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Safety of vaccines: Lessons learned

WHO, R&D Blueprint, 25 October, 2021

Marco Cavaleri, Head of Biological Health Threats and Vaccine Strategy, European Medicines Agency

COVID-19 vaccines approved in the EU

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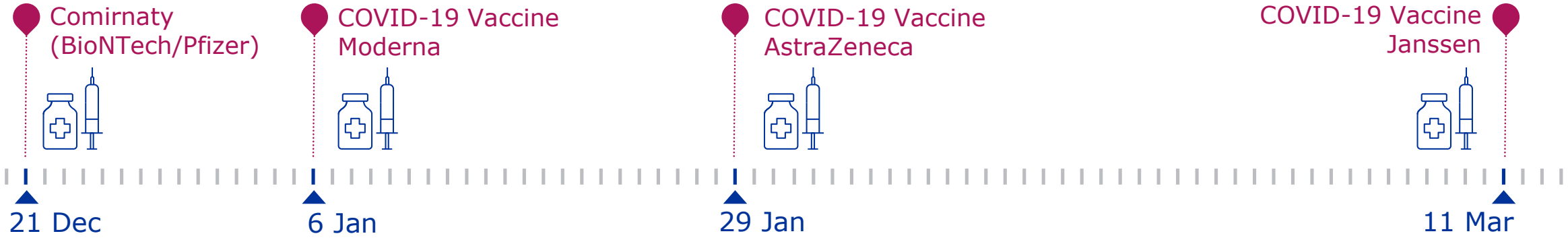
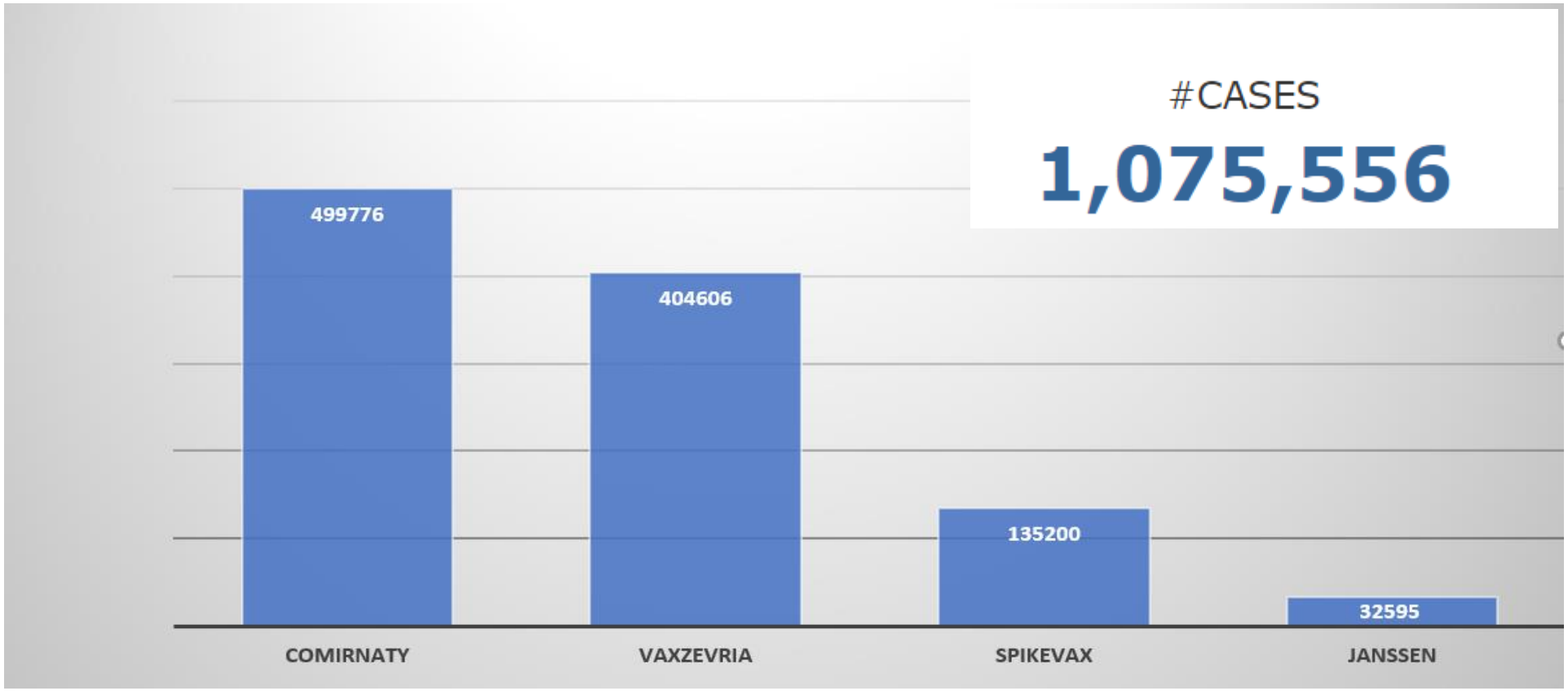
4 vaccines **authorised in the EU**

- Approval via Conditional Marketing Authorisation based on RCTs recruiting several thousands subjects
- Rare adverse reactions with frequency lower than 1 in 10,000 could not be determined pre-approval and required post-authorisation monitoring via active and passive surveillance
- **No signicant safety concerns were emerging at time of approval**



More reports received with 4 vaccines than all other Centrally authorised products in 1 year



Represents data received in EudraVigilance (EVDAS) as of 6th Oct 2021

Vaxzevria-Signal of rare cases of thrombosis with thrombocytopenia (TTS)

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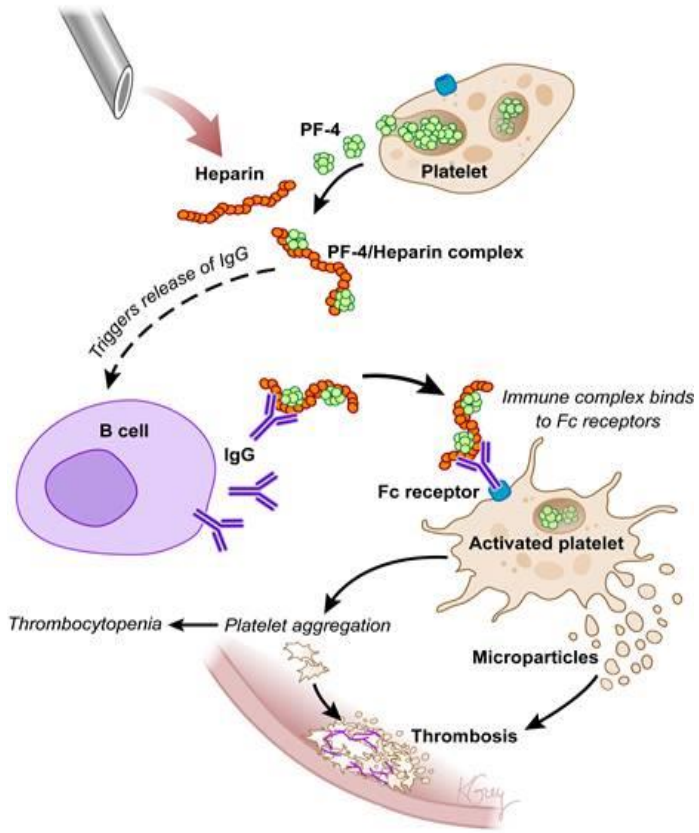
- Cases picked up initially in unusual location (e.g. CVST, Splanchnic Thrombosis, DIC)
- Cases in EV appear similar to HIT-like syndrome
- New clinical entity was identified Thrombosis Thrombocytopenia Syndrome (**TTS**)= platelets count decreased + thromboembolism
- Frequency: about **1/100.000** vaccinees
- Same risk was confirmed also for Janssen
- Second doses did not show same size of the risk
- Continuous monitoring of the new cases + frequency
- Further research to characterise TTS and pathophysiology



Temporary pause of vaccination programme

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Requirement for "real time" data concerning safety monitoring to ensure appropriate decision making → inform policy makers/public health agencies.

- Temporary pause in vaccination programme in several EEA countries (e.g. NL, IE, DK etc.) →pending outcome of extraordinary PRAC on 18th March.

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EMA's safety committee continues investigation of COVID-19 Vaccine AstraZeneca and thromboembolic events – further update

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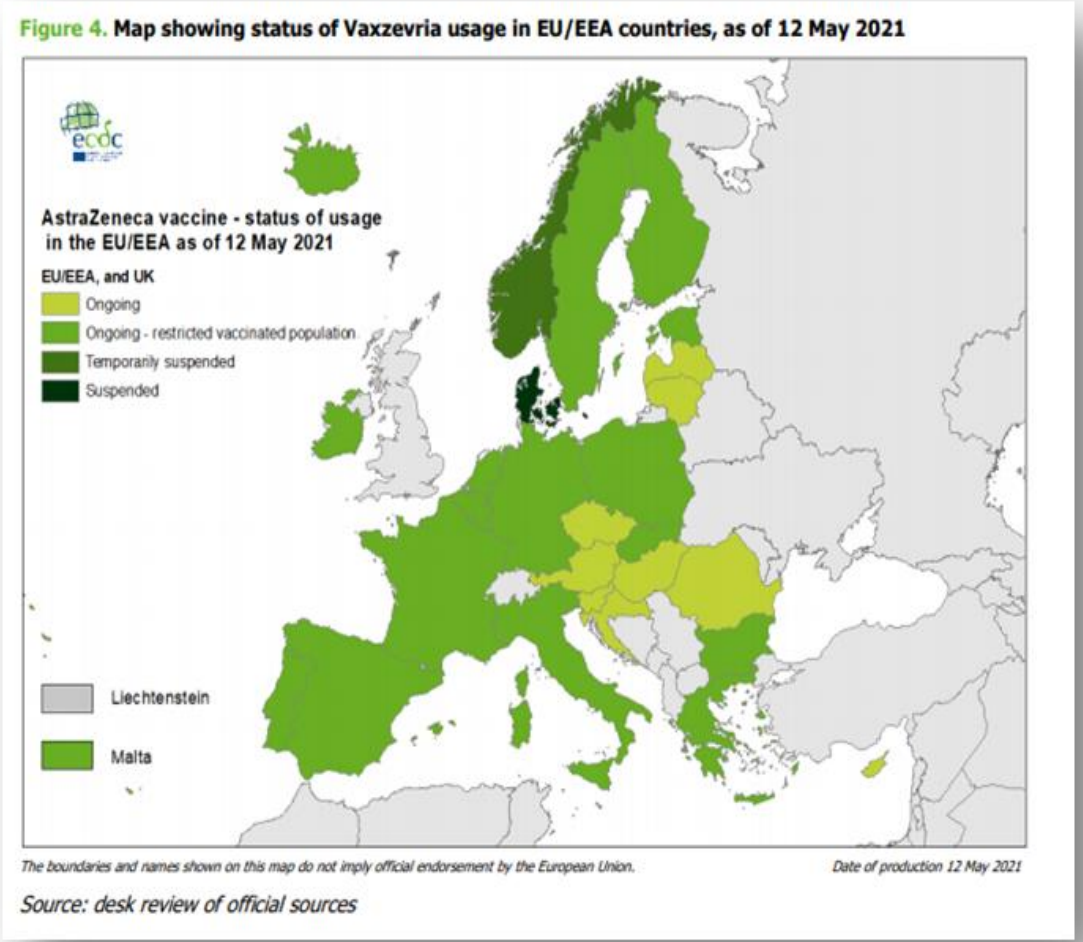
Several authorities responsible for national vaccine campaigns in EU countries have temporarily paused vaccination with Vaxzevria (previously COVID-19 Vaccine AstraZeneca). This is a precaution taken in the light of their national situation while EMA investigates a number of events of blood clots in people who had received the vaccine, as previously reported.

- Resumed use of Vaxzevria® within the vaccination programme on the 18th March but subsequently imposed restrictions concerning use of COVID-19 non-replicant adenovirus vector-based vaccines:
  - Twelve EU/EEA countries based their recommendation on information concerning benefit risk contextualization provided by EMA within the context of Article 5(3) procedure (as reported to ECDC (12 May 2021)



Risk contextualisation of vaccination with Vaxzevria

Medium infection rate*

per 100,000 people, after 1st dose

Age	Cases of COVID-19 **ICU admissions prevented**	Cases of blood clots with low platelets
20-29	3	1.9
30-39	5	1.8
40-49	10	2.1
50-59	15	1.1
60-69	28	1
70-79	39	0.5
80+	29	0.4

* "Medium" exposure: using virus circulation for March 2021 (incidence 401/100,000 population)

Risk contextualisation of vaccination with Vaxzevria

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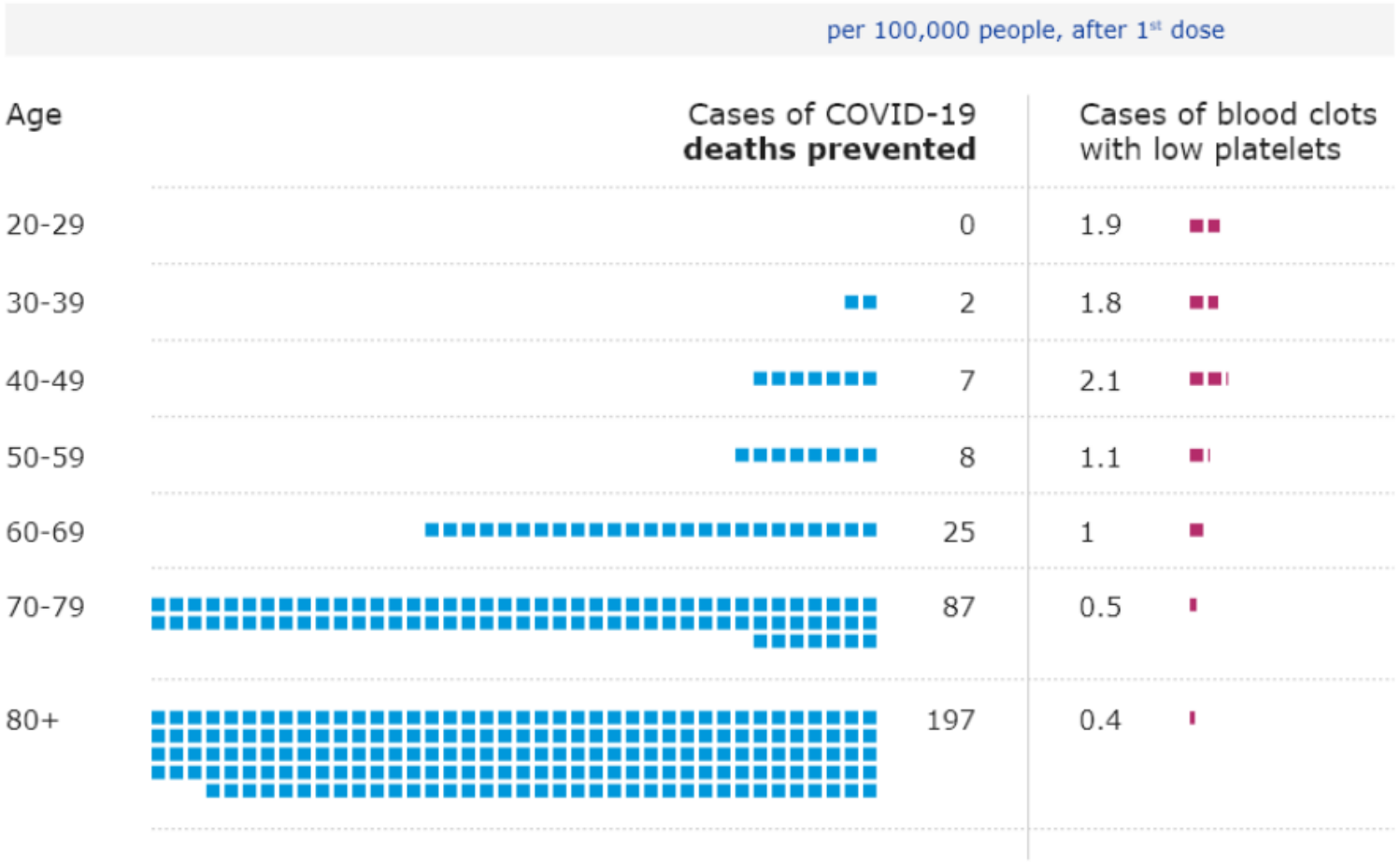

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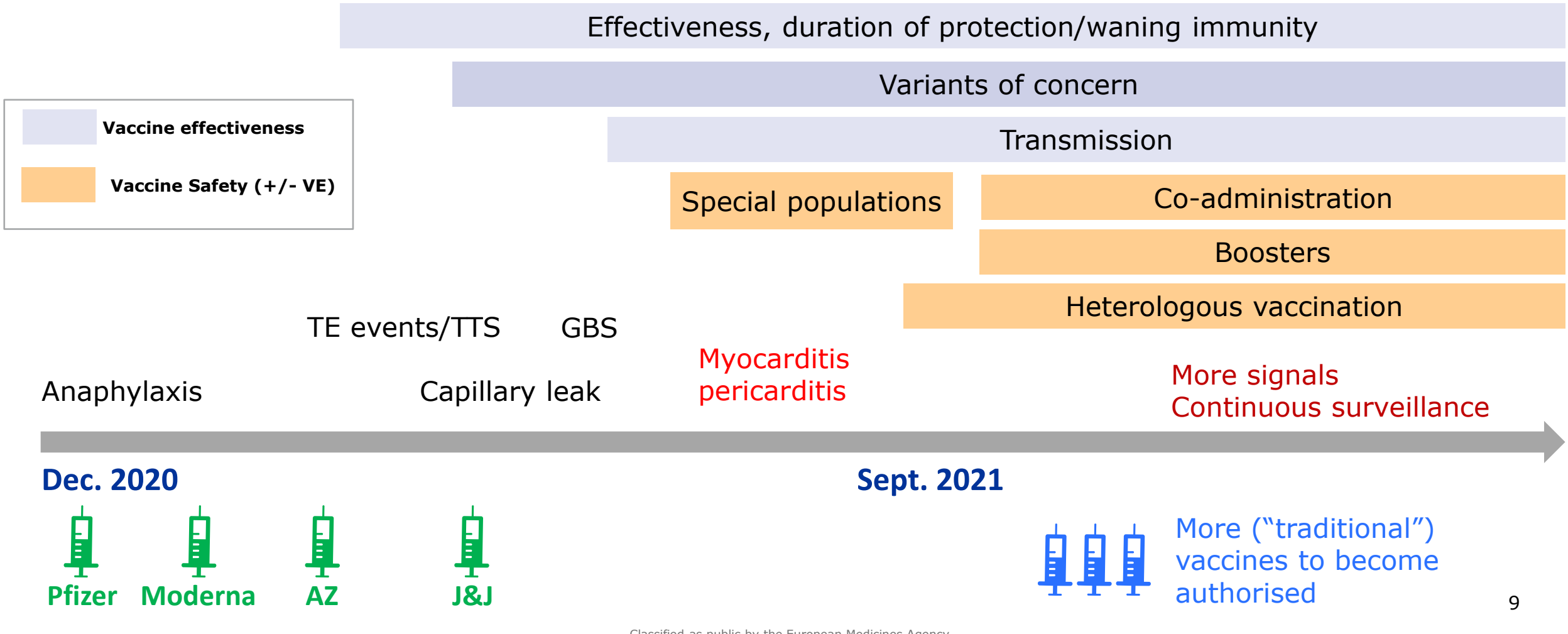
Challenges

- Background rates ≠ predefined AESI →need for rapid generation for new signals.
- Readiness/limitations of EHRs (impact of lagtime on data availability, outcome ascertainment, linkage to hospital data).
- Case definitions, phenotypes for case finding.
- Pharmacogenomic & lab data→availability & validity.
- Quantifying associations: appropriate adjustments (risk factor data), design to allow measure of AR.
- Risk periods (TTO from spontaneous reports, biological plausibility).
- Impact of pandemic on healthcare systems.

Learnings

- Primary data collection using modern tools for prospective monitoring (apps) allowing near-real time surveillance.
- Value of large healthcare databases (sample size, hospital data, federated networks, common data models, rapid analyses possible).
- Value of EMA framework contracts.
- Consortia with demonstrated capacity/expertise.
- International collaborations with other regulators.
- Mechanistic studies to elucidate pathophysiology

Research questions mirror the deployment of the vaccination campaigns and the accumulating post-authorisation experience



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Further information

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