



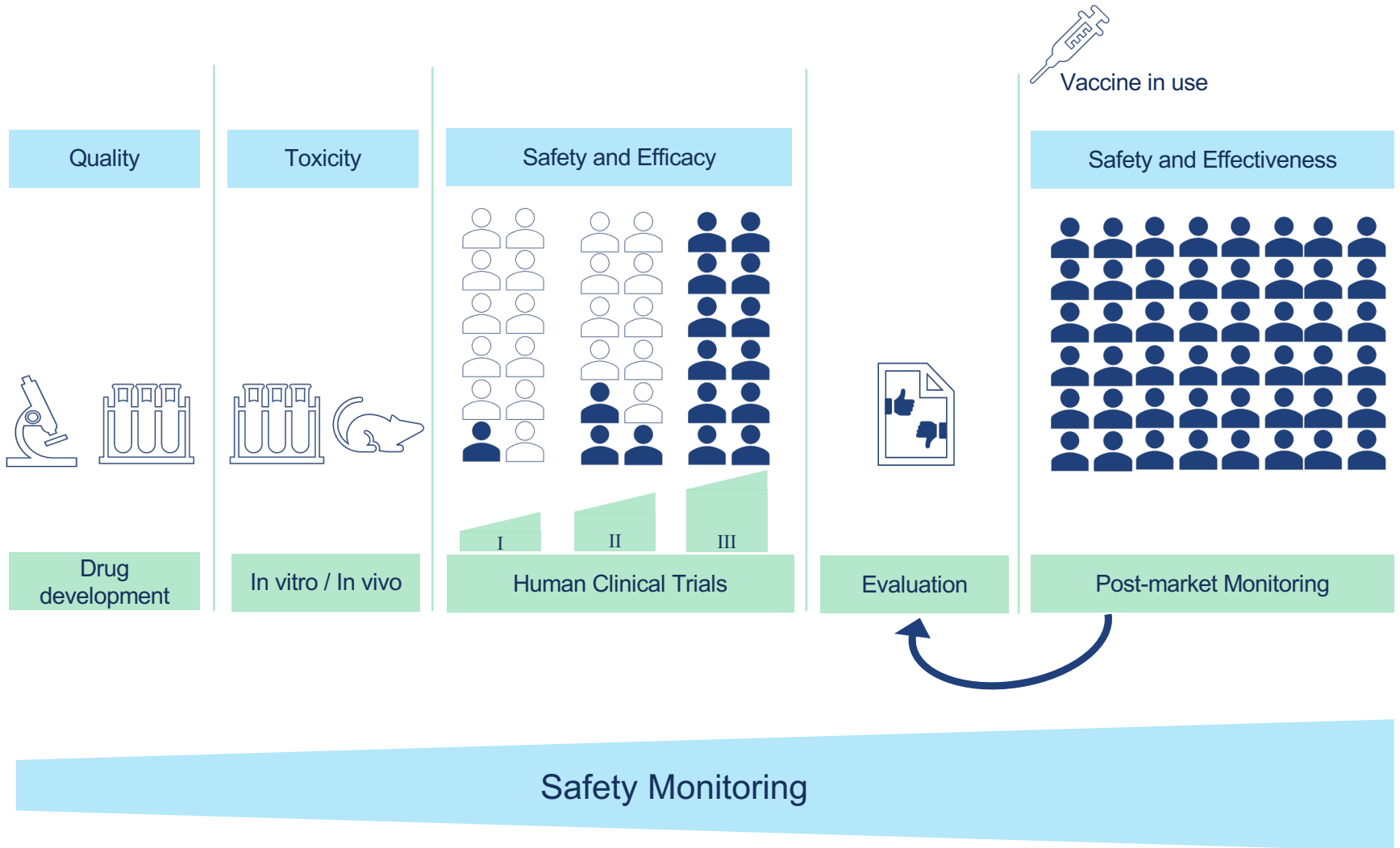
# Monitoring Vaccine Safety After Market Approval: How do we move forward?

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# Outline

- ① Was safety compromised with a faster development?
- ② Why and how do we monitor vaccine safety after approval?
- ③ What does the safety profile look like?
- ④ What are the long-term effects?
- ⑤ Who should get vaccinated?
- ⑥ How many people need to be vaccinated?
- ⑦ Q&A

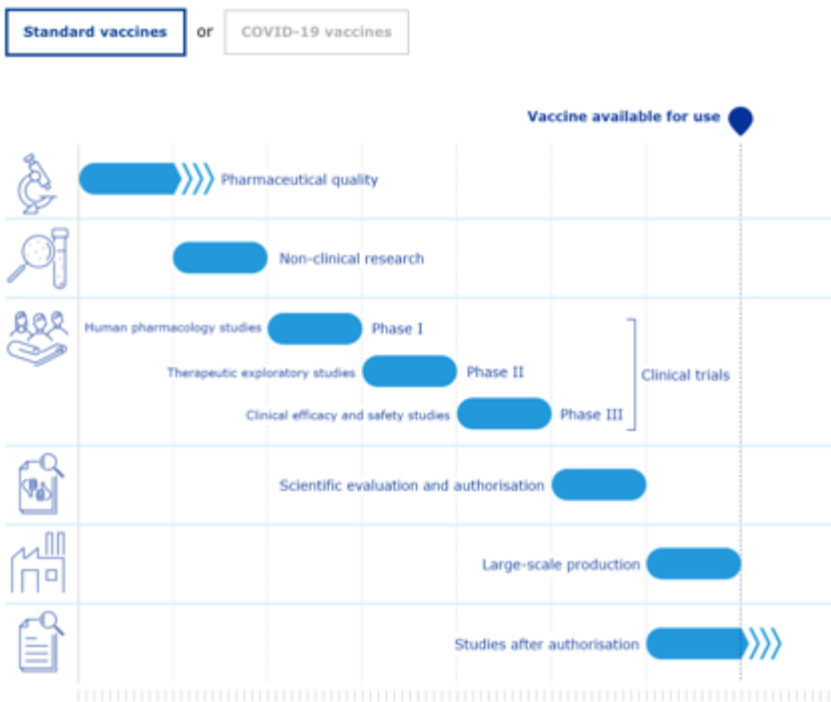
# Life cycle of vaccines from development to use



# Was the approval process different?

- Minimum level of efficacy for vaccine approval<sup>1</sup>:
  - At least one phase III study with many thousands (>30K) participants
  - Minimum efficacy of 50%
  - Demonstrated evidence that the benefit (efficacy) outweighs harms (safety)
- No difference in safety criteria required for the COVID-19 vaccine approval
- The speed of the COVID-19 vaccine development was due to a number of fortuitous circumstances:
  - Scientific advancement in vaccine development
  - Expedited procedural aspects, not expedited trial time
  - Testing during an active pandemic with high case numbers
  - Working in parallel not in sequence

# Was the approval process different?



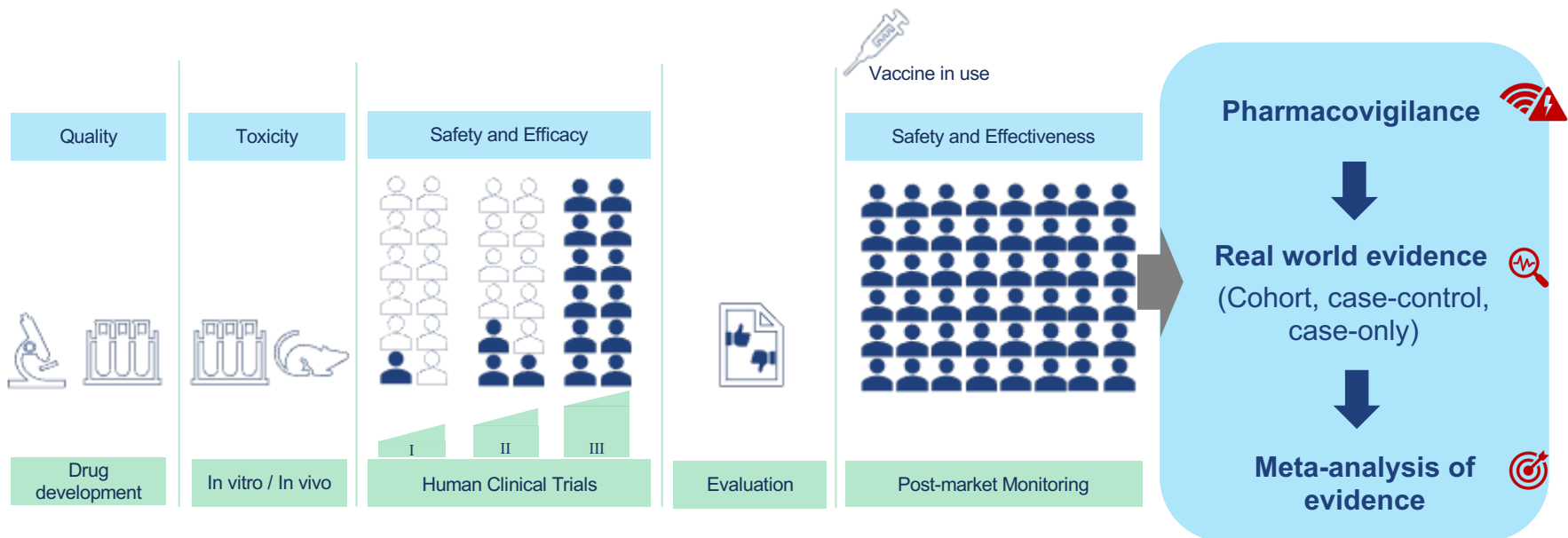
# Why study safety after market approval?

- No drug is 100% safe, vaccines are no different
- At the time of market approval we know the benefits outweigh the risks, but...
  - Common adverse events are mild, and known at approval
  - Very rare events may only be known when millions are vaccinated
  - Continued monitoring to weigh the risk of a serious adverse event against the prevention of serious illness, like COVID-19



# How is safety monitored after market approval?

- Moving from signal detection (pharmacovigilance) to causality (Pharmacoepidemiology)



# How is safety monitored after market approval?


- Pharmacovigilance: Comprehensive safety monitoring systems already in place
  - EudraVigilance (EU adverse events)
  - WHO VigiBase
  - US Vaccine Adverse Event Reporting System (VAERS)
- Health authorities and manufacturers are required to report any adverse event
- Allow assessment of:
  - Reported adverse events
  - Detection of new adverse events
  - Assessment of disproportionality (is the adverse event occurring more often than expected)











# What does the safety profile look like?

← → ↻ wonder.cdc.gov

 Centers for Disease Control and Prevention  
CDC 24/7: Saving Lives. Protecting People™

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## The Vaccine Adverse Event Reporting System (VAERS) Request

Request Form    Results    Map    Chart    Report    About

[Dataset Documentation](#)    [Other Data Access](#)    [Data Use Restrictions](#)    [How to Use WONDER](#)       

*Make all desired selections and then click any **Send** button one time to send your request.*

### 1. Organize table layout:

   [Help](#)

**Group Results By:**  **Notes:**

**And By:**  • Data contains VAERS reports processed as of **02/12/2021**.

**And By:**  • Must group by VAERS ID when selecting any of the Optional Measures.

**And By:**  • When grouping by **VAERS ID**, results are initially displayed with Events Reported, Percent, and totals not shown.

**And By:**

**Optional Measures** (Check box to include in results.)

**Adverse Event Description**

**Lab Data**

**Current Illness**

**Adverse Events After Prior Vaccinations**

**Medications At Time Of Vaccination**

**History/Allergies**

**Title**

### 2. Select symptoms:

   [Help](#)

**Click the Advanced Finder Options link for more complex searches.**

**Browse** or **search** to find items in the Symptoms Finder Tool, then **highlight** the items to use for this request.  
(The *Currently selected* box displays all current request items.)

[Finder Tool Help](#)    [Advanced Finder Options](#)

Browse    Search    Details

**Symptoms**    *Currently selected:*

# Safety Profile in VAERS (17-02-2021)

## Messages:

- ▶ VAERS data in CDC WONDER are updated every Friday. Hence, results for the same query can change from week to week.
- ▶ These results are for 12,697 total events.
- ▶ Rows with zero Events Reported are hidden. Use Quick Options above to show zero rows.

Symptoms ↓	Events Reported ↑↓	Percent (of 12,697) ↑↓
<b>Total</b>	<b>58,010</b>	<b>456.88%</b>
HEADACHE	2,602	20.49%
FATIGUE	1,907	15.02%
PYREXIA	1,791	14.11%
DIZZINESS	1,770	13.94%
CHILLS	1,726	13.59%
NAUSEA	1,665	13.11%
PAIN	1,654	13.03%
INJECTION SITE PAIN	1,163	9.16%
PAIN IN EXTREMITY	1,050	8.27%
DYSPNOEA	949	7.47%
MYALGIA	837	6.59%
SARS-COV-2 TEST POSITIVE	808	6.36%
PARAESTHESIA	775	6.10%
PRURITUS	694	5.47%
RASH	646	5.09%
ARTHRALGIA	627	4.94%
VOMITING	592	4.66%
HYPOAESTHESIA	578	4.55%
COUGH	555	4.37%
FLUSHING	552	4.35%
DEATH	536	4.22%
MALAISE	534	4.21%
URTICARIA	500	3.94%
PALPITATIONS	494	3.89%
ASTHENIA	486	3.83%
TACHYCARDIA	452	3.56%
HEART RATE INCREASED	449	3.54%
SARS-COV-2 TEST NEGATIVE	448	3.53%
DIARRHOEA	441	3.47%
ANAPHYLACTIC REACTION	137	1.08%
ANAPHYLACTIC SHOCK	10	0.08%
ANAPHYLACTOID REACTION	8	0.06%

# How does it compare to the other vaccines?

- Overall the safety profile of commonly reported adverse events are similar

	COVID-19	456.88%
HEADACHE		20.49%
FATIGUE		15.02%
PYREXIA		14.11%
DIZZINESS		13.94%
CHILLS		13.59%
NAUSEA		13.11%
PAIN		13.03%
INJECTION SITE PAIN		9.16%
PAIN IN EXTREMITY		8.27%
DYSPNOEA		7.47%

	Influenza	389.34%
PYREXIA		13.42%
PAIN		11.22%
INJECTION SITE PAIN		10.72%
INJECTION SITE ERYTHEMA		10.36%
PAIN IN EXTREMITY		8.59%
HEADACHE		7.76%
ERYTHEMA		7.56%
INJECTION SITE SWELLING		7.55%
CHILLS		6.10%
DIZZINESS		5.80%

- Increase in proportion of reported deaths and anaphylaxis in VAERS data

	COVID-19	H1N1	Influenza
Anaphylaxis	1.08%	0.88%	0.42%
Death	4.22%	0.75%	0.64

- But...difficult to interpret & needs to be monitored!

# What about long-term effects?

**Messages:**

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- ▶ These results are for 12,697 total events.

Onset Interval ↓	→ Events Reported ↑↓	← Percent (of 12,697) ↑↓
0 days	6,721	52.93%
1 day	2,764	21.77%
2 days	622	4.90%
3 days	358	2.82%
4 days	240	1.89%
5 days	169	1.33%
6 days	142	1.12%
7 days	162	1.28%
8 days	109	0.86%
9 days	85	0.67%
10-14 days	222	1.75%
15-30 days	155	1.22%
31-60 days	18	0.14%
61-120 days	2	0.02%
Over 120 days	17	0.13%
Unknown	911	7.17%
<b>Total</b>	<b>12,697</b>	<b>100.00%</b>



Note: Submitting a report to VAERS does not mean that healthcare personnel or the vaccine caused or contributed to the adverse event (possible side effect).

# What about long-term effects?

- History has shown that most adverse events associated with vaccines occur within the first 30-days<sup>2</sup>
- Serious rare adverse events have been reported for other vaccines
  - All occurred within 8-weeks (60-days) of vaccination
  - Majority of adverse events could also be caused by getting infected with the virus
- Emergency approval of COVID-19 vaccines only considered after 60-days from when 50% of trial participants received their 2<sup>nd</sup> dose
- There are no known long-term adverse events beyond 60-days with any vaccine

# Who should get vaccinated?

- Anyone eligible for the vaccine should be vaccinated
  - [www.foph-coronavirus.ch](http://www.foph-coronavirus.ch)
- Vaccination still recommended if you've had COVID-19, **but...**
- Priority setting for early roll-out based on risk of adverse outcome if COVID-19 were contracted



Person A	Person B
	
<ul style="list-style-type: none"><li>• I have a <u>high risk because I have a chronic disease</u></li><li>• I am <u>at least 60 years</u></li><li>• If I get infected I will normally infect 1 other person</li><li>• My profession <u>is essential</u></li></ul>	<ul style="list-style-type: none"><li>• I have <u>no underlying conditions</u></li><li>• I am <u>younger than 60 years</u></li><li>• If I get infected I will normally infect <u>10 other person</u></li><li>• My profession is <u>not essential</u></li></ul>

Adapted from: Luyten et al. (2020) Covid Economics 57



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# How many people need to be vaccinated?

- Still largely unknown
- Calculation for vaccination rates derived from the replication rate ( $R^0$ )

$$\text{Vaccination rate} = 1 - \left(\frac{1}{R^0}\right)$$

COVID-19



$R^0$ : 2.5 - 3

66%

Influenza



$R^0$ : 1 - 1.5

30 - 50%

Ebola



$R^0$ : 2

50%

Measles



$R^0$ : 12 - 18

90%



# How many people need to be vaccinated?

- Still largely unknown
- Calculation for vaccination rates derived from the replication rate ( $R^0$ )

$$\text{Vaccination rate} = 1 - \left(\frac{1}{R(0)}\right)$$

COVID-19



$R^0$ : 4

75%

Influenza



$R^0$ : 1 – 1.5

30 – 50%

Ebola



$R^0$ : 2

50%

Measles



$R^0$ : 12 - 18

90%

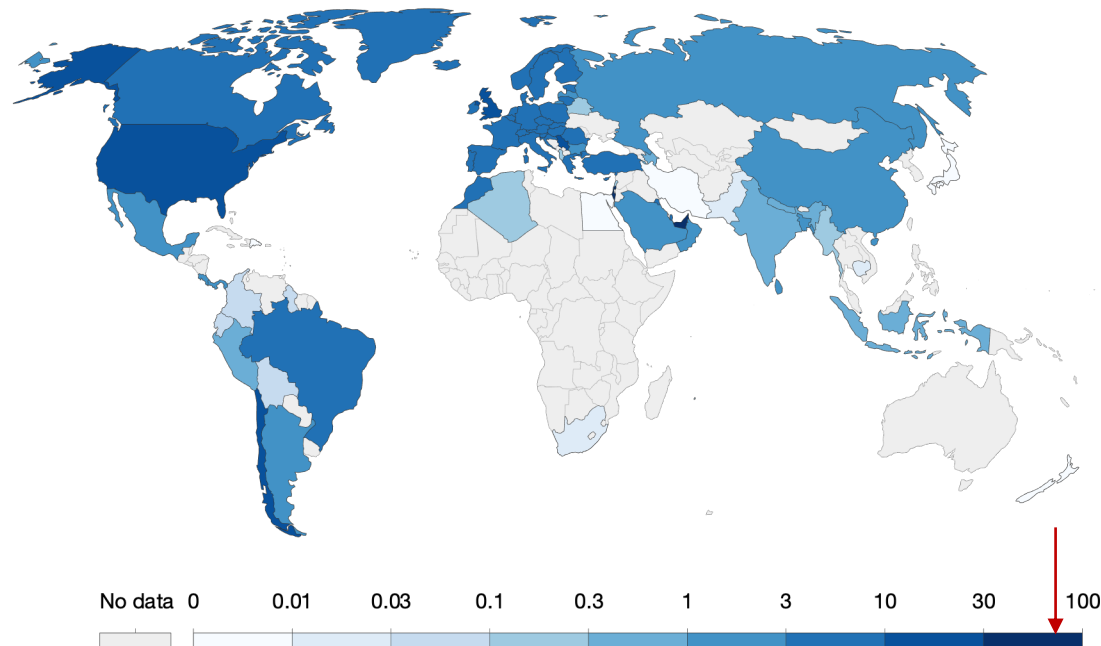
# How many people need to be vaccinated?

- When can we expect to have global vaccination coverage?

## COVID-19 vaccine doses administered per 100 people, Feb 21, 2021

Total number of vaccination doses administered per 100 people in the total population. This is counted as a single dose, and may not equal the total number of people vaccinated, depending on the specific dose regime (e.g. people receive multiple doses).

Our World  
in Data



Source: Official data collated by Our World in Data – Last updated 22 February, 10:20 (London time) [OurWorldInData.org/coronavirus](https://OurWorldInData.org/coronavirus) • CC BY

# Q & A

## Thank you for your attention!

