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Phenotype Algorithms for the Identification and Characterization of Vaccine-Induced Thrombotic Thrombocytopenia in Real World Data: A Multinational Network Cohort Study

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Vaccine safety workgroup

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Background

- VITT has been identified as a rare but serious adverse event associated with coronavirus disease 2019 (COVID-19) vaccines.
- The Brighton collaboration published an interim case definition for VITT, oriented towards identification and treatment of cases
- There is yet no consensus (or a clear guidance) on how to identify VITT cases in real world data (RWD) including claims and electronic health records (EHR).
- RWD can be used to generate important evidence such as, estimating TTS background rate and characterizing the profile of patients who had thrombocytopenia with thrombosis in the past

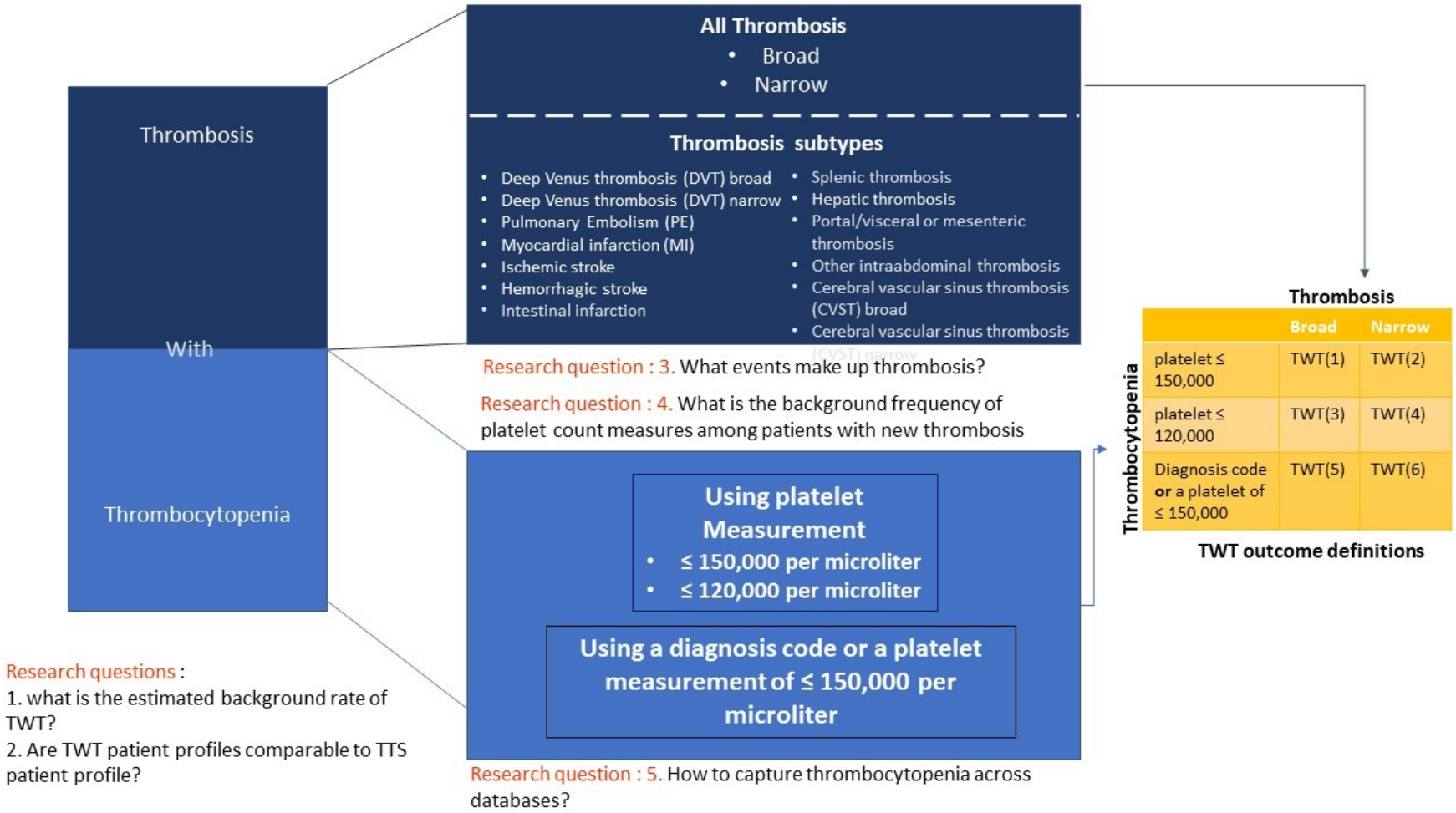
Data

We explored the historical trend of the co-occurrence of thrombosis with thrombocytopenia (TWT) through an international network cohort study using routinely collected primary care and hospital patient records from 17 data sources across the United States (US), Australia, Japan and Europe

Data source	Country	Type	Explicit observation period	Inpatient diagnosis	Outpatient diagnosis	Inpatient measurements	Outpatient measurements	Outpatient drug	Inpatient drug
IBM MarketScan Commercial Claims and Encounters Database (CCAE_US)	USA	Claims	Available	Available	Available	Not Available	Partially availab	Available	Not Available
Optum® De-Identified Clinformatics® Extended Data Mart Database – Date of death (optum_extended_dod_US	USA	Claims	Available	Available	Available	Not Available	Partially availab	Available	Not Available
IBM MarketScan Multi-State Medicaid Database (MDCD_US)	USA	Claims	Available	Available	Available	Not Available	Not Available	Available	Not Available
IBM MarketScan Medicare Supplemental and Coordination of Benefits Database (MDCR_US)	USA	Claims	Available	Available	Available	Not Available	Partially availab	Available	Not Available
Optum® de-identified Electronic Health Record Dataset (OPTUM_EHR_US)	USA	EHR	Not Available	Available	Partially availab	Available	Partially availab	Partially avail	Available
Columbia University Irving Medical Center (CUMC_US)	USA	Hospital EHR	Not Available	Available	Partially availab	Available	Available	Partially avail	Available
Clinical Practice Research Datalink (CPRD)	UK	GP records	Available	Not Available	Available	Not Available	Available	Available	Not Available
UK biobank (UK biobank)	UK	Registry	Available	Partially availab	Available	Not Available	Available	Available	Not Available
Health Informatics Centre from University of Dundee (HIC)	Scotland	Hospital EHR	Available	Available	Available	Available	Available	Available	Not Available
Integrated Primary Care Information (IPCI_NETHERLANDS)	Netherlan	GP records	Not Available	Not Available	Available	Not Available	Available	Not Available	Available
Health Data Warehouse of Assistance Publique - Hopitaux de Marseille (APHM)	France	Hospital EHR	Available	Available	Not Available	Available	Available	Not Available	Available
Information System for Research in Primary Care (SIDIAP)	Spain	EHR	Available	Available	Available	Not Available	Available	Available	Not Available
Information System of Parc Salut Mar Barcelona (FIMIM)	Spain	Hospital EHR	Available	Available	Partially availab	Available	Not Available	Not available	Available
IQVIA Disease Analyser Germany (IQVIA_GERMANY)	Germany	GP records	Not Available	Not Available	Available	Not Available	Partially availab	Available	Not Available
University Clinical Center of Serbia (CC-SERBIA)	Serbia	Hospital EHR	Not Available	Available	Available	Available	Available	Not available	Available
IQVIA® Australia Longitudinal Patient Data (IQVIA Australia)	Australia	GP records	Not Available	Not Available	Available	Not Available	Available	Available	Not Available
Japan Medical Data Center (JMDC_JAPAN)	Japan	Claims	Available	Available	Available	Not Available	Not Available	Available	Available

VITT Definition

Patients with a diagnosis of embolic or thrombotic arterial or venous events and a diagnosis or measurement of thrombocytopenia within 7 days



Results

Background incidence rate and patient's profiles

- The overall incidence rate ranged from 1.62 (in CPRD) to 150.65 (in MDCR) per 100,000 person-years.
- Substantial heterogeneity across data sources and by age group and sex within the same data source.
- Higher rates were observed among men of older age groups.
- Identified cases were likely to have preexisting conditions such heart disease, malignancies and liver disease.
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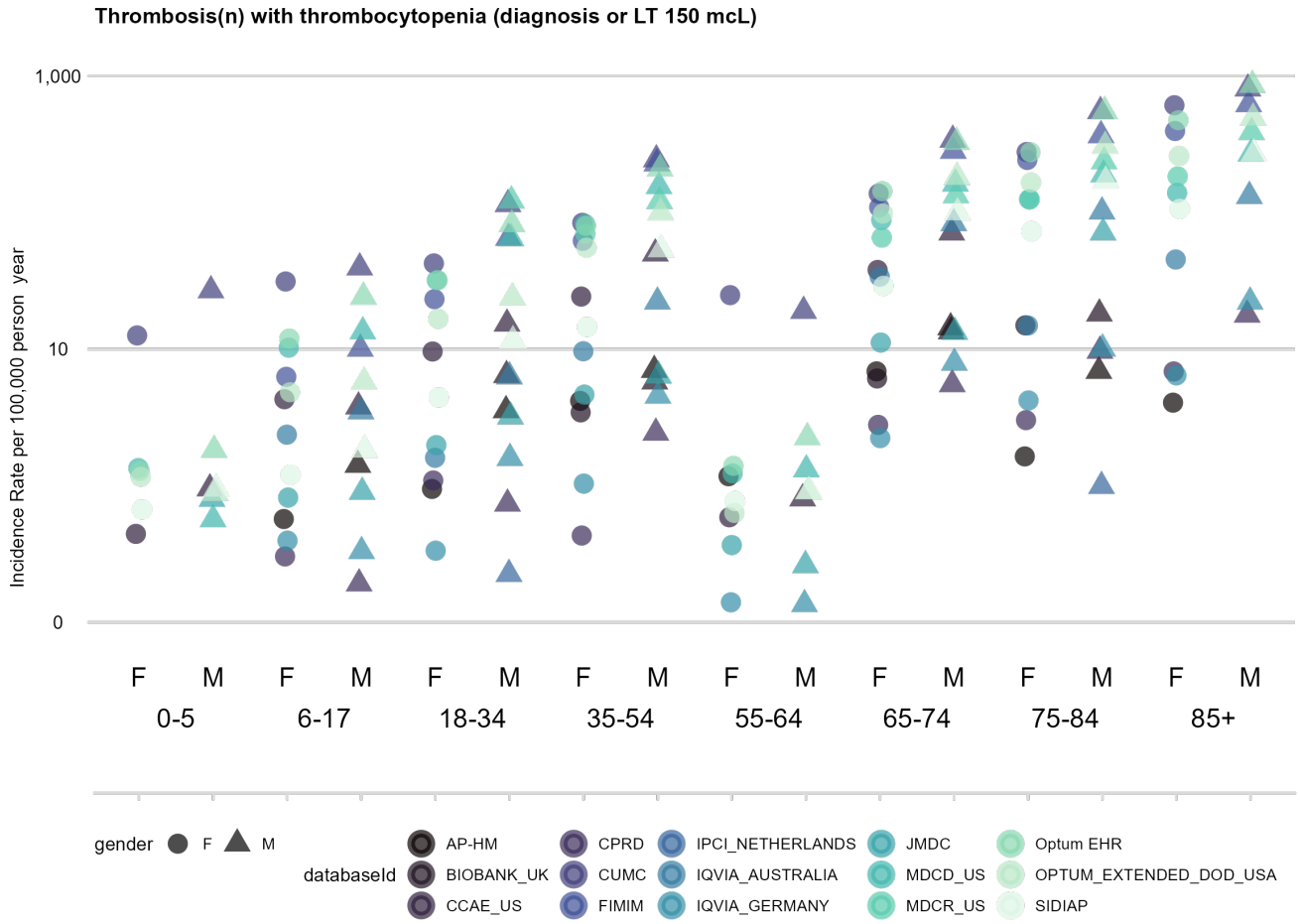

Conclusion

- Thrombocytopenia does co-occur frequently with thrombosis in RWD
- Current definitions is likely to capture cases that are not a true representation of the new emerging clinical phenomena of VITT but merely a coincidental co-occurrence of two common clinical events
- Can't reliably generate background rates of VITT from observational data
- If RWE is to be used to explore, further evaluation of cases will be required
- The vaccine safety workgroup is the best team I ever worked with

- Thank you ☺

Results

Patients' medical history

- likely to be men of older age with various comorbidities.
- An average of 66.65% had a heart disease at baseline
- Chronic liver disease ranged from 1.3% to 15.1% .
- Renal impairment ranged from 3.5% to 48.9%
- Malignant neoplastic disease ranged from 8.3% to 36.50%

characteristic	CCAE_US	Optum_extended_	MDCD_US	MDCR_US	OPTUM_E	CUMC_US	CPRD
Gender = female	39.40%	41.00%	49.40%	40.30%	37.60%	41.70%	34.70%
Medical history							
Chronic liver disease	11.10%	8.50%	15.10%	5.00%	6.00%	6.10%	1.30%
Diabetes mellitus	26.80%	38.30%	35.00%	34.10%	29.50%	15.90%	3.00%
Hyperlipidemia	40.00%	63.90%	36.90%	51.50%	47.70%	18.40%	0.80%
Hypertensive disorder	55.60%	76.90%	65.20%	72.40%	60.40%	35.70%	3.60%
Renal impairment	27.30%	48.90%	42.90%	38.00%	37.00%	20.90%	8.20%
Heart disease	66.00%	79.90%	73.40%	83.90%	74.50%	69.60%	36.10%
Obesity	16.40%	17.50%	15.10%	7.80%	16.30%	4.10%	0.50%
Malignant neoplastic disease	23.50%	26.80%	17.90%	30.70%	15.80%	14.90%	15.00%
Heparin use in the last 30 days	8.60%	8.10%	6.80%	5.00%	54.80%	28.70%	9.40%

Results

Make up of thrombosis

- Despite variation in coding practices and granularity of medical terms used across different data sources; the most occurring thrombotic events were MI, ischemic and hemorrhagic strokes, DVT and PE