82 (70 to 95)	27 (24 to 31)	27 (24 to 31)	IQVIA LPD France
Splanchnic vein thrombosis with thrombocytopenia	14 (7 to 24)	99 (78 to 123)	35 (28 to 43)	35 (28 to 43)	IQVIA LPD Italy
	10 (8 to 12)	188 (176 to 201)	1,072 (1,036 to 1,110)	248 (240 to 255)	SIDIAP CMBD-HA
	1 (1 to 2)	10 (8 to 12)	37 (33 to 43)	10 (9 to 11)	CPRD AURUM
Deep vein thrombosis with thrombocytopenia	1 (0 to 2)	8 (5 to 12)	32 (25 to 42)	9 (7 to 11)	CPRD GOLD
	55 (42 to 71)	201 (167 to 238)	553 (488 to 625)	205 (186 to 224)	HIC Dundee
	6 (2 to 13)	21 (11 to 35)	6 (4 to 9)	6 (4 to 9)	IPCI
	2 (1 to 3)	11 (9 to 14)	35 (30 to 40)	15 (13 to 16)	IQVIA DA Germany
	2 (1 to 4)	13 (9 to 19)	5 (3 to 6)	5 (3 to 6)	IQVIA LPD France
Cerebral venous sinus thrombosis with thrombocytopenia	7 (6 to 9)	62 (55 to 70)	207 (191 to 224)	58 (54 to 62)	IQVIA LPD Italy
	0 (0 to 1)	2 (2 to 4)	3 (2 to 5)	1 (1 to 2)	SIDIAP CMBD-HA
	4 (3 to 5)	43 (37 to 49)	59 (51 to 68)	24 (22 to 27)	CPRD AURUM
Myocardial infarction or ischemic stroke with thrombocytopenia		22 (12 to 37)	47 (29 to 71)	18 (13 to 25)	CPRD GOLD
		1 (0 to 2)	1 (1 to 3)	1 (0 to 1)	HIC Dundee
					IPCI
Pulmonary embolism with thrombocytopenia					IQVIA DA Germany
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					CPRD GOLD

E Burn et al. Pharm Drug Saf 2022

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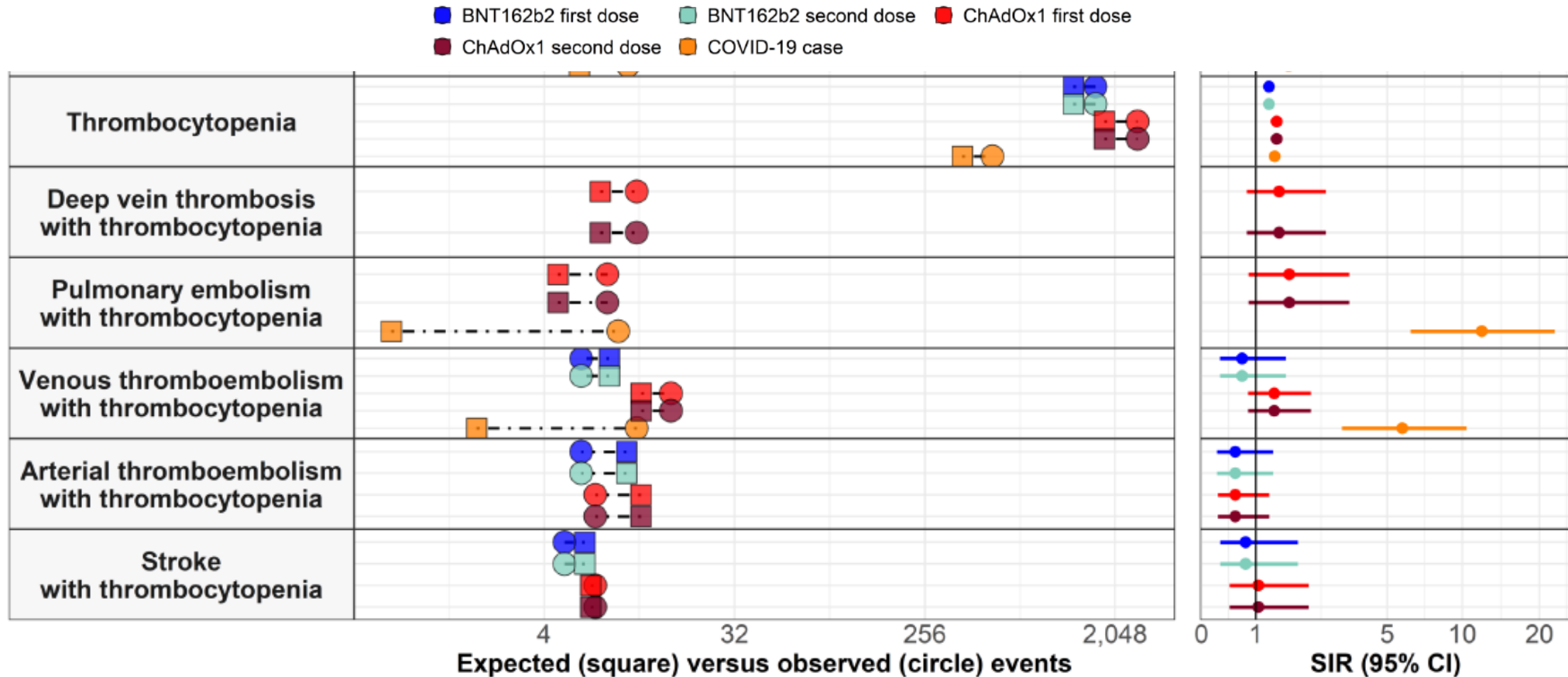
Obs (post-vaxx) / Expected (background) in CPRD AURUM (UK) data



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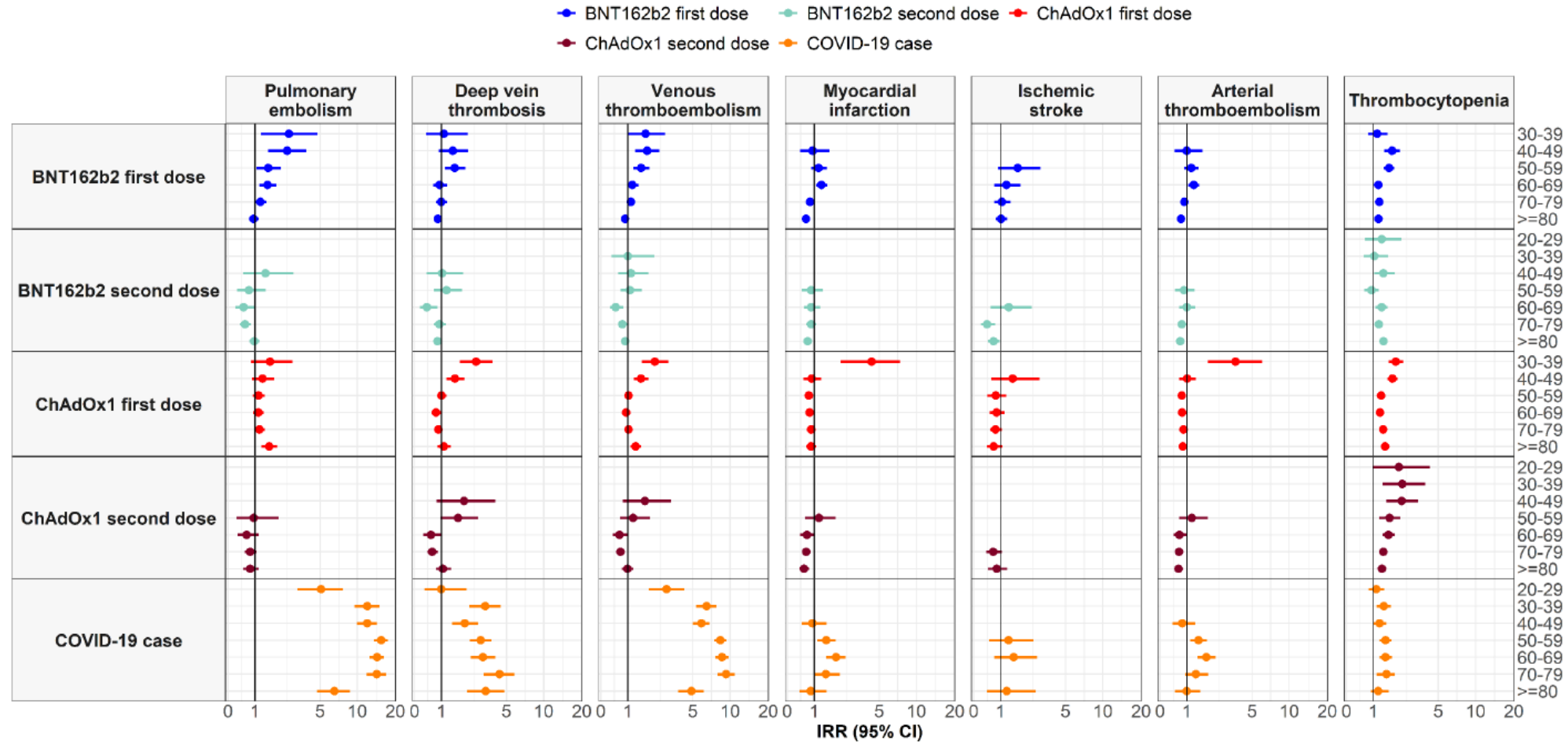
Classified as internal/staff & contractors by the European Medicines Agency

Obs (post-vaxx) / Expected (background) in CPRD AURUM (UK) data (ii)



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Obs (post-vaxx) / Expected (background) in CPRD AURUM (UK) data (iii)



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Questions?

