糖尿病族群LTBI檢驗及治療經驗分享

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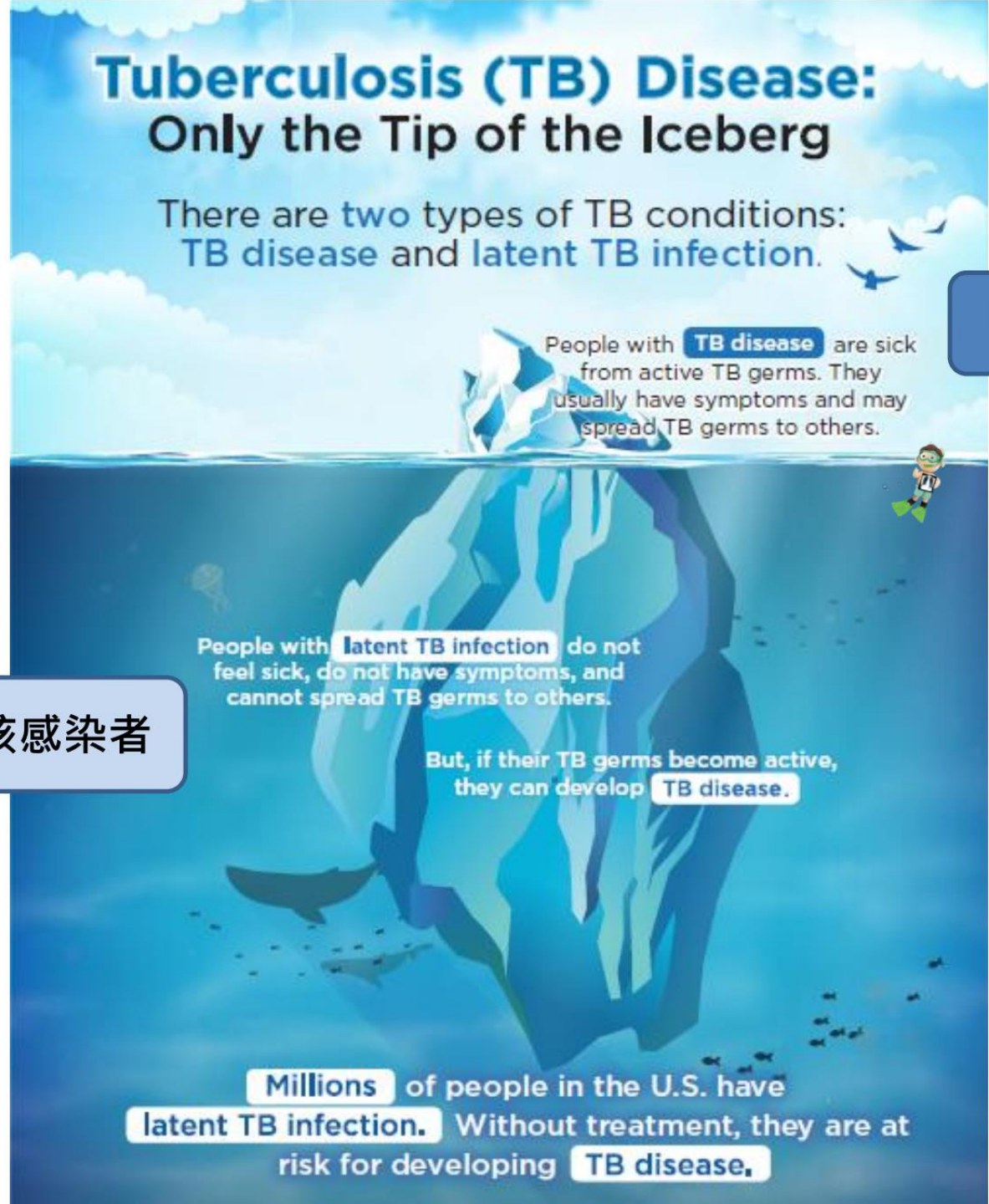
為什麼需要治療糖尿病病人的潛伏結核感染?



結核病人

潛伏結核感染者

Table 1 Risk factors for TB activation

Risk factor	TB risk[a]	Reference(s)	WHO's recommendation for screening and treatment for LTBI[41]	
			Country A[b]	Country B[c]
High-risk factors				
HIV/AIDS	10–100	Landry *et al.*,[4] Hourburgh *et al.*[9] and WHO[14]	Required	Required
Close contacts	15	Landry *et al.*[4] and Sutherland *et al.*[15]	Required	Required for close contacts (<five years old)
Organ-transplantation recipients	20–70	Aguado *et al.*[16] and Sakhuja *et al.*[17]	Required	Not mentioned
Chronic renal failure requiring dialysis	6.9–52.5	Andrew *et al.*,[18] Lundin *et al.*,[19] Belcon *et al.*[20] and Hussein *et al.*[21]	Required	Not mentioned
TNF-alpha blockers	1.6–25.1	Solovic *et al.*[22]	Required	Not mentioned
Silicosis	2.8	Cowie *et al.*[23]	Required	Not mentioned
Moderate-risk factors				
Fibronodular disease on chest x-ray	6–19	Grzybowski *et al.*[24]	Not mentioned	Not mentioned
Immigrants from high-TB-prevalence countries	2.9–5.3	Baussano *et al.*[25]	Options to be considered	Not mentioned
Health-care workers	2.55	Chu *et al.*[26]	Options to be considered	Not mentioned
Prisoners, homeless persons, illicit drug users	–	–	Options to be considered	Not mentioned
Low-risk factors				
Diabetes mellitus	1.6–7.83	Harries *et al.*,[27] Dobler *et al.*,[28] Jeon *et al.*,[29] Boucot *et al.*,[30] Kim *et al.*[31] and Baker *et al.*[32]	Not recommended	Not mentioned
Smoking	2–3.4	Altet *et al.*,[33] Slama *et al.*[34] and Maurya *et al.*[35]	Not recommended	Not mentioned
Use of corticosteroids	2.8–7.7	Jick *et al.*[36]	Not recommended	Not mentioned
Underweight	2–3	Palmer *et al.*[37] and Comstock *et al.*[38]	Not recommended	Not mentioned

[a] Relative risk of TB compared to the general population.

[b] In high- and upper-middle-income countries with an estimated TB incidence less than 100/100,000 population.

[c] For resource-limited countries and other middle-income countries that do not belong to country A.

Ai JW, et al. Emer Micro Infec 2016

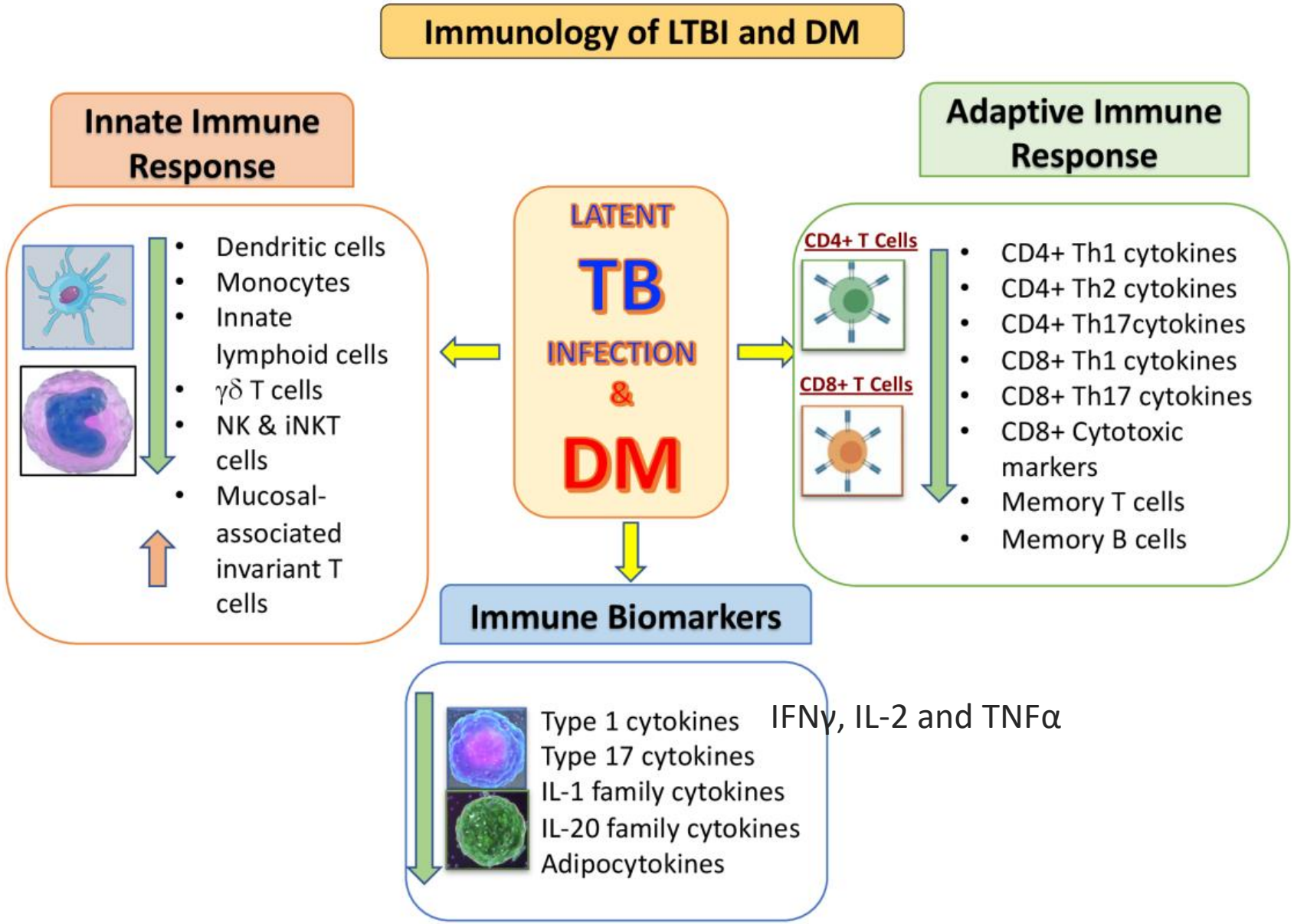


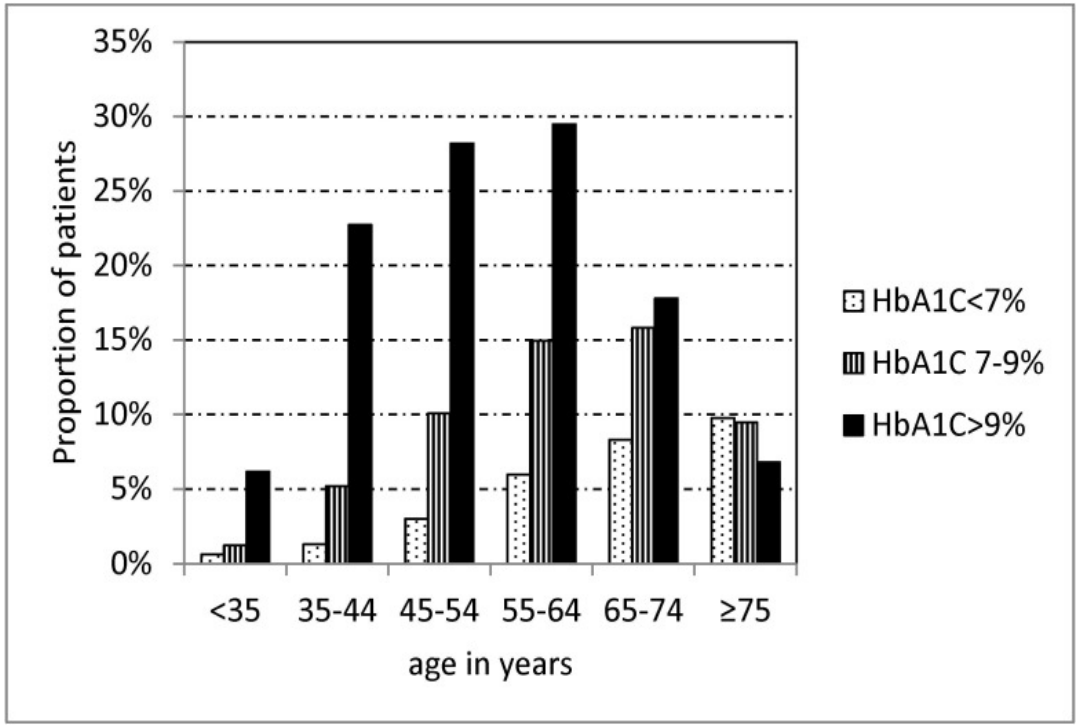
FIGURE 1
Summary of the immunological interactions between latent tuberculosis infection (LTBI) and type 2 diabetes mellitus **(DM)**. The outcomes of DM on the distinctive arms of the innate and adaptive immune systems is represented by arrows indicating increased or decreased function compared to LTBI without DM.

Front. Clin. Diabetes Healthc., 26 January 2023

為何選擇45歲以上HbA1c>9.0%的糖尿病人進行LTBI檢驗及治療?

- 在臺灣，65歲以上的糖尿病盛行個案數超過200萬以上。
- 過去的研究發現：罹患糖尿病者發生TB的風險是沒有糖尿病者的2-3倍;
- 臺灣的研究發現：在<65歲糖尿病患血糖控制不佳者的TB發病風險是沒有DM者的3.38倍。

Covariate	Diabetes Status	Number of Cases*	aHR (95% CI)**	*p*-Value
Overall	No DM	264	Ref	
	DM with good glycemic control	9	0.69 (0.35–1.36)	0.281
	DM with poor glycemic control	54	2.21 (1.63–2.99)	<0.001
Age				
<65 y old	No DM	148	Ref	
	DM with good glycemic control	2	0.63 (0.16–2.54)	0.513
	DM with poor glycemic control	29	3.38 (2.25–5.09)	<0.001
≥65 y old	No DM	116	Ref	
	DM with good glycemic control	7	0.69 (0.32–1.49)	0.345
	DM with poor glycemic control	25	1.63 (1.05–2.53)	0.028



Proportion of patients with HbA1C<7%, HbA1C 7–9%, HbA1C>9% by age groups of consecutive culture positive pulmonary tuberculosis patients with diabetes mellitus who had results of pretreatment HbA1C treated in three referral hospitals in Taiwan, 2005–2010.

Sheen et al. JFMA 2019
Lee et al. Plos Med 2016
Chiang et al. PLoS One 2015

我國各種結核病高風險族群成年人之潛伏結核感染率暨未進行治療之結核病發病率及相關指標

Risk Population	Sample Size	Age · Mean (year)	IGRA (+) 人數(%)	IGRA結果 Indeterminate 人數(%)	Active TB in IGRA positive 人數 (%)	Active TB in IGRA positive (每100人年)	Number needed to treat ***	Number needed to screen ****
Adult Contact [3]	2203	45	414 (18.8%*)		10 (2.4%)		42	222.2
Leukemia and Hemaoncology[2]	49	55.5	7 (14.3%)	12 (24.5%)	2 (28.6%)	25.6 (2/7.8人年)	3.5	24.4
Lung Cancer[2]	244	68.6	63 (25.8%)	22 (9.0%)	1 (1.6%)	0.7 (1/150人年)	62.5	250.0
HIV[4](Heterosexual)	97	39.8	10 (10.3%*)	(1.9%)	1 (10.0%)		10	97.1
HIV[6] (mainly IVDU)	772	36.8	90 (11.7%)	31 (4%)	6 (6.7%)		14.9	125
HIV[4](IVDU)	362	36.4	42 (11.6%*)	(3.9%)	1 (2.4%)		41.7	357.1
IVDU[5](HIV+)	4298				13**			333.3
HIV[4] (MSM)	450	35.5	29 (6.4%*)	(4.7%)	3 (10.3%)		9.7	149.3
HIV[7] (mainly MSM)	608		64 (10.5%)	10 (1.6%)	1 (1.6%)		62.5	500
IVDU[5](HIV-)	32430				33**			1000
Type [2] DM[2]	1316	56.6	313 (23.8%)	7 (0.5%)	2 (0.6%)	0.2 (2/817人年)	166.7	666.7
CKD[2]	63	61.8	7 (11.1%)	2 (3.2%)	0 (-)			
For Kidney Transplantation Evaluation[2]	109	47.5	9 (8.3%)	10 (9.21%)	0 (-)			
Dialysis[2]	940	59.3	193 (20.5%)	34 (3.6%)	3 (1.6%)	0.48	64.3	313
RA with TNF α Blocker[1]	242	54.7	45 (18.6%)	9 (3.7%)	3 (6.7%)		14.9	80.6
RA and other Autoimmune Diseases (RA: 55%,22% on TNF α Blocker)[2]	229	50.1	26 (9.3%)	24 (8.6%)	0 (-)			
RA with TNF α Blocker[2]	136		19 (14%)	10 (7.7%)	2 (1.5%)		9.5	68
RA without TNF α Blocker[2]	173		24 (14%)	11 (6.4 %)	0 (-)			

結核病診治指引

高風險共病族群LTBI檢驗及治療專案

建議執行對象

具共病者包含藥癮者、腹膜/血液透析、糖尿病、 COPD 、塵肺症、接受器官移植者、生物製劑使用者、愛滋感染者，法定傳染病醫療服務費用支付作業規範(健保代收代付)已納入共病族群為申報對象。

歷年執行情形

	檢驗	檢驗陽性	加入治療	完成治療*
腹膜/血液透析2017-2023	10,435人	1,559人 (15%)	1,028人 (66%)	669人 (65%)
糖尿病 2018-2023	8,487人	1,845人 (22%)	1,253人 (68%)	985人 (79%)
COPD 2021-2023	2,487人	529人 (21%)	368人 (70%)	250人 (68%)
IDU藥癮者 2022-2023	233人	20人 (9%)	10人 (50%)	8人 (80%)

*僅計追蹤治療期滿者

糖尿病病人潛伏結核治療選擇

潛伏結核感染治療處方一覽表

處方	處方藥品		總劑數與療程頻率	劑量			常見副作用	使用限制	都治 (DOPT)	推薦順序 (接觸者除指標抗藥或使用限制外)
				每日最大劑量	兒童	成人				
1HP[a]	複方	Isoniazid(INH) 300mg+ Rifapentine (RPT) 300mg	28天 (1個月) 每日服用	300mg	固定1顆		皮疹(蕁麻疹)為主、(少數)肝毒性	◆ 指標個案INH或RMP抗藥之接觸者 ◆ <13歲兒童 ◆ 孕婦[c]	必須	推薦處方
		Rifapentine (RPT) 150mg		300mg	◆ 35-45 kg 1顆 ◆ >45 kg 2顆					
	單方	Isoniazid (INH) 300mg	28天 (1個月) 每日服用	300mg	300 mg					
		Rifapentine (RPT) 150mg		600mg	◆ <35 kg 300 mg ◆ 35-45 kg 450mg ◆ >45 kg 600 mg					
3HP[a]	複方	Isoniazid(INH) 300mg+ Rifapentine (RPT) 300mg	12個劑量 (3個月) 每週服用	900 mg	體重50kg以上 固定劑量3顆		皮疹、類流感症狀、過敏反應、(少數)肝毒性	◆ 指標個案INH或RMP抗藥之接觸者 ◆ 孕婦[c]	必須	推薦處方
	單方	Isoniazid (INH) 300mg	12個劑量 (3個月) 每週服用	900 mg	◆ 2-11 歲 25mg/kg ◆ 12 歲(含)以上15mg/kg		皮疹、類流感症狀、過敏反應、(少數)肝毒性	◆ 指標個案INH或RMP抗藥之接觸者 ◆ <2歲兒童 ◆ 孕婦[c]	必須	推薦處方
		Rifapentine (RPT) 150mg		900 mg	◆ 10.0–14.0 kg 300 mg ◆ 14.1–25.0 kg 450 mg ◆ 25.1–32.0 kg 600 mg ◆ 32.1–49.9 kg 750 mg ◆ ≥50.0 kg 900 mg					
4R	Rifampin (RMP) 300mg		120天 (4個月) 每日服用	600 mg	15 (10-20)mg/kg	10 mg/kg	皮疹、腸胃不適/腸胃障礙、(少數)肝毒性	指標個案RMP抗藥之接觸者	必須	推薦處方
3HR[b]	Isoniazid (INH) 100mg		90天 (3個月) 每日服用	300 mg	10 (7-15)mg/kg	5 mg/kg	過敏反應、(少數)肝毒性	指標個案INH或RMP抗藥之接觸者	必須	推薦處方
	Rifampin (RMP) 300mg			600 mg	15 (10-20)mg/kg	10 mg/kg				
6H /9H	Isoniazid(INH) 100mg		180天(6個月) /270天(9個月) 每日服用	300 mg	10 (7-15)mg/kg	5 mg/kg	皮疹、周邊神經病變、肝毒性	指標個案INH抗藥之接觸者	建議	替代處方

藥品使用同意書下載點

a. 1HP及3HP處方使用之INH300mg及HP複方為 專案進口藥品，須請個案簽立藥品使用同意書
b. 3HR可依體重使用INH+RMP之二合一劑型
c. 目前尚未有足夠之孕婦臨床安全性相關試驗數據

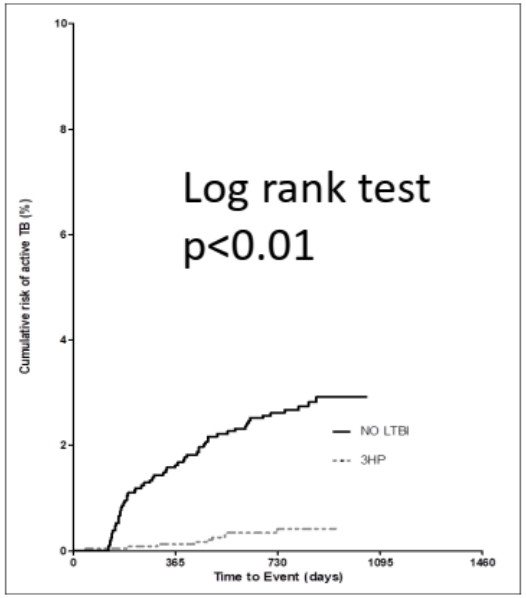
參考資料：WHO operational handbook on tuberculosis (Module 1 – Prevention): Tuberculosis preventive treatment. (2020)及疾病管制署結核病診治診引

接受LTBI治療之保護效果 (科技計畫成果2016/1-2017/6 五歲及以上,N=11923)

	發生率 (人年)	RR	95%CI		發生率 (人年)	RR	95%CI
3HP	**0.18**	0.13	(0.07-0.27)	3HP	**0.18**	0.64	(0.27-1.52)
未曾接受治療	**1.35**			9H	**0.28**		

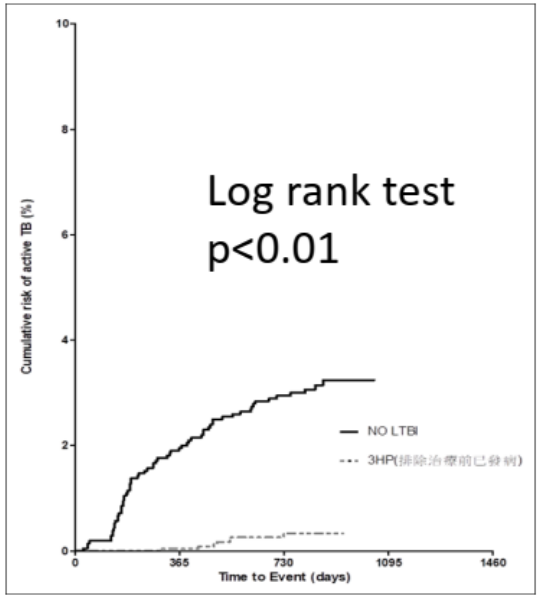
接觸者接受LTBI治療是最具效益的防治策略

LTBI 接觸者接受治療的保護力約87%



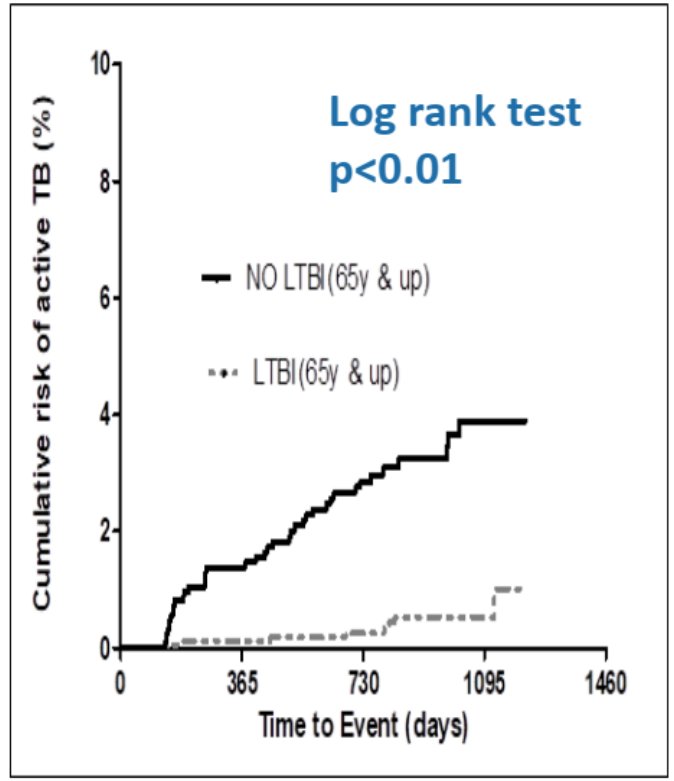
3HP vs. 未治療

LTBI 接觸者 (治療前已發病視為無治療) 接受治療的保護力約94%



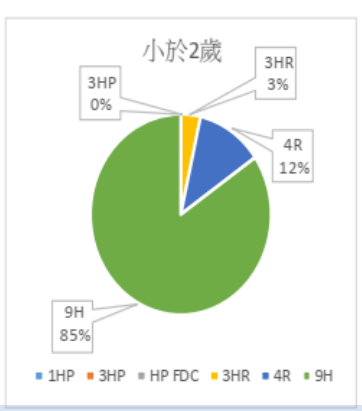
3HP vs. 未治療
(經病歷及影像調閱判斷)

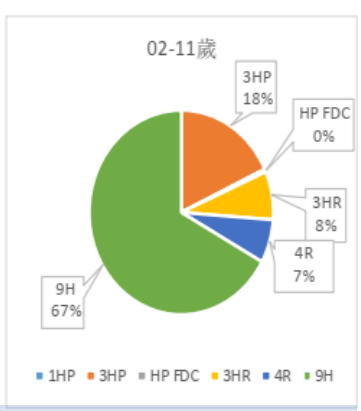
即使在65歲以上老年族群的保護力也達85%

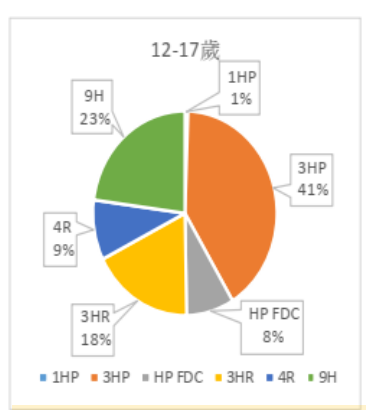


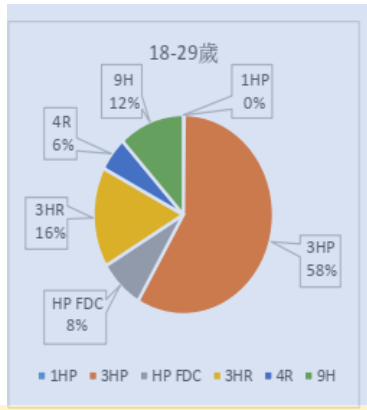
接觸者潛伏感染各類處方使用情況

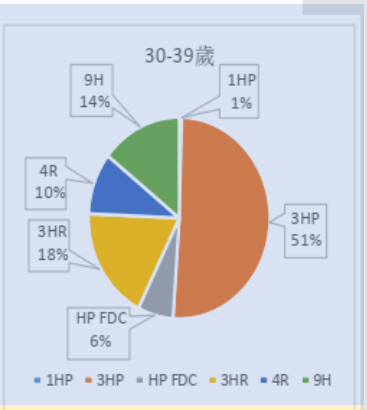
- 2021-2022.7 接觸者
- 短程處方在12歲到84歲都超過55%的佔比，18～29歲更是高達88%。3HP/HP FDC在12～64歲間各年齡層的比例皆為處方之冠（49%～66%不等）

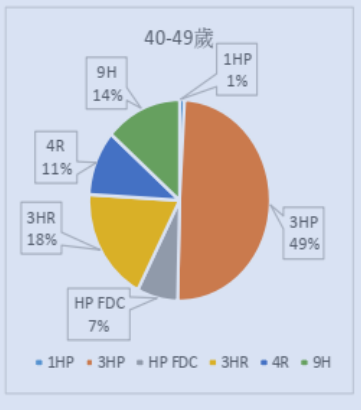


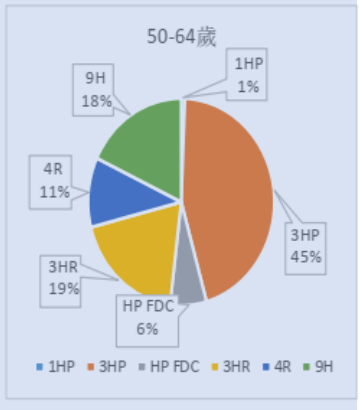


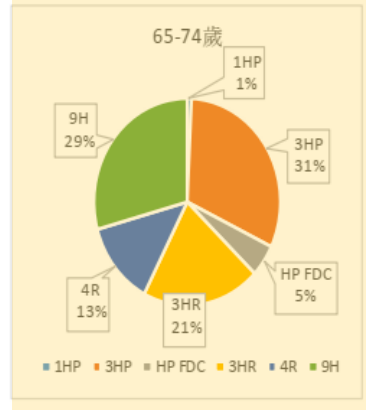


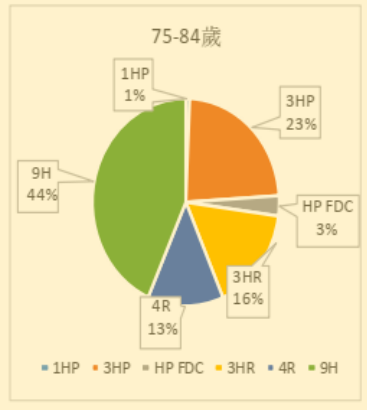


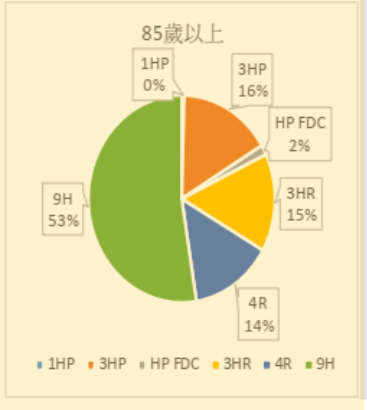












固定劑量組合及多重抗藥性結核病接觸者之潛伏結核感染治療介入安全性及成效評估 MOHW111-CDC-315-112103

糖尿病病人潛伏結核治療遭遇的問題

醫生，我年紀大/身體毛病多，受不了副作用

Safety Profile of 3HP in 579 Cases – Severe AE

Age Group	All (n=579)	< 35 (n=165)	35 ~ 65 (n=280)	≥ 65 (n=134)
Systemic drug reaction	65 (11.2%)	8 (4.8%)	48 (17.1%)	9 (6.7%)
Flu-like syndrome	47 (8.1%)	6 (3.6%)	34 (12.1%)	7 (5.2%)
Hypotension	10 (1.7%)	2 (1.2%)	7 (2.5%)	1 (0.7%)
Urticaria	6 (1.0%)	0 (0%)	6 (2.1%)	0 (0%)
Conjunctivitis	4 (0.7%)	0 (0%)	3 (1.1%)	1 (0.7%)
Severe hepatotoxicity	7 (1.2%)	0 (0%)	6 (2.1%)	1 (0.7%)

Huang HL. *Clin Infect Dis*. 2020;ciaa1741.

Safety Profile of 3HP in 579 Cases – Individual Symptoms

Age Group	All (n=579)	< 35 (n=165)	35 ~ 65 (n=280)	≥ 65 (n=134)
Flu-like symptoms				
Malaise	261 (45.1%)	60 (36.4%)	135 (48.2%)	66 (49.3%)
Febrile sensation	81 (14.0%)	15 (9.1%)	50 (17.9%)	16 (11.9%)
Fever	147 (25.4%)	26 (15.8%)	87 (31.1%)	34 (25.4%)
Dizziness	184 (31.8%)	31 (18.8%)	111 (39.6%)	42 (31.3%)
Headache	158 (27.3%)	33 (20.0%)	101 (36.1%)	24 (17.9%)
Chills	85 (14.7%)	10 (6.1%)	59 (21.1%)	16 (11.9%)
Myalgia	138 (23.8%)	23 (13.9%)	92 (32.9%)	23 (17.2%)
URI symptoms	87 (15.0%)	22 (13.3%)	51 (18.2%)	14 (10.4%)
Dyspnea	34 (5.9%)	6 (3.6%)	20 (7.1%)	8 (6.0%)
GI symptoms				
UGI symptoms	199 (34.4%)	42 (25.5%)	101 (36.1%)	56 (41.8%)
Diarrhea	28 (4.8%)	5 (3.0%)	17 (6.1%)	6 (4.5%)
Cutaneous reaction	101 (17.4%)	21 (12.7%)	60 (21.4%)	20 (14.9%)
Cardiovascular symptoms				
Palpitation	35 (6.0%)	7 (4.2%)	22 (7.9%)	6 (4.5%)
Hypertension	22 (3.8%)	0 (0%)	7 (2.5%)	15 (11.2%)

Huang HL. *Clin Infect Dis*. 2020;ciaa1741.

Clinical Infectious Diseases

MAJOR ARTICLE

Completion Rate and Safety of Programmatic Screening and Treatment for Latent Tuberculosis Infection in Elderly Patients With Poorly Controlled Diabetic Mellitus: A Prospective Multicenter Study

Hung-Ling Huang,[1,2,3,4,a] Wei-Chang Huang,[5,6,7,8,9,a] Kun-Der Lin,[4,10] Shin-Shin Liu,[11] Meng-Rui Lee,[12,13,14] Meng-Hsuan Cheng,[2,3,4] Chun-Shih Chin,[5] Po-Liang Lu,[3,15] Chau-Chyun Sheu,[2,3,4] Jann-Yuan Wang,[13,14,b] I-Te Lee,[9,16,17,18,b] and Inn-Wen Chong[2,3,4,19,20]

Table 3. Treatment Course and Outcome of Patients Undergoing Either the 3-Month Weekly Isoniazid Plus Rifapentine (3HP) or 9-Month Daily Isoniazid (9H) Regimen

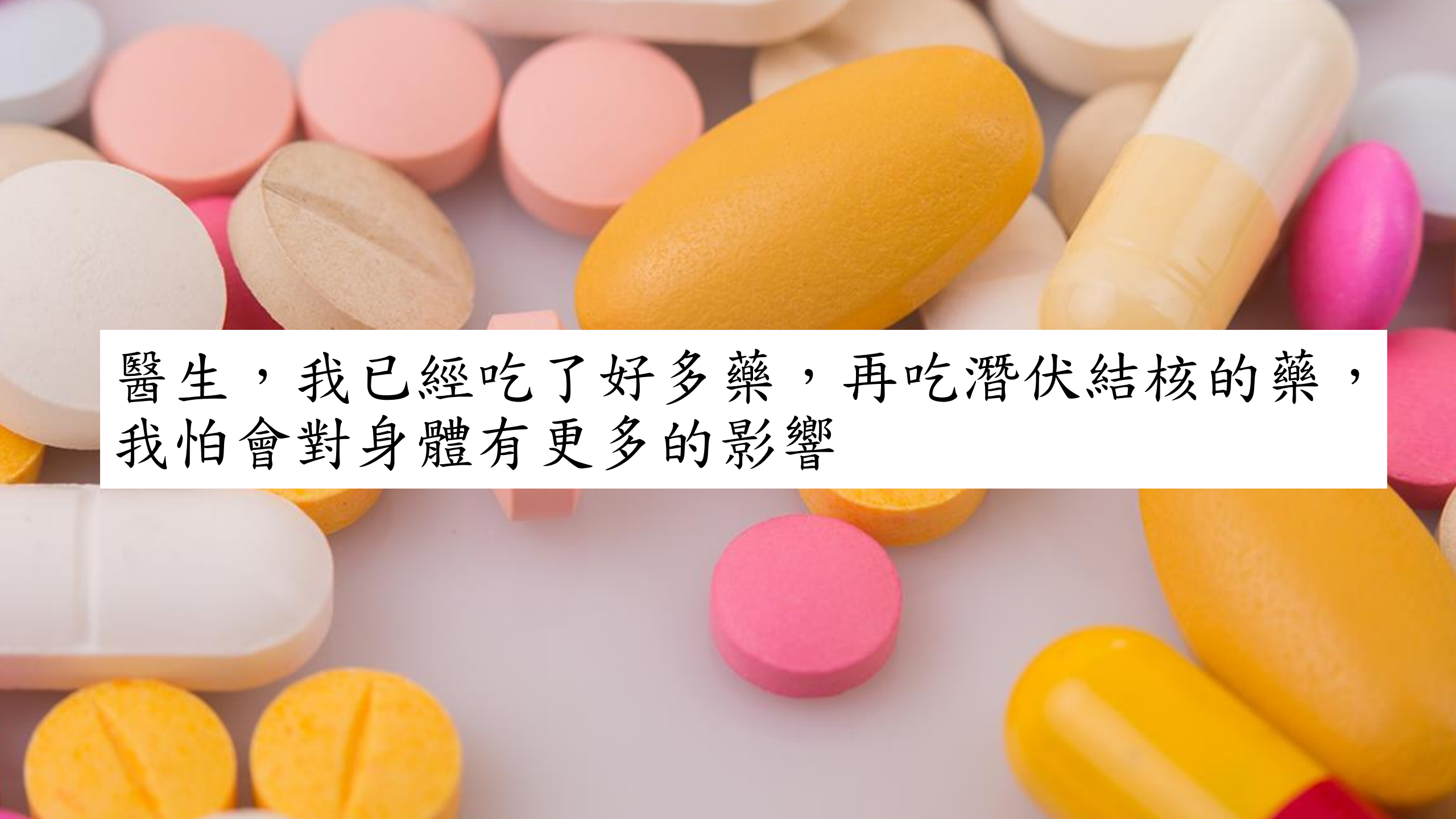
	Total (n = 200)	3HP (n = 138)	9H (n = 62)	*P*-value
Complete treatment	165 (82.5%)	116 (84.1%)	49 (79.0%)	.494
No adverse drug reactions	59 (29.5%)	30 (21.7%)	29 (46.8%)	<.001
Permanent discontinuation	35 (17.5%)	22 (15.9%)	13 (21.0%)	.494
Dose received		5.0 ± 2.7	56.7 ± 40.8	
Cause of discontinuation				
Adverse drug reaction	28 (14.0%)	20 (14.5%)	8 (12.9%)	.764
Systemic drug reaction	6 (3.0%)	6 (4.3%)	0	.223
Hypotension	1 (0.5%)	1 (0.7%)	0	.680
Flu-like syndrome	5 (2.5%)	5 (3.6%)[a]	0	.301
Urticaria	1 (0.5%)	1 (0.7%)	0	.680
Hepatotoxicity	4 (2.0%)	2 (1.4%)	2 (3.2%)	.776
Other adverse drug reactions	18 (9.0%)	12 (8.7%)	6 (9.7%)	.822
Patient refusal	5 (2.5%)	2 (1.4%)	3 (4.8%)	.352
Other reasons	2 (1.0%)	0	2 (3.2%)[b]	.176

Table 4. Details of Adverse Drug Reactions (ADRs) in Patients Receiving 3-Month Weekly Isoniazid and Rifapentine (3HP) or 9-Month Daily Isoniazid (9H)

	Total (n = 200)	3HP (n = 138)	9H (n = 62)	*P*-value
Any ADR	141 (70.5%)	108 (78.3%)	33 (53.2%)	<.001
Systemic drug reaction	9 (4.5%)	9 (6.5%)	0	.091
Flu-like syndrome	8 (4.0%)	8 (5.8%)	0	.122
Hypotension	1 (0.5%)	1 (0.7%)	0	.680
Urticaria	2 (1.0%)	2 (1.4%)	0	.854
Hepatotoxicity	8 (4.0%)	4 (2.9%)	4 (6.5%)	.426
Grade 3	1 (0.5%)	1 (0.7%)	0	.680
Grade 2	3 (1.5%)	1 (0.7%)	2 (3.2%)	.473
Gastrointestinal ADRs	93 (46.5%)	78 (56.5%)	15 (24.2%)	<.001
Nausea	53 (26.5%)	42 (30.4%)	11 (17.7%)	.060
Gr. 2	26 (13.0%)	23 (16.7%)	3 (4.8%)	.021
Epigastralgia	29 (14.5%)	25 (18.1%)	4 (6.5%)	.030
Gr. 2	18 (9.0%)	16 (11.6%)	2 (3.2%)	.056
Anorexia	29 (14.5%)	20 (14.5%)	9 (14.5%)	.997
Gr. 2	5 (2.5%)	3 (2.2%)	2 (3.2%)	.961
Diarrhea	9 (4.5%)	9 (6.5%)	0	.091
Flu-like symptoms	88 (44.0%)	74 (53.6%)	14 (22.6%)	<.001
Dizziness	59 (29.5%)	51 (37.0%)	8 (12.9%)	.001
Gr. 3	1 (0.5%)	1 (0.7%)	0	.680
Gr. 2	13 (6.5%)	11 (8.0%)	2 (3.2%)	.343
Malaise	44 (22.0%)	40 (29.0%)	4 (6.5%)	<.001
Gr. 2	6 (3.0%)	5 (3.6%)	1 (1.6%)	.747
Lethargy	27 (13.5%)	21 (15.2%)	6 (9.7%)	.289
Myalgia and arthralgia	24 (12.0%)	24 (17.4%)	0	<.001
Gr. 2	13 (6.5%)	13 (9.4%)	0	.029

對於副作用的擔心

- 考慮糖尿病控制不良病人，因免疫能力下降對結核菌造成的影響，應考慮治療成功率較高的處方。
- 但是病人擔心3HP/1HP副作用該怎麼做?
  - 仔細解釋可能會有的副作用，但是不過度強調。
  - 短期3個月的治療，一周吃藥一次，總治療時間短，藥物造成的副作用也短。
  - 治療醫師不要因為擔心發生副作用處理麻煩，而不敢處方3HP。
  - 若真的因副作用無法耐受，也可以轉換成9H/6H。
  - 病人表現出十足的抗拒時，願意接受治療最重要，仍可以處方9H/6H，但是要能安排好後續的回診，增加病人願意完整接受治療意願。


醫生，我已經吃了好多藥，再吃潛伏結核的藥，
我怕會對身體有更多的影響

Drug–Drug Interaction Potential with Once-Weekly Isoniazid/ Rifapentine (3HP) for the Treatment of Latent Tuberculosis Infection

Catia Marzolini[1,2] · Sara Gibbons[2] · Joep J. van Oosterhout[3,4] · Saye Khoo[2]

Therapeutic class	Comedication (main metabolic pathway)	Effect on co-medication	Recommendation/comment
	Chloroquine (CYP2C8/3A4/2D6)	↓	Moderate decrease in chloroquine exposure is expected. Monitor clinical and parasitological responses
	Lumefantrine (CYP3A4)	↓	Avoid because of the substantial decrease in lumefantrine exposure and the related potential treatment failure
	Piperaquine (CYP3A4)	↓	Avoid because of the substantial decrease in piperaquine exposure and the related potential treatment failure
	Primaquine (non-CYP)	↑m	Use with caution because of increased metabolism towards hemotoxic metabolites
	Proguanil (partly CYP2C19)	↓↑	Isoniazid inhibits whereas rifapentine induces CYP2C19. Monitor the clinical and parasitological responses
	Quinine (CYP3A4)	↓	Avoid because of the substantial decrease in quinine exposure and the related potential treatment failure
Antihypertensives	Amlodipine (CYP3A4)	↓	Monitor blood pressure and adjust amlodipine dosage as needed
	Nifedipine (CYP3A4)	↓	Monitor blood pressure and adjust nifedipine dosage as needed

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Therapeutic class	Comedication (main metabolic pathway)	Effect on co-medication	Recommendation/comment
Statins	Atorvastatin (CYP3A4)	↓	Monitor cholesterol levels and increase atorvastatin dosage if needed
	Simvastatin (CYP3A4)	↓	Monitor cholesterol levels and increase simvastatin dosage if needed
Anticoagulants/antiplatelets	Clopidogrel (CYP2C19/3A4/2B6)	↓↑	The net effect of interaction is unknown. Isoniazid inhibits CYP2C19 and may prevent the conversion to the active metabolite. Rifapentine induces CYP3A4 and may increase the conversion to the active metabolite and thereby increase the risk of bleeding
	Warfarin (CYP3A4/1A2/2C9)	↓	Monitor INR and adjust warfarin dose as needed
Anti-diabetic agents	Glibenclamide (CYP3A4)	↓	Monitor clinical effect and increase glibenclamide dosage if needed
	Gliclazide (CYP2C9)	↓	Moderate decrease in gliclazide exposure expected. Monitor glucose and adjust gliclazide dosage as needed

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Catia Marzolini[1,2] · Sara Gibbons[2] · Joep J. van Oosterhout[3,4] · Saye Khoo[2]

Therapeutic class	Comedication (main metabolic pathway)	Effect on co-medication	Recommendation/comment
Others	Aminophylline (CYP1A2)	↓	Given the narrow therapeutic index of the constituent theophylline, monitor concentrations and adjust dosage
	Colchicine (CYP3A4)	↓	Dose adjustment of colchicine may be considered as clinically needed
	Digoxin (P-gp substrate)	↓	Monitor serum digoxin concentrations and adjust dosage accordingly
	Ergometrine (CYP3A4)	↓	Dose adjustment of ergometrine may be considered as clinically needed
	Ketoconazole (CYP3A4)	↓	Avoid because of the substantial decrease in ketoconazole exposure and the related loss of efficacy
	Loperamide (CYP3A4/2C8)	↓	Dose adjustment of loperamide may be considered as clinically needed
	Paracetamol (partly CYP2E1)	↑m	Risk of hepatotoxicity related to conversion to toxic metabolites via CYP2E1 induction by isoniazid [14] However, paracetamol can increase isoniazid concentrations. Limit daily dose of paracetamol

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Table 2 Crossed metabolic pathways of rifapentine/rifampicin and oral antidiabetics

Oral hypoglycemic agent	Antituberculosis drug	
	Rifapentine	Rifampicin
Meglitinides		
Nateglinide (Starlix®)	3A4/2C9	3A4/2C9
Repaglinide (Prandin®)	3A4/2C8	3A4/2C8
Thiazolidinediones		
Pioglitazone (Actos®)	3A4/2C8	3A4/2C8
Rosiglitazone (Avandia®)	2C8/9	2C8/9
Sulfonylureas		
Glibenclamide (Glyburide®)	3A4	3A4
Gliclazide (Diamicron®)	2C8/9	2C8/9/19
Gliquidone (Glurenorm®)	3A4/2C9	3A4/2C9/19/1A2
DPP-IV inhibitors		
Sitagliptin (Januvia®)	3A4/2C8	3A4/2C8
Saxagliptin (Onglyza®)	3A4	3A4
Other		
Bromocriptine mesylate (Cycloset®)	3A4	3A4

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Table 3 Possible PK interactions between rifapentine/rifampicin and hypoglycemic agents and their expected clinical effects

Interaction level	Possible PK interaction	Expected clinical effect
Transporter level (ABCB1)	Rifapentine: competition with SU and SGLT-2 inhibitors. Decreased levels of SU and SGLT-2 inhibitors	Lack of hypoglycemic efficacy, possibly greater with rifampicin
	Rifampicin: competition with SU and SGLT-2 inhibitors and induction of ABCB1. Decreased levels of SU and SGLT-2 inhibitors	
Protein-binding level	Rifapentine: competition for protein-binding sites with SU, glinides, SGLT-2 inhibitors, detemir, degludec, and liraglutide. Increased levels of oral antidiabetic drugs and/or rifapentine	Possible potentiation of hypoglycemic and/or antituberculosis effects, and increased risk of dose-dependent adverse effects.
	Rifampicin: competition for protein-binding sites with SU, glinides, SGLT-2 inhibitor[illegible] drugs an[illegible]	The interaction may be stronger with rifapentine than with rifampicin
Hepatic metabolism level	Rifapenti[illegible] nateglinide, repaglinide, pioglitazone, rosiglitazone, glibenclamide, gliquidone, gliclazide, sitagliptin, and saxagliptin	Rifapentine: hyperglycemia
	Rifampicin: induction of CYP3A4, CYP2C8/9/19, CYP1A2, and auto-induction. Decreased levels of nateglinide, repaglinide, pioglitazone, rosiglitazone, glibenclamide, gliquidone, gliclazide, sitagliptin, saxagliptin, and rifampicin itself	Rifampicin: hyperglycemia and diminished antituberculosis efficacy over time
	Rifapentine/rifampicin: induction by antidiabetics with CYP3A4-inducing potential, like bromocriptine. Decreased levels of both rifapentine and rifampicin	Lack of antituberculosis efficacy, possibly greater with rifampicin owing to auto-induction
	Rifapentine/rifampicin/antidiabetics: inhibition of CYP450 in severe infection. Increased levels of oral antidiabetic drugs and/or rifapentine/rifampicin	Possible potentiation of hypoglycemic and/or antituberculosis effects, and increased risk of dose-dependent adverse effects

血糖可能會稍微升高

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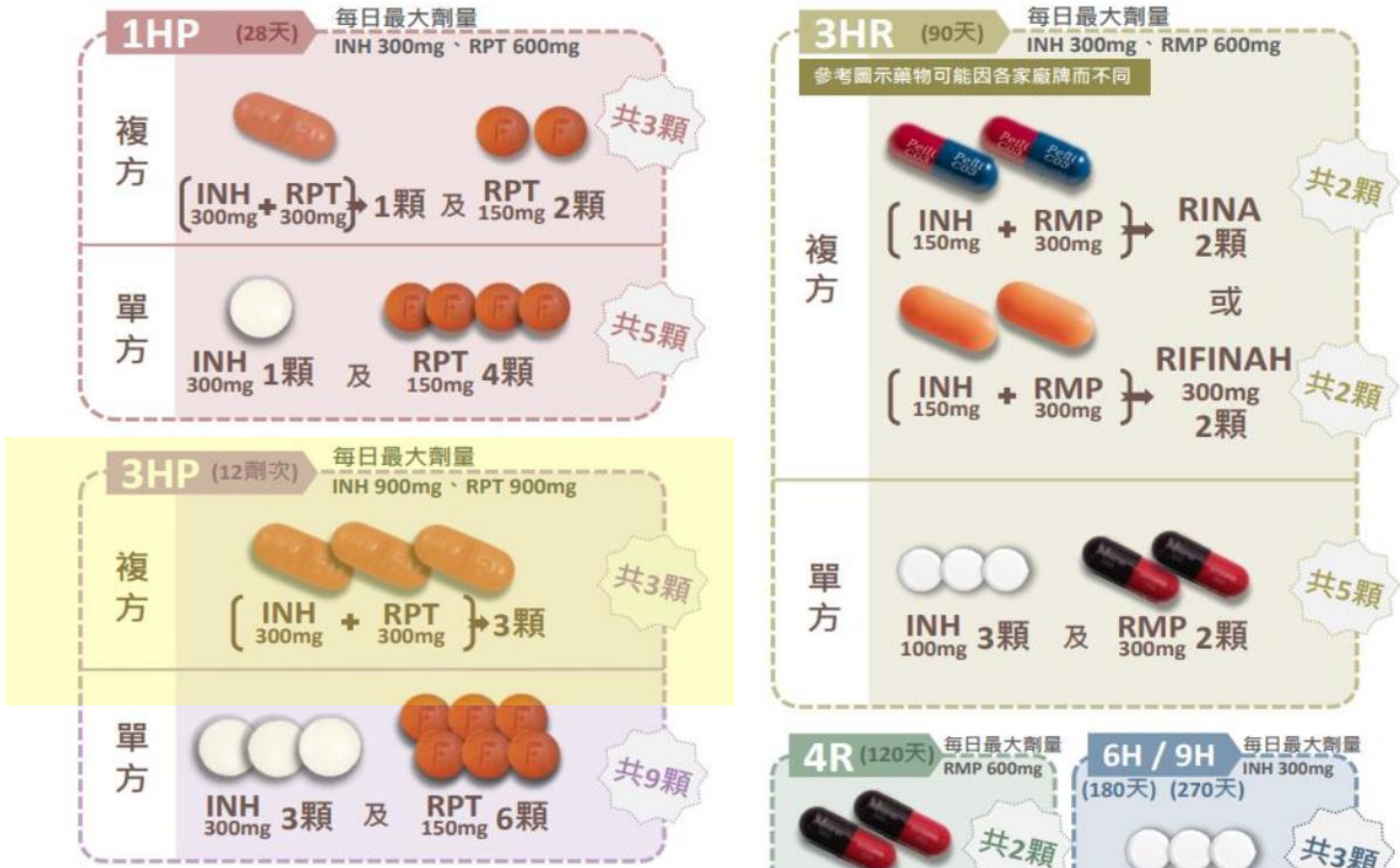
對於藥物交互作用的擔心

- 雖然會有藥物交互作用，但是在糖尿病患者常用藥物中，大多不會有重大的影響。
- 注意血糖原本就控制不良的病人，若是使用3HP的治療，要請病人更加注意血糖的監測。
- 若有使用warfarin/NOAC的高風險病人，要注意可能會導致藥效降低的血栓風險增加。

醫生，我不想再吃那麼多藥了

潛伏結核感染治療處方一覽表(藥品圖示)



使用Isoniazid 300 mg/tab(INH)、Rifapentine 150 mg/tab (RPT) 、 Isoniazid/Rifapentine Coated Tablets 300 mg / 300 mg 複方錠 (HP FDC)，須請個案簽立藥品使用同意書

已服用3HP治療轉換處方建議表

已服用3HP劑次 每週服用(總療程12週)	轉換為3HR處方 每天服用(總療程90天)	轉換為4R處方 每天服用(總療程120天)	轉換為9H處方 每天服用(總療程270天)	轉換為6H處方 每天服用(總療程180天)	轉換為1HP處方 每天服用(總療程28天)
已服用1劑次	餘83天	餘110天	餘248天	餘165天	餘26天
2	75	100	225	150	24
3	68	90	203	135	21
4	60	80	180	120	19
5	53	70	158	105	17
6	45	60	135	90	14
7	38	50	113	75	12
8	30	40	90	60	10
9	23	30	68	45	7
10	15	20	45	30	5
11	8	10	23	15	3

註:轉換處方後藥量原則上不要少於此建議表

結論:

- 考慮糖尿病控制不良病人，因免疫能力下降對結核菌造成的影響，應考慮治療成功率較高的處方。
- 透過詳細解釋及溝通技巧，減少病人對副作用的疑慮，並願意全程接受治療。
- 注意藥物交互作用，減少病人風險。
- 不管是3HP短期處方或是9H/6H的長期治療，在醫師/個管師/公衛夥伴的合作之下，讓病人能完成完整治療療程才是最終目標。