

# 免疫低下族群面對疫情之困境與COVID19疫苗保護效果

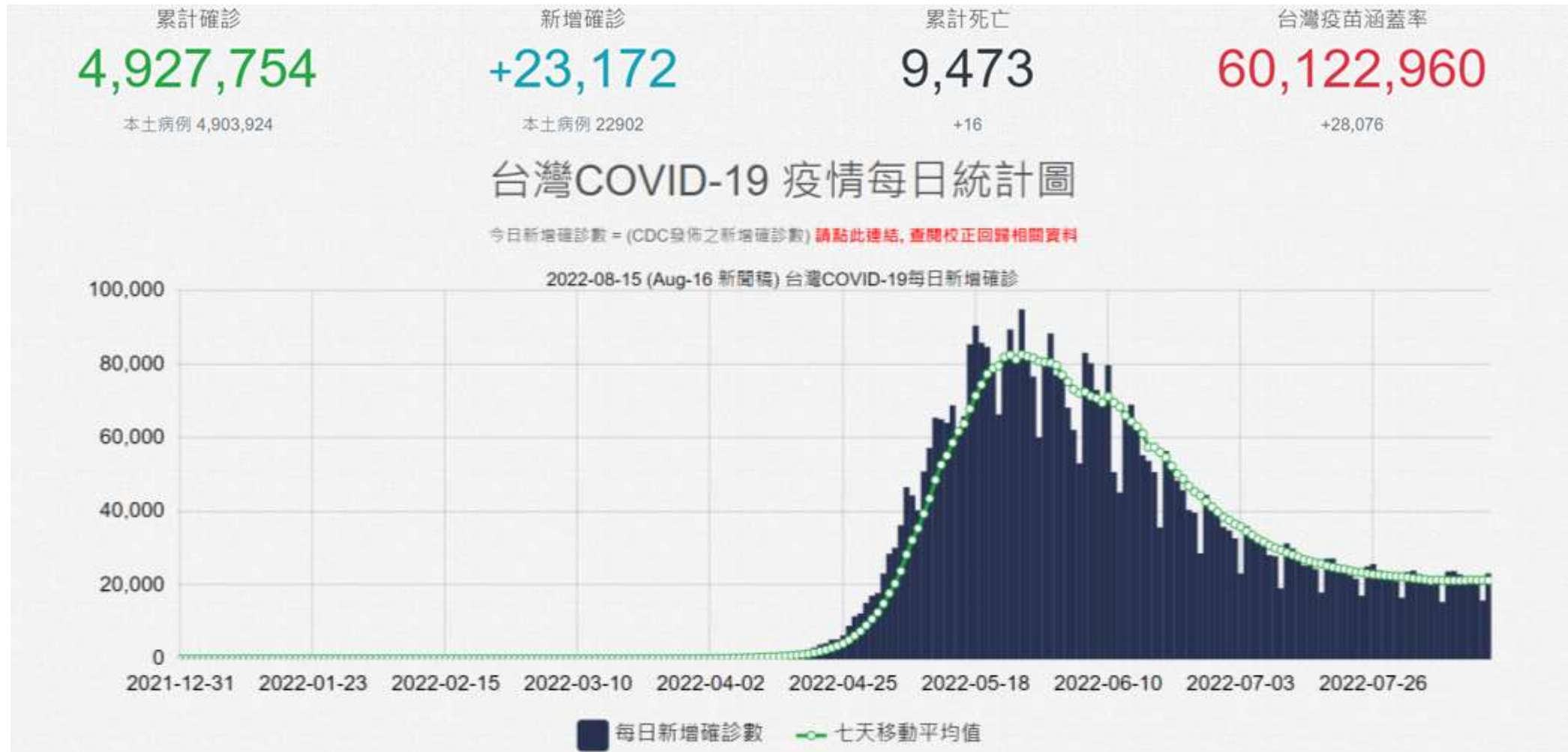
臺大醫院家庭醫學部

張皓翔

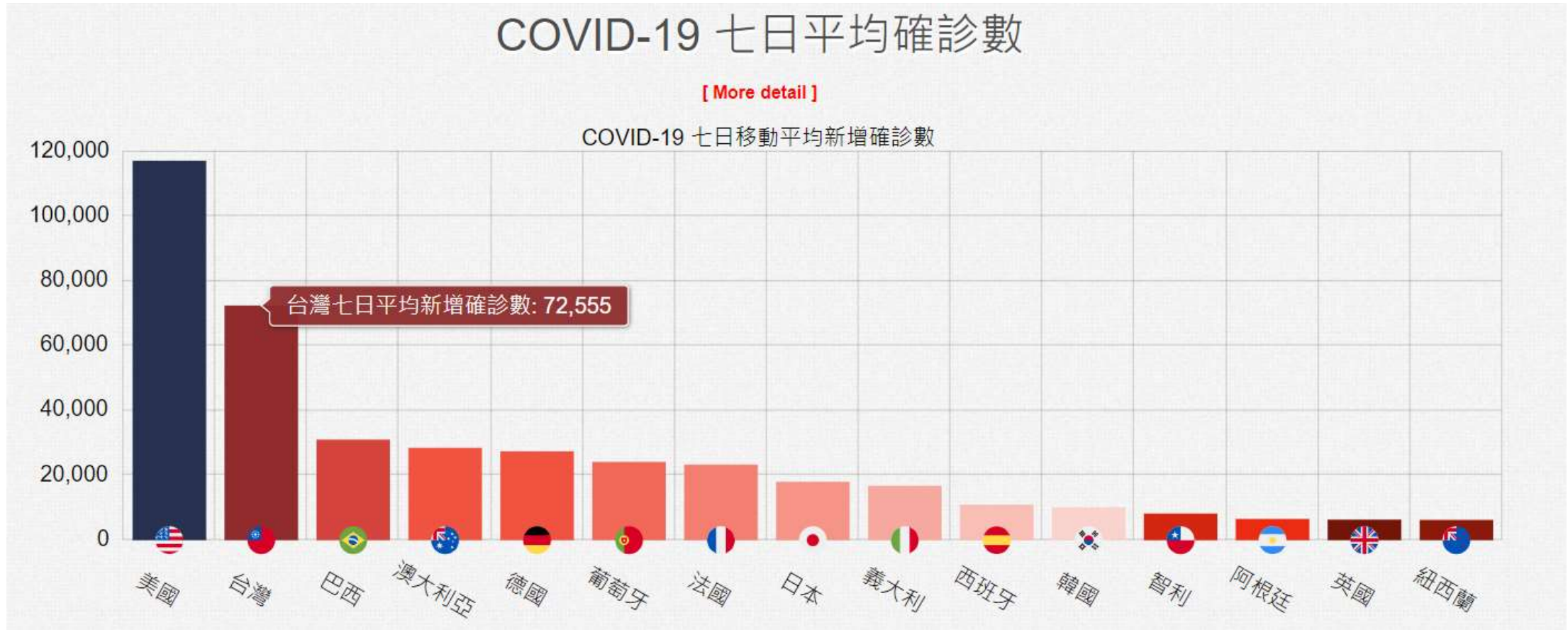
2022.08.20

# 台灣新冠疫情統計

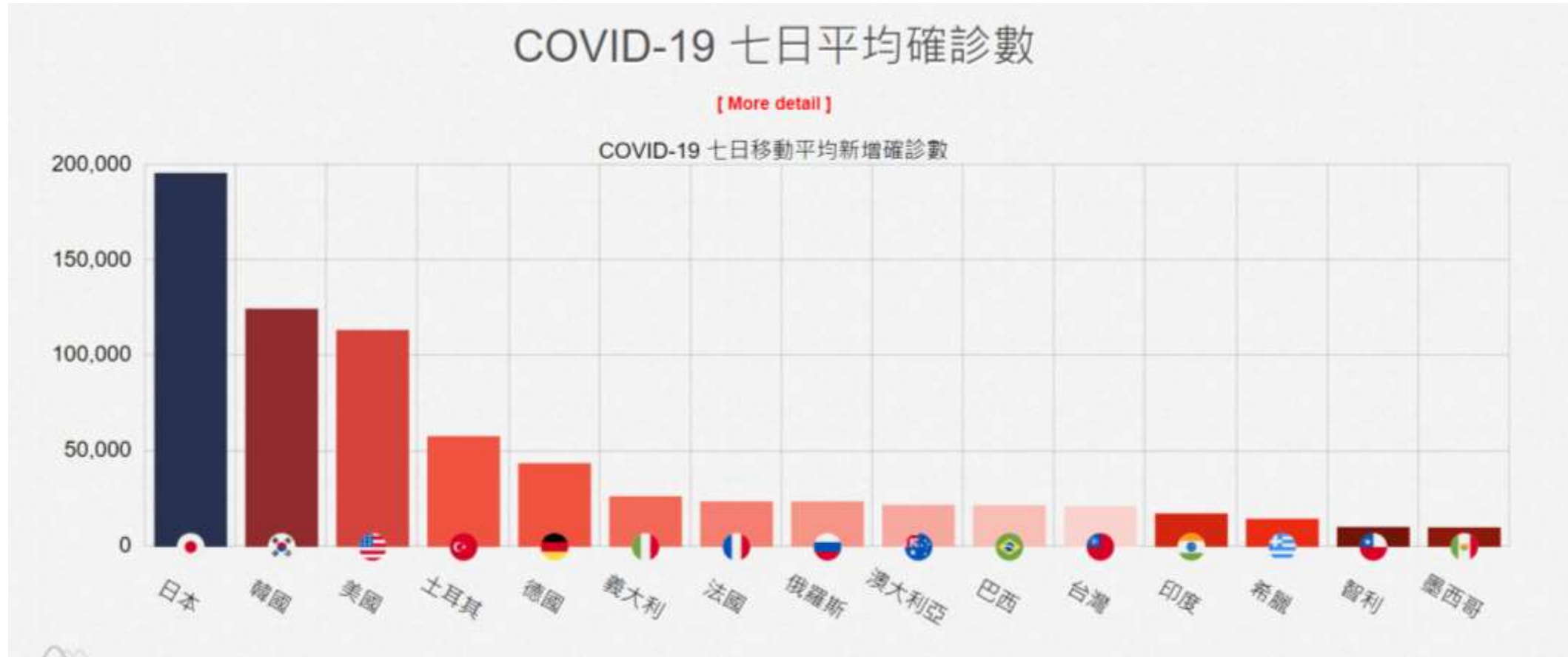
## (2022春節開放、清明變盤、暑假趨緩....)



# 七日平均確診數(6/1~6/7)僅次於美國

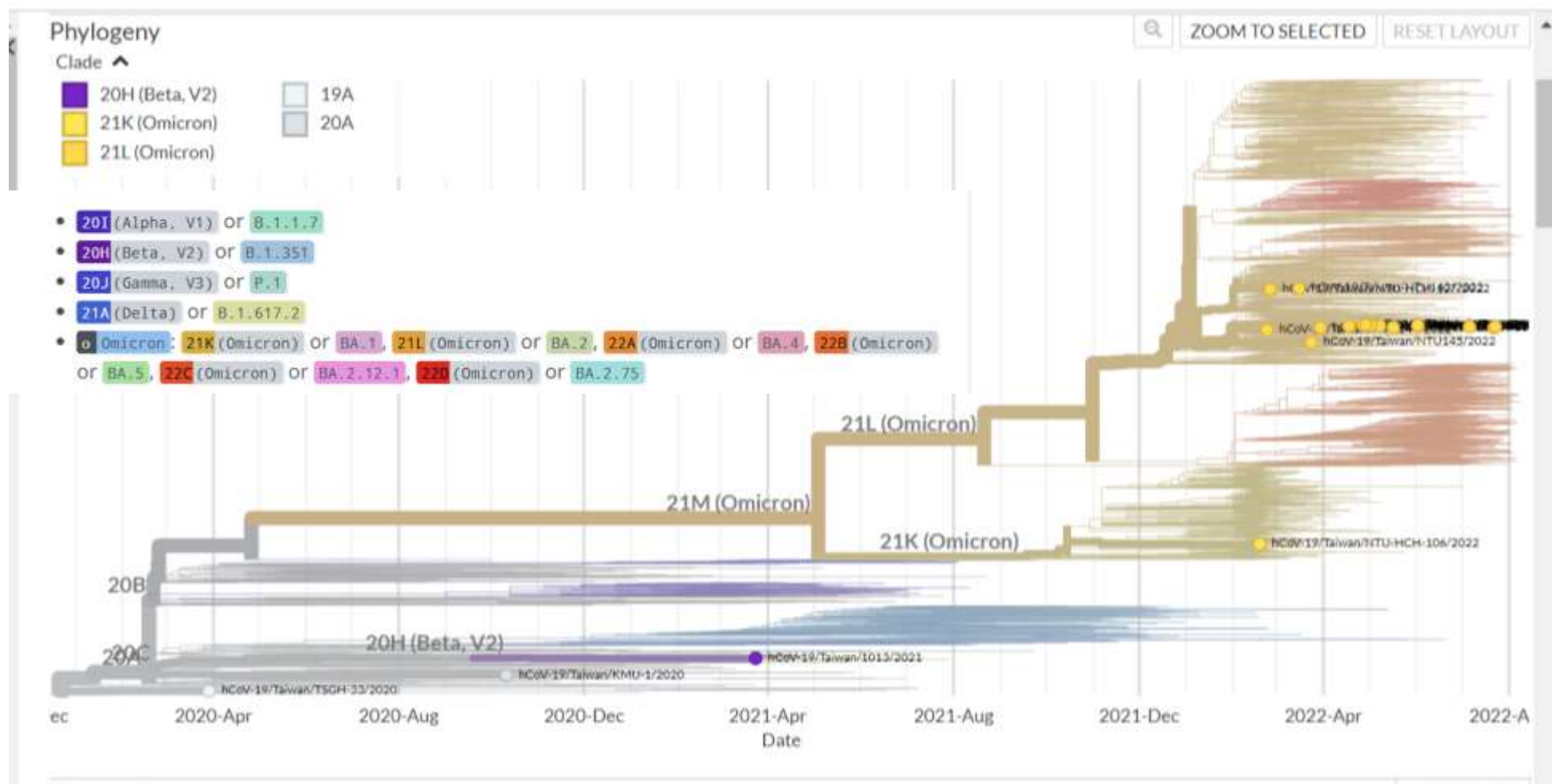


# 七日平均確診數(6/1~6/7)排名第10





# 台灣: 基因型

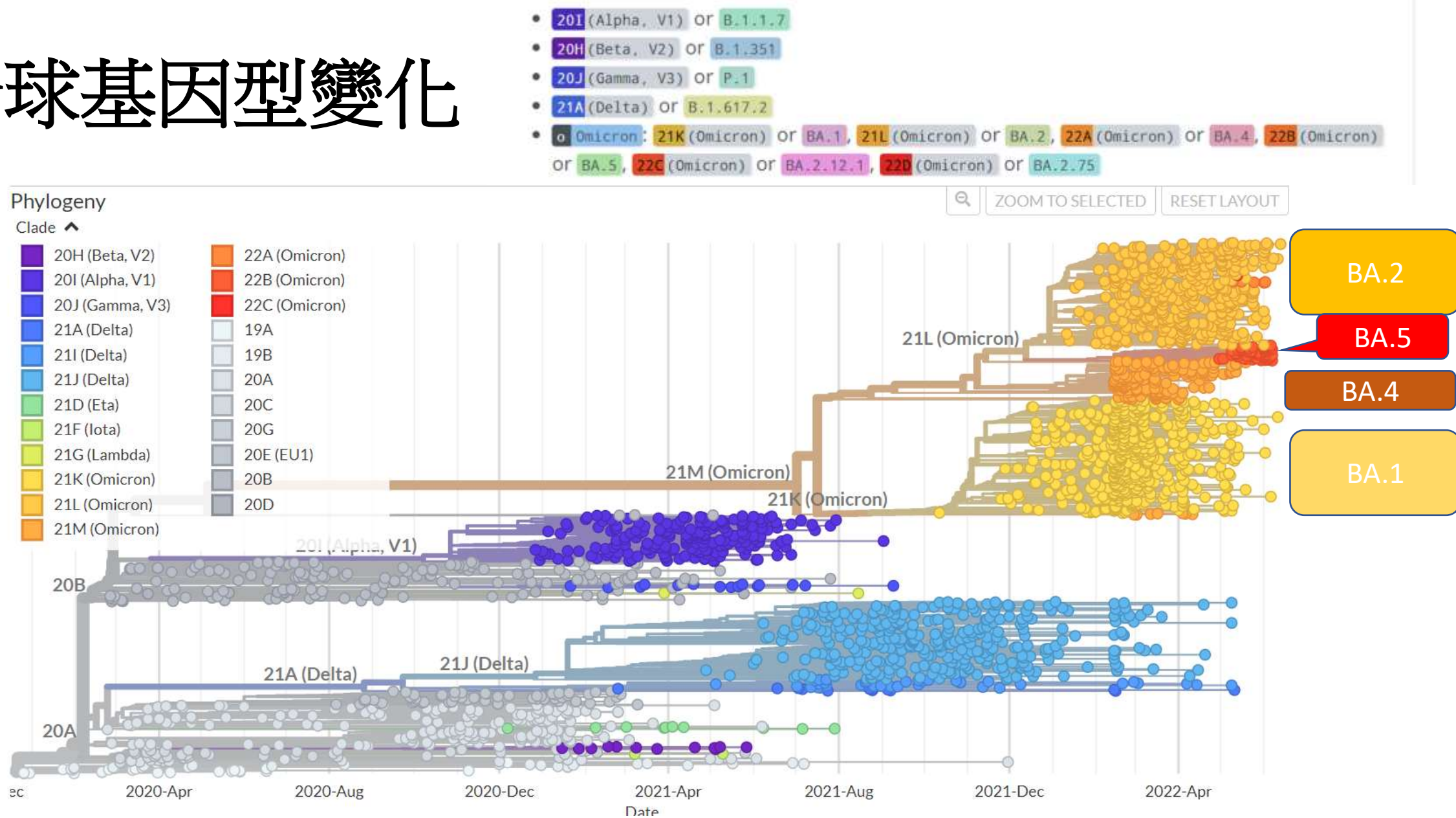


BA.2

BA.1

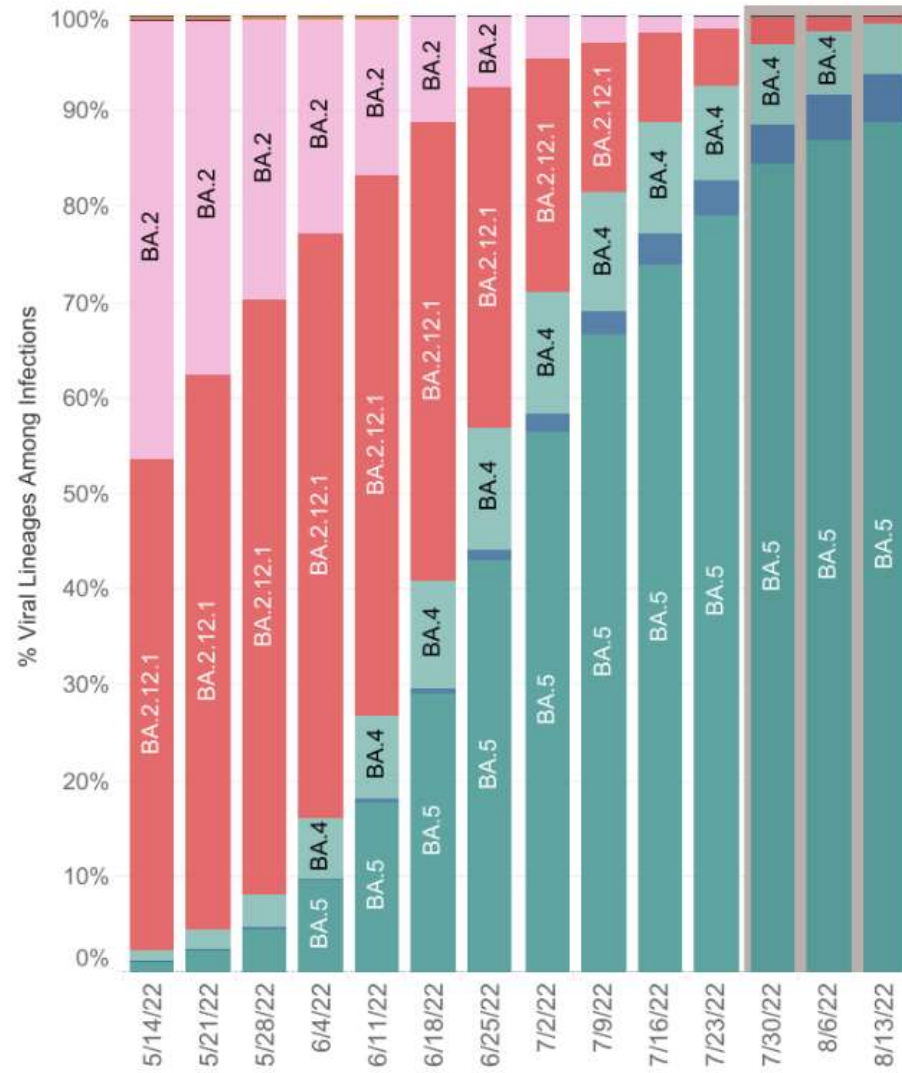
[https://nextstrain.org/ncov/gisaid/global/6m?f\\_country=Taiwan](https://nextstrain.org/ncov/gisaid/global/6m?f_country=Taiwan)

# 全球基因型變化



<https://nextstrain.org/groups/swiss/ncov/CH-omicron-21M>

# BA.4, BA.5已成主流



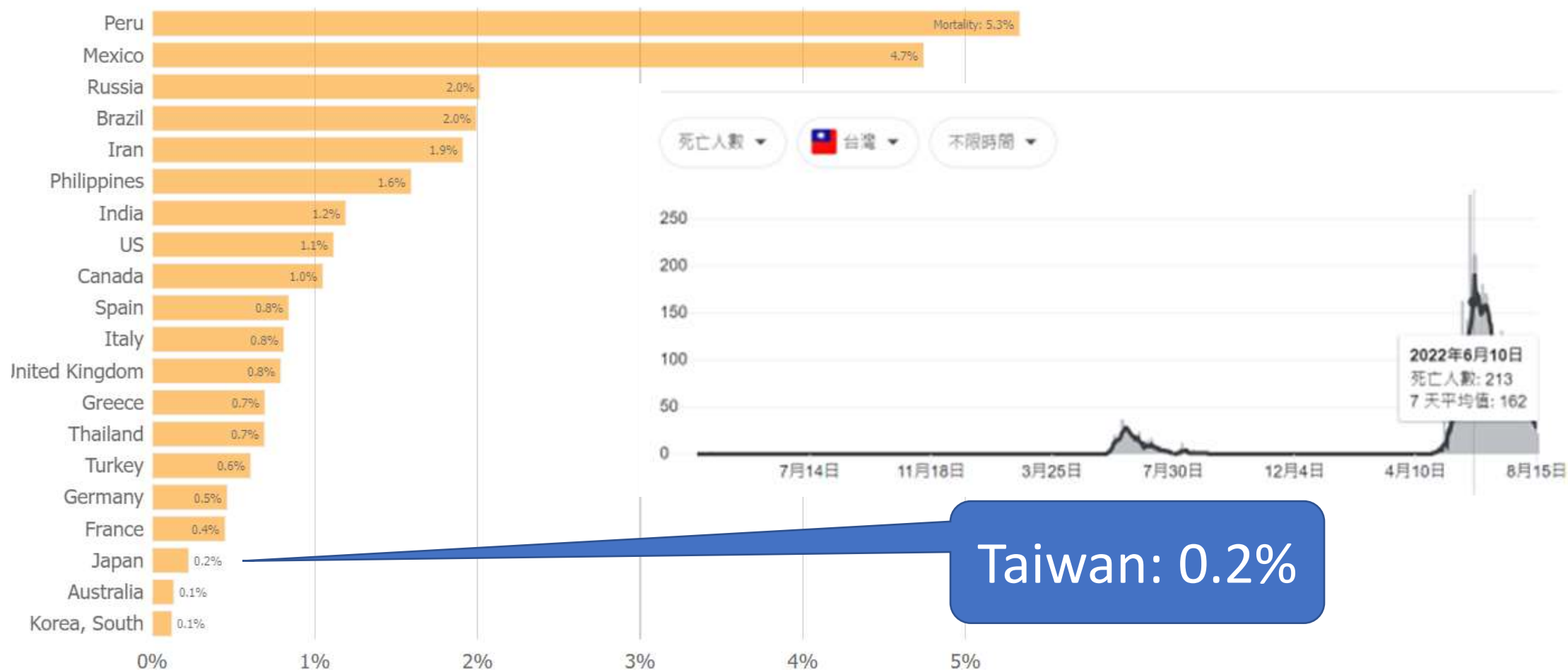
USA				
WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	88.8%	87.5-90.0%
	BA.4	VOC	5.3%	4.9-5.7%
	BA.4.6	VOC	5.1%	4.1-6.4%
	BA.2.12.1	VOC	0.8%	0.7-0.9%
	BA.2	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

\* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.

\*\* These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

# AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data,

# 個案死亡率(Case Fatality Ratio)



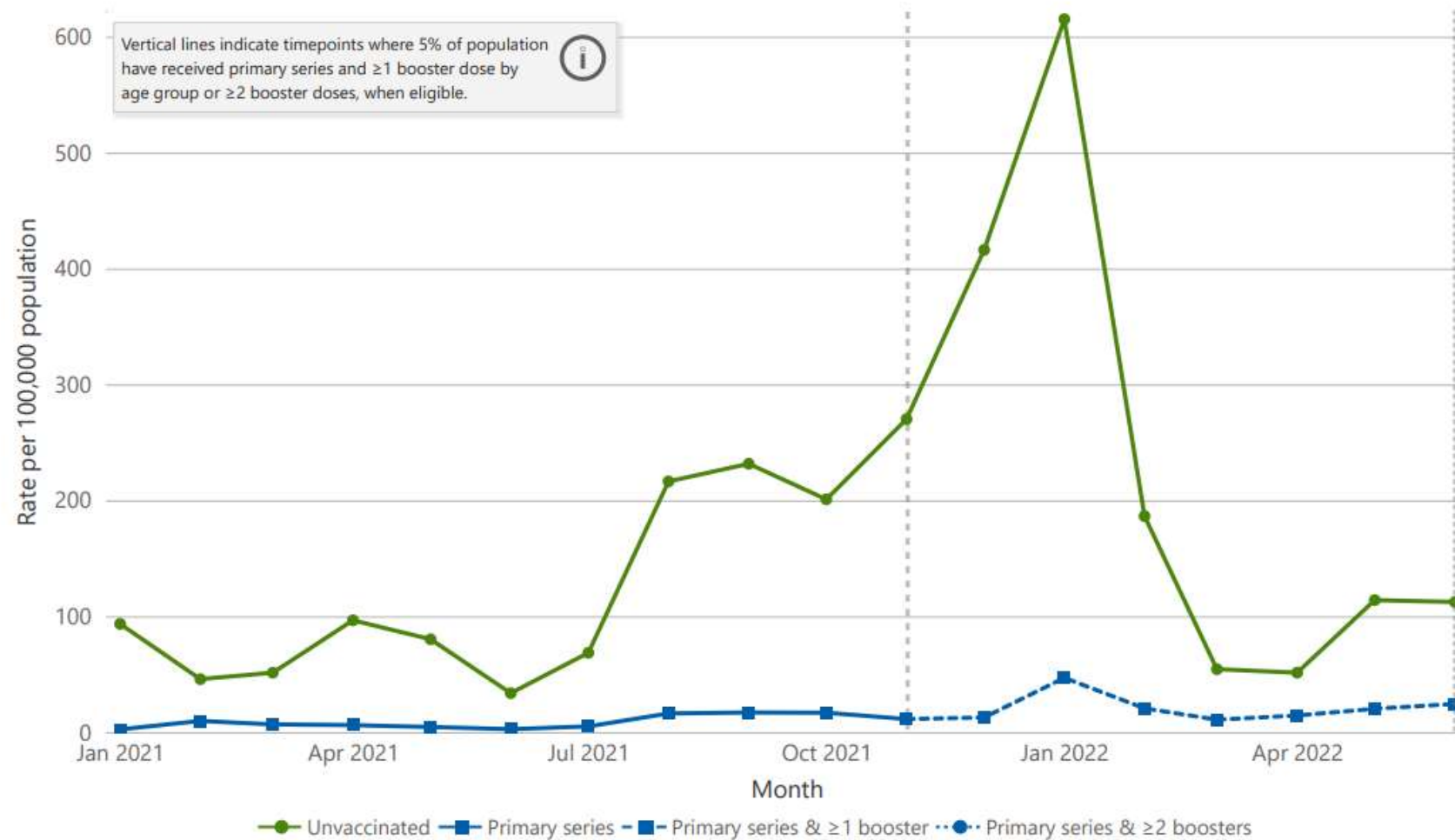


# 台灣現有的疫苗

AZ, Moderna, BNT, Medigen, Novavax



# COVID-19 住院by Vaccine Status(USA>18歲)



<https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html>

# 18歲以上疫苗注射降低COVID 19 住院風險

**4.6x Higher in Unvaccinated Adults Ages 18 Years and Older**

**1.7x Higher**  
in Unvaccinated Children  
Ages 5-11 Years

**2.0x Higher**  
in Unvaccinated Adolescents  
Ages 12-17 Years

**2.8x Higher**  
in Unvaccinated Adults  
Ages 18-49 Years

**3.6x Higher**  
in Unvaccinated Adults  
Ages 50-64 Years

**6.3x Higher**  
in Unvaccinated Adults  
Ages 65 Years and Older

in  
Unvaccinated  
Children  
Ages 5-11  
Years

in  
Unvaccinated  
Adolescents  
Ages 12-17  
Years

in  
Unvaccinated  
Adults  
Ages 18-49  
years

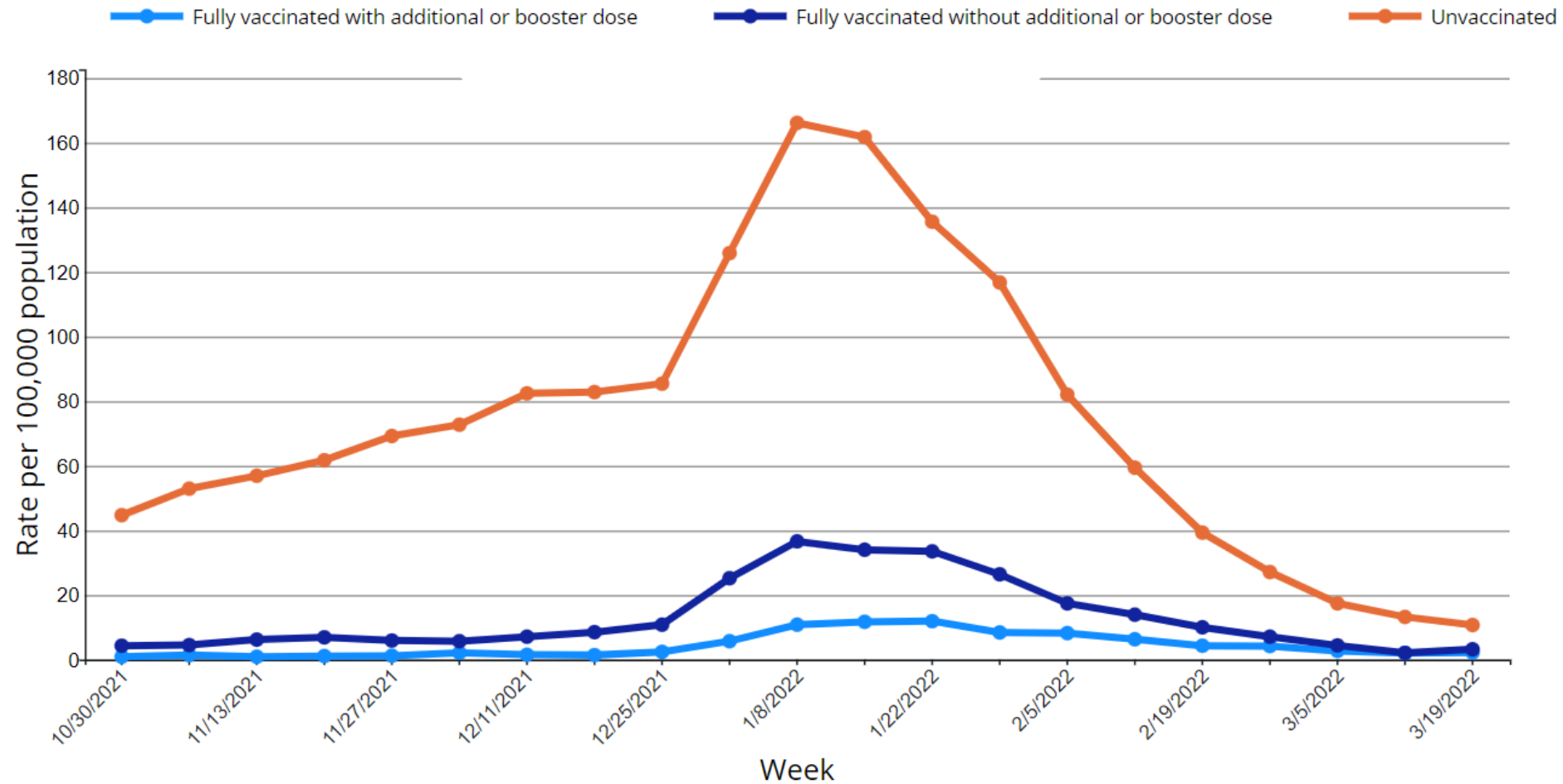
in  
Unvaccinated  
Adults  
Ages 50-64  
years

in  
Unvaccinated  
Adults  
Ages 65 Years  
and Older

For more information about COVID-NET, please see

<https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html>

# COVID-19 住院 by Vaccine Status追加(USA)



<https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html>



**6X**

*Risk of Dying from COVID-19*

**2.0X**

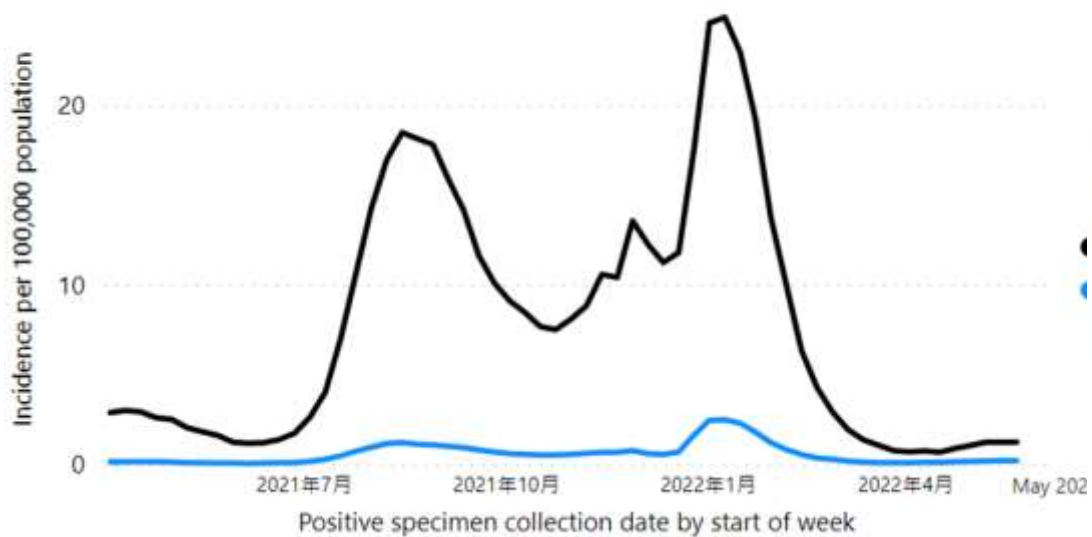
*Risk of Testing Positive for COVID-19*

**2.8X**

*Risk of Testing Positive for COVID-19*

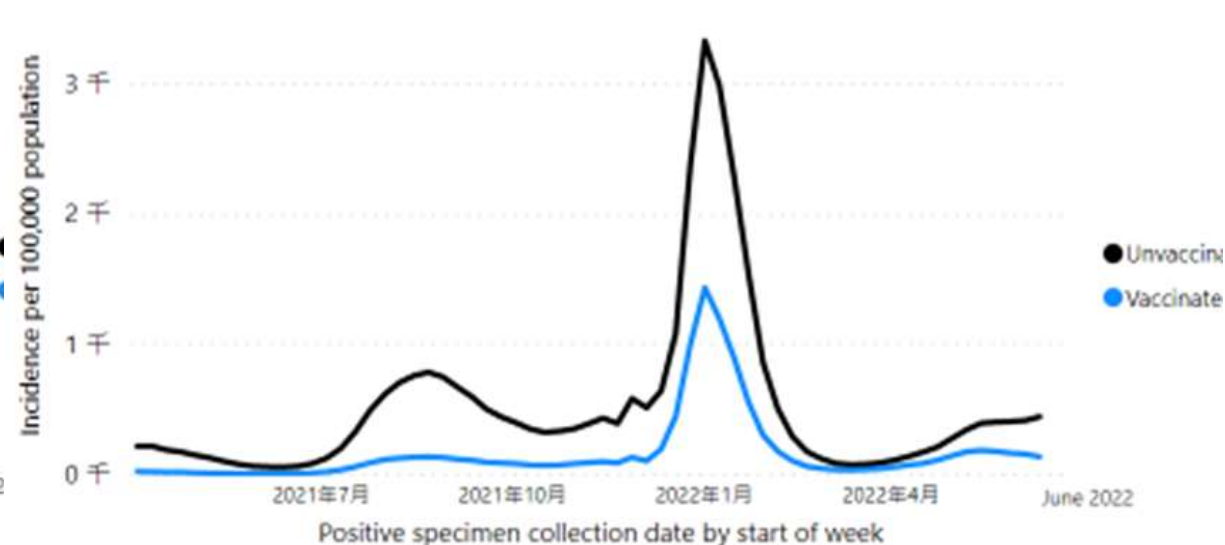
**Rates of COVID-19 Deaths by Vaccination Status in Ages 5+**

April 04, 2021–May 28, 2022 (30 U.S. jurisdictions)



**Rates of COVID-19 Cases by Vaccination Status in Ages 5+ Years**

April 04, 2021–June 18, 2022 (31 U.S. jurisdictions)



# 台灣： 接種完整疫苗可有效降低死亡率

3日內死亡多  
老人小孩多  
沒打疫苗多  
人數倍增快

## 未打疫苗者，死亡率為 打過三劑者的6倍

(統計至2022/05/16)

COVID-19疫苗追加劑接種者較未接種者在染疫後可降低83%的死亡率

	每百萬人口 無接種疫苗染 疫死亡率	每百萬人口 接種1劑疫苗後 染疫死亡率	每百萬人口 接種2劑疫苗後 染疫死亡率	每百萬人口 接種三劑疫苗後 染疫死亡率	第三劑vs未接種 之疫苗效力(95%C.I.)
0-4歲	2.20	-	-	-	-
5-11歲	0.00	0.00	0.00	0	-
12-17歲	0.00	0.00	0.00	0.00	-
18-49歲	66.52	1.74	0.81	0.13	0.998(0.984, 1.000)
50-64歲	30.90	21.00	6.42	2.73	0.912(0.810, 0.959)
65-74歲	115.24	121.77	41.79	7.59	0.934(0.877, 0.965)
75+歲	237.85	259.30	238.31	77.52	0.674(0.550, 0.764)
總計	38.88	29.16	11.35	6.51	0.833(0.783, 0.871)

中央流行疫情指揮中心

2022/05/19

## 致死率達萬分之10.5



46% 3天內死亡

0-3天	1260人
4-7天	698人
8-15天	602人
16天以上	171人

90% 60歲以上

0-9歲	15人
10-19歲	4人
20-59歲	227人
60歲以上	2485人

43% 沒打疫苗

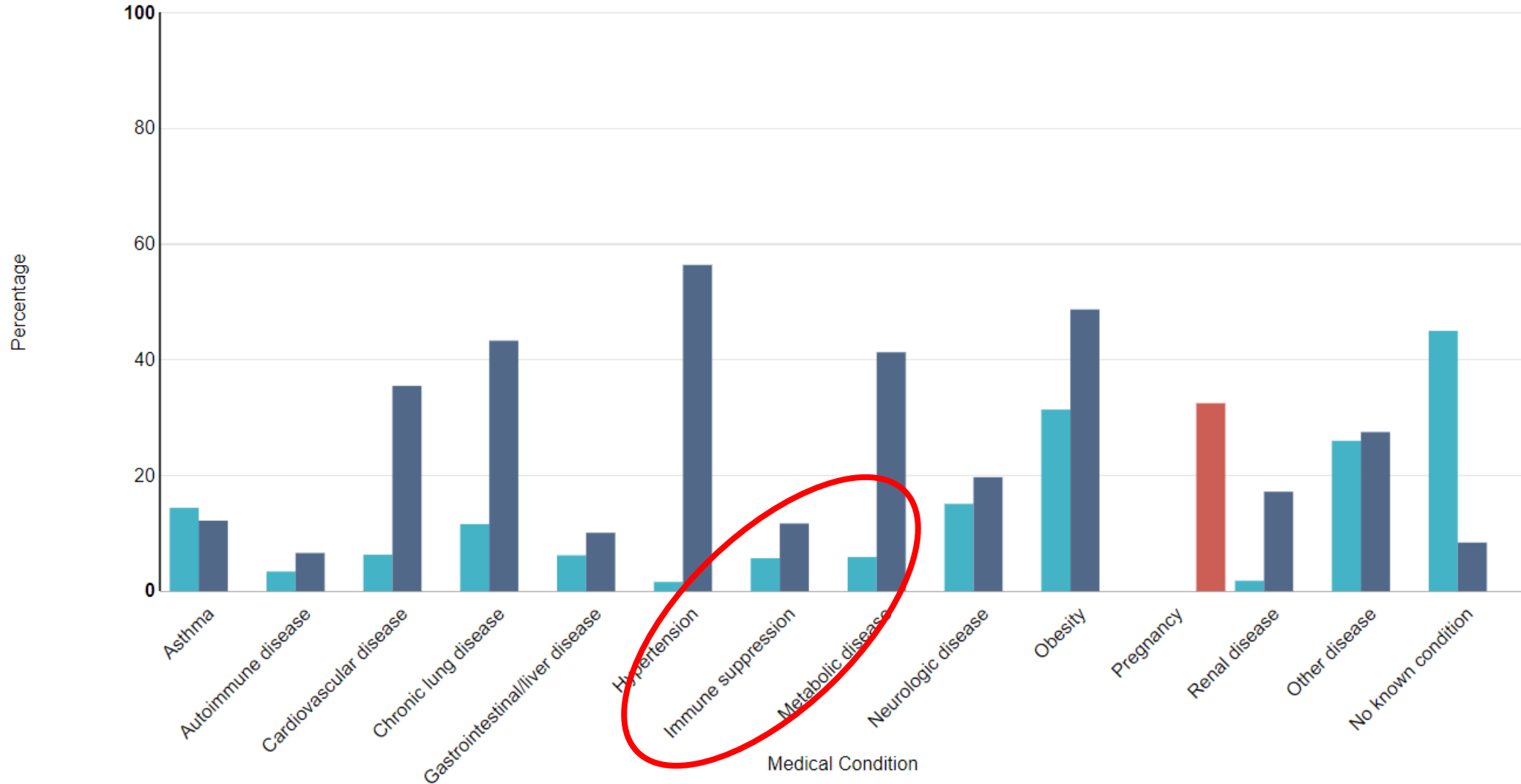
0劑	1177人
1劑	284人
2劑	385人
3劑以上	885人

## 翻倍死亡天數

蒙特塞拉特	▶ 12
台灣	▶ 13
薩摩亞	▶ 44
紐西蘭	▶ 48
萬那杜	▶ 48
東加	▶ 68
不丹	▶ 69
南韓	▶ 82
香港	▶ 85
新加坡	▶ 193
日本	▶ 297
全球	▶ 414
歐洲	▶ 433
美國	▶ 469
中國大陸	▶ 835

註／依各國最新累計死亡人數，對照死亡數一半的日期，計算期間天數，統計至6/8

# COVID住院病患的慢性病狀態



# 免疫功能低下族群

一、先天性免疫不全：分為

(1)細胞性免疫缺損(Cellular/T-cell immunodeficiency)

(2)體液性免疫缺損 (Humoral/B-cell immunodeficiency)

(3)補體缺損(Complement deficiency)

(4)吞噬細胞功能缺損(Phagocyte deficiency)。

二、人類免疫缺乏病毒(Human Immunodeficiency Virus，HIV)感染者

三、其他影響免疫功能的疾病，包括腎臟病、糖尿病、肝硬化及慢性肝病、無脾症及自體免疫疾病正接受類固醇或其他免疫調節劑治療者。

## 免疫功能低下者

關鍵字搜尋:

搜尋

移植患者預防接種建議

癌症病人預防接種建議

免疫不全病人預防接種建議

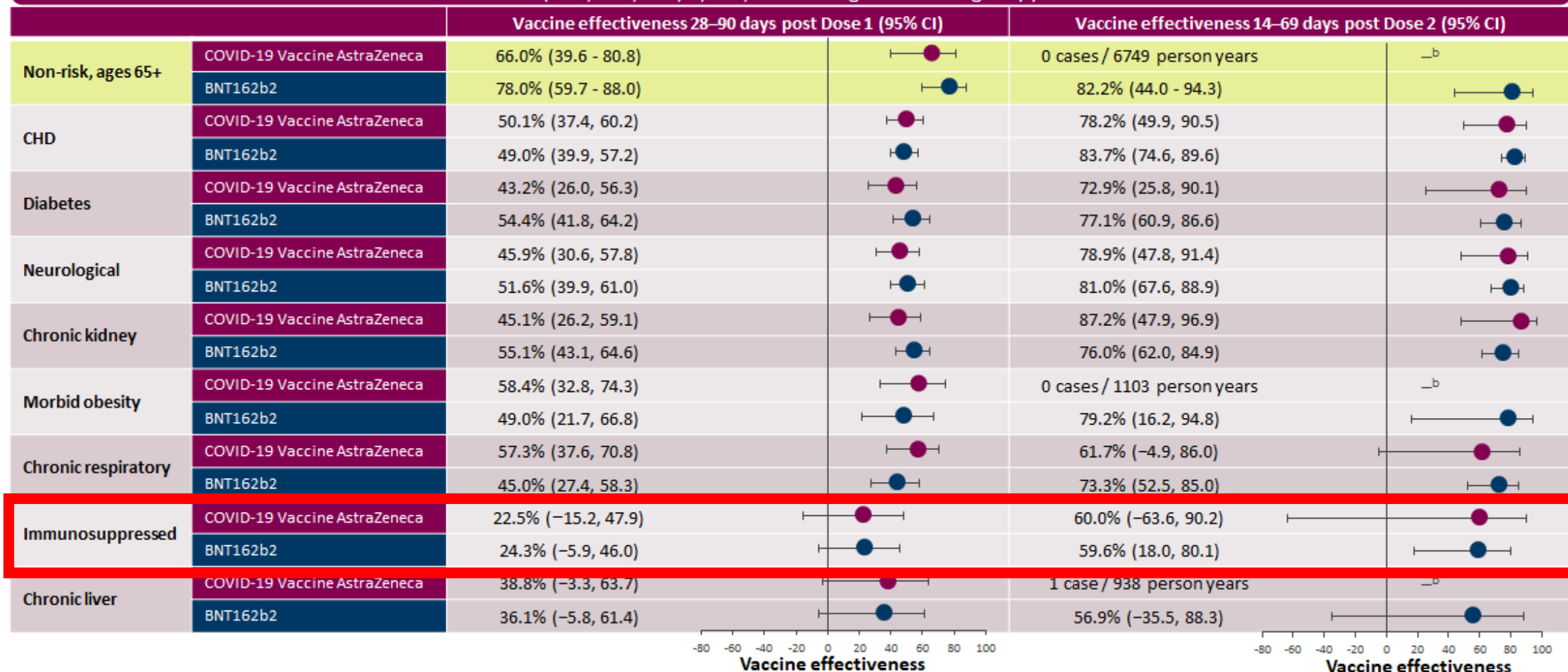
慢性腎臟疾病及洗腎患者疫苗接種建議



# 免疫低下者疫苗效力較差

UK

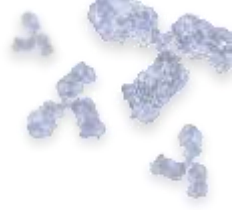
Cohort and nested test-negative case-control vaccine efficacy<sup>a</sup> analyses were conducted in the UK  
(n=5,642,687; 1,054,510 belonged to a risk group)



<sup>a</sup>Caccine effectiveness against symptomatic medically attended disease; <sup>b</sup>insufficient number of cases  
CHD = chronic heart disease and vascular disease; CI = confidence interval; COVID-19 = coronavirus disease 2019.  
Whitaker HJ et al. Online ahead of print. *J infect.* 2022.



# 免疫低下族群對疫苗Low response rate ( COVID-19 vaccine- 162 studies, 25,209 IC patients)



## **Solid organ transplant**

Heart: 12 - 75 %  
Liver: 37 - 84 %  
Lung: 0 - 41 %  
Kidney: 2 - 65 %



## **Hematologic malignancy**

39-86%

## **B cell depleting treatment**

42-70%



## **Inflammatory immune diseases**

37-100%

- Rheumatoid arthritis,  
Inflammatory bowel diseases  
Multiple sclerosis
- **B-cell depleting agents,**  
Methotrexate  
Disease-modifying  
antirheumatic drugs (DMARDs)  
Corticosteroids

# 預防嚴重COVID的效果：風險族群分析

## REACT-SCOT case-control study

1. Solid organ transplant recipient
2. Cancer of the blood or bone marrow at any stage of treatment, or people with cancer receiving treatments that affect the immune system
3. Severe respiratory conditions including cystic fibrosis, severe asthma and severe chronic obstructive airway disease, on home oxygen, severe bronchiectasis, pulmonary hypertension)
4. Rare diseases that increase the risk of infections such as severe combined immunodeficiency and homozygous sickle-cell disease
5. People on immunosuppression therapies sufficient to increase risk of infection
6. Pregnant with heart disease
7. Additional conditions, including people on renal dialysis, those who had a splenectomy and others identified by clinicians as requiring shielding advice.

Table 2. Rate ratios for severe COVID-19 within risk groups associated with vaccine dose: unvaccinated as reference category

Effect	1 dose vaccine			2 doses vaccine		
	Rate ratio (95% CI)		p-value	Rate ratio (95% CI)		p-value
No risk condition	0.35 (0.28, 0.45)	65%	$1 \times 10^{-17}$	0.07 (0.05, 0.10)	93%	$9 \times 10^{-41}$
Moderate risk condition	0.45 (0.37, 0.54)	55%	$3 \times 10^{-16}$	0.11 (0.08, 0.15)	89%	$4 \times 10^{-41}$
Eligible for shielding	0.49 (0.36, 0.67)	51%	$1 \times 10^{-5}$	0.34 (0.24, 0.48)	66%	$8 \times 10^{-10}$

Table 3. Rate ratios for severe COVID-19 associated with vaccine dose within clinically extremely vulnerable subgroups/2, 1

Effect	1 dose vaccine		2 doses vaccine	
	Rate ratio (95% CI)	p-value	Rate ratio (95% CI)	p-value
Solid organ transplant	0.79 (0.18, 3.53)	0.8	0.39 (0.11, 1.33)	0.1
Specific cancers	0.48 (0.21, 1.08)	0.08	0.44 (0.22, 0.89)	0.02
Severe respiratory	0.63 (0.41, 0.98)	0.04	0.20 (0.13, 0.32)	$3 \times 10^{-11}$
Rare diseases	0.59 (0.18, 1.91)	0.4	0.23 (0.05, 1.03)	0.05
On immunosuppressants	0.47 (0.19, 1.14)	0.1	1.09 (0.48, 2.49)	0.8
Additional conditions	0.19 (0.09, 0.41)	$2 \times 10^{-5}$	0.37 (0.20, 0.69)	0.002

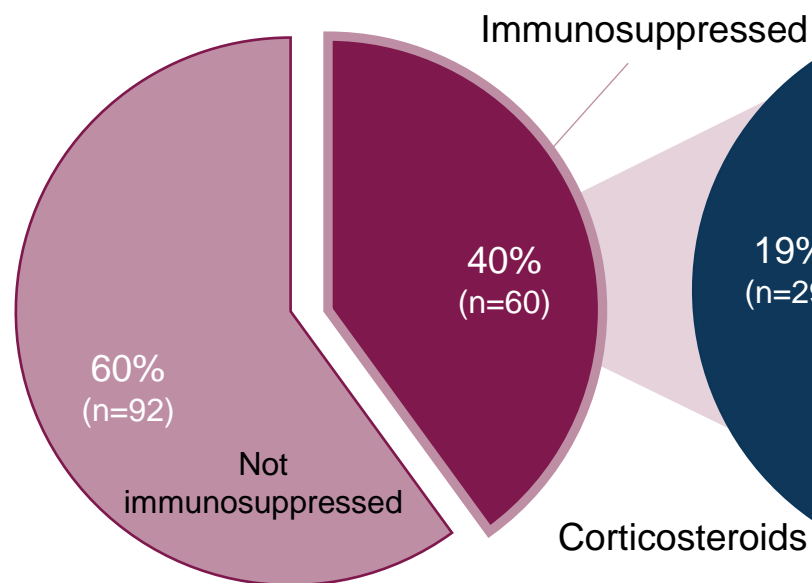
# 免疫低下者占突破性感染住院較高比率



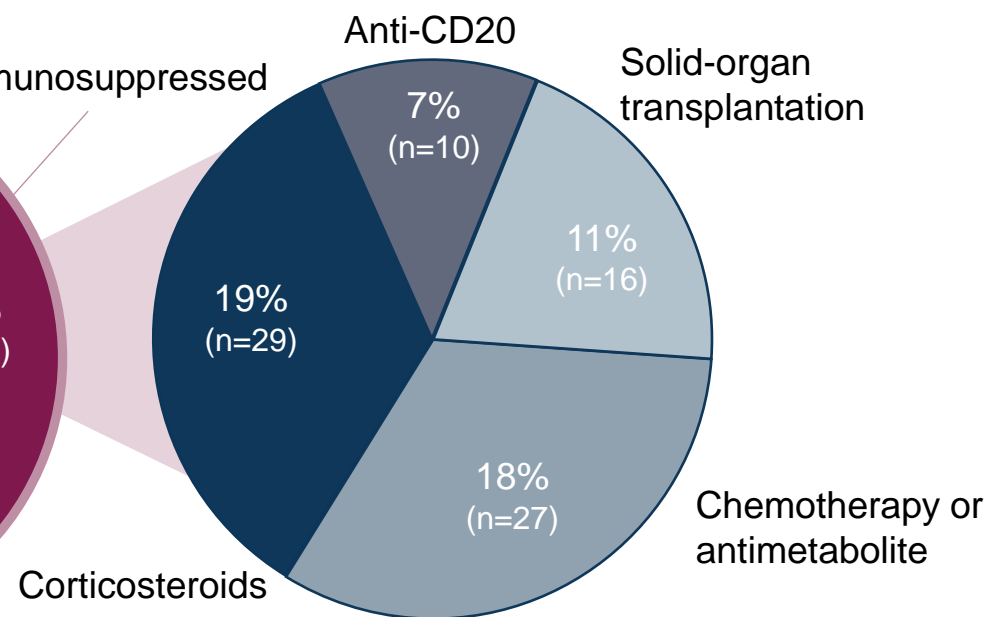
Vaccinated patients<sup>b,c</sup> (N=152) admitted to any of 17 participating hospitals in Israel with severe COVID-19 and confirmed PCR diagnosis<sup>5,a-c</sup>

**40% of vaccinated patients hospitalized breakthrough cases of COVID-19 were immunocompromised, that have increased vulnerability to COVID-19<sup>1-4</sup>**

**Immunosuppression was enriched in the admitted patients**



**Common causes of immunosuppression included:**



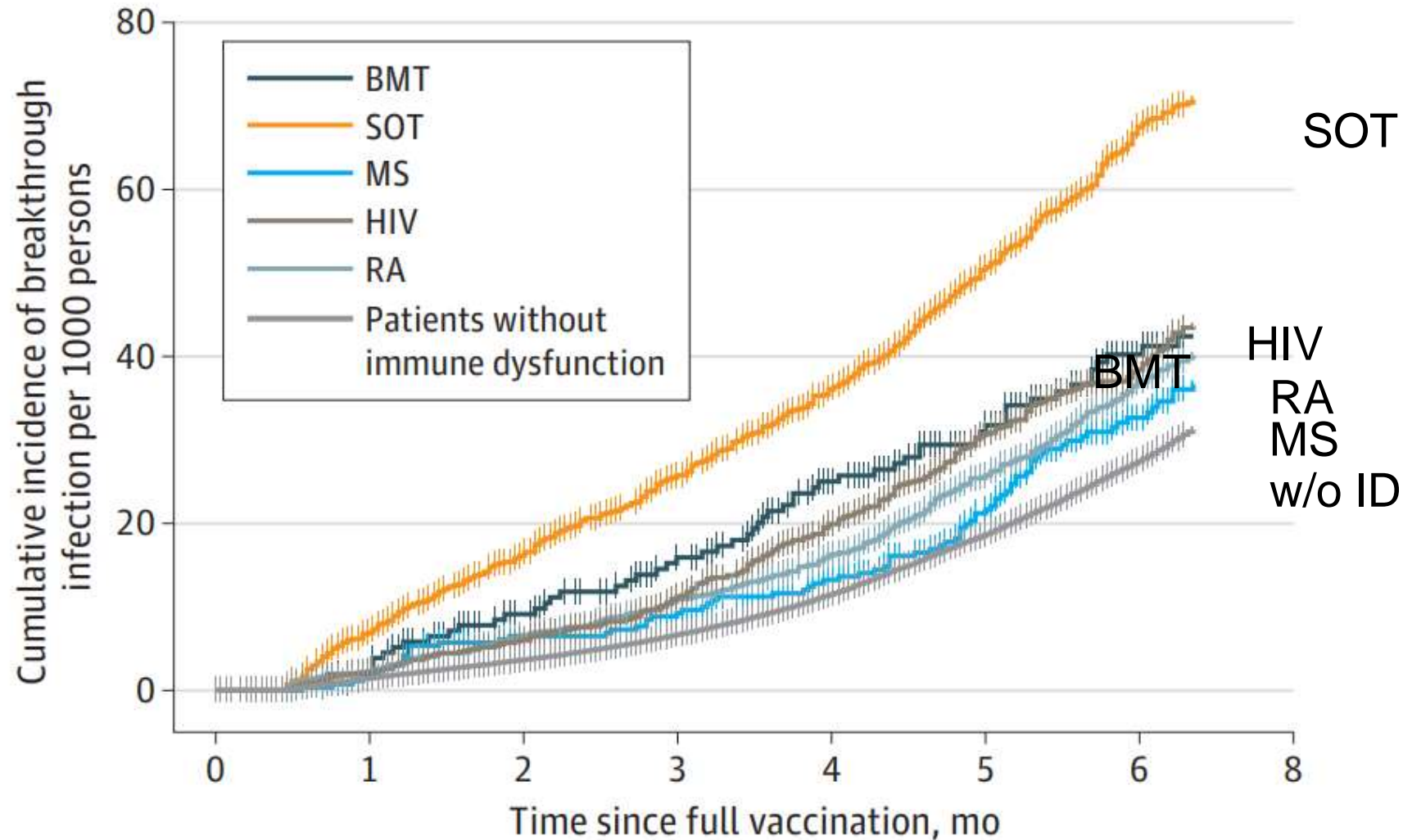
<sup>a</sup>COVID-19 mRNA vaccines are highly efficacious; these offer ~94%-95% efficacy in Phase III trials; <sup>b</sup>All of the study participants had their disease onset 8 or more days after their second vaccine dose, although in most of the cases disease onset occurred much later, with a median time to admission exceeding 1 month; <sup>c</sup>BNT162b2 COVID-19 vaccine, which showed 80%-91% effectiveness after a single dose. COVID-19 = coronavirus disease 2019; mRNA = messenger ribonucleic acid; PCR = polymerase chain reaction.

1. In House Data, AstraZeneca Pharmaceuticals LP. Up to 2% of the Targeted Patients for LAAB Treatment Are Immunocompromised; 2. Harpaz R et al. *JAMA*. 2016;316:2547-2448; 3. Centers for Disease Control and Prevention. COVID-19 vaccines for moderately or severely immunocompromised people. <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html>; 4. Abbasi J. *JAMA*. 2021;325:2033-2035; Brosh-Nissimov T et al. Online ahead of print. *Clin Microbiol Infect*. 2021.





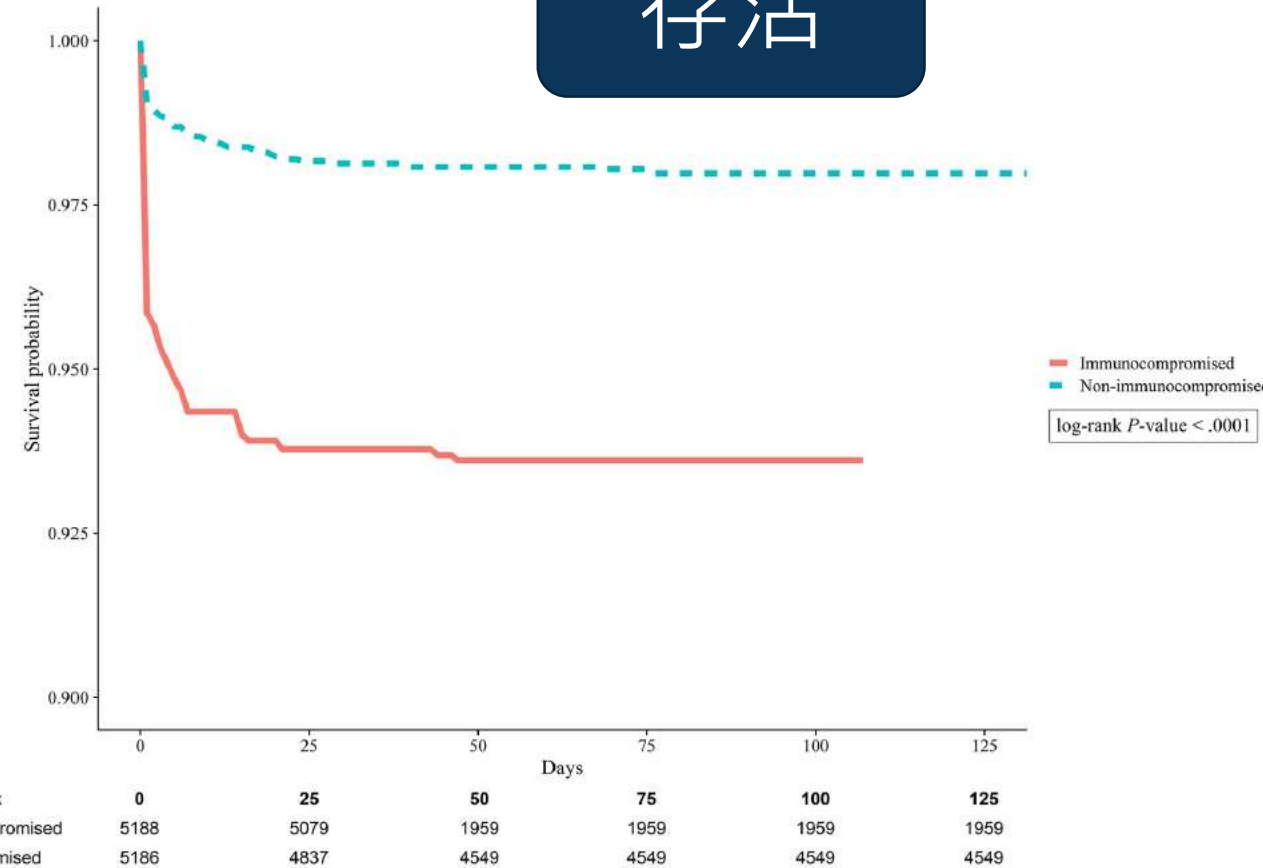
# 免疫低下者突破性感染風險較高



# 免疫低下のCOVID-19確診者癒後較差

存活

Outcomes	COVID-19 patients after IPTW		P-value
	Immunocompromised	Non- immunocompromised	
	(n = 5,186)	(n = 5,188)	
In-hospital mortality	330 (6.4)	101 (2.0)	< .001
Conventional oxygen therapy	973 (18.8)	608 (11.7)	< .001
High flow nasal cannula	249 (4.8)	105 (2.0)	< .001
Mechanical ventilation	138 (2.7)	69 (1.3)	< .001
ECMO	22 (0.4)	10 (0.2)	0.034
Vasopressor use	179 (3.5)	91 (1.8)	< .001
Renal replacement therapy	28 (0.6)	11 (0.2)	0.007
Acute heart failure	469 (9.0)	277 (5.4)	< .001



IPTW: Inverse probability of treatment weighting; ECMO: Extracorporeal membrane oxygenation.

Moon Seong Baek et al. PLoS One. 2021 Oct 1;16(10):e0257641

# 面對Omicron接受器官移植者更易受到感染、住院,死亡率較低



Single  
center

During the  
*Omicron*  
surge,  
**12/22/21  
– 2/9/22**



**347**

SOT recipients had a  
positive COVID-19  
test



**26%**

(90/347) were  
hospitalized



**2%**

(8/347) died

97% of all  
positive  
SARS-CoV2  
PCR results  
at our  
center in  
this period  
were  
*Omicron*.

Compared to  
3/1/2020 –  
11/30/2020

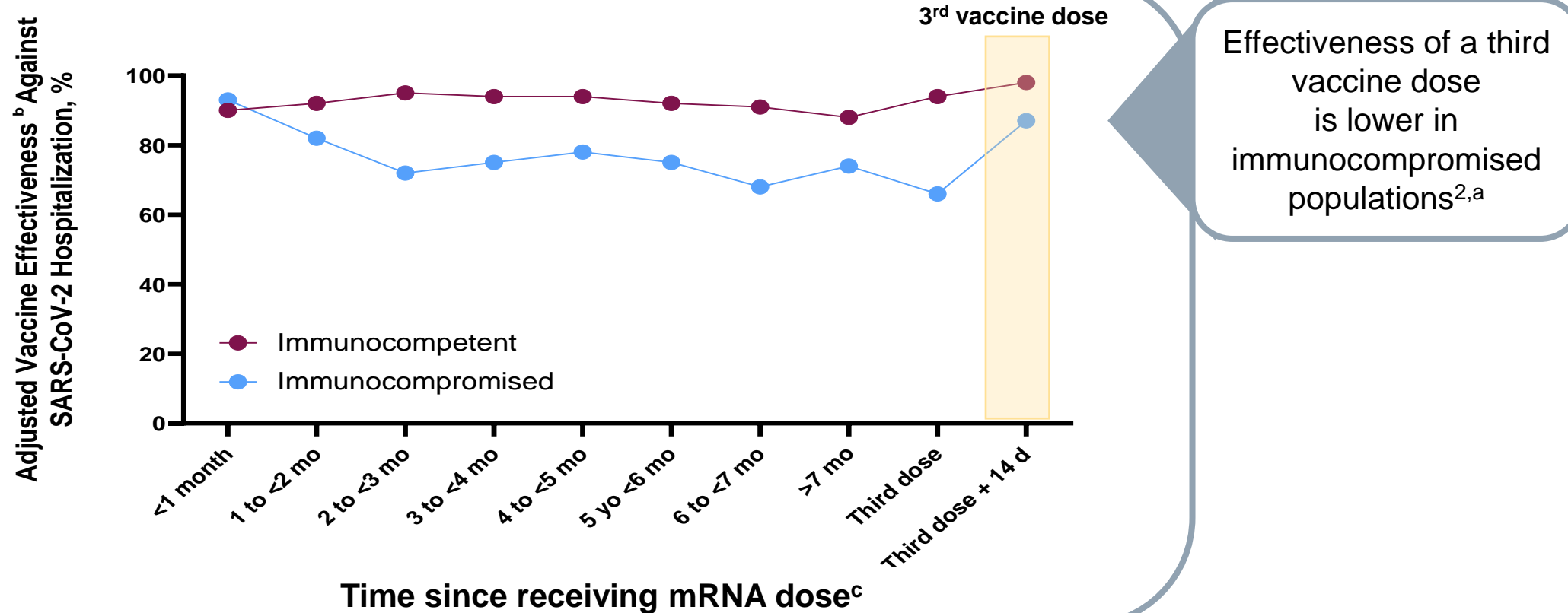
129  
cases

77 cases  
60%  
hospitalized

13 cases  
10%  
died

# 接受mRNA疫苗後,免疫低下族群保護力下降較快

Protection wanes faster after 2 COVID-19 vaccines doses in immunocompromised populations<sup>2,a</sup>



<sup>a</sup>Immunocompromising conditions included participants with ICD10 codes corresponding to hematologic malignancy, HIV/AIDS, intrinsic immune compromising conditions, those on the solid organ or hematopoietic stem cell registries, and those taking systemic immunosuppressive medications <sup>b</sup>Relative to unvaccinated. Retrospective cohort study in adults receiving the BNT162b2 vaccine; <sup>c</sup>mRNA vaccine defined as BNT162b2.

1. Embi PJ et al. *MMWR Morb Mortal Wkly Rep.* 2021;70:1553-1559; 2. Tartof SR et al. *The Lancet Regional Health – Americas.* 2022;00: 100198. <https://doi.org/10.1016/j.lana.2022.100198>.





# 美國CDC對中重度免疫功能不全病患的新冠 疫苗注射建議(增加基礎加強劑)

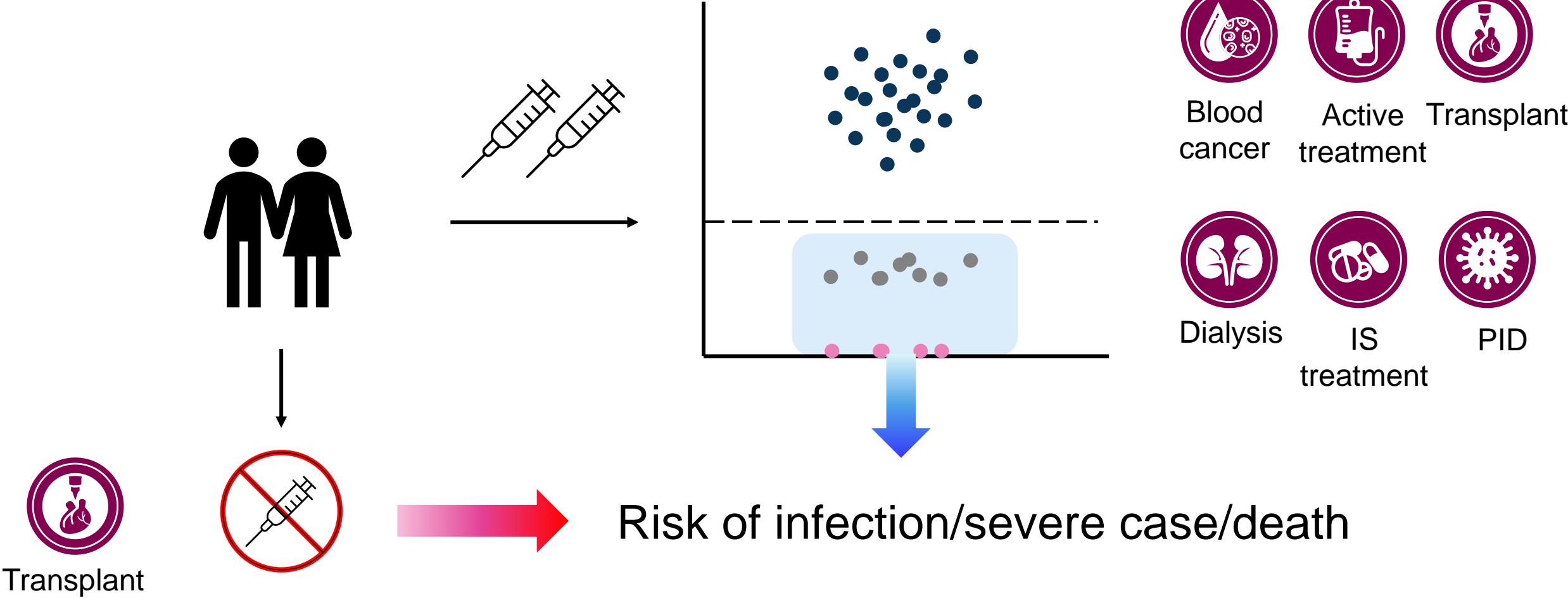


Vaccine	0 month	1 month	2 month	3 month	4 month	5 month	6 month	7 month	8 month	9 month
<b>Pfizer-BioNTech</b> (ages 5 years and older)	1 <sup>st</sup> dose	2 <sup>nd</sup> dose (3 weeks after 1 <sup>st</sup> dose)	3 <sup>rd</sup> dose (at least 4 weeks after 2 <sup>nd</sup> dose)			Booster dose* (at least 3 months after 3 <sup>rd</sup> dose)				2 <sup>nd</sup> booster dose for eligible people† (at least 4 months after 1 <sup>st</sup> booster)
<b>Moderna</b> (ages 18 years and older)	1 <sup>st</sup> dose	2 <sup>nd</sup> dose (4 weeks after 1 <sup>st</sup> dose)	3 <sup>rd</sup> dose (at least 4 weeks after 2 <sup>nd</sup> dose)			Booster dose* (at least 3 months after 3 <sup>rd</sup> dose)				2 <sup>nd</sup> booster dose† (at least 4 months after 1 <sup>st</sup> booster dose)
<b>Janssen</b> (ages 18 years and older)	1 <sup>st</sup> dose	2 <sup>nd</sup> (additional dose‡ using an mRNA COVID-19 vaccine (at least 4 weeks after 1 <sup>st</sup> dose)		Booster dose* (at least 2 months after additional dose)				2 <sup>nd</sup> booster dose† (at least 4 months after 1 <sup>st</sup> booster dose)		

Vaccine	0 month	1 month	2 month	3 month	4 month	5 month	6 month	7 month	8 month	9 month	10 month	11 month
<b>Pfizer-BioNTech</b> (ages 5 years and older)	1 <sup>st</sup> dose	2 <sup>nd</sup> dose† (3 weeks after 1 <sup>st</sup> dose)					Booster dose‡ (at least 5 months after 2 <sup>nd</sup> dose)				2 <sup>nd</sup> booster dose for eligible people§ (at least 4 months after 1 <sup>st</sup> booster)	

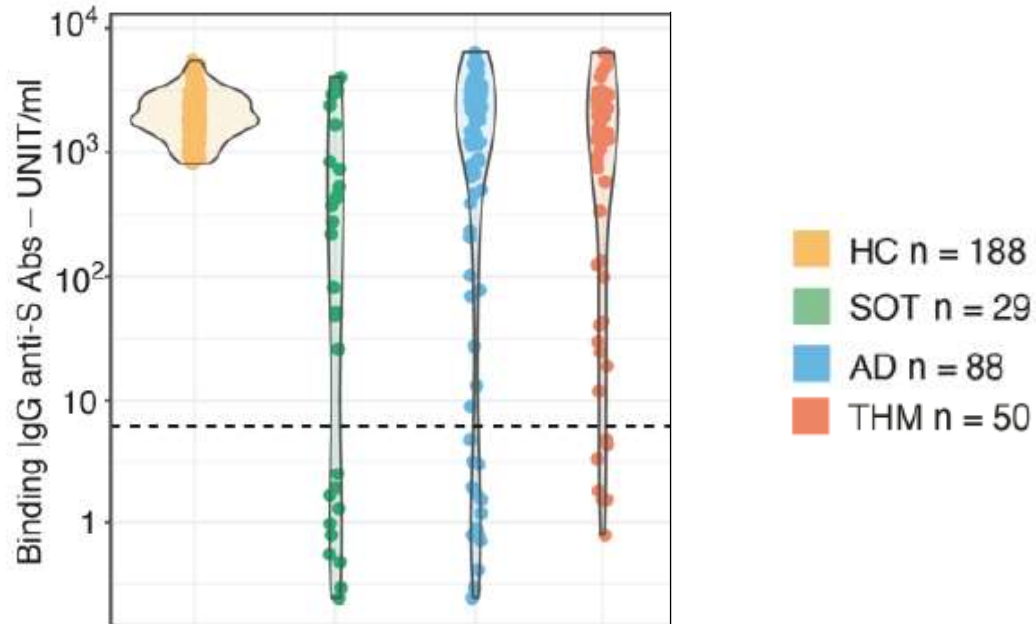
# 免疫低下族群的困境： 因害怕而未接受疫苗注射、疫苗效果較差



# 免疫低下病患的抗體效價較低



Anti-S IgG levels were measured in healthy controls and immunocompromised groups after 2 mRNA vaccine doses<sup>1,a</sup>



Compared to healthy controls, levels of anti-S IgG antibodies were significantly reduced after 2 doses of mRNA vaccine<sup>1,a</sup>

Solid organ  
transplant  
**23X**

Autoimmune  
disease  
**1.2X**

Treated  
hematologic  
malignancy  
**1.4X**

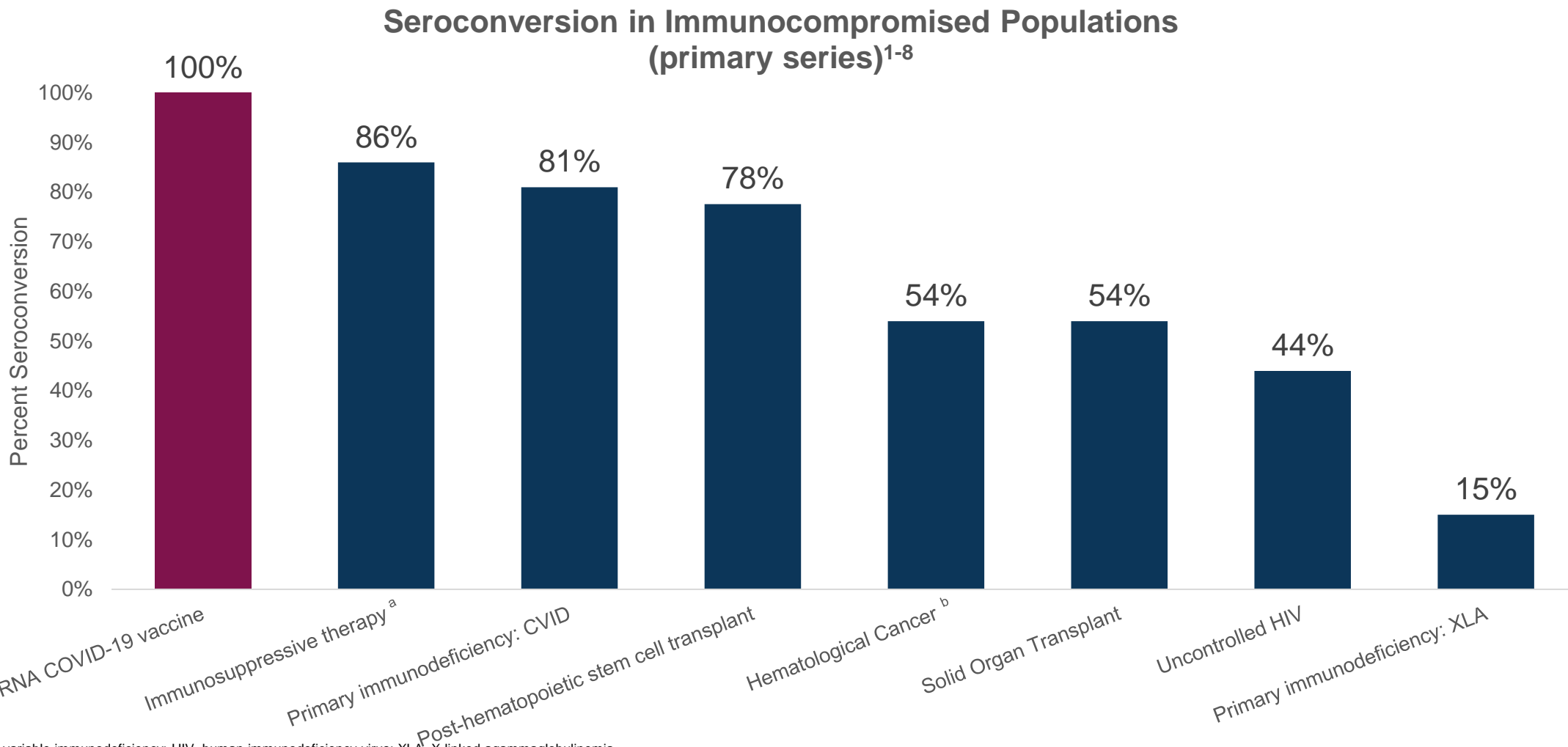
<sup>a</sup>1 month after a second dose of mRNA vaccine.

AD = autoimmune diseases; HC = healthy control; SOT = solid organ transplant; THM = treated hematological malignancy; TSC = treated solid cancer; UHM = untreated hematological malignancy; USC = untreated solid cancer.

1. Obeid M et al. *JAMA Oncol*. Published online March 10, 2022.



# 免疫低下族群血清免疫轉換(Seroconvert):兩劑注射後



CVID, common variable immunodeficiency; HIV, human immunodeficiency virus; XLA, X-linked agammaglobulinemia.

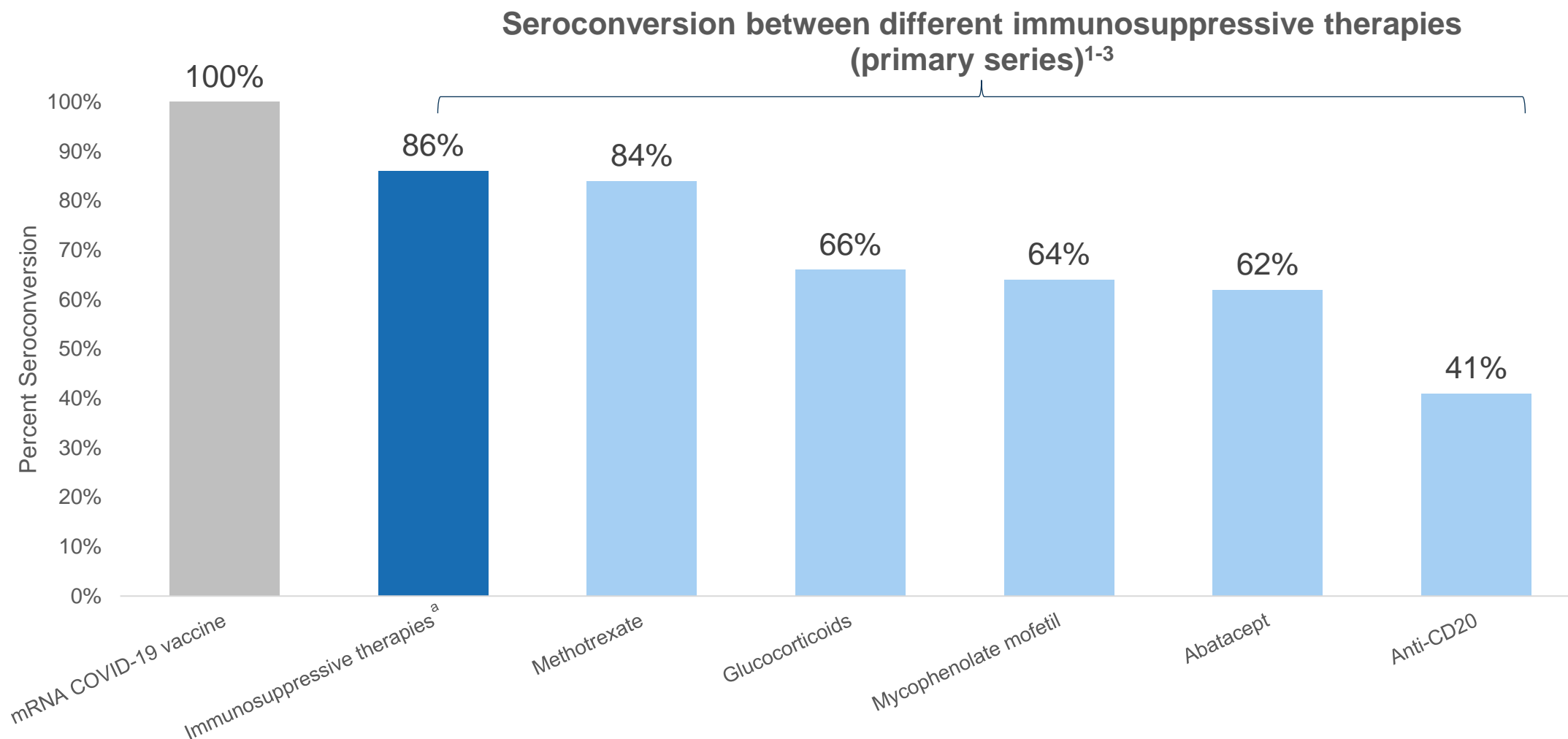
<sup>a</sup>Included glucocorticoids, conventional synthetic disease-modifying antirheumatic drugs (DMARDs), biologic DMARDs, and Janus kinase inhibitors. <sup>b</sup>Included multiple myeloma, lymphomas, B-cell chronic lymphocytic leukemia, and other myeloid malignancies.

1. Mulligan MJ et al. *Nature*. 2020;586, 589-593; 2. Jackson LA et al. *N Engl J Med*. 2020; 383:1920-1931; 3. Furer V et al. *Ann Rheum Dis*. 2020;80:1330-1338; 4. van Leeuwen LPM et al. *J Allergy Clin Immunol* 2022. 5. Shem-Tov N et al. *British Journal of Haematology*. 2022;196:884-891; 6. Agha ME et al. *Open Forum Infectious Diseases*. 2021;8(7); 7. Boyarsky BJ et al. *JAMA*. 2021;325(21):2201-2206; 8. Nolan H et al. *AIDS*. 2022;35(4):F1-F5.





# 不同免疫抑制藥物使用與血清免疫

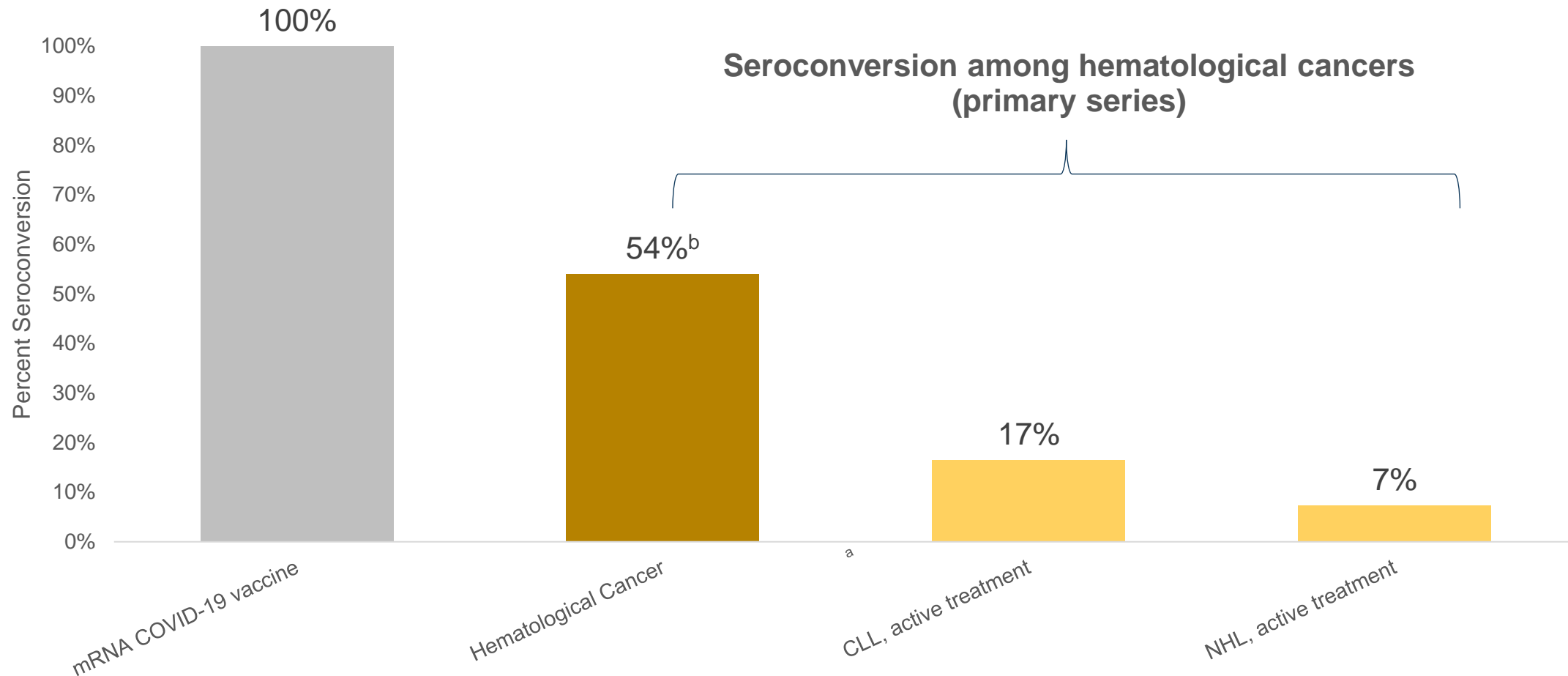


<sup>a</sup>Included glucocorticoids, conventional synthetic disease-modifying antirheumatic drugs (DMARDs), biologic DMARDs, and Janus kinase inhibitors.

1. Furer V et al. *Ann Rheum Dis.* 2020;80:1330-1338; 2. Mulligan MJ et al. *Nature.* 2020;586, 589-593; 3. Jackson LA et al. *N Engl J Med.* 2020; 383:1920-1931.



# 血液腫瘤治療者的血清免疫轉換



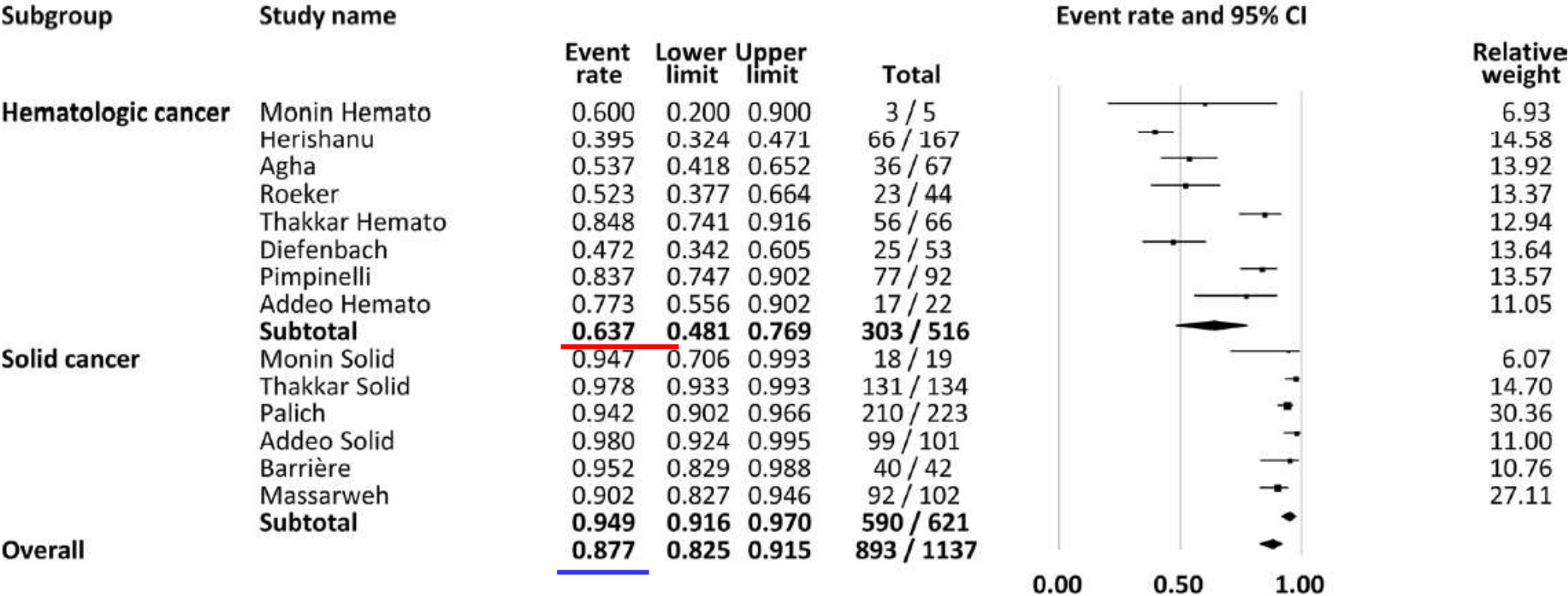
CLL, chronic lymphocytic leukemia; NHL, non-Hodgkin lymphoma.

<sup>a</sup>Included multiple myeloma, lymphomas, B-cell chronic lymphocytic leukemia, and other myeloid malignancies.

1. Mulligan MJ et al. *Nature*. 2020;586, 589-593; 2. Jackson LA et al. *N Engl J Med*. 2020; 383:1920-1931; 3. Agha ME et al. *Open Forum Infectious Diseases*. 4. Herishanu Y et al. *Blood*. 2021;137(23):3165-3173; 5. Perry C et al. *Blood Adv*. 2021;5(16):3053-3061.

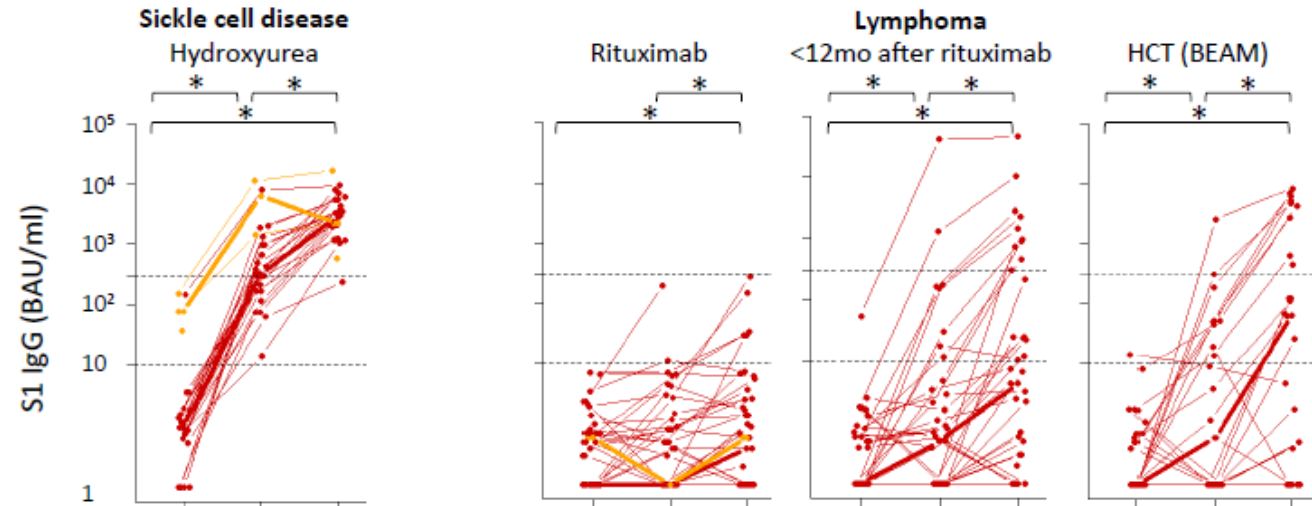


# 腫瘤病患疫苗血清免疫較低(尤其是血腫)

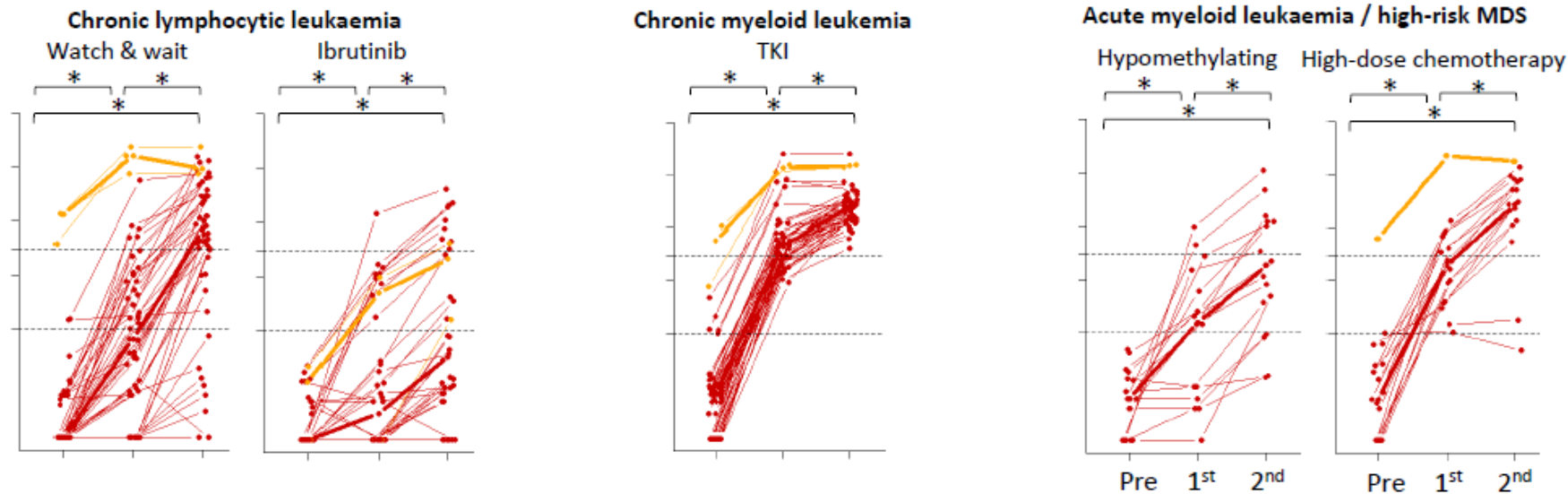


Hemato: Heterogeneity:  $I^2 = 89.49\%$ ,  $Q = 66.59$ ,  $P < 0.001$   
Solid: Heterogeneity:  $I^2 = 39.79\%$ ,  $Q = 8.31$ ,  $P = 0.14$   
Overall: Heterogeneity:  $I^2 = 94.22\%$ ,  $Q = 224.81$ ,  $P < 0.001$

# 注射疫苗後S 抗體反應 (不同血腫)

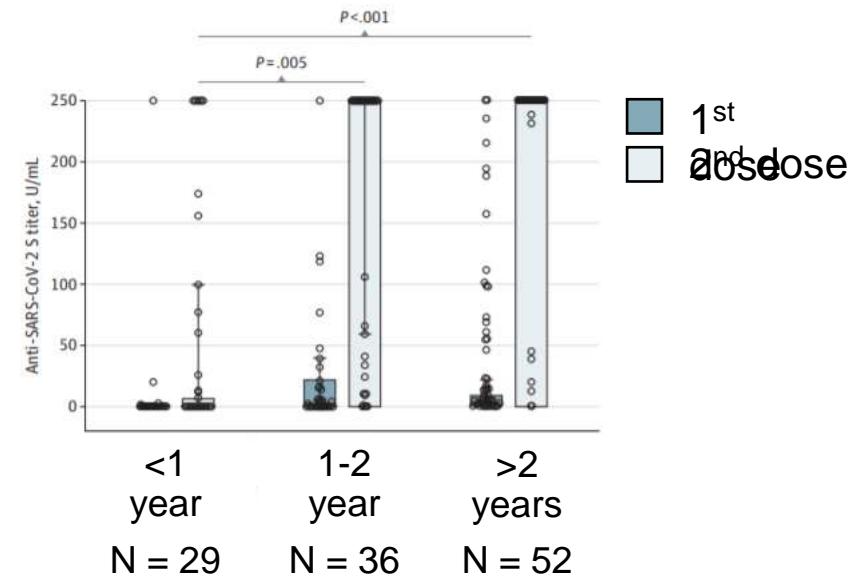
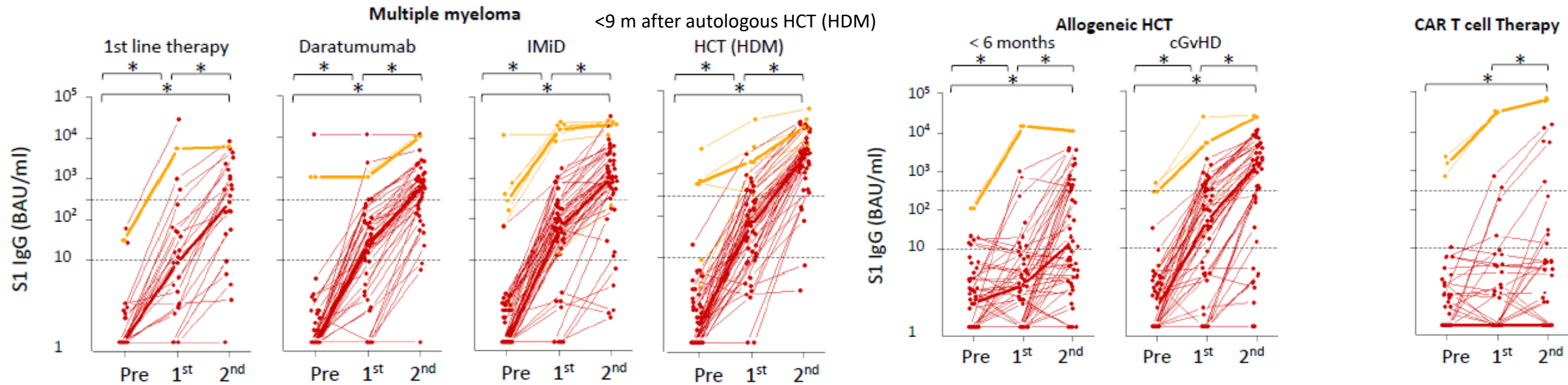


10: seroconversion  
300:adequate titer



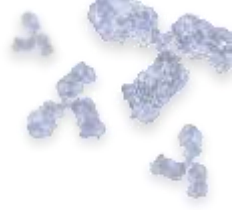


# 注射疫苗後S 抗體反應 (不同血腫)續



1. Sabine Haggengburg Blood Adv. 2022 Feb 3;bloodadvances.2021006917. doi: 10.1182/bloodadvances.2021006917; 2. Amandine Le Bourgeois et al. JAMA Netw Open. 2021 Sep 1;4(9):e2126344.

# 疫苗抗體反應 by rituximab or HCT



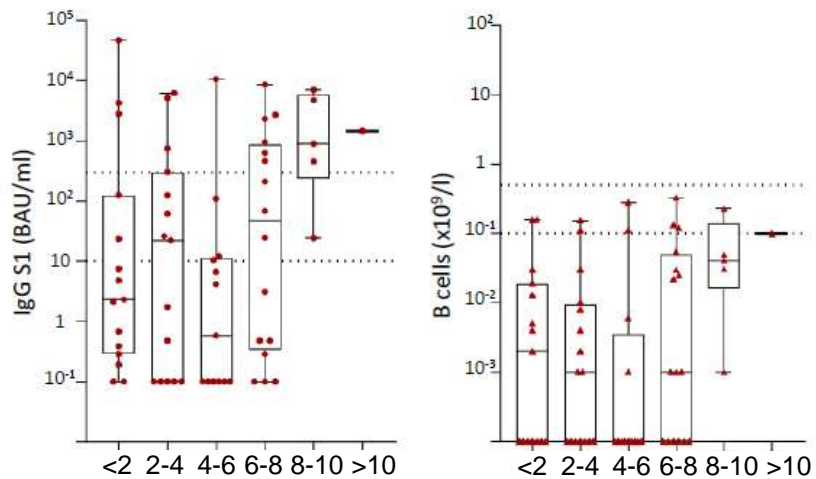
Lymphoma

Multiple myeloma

Allogeneic HCT

Ab

B cell No.

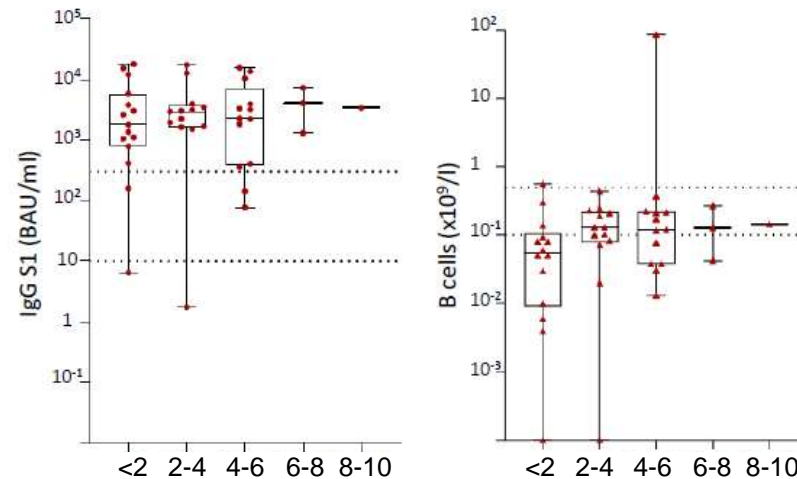


Time after end of rituximab/HCT (months)

Anti-CD 20

Ab

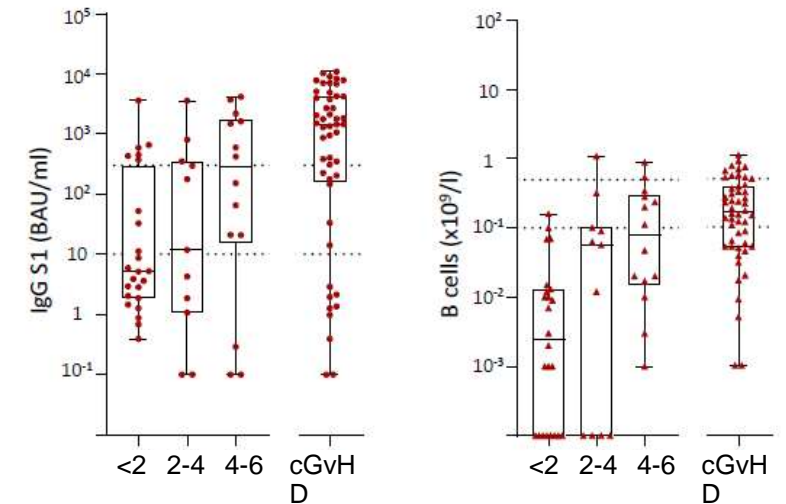
B cell No.



Time after HCT (months)

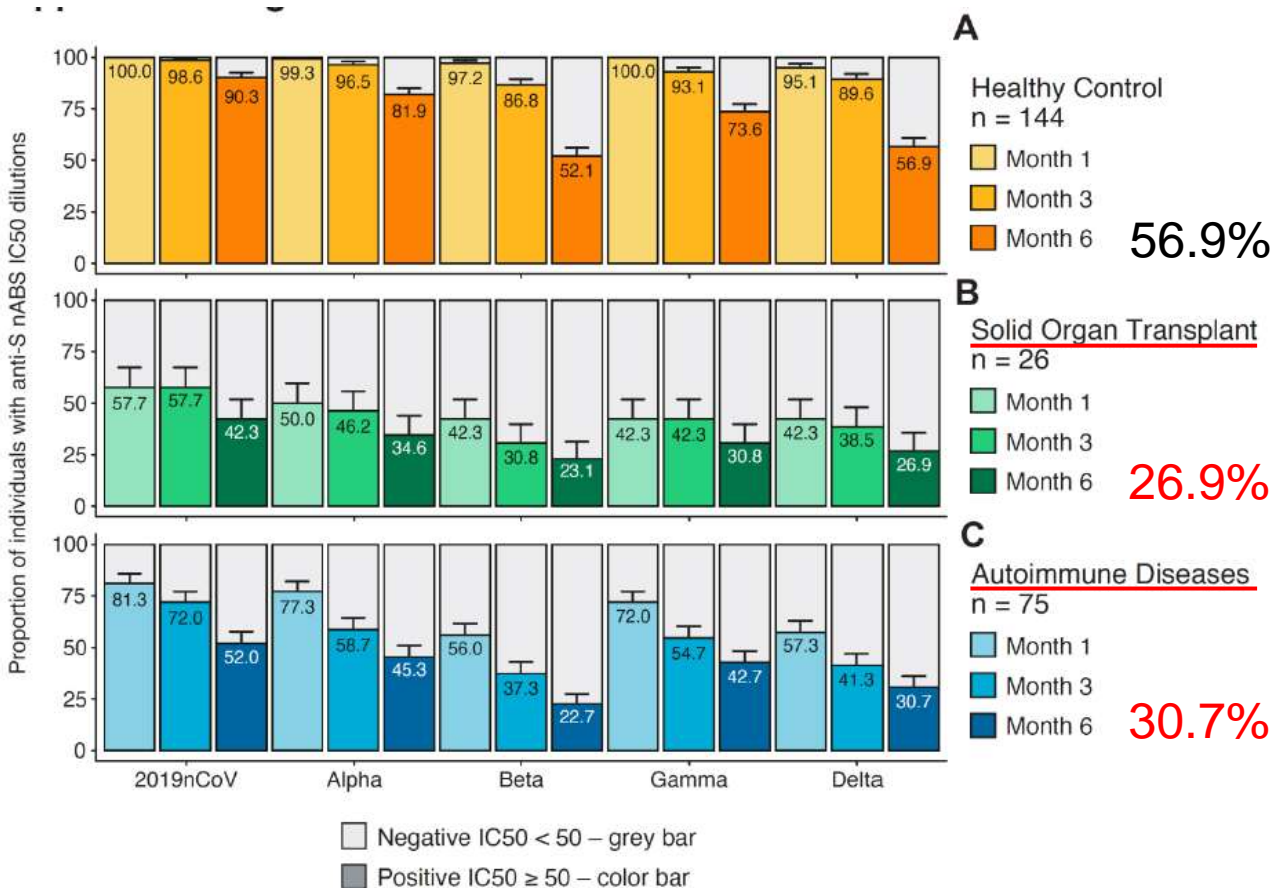
Ab

B cell No.

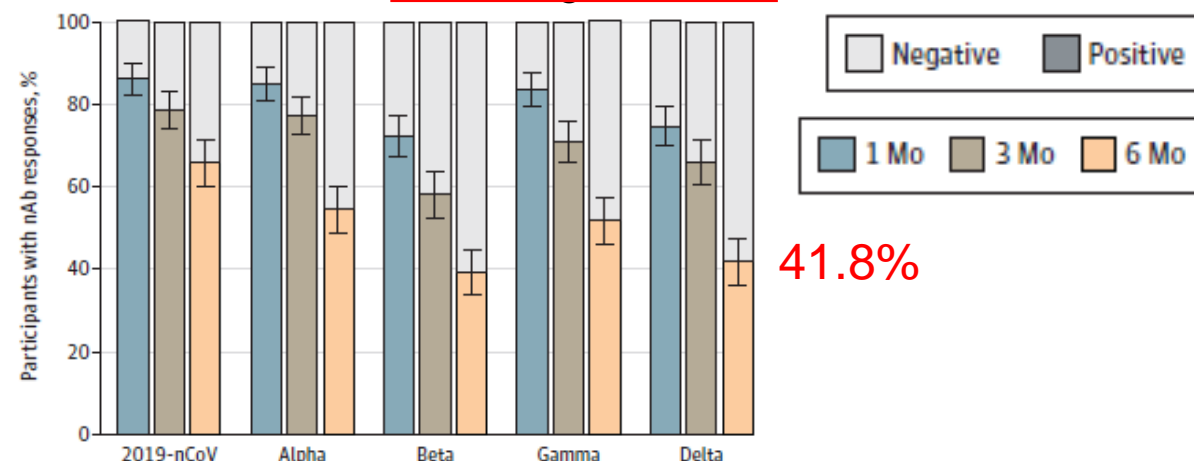


Time after HCT (months)

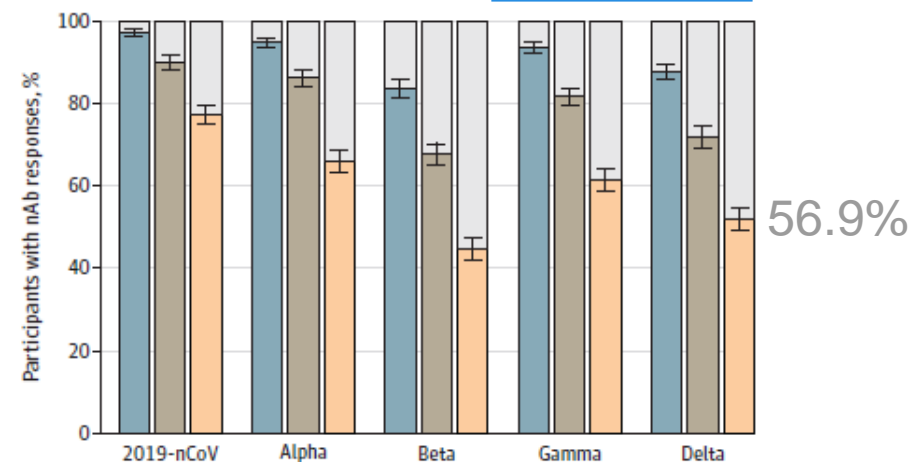
# 即使接種第二劑疫苗，抗體反應仍會持續性的 弱化，特別是免疫低落的族群



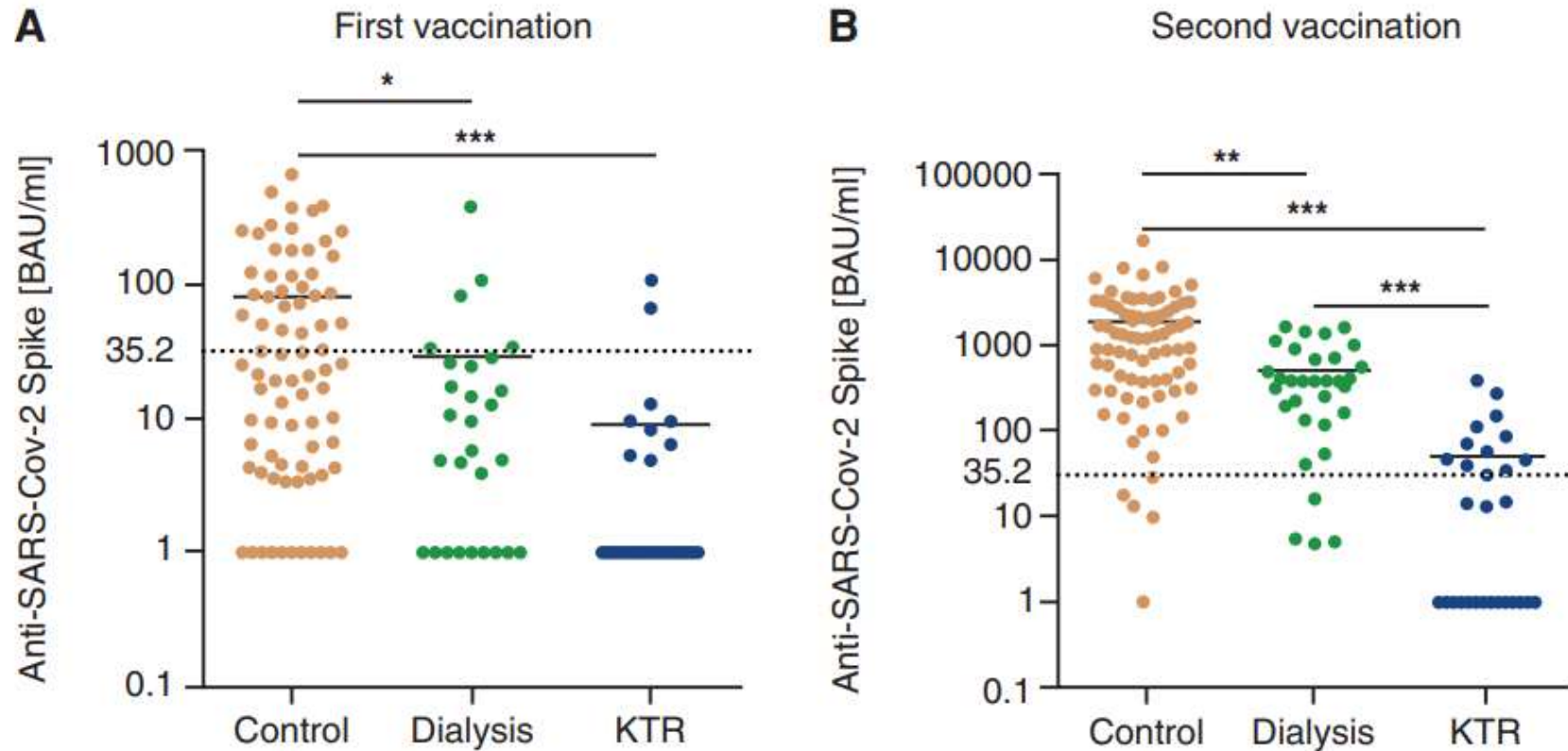
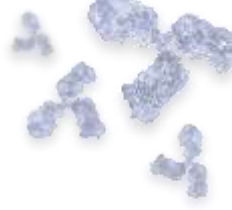
## Untreated & treated hematologic cancers



## Untreated & treated solid cancers

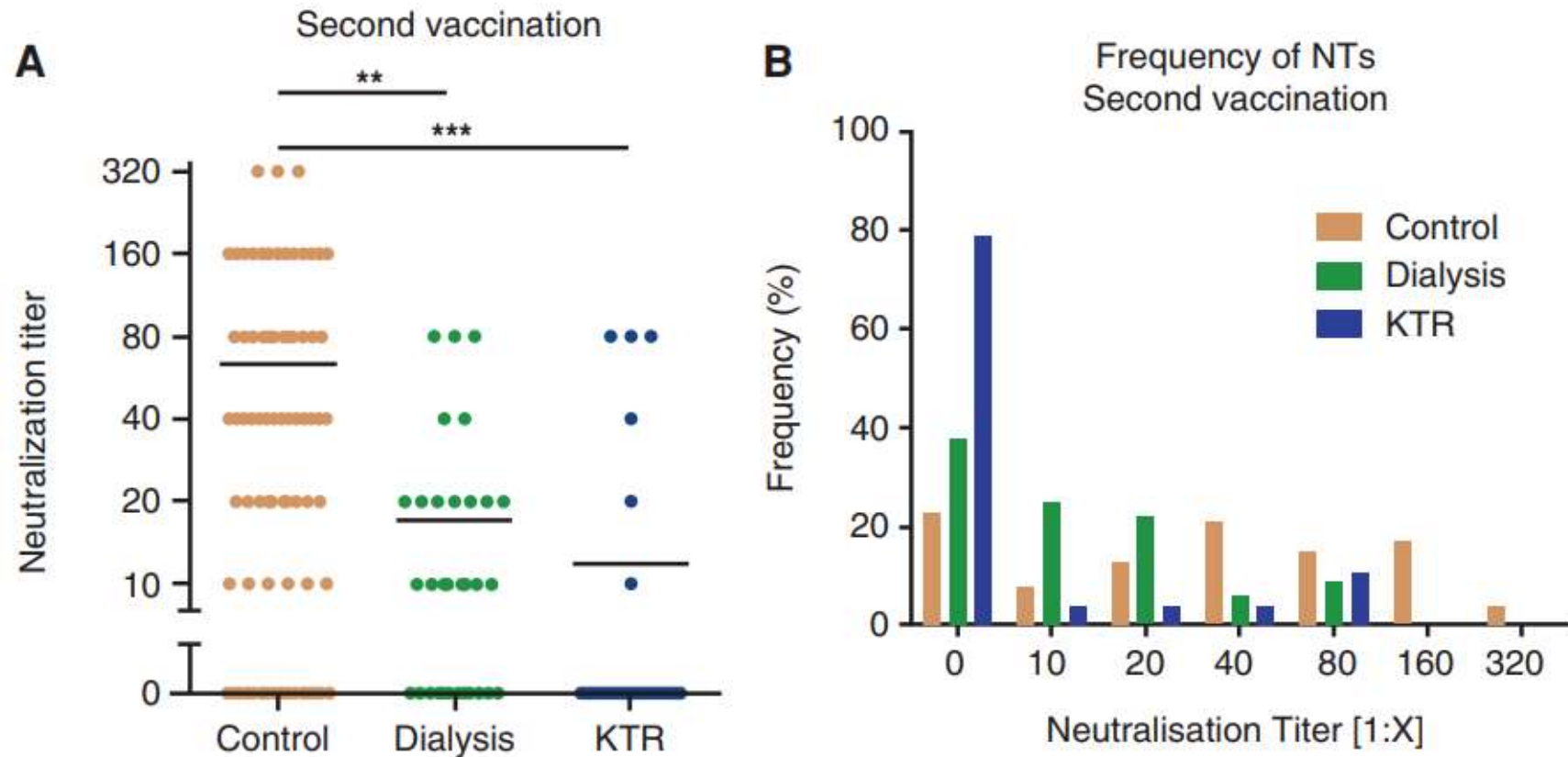


# 洗腎與腎移植病患:疫苗反應較差 (S抗體濃度)





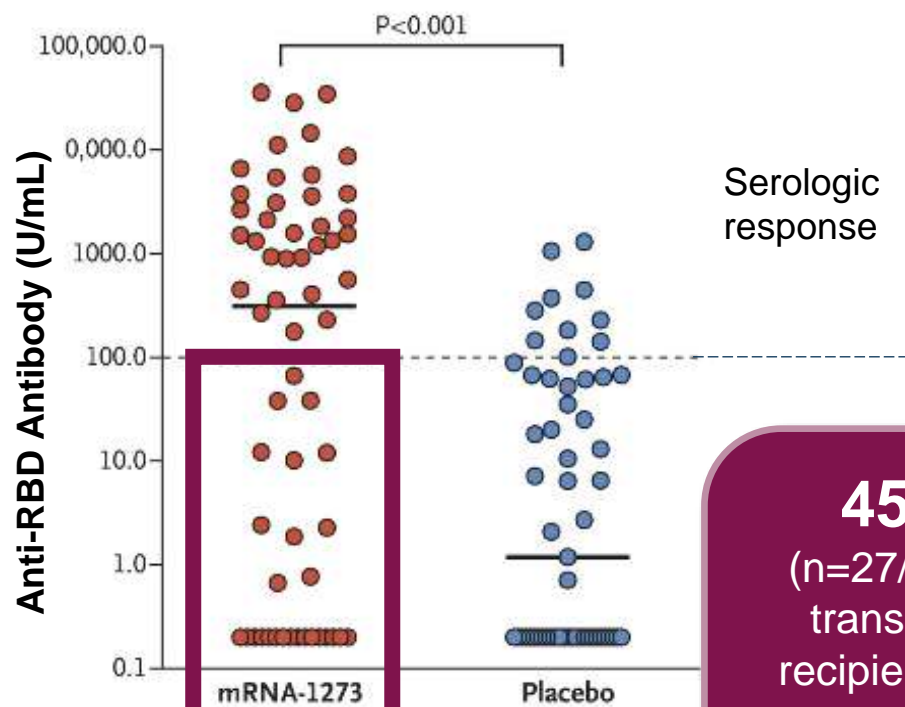
# 洗腎與腎移植病患:疫苗反應較差 (中和抗體濃度)



# 器官移植者接受第三劑 約50%能達到足夠抗體濃度

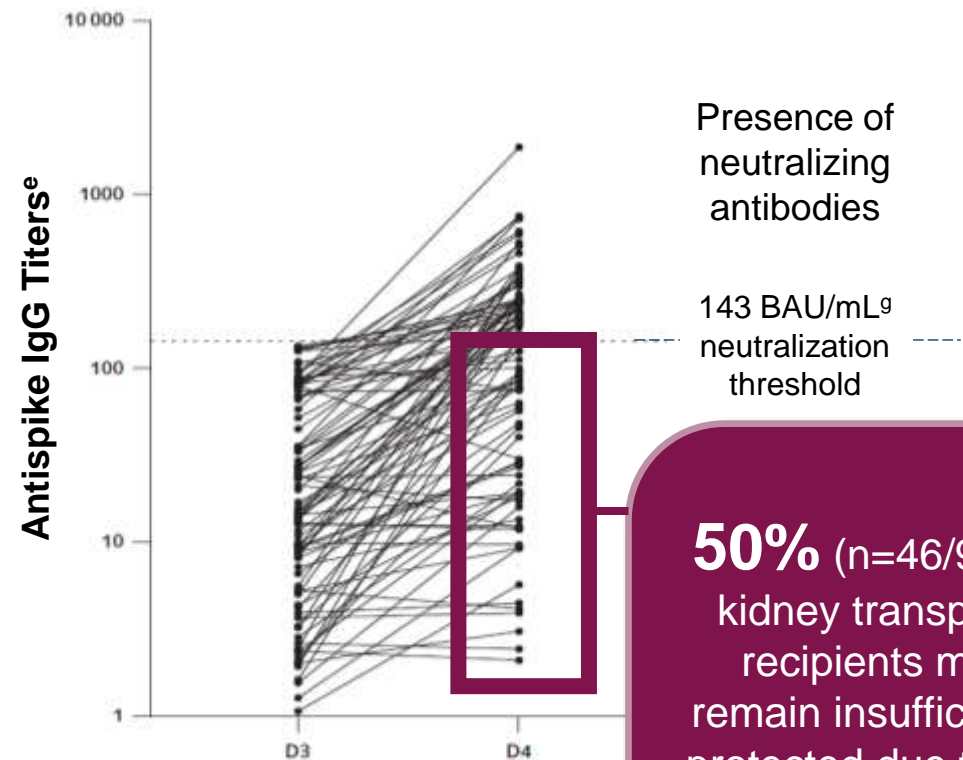


Antibody levels after third dose of mRNA vaccine<sup>a</sup>  
in transplant recipients<sup>1,b,c</sup>



**45%**  
(n=27/60) of  
transplant  
recipients did  
not mount an  
optimal immune  
response<sup>d</sup> **after  
the third dose**

Antibody levels after a third and fourth mRNA vaccine<sup>f</sup> doses  
in kidney transplant recipients<sup>2</sup>



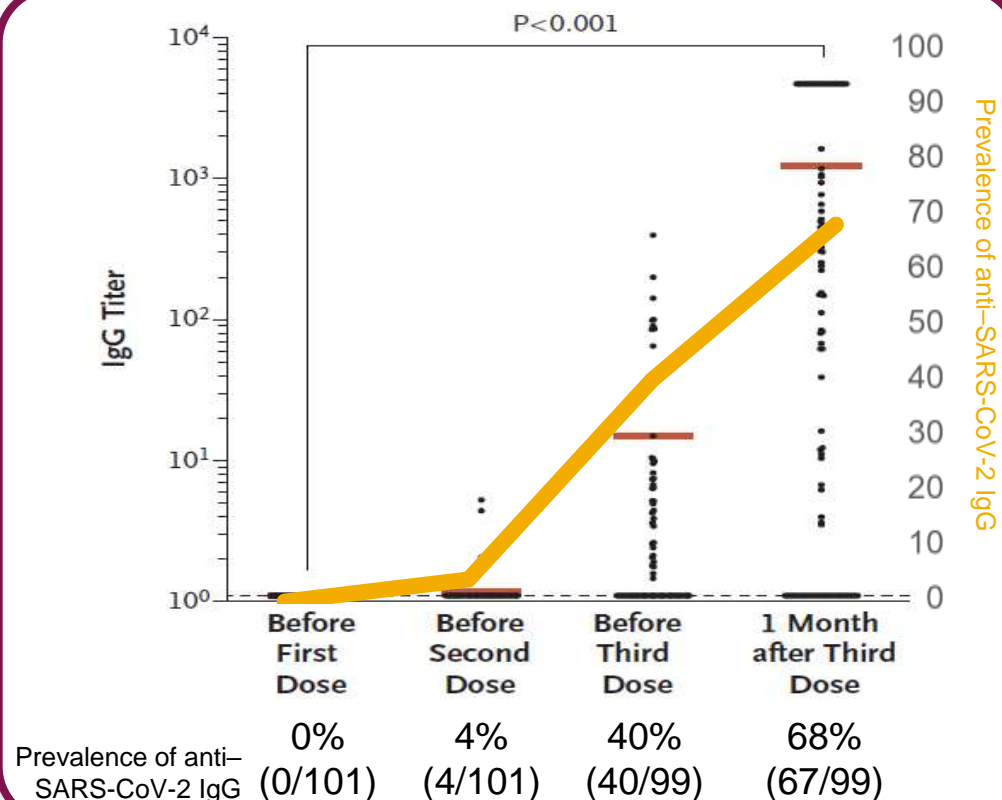
**50%** (n=46/92) of  
kidney transplant  
recipients may  
remain insufficiently  
protected due to low  
antispike IgG titers

1. Hall VG et al. *N Engl J Med*. 2021;385:1244-1246.
2. 2. Caillard S et al. *Ann Intern Med*. 2022.

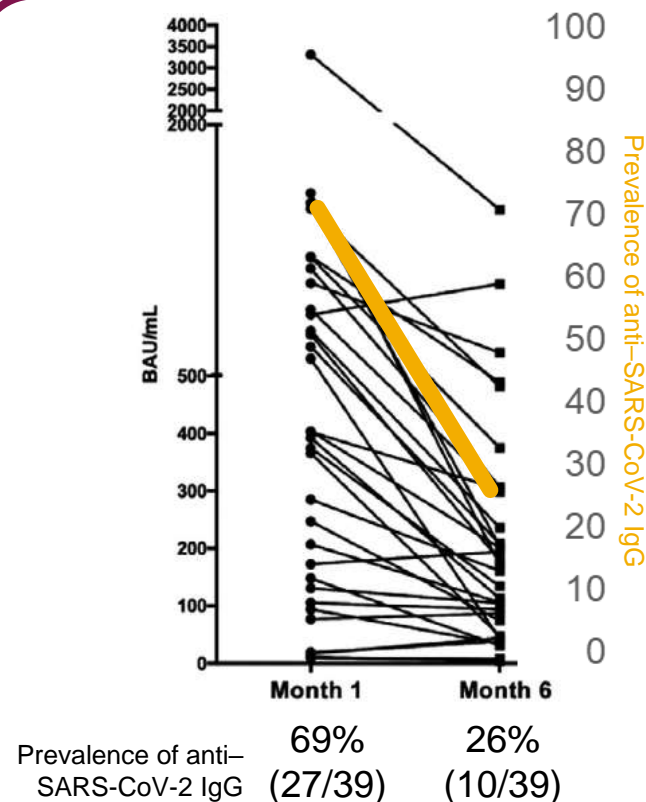


# 免疫功能低下者對疫苗的反應較差，抗體效價較快的速度較快

After the 3<sup>rd</sup> dose, SOT patients show an immune response<sup>1,a-c</sup>



SOT seropositive<sup>d</sup> individuals showed a decline over time<sup>2</sup>



**63.8%**

Median decrease in  
IgG titers within SOT  
responders  
(Month 1 vs. 6)

<sup>a</sup>The group included 78 kidney-transplant recipients, 12 liver-transplant recipients, 8 lung-transplant or heart-transplant recipients, and 3 pancreas-transplant recipients;

<sup>b</sup>The first two doses were given 1 month apart, and the third dose was administered 61±1 days after the second dose; <sup>c</sup>Patients received BNT162b2;

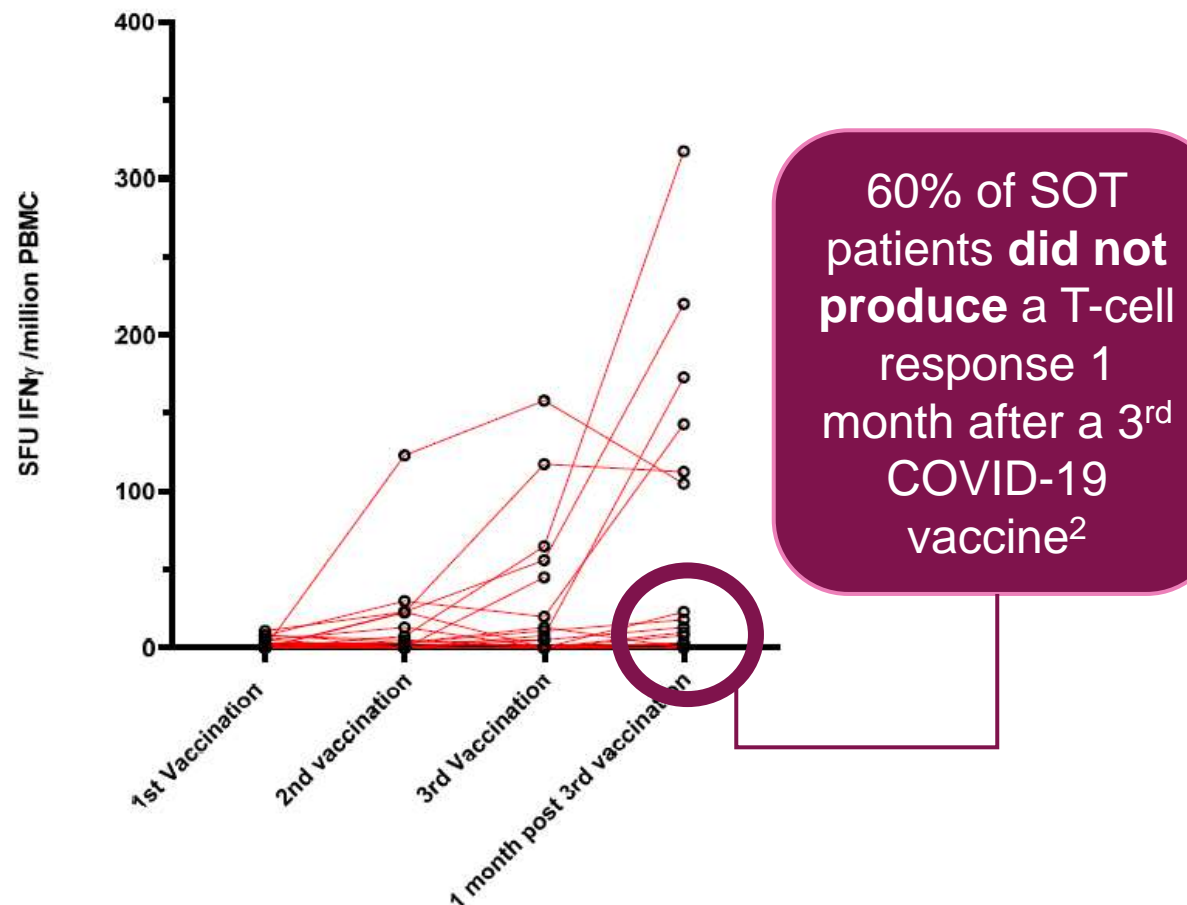
<sup>d</sup>Had immune response 1 month after the third dose. BAU = binding antibody units; COVID-19 = coronavirus disease 2019; IgG = immunoglobulin G; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SOT = solid-organ transplant.

1. Kamar N et al. *N Engl J Med.* 2021;385:661-662; 2. Bertrand D et al. Online ahead of print. *Am J Transplant.* 2022



# 免疫功能低下者:T細胞免疫反應較差

Immunocompromised (SOT) patients produce a low cellular immune response after COVID-19 vaccination<sup>2</sup>

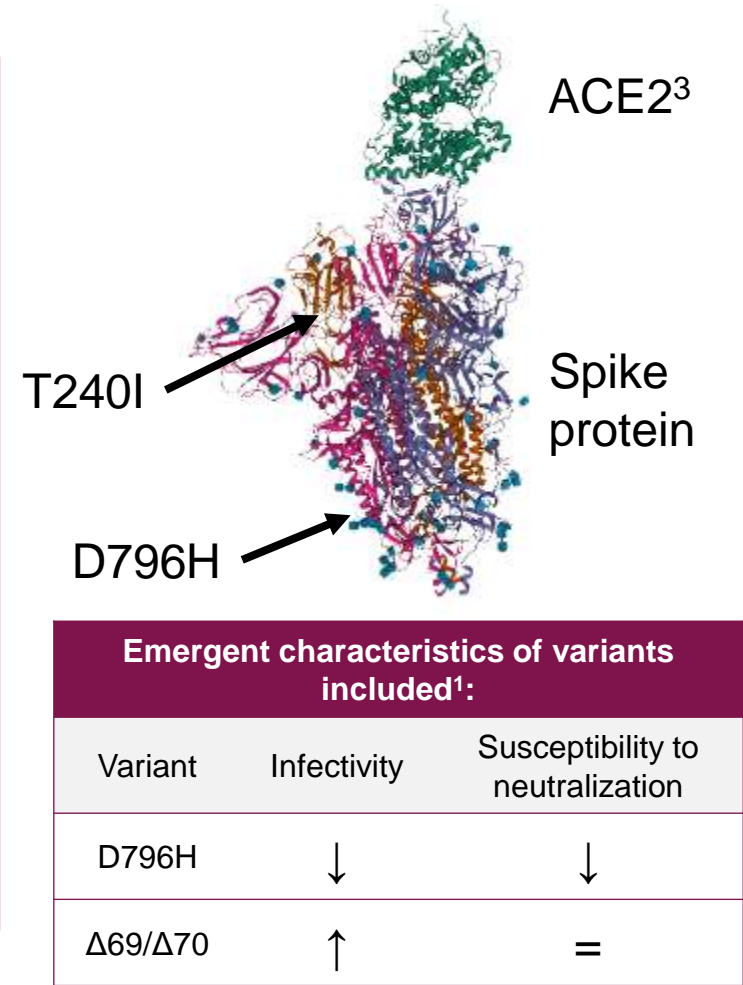
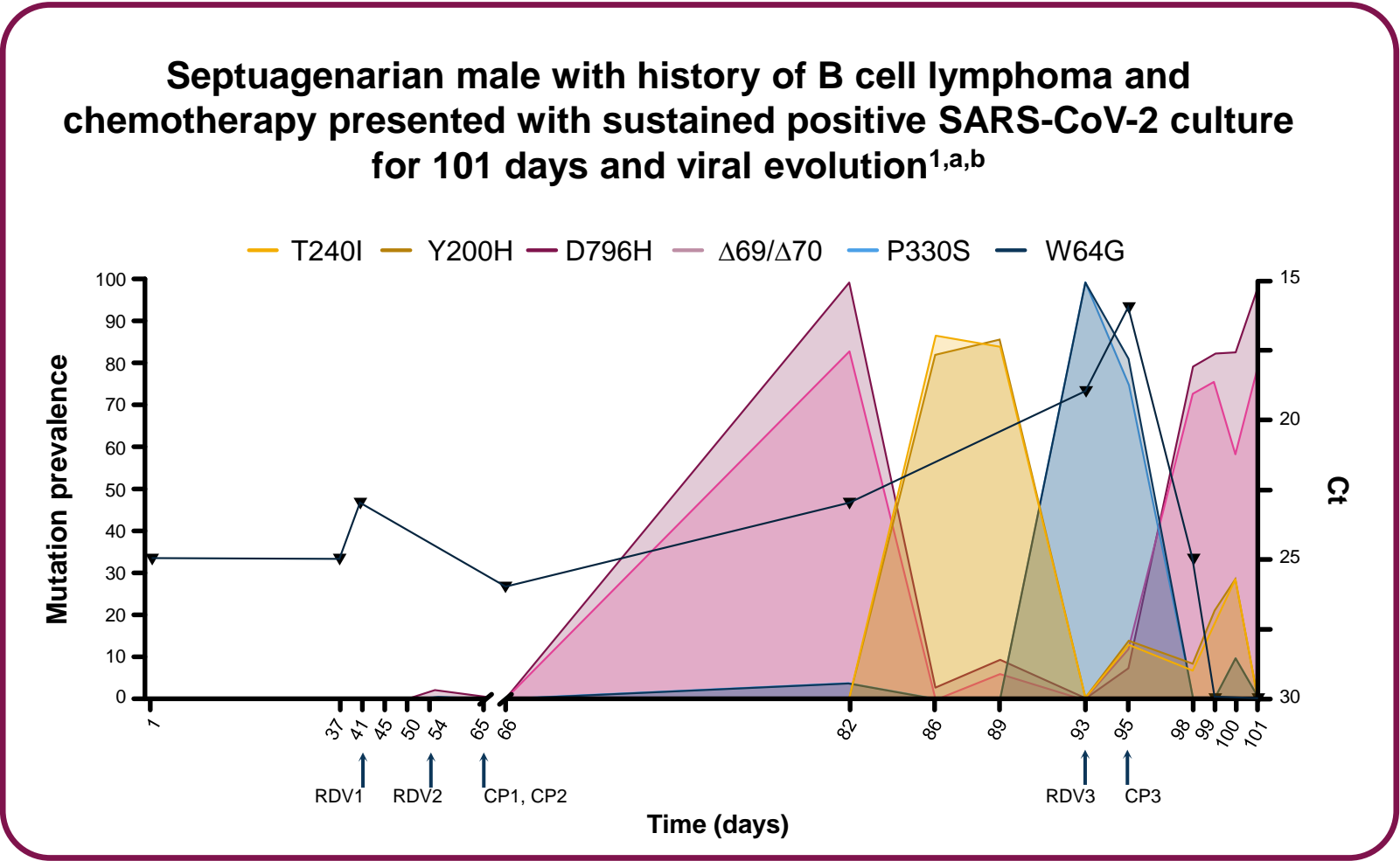


器官移植者接受3劑疫苗仍有60%無法產生細胞免疫





# 免疫功能低下者Prolonged Infection 可能導致變種



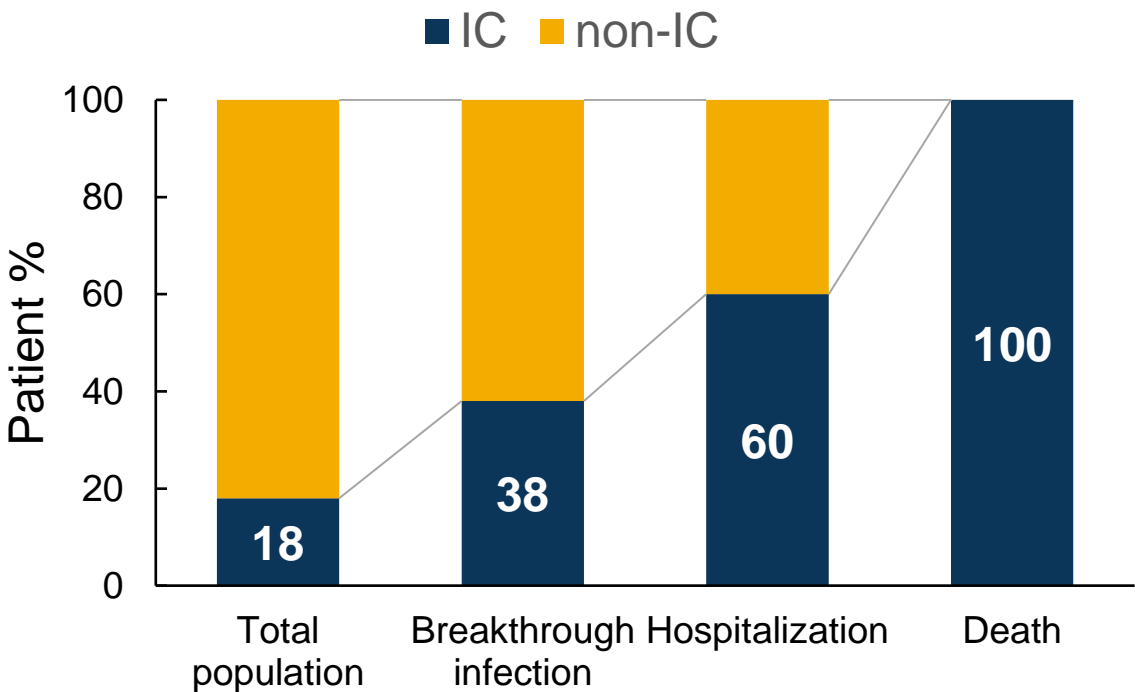
<sup>a</sup>Quantitative real-time polymerase chain reaction<sup>1</sup>; <sup>b</sup>Patient was likely not vaccinated due to the date of the CDC EUA of the Pfizer vaccine compared to when the patient was hospitalized.<sup>4</sup>  
CDC = Centers for Disease Control and Prevention; Ct = cycle threshold; CP = convalescent plasma; EUA = Emergency Use Authorization; RDV = remdesivir; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.  
1. Kemp SA et al. *Nature*. 2021;592:277-282; 2. Pfizer-BioNTech COVID-19 vaccine. <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine>. Accessed August 17, 2021; 3. 7DF4. <https://www.rcsb.org/structure/7DF4>. Accessed August 23, 2021.



# 免疫功能低下者突破性感染、住院、死亡較高



US HealthVerity database (12/10/2020-7/8/2021)  
N = 1,277,747



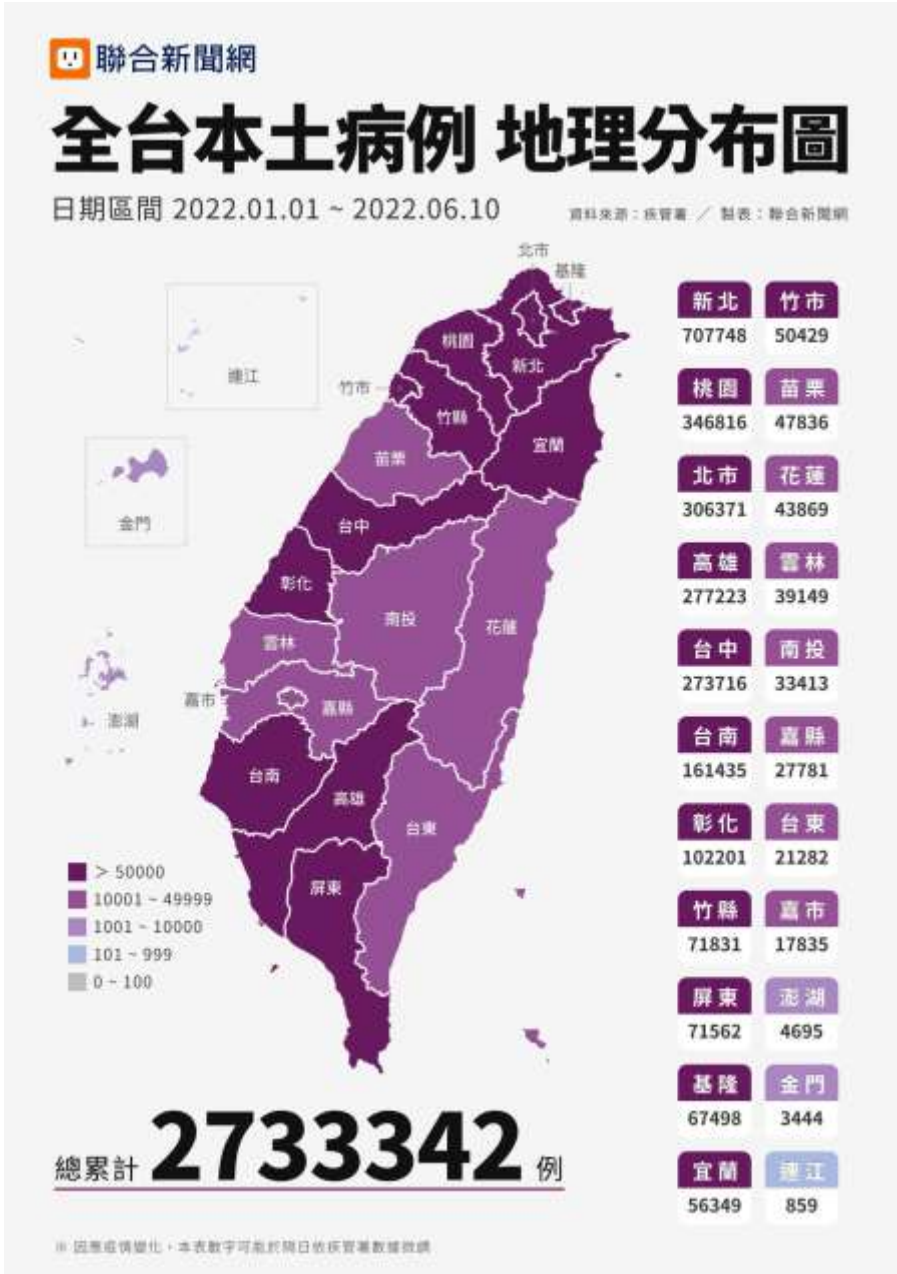
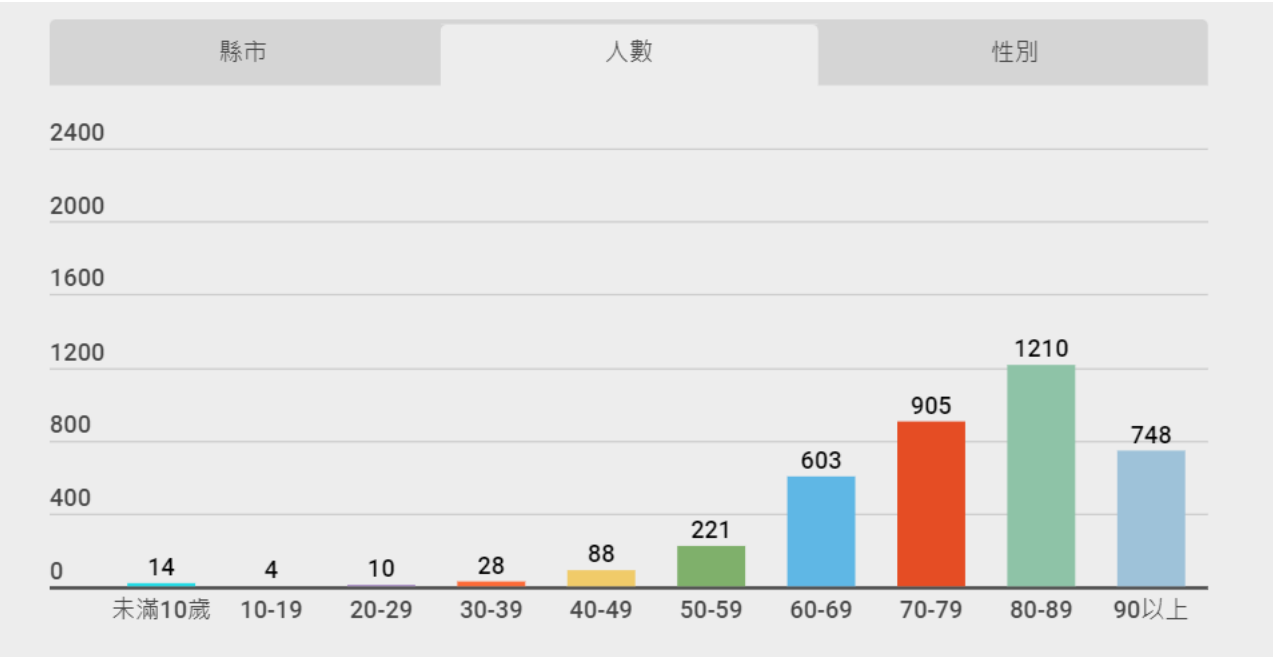
IC: immunocompromised  
Manuela Di Fusco et al. medRxiv preprint J Med Econ. Jan-Dec 2021;24(1):1248-1260

Population	IR per 100 person-year
Non-IC	0.34 (0.32-0.37)
IC	0.89 (0.80-0.98)
HIV/AIDS	0.71 (0.15-2.07)
Solid malignancy	0.56 (0.40-0.70)
Bone marrow transplant	0.00 (NA)
Organ transplant	3.66 (1.19-8.54)
Rheumatologic condition	0.82 (0.62-1.06)
Primary Immunodeficiency	1.13 (0.45-2.33)
Other immune condition	0.27 (0.03-0.99)
CKD or ESRD	0.95 (0.75-1.19)
Hematological malignancy	1.09 (0.30-2.80)
IS medication usage ≥ 14 Days	0.48 (0.28-0.76)
antimetabolite usage ≥ 14 Days	1.48 (0.18-5.35)
> 1 IC condition	1.70 (1.41-2.03)

2.6X

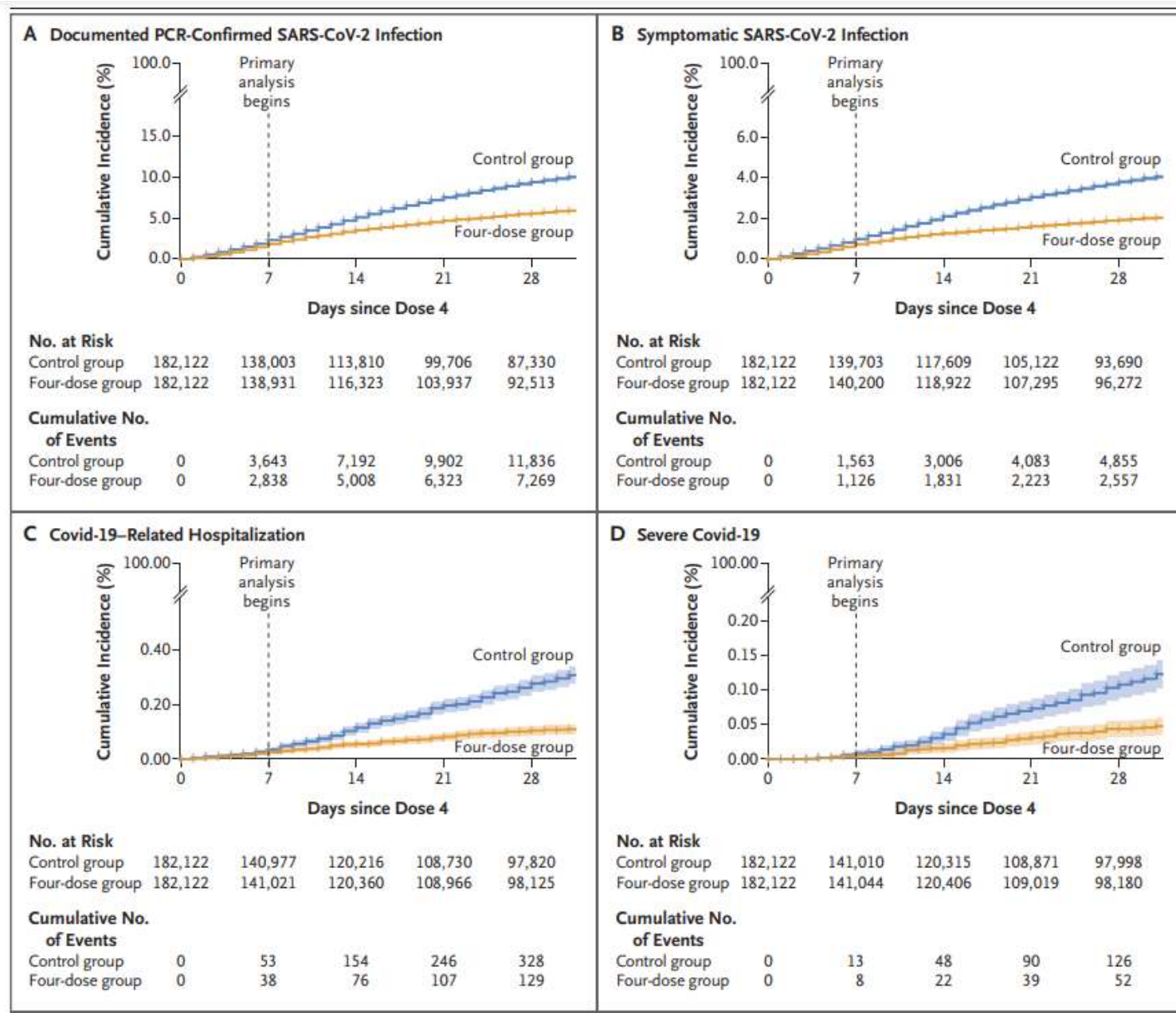
# 台灣疫情地圖、死亡人數

至2022.6.11  
累計死亡人數4008



# 第4劑?

- Age > 60
- 4<sup>th</sup> dose (BNT) at least 4 months after 3<sup>rd</sup> dose
- 182,122 (4 dose) VS 44,362 (control)
- 第4劑有效降低染病、住院及嚴重個案!





# 死亡與使用呼吸器之新冠突破感染病患： 40.1% 免疫功能低下



Characteristic	COVID-19 test-negative controls, no. (%) (n = 6,104)	Case patients with IMV or death, no. (%)		P-value <sup>†</sup>
		Vaccinated (n = 307)	Unvaccinated (n = 1,133)	
Age, median, yrs (IQR)	63 (50–72)	69 (60–77)	55 (42–66)	<0.001
LTCF resident, <sup>¶</sup> no./total no. (%)	330/5,920 (5.6)	32/284 (11.3)	20/1,023 (2.0)	<0.001
One or more previous hospitalizations in the last year, no./total no. (%)	3,097/5,674 (54.6)	125/284 (44.0)	217/975 (22.3)	<0.001
Immunocompromising condition, no./total no.	1,504 (24.6)	123 (40.1) <b>40.1%</b>	109 (9.6)	<0.001
Among immunocompetent, no. of chronic medical condition types, median (IQR)	2 (1–3)	2 (1.5–3)	1 (0–2)	<0.001
<b>Specific categories of conditions</b>				
Chronic cardiovascular disease	4,246 (69.6)	252 (82.1)	571 (50.4)	<0.001
Chronic pulmonary disease	2,016 (33.0)	91 (29.6)	213 (18.8)	<0.001
Diabetes mellitus	1,991 (32.6)	140 (45.6)	323 (28.5)	<0.001

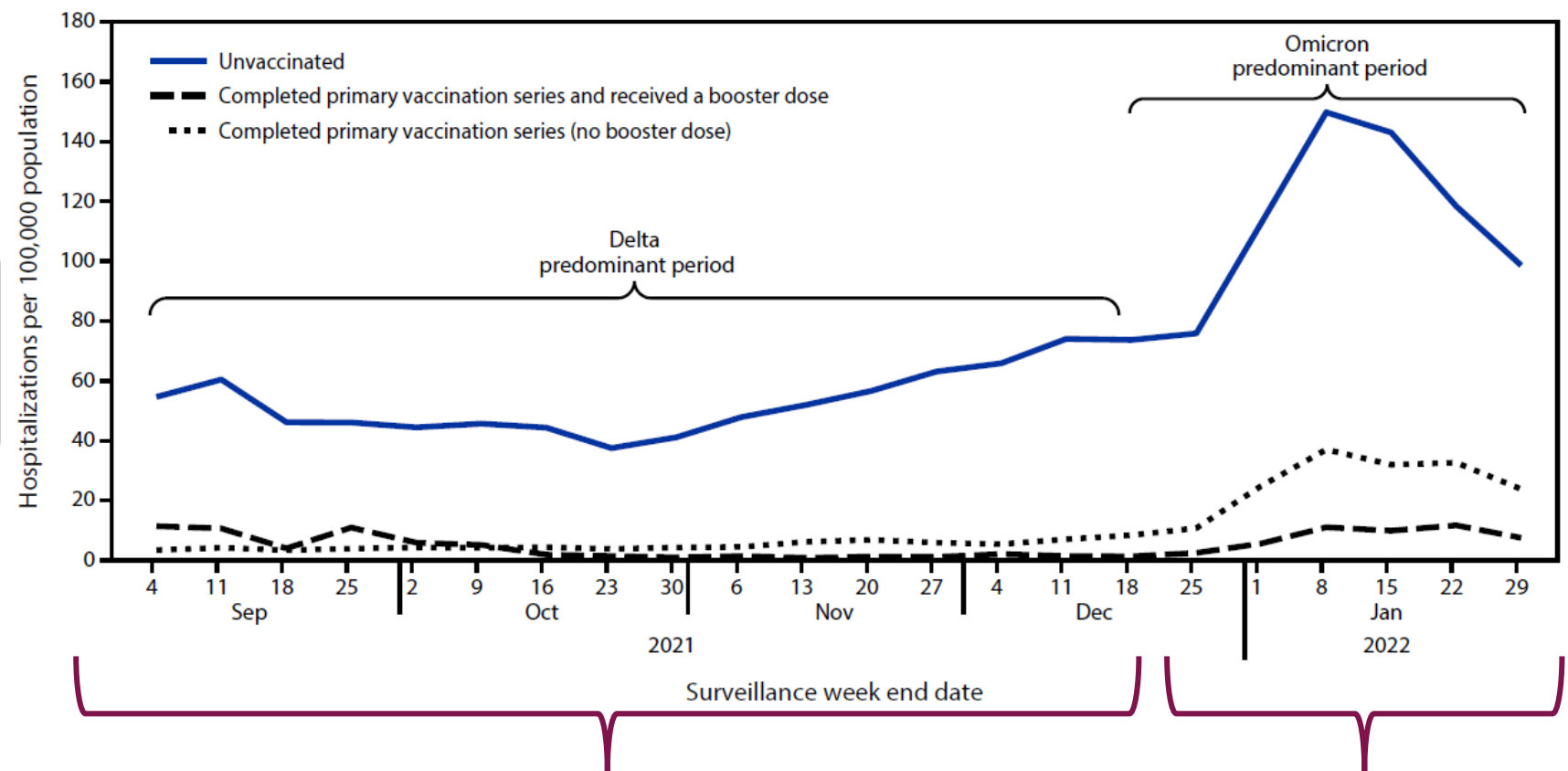
Group/Characteristic	No. of vaccinated case-patients with IMV or death/ total no. of case-patients (%)	No. of vaccinated control-patients/ total no. of control-patients (%)	Vaccine effectiveness, % (95% CI)
<b>Health status</b>			
Immunocompromised	123/232 (53.0)	1,090/1,504 (72.5)	74 (64–81)
Immunocompetent	184/1,208 (15.2)	2,930/4,600 (63.7)	92 (91–94)

**Vaccine effectiveness**  
IC vs Normal  
**74% vs 92%**



# 無論delta或omicron 免疫低下都是突破性感染住院高風險

What proportion of hospitalized patients are immunocompromised?



44.7% of 3 doses vaccinated patients were immunosuppressed

69.5% of 3 doses vaccinated patients were immunosuppressed

<sup>a</sup>Includes current treatment of recent diagnosis of an immunosuppressive condition or use of an immunosuppressive therapy during the preceding 12 months.  
1. Taylor CA et al. *MMWR Morb Mortal Wkly Rep.* 2022;71:466-472.



# 免疫功能低下者即便注射疫苗仍是嚴重新冠、死亡的高風險

Although all fully vaccinated people remain at risk of COVID-19<sup>a</sup>, the immunocompromised are at greater risk of adverse outcomes<sup>1</sup>

Among patients hospitalized for COVID-19, immunocompromised individuals are<sup>2,3,b</sup>

**3X**

more require  
hospitalization

**1.5X**

more likely to  
need ICU care

**2X**

more likely to need  
vasopressor  
support

**2X**

more likely  
to die

<sup>a</sup>There is an estimated <1% rate of hospitalizations in the fully vaccinated overall population<sup>3</sup>; <sup>b</sup>A retrospective study of SOT patients (n=128) and non-SOT controls (n=3907) who had been hospitalised for COVID-19.<sup>2</sup> Some of the information provided is based off a preprint research paper that has not been peer reviewed. COVID-19 = coronavirus disease 2019; ICU = intensive care unit.

1. Embi PJ et al. *MMWR Morb Mortal Wkly Rep.* 2021;70:1553-1559; 2. Fisher AM et al. *Clin Transplant.* 2021;35:e14216; 3. Kates J et al. COVID-19 vaccine breakthrough cases: data from the states.

<https://www.kff.org/policy-watch/covid-19-vaccine-breakthrough-cases-data-from-the-states/>. Accessed December 1, 2021; 3. Suleyman G, et al. *Open Forum Infect Dis*

. 2022 Mar 7;9(5).



# 面對COVID大流行的威脅免疫低下族群的挑戰!



**Immunocompromised (IC) people** are not able to **mount a good enough immune response against COVID-19, even after** vaccination

- Despite availability of vaccines, immunocompromised (IC) populations remain at risk of COVID-19
- IC individuals show a reduced response to COVID-19 vaccine (decreased seroconversion)
  - Different immunosuppressive therapies and specific hematological cancers reduce seroconversion even further
- Even with booster doses ~50% of certain immunocompromised individuals may still not be protected against COVID-19

The immune response in IC is **affected in terms of quantity, quality and durability**

- 1.2-23X lower antibody levels compared to healthy people
- To have the same neutralization activity against SARS-CoV-2 as healthy controls, IC populations require 64X more serum
- Antibodies responses decline twice as fast in IC versus healthy individuals
- 60% of IC patients (SOT) did not produce a T-cell response 1 month after a 3rd COVID-19 vaccine



**IC people tend to harbour new variants**, as the immune system is not strong enough to kill the virus and it often takes months to clear the virus, enabling it to escape, and posing a potential public health risk.



These IC populations **represent 2% of the total population**, yet **account for over 40%** of vaccinated patients hospitalized **breakthrough cases** of COVID-19



IC populations are **2X more likely to die** and up to **3X more likely** to be **hospitalized** due to COVID-19; resulting in **significant morbidity/mortality and societal burden, even when vaccinated**

## ***Clinical Profile of Target Patient***

- *Blood Cancer & Active Chemo Patients*
- *Transplant*
- *Taking Immunosuppressants*
- *Dialysis/Chronic Kidney Disease*
- *Primary Immune Deficiency*

# 完整接種COVID疫苗重要!

- 降低罹病率，使疫情不致於瞬間暴增
- 降低重症及死亡率，高齡者、免疫不全者的完整接種尤其重要
- 趕快施打，沒有來不及的議題

打好打滿!

## 疫苗3新措施 兒童就醫12指標

6-11歲

打莫德納

- 第1、2劑間隔  
4~8周
- 成人劑量1/2  
(50微克)
- 5月上旬開打

12-17歲

打第3劑

- 與第2劑  
間隔5個月
- 5月下旬開打，  
多集中在6月

高風險成人

打第4劑

- 與第3劑  
間隔5個月
- 6月上旬開打  
註/65歲以上、長照  
住民、免疫力低下

# 防疫新常態:做好個人防護

## 預防COVID-19(武漢肺炎)



保持手部清潔



定期量體溫



人多時戴口罩





# 盡快使用抗病毒藥物



## 即日起修訂未滿65歲口服抗病毒藥物適用條件

Paxlovid	莫納皮拉韋 (Molnupiravir)
輕度至中度未使用氧氣且發病5天之 12歲(含)以上且體重40(含)公斤以上 病人，並有下列任一情形者	輕度至中度未使用氧氣且於發病5天之18歲 (含)以上病人，有以下任一情形(不含懷孕)，且 無法使用其他建議藥物者
<ul style="list-style-type: none"><li>◆癌症 ◆糖尿病 ◆慢性腎病</li><li>◆心血管疾病(不含高血壓) ◆孕婦與產後6週內婦女(僅適用Paxlovid, 不適用莫納皮拉韋)</li><li>◆慢性肺疾 (間質性肺病、肺栓塞、肺高壓、氣管擴張、慢性阻塞性肺病)</li><li>◆結核病</li><li>◆慢性肝病 (肝硬化、非酒精性脂肪性肝炎、酒精性肝病與免疫性肝炎)</li><li>◆失能(注意力不足及過動症、腦性麻痺、先天性缺陷、 發展或學習障礙、脊髓損傷)</li><li>◆精神疾病(情緒障礙、思覺失調症)、失智症</li><li>◆BMI ≥ 30 (或12-17歲兒童青少年BMI 超過同齡第95百分位)</li><li>◆影響免疫功能之疾病(HIV感染、先天性免疫不全、實體器官或血液幹細胞移植、使用類固醇或 其他免疫抑制劑)</li></ul> <p>註：原列入重症高風險因子之「吸菸或已戒菸者」，即日起依專家會議決議自用藥條件移除，「吸菸或已戒菸者」須搭配任一其他風險因子，方符合用藥條件</p>	

目前尚無Paxlovid  
用於孕婦及產後婦  
女之臨床資料，若  
臨床醫師評估使用  
效益大於風險，經  
充分告知並獲同意  
後可使用。

2022/05/23

中央流行疫情指揮中心

# THE END!謝謝聆聽

Q&A

