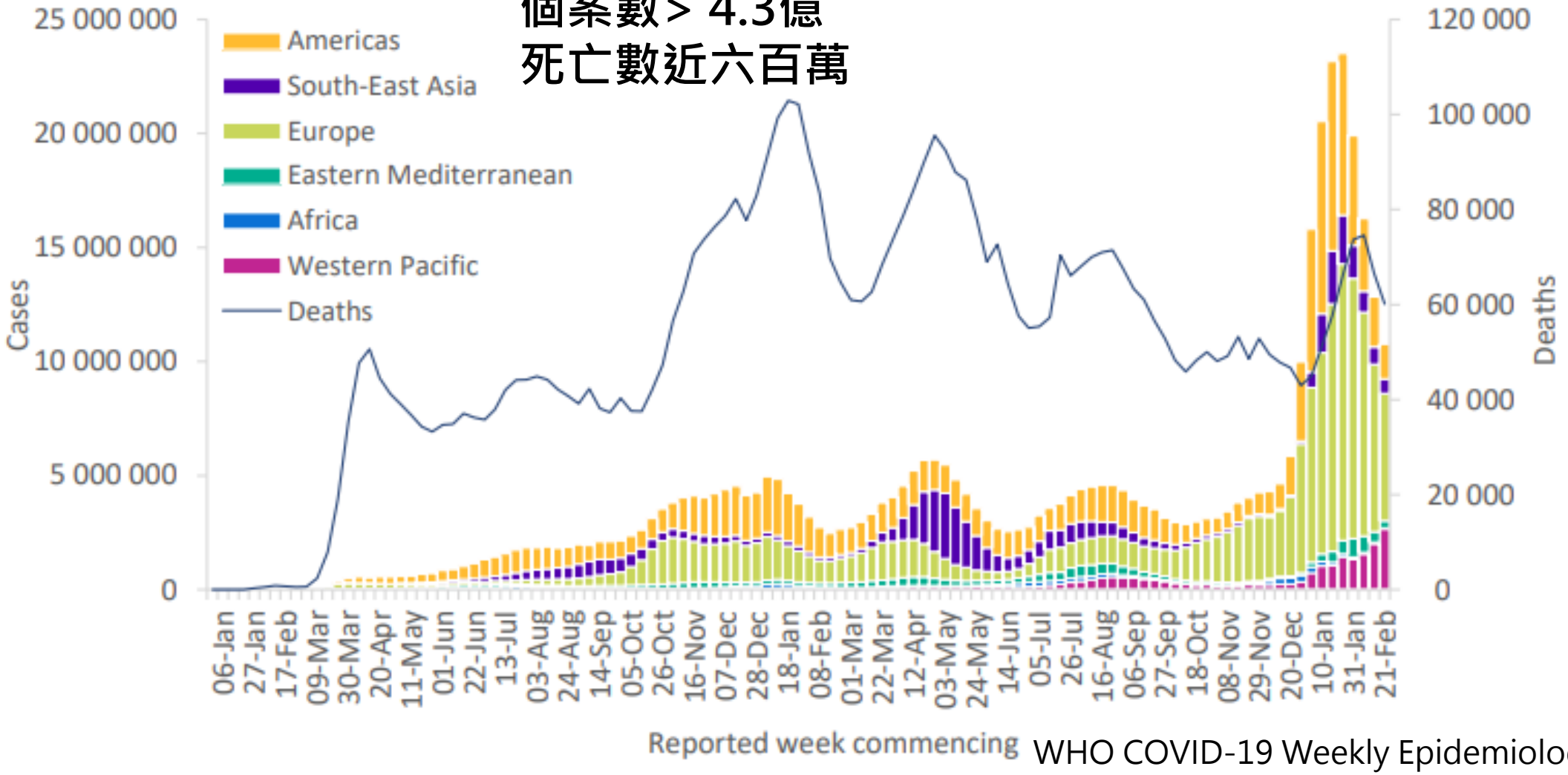
COVID-19疫苗與Omicron病毒變異株

報告大綱

- COVID-19疫苗進展更新
- Omicron病毒變異株對疫苗保護力的影響
- 疫苗基礎加強劑和追加劑
- 結論

COVID-19全球疫情現況 (2022/3/1)

個案數> 4.3億
死亡數近六百萬



WHO COVID-19 Weekly Epidemiological Update

發展中的COVID-19疫苗 (2022/2/18)

- 共有144種COVID-19疫苗正在臨床試驗(clinical)階段中
  - Phase III 32種、Phase IV 10種
- 另有195種COVID-19疫苗於臨床前期發展階段(preclinical)中
- >90%的疫苗採用肌肉注射方式

https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

通過WHO EUL程序的COVID-19疫苗 (2022/2/14)

EUL : Emergency Use Listing

Pfizer BIONTECH

moderna

Sinopharm / BIBP[1]

sinovac

SERUM INSTITUTE OF INDIA PVT. LTD.
Cyrus Poonawalla Group

AstraZeneca OXFORD

NOVAVAX

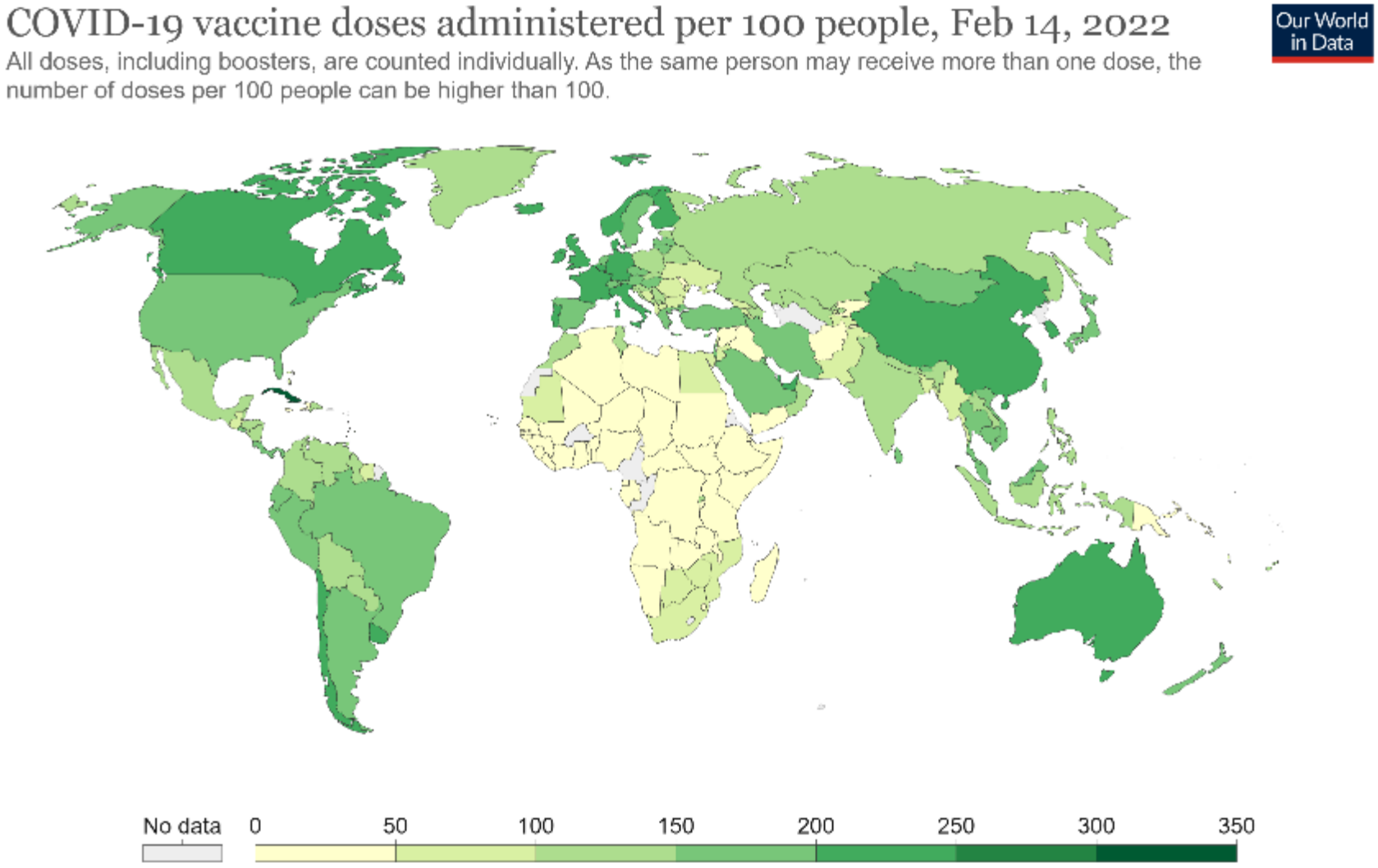
janssen Infectious Diseases & Vaccines
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

THE GAMALEYA NATIONAL CENTER
OF EPIDEMIOLOGY AND MICROBIOLOGY

BHARAT BIOTECH
Lead Innovation

https://www.who.int/teams/regulation-prequalification/eul/covid-19

全球已接種超過100億劑COVID-19疫苗(2022/2/14)



Omicron病毒變異株對疫苗保護力的影響

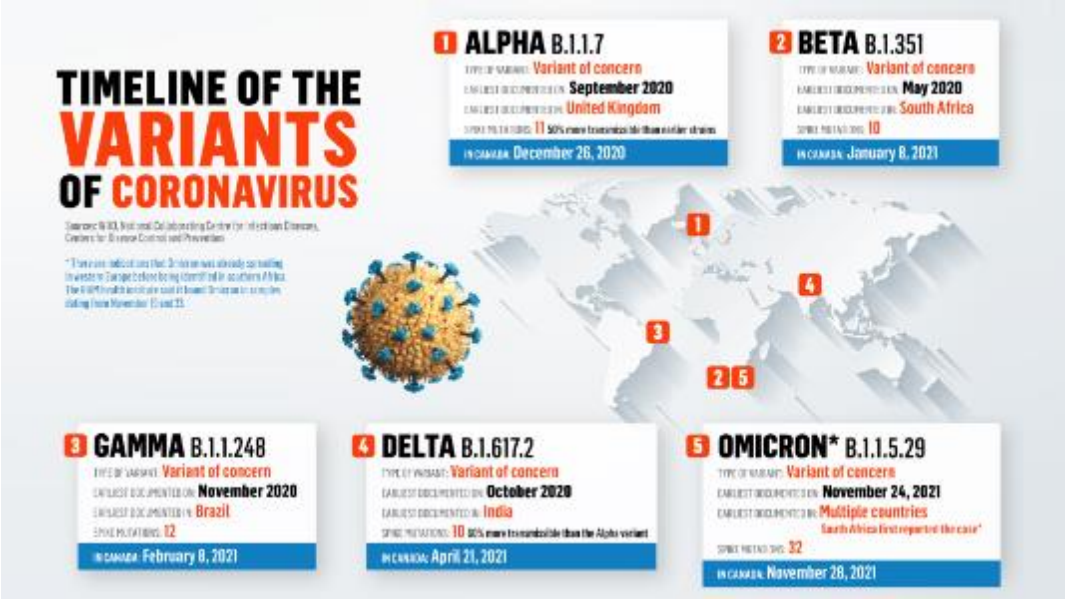


Photo credit: https://www.ctvnews.ca/health/coronavirus/timeline-of-the-covid-19-variants-of-concern-1.5691314

Omicron病毒變異株新增許多未曾出現過的突變點

主要變異株VOC名稱:（PANGO lineage）	Alpha (B.1.1.7)	Beta (B.1.351)	Gamma (P.1)	Delta (B.1.617.2)	Omicron(B.1.1.529)
最早發現的地區	英國	南非	巴西、日本（巴西移入）	印度	南非、波札那
主要突變的位點:					三個缺失、一個插入, 且至少有30個氨基酸出現取代(其中有15個位在受體結合區域receptor binding domain, RBD)
缺失(deletion)	del69-70, del144	del241-243		del156-157	del69-70*, del142-144, del211
取代(substitution)	D614G、N501Y、P681H、A570D	D614G、K417N、E484K、N501Y	D614G、K417T、E484K、N501Y	D614G、L452R、T478K、P681R	D614G, S477N, T478K, N501Y.....
插入(insertion)					ins214EPE**

Omicron有BA.1、BA.2、BA.3三分支, *del69-70出現在BA.1及BA.3, **ins214EPE出現在BA.1

ECDC: SARS-CoV-2 variants of concern as of 3 December 2021. https://www.ecdc.europa.eu/en/covid-19/variants-concern
WHO:
Enhancing Readiness for Omicron(B.1.1.529): Technical Brief and Priority Actions for Member States. https://reurl.cc/oemRXv
Weekly epidemiological update on COVID-19 - 8 February 2022. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---8-february-2022

Omicron病毒變異株傳播力及再次感染風險均增加

主要變異株VOC名稱: （PANGO lineage）	Omicron(B.1.1.529)
傳播力	增加 more transmissible than **Delta**(36.5%, 95% CI 20.9-60.1)
二次傳播率 (secondary attack rate)	增加(compared to **Delta:** **Household transmission:** The odds ratio: 2.9, 95% CI: 2.4-3.5; **Secondary attack rate:** The odds ratio: **Omicron:**15.8%, 95% CI: 14.3-17.5 **Delta:** 10.3%, 95% CI: 10.1-10.5)
再次感染(risk of reinfection)	增加(compared to **non-Omicron variant**, the risk ratio: 3.3, 95%CI: 2.8-3.8)

UK Health Security Agency: SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 36. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1054357/Technical-Briefing-36-11February2022_v2.pdf
CDC: Science Brief: Omicron (B.1.1.529) Variant. https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/scientific-brief-omicron-variant.html
ECDC: Threat Assessment Brief: Implications of the emergence and spread of the SARS-CoV-2 B.1.1. 529 variant of concern (Omicron) for the EU/EEA. https://reurl.cc/NZWAQx
WHO: Weekly epidemiological update on COVID-19 - 8 February 2022. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---8-february-2022
WHO: Enhancing Readiness for Omicron(B.1.1.529): Technical Brief and Priority Actions for Member States. https://reurl.cc/oemRXv

Omicron病毒變異株嚴重度可能較低

變異株VOC名稱: （ PANGO lineage ）	Omicron(B.1.1.529)
嚴重度:	
住院率:	降低(29% lower, compared to the D614G mutation in South Africa's first wave in mid-2020)
重症率:	降低 (compared to **Delta:** significantly reduced odds in earlier epidemic waves, aOR: 0.3, 95% CI: 0.2-0.5)
死亡率:	降低 (compared to **Delta:** reductions in mortality, HR: 0.01, 95% CI: 0.01-0.75)

雖然與 Delta 相比，感染Omicron 嚴重度較低，但快速增加的病例仍將導致住院人數增加，從而給治療 COVID-19 和其他疾病患者的醫療保健體系和社會帶來龐大壓力。
目前對 Omicron 嚴重程度的估計仍有不確定性，需要進一步研究，包括按年齡組別、先前感染和疫苗接種情形進行分析，以提供更可靠的科學證據。

Discovery Health. Real-world analysis of Omicron outbreak based on 211000 COVID-19 test results in South Africa. 2021. https://www.discovery.co.za/corporate/news-room
ECDC: Assessment of the further emergence and potential impact of the SARS-CoV-2 Omicron variant of concern in the context of ongoing transmission of the Delta variant of concern in the EU/EEA, 18th update. https://reurl.cc/2D7YN4
Threat Assessment Brief: Implications of the emergence and spread of the SARS-CoV-2 B.1.1. 529 variant of concern (Omicron) for the EU/EEA. https://reurl.cc/pWpeda
WHO: Enhancing Readiness for Omicron(B.1.1.529): Technical Brief and Priority Actions for Member States. https://reurl.cc/oemRXv
WHO: Weekly epidemiological update on COVID-19 - 8 February 2022. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---8-february-2022
Nealon J, Cowling BJ. Omicron severity: milder but not mild. Lancet. 2022;399(10323):412-413. doi:10.1016/S0140-6736(22)00056-3

Omicron 變異株皆會降低各疫苗保護力

	ChAdOx1 (AstraZeneca)	BNT162b2 (Pfizer-BioNTech)	mRNA-1273 (Moderna)
對疫苗保護力的影響: (完整接種)			
對感染/有症狀的保護力	降低: ***Two to 4 week*** *after receiving 2 doses of the AstraZeneca vaccine: 45-50% against symptomatic disease*	降低: ***Two to 4 weeks*** *after receiving 2 doses of the Pfizer vaccine: 65% against symptomatic disease*	降低: ***Two to 4 weeks*** *after receiving 2 doses of the Moderna vaccine: 70% against symptomatic disease*
對重症/住院的保護力	降低: ***20-24 week*** *after receiving 2 doses of the AstraZeneca vaccine: approximately* ***55% against hospitalization*** ***After 25+ weeks: 35% against hospitalization***	降低: ***Two to 4 weeks*** *after receiving 2 doses of the Pfizer vaccine: approximately* ***75% against hospitalization*** ***After 25+ weeks: 35% against hospitalization***	未知

Andrews N, Stowe J, Kirsebom F, et al. Effectiveness of COVID-19 vaccines against the Omicron (B.1.1.529) variant of concern. 2021. https://reurl.cc/emjq4x
UK Health Security Agency: COVID-19 vaccine surveillance report: 17 February 2022 (week 7)
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1055620/Vaccine_surveillance_report_-_week_7.pdf
ECDC: Assessment of the further emergence and potential impact of the SARS-CoV-2 Omicron variant of concern in the context of ongoing transmission of the Delta variant of concern in the EU/EEA, 18th update. https://reurl.cc/2D7YN4
WHO: Weekly epidemiological update on COVID-19 - 8 February 2022. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---8-february-2022

COVID-19疫苗

基礎加強劑(Additional dose)

追加劑(Booster dose)

Photo credit: https://www.health.gov.au/news/booster-doses-of-the-covid-19-vaccine

Additional dose (基礎加強劑) vs Booster dose (追加劑)

- 基礎劑
  - 完成兩劑COVID-19疫苗接種
- 基礎加強劑
  - 免疫不全或免疫力低下病人，完成基礎劑後可能無法獲得足夠保護力，故建議應接種第3劑基礎加強劑，並按時程完成追加劑
- 追加劑
  - 疫苗保護力會隨著接種時間過去而逐漸下降，加上病毒變異，即使完成基礎劑接種後仍有突破性感染風險，故建議接種追加劑

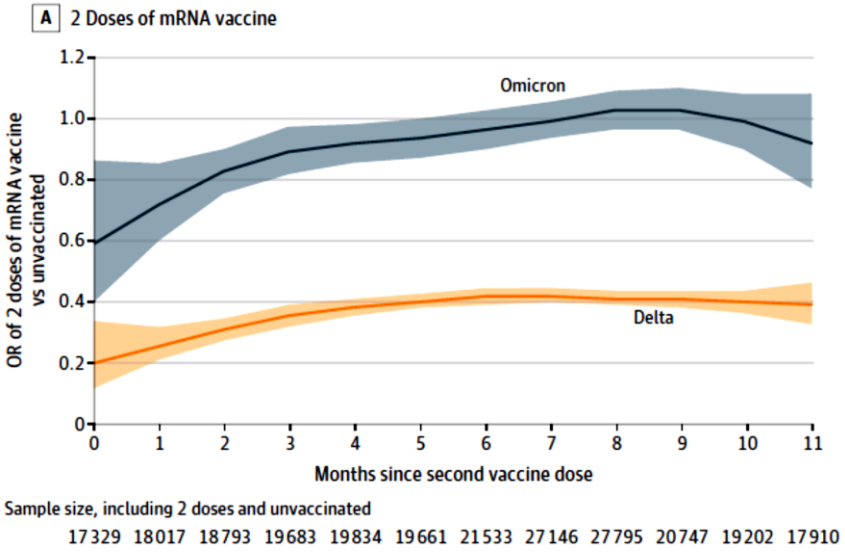
COVID-19疫苗基礎加強劑建議對象

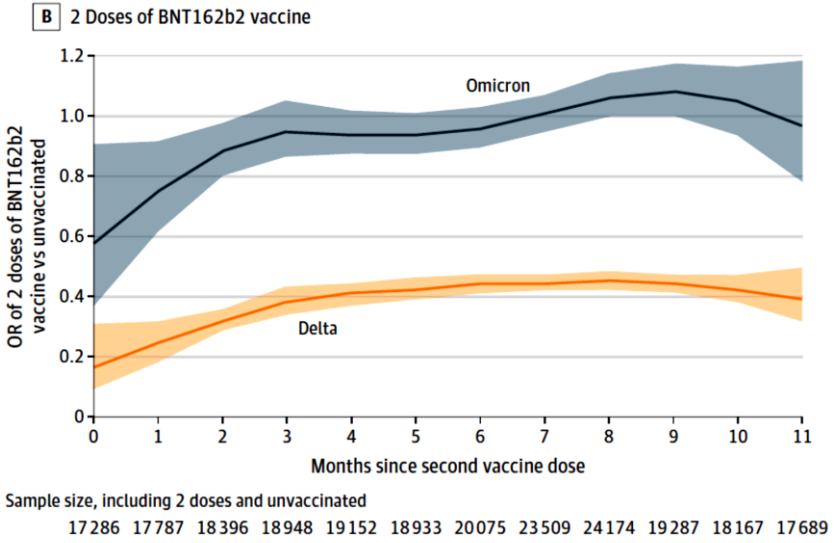
- 12歲以上，經醫師評估病情穩定之免疫不全及免疫力低下對象
  - 目前正進行或1年內曾接受免疫抑制治療之癌症患者
  - 器官移植或幹細胞移植患者
  - 中度或嚴重先天性免疫不全患者
  - 血液透析患者
  - HIV陽性患者
  - 目前正使用高度免疫抑制藥物者
  - 過去6個月內接受化學治療或放射線治療者
  - 以及其他經醫師評估因免疫不全或免疫力低下者
- 與第二劑COVID-19疫苗間隔至少28天

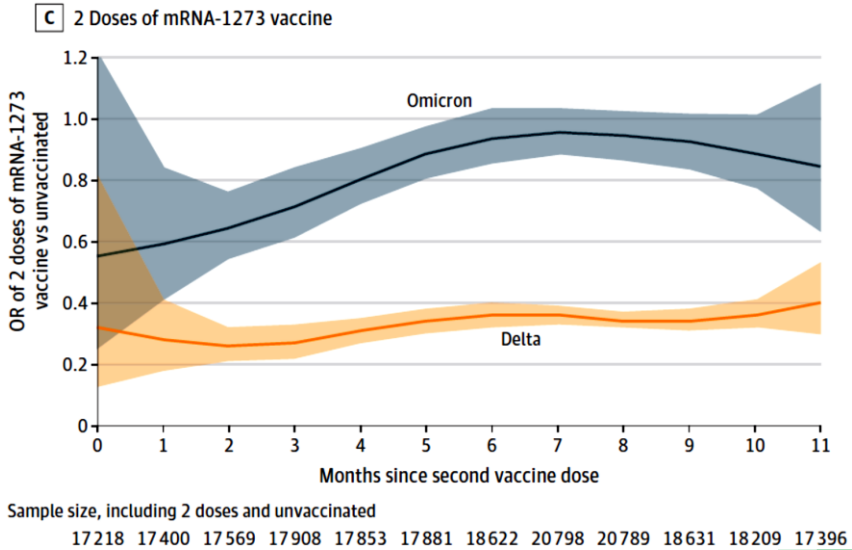
COVID-19疫苗追加劑建議對象

- 滿18歲以上民眾均建議接種追加劑
- 下列對象建議優先接種追加劑
  - 65歲以上長者
  - 長照機構住民與工作者
  - 醫護人員、防疫工作人員及高風險工作人員 (公費對象1-3類)
  - 容易感染及疾病嚴重風險者 (公費對象第9類)
- 已完成基礎劑接種且間隔滿3個月

接種追加劑: 因接種兩劑疫苗後, 隨時間對有症狀感染的疫苗效果(Effectiveness)漸漸降低



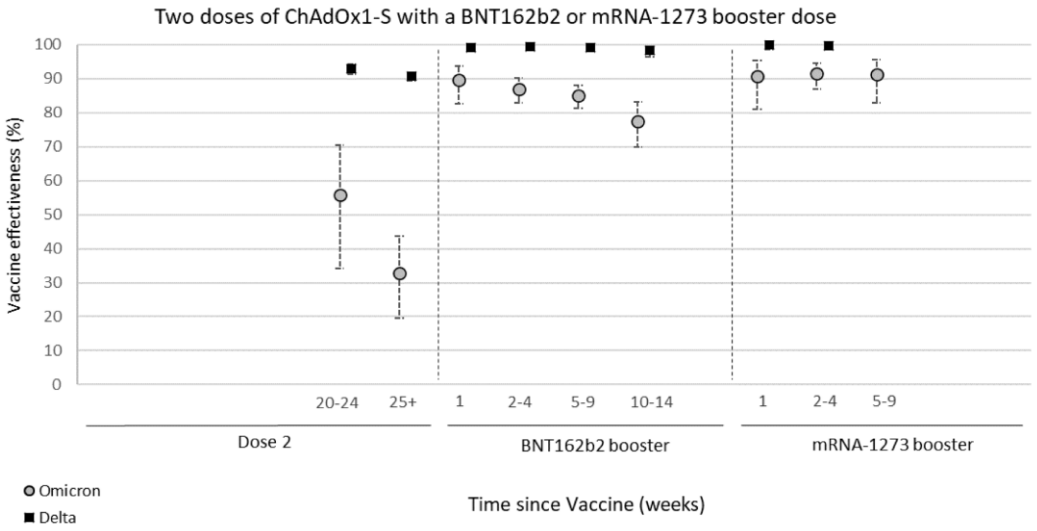


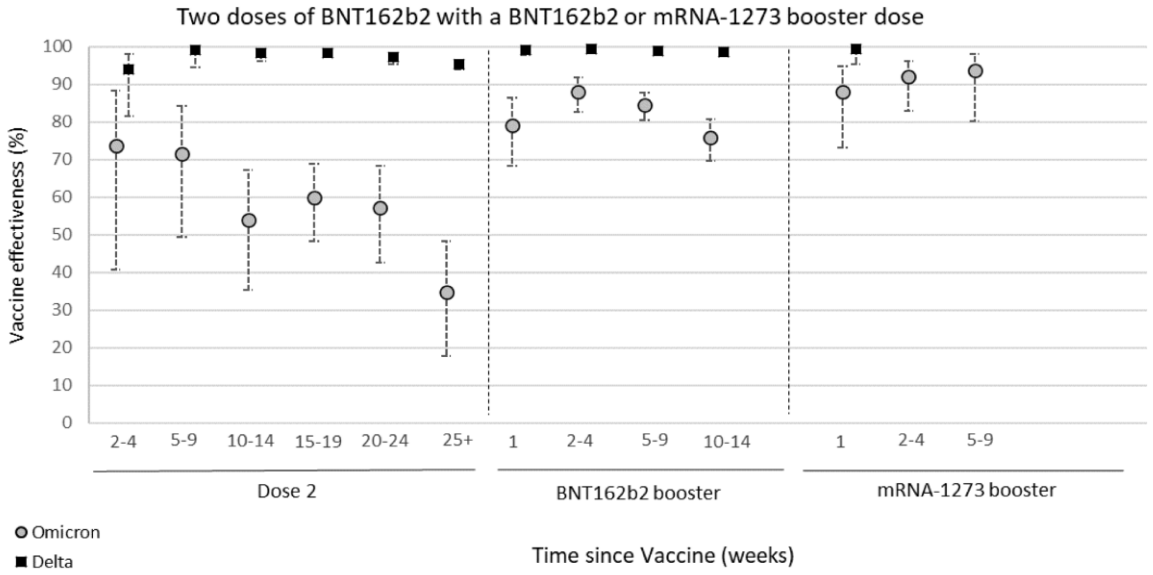


- 打完兩劑疫苗者, 與未接種疫苗相比:
- 無論是**哪個廠牌的mRNA疫苗, 超過6個月後**, 對**Omicron變異株有症狀感染**幾乎**沒有疫苗效果**, 預防**Delta有症狀感染**的保護力也**隨時間消退**

Accorsi EK, et al. JAMA. 2022 Jan 21. doi: 10.1001/jama.2022.0470.

對於Omicron 變異株，其預防需住院的疫苗效果也隨時間而降低



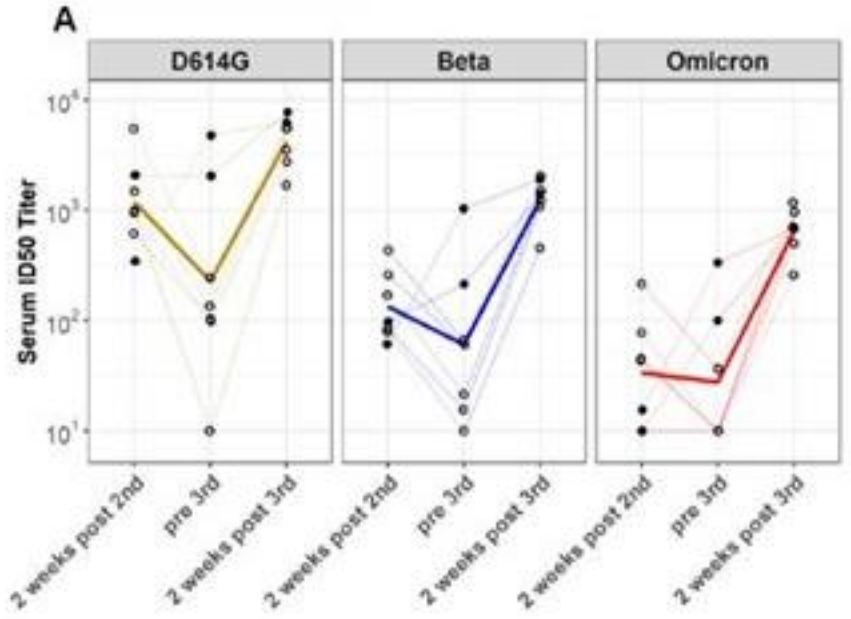


- 完成兩劑AZ 或BNT 疫苗25週後，其預防Omicron住院之疫苗效果降為25 - 35%
- 接種BNT或Moderna追加劑後，預防Omicron住院之疫苗效果可以提升至75-95%

UK Health Security Agency. COVID-19 vaccine surveillance report. Week 9. 3 March 2022

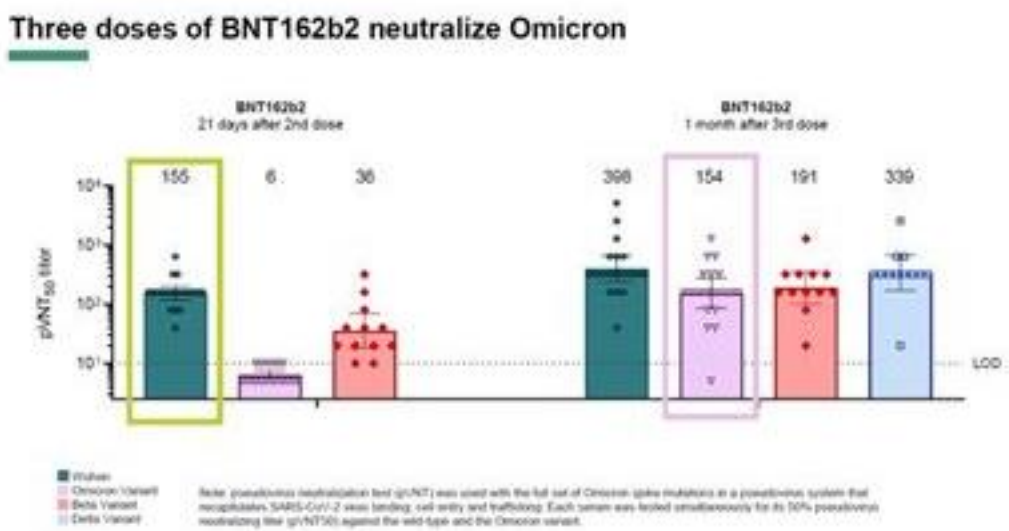
接種追加劑後可有效增加中和抗體

Moderna



接種第2劑後，中和抗體逐漸下降。接種第3劑後，抗體明顯增加(包括Omicron變異株中和抗體)

BNT



接種第2劑後3周，中和抗體無法中和Omicron變異株。接種第3劑1個月後，Omicron變異株中和抗體明顯增加

接種追加劑: 無論是對Omicron 或Delta變異株, 有症狀感染者比率較未接種者低

- 美國針對2021/12/10-2022/1/1間，18歲以上**有症狀**(且非免疫力低下)，至全國4666個篩檢站做**鼻咽PCR**者，分析**疫苗施打劑次**(接種的疫苗均為mRNA疫苗)、是否為**有症狀感染**、及**感染變異株**的結果：
  - 46764人為對照組, **23391人為有症狀**感染:
    - 13098例為Omicron (施打兩劑: 7245人, 三劑: 2441人, 未施打疫苗: 3412人)
    - 10293例為Delta (施打兩劑: 4570人, 三劑: 679人, 未施打疫苗: 5044人)

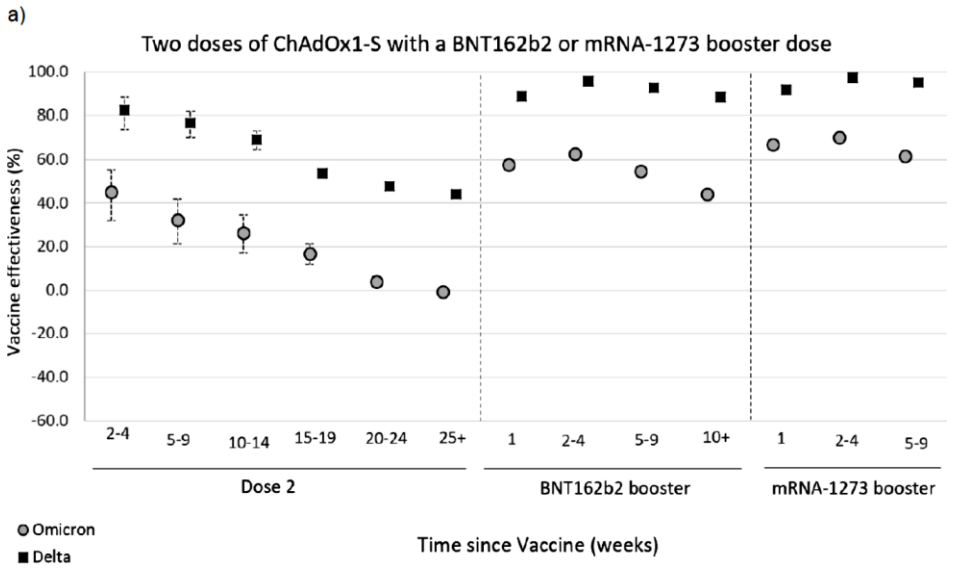
Table 2. Association Between Omicron or Delta Symptomatic SARS-CoV-2 Infection and Prior mRNA COVID-19 Vaccination Among Adults 18 Years or Older Tested in the Increasing Community Access to Testing Platform, December 10, 2021, to January 1, 2022

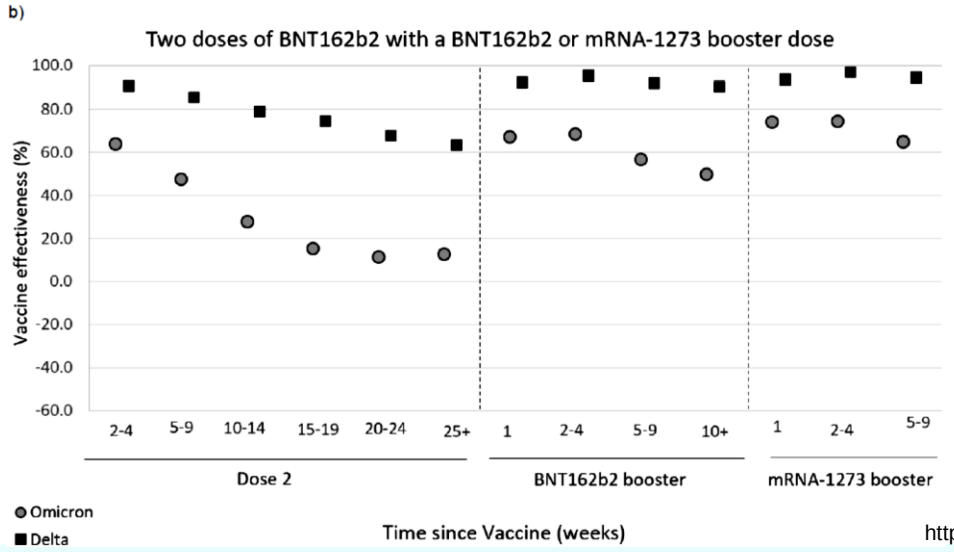
Vaccine type evaluated	SARS-CoV-2 variant	Total test-positive cases	Total test-negative controls	OR (95% CI)		Q value[b]
				Crude	Adjusted[a]	
3 Doses vs unvaccinated[c]						
Any 3 doses of mRNA vaccine[d]	Delta	5723	27 308	0.063 (0.058-0.069)	0.065 (0.059-0.071)	<.001
	Omicron	5853	27 308	0.34 (0.32-0.36)	0.33 (0.31-0.35)	
3 Doses of BNT-162b2[e]	Delta	5508	19 239	0.076 (0.069-0.084)	0.077 (0.070-0.086)	<.001
	Omicron	4906	19 239	0.36 (0.34-0.39)	0.35 (0.32-0.38)	
3 Doses of mRNA-1273[f]	Delta	5216	15 395	0.045 (0.038-0.052)	0.045 (0.038-0.053)	<.001
	Omicron	4143	15 395	0.28 (0.26-0.31)	0.28 (0.26-0.31)	
3 vs 2 Doses[c,g]						
Any 3 doses of mRNA vaccine[d]	Delta	5249	38 043	0.16 (0.14-0.17)	0.16 (0.14-0.17)	<.001
	Omicron	9686	38 043	0.35 (0.34-0.37)	0.34 (0.32-0.36)	
3 Doses of BNT-162b2[e]	Delta	3526	22 581	0.17 (0.16-0.19)	0.17 (0.16-0.19)	<.001
	Omicron	6208	22 581	0.36 (0.34-0.39)	0.35 (0.32-0.37)	
3 Doses of mRNA-1273[f]	Delta	1670	14 039	0.13 (0.11-0.15)	0.13 (0.11-0.15)	<.001
	Omicron	3251	14 039	0.32 (0.29-0.35)	0.31 (0.28-0.34)	

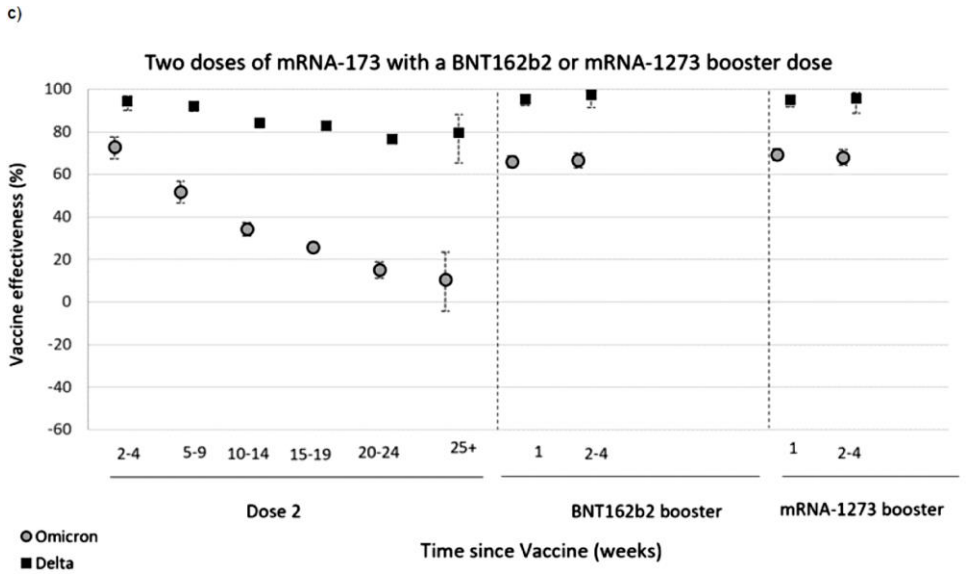
- 無論是施打哪種mRNA疫苗:
- **施打三劑疫苗**(於施打完後至少14天檢測), 與**兩劑疫苗**(於施打完後超過6個月檢測)或**未施打疫苗**者相比: **有症狀感染者**較**少**, 且達統計上的差異
  - **施打三劑疫苗** vs **施打兩劑疫苗**:
    Adjusted OR:
    Omicron: 0.34 (95%CI: 0.32-0.36)
    Delta: 0.16 (95%CI: 0.14-0.17)
  - **施打三劑疫苗** vs 未**施打疫苗**:
    Adjusted OR:
    Omicron: 0.33 (95%CI: 0.31-0.35)
    Delta: 0.065 (95%CI, 0.059-0.071)

Accorsi EK, et al. JAMA. 2022 Jan 21. doi: 10.1001/jama.2022.0470.

接種mRNA追加劑: 降低有症狀感染的比率







- 前面兩劑無論是接種AZ或mRNA疫苗:
  - 打完**第二劑20週後**, 對**Omicron有症狀感染**的疫苗效果降低(AZ: almost no effect, BNT & Moderna: 10%)
  - 接種完**mRNA追加劑**後, 疫苗效果再次提升

UK Health Security Agency: COVID-19 vaccine surveillance report: 20 January 2022(Week 3)
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1049160/Vaccine-surveillance-report-week-3-2022.pdf

接種追加劑: 因感染住院或重症的比率均較低

Table 2. Summary of evidence on vaccine effectiveness against different outcomes (a) Omicron (b) Delta (all vaccines combined)

a)

	Dose 2			Dose 3		
	0 to 3 months	4 to 6 months	Over 6 months	0 to 3 months	4 to 6 months	Over 6 months
Infection	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Symptomatic disease	25 to 70%	5 to 30%	0 to 10%	50 to 75%	40 to 50%	Insufficient data
Hospitalisation	65 to 85%	55 to 65%	30 to 35%	80 to 95%	75 to 85%	Insufficient data
Mortality	Insufficient data	Insufficient data	40 to 70%	85 to 99%	Insufficient data	Insufficient data

b)

	Dose 2			Dose 3		
	0 to 3 months	4 to 6 months	Over 6 months	0 to 3 months	4 to 6 months	Over 6 months
Infection	65 to 80%	50 to 65%	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Symptomatic disease	65 to 90%	45 to 65%	40 to 60%	90 to 99%	90 to 95%	Insufficient data
Hospitalisation	95 to 99%	80 to 90%	70 to 85%	95 to 99%	Insufficient data	Insufficient data
Mortality	95 to 99%	90 to 95%	80 to 99%	95 to 99%	Insufficient data	Insufficient data

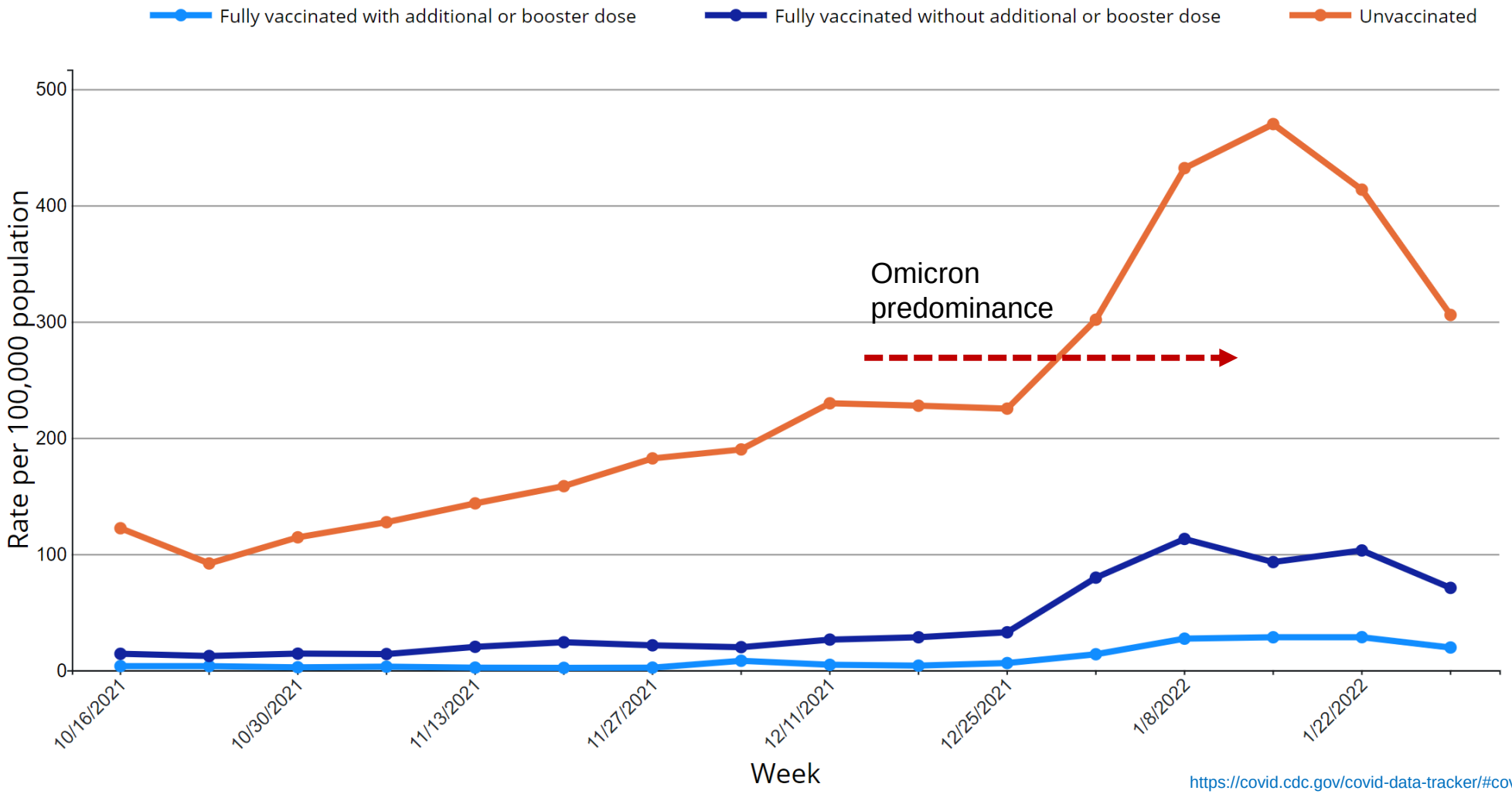
- **可降低因感染Omicron**(接種疫苗後0-6個月)**或Delta**(接種疫苗後0-3個月)**住院**, 以及**對感染Delta重症**(接種疫苗後0-3個月)的比率

UK Health Security Agency: COVID-19 vaccine surveillance report: 20 January 2022(Week 3)
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1049160/Vaccine-surveillance-report-week-3-2022.pdf

Omicron 對於未接種疫苗之年長者威脅仍高

US CDC 資料

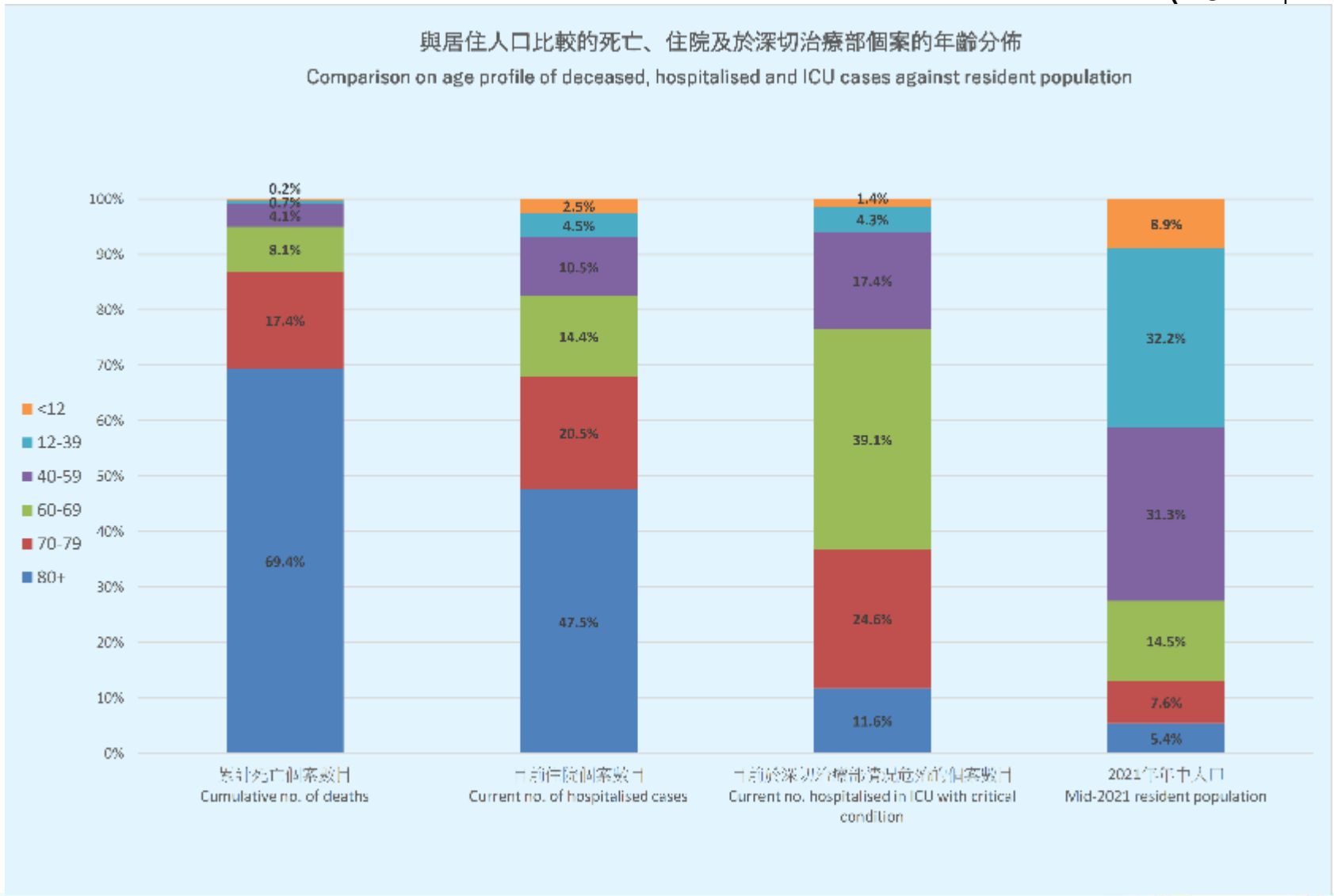
Rates of COVID-19-Associated Hospitalizations by Vaccination Status in Adults Ages ≥65 Years, October 2021–January 2022



https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination

香港2019冠狀病毒病第5波疫情

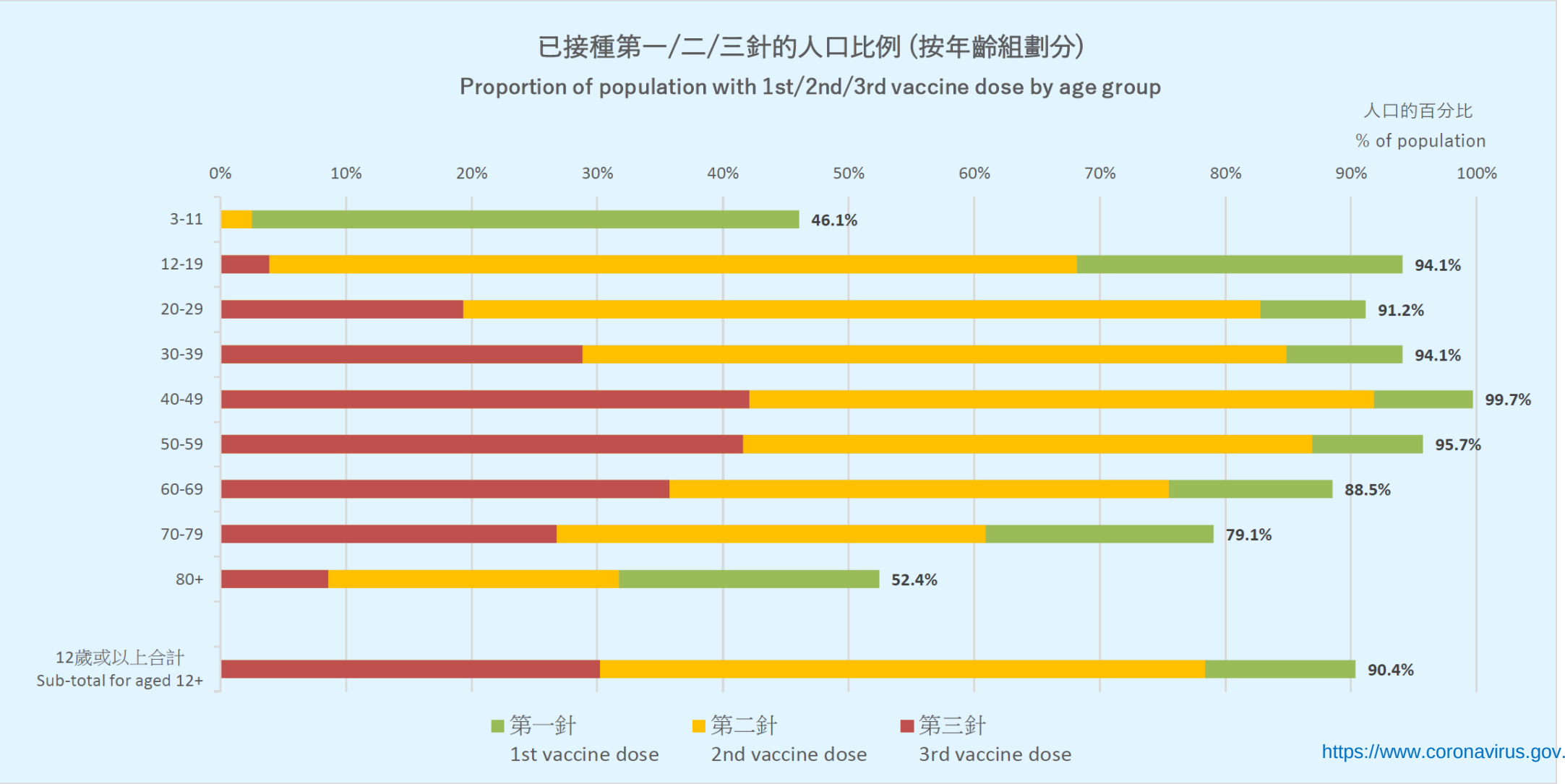
(2021年12月31日至2022年3月8日00:00)



現需住院及死亡個案以年長者為主

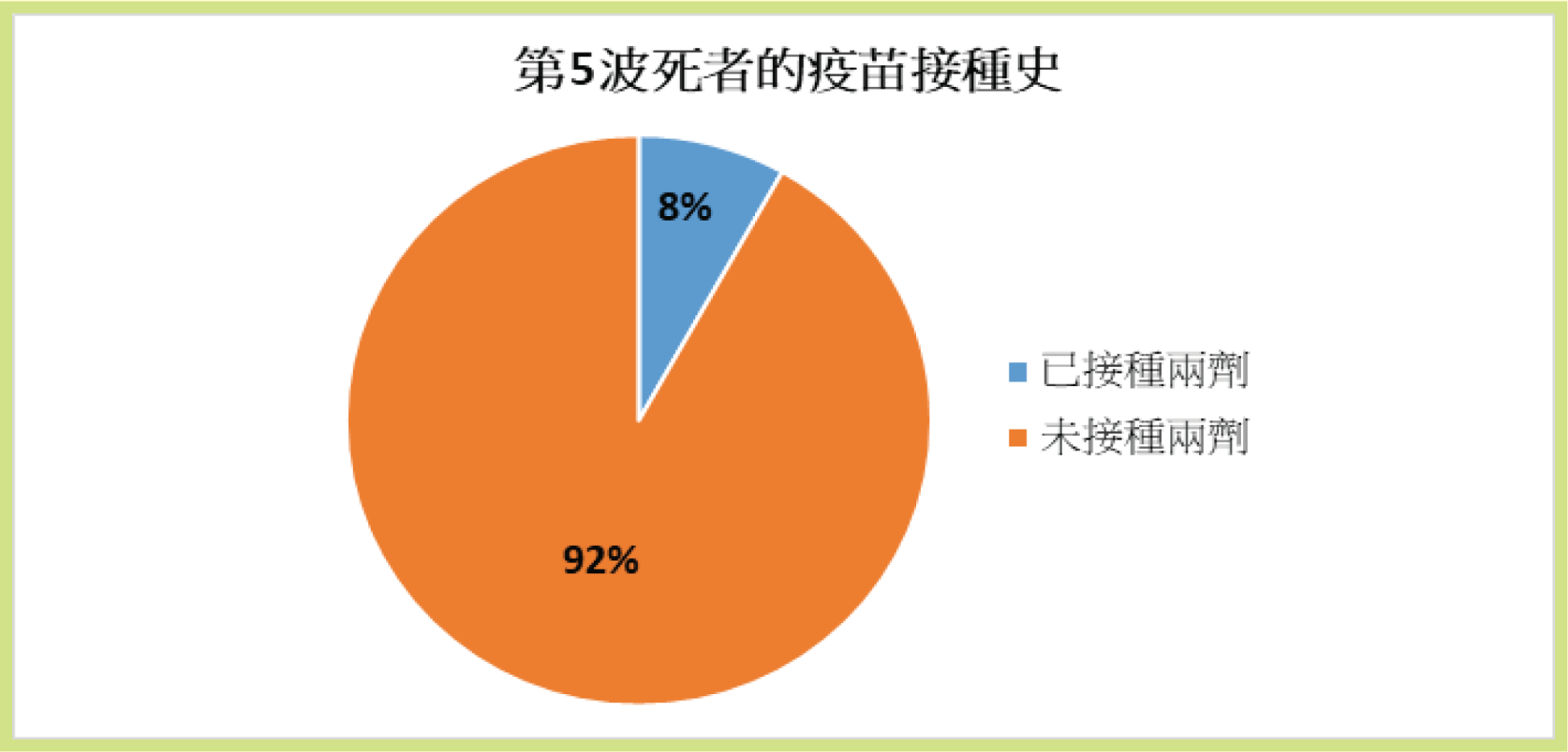
https://www.coronavirus.gov.hk/chi/index.html

香港各年齡層疫苗接種率：年長者接種率相對較低



https://www.coronavirus.gov.hk/chi/index.html

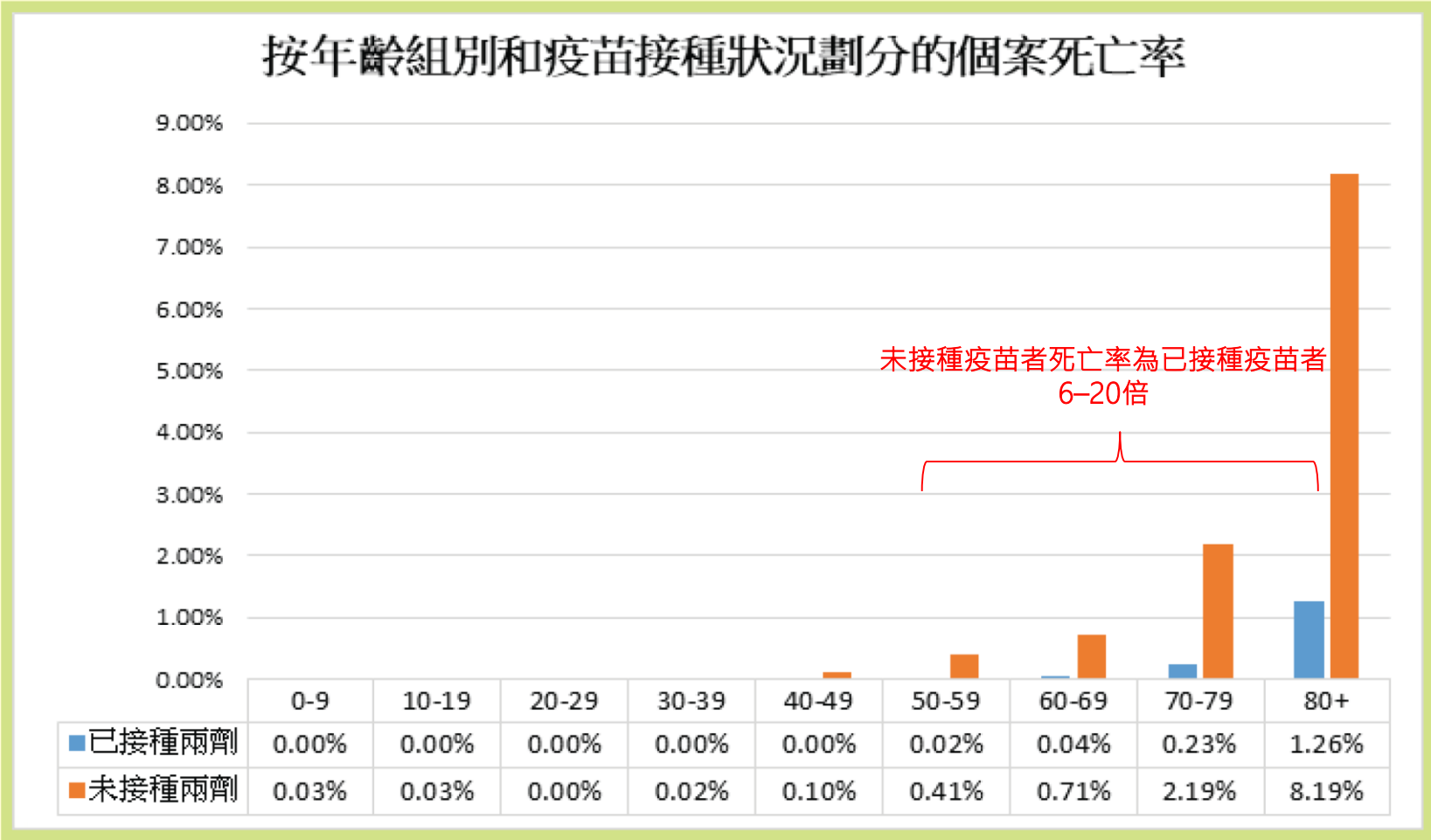
香港死亡個案分析(n = 1153)



第5波死者中，超過九成人士未接種兩劑疫苗

https://www.coronavirus.gov.hk/chi/index.html

按年齡組別和疫苗接種情形之死亡率差異



	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80+
已接種兩劑	0.00%	0.00%	0.00%	0.00%	0.00%	0.02%	0.04%	0.23%	1.26%
未接種兩劑	0.03%	0.03%	0.00%	0.02%	0.10%	0.41%	0.71%	2.19%	8.19%

接種兩劑疫苗人士 死亡率低至少5倍

https://www.coronavirus.gov.hk/chi/index.html

結論

- 疫苗對有症狀感染的保護力，可隨完成接種時間漸漸降低，而接種追加劑後可有效增加中和抗體，降低有症狀感染的比率及住院的風險
- 雖然感染Omicron 嚴重程度較低，但對於未接種疫苗族群仍有健康威脅，而快速增加的病例將導致醫療保健體系衝擊
- 因應Omicron 變異株，完整接種疫苗並按時程完成追加劑接種，可有效預防感染及預防重症和死亡的發生