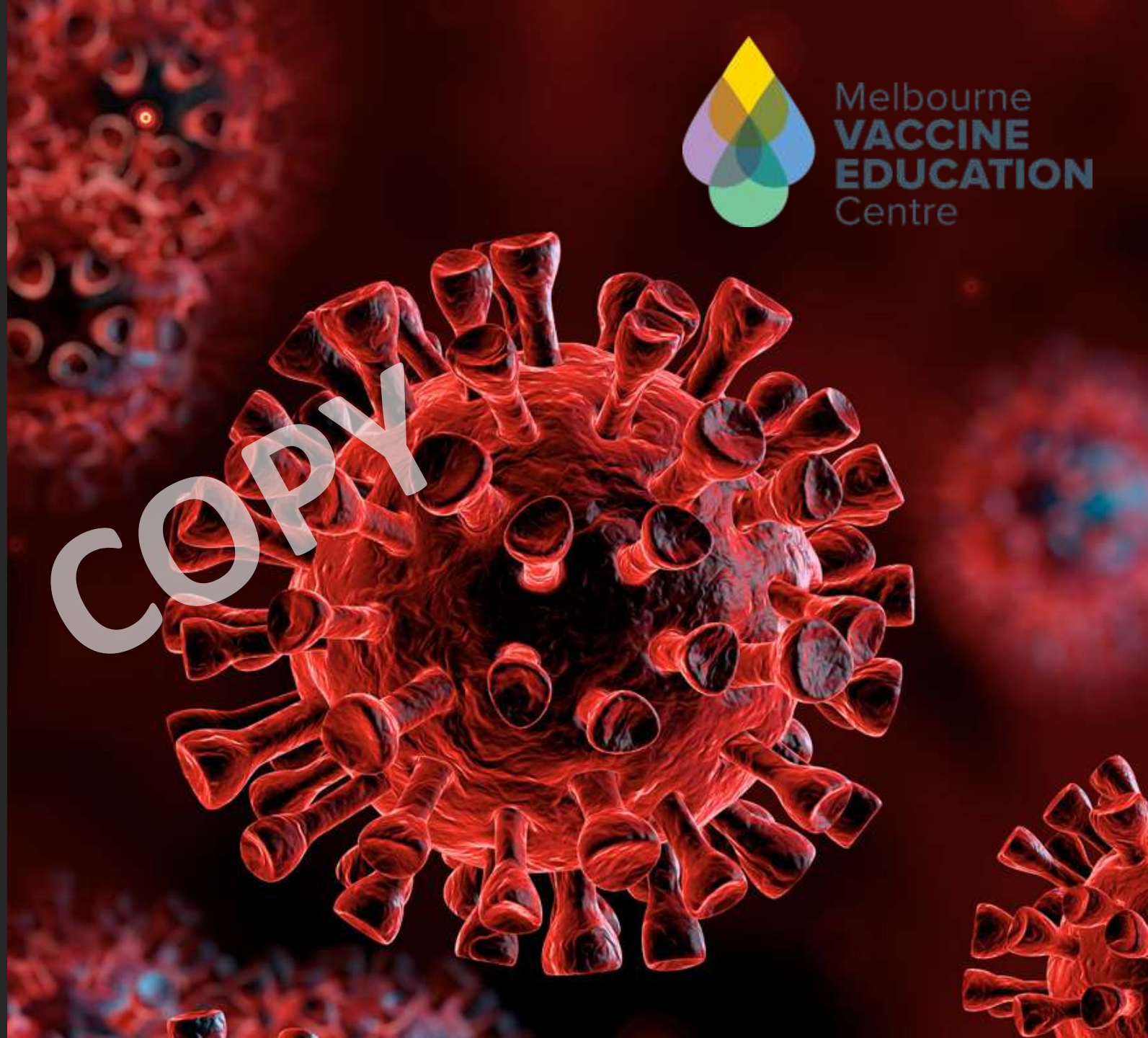
COVID-19 Vaccine Safety Update

CVU mini-series March 2021

Nigel Crawford



Declarations of interest (DOI)

Melbourne VACCINE EDUCATION Centre

Director of SAEFVIC (Victorian Vaccine safety service) based at MCRI and and member of Australian Technical Advisory Group on Immunisation (ATAGI) .

This presentation presents my own views and not necessarily those of my affiliations.

Nil pharmaceutical industry declarations.

SAEFVIC

Melbourne VACCINE EDUCATION Centre

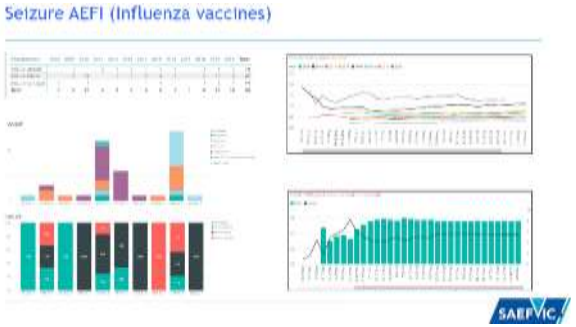
Business as usual (BAU)

- SAEFVIC- Victorian vaccine safety service
  - https://www.safevac.org.au/Home/Info/VIC

  - Established in 2007
  - Supported every vaccine program on the NIP
    - HPV
    - Rotavirus
    - PCV13
    - Meningococcal….
  - Enhanced spontaneous reporting with clinical follow-up/ feedback
  - Supervised observation for vaccine(s) – AEFI recurrence rates

Immunisation workforce
Consumers
Aged care

Harmonised
Easier
Visualised



Education & Comms

Spontaneous surveillance

Collaboration

Active surveillance

National
Jurisdictional
International

Solicited
Syndromic
Data-linking

vaccine safety net

https://www.who.int/vaccine_safety/initiative/communication/network/vaccine_safety_websites/en/

AusVaxSafety
An NCIRS led collaboration

SmartVax
NSW Health
Hunter New England Local Health District

Vaxtracker Project

SAFESIG

Slide acknowledgement Jim Buttery

Australian Vaccine Safety

- Therapeutic Goods Administration (TGA)
  - Advisory committee of vaccines (ACV)
    - Provides recommendations re provisional approval of COVID19 vaccines
    - Vaccine causality panels
  - Jurisdictional-TGA meeting (monthly)- weekly for COVID19
  - Adverse Event Monitoring System (AEMS) database
  - Linking with other international regulators (FDA, EMA)- rolling reviews, pharmacovigilance plans etc.
  - Weekly report- including AVS
  - https://www.tga.gov.au/periodic/covid-19-vaccine-weekly-safety-report-1-03-03-2021

Australian Vaccine Safety

- Clinical Assessment Network [AEFI-CAN]
  - Currently meet 6-weekly
  - Discuss adverse events following immunisation (AEFI) cases
  - Paediatric and adult vaccine specialists
  - TGA and Commonwealth Immunisation representatives
  - Research projects and international collaborations

  - Newly formed ‘International Specialist Immunisation Services’
    - InSIS network
  - Flagship- ‘vaccine allergy project’

Victorian Specialist Immunisation Services

VicSIS

- Victorian Department Health (DH) initiative
- ‘System strengthening’ in the COVID19 pandemic

Victorian Specialist Immunisation services (VicSIS) - Background

Given that COVID-19 vaccine rollout in Victoria will prioritise high risk adults…

- COVID-19 vaccine rollout commenced February 2020 with a phased approach throughout 2021
- Initial target cohort includes **healthcare workers and aged care residents**
- **Specialist services typically required** to address queries and to safely provide vaccination under supervision, where required

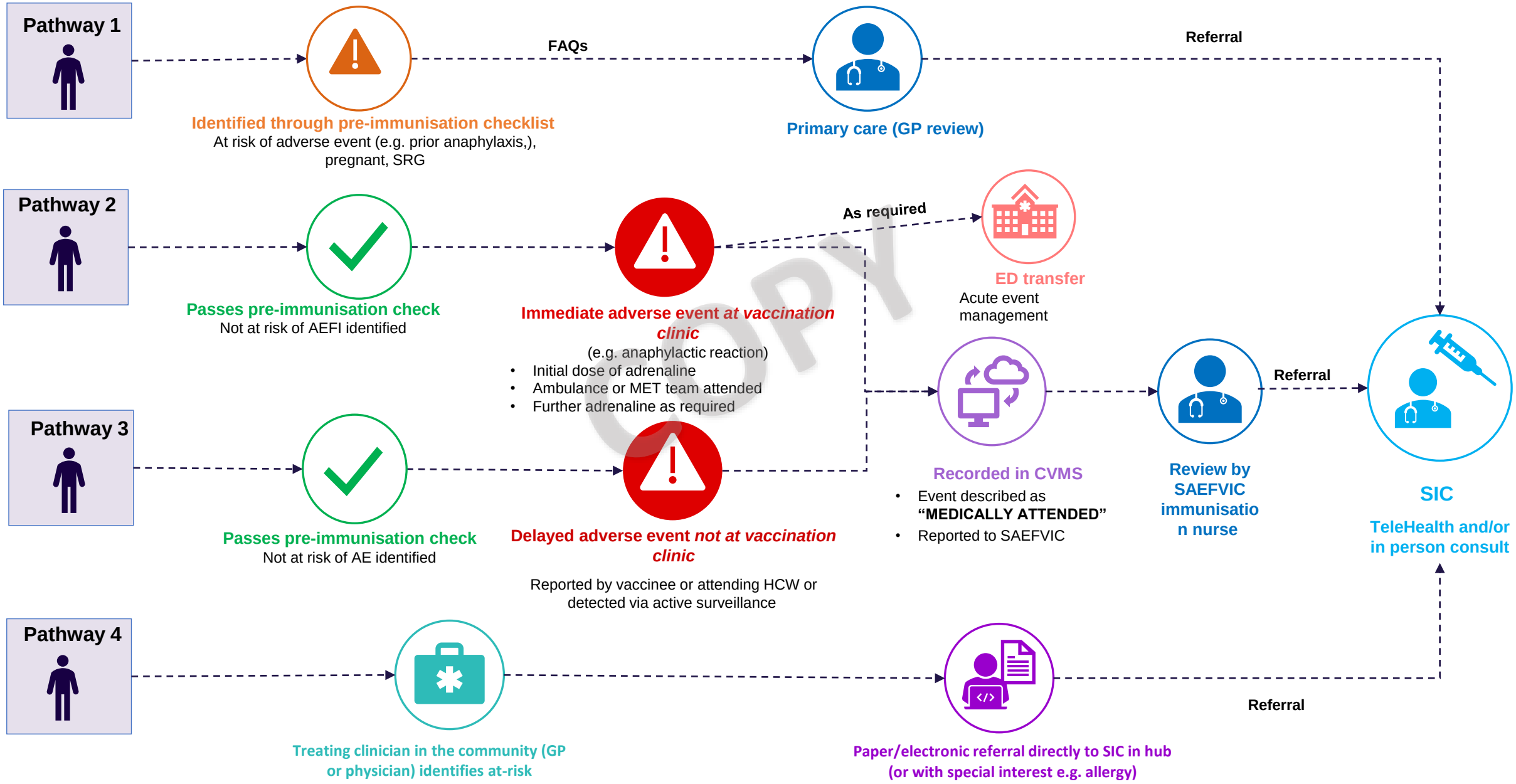
… and current vaccine safety services in VIC, managed by SAEFVIC, have predominantly focused on paediatrics…

- **Surveillance of Adverse Events Following Vaccination In the Community** (SAEFVIC), based at MCRI in Parkville, coordinates the management, monitoring and reporting of **adverse events following immunisation** (AEFI)
- Includes AEFIs at **time of vaccination**, as well as **delayed reactions** - both of which will be important within the COVID-19 vaccine space
- Data collected by SAEFVIC and the COVID-19 Vaccine Management System (CVMS) will be **forwarded to the TGA** as a part of phase IV pharmacovigilance

… there is a need to rapidly enhance adult immunisation services within the state.

- The aim is rapidly to expand the number of adult services that can provide this support to the LPHUs via a **Victorian Specialist Immunisation Services (VicSIS**) network
- **Monash** and **Sunshine** hospitals currently have DHHS-supported immunisation clinics – **scope to enhance these services**
- Rapidly expanded **adult specialist immunisation services (inclusive of clinics)** – to be **aligned with LPHUs**

VicSIS - Referral Pathways to Specialist Immunisation Clinics (SICs)



VicSIS sites- vaccine safety coordinated by SAEFVIC

VicSIS clinic	SIS leads	Referrals*
Monash Health (includes specialist allergy clinic)	Tony Korman, Sara Barnes, Jeremy Carr, Jo Hickman, Karen Bellamy	screferralmanagement@monashhealth.org
Austin Hospital (includes specialist allergy clinic)	Jason Trubiano, Joseph DeLuca	antibiotic.allergy@austin.org.au
Alfred Hospital	Michelle Giles, Allen Cheng	specialistimmunisationservice@alfred.org.au
Royal Melbourne Hospital	Katherine Gibney, Lyn Kiers	specialistimmunisationservice@mh.org.au
Peter MacCallum Cancer Centre	Ben Teh	ICOutpatientReferral@petermac.org
Barwon Health	Callum Maggs	VicSIS@barwonhealth.org.au
Sunshine Hospital	Marion Kainer, Michelle Giles	COVIDvaccinationsSIS@wh.org.au
Northern Hospital	Craig Aboltins	TBC
Royal Children's Hospital	Teresa Lazzaro, Sonja Elia	immunisation.centre@rch.org.au

*referral form soon to be available on MVEC website

VicSIS Subject Matter Experts (SME)

- A rapid review team will be set up for the assessment of AESI or AEFI in high or special-risk groups
- This team will be made up of a VicSIS on-call clinician and subject matter experts
- SME include: allergy, serious acute neurological event (SANE), geriatrics, immunosuppressed, cancer

- Acknowledgement of Victorian DH COVID19 vaccine safety & data team
  - Michelle Wolthuzien
  - Hazel Clothier
  - Emma Roney
  - Eleanor Duckworth
  - Sally Gordon

Vaccine errors

- Thinks of error that could be made @ any step of the “immunisation pathway”
- It has happened….
- Errors will have an impact on ‘vaccine confidence’
- How can we minimse them?

https://theconversation.com/when-vaccinating-26-million-australians-expect-a-mistake-or-two-but-we-can-minimise-the-risk-of-repeating-queenslands-overdose-incident-155945

Learning from COVID vaccine errors

- **Dilution errors** reported with the Pfizer-BioNTech COVID-19 vaccine include administering too much or too little vaccine, an inadequate volume of diluent
- **Syringe malfunctions** and use of syringes not adequate to extract a vial's full contents caused wastage
- **Leftover vaccine** due to cancellations and no-shows led to wastage, as did leftover doses at the end of the day; the vaccines must be discarded if not used within 6 hours after dilution (Pfizer)
- **Inadequate recipient screening** led to vaccination of youths for whom the vaccine was not authorized
- **Second dose errors** occurred due to misspelling of patient names or email addresses and, consequently, failure to inform or remind patients of second dose appointments
- **Allergic reactions** occurred in 29 individuals, most with documentation of previous allergic reaction to the Pfizer vaccine

https://www.ismp.org/resources/learning-errors-new-covid-19-vaccines

International vaccine safety

- CDC vaccine safety updates @ ACIP

- Tom Shimabukuro [1st March 2021]

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covid-Shimabukuro.pdf

- Over 75 million doses of mRNA vaccines
  - [Pfizer and Moderna]
- Excellent safety profile in line with phase 3 studies

v-safe℠ after vaccination health checker

V-safe pregnancy registry enrollment as of February 19, 2021

Registry participants to date (N = 1,949)	
Enrolled	1,815
Not eligible*	103
Refused/declined†	31

- In the enrolled population, there have been 275 completed pregnancies, including 232 live births
  - Other outcomes include miscarriage, stillbirth, ectopic/tubal, other

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covid-Shimabukuro.pdf

Adverse events of special interest (AESI)

Preliminary results of the VSD **unvaccinated concurrent comparator** analysis for COVID-19 vaccine safety after either dose of any mRNA vaccine as of February 13, 2021

VSD Rapid Cycle Analysis prespecified outcomes for COVID-19 vaccines	Concurrent comparator analysis	Risk interval	Events in vaccinated	Adjusted expected events in risk interval
Acute disseminated encephalomyelitis	Unvaccinated	1-21 days	0	0
Acute myocardial infarction	Unvaccinated	1-21 days	23	26.0
Acute respiratory distress syndrome	Unvaccinated	N/A	0	N/A
Anaphylaxis	Unvaccinated	0-1 days	20	N/A
Appendicitis	Unvaccinated	1-21 days	31	23.6
Bell's palsy	Unvaccinated	1-21 days	21	20.3
Convulsions/seizures	Unvaccinated	1-21 days	10	9.6
Disseminated intravascular coagulation	Unvaccinated	1-21 days	1	1.1
Encephalitis/myelitis/encephalomyelitis	Unvaccinated	1-21 days	1	.1
Guillain-Barré syndrome	Unvaccinated	1-21 days	1	.6
Thrombotic thrombocytopenic purpura	Unvaccinated	1-21 days	0	0
Immune thrombocytopenia	Unvaccinated	1-21 days	1	1
Kawasaki disease	Unvaccinated	1-21 days	0	0
MIS-C and MIS-A	Unvaccinated	N/A	0	N/A
Myocarditis/pericarditis	Unvaccinated	1-21 days	2	2.1
Narcolepsy and cataplexy	Unvaccinated	N/A	2	N/A
Stroke, hemorrhagic	Unvaccinated	1-21 days	8	10
Stroke, ischemic	Unvaccinated	1-21 days	41	38.8
Transverse myelitis	Unvaccinated	1-21 days	0	0

- No statistically significant increased risks detected for any prespecified outcomes

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covid-Shimabukuro.pdf

Incidents after vaccination with AstraZeneca's COVID-19 vaccine NEW

messages in brief | 07/03/2021

The Federal Office for Safety in Health Care (BASG) has received two reports in temporal connection with a vaccination from the same batch (ABV 5300) of the AstraZeneca vaccine in the district of Zwettl: a woman (49 y) died as a result of severe coagulation disorders, another woman (35 y) who developed a pulmonary embolism is on the way to recovery.

Currently, there is no evidence of a causal relationship with vaccination. Based on the known clinical data, a causal relationship cannot be established, as thrombotic events in particular are not among the known or typical side effects of the vaccine in question. According to current knowledge, the clinical data do not show any worrying data or signals in this respect compared to placebo. The immediately initiated international analysis of side effect reports also shows no accumulation of similar case reports so far.

At present, all necessary investigations involving the respective experts are running at full speed in order to be able to completely exclude a possible connection. To be on the safe side, the remaining stocks of the affected vaccine batch will no longer be distributed and vaccinated.

https://www.basg.gv.at/en/market-surveillance/official-announcements/detail/zwischenfaelle-nach-impfung-mit-covid-19-impfstoff-von-astrazeneca

UK “yellow card” system

- As of 21 February 2021, for the UK:
  - 9.4 million first doses of the Pfizer/BioNTech vaccine & 8.4 million doses of the Oxford University/AstraZeneca vaccine administered
  - 0.6 million second doses, mostly the Pfizer/BioNTech vaccine.
  - 29,715 Yellow Cards have been reported for the Pfizer/BioNTech
  - 42,917 have been reported for the Oxford University/AstraZeneca vaccine
  - both vaccines the overall reporting rate is around 3 to 5 Yellow Cards per 1,000 doses
  - At the time of this report, more than 120,000 people in the UK have died within 28 days of a positive test for coronavirus

- AEFI Reporting predominantly expected reactions; monitoring for allergy, Bells palsy + other AESI, including deaths in the elderly

https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting

UK “real-world” vaccine effectiveness (VE) - frail elderly (pre-publicaiton)

Background However, few data exist regarding the effectiveness of these vaccines in elderly frail people. Evaluation following implementation to determine the effectiveness of one dose in reducing hospitalisations due to SARS-CoV-2 infection in elderly adults is urgent.

Methods: A prospective single-centre test-negative design case-control study of adults aged ≥80 years hospitalised with COVID-19 disease or other acute respiratory disease. We conducted logistic regression controlling for time (week), gender, index of multiple deprivations (IMD), and care residency status (CRS), and sensitivity analyses matched for time and gender using a conditional logistic model adjusting for IMD and CRS.

Findings: First dose vaccine effectiveness of BNT162b2 was 71.4% (95% confidence interval [CI] 46.5-90.6). ChAdOx1nCoV-19 first dose vaccine effectiveness was 80.4% (95% CI 36.4-94.5). When effectiveness analysis for BNT162b2 was restricted to the period covered by ChAdOx1nCoV-19, the estimate was 79.3% (95% CI 47.0-92.5).

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3796835