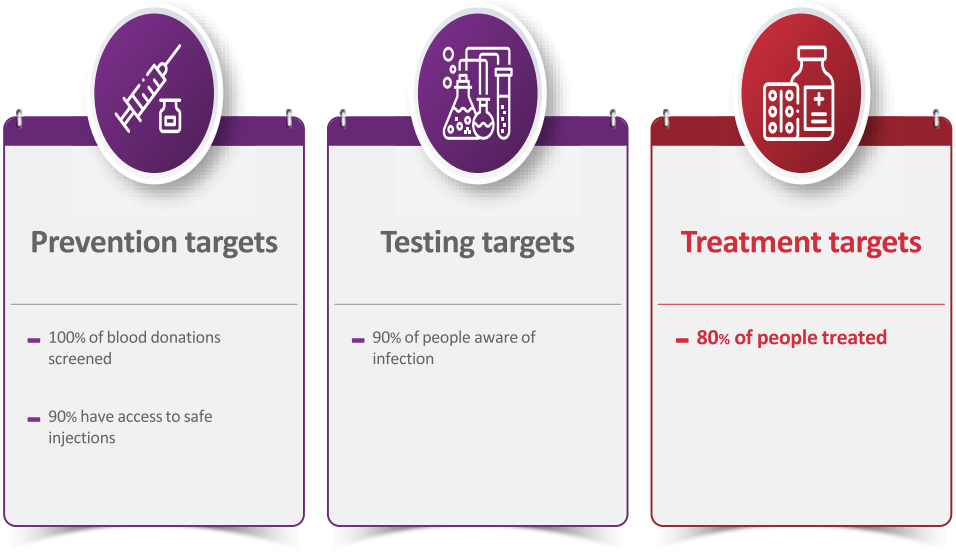
B型肝炎篩檢與治療的臨床實務

劉俊人

台大醫學院內科暨臨床醫學研究所、
台大醫院內科部暨肝炎研究中心

WHO 希望全球消滅 HBV & HCV（2030）



WHO. Global health sector strategy on viral hepatitis 2016–2021.
Available at: http://apps.who.int/iris/bitstream/10665/246177/1/WHO-HIV-2016.06-eng.pdf?ua=1 (accessed April 2018)

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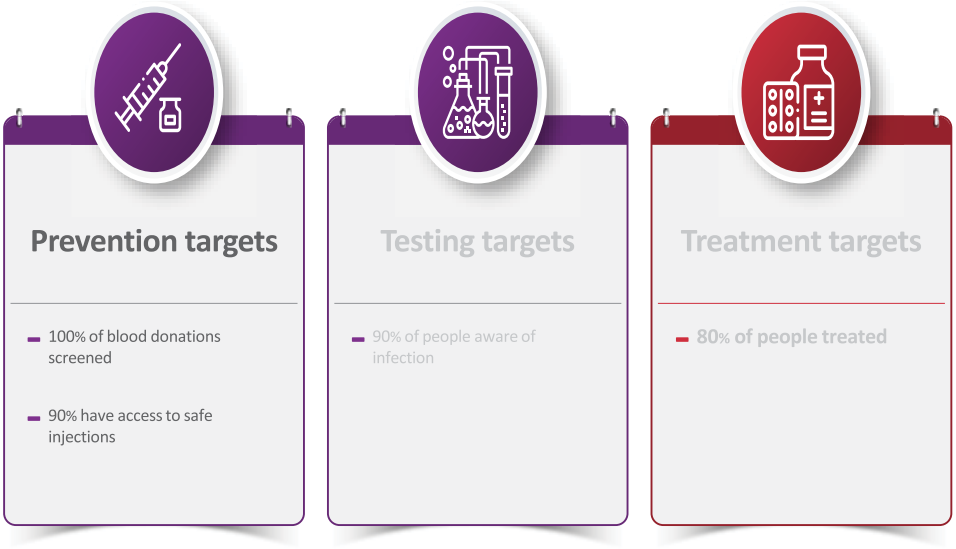
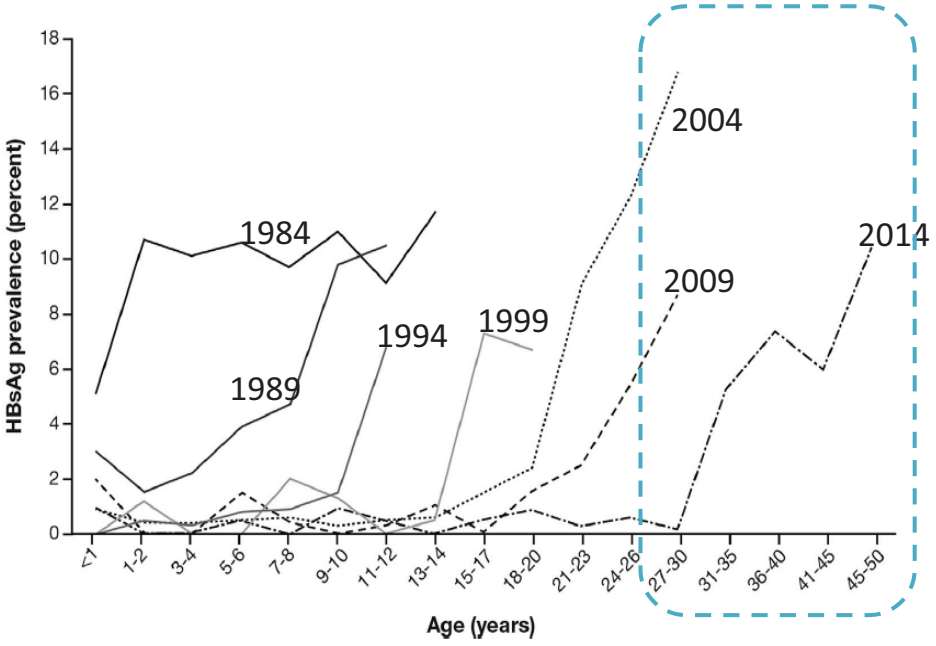


Eliminate viral hepatitis as a public health issue by 2030

WHO. Global health sector strategy on viral hepatitis 2016–2021.
Available at: http://apps.who.int/iris/bitstream/10665/246177/1/WHO-HIV-2016.06-eng.pdf?ua=1 (accessed April 2018)

臺灣經驗:30年疫苗注射計畫有效減少新世代B肝帶原者

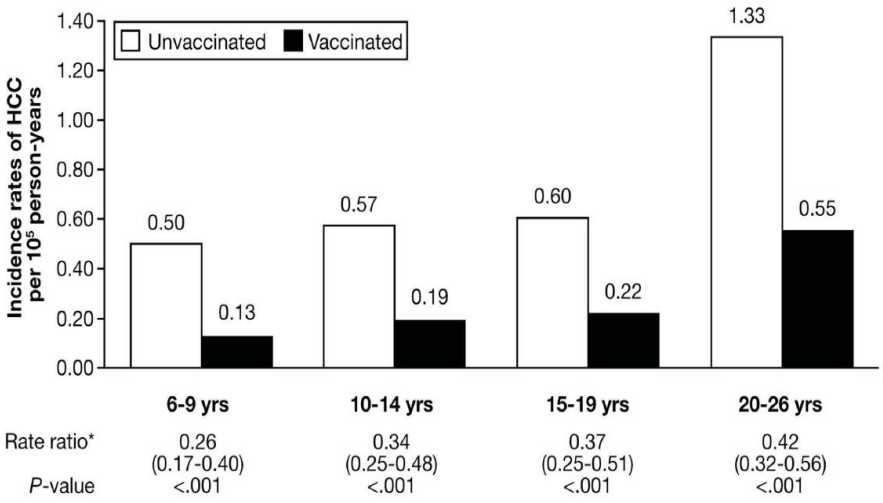
- 疫苗注射涵蓋率:97.7%
- B肝帶原率: 6.7% → 0.5%



YH Ni et al. Clin Gastroenterol Hepatol. 2016 Sep;14(9):1324-30.

臺灣經驗:30年疫苗注射計畫有效減少B肝相關肝細胞癌發生

Incidence for HCC by age for birth cohorts born before vs. after universal HBV vaccination program



	6-9 yrs	10-14 yrs	15-19 yrs	20-26 yrs
Rate ratio*	0.26 (0.17-0.40)	0.34 (0.25-0.48)	0.37 (0.25-0.51)	0.42 (0.32-0.56)
P-value	<.001	<.001	<.001	<.001

*Rate ratio of vaccinated/unvaccinated birth cohort

* Significant reduction in the incidence of HCC in vaccinated birth cohorts in all age groups between 6 and 26 years old.

Chang et al., NEJM 1997; Chang et al., JAMA 2000; Chang et al., JNCI 2009; Chang et a. Gastroenterology 2016.

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國人107年因肝病而死亡者

- 肝癌：8222人
- 慢性肝病及肝硬化：4554人

合計：約一萬三千人

內容

- 國人B型肝炎的篩檢與治療
  - 目前國內外篩檢防治B型肝炎的策略
  - 各種B型肝炎治療的優缺點與限制
  - 國內防治慢性病毒性肝炎的成效
    - 減少肝硬化和肝細胞癌
    - 改善存活
- 待解決的臨床議題
  - 停藥後的追蹤與再次治療
  - 臨床預測指標
- 結論與展望

如何知道自己有無肝病？

- 肝功能檢查
- B型肝炎檢驗
- C型肝炎檢驗
- 甲種胎兒蛋白檢查
- 腹部超音波檢查

免費健康檢查

年滿45-79歲民眾，終身1次B、C肝篩檢
別讓您的權益睡著

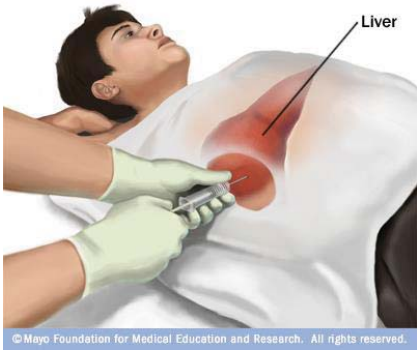
2020/9/28

- 國民健康署目前提供民國55年次或以後出生且滿45歲及年滿40至60歲具原住民身分的民眾，搭配成人預防保健終身可接受1次B、C型肝炎篩檢服務。
- 為配合國家消除C肝政策，業核定擴大放寬年滿45至79民眾，都可接受終身一次的B、C型肝炎篩檢服務，以早期發現、提供適當治療，避免演變為慢性肝病及肝硬化。

B型肝炎誰需要接受治療?

- 血清病毒濃度高
- 反覆發炎與修復：血清ALT異常
- 肝臟纖維化較嚴重：發炎越久，病程越嚴重
- 有機會自我免疫控制改善：觀察3~6個月

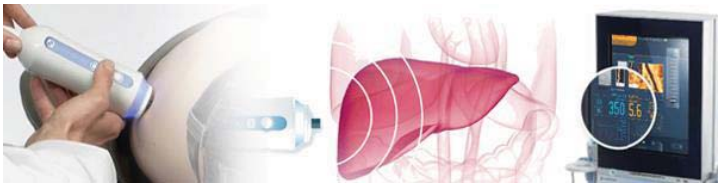
評估肝臟纖維化



- 肝穿刺 (Liver biopsy)
- 抽血檢驗 (Noninvasive tests)
  - APRI
  - FIB-4
  - Fibrotest
  - BioFibroScore
- 纖維檢測儀 (Elastography)
  - Transient elastography (Fibroscan®)
  - MR elastography
- ARFI

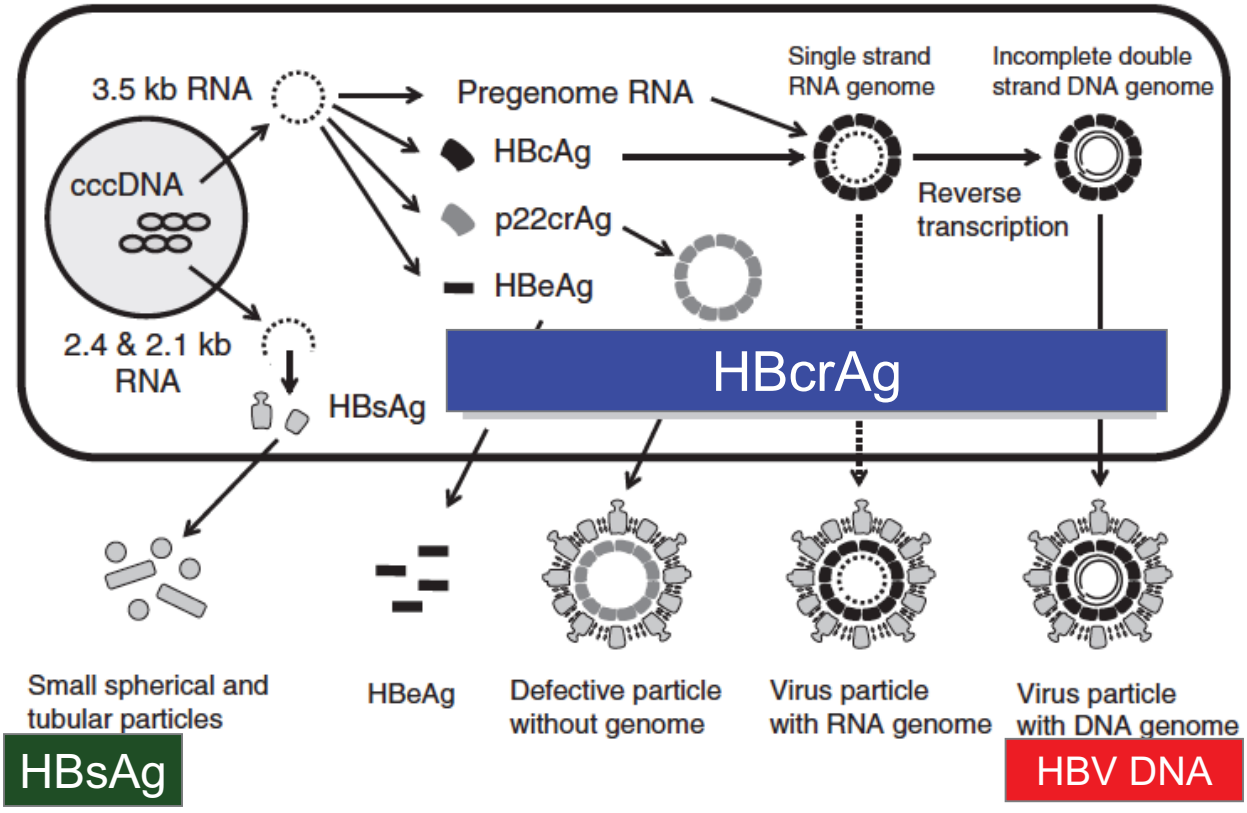
$$\text{APRI} = \frac{\frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelet Count } (10^9/\text{L})} \times 100$$

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count } (10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}}$$



B型肝炎患者發生肝細胞癌風險之預測標誌

HBV血清生物標誌

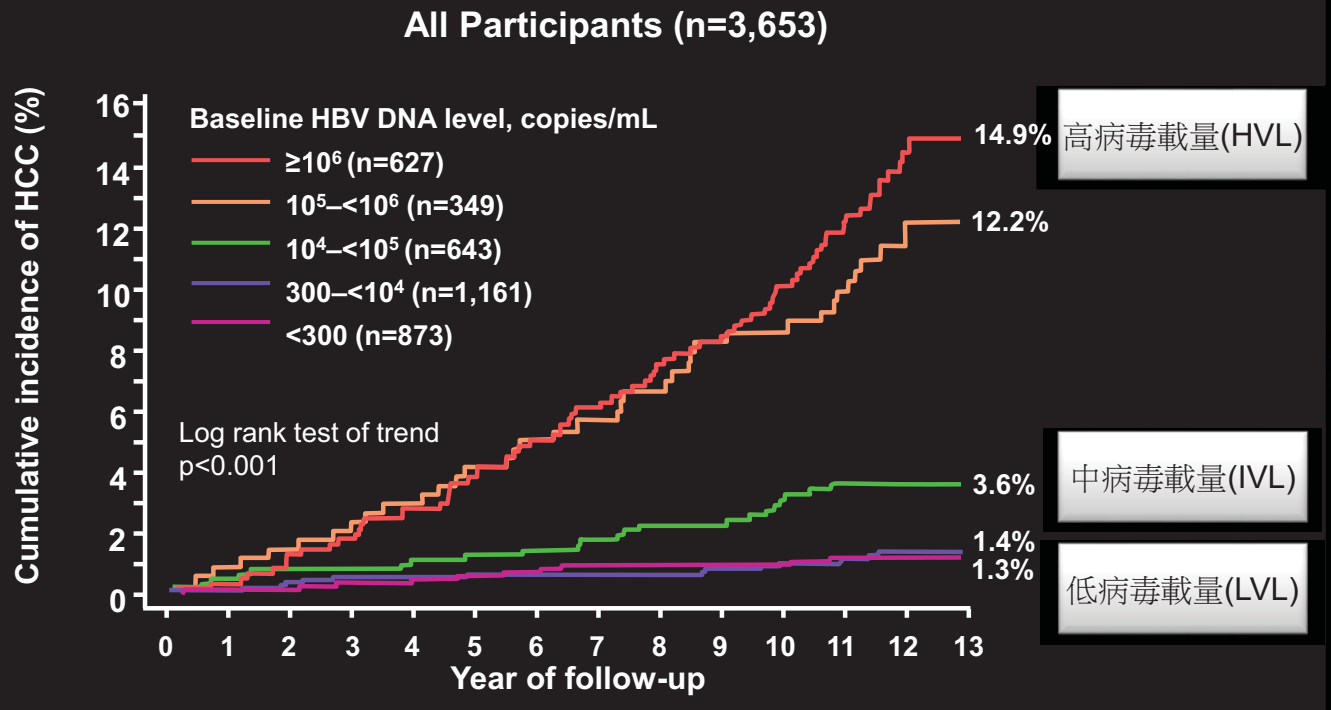


Modified from Tanaka et al. Hepatol Res 2013.

病毒量(HBV DNA)

- 直接代表病毒複製的情形
- 隨著感染的時間，會有自然的變化
  - 免疫耐受期、免疫清除期、不活動期、再活化期
- 高病毒量：長期肝硬化、肝癌的風險較高
- 目前高病毒量的定義
  - e抗原陽性： > 20,000 IU/mL
  - e抗原陰性：> 2,000 IU/mL
- 藥物治療的短期目標：病毒量消失

R.E.V.E.A.L.: 高病毒載量增加肝細胞癌風險



Chen et al. JAMA 2006; 2006;295:65.

肝癌風險計算機
(HCC Risk calculator)

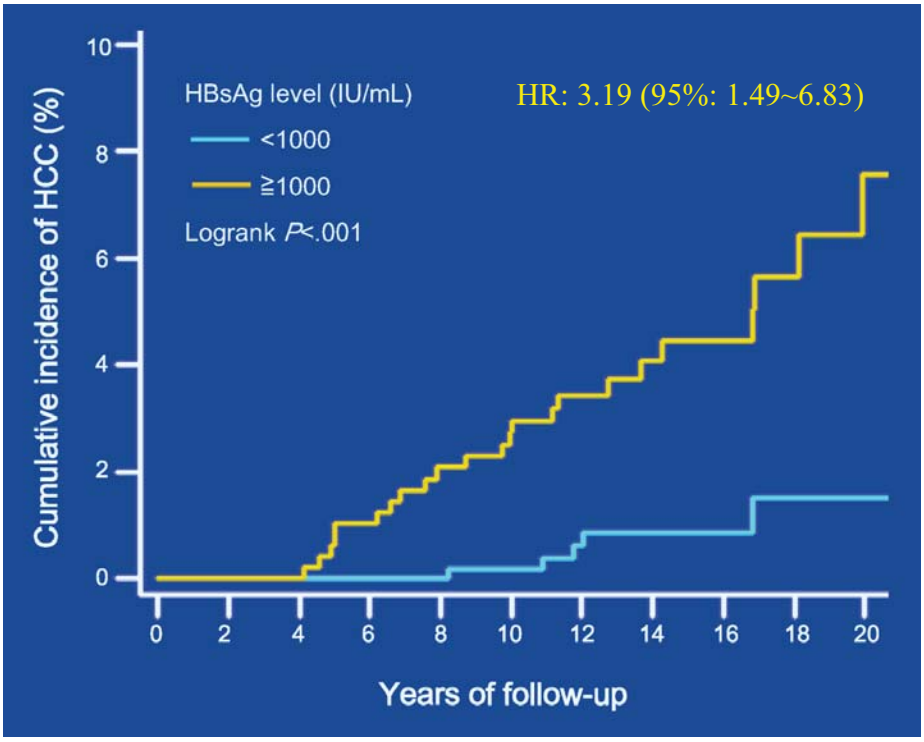
REACH-B HCC risk score developed using REVEAL cohort (n=3,584)

Risk predictor	Risk score
Gender	
Female	0
Male	2
Age	
30-34	0
35-39	1
40-44	2
45-49	3
50-54	4
55-59	5
60-65	6
ALT, U/L	
<15	0
15-44	1
≥45	2
HBeAg	
Negative	0
Positive	2
HBV DNA level, copies/mL	
<300 (Undetectable)	0
300-9999	0
10000-99999	3
100000-999999	5
≥10^6	4

Cumulative risk score	HCC risk		
	At 3rd year	At 5th year	At 10th year
0	0.0%	0.0%	0.0%
1	0.0%	0.0%	0.1%
2	0.0%	0.0%	0.1%
3	0.0%	0.1%	0.2%
4	0.0%	0.1%	0.3%
5	0.1%	0.2%	0.5%
6	0.1%	0.3%	0.7%
7	0.2%	0.5%	1.2%
8	0.3%	0.8%	2.0%
9	0.5%	1.2%	3.2%
10	0.9%	2.0%	5.2%
11	1.4%	3.3%	8.4%
12	2.3%	5.3%	13.4%
13	3.7%	8.5%	21.0%
14	6.0%	13.6%	32.0%
15	9.6%	21.3%	46.8%
16	15.2%	32.4%	64.4%
17	23.6%	47.4%	81.6%

Yang HI et al. *Lancet Oncol* 2011;12:568-574

HBeAg陰性而且病毒濃度<2000 IU/mL之1068位患者，HBsAg濃度協助預測肝細胞癌發生

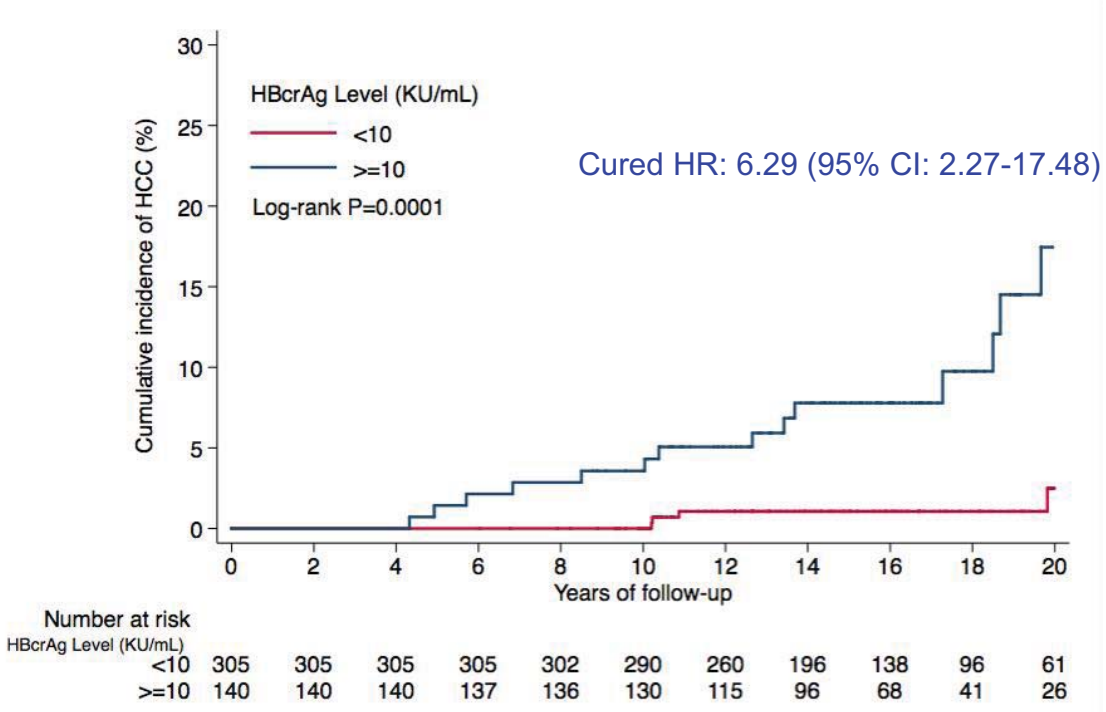


Tseng TC et al, Gastroenterology 2012;142:1140-9

HBcrAg的病毒學意義與臨床應用

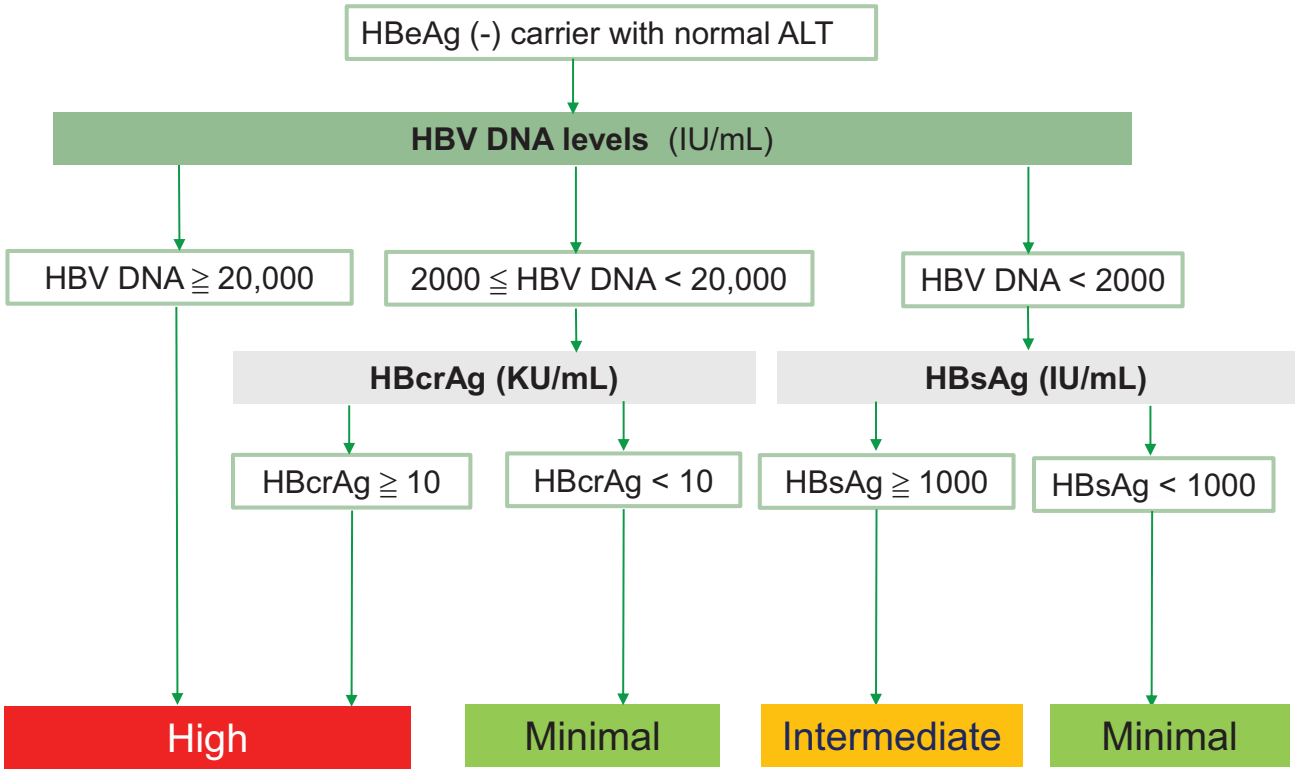
- HBcrAg由HBV前C/C區編碼的HBcAg、HBeAg與P22cr（22 kD precore protein）3種蛋白質組成（共用C基因編碼的*149*個胺基酸序列），其中P22cr是HBeAg 形成前的中間產物，包含從-28~*150*的胺基酸序列的一種前核心蛋白，但缺少C末端的精氨酸富集區域，常存在於空缺的、不含病毒核心的病毒顆粒中。

針對445 eAg^{neg} 患者屬於IVL+ALT<40 U/L時，HBcrAg可以分辨HCC之風險



Tseng TC et al, Gastroenterology. 2019 ;157:1518-1529

利用血清生物標誌預測預後



Tseng, Liu and Kao et al, Gastroenterology 2012 & 2019

慢性B型肝炎之治療目標

- 清除/壓抑病毒
  - ＊ 減少致病原
  - ＊ 減少傳染性
- 減少肝發炎壞死
  - ＊ 肝炎緩解（逆轉肝纖維化）
  - ＊ 預防肝衰竭
- 遏止病程進展
  - ＊ 減少急性發作，肝硬化和肝細胞癌
- 改善存活率

慢性B型肝炎之治療選擇

- 傳統型干擾素
- 長效型干擾素(Peginterferon alfa-2a)
  - 佩格西施(Pegasys)
- 干安能 (lamivudine)
- 干適能 (adefovir dipivoxil)
- 貝樂克 (entecavir)
- 喜必福 (telbivudine)
- 惠立妥 (Tenofovir disoproxil fumarate, TDF)
- 韋立得 (Tenofovir alafenamide, TAF)

抗病毒藥物的特性比較(1)

Treatment	Preferred	Notes
Entecavir	Yes	High potency, high genetic barrier to resistance
Tenofovir Alafenamide (TAF)	Yes	High potency, high genetic barrier to resistance, lower risk of kidney and bone adverse effects
Tenofovir (TDF)	Yes	High potency, high genetic barrier to resistance
PegIFN	Yes	Less safe in patients with cirrhosis, contraindicated in patients with decompensated cirrhosis
Adefovir	No	Low genetic barrier to resistance
Lamivudine	No	Low genetic barrier to resistance
Telbivudine	No	Low genetic barrier to resistance

Terrault. Hepatology. 2018;67:1560. www.aasld.org.
EASL. J Hepatol. 2017;67:370.

抗病毒藥物的特性比較(2)

Comparative Measure	ETV	TAF	TDF
Dose	0.5 mg/day	25 mg/day	300 mg/day
Presence of LAM resistance	Increase dose	Active	Active
Anticipated pregnancy	Pregnancy Category C	No human data in pregnancy	Pregnancy Category B
Renal disease	Decrease dose if CrCl < 50 mL/min	Decrease dose is not require	Decrease dose if CrCl < 50 mL/min
Bone disease	Recommended	Recommended	Recommended

Terrault. Hepatology. 2018;67:1560.

短期治療的療效指標與比較

第一線抗病毒藥物療效比較

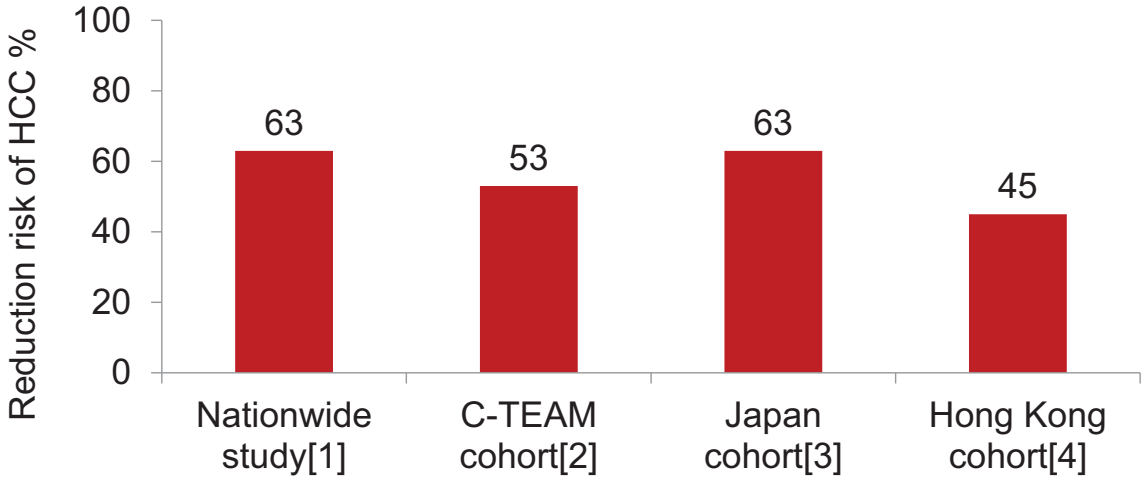
HBeAg Positive	Peg-IFN*	Entecavir†	Tenofovir Disoproxil Fumarate†	Tenofovir Alafenamide‡
% HBV-DNA suppression (cutoff to define HBV-DNA suppression)§	30-42 (<2,000-40,000 IU/mL) 8-14 (<80 IU/mL)	61 (<50-60 IU/mL)	76 (<60 IU/mL)	73 (<29 IU/mL)
% HBeAg loss	32-36	22-25	—	22
% HBeAg seroconversion	29-36	21-22	21	18
% Normalization ALT	34-52	68-81	68	—
% HBsAg loss	2-7 11 (at 3 years posttreatment)	4-5	8	1

HBeAg Negative	Peg-IFN	Entecavir	Tenofovir Disoproxil Fumarate†	Tenofovir Alafenamide‡
% HBV-DNA suppression (cutoff to define HBV-DNA suppression)‖	43 (<4,000 IU/mL) 19 (<80 IU/mL)	90-91 (<50-60 IU/mL)	93 (<60 U/mL)	90 (<29 IU/mL)
% Normalization ALT¶	59	78-88	76	81
% HBsAg loss	4 6 (at 3 years posttreatment)	0-1	0	<1

Terrault NA et al. Hepatology 2018

長期治療的好處

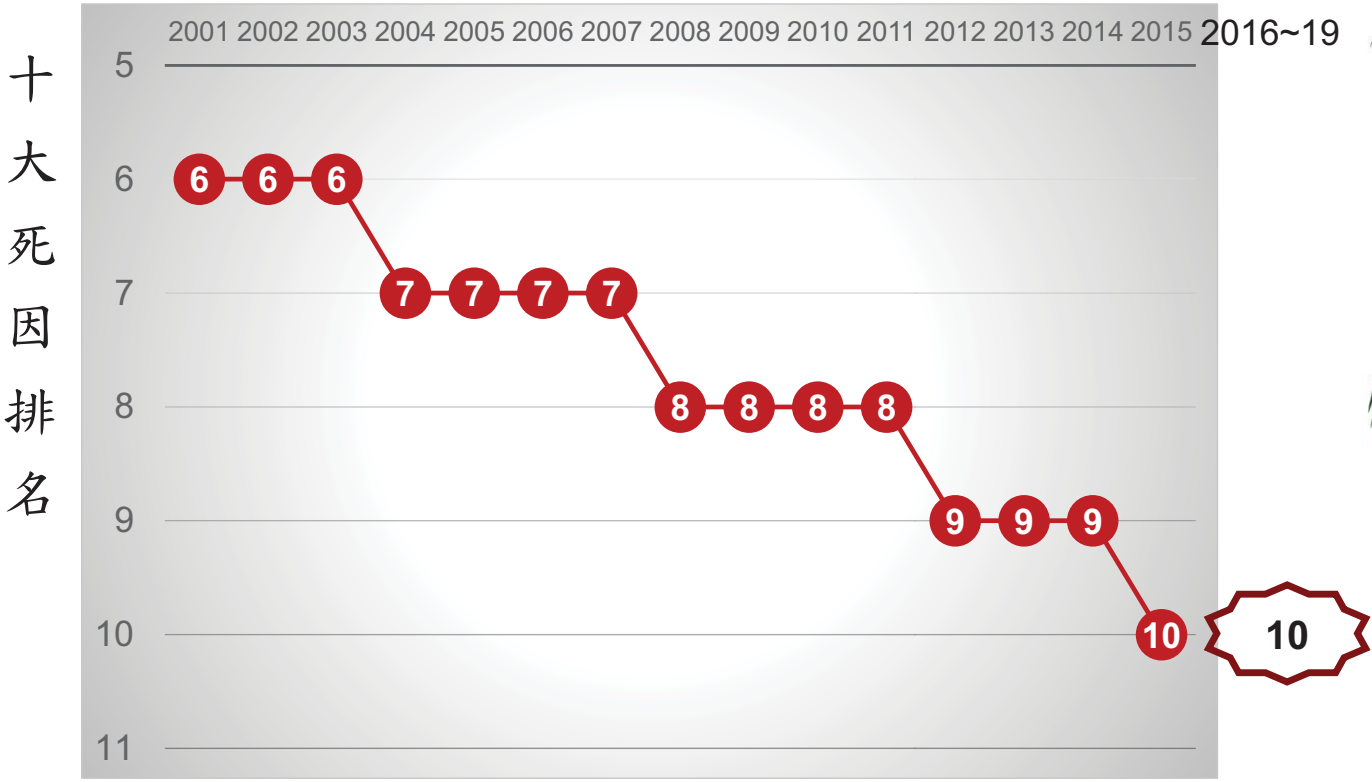
口服藥治療可以降低HCC發生率：亞太各國資料



Patients	CHB	Cirrhosis	CHB	Cirrhosis
Treated	21595	1315 (ETV)	316 (ETV)	482 (ETV)
Untreated	21595	503	316	69

1. Wu CY et al. JAMA 2012 (Propensity score matching study)
2. Su TH et al. Liver Int. 2016;36:1755
3. Hosaka et al. Hepatology 2013 (Propensity score matching study)
4. Wong et al. Hepatology 2013

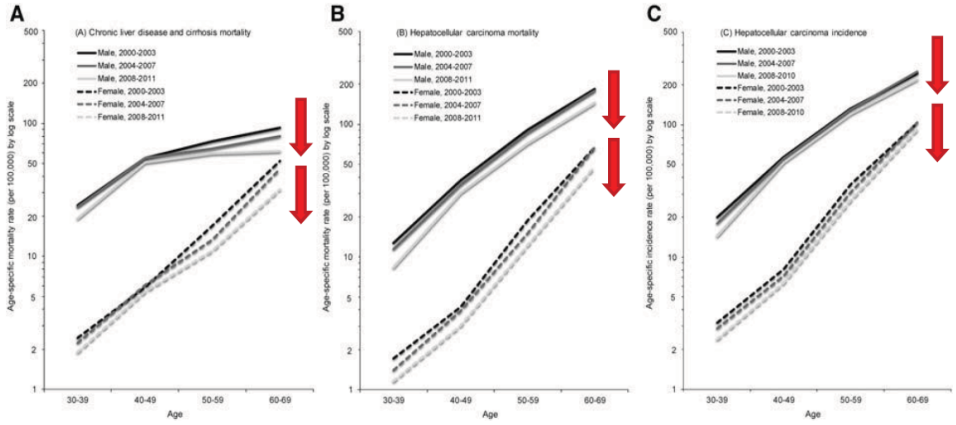
國人十大死因：慢性肝病排名逐年下降



衛福部統計處

國內健保給付治療B肝之長期療效:全國資料

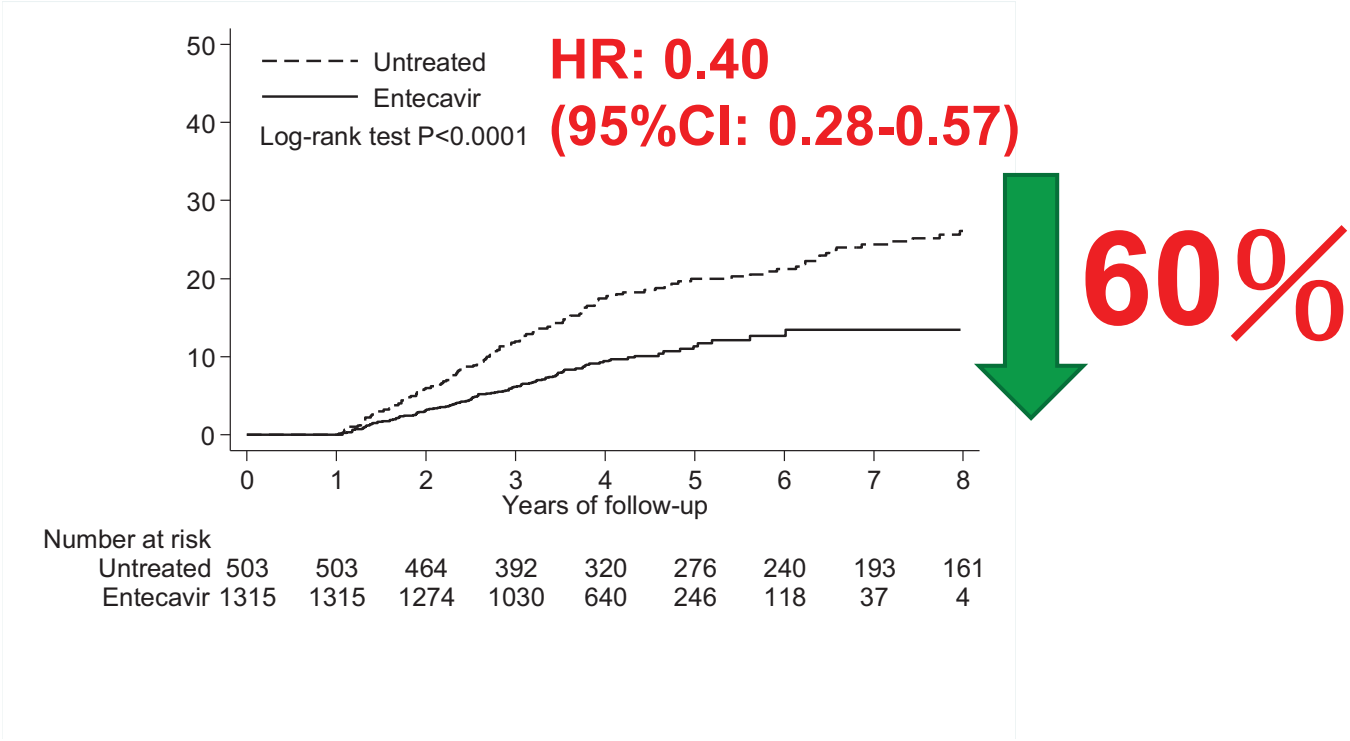
Age-sex-specific mortality and incidence rates before and after the launch of chronic viral hepatitis therapy program since October 2003 in Taiwan



Year	CLD Mortality	HCC Mortality	HCC Incidence
2000-2003	1.00 (referent)	1.00 (referent)	1.00 (referent)
2004-2007	0.92 (0.90-0.94)	0.95 (0.93-0.97)	0.98 (0.96-0.99)
2008-2011	0.78 (0.76-0.80)	0.76 (0.75-0.78)	0.86 (0.85-0.88)

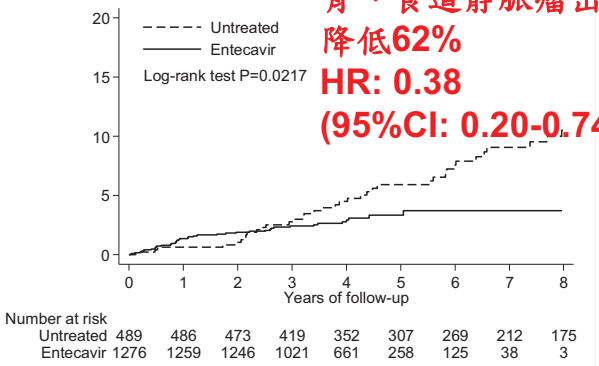
Chiang CJ et al. Hepatology 2015

長期抗病毒藥物治療降低6成肝硬化患者之肝癌發生率：多中心觀察

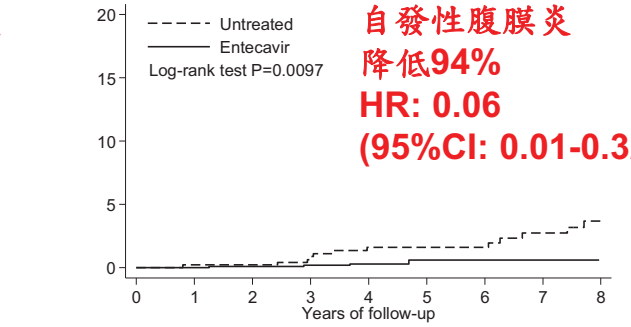


Su and Kao et al., Liver Int. 2016 Dec;36(12):1755-1764

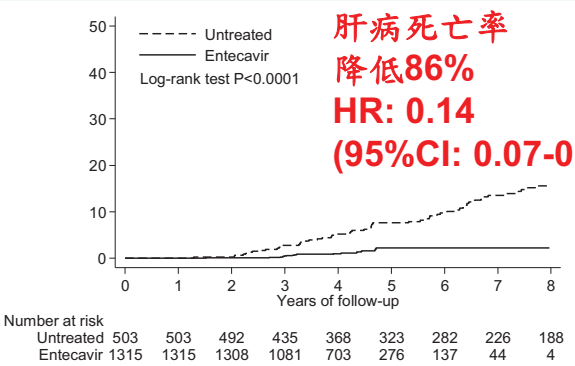
長期抗病毒藥物治療降低肝硬化併發症及死亡率



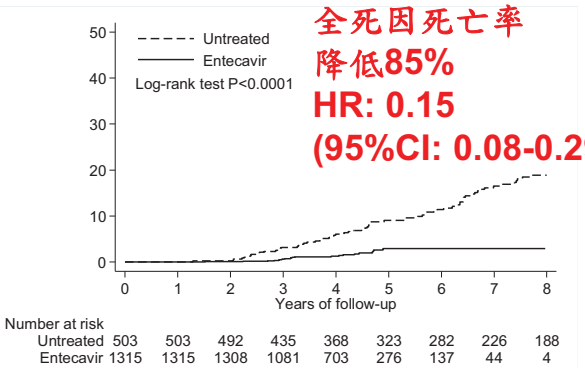
胃、食道靜脈瘤出血
降低62%
HR: 0.38
(95%CI: 0.20-0.74)



自發性腹膜炎
降低94%
HR: 0.06
(95%CI: 0.01-0.32)



肝病死亡率
降低86%
HR: 0.14
(95%CI: 0.07-0.30)



全死因死亡率
降低85%
HR: 0.15
(95%CI: 0.08-0.29)

Su and Kao et al., Liver Int. 2016 Dec;36(12):1755-1764

2003~2020

肝炎健保給付大躍進

台灣B肝健保給付里程碑

2008.08

- 給付新一代B肝口服抗病毒藥物

2009.11

- 口服藥物給付18個月改為36個月
- DNA取代biopsy

台灣B肝健保給付里程碑

2010.07

Jan. 2019: NUC for HBV post HCC curative treatment
May 2019: TAF (tenofovir alafenamide) for CHB

- e抗原陽性病患取消口服藥物3年限制，治療至e抗原轉陰
- 針劑干擾素治療由6個月延長為12個月
- 非肝硬化B肝患者停藥復發，不限制再治療次數

全民健康保險慢性B型肝炎治療試辦計畫
口服藥給付規定及流程

2019修訂

HBeAg 陽性病患	HBeAg 陰性病患	肝代償不全病患
• HBsAg (+) > 6 個月 • HBeAg (+) > 3個月 • ALT ≥ 5倍 ULN 或 • 2倍 ≦ALT <5倍 ULN 且HBV DNA ≥ 20,000 IU/mL 或肝組織切片 HBcAg (+)（血友病患及類血友病患得不做切片）	• HBsAg (+) > 6 個月 • HBeAg (-) > 3個月 • ALT ≥ 2倍 ULN (半年有兩次以上,每次間隔3個月)且HBV DNA ≥ 2,000 IU/mL，或肝組織切片HBcAg (+)（血友病患及類血友病患得不做切片）	HBsAg (+)且已發生肝代償不全 *已發生肝代償不全 1. PT延長≥3秒 或 2. T-Bil. ≥ 2 mg/dL

Entecavir (0.5 mg), TDF, Telbivudine, Lamivudine, TAF擇一 給付
HBeAg (-)病患治療至少2年，每次療程至多給付36個月
HBeAg (+)患者治療至e抗原轉陰並再多給付最多12個月

(肝代償不全者Entecavir使用1mg)

治療完成後，觀察3 - 6個月，復發且符合治療條件

Entecavir (0.5 mg), TDF, Lamivudine, Telbivudine, TAF 再次給付

全民健康保險慢性B型肝炎治療試辦計畫
口服藥給付規定及流程

2019修訂

長期給予	預防性使用	B型肝炎發作出現抗藥株
		(指於治療中一旦HBV DNA從治療期間之最低值上升超過一個對數值 1 log IU/mL)
•HBsAg (+) •肝硬化病患* •接受非肝臟器官移植後或接受癌症化學治療法中B型肝炎發作者 •接受肝臟器官移植後，持續接受免疫抑制劑者	•HBsAg (+) •接受肝臟器官移植或接受癌症化學療法的病患預防性使用 •異體造血幹細胞移植，捐贈者可接受預防性投藥至HBV DNA偵測不到，受贈者移植前一週開始給付，至免疫抑制劑停用後6個月	• 原藥物加上Adefovir 3年 • Entecavir 1mg (限Lamivudine抗藥) 3年 • Tenofovir 3年 • Interferon, pegylated interferon 1年
•Entecavir 0.5mg, TDF, Telbivudine, Lamivudine, TAF長期給予	•Entecavir 0.5mg, TDF, Telbivudine, Lamivudine, TAF 化療前一週至結束後6個月	• 若停藥後復發，得以合併療法或TDF或TAF治療3年或干擾素再治療1年 • 再復發時得再治療，不限治療次數 • 多重抗藥性時，可用TDF或TAF或合併Entecavir 1mg治療3年

* 肝硬化條件為需同時符合下列二項條件：

(一) HBsAg (+)且血清HBV DNA ≥ 2,000 IU/mL者。

(二) 診斷標準：1. 肝組織切片 (Metavir F4或Ishak F5以上，血友病患及類血友病患經照會消化系專科醫師同意後，得不作切片) 或 2. 超音波診斷為肝硬化併食道或胃靜脈曲張，或肝硬化併脾臟腫大。

B肝健保給付大躍進
---與亞太治療指引接軌

給付時間

一年　三年　不以時間為限

給付次數

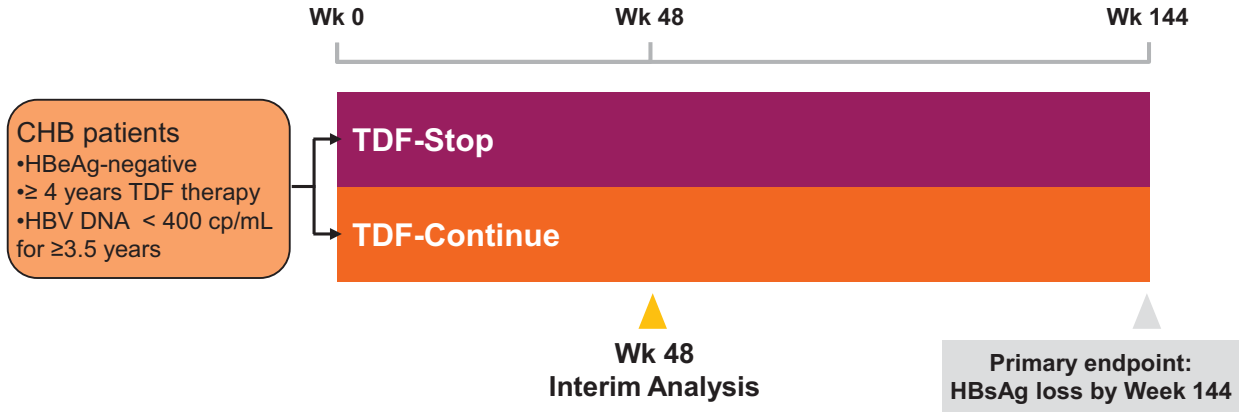
初次治療　可再次治療　不限次數 再治療

B型肝炎患者達成治療目標時，可以考慮停止藥物治療

TDF FINITE CHB

停止藥物治療的臨床試驗(1)：HBeAg-Negative CHB

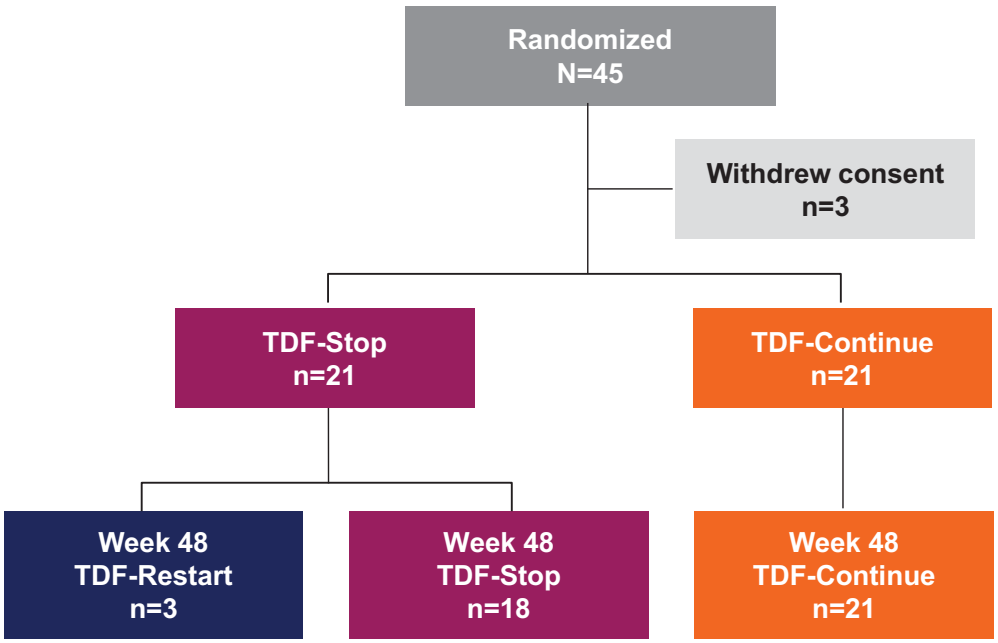
Open-label, multicenter, randomized, controlled trial



Berg T et al. J Hepatol 2017;67:918-924

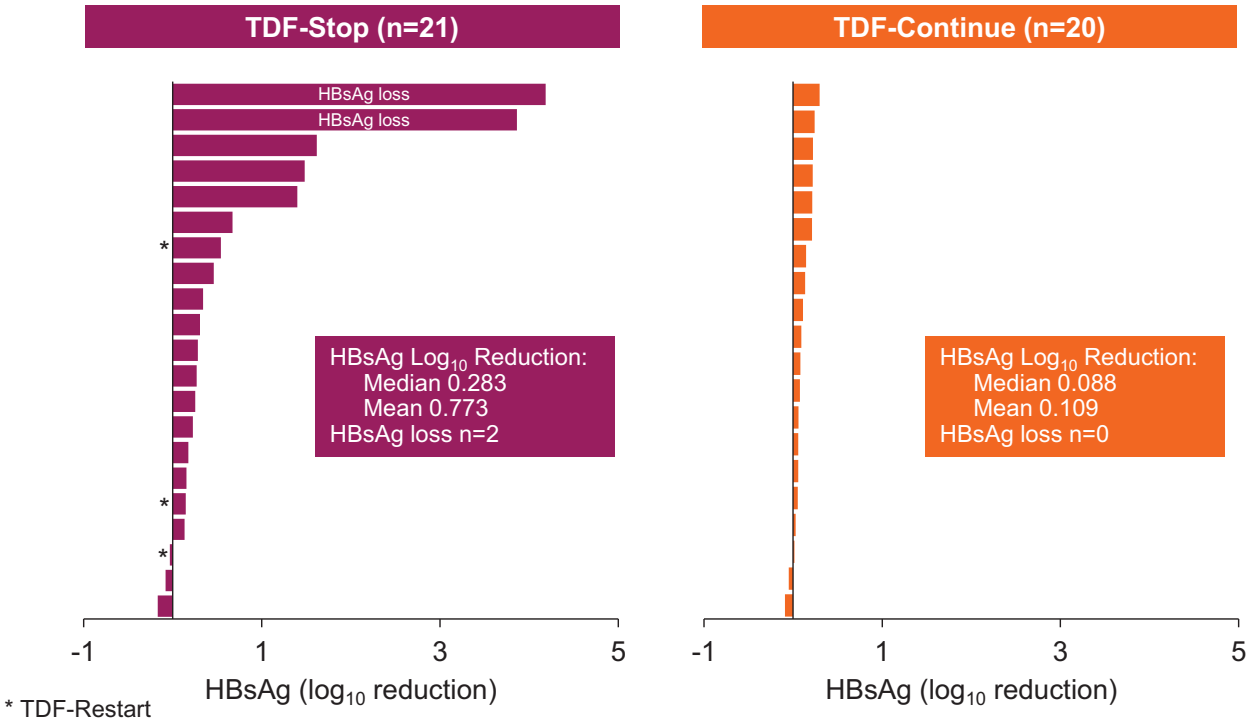
FINITE CHB

停止藥物治療的臨床試驗(1)：HBeAg-Negative CHB



Berg T et al. J Hepatol 2017;67:918-924

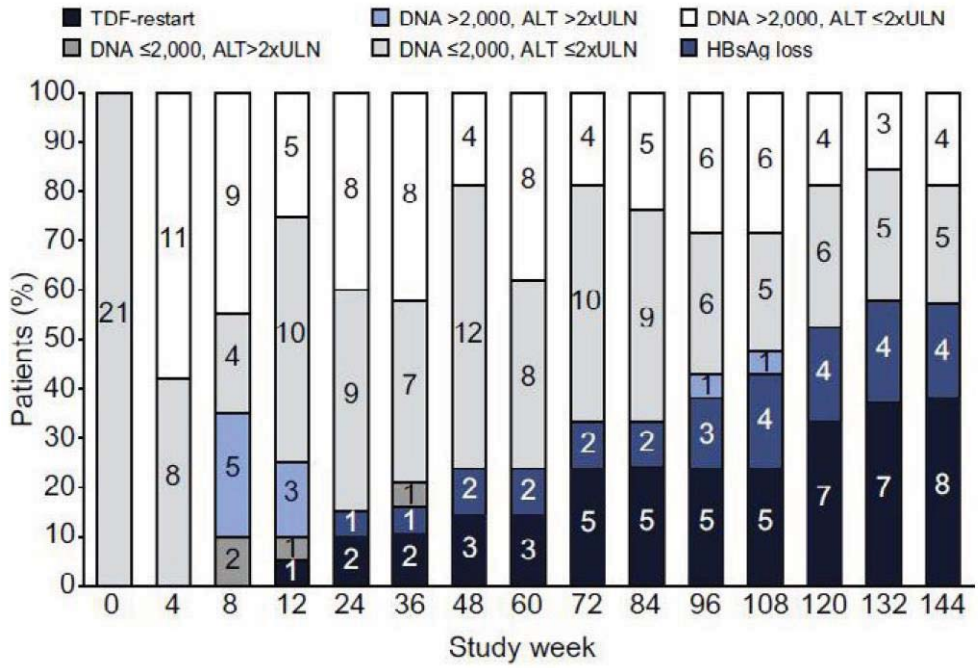
Week 48 HBsAg log_{10} Reduction (Individual Patients)



* TDF-Restart

Berg T et al. J Hepatol 2017;67:918-924

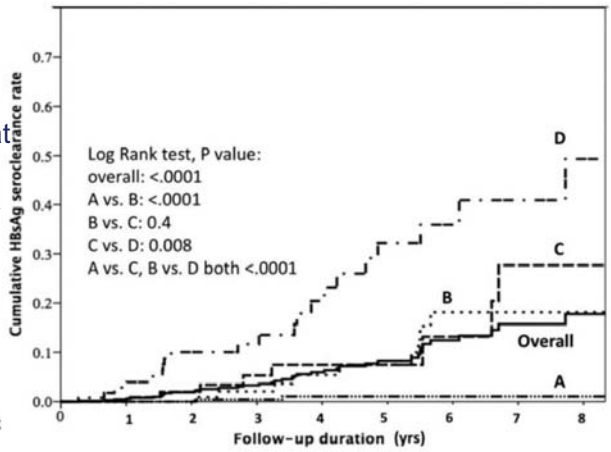
血清HBV DNA, ALT, 和HBsAg變化以及TDF再治療：停藥後144週觀察



Berg T et al. J Hepatol 2017;67:918-924

停止藥物治療的臨床觀察：
HBeAg-Negative CHB

A: CR, retreat
B: CR, not retreat
C: VR, no CR
D: no VR, no CR



Patient at risk

Overall			691	595	472	351	237	150	101	61	31
A	CR+	reTx	269	262	226	179	126	77	47	29	13
B	CR+	reTx-	150	135	107	77	49	36	25	15	9
C	CR-	VR+	128	109	76	47	33	17	15	8	6
D	CR-	VR-	144	89	63	48	29	20	14	9	3

Annual HBsAg loss cumulative incidence:

-DC group: 1.78%.
-Continue group: 0.15%

- **The incidence of HBsAg seroclearance after stopping NUC was much higher than that during therapy**
- **Higher incidence of HBsAg clearance in patients with clinical relapse who remained untreated than those who received retreatment**

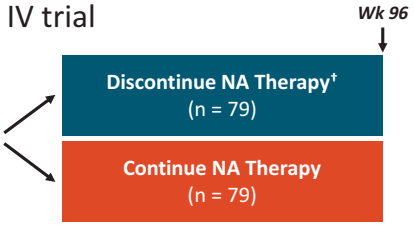
Jeng WJ, et al. Hepatology. 2018;68:425-434

停止藥物治療的臨床試驗(2)：
HBeAg-Negative CHB

Stop-NUC: Discontinuation of Long-term NA Therapy in Patients With HBeAg Negative CHB

- Multicenter, prospective, randomized phase IV trial

Adult patients with HBeAg negative CHB and normal ALT receiving NA therapy* with HBV DNA < 1000 IU/mL for ≥ 4 yrs; no advanced fibrosis or cirrhosis, HCC, or HCV, HDV, HIV coinfection (N = 158)



Enrolled patients had HBeAg status and ALT data available for period before NA therapy, were known to have pre-treatment HBV DNA > 2000 IU/mL. Liver function, HBV virology and serology regularly evaluated on study for all patients. *TDF (51%), ETV (39%), telbivudine (6%), or lamivudine (4%). **†Patients retreated upon severe acute or chronic hepatitis reactivation (ie, confirmed ALT > 10 x ULN, ALT > 5 x ULN and ≤ 10 x ULN for ≥ 28 days, ALT > 2 x ULN and ≤ 5 x ULN for ≥ 112 days with HBV DNA > 20,000 IU/mL, or total bilirubin increase > 1.5 x ULN at 2 consecutive measurements within 1 wk).**

- Primary endpoint: HBsAg loss up to Wk 96
- Secondary endpoints: time to HBsAg loss, time to HBsAg seroconversion, virologic response (HBV DNA < 12 IU/mL), biochemical response (ALT ≤ ULN), time to fulfill retreatment criteria, sustained remission (HBV DNA < 2000 IU/mL and normal ALT)

van Bömmel. EASL 2020. Abstr LBO06. EudraCT 2013-004882-15.

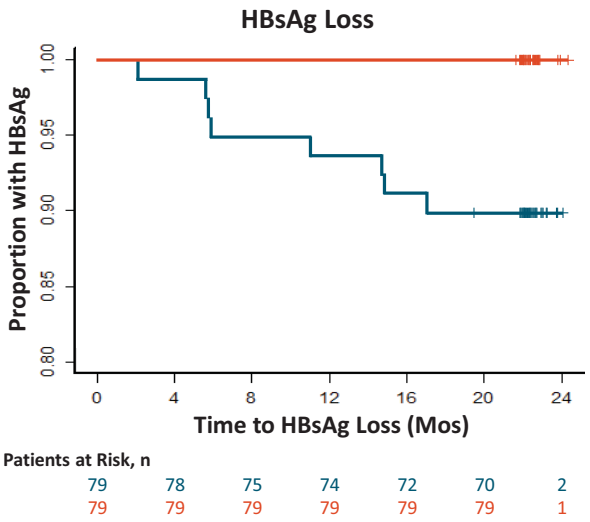
Slide credit: clinicaloptions.com

停止藥物治療的臨床試驗(2)：
停藥組有較高HBsAg消失機會

Stop-NUC: Retreatment and Time to HBsAg Loss

Outcome at Wk 96, n (%)	Discontinue NA (n = 78)
HBsAg loss	8 (10.3)*
No retreatment indicated	53 (67.9)
Retreatment indicated	6 (7.7)
Retreatment initiated	11 (14.1)†

*Compared with 0 patients achieving HBsAg loss in **NA continuation arm** (*P* = .006).
†Per predetermined criteria, n = 9; by decision of treating physician, n = 3.



van Bömmel. EASL 2020. Abstr LBO06.

停止藥物治療的臨床試驗(2)：
HBsAg消失者的基本特色

Baseline Characteristic, n (%)	HBsAg Loss	No HBsAg Loss	*P* Value
HBsAg < 1000 U/mL			
• Yes	7 (28)	18 (72)	.001
• No	1 (1.9)	53 (98.1)	
Previous NA therapy			
ETV or TDF	7 (10)	63 (90)	1
Lamivudine or telbivudine	1 (11.1)	8 (88.9)	

van Bömmel. EASL 2020. Abstr LBO06.

停止藥物治療的臨床試驗(2)：
停藥後第96週的病毒學與臨床復發

Outcome at Wk 96 in Patients Without Retreatment, n (%)	Discontinue NA (n = 79)
Virologic response	
▪ HBV DNA > 20 IU/mL	53 (67.1)
▪ HBV DNA ≤ 20 IU/mL	14 (17.7)
Biochemical response	
▪ ALT > ULN	7 (8.8)
▪ ALT ≤ ULN	61 (77.2)
Sustained remission*	
▪ No	36 (45.6)
▪ Yes	32 (40.5)

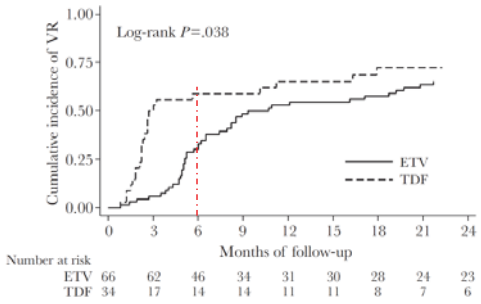
*HBV DNA < 2000 IU/mL and normal ALT.

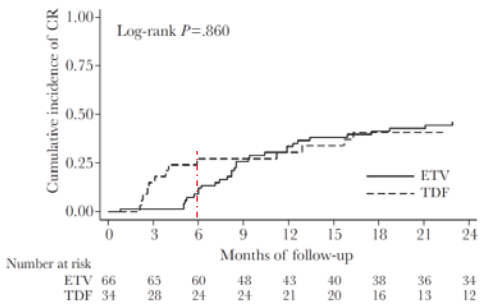
- Mean AEs per patient: 3.19 vs 2.06
- Severe AEs: 8 vs
  - Bone fractures, abortion, ventricular tachycardia, artrial fibrillation, acute myocardial infarction, subileus and gastritis influenca
  - Gastritis, cerebrovascular accident
  - No severe AE related to study intervention

van Bömmel. EASL 2020. Abstr LBO06.

B型肝炎患者完成治療後，須監測與治療B型肝炎復發

停止口服藥物後，須監測B型肝炎復發





Relapse type, Time after EOT	ETV, % (95% CI)	TDF, % (95% CI)	P
VR			
3 mo	6.1 (2.3-15.4%)	52.9 (37.5-70.2)	<0.001
6 mo	33.3 (23.4-46.1)	58.8 (43.1-75.2)	0.014
12 mo	53.0 (41.6-65.4)	65.2 (49.3-80.5)	0.248
CR			
3 mo	1.5 (0.2-10.3)	15.2 (6.6-32.6)	0.007
6 mo	12.1 (6.3-22.8)	27.3 (15.2-45.9)	0.060
12 mo	33.7 (23.6-46.5)	30.6 (17.8-49.4)	0.877

Su TH et al JID 2018

HBeAg-Negative CHB患者經口服藥物治，依照APASL指南停藥後復發的風險

Study	Number	Viral Relapse	Clinical Relapse
Ha et al 48	145	95 (65.5%)	93 (64.1%)
Jeng et al 24	95	55 (57.9%)	43 (45.3%)
kim et al 49	45	33 (73.3%)	24 (53.3%)
Chen et al 22	169	108 (64.3%)	87 (51.6%)
Jiang et al 50	39	25 (64.1%)	19 (48.7%)
Lee et al 51	64	50 (77.7%)	26 (41.9%)
Seto et al 31	184	168 (91.4%)	42 (22.8%)
Jung et al 52	68	37 (54.4%)	19 (28.9%)
Overall (total)	809	571	353
Overall (%)		70.5%	43.6%

B肝高病毒濃度孕婦使用抗病毒藥物預防母嬰B型肝炎傳染

Antiviral Therapy During the Third Trimester can Reduce MTCT of HBV

- **TDF is Reimbursed in Pregnant Women in Taiwan Since Feb. 1, 2018:**

血清**HBV DNA** ≧10^6 **IU/mL** 之懷孕者，可於懷孕滿**27** 週後開始給付使用**telbivudine** 或**tenofovir**，直至產後**4** 週。

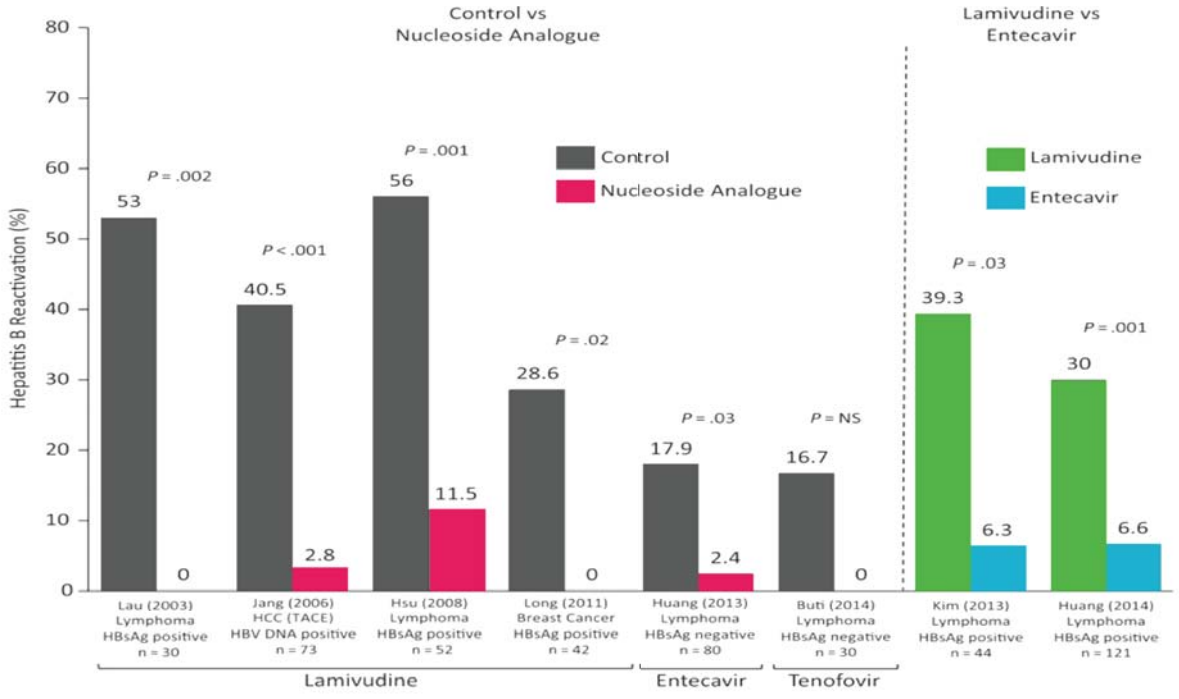
- **HBIG can be Applied to all Pregnant Women with HBsAg Carriage in Taiwan Since July 2019**
- 母親**HBsAg**陽性幼兒滿**12**個月可抽血檢驗，若**anti-HBs(-) and HBsAg (-)**，可以免費追加一劑疫苗

1. Chen, AASLD, 2014, Poster #1632
2. Pan CQ, et al. *N Engl J Med*. 2016;374:2324–34

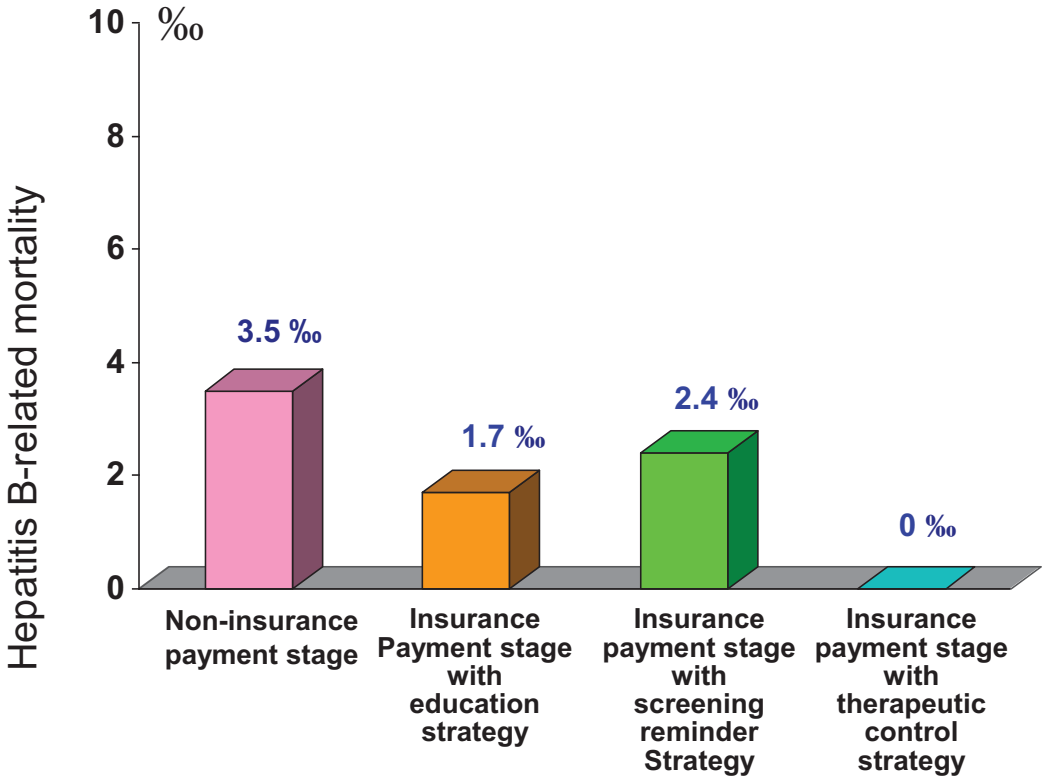
ITT analysis included infants born to all enrolled participants except for those who withdrew consent before the initiation of treatment.
PP analysis excluded infants born to women who withdrew consent, were lost to follow-up, or discontinued treatment for any reason. MTCT: mother-to-child transmission; PP: per protocol

癌症患者接受化學治療中預防B型肝炎復發

Prospective RCTs evaluating antiviral prophylaxis for HBVr



Gonzalez SA, Perrillo RP. *Clin Infect Dis* 2016;**62** Suppl 4:S306-13.



Hepatitis B-related mortality rate in cancer patients receiving chemotherapy

Hsu PI et al. Hepatology 2015

需積極接受治療的患者

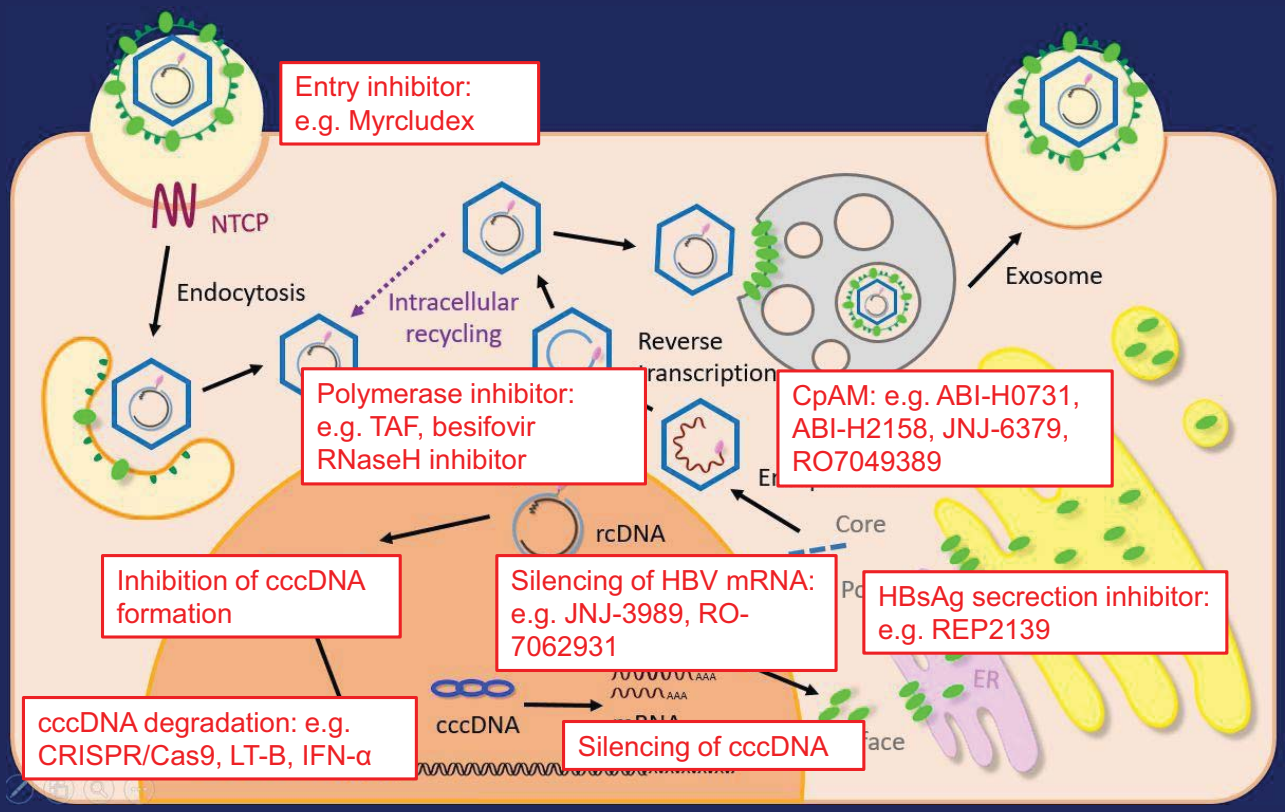
- 慢性B型肝炎：
  - ALT 數值超過正常值上限2倍
- 代償良好之活動性肝硬化
- 代償失調之活動性肝硬化
- 40歲以上且肝切片顯示有顯著肝纖維化
- 器官 (肝臟) 移植前後
- 接受免疫抑制劑或化學藥物治療
  - 接受rituximab治療

結論及未來方向

- 慢性B型肝炎之治療仍有努力的空間
- 發展更有效的口服抗病毒藥物和免疫調節劑
- 合併療法是未來努力的方向，但最佳之處方尚待發掘
- 依宿主、病毒和肝病狀況訂做個人化療法

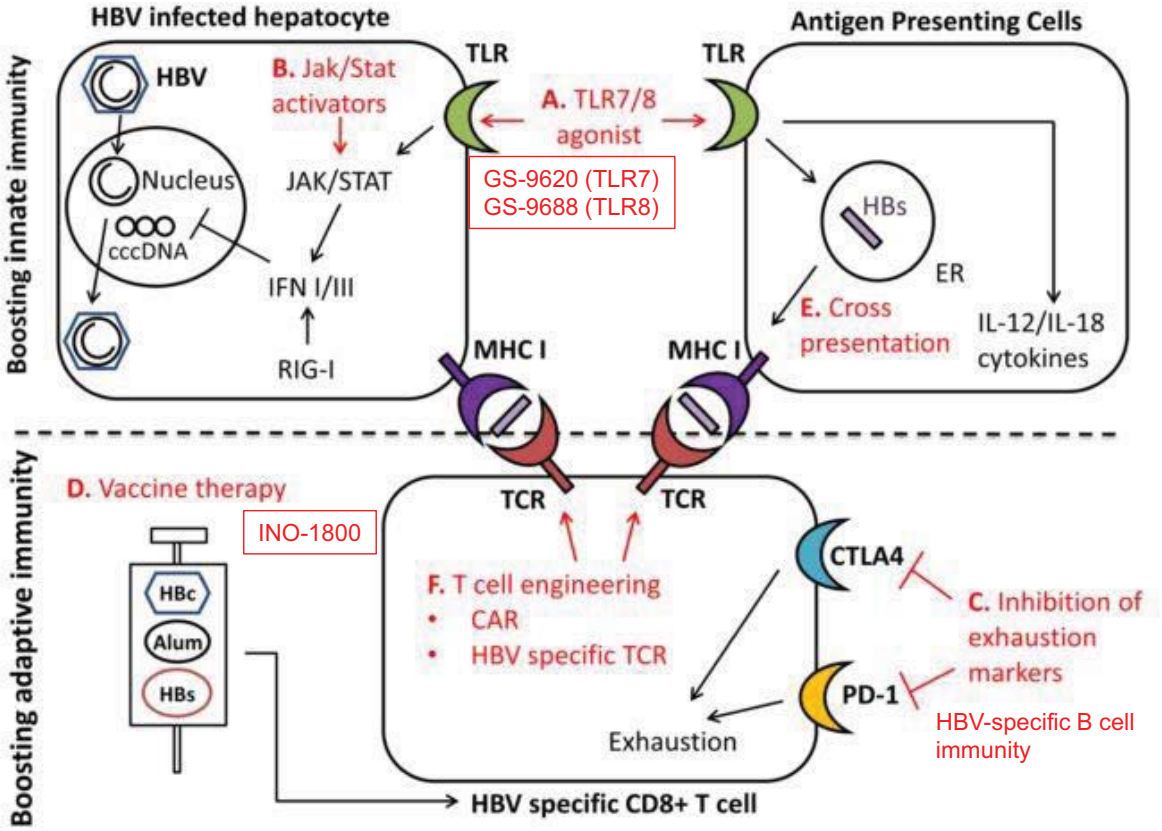
研發中B型肝炎之治療策略

HBV life cycle and antiviral targets

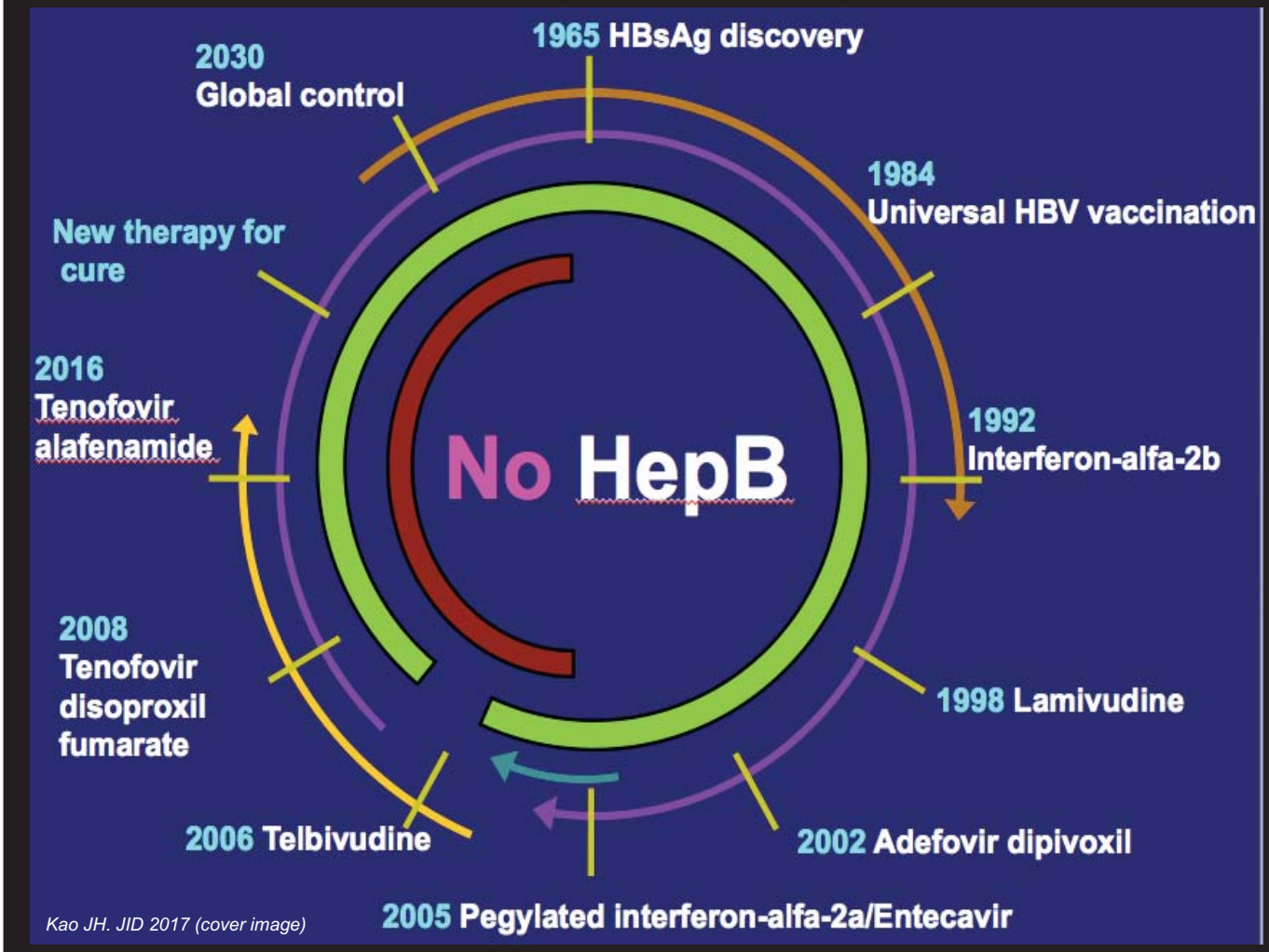


Modified from Yang HC & Chen PJ, Viruses 2017 (modified)

Potential Immunotherapeutic targets



Yang N & Bertoletti A, Hepatol Int, 2015 (modified)



Kao JH. JID 2017 (cover image)

謝謝大家聆聽