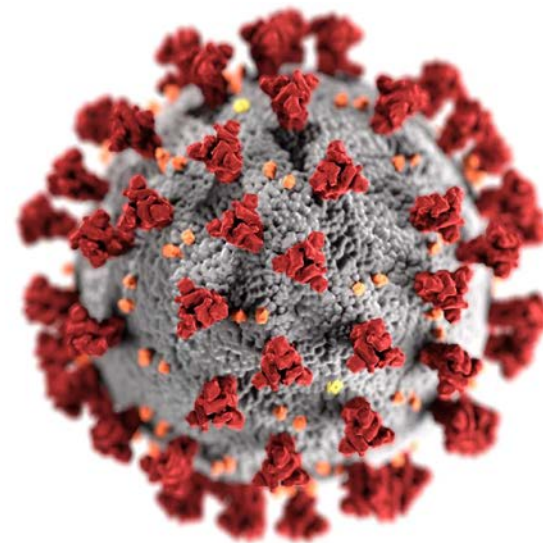


新冠病毒的病毒學與 流行病學

新冠病毒對於兒童健康之衝擊研討會

2020/11/21

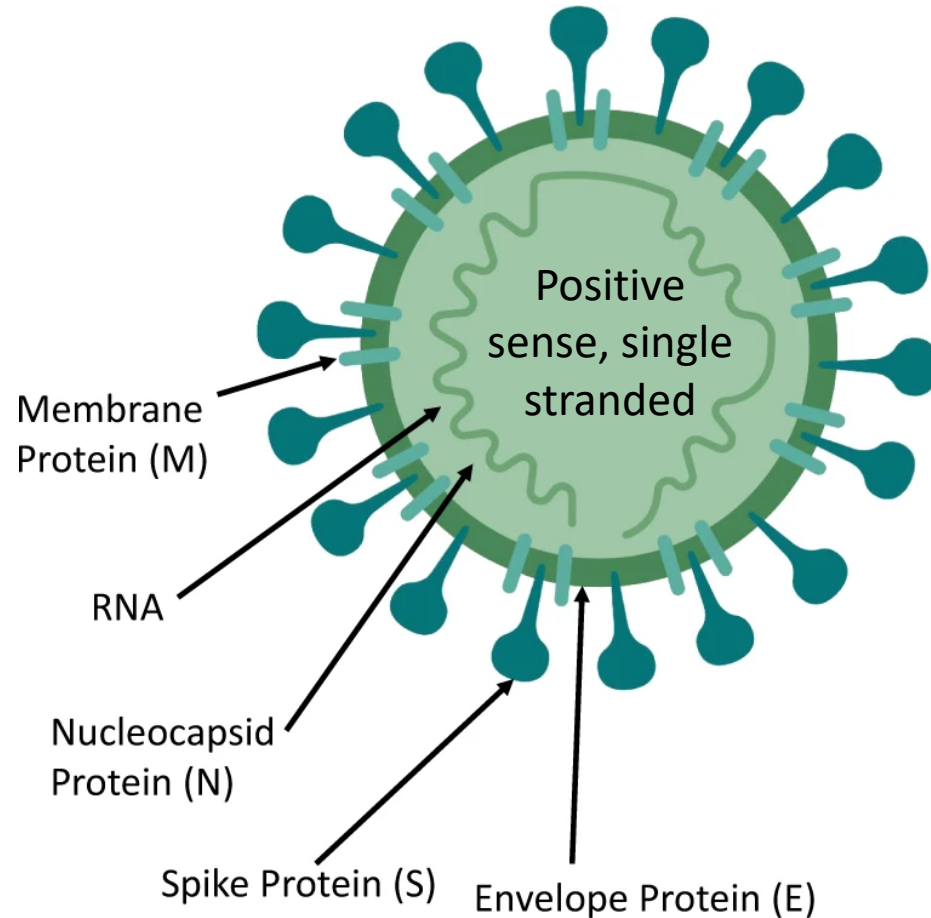
疾病管制署 陳孟妤醫師





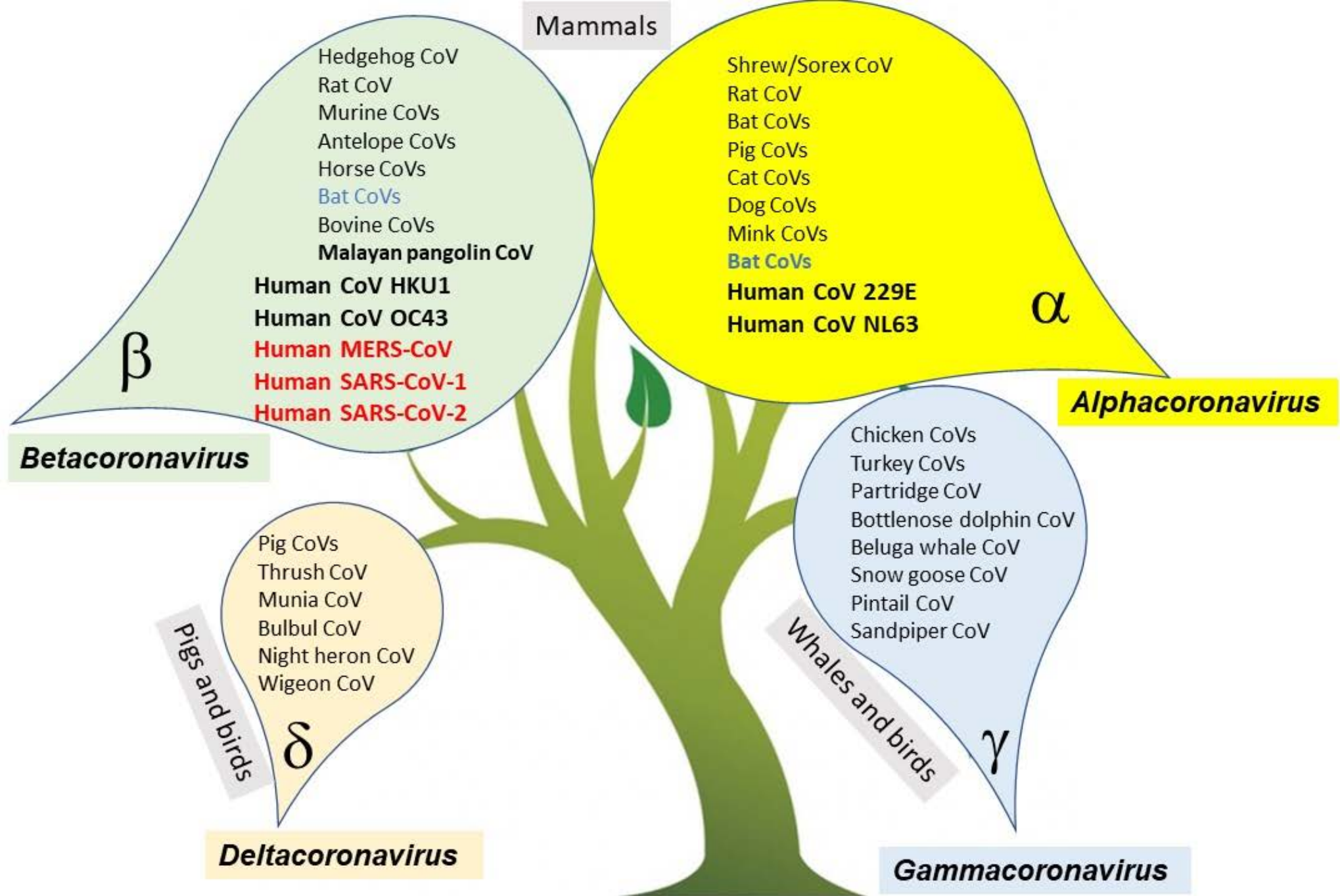
Join at
slido.com
#28316

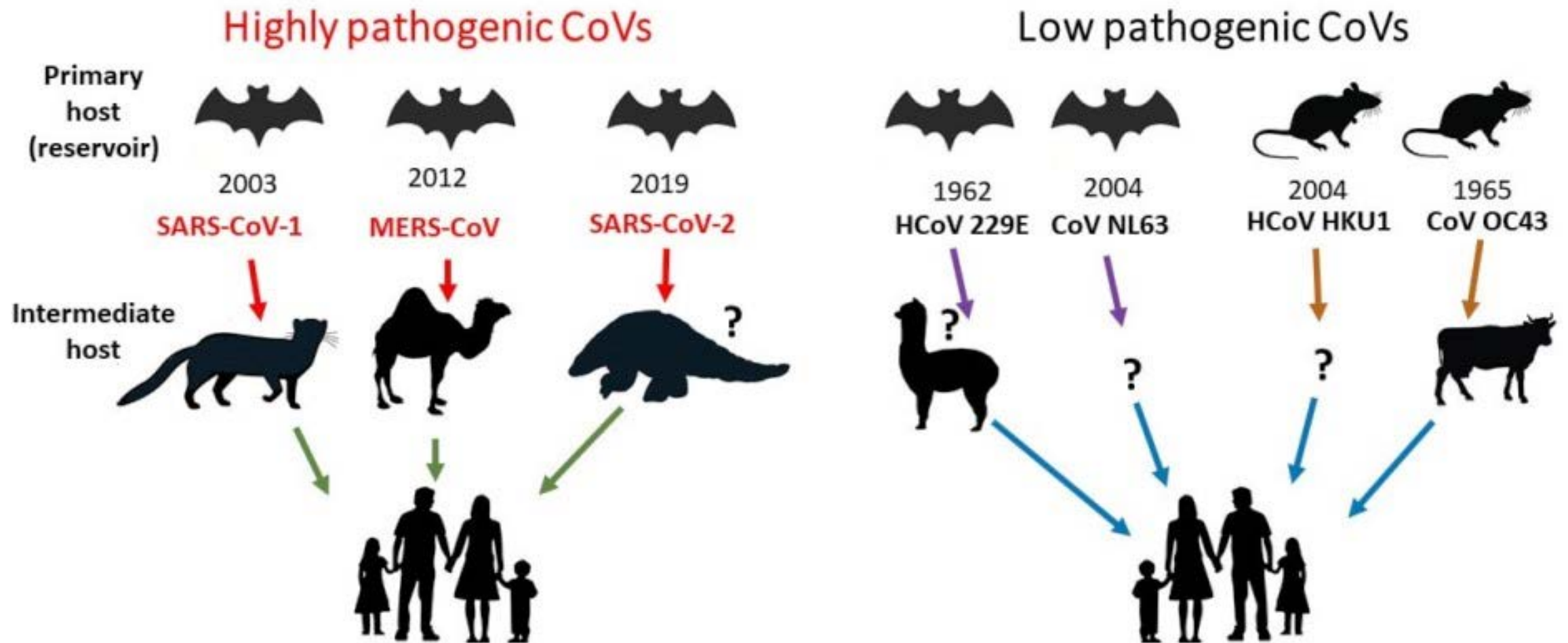
冠狀病毒的結構



Structural Protein	Function of Protein
Nucleocapsid Protein (N) 核殼蛋白	Bound to RNA genome to make up nucleocapsid
Spike Protein (S) 棘蛋白	Critical for binding of host cell receptors to facilitate entry of host cell
Envelope Protein (E) 封套蛋白	Interacts with M to form viral envelope
Membrane Protein (M) 膜蛋白	- Central organiser of CoV assembly - Determines shape of viral envelope

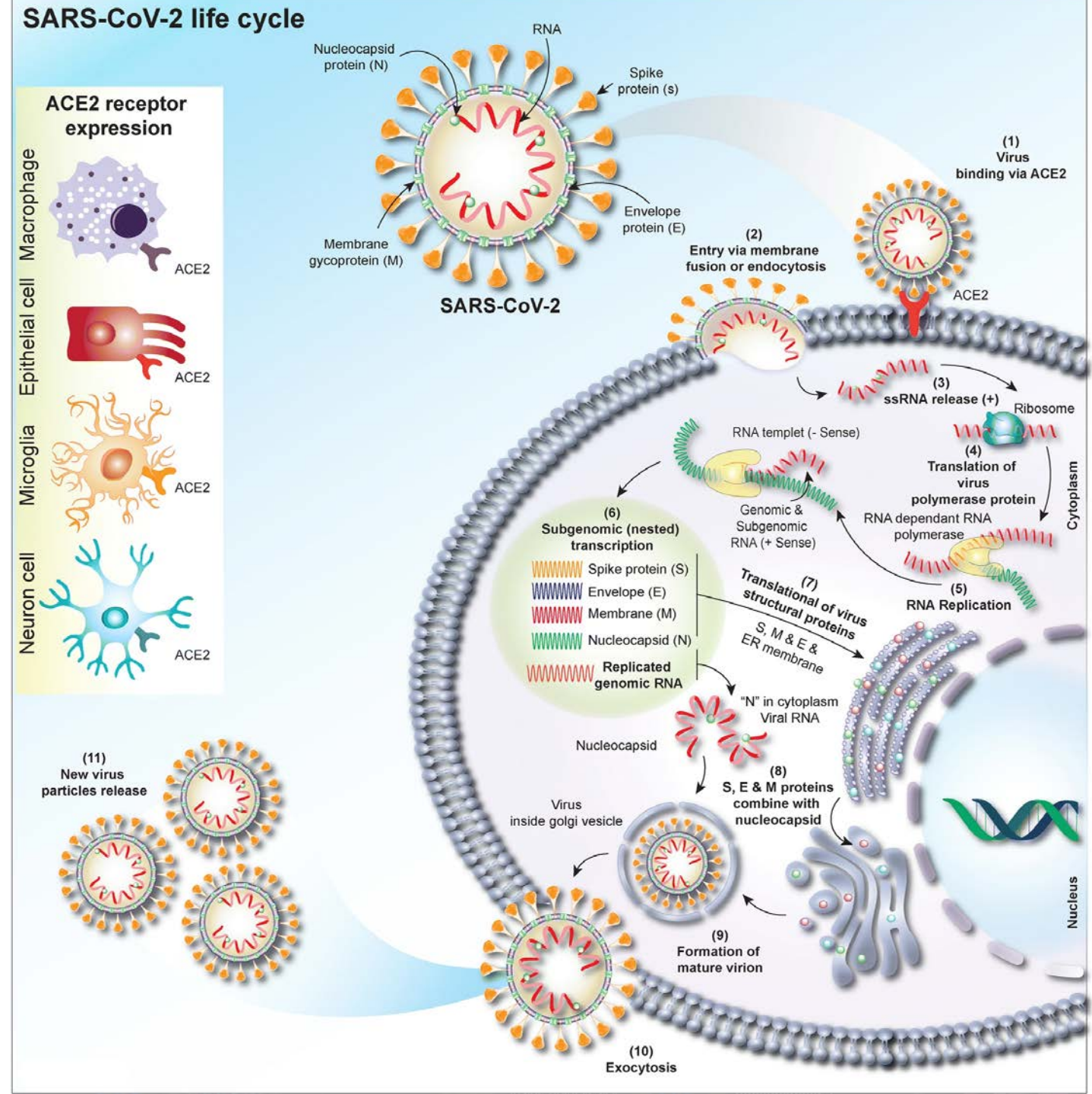
- It has been noted that some CoVs do not need to have the full ensemble of structural proteins to make virions, highlighting that certain proteins may be dispensable or compensated by the function of non-structural proteins.



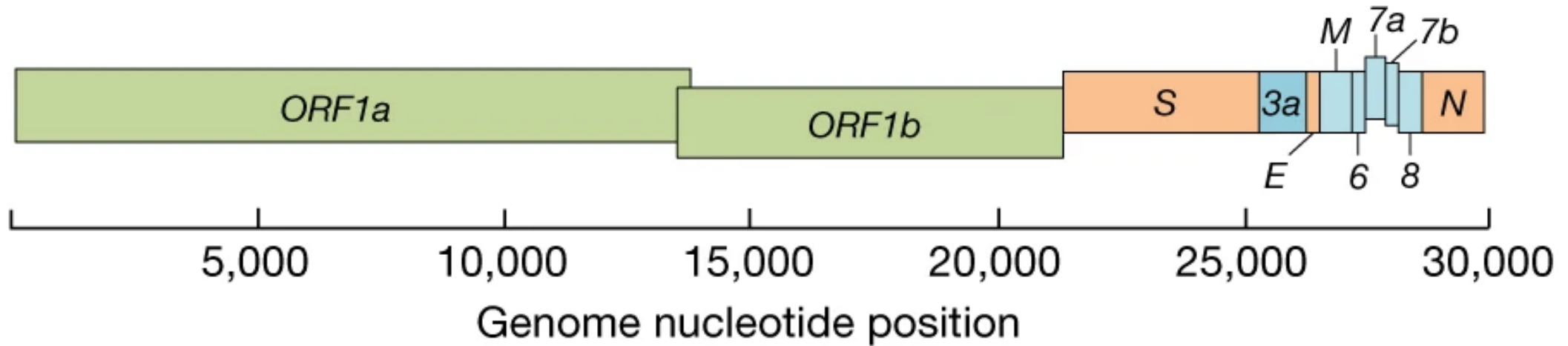


SARS-CoV-2 透過ACE2 receptor進入細胞

J Neuroimmune Pharmacol **15**, 359–386 (2020).
<https://link.springer.com/article/10.1007/s11481-020-09944-5>



SARS-CoV-2 基因序列



核酸複製蛋白酶

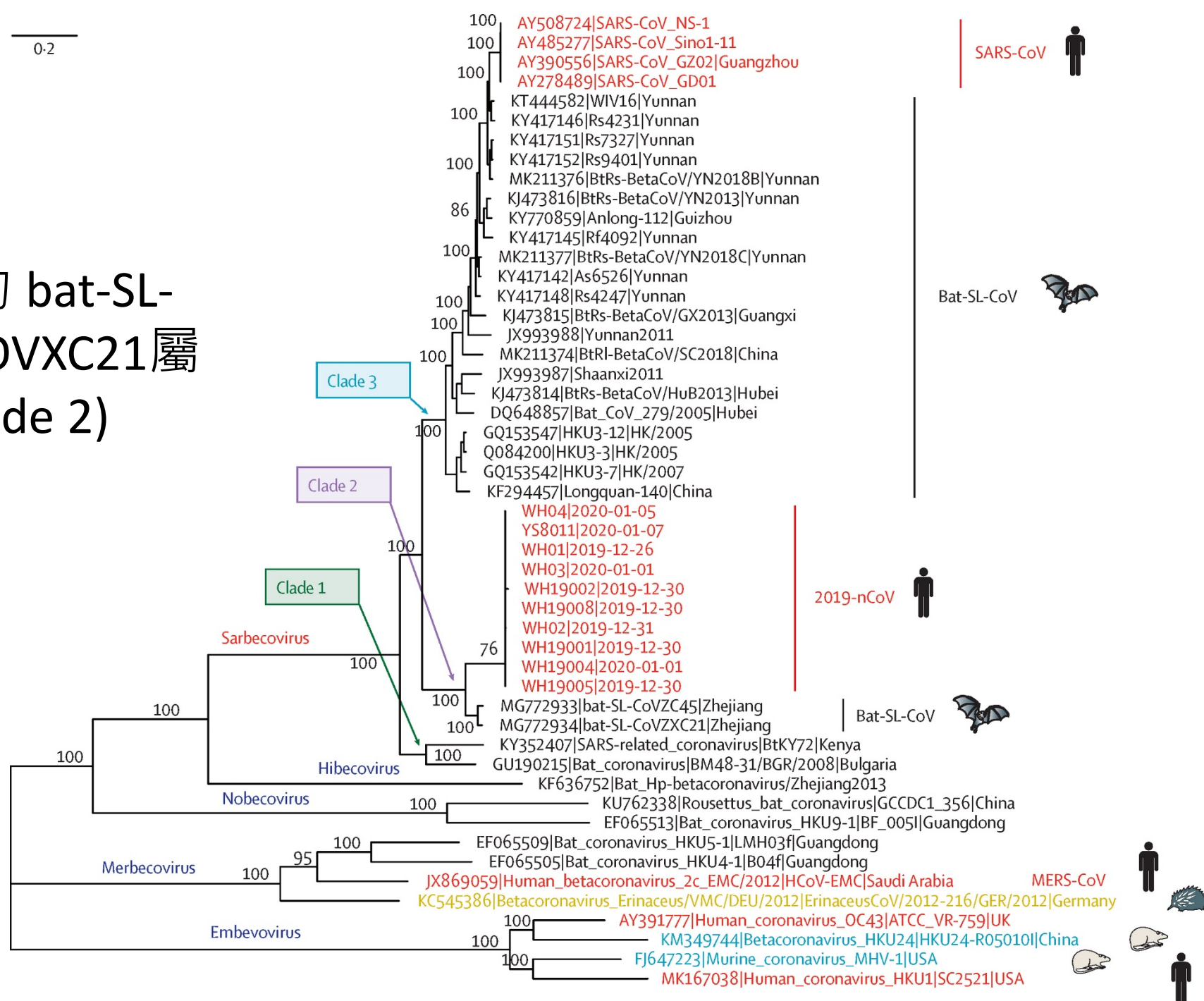
(Replicase gene)

結構蛋白及其他

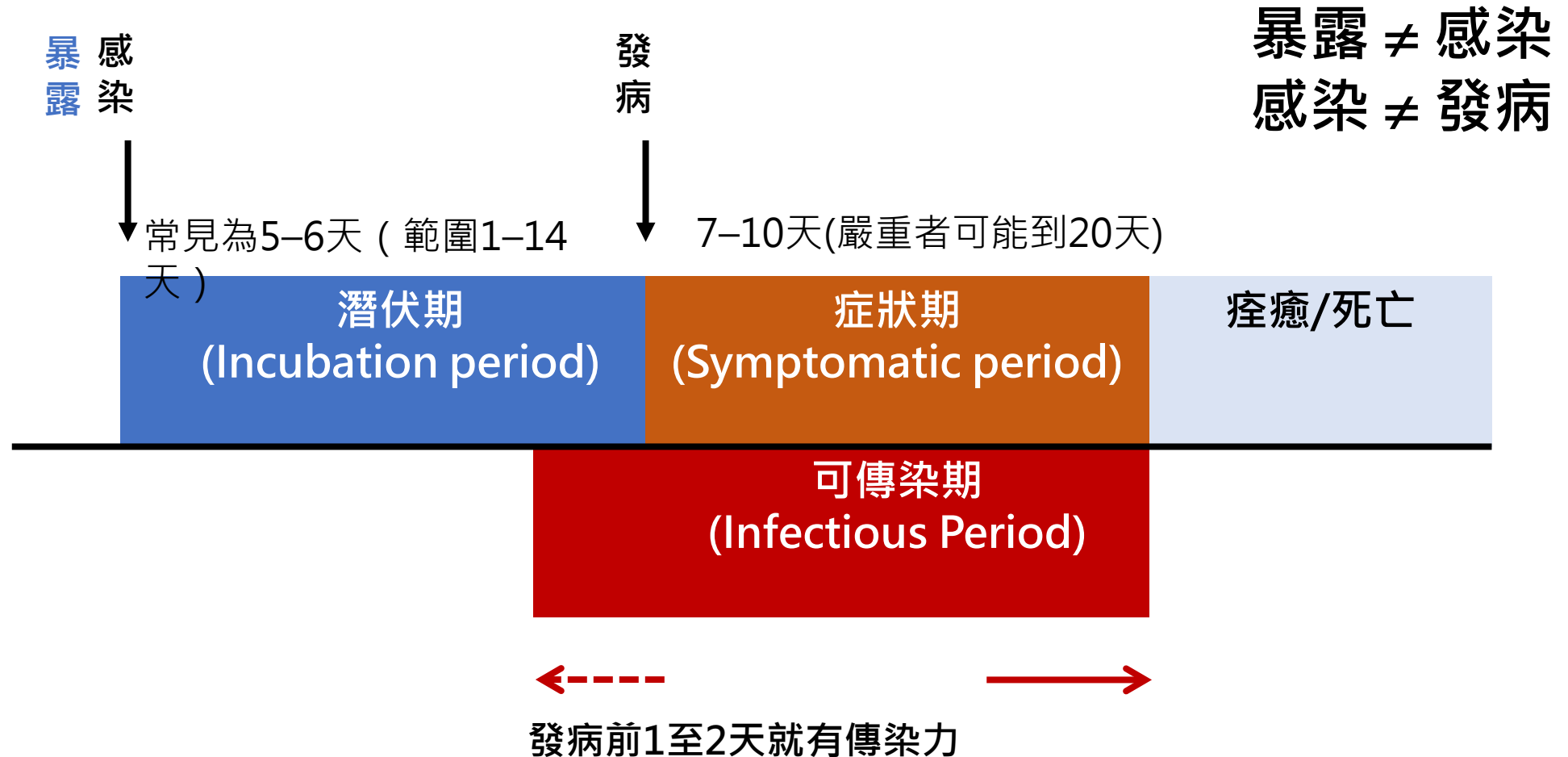
(Structural & accessory gene)

演化分析

SARS-CoV-2與舟山的 bat-SL-COVZC45、bat-SL-COVXC21屬於第二個演化支(Clade 2)

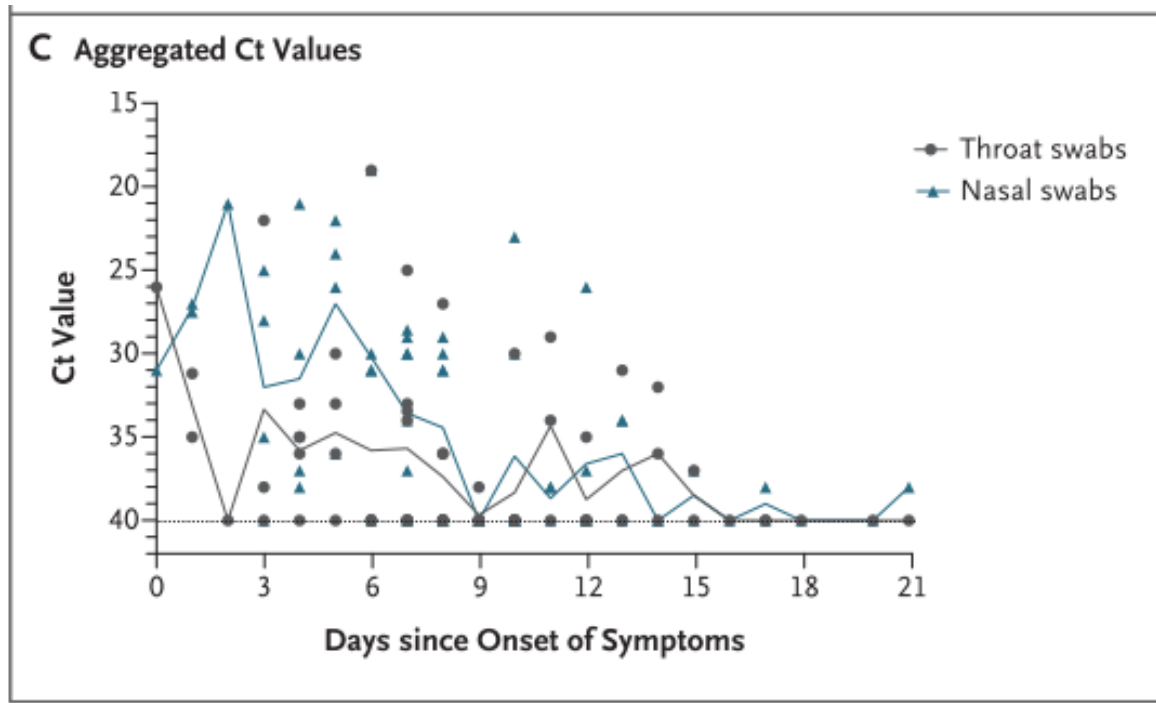


COVID-19 疾病傳播特性

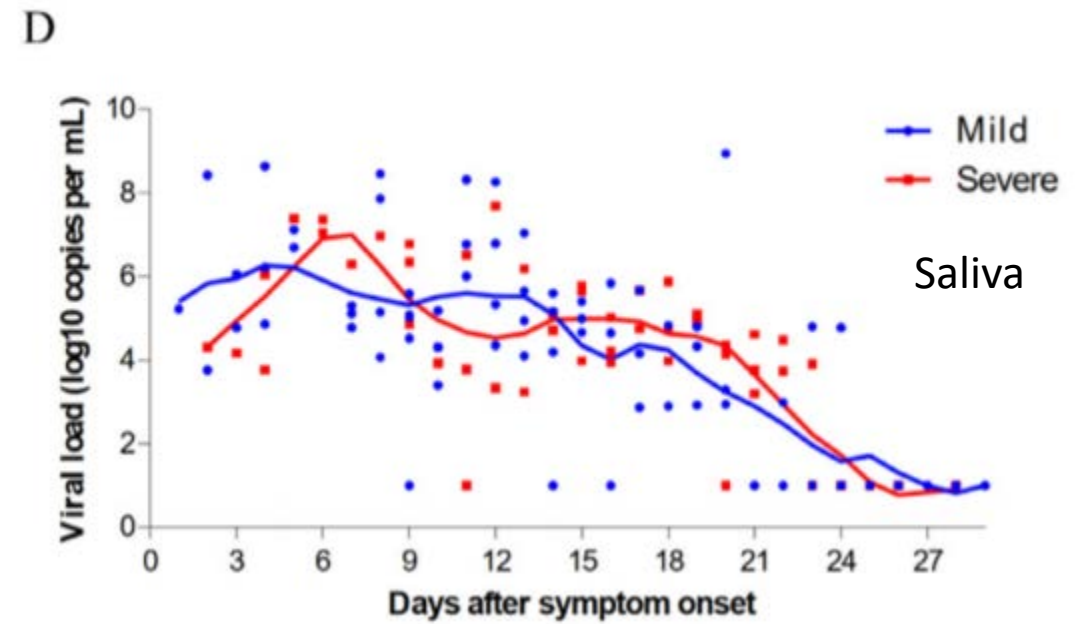


上呼吸道可檢驗到病毒核酸的時間

- COVID-19病人於發病前即可檢驗到病毒核酸
- 症狀出現後，核酸濃度即開始下降(Ct 值上升)



N Engl J Med 2020; 382:1177-1179



J Infect. 2020 Sep; 81(3): e48–e50.

病毒核酸可持續數週

- 義大利研究176名康復個案(症狀恢復，PCR二次陰性)
- 其中32名個案(18.6%)持續驗出病毒核酸，平均達48.6天
- 其中有一名培養陽性

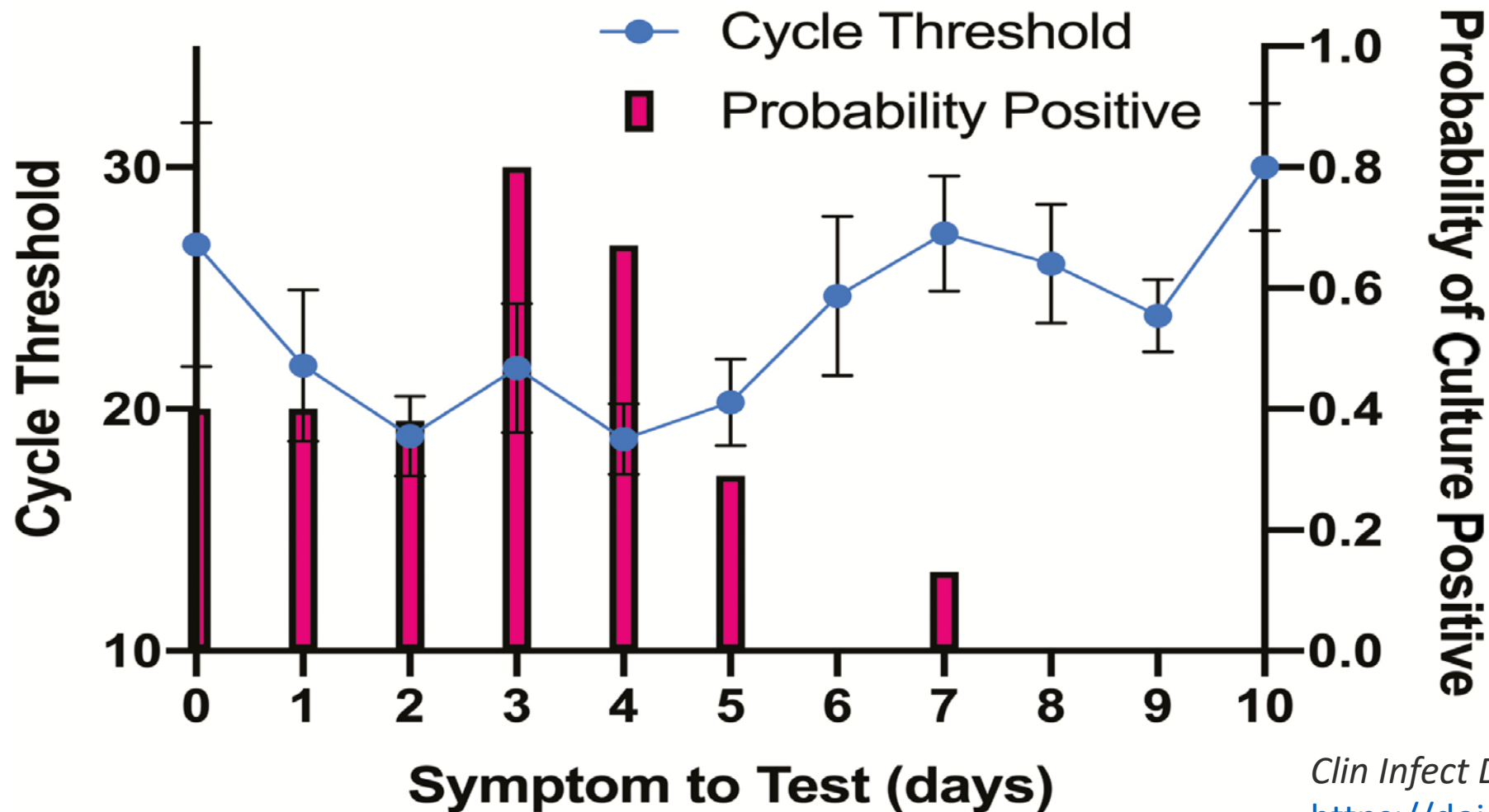
Table. Testing Results for NOS Samples Obtained at COVID-19 Diagnosis or After COVID-19 Recovery in 32 Study Patients^a

Sample No.	COVID-19 samples tested				Recovery								Days of recovery sampling since diagnosis
	Diagnosis												
	Genomic RNA (C _t value)		Subgenomic RNA (C _t value)		Genomic RNA (C _t value)		Subgenomic (C _t value)		RNA load, copies/mL		Serology (positive or negative result)		
E gene	RdRP gene	N gene	E gene	E gene	RdRP gene	N gene	E gene	N gene	IgG	IgA			
1	31.6	31.3	31.2	34.5	29.3	30.7	31.2	39.1	1.2 × 10 ⁴	Positive	Positive	39	
2	27.0	26.9	30.0	36.0	30.0	30.5	31.2		8.9 × 10 ³	Positive	Positive	31	
3	19.3	20.8	22.1	35.2	31.5	34.7	32.8		3.3 × 10 ³	Positive	Negative	44	
4	21.6	22.0	22.9	36.4	31.8	31.4	32.3		5.5 × 10 ³	Positive	Positive	34	
5	30.0	32.8	38.1	30.2	31.8	34.3	34.5		3.2 × 10 ³	Positive	Positive	62	
6	20.8	20.9	22.3	37.3	32.2	32.8	34.1		5.3 × 10 ³	Positive	Positive	37	
7	27.3	29.9	31.3	36.9	32.3	30.9	32.7		6.4 × 10 ³	Positive	Positive	39	
8	26.9	27.0	31.2	38.1	35.0	34.4	36.1		4.0 × 10 ²	Positive	Positive	71	
9	22.5	23.7	24.9	31.0	38.8	33.6	33.9		2.6 × 10 ³	Negative	Negative	42	
10	21.3	21.4	28.9	38.9		32.2	33.4		1.2 × 10 ⁴	Positive	Positive	56	
11	26.6	26.9	28.1	33.0		32.8	33.2		1.3 × 10 ⁴	Positive	Positive	54	
12	22.8	24.2	25.3	31.0		34.2	33.7		6.9 × 10 ³	Positive	Positive	55	
13	25.8	25.8	26.1	39.8	NA	34.8	39.1		3.0 × 10 ²	Positive	Positive	36	
14	20.8	20.4	21.1	32.0		35.0	35.1		1.9 × 10 ³	Positive	Positive	56	
15	29.4	30.1	32.2	37.0		36.5	39.2		3.2 × 10 ³	Positive	Positive	36	
16	27.9	29.1	31.1	32.0		38.1	39.3		1.6 × 10 ¹	Positive	Positive	77	
17	30.6	29.9	31.8	32.1			35.7	NA	5.4 × 10 ³	Positive	Positive	53	
18	28.5	29.1	30.8	36.8			36.8		2.9 × 10 ³	Positive	Positive	43	
19	26.9	22.2	26.1	30.1			37.5		1.1 × 10 ³	Positive	Positive	36	
20	25.7	25.2	28.9	38.0			37.9		2.6 × 10 ³	Positive	Positive	48	
21	27.0	29.0	30.2	32.3			38.1		1.9 × 10 ³	Positive	Positive	41	
22	28.5	29.4	30.0	32.3			38.4		4.9 × 10 ¹	Positive	Negative	76	
23	27.1	28.6	29.3	36.1			38.9		4.5 × 10 ²	Positive	Positive	29	
24	25.4	22.9	24.1	34.8			39.0		5.6 × 10 ¹	Positive	Positive	70	
25	28.7	29.5	31.4	37.3	NA		39.1		5.4 × 10 ³	Negative	Positive	46	
26	27.1	27.7	29.2	37.1			39.1		1.9 × 10 ³	Positive	Positive	34	
27	26.7	27.7	29.6	39.2			39.2		2.0 × 10 ³	Positive	Positive	45	
28	17.1	19.1	19.9	33.0			39.2		8.5 × 10 ²	Positive	Positive	40	
29	27.0	28.9	30.0	32.1			39.3		5.0 × 10 ¹	Positive	Positive	56	
30	22.9	23.8	25.8	37.1			39.4		1.6 × 10 ²	Positive	Positive	55	
31	28.6	30.4	30.9	33.0			39.6		5.3 × 10 ²	Positive	Positive	61	
32	29.1	28.0	30.9	36.2			39.8		3.4 × 10 ²	Positive	Positive	53	

Abbreviations: COVID-19, coronavirus disease 2019; C_t, cycle threshold; E gene, envelope gene; NA, not applicable; N gene, nucleocapsid gene; RdRP, RNA-dependent RNA polymerase; RT-PCR, real-time polymerase chain reaction.

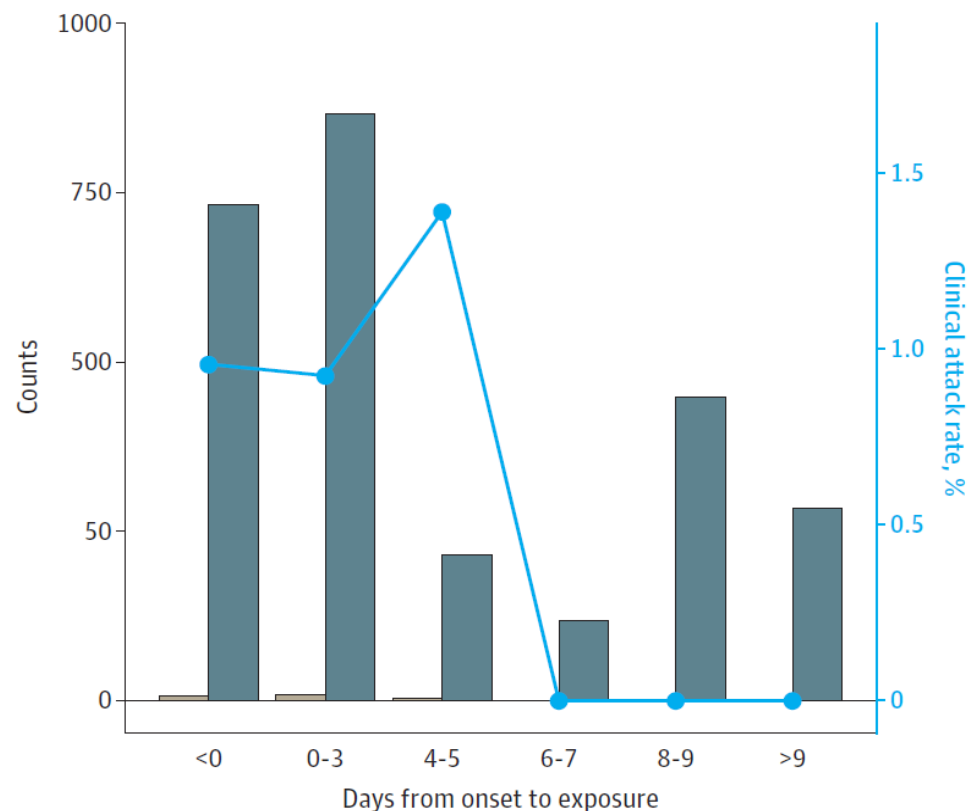
^a For RT-PCR testing, the Seegene Allplex 2019-nCoV and Clonit Quanty COVID-19 assays were used for total RNA detection and quantification, respectively, whereas replicative (E gene) RNA was detected by an in-house RT-PCR assay.⁴ Results were expressed as C_t values (<40 for positive detection) or quantified as RNA (N gene) copies per mL. NA indicates the absence of positive detection for the indicated gene. For serological testing, SARS-CoV-2 IgG/IgA Euroimmun enzyme-linked immunoassays were used, and positive and negative results were assessed using the 1.1 or greater or less than 1.1 times the manufacturer's cutoffs as reference IgG/IgA values, respectively.

病毒成功培養的機率隨發病後天數下降

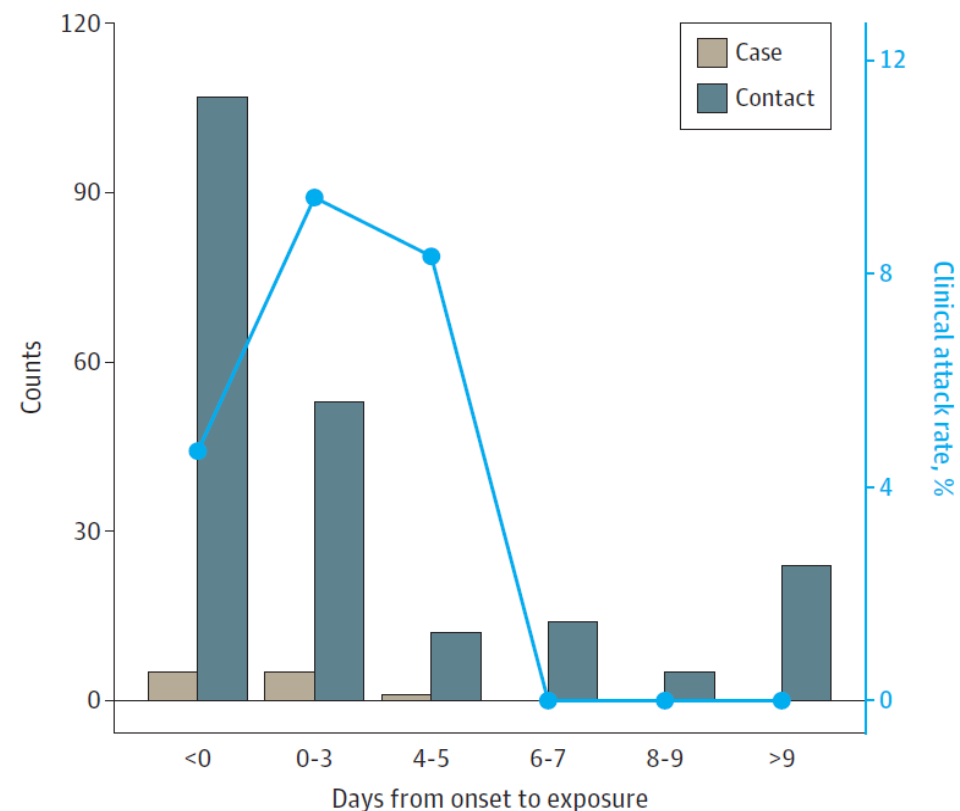


發病後一週的接觸，無次波感染

A All types of contact 所有接觸者

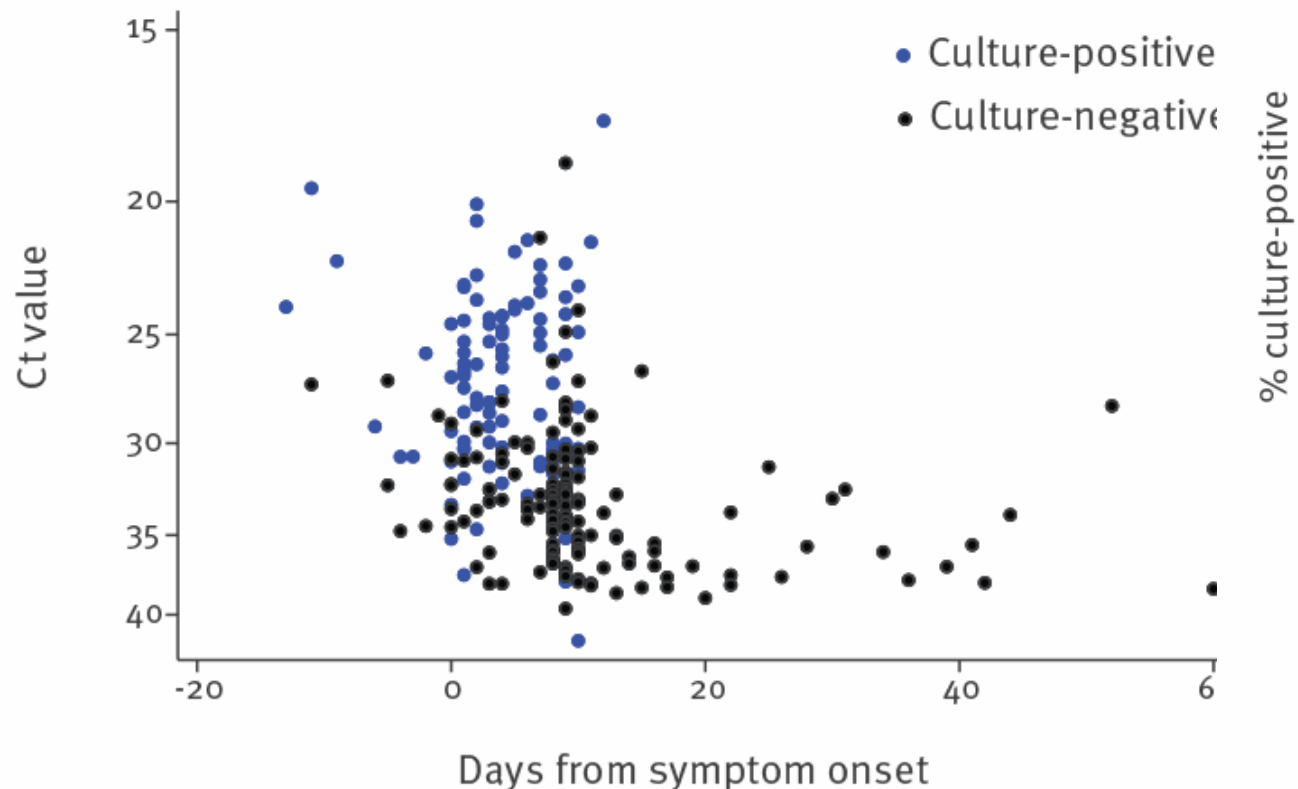


B Household and family contact 家戶接觸者

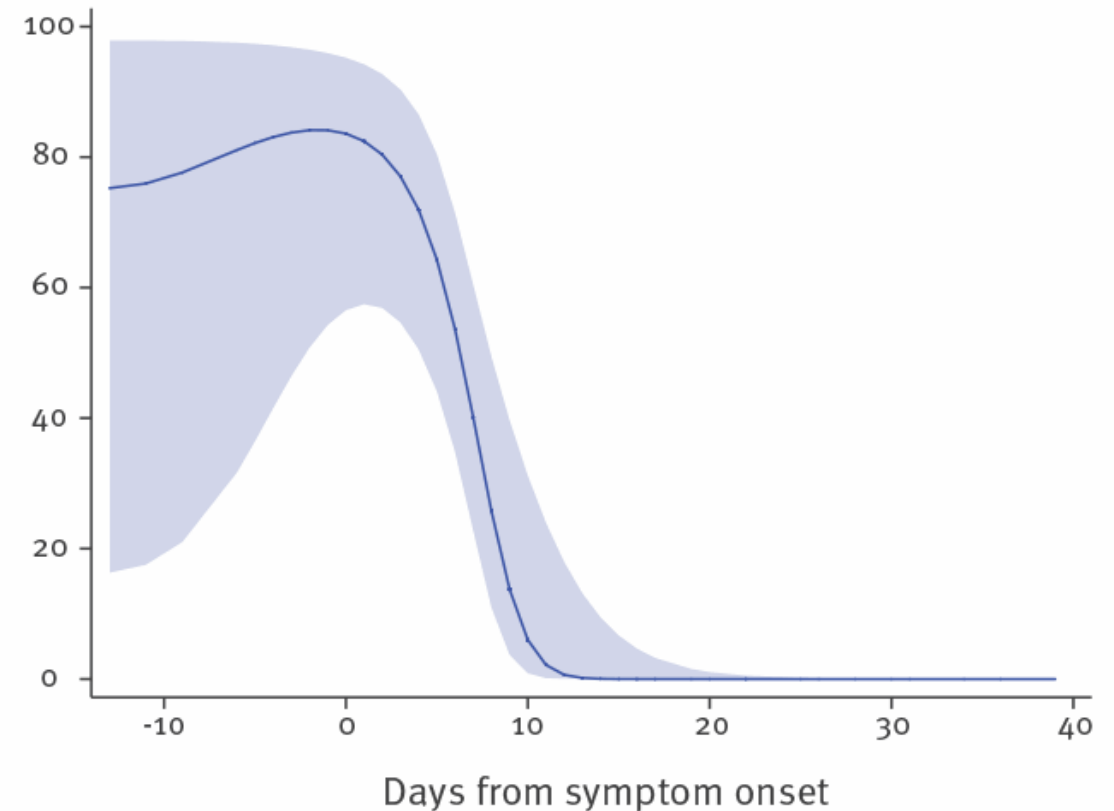


症狀前期(Presymptomatic)與出現症狀時之病毒培養陽性率相當

A. Culture positivity, Ct value and timing of each individual sample.



B. Mixed effects logistic regression analysis.

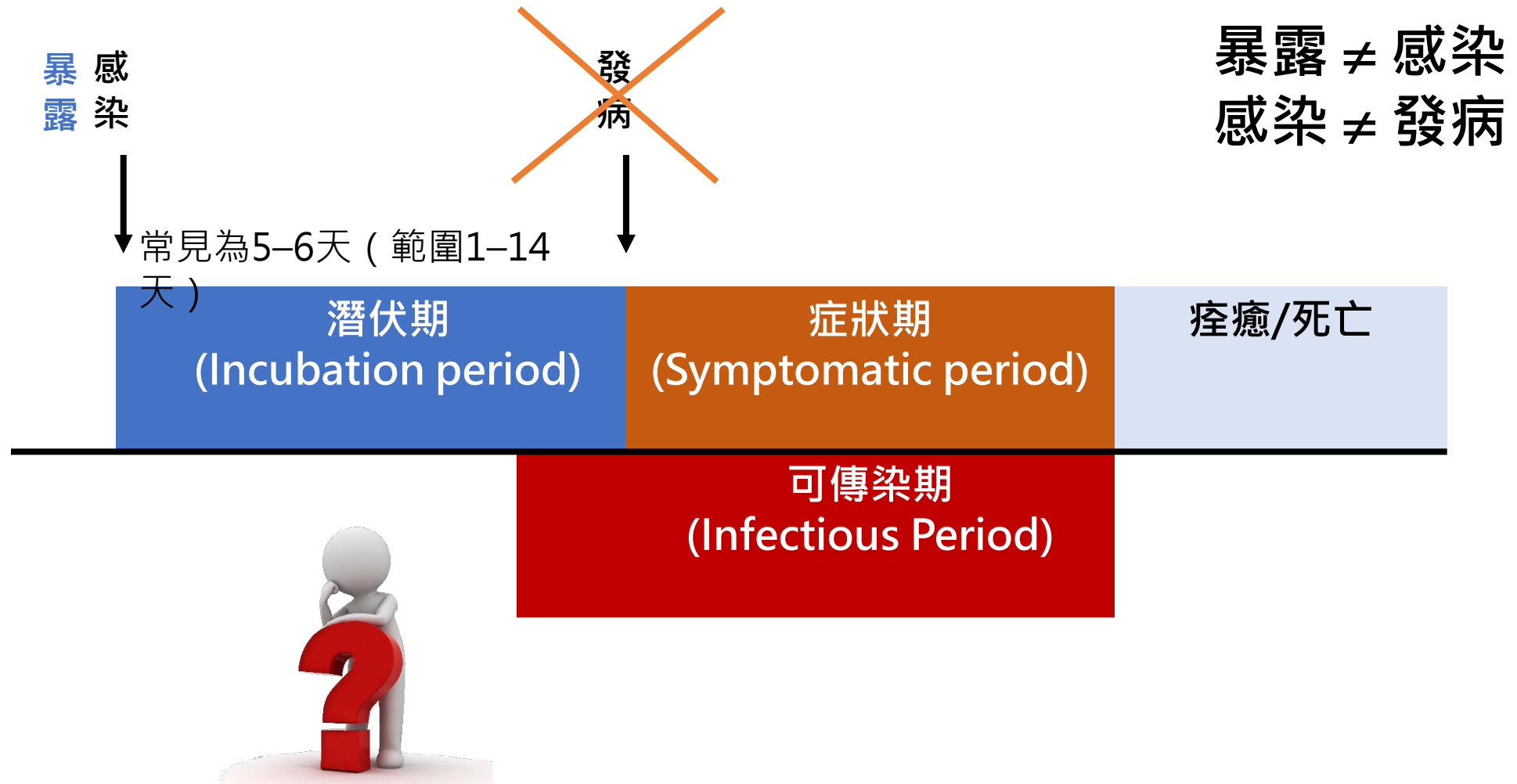


無症狀感染者

- 需區分是Asymptomatic或是Pre-symptomatic
 - ✓ Asymptomatic: 採檢時無症狀，且後續追蹤時持續無症狀
 - ✓ Pre-symptomatic: 採檢時無症狀，但後續追蹤時出現症狀
- 約40-45%個案為採檢時無症狀 (presymptomatic and/or asymptomatic)
- 約49%個案採檢時無症狀者，後續出現症狀(presymptomatic)
- 約20%個案持續無症狀 (asymptomatic)
- Asymptomatic 與有症狀者相比，造成接觸者次波感染的比例低

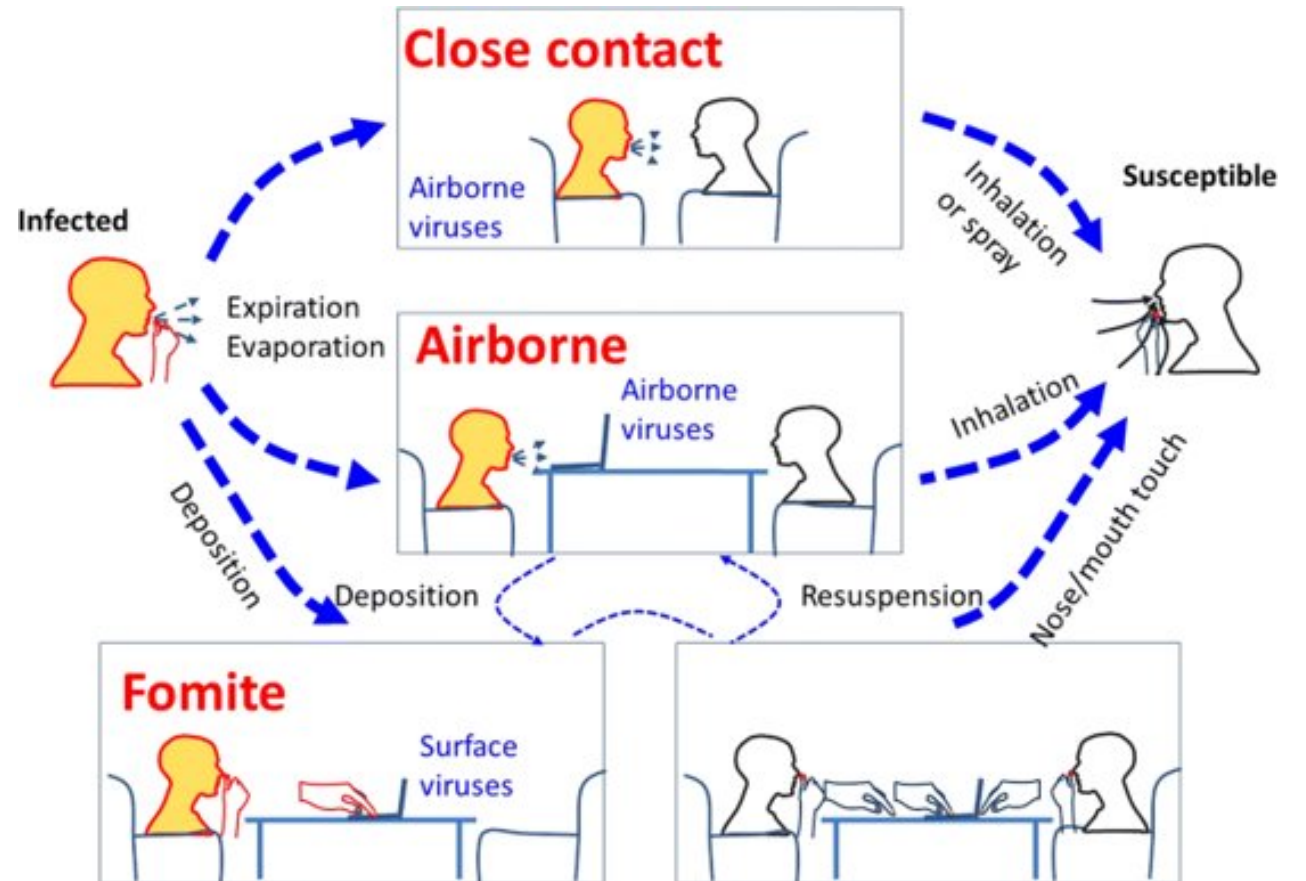
Ann Intern Med. 2020 Sep 1;173(5):362-367
J Med Virol. 2020 Jul 21;10.1002/jmv.26326
PLoS Med. 2020 Sep 22;17(9):e1003346.

無法明確知道無症狀感染者 (asymptomatic)何時開始具有傳染力



COVID-19 傳播途徑

- 飛沫 (Droplet transmission)
- 空氣 (Airborne transmission)
- 接觸 (Contact transmission)



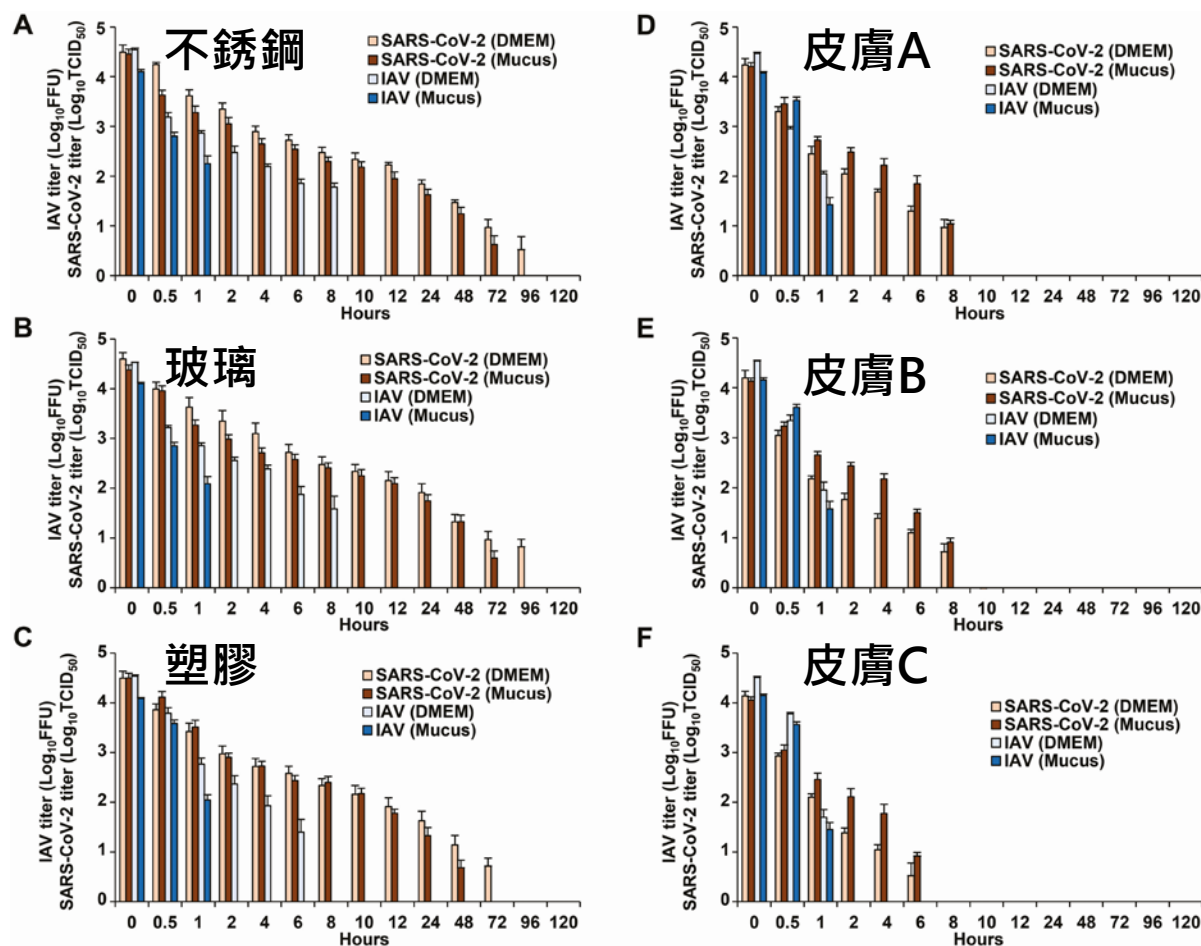
口罩與飛沫傳播



美國CDC 2020/11/10最新建議：

"CDC recommends community use of masks, specifically non-valved **multi-layer cloth masks**, to prevent transmission of SARS-CoV-2. Masks are primarily intended to reduce the emission of virus-laden droplets ("**source control**"), which is especially relevant for asymptomatic or presymptomatic infected wearers who feel well and may be unaware of their infectiousness to others, and who are estimated to account for more than 50% of transmissions. Masks also help reduce inhalation of these droplets by the wearer ("**filtration for personal protection**"). The community benefit of masking for SARS-CoV-2 control is due to the combination of these effects; individual prevention benefit increases with increasing numbers of people using masks consistently and correctly."

SARS-CoV-2在環境中的穩定性



- 在皮膚上約9小時後失去活性
- 在皮膚上活性時間較其他物質上短
- 與流感病毒相比，SARS-CoV-2穩定性較高
- 使用酒精即可很快的去活性

感染的高風險族群或場所

- 經常與人接觸的職業(醫護人員、導遊、司機)
- 與疑似個案長時間近距離之接觸(家戶接觸、醫療照護)
- 通風不佳之場所
- 人員密集之場所(郵輪、教堂、辦公場所)

多樣的疾病表現

12 Possible Symptoms of COVID-19

Symptoms vary by case and typically appear 2-14 days after exposure to the virus.



Fever or Chills



Cough



Shortness of
Breath or
Difficulty
Breathing



Fatigue



Muscle or
Body Aches



Headache



New Loss
of Taste



New Loss
of Smell



Sore Throat



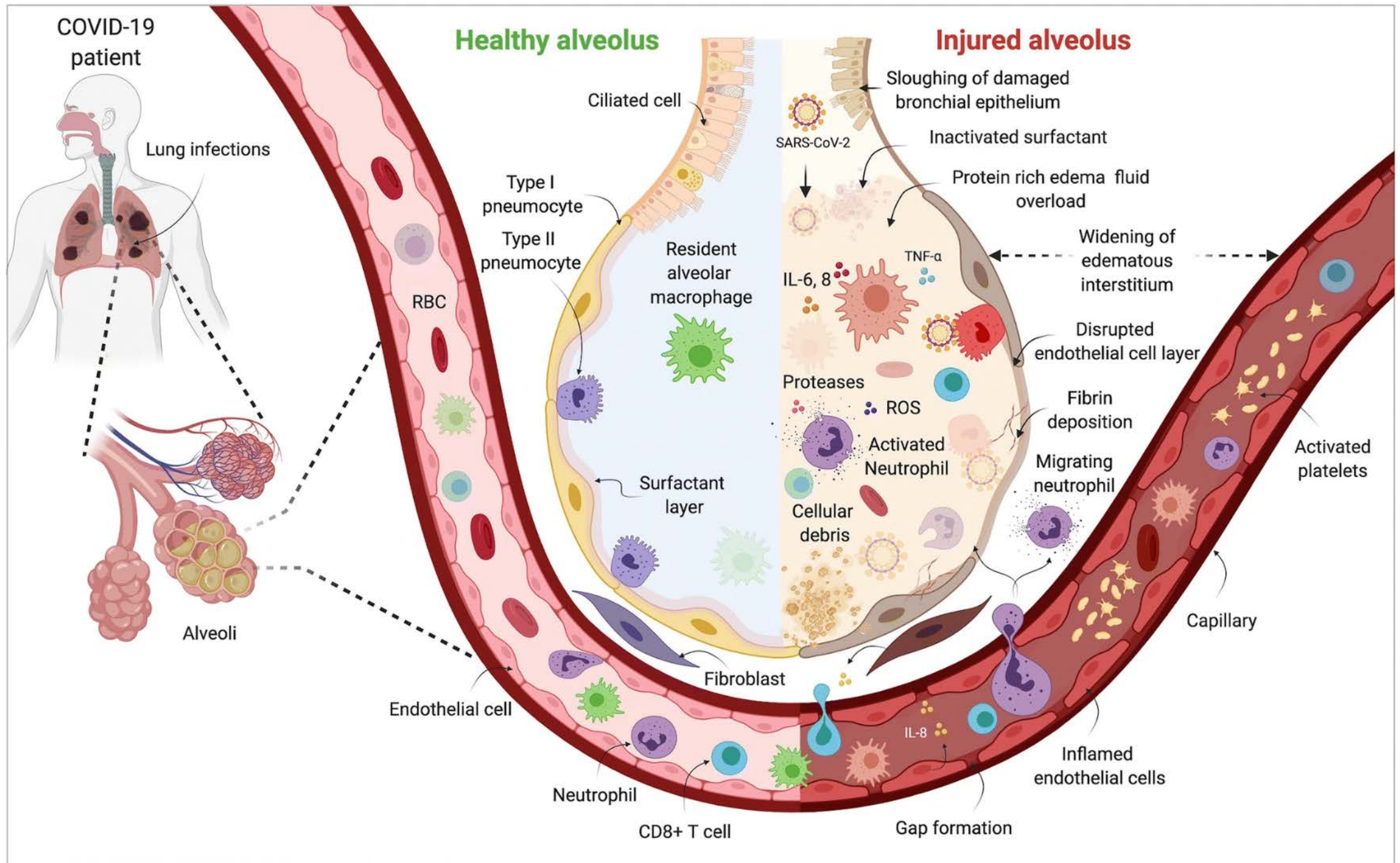
Congestion or
Runny Nose



Nausea or
Vomiting



Diarrhea



重症高風險族群

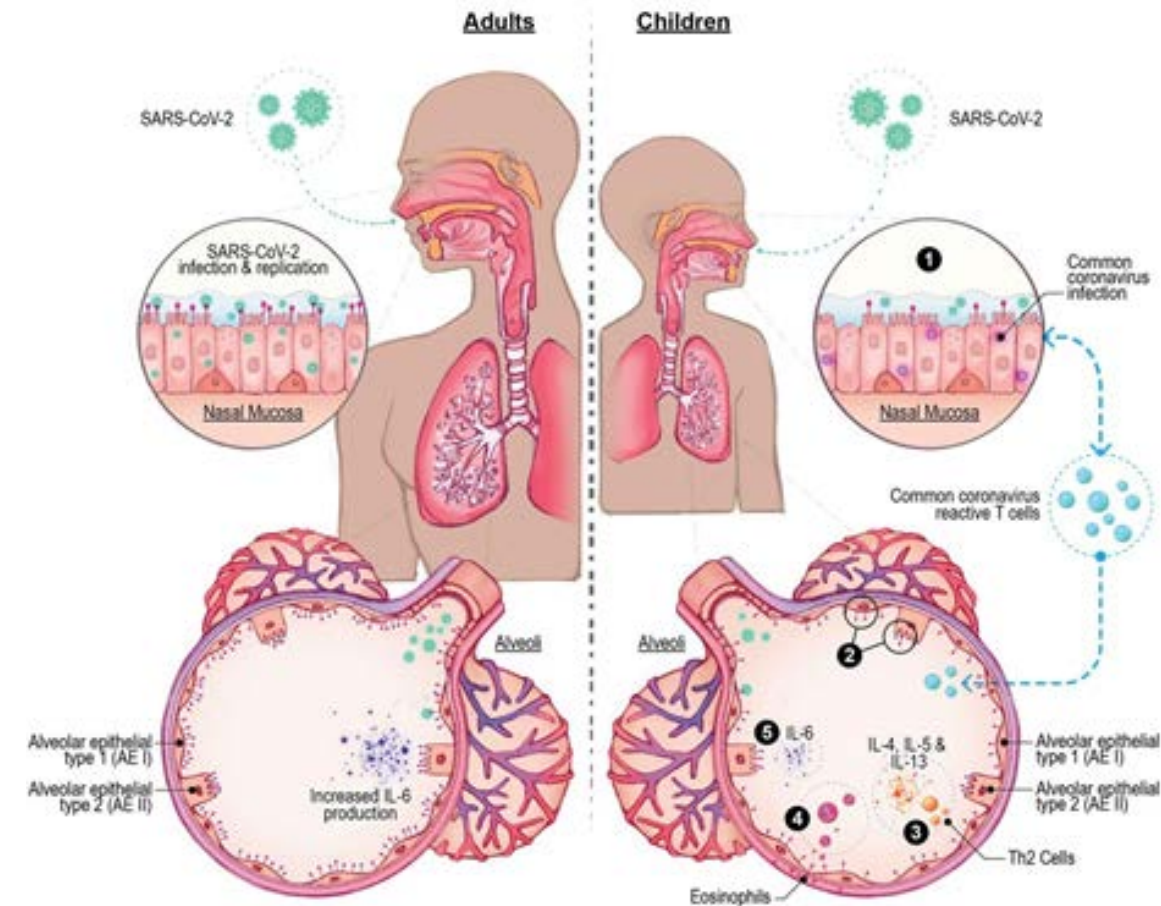
- 年長者(>65歲)
- 機構住民
- 具慢性疾病史
 - 慢性肺病
 - 心血管疾病
 - 肥胖
 - 糖尿病
 - 慢性腎病
 - 免疫不全者

兒童

- 多為輕症且為自限性
- 感染的比例較成人為低
- 非主要的感染源
- 少數病患有全身炎症之重症表現

兒童較不易感染的原因

- ACE2 receptor較少
- 感冒提供的交叉保護力
- Th2免疫、Eosinophilia提供保護
- 發炎物質生成量低

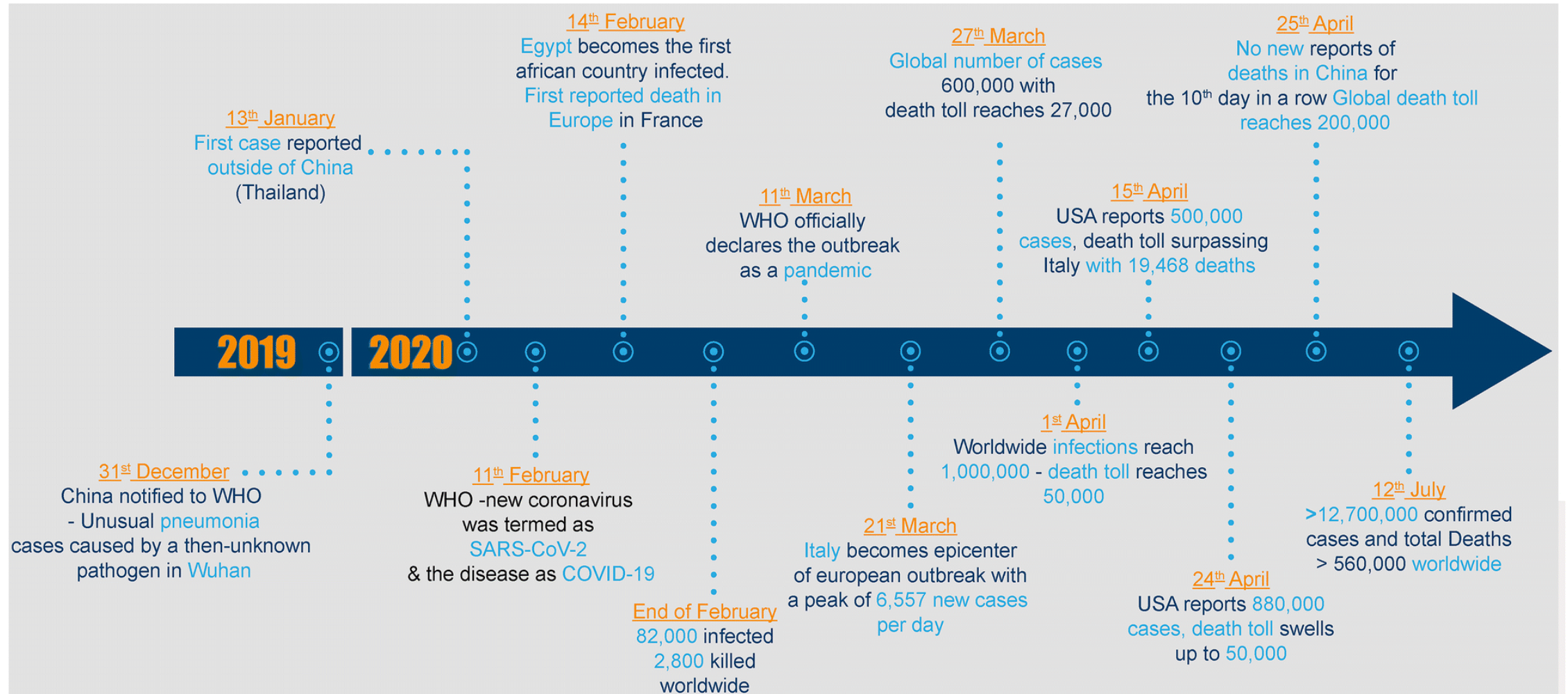


Legend

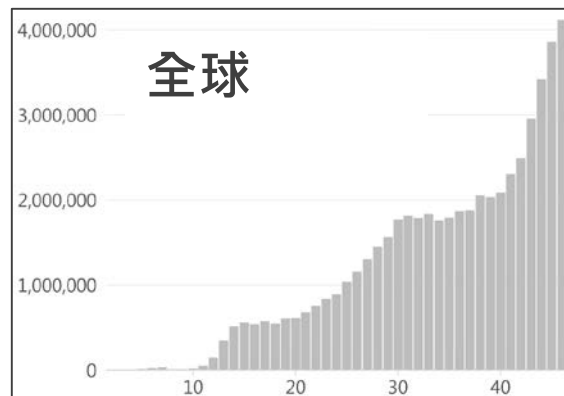
- SARS-CoV-2 Virus
- Common Coronavirus
- ACE2
- TMPRSS2
- T helper cells (Th2)
- Common coronavirus reactive T cells
- Eosinophil

- 1 Coronavirus associated with common colds in children may offer some protection, due to cross-reactive T cell immunity between common coronaviruses and SARS-CoV-2, and due to reduced ACE2 in nasal mucosa of children.
- 2 Reduced TMPRSS2 in children in type I alveolar epithelial cells (AEI). Reduced ACE2 in children in type II alveolar epithelial cells (AEII).
- 3 Protective Th2 immunity in children.
- 4 Surprising protection from eosinophilia driven by Th2 cytokines including IL-4, IL-5, and IL-13 (for example childhood asthma).
- 5 Children produce lower levels of inflammatory cytokines, IL-6 production increases with age.

COVID-19 全球疫情發展



全球疫情概況



截至11/16 24:00

受影響國家/地區數：190

確診病例數：55,068,799 (+591,410 /day) ▲

死亡數：1,329,125 (+9,039 /day) ▲

CFR：2.4% ▼

*紅字表示近1週新增數

新增
確診
數

2,000,000

1,500,000

1,000,000

500,000

0

- 全球疫情持續創新高▲7%
- ✓ 歐洲仍嚴峻，居各區第一
- ✓ 美洲快速惡化▲35%
- ✓ 東地中海仍上升▲11%

10

20

30

40

報告週

歐洲

美洲

東南亞

東地中海

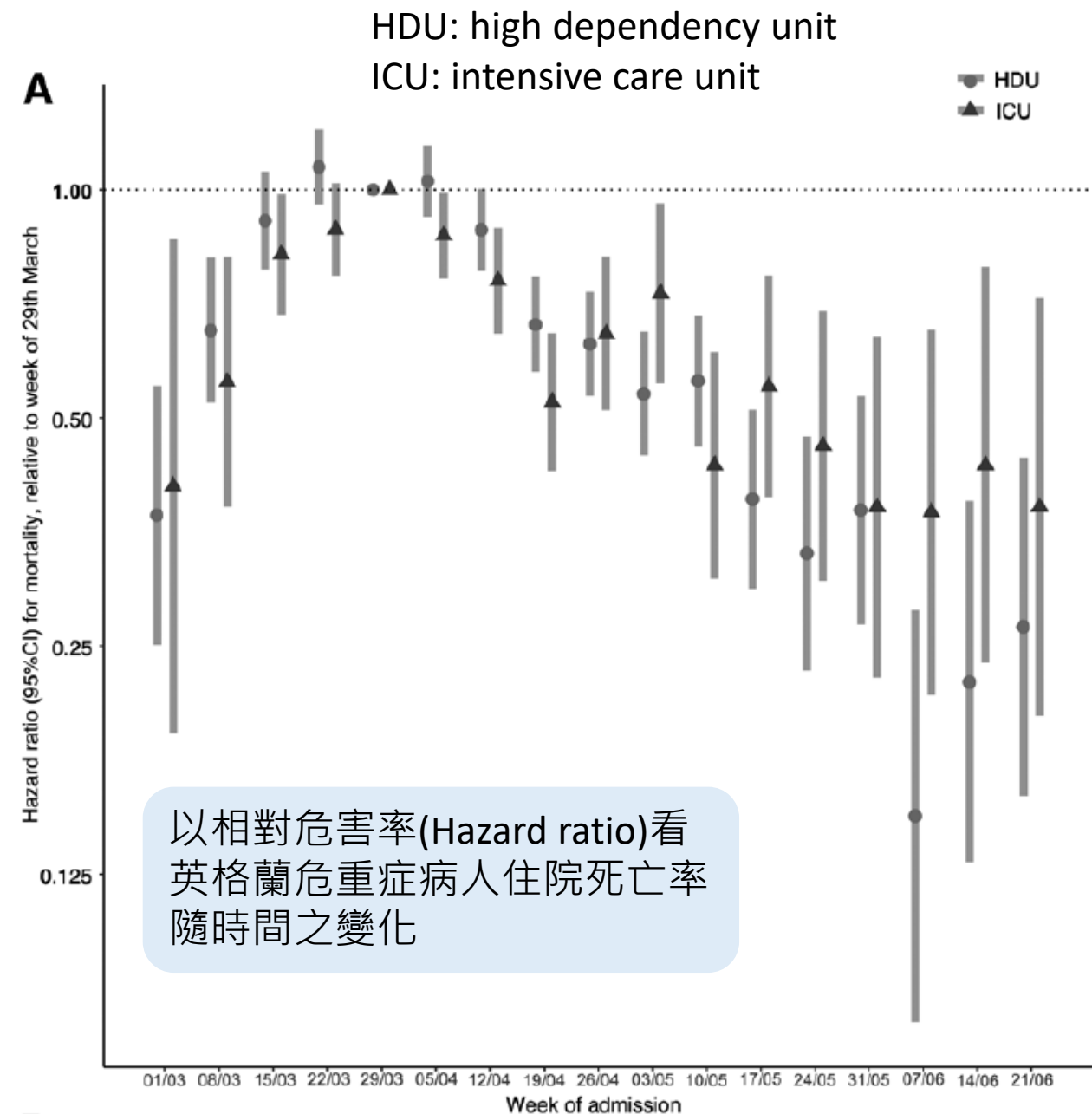
非洲

西太平洋

26

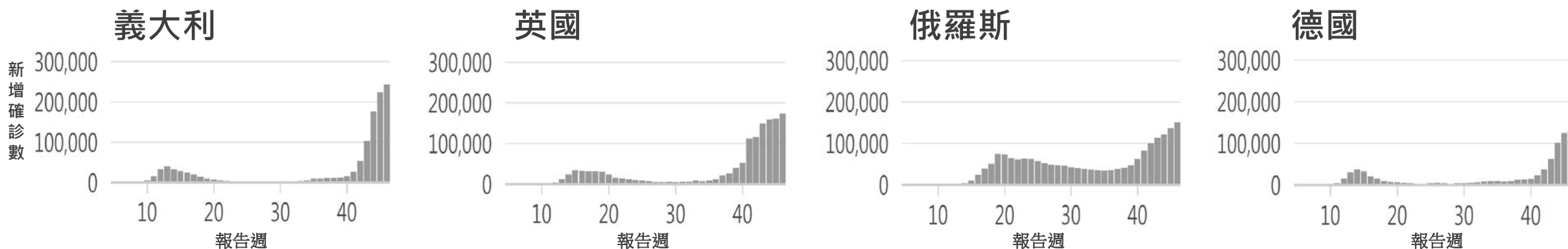
死亡率隨疫情的變化

- 感染族群的改變(年齡、潛在疾病)
- 檢驗的改變(輕症接受檢驗)
- 醫療照護的改善
- 病毒的變化



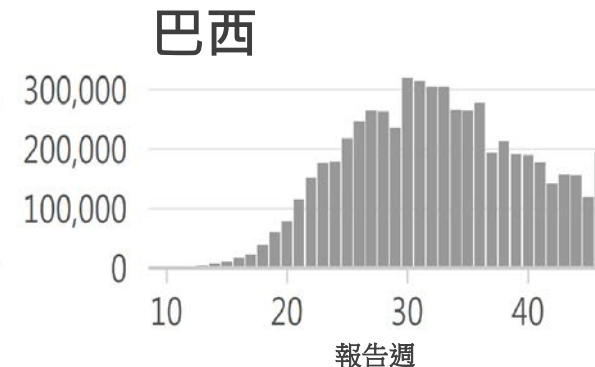
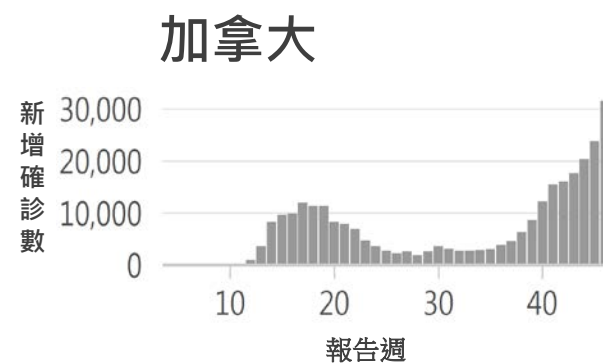
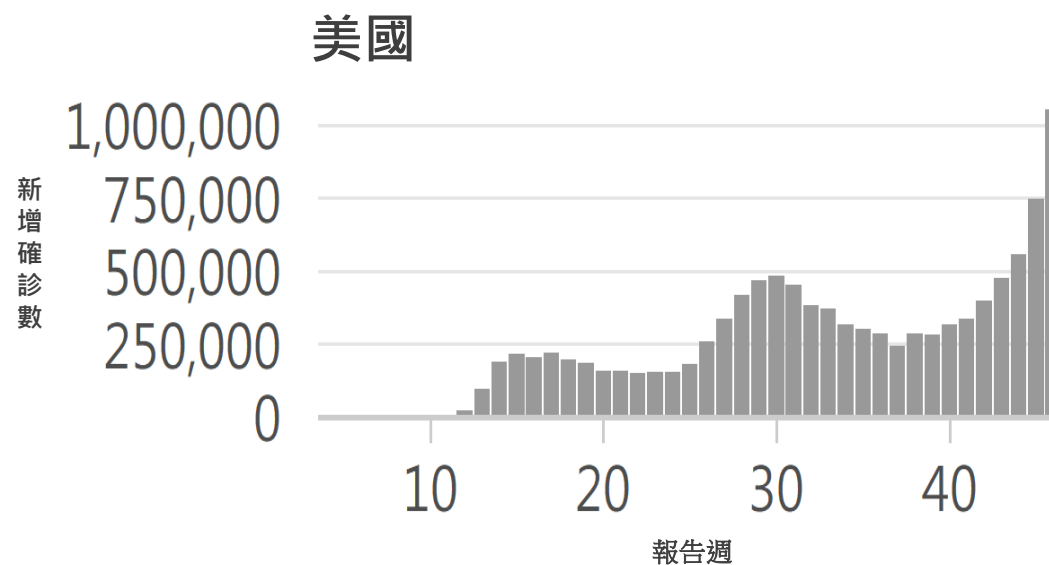
歐洲疫情概況：確診及死亡數均略降，死亡數已逾首波高峰

- 義大利、英國、俄羅斯、德國及烏克蘭仍上升，且近1週日增均逾萬例
- 部分國家高強度管制措施奏效，法國、比利時、瑞士、捷克、荷蘭等國近期趨緩



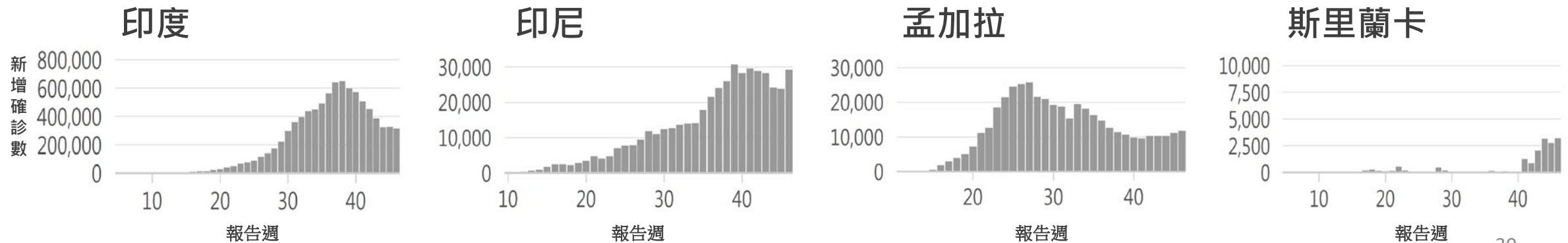
美洲疫情概況

- 美國確診數較前週增加41%，近4週死亡數加速增加；多州已加強管制措施
- 加拿大加速升溫，病例多來自脆弱族群，包括老年人、長照住民及原住民
- 中南美洲持續趨緩，惟仍嚴峻
 - ✓ 巴西、墨西哥、巴拿馬等近期回升



東南亞疫情概況

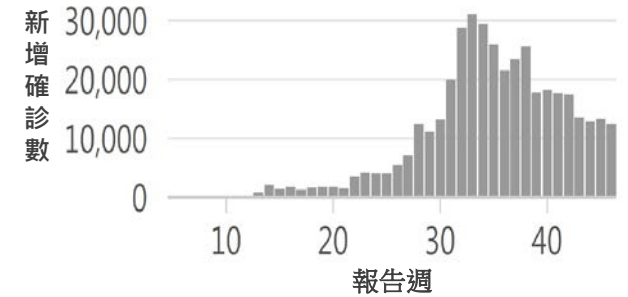
- 印度近3週持平，日增逾41,000例回到全球第二位，佔本區8成
- 印尼及孟加拉近期回升，斯里蘭卡持續，尼泊爾及緬甸過高峰趨緩，惟仍嚴峻
 - ✓ 印尼近期近5成病例來自雅加達、東爪哇及西爪哇省



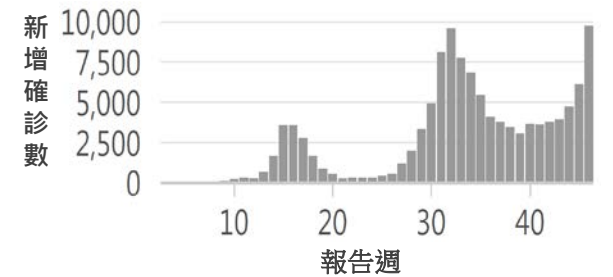
西太平洋疫情概況：近1週較10月初上升36%

- **菲律賓**持續緩降，近1週日增約1,600例，佔本區逾4成
- **日本**近期連3日新增約1,700例創新高，已逾前二波高峰，高齡感染者佔比上升；近1週發生率前五名為北海道、大阪府、沖繩縣、東京都及愛知縣
- **韓國**10月中起持續回升，近期病例多來自首爾及京畿道；11/13起公共交通工具及場所強制戴口罩
- **中國大陸**天津與上海/安徽近期分別報告零星冷鏈及機場貨運相關感染個案，疫情暫無擴散

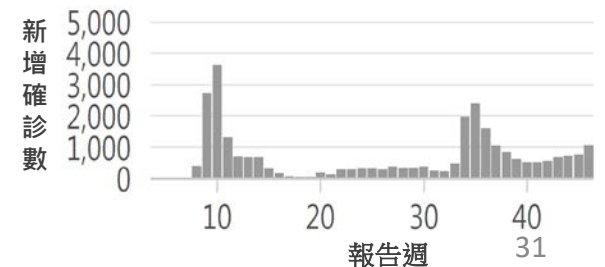
菲律賓



日本

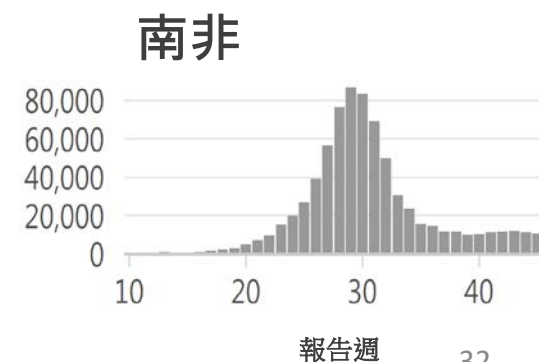
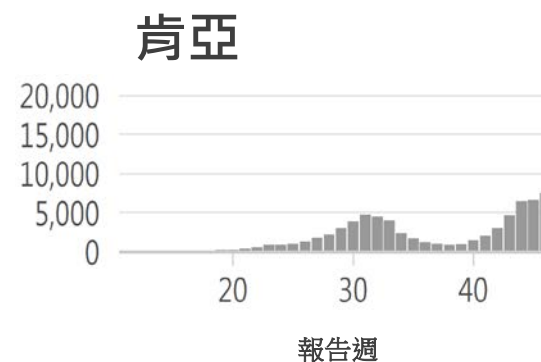
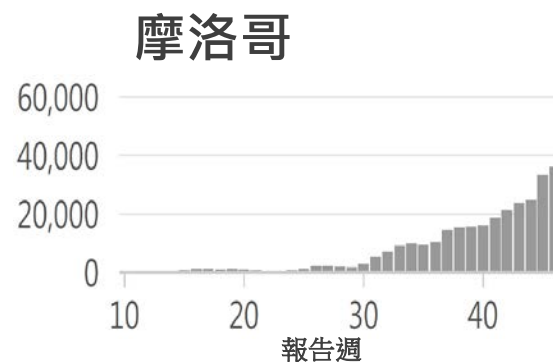
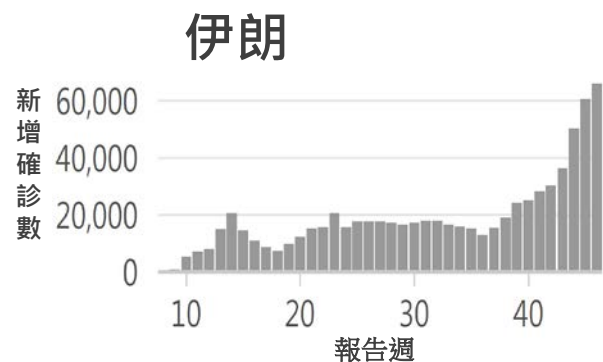


韓國

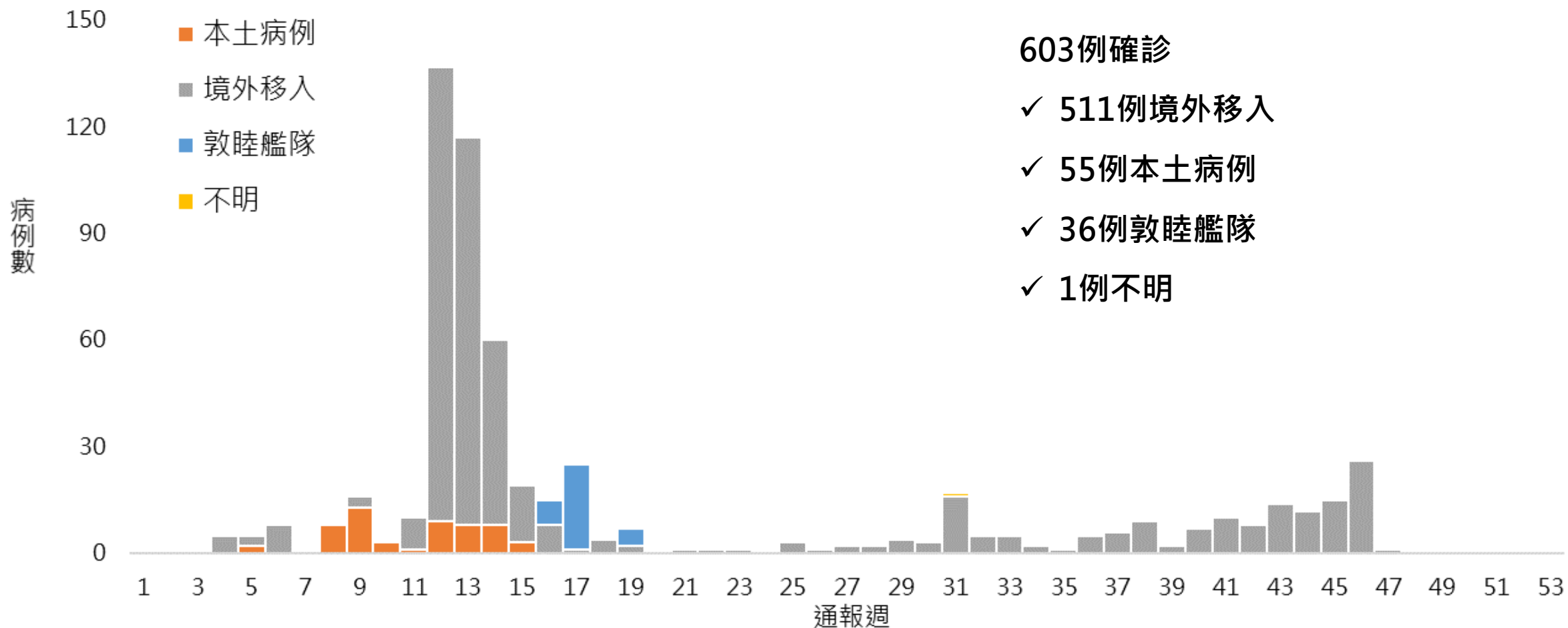


東地中海及非洲疫情概況

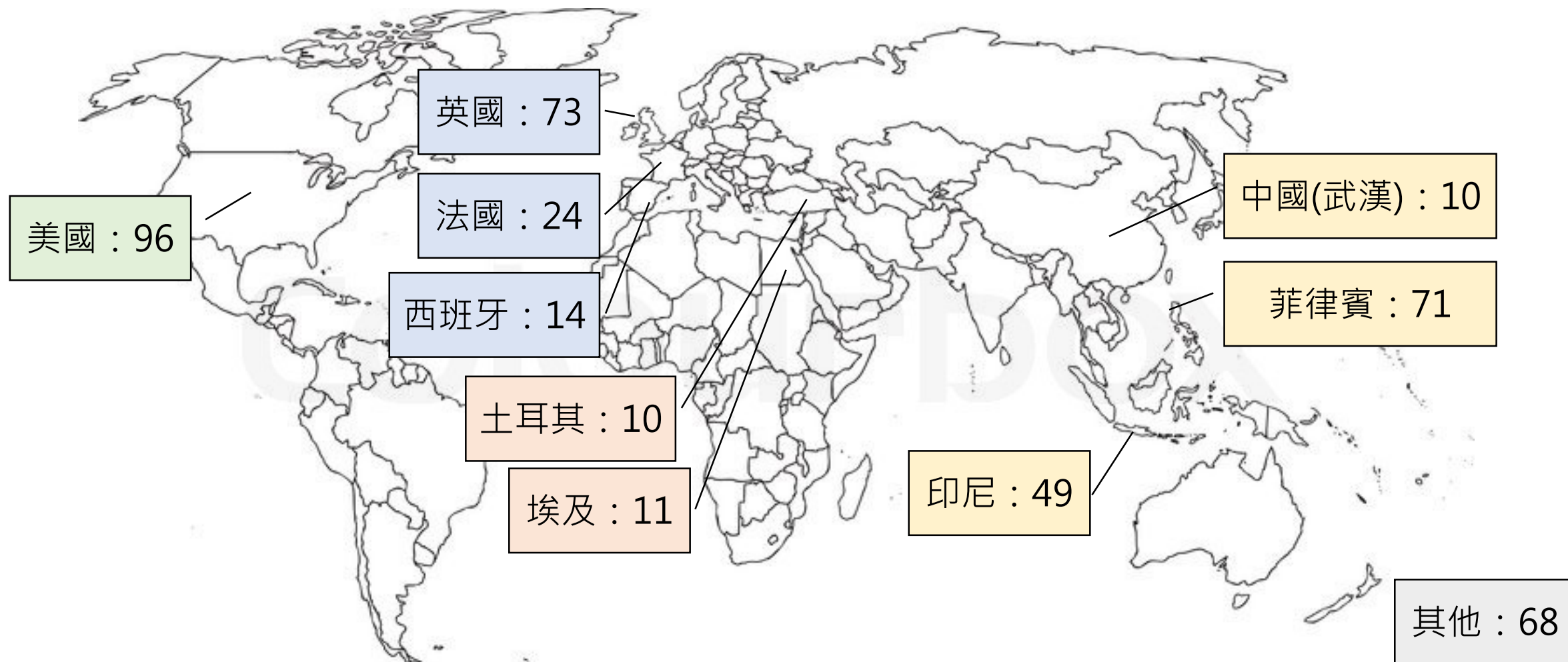
- 東地中海整體持續創新高
 - ✓ 伊朗、摩洛哥及約旦維持上升，其中伊朗近1週日增逾萬例為本區最高，死亡數亦加速上升
- 非洲10月中起緩升
 - ✓ 肯亞及阿爾及利亞持續上升，均逾7月下旬高峰
 - ✓ 南非持平



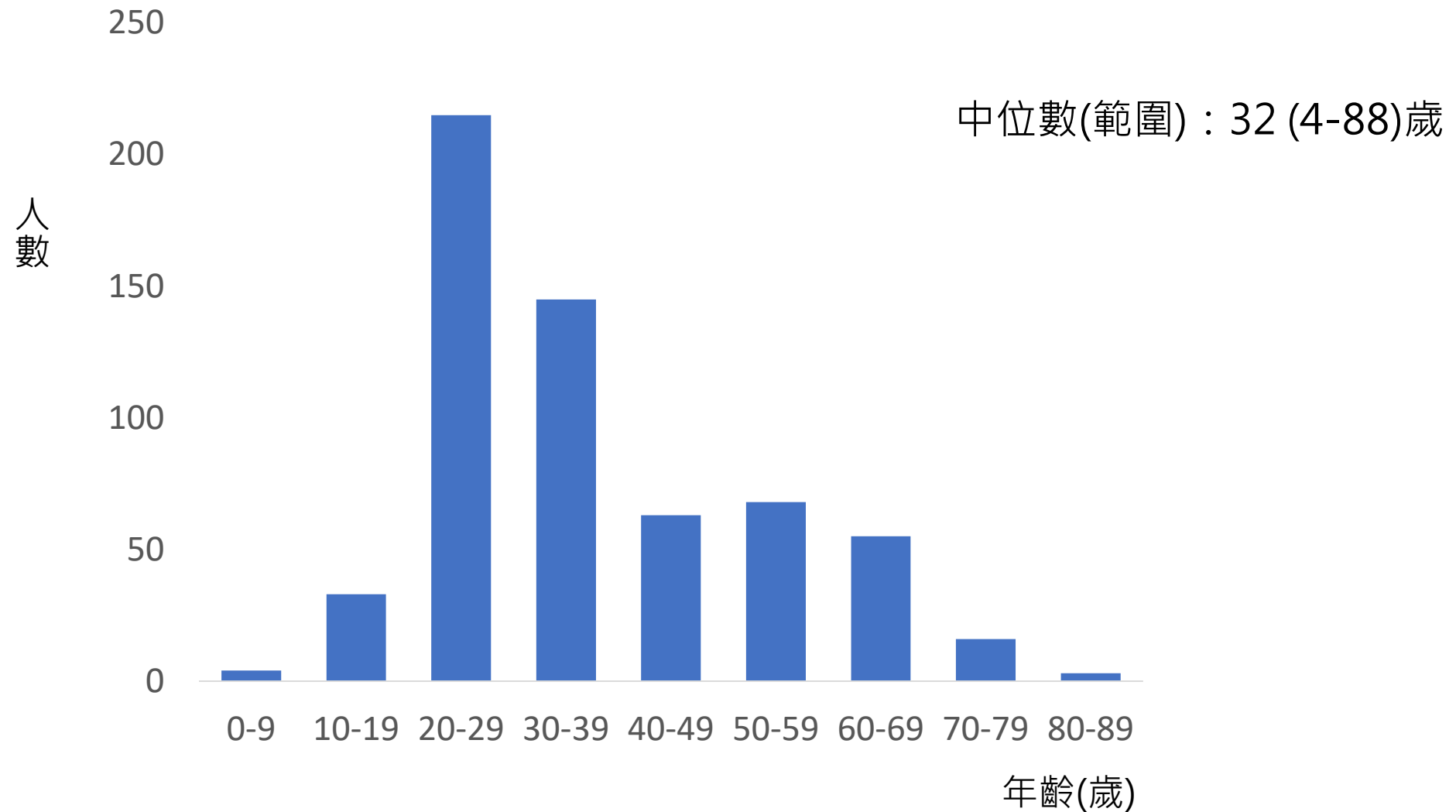
我國嚴重特殊傳染性肺炎個案通報趨勢



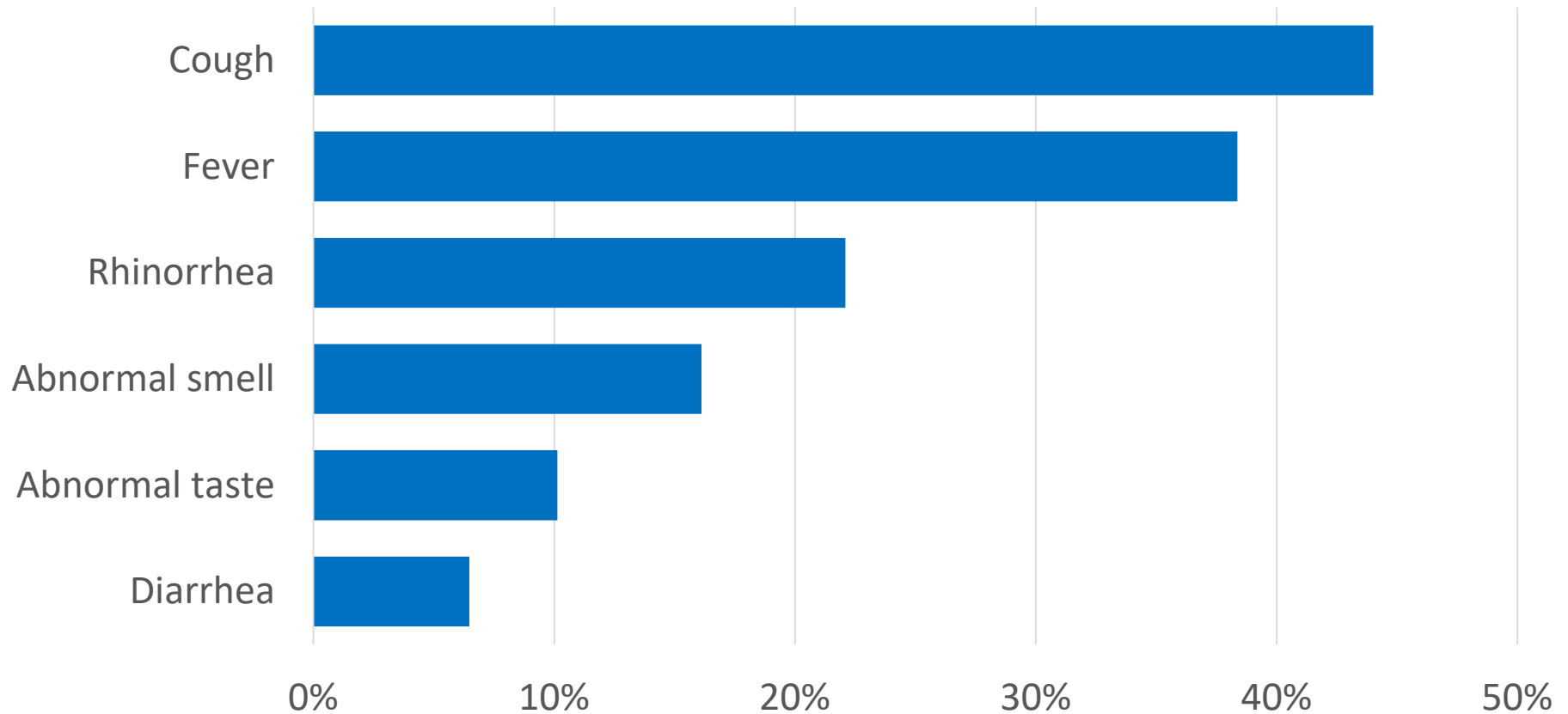
境外移入(n=511)感染國家



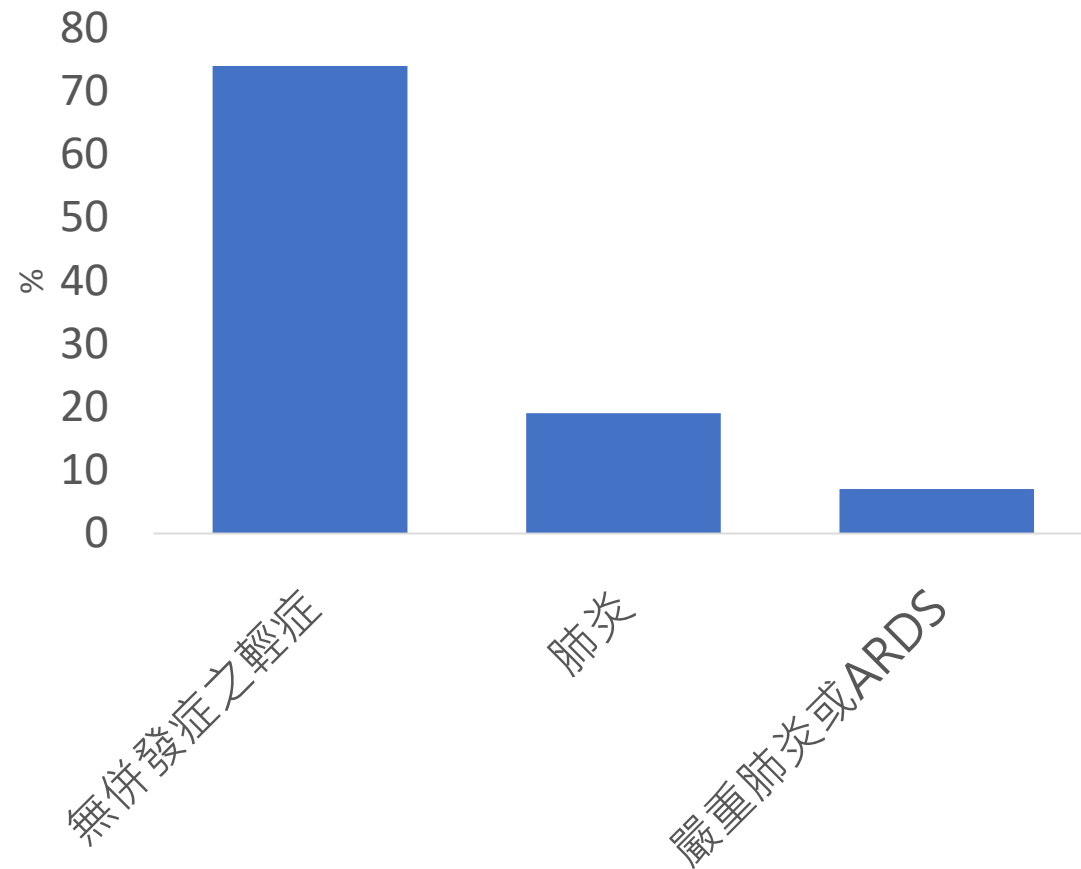
我國確診個案年齡分佈 (n=603)



我國確診個案初始症狀分佈(n=603)



嚴重度分類及預後 (n=603)



- 出院：536
- 隔離中：60
- 死亡：7 (1.2%)

Pacific islands which escaped the 1918–1919 influenza pandemic and their subsequent mortality experiences

Island	Location in Pacific	Influenza epidemics	Mortality outcomes	Ref.
American Samoa	North of Tonga near western Samoa	1926 1929/1930	Approx. 25 % ill in 1926 with estimated 1 : 1000 mortality	[2, 4, 5]
New Caledonia	East of Queensland, Australia	1921	Widespread illness with estimated 1 : 1000 mortality	[6]
Rotuma	Between Fiji and Tuvalu	1927/1928 1947/1948	3·8 % died in 1927/1928 and 1·9 % died in 1947/1948	[7, 8]
Yule Island	Papuan south coast north of Australia	1920 1931/1932 1940–1942	Baseline annual mortality of 3 % increasing up to 6·8 % during epidemic years	[9]
Niue	Between Tonga and Cook Islands	1921? 1942 1944	Estimated 4% of population including all ages died during 1944 epidemic	[10]
Jaliut	Southern Marshall Islands	1931	8·6 % died in 1931 epidemic	[11]

very isolated

結語

- 依基因序列的相似度，推測SARS-CoV-2可能源自於感染蝙蝠的冠狀病毒
- S蛋白是病毒進入細胞的關鍵，同時也是目前疫苗研發主要標的
- SARS-CoV-2在環境中穩定，但一般消毒方式(熱、消毒劑、酒精)即可去其活性
- COVID-19主要藉由飛沫傳播，感染者發病前即具有傳染力
- 目前全球疫情持續，以歐洲、美洲疫情最嚴竣



謝謝聆聽

mengyuchen@cdc.gov.tw

