酒癮治療經驗及社區防治新面向

方俊凱 MD MSC PHD

馬偕紀念醫院精神醫學部資深主治醫師

臺北護理健康大學生死與健康心理諮商系 副教授

定風波

蘇軾

1082

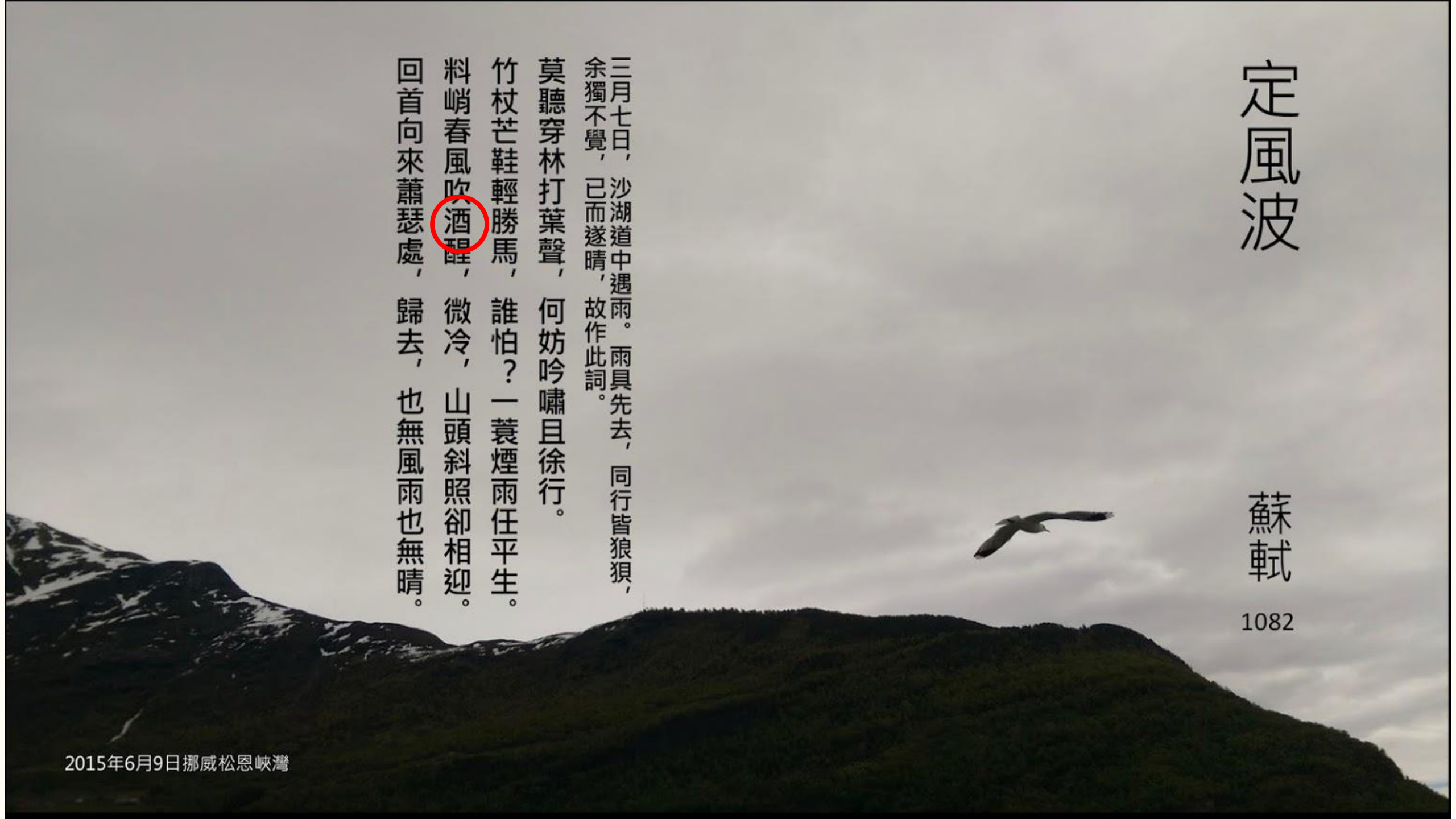
三月七日，沙湖道中遇雨。雨具先去，同行皆狼狽，余獨不覺，已而遂晴，故作此詞。

莫聽穿林打葉聲，何妨吟嘯且徐行。

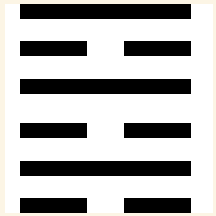
竹杖芒鞋輕勝馬，誰怕？一蓑煙雨任平生。

料峭春風吹酒醒，微冷，山頭斜照卻相迎。

回首向來蕭瑟處，歸去，也無風雨也無晴。



2015年6月9日挪威松恩峽灣



未濟卦火水未濟

- 未濟，亨。小狐汔濟，濡其尾，无攸利。初六，濡其尾，吝。
- 九二，曳其輪，貞吉。六三，未濟，征凶，利涉大川。
- 九四，貞吉，悔亡，震用伐鬼方，三年有賞于大國。
- 六五，貞吉无悔，君子之光，有孚，吉。
- **上九，有孚于飲酒，无咎。濡其首，有孚，失是。**
  - 《象》曰：飲酒濡首，亦不知節也。
    - 相信於飲食喝酒之宴樂，沒有罪咎。但若喝酒喝到頭都埋於酒中而濕了頭，那麼相信也將會失去這一切。
    - 未濟已過，將轉既濟。信於既濟（有孚），適度的飲酒逸樂無傷大雅，但告戒君子當有所節制，不能耽溺。

挪亞方舟 創世記第9章18-23節

18.出方舟挪亞的兒子就是閃、含、雅弗。含是迦南的父親。

19.這是挪亞的三個兒子，他們的後裔分散在全地。

20.挪亞作起農夫來，栽了一個葡萄園。

21.他喝了園中的酒便醉了，在帳棚裡赤著身子。

22.迦南的父親含看見他父親赤身，就到外邊告訴他兩個弟兄。

23.於是閃和雅弗拿件衣服搭在肩上，倒退著進去，給他父親蓋上；他們背著臉就看不見父親的赤身。

挪亞方舟 創世記第9章24-29節

24.挪亞醒了酒，知道小兒子向他所做的事，

25.就說：迦南當受咒詛，必給他弟兄作奴僕的奴僕；

26.又說：耶和華─閃的神是應當稱頌的！願迦南作閃的奴僕。

27.願神使雅弗擴張，使他住在閃的帳棚裡；又願迦南作他的奴僕。

28.洪水以後，挪亞又活了三百五十年。

29.挪亞共活了九百五十歲就死了。

救贖後的悲哀──挪亞之醉

方俊凱
（馬偕紀念醫院安寧療護教育示範中心主任/臺北護理健康大學生死與健康心理諮商系兼任副教授）

諮商與輔導　第445期　2023.1.5　第38-40頁

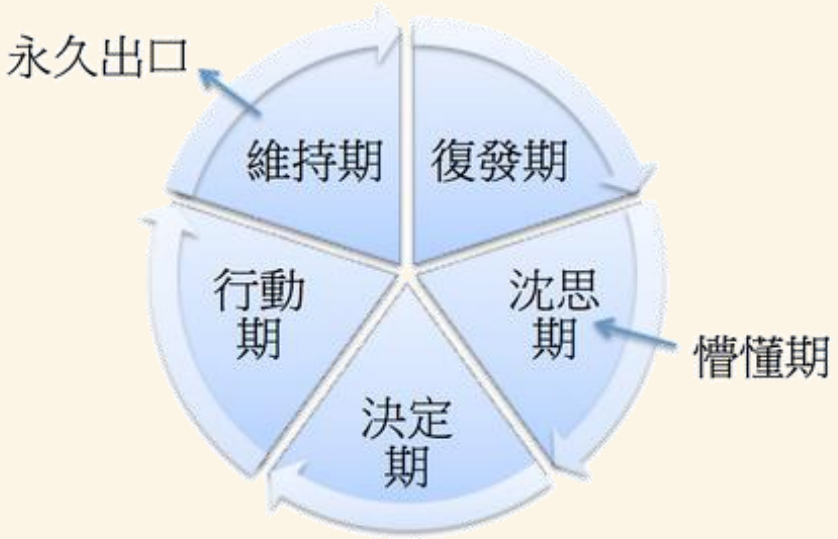
蘋果即時

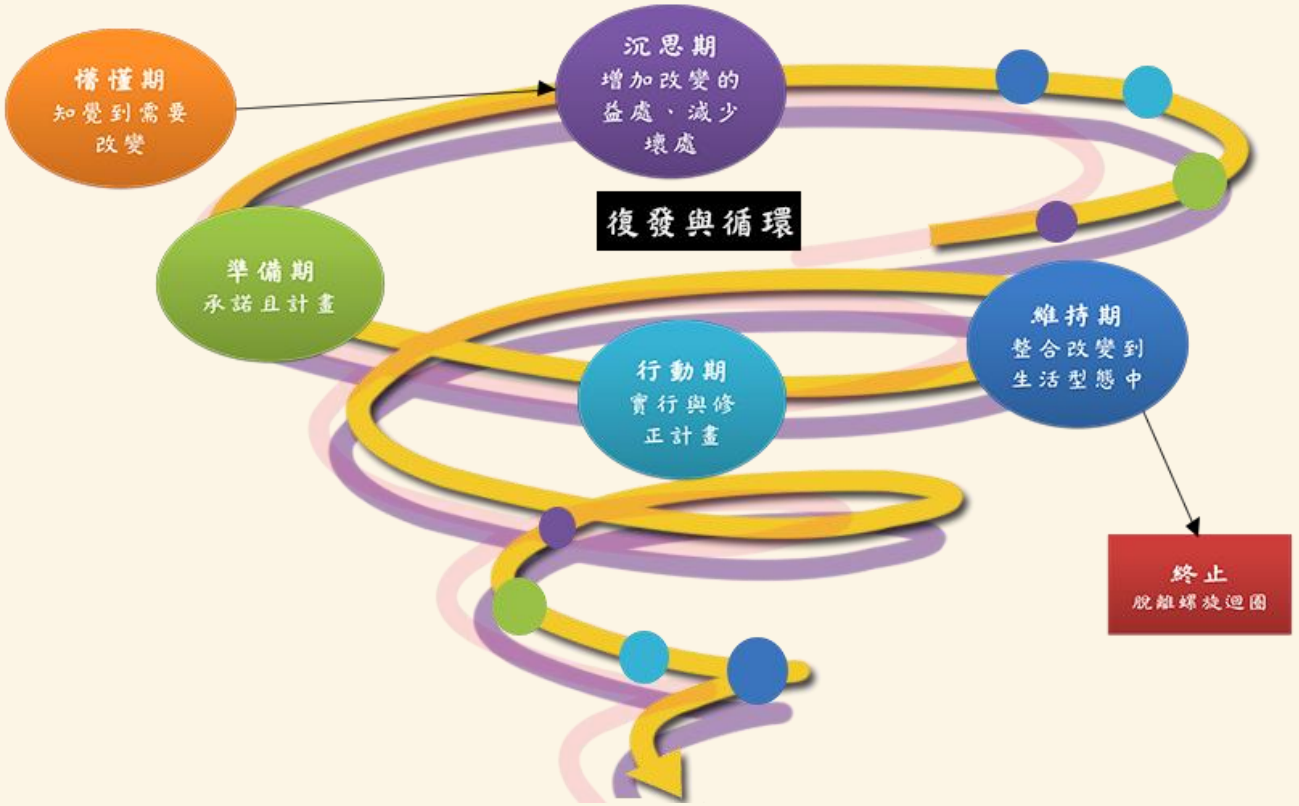
意志力戒酒 醫界：不可能任務

更新時間： 2019/08/14 05:00

方俊凱以專業角度分析，為何戒酒靠意志力行不通。他表示，「意志力」是要靠大腦來運作，也就是大腦前額葉皮質區。一般人在沒有什麼特別的壓力就想喝上一杯念頭，指令來自於中腦多巴胺神經系統；像觸景傷情動起想喝酒念頭，是在大腦另外一區顳葉內側海馬迴。方主任指出，這兩個區域都是屬於比較原始的區域，是不受意志力控制的，倒過來講是這兩區起心動念反而來動搖意志力。而有酒癮的人腦部神經系統受損，換句話來說，「意志力再怎麼堅強都沒辦法！

戒酒是意志力、是認知、是行動？





大家都愛用這個理論　結果就是團團轉

題西林壁

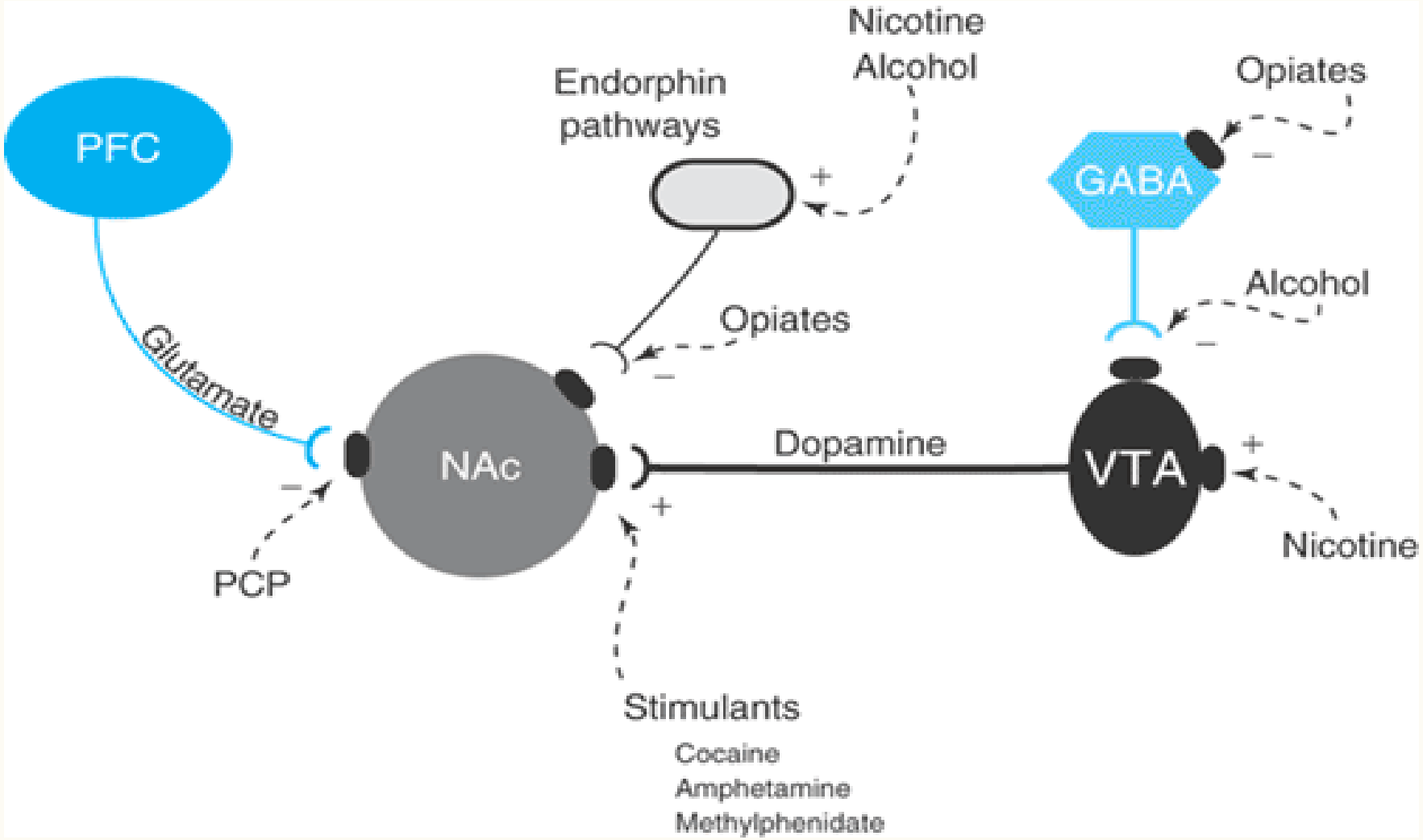
宋　蘇軾

橫看成嶺側成峯
遠近高低各不同
不識廬山真面目
只緣身在此山中

不識自己真面目
只緣認知受損中

Addictions Change the Brain

聖經：這樣，我願意行的善，我沒有去行；我不願意做的惡，我反而去做。 羅馬書7:19



AIMS Neuroscience

AIMS Neuroscience, 8(3): 390–413.
DOI: 10.3934/Neuroscience.2021021
Received: 20 January 2021
Accepted: 01 March 2021
Published: 09 April 2021

http://www.aimspress.com/journal/neuroscience

Review

Effect of alcohol on the central nervous system to develop neurological disorder: pathophysiological and lifestyle modulation can be potential therapeutic options for alcohol-induced neurotoxication

Zinia Pervin[1,*], Julia M Stephen[2]

[1] Department of Biomedical Engineering, University of New Mexico, Albuquerque, NM 87131, USA
[2] The Mind Research Network and Lovelace Biomedical and Environmental Research Institute, Albuquerque, NM 87106, USA

Abstract: The central nervous system (CNS) is the major target for adverse effects of alcohol and extensively promotes the development of a significant number of neurological diseases such as stroke, brain tumor, multiple sclerosis (MS), Alzheimer's disease (AD), and amyotrophic lateral sclerosis (ALS). Excessive alcohol consumption causes severe neuro-immunological changes in the internal organs including irreversible brain injury and it also reacts with the defense mechanism of the blood-brain barrier (BBB) which in turn leads to changes in the configuration of the tight junction of endothelial cells and white matter thickness of the brain. Neuronal injury associated with malnutrition and oxidative stress-related BBB dysfunction may cause neuronal degeneration and demyelination in patients with alcohol use disorder (AUD); however, the underlying mechanism still remains unknown. To address this question, studies need to be performed on the contributing mechanisms of alcohol on pathological relationships of neurodegeneration that cause permanent neuronal damage. Moreover, alcohol-induced molecular changes of white matter with conduction disturbance in neurotransmission are a likely cause of myelin defect or axonal loss which correlates with cognitive dysfunctions in AUD in developing a neuroprotective environment, we need to EtOH) metabolism and its effect on the CNS. Recent epid mal research have revealed the association between excessi ration. This review supports an interdisciplinary treatment p nd to improve the cognitive outcomes of patients who suffer from alcohol related neurodegeneration as well as clarify the pathological involvement of alcohol in causing other major neurological disorders.

stroke
brain tumor

Keywords: alcohol use disorder; central nervous system; oxidative stress response; neuropathology, blood-brain barrier dysfunction; neuroimaging, antioxidant

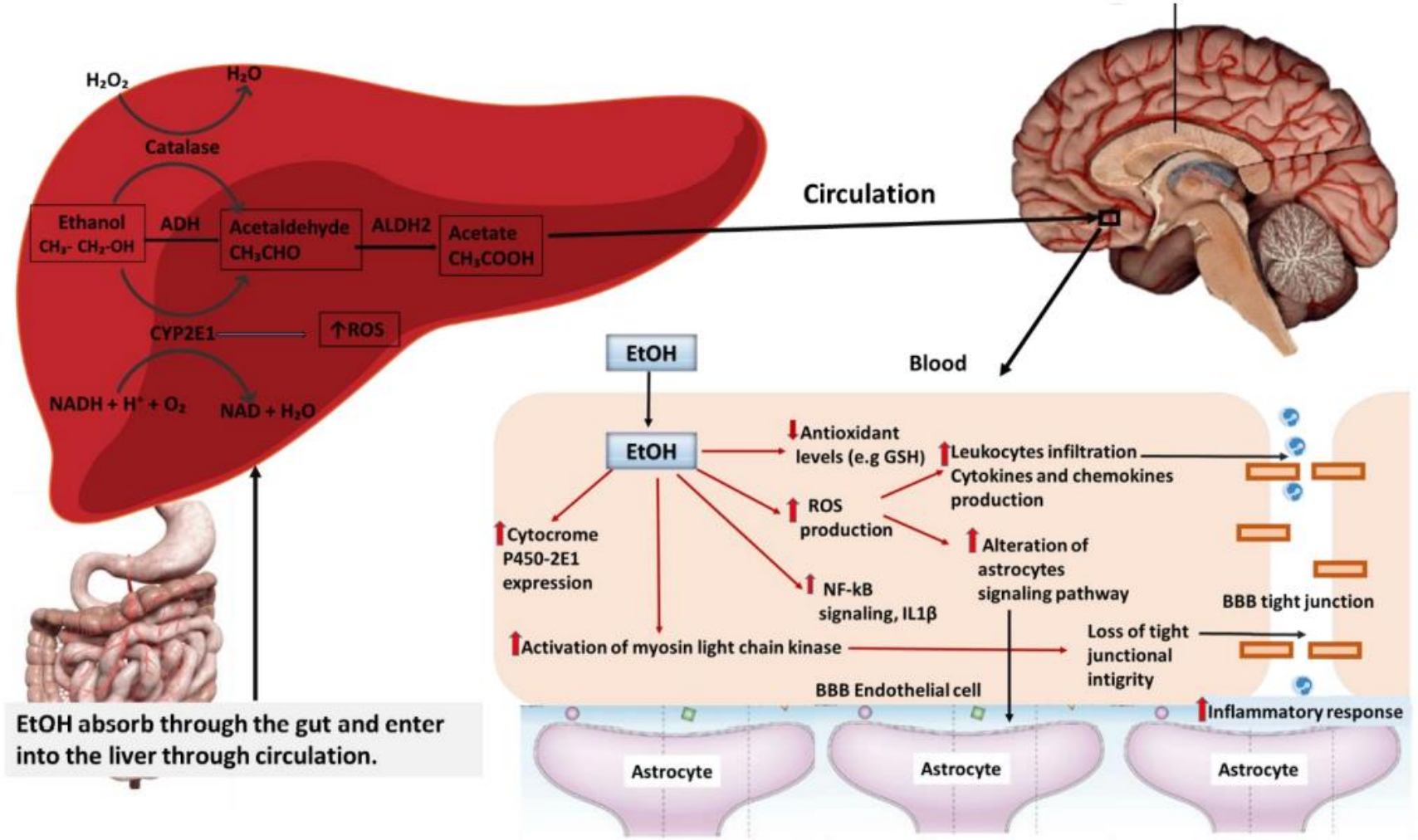


Figure 1. Schematic of ethanol metabolism through the liver and hypothetical involvement of ethanol metabolites for BBB dysfunction. In the presence of alcohol dehydrogenase (ADH) and cytochrome P450 enzymes, alcohol undergoes 1st and 2nd pass metabolism in the liver. Increased ROS and ethanol metabolites in the blood alter the signaling pathways of BBB endothelial cells and down-regulate the tight junction, which ultimately enhances leukocyte leakage and neuroinflammation [41,42,25].

Table 1. Evidence-based study about the relationship between alcohol and neurodegeneration.

Neurodegenerative disorder	Study type	The number of subjects with alcohol exposure history. Cases/control	Brief Description of neurodegenerative risk.	References
Alzheimer's disease	Population-based longitudinal study	111/3,202	The increased risk, an excessive amount of alcohol enhances tau phosphorylation and β- amyloid accumulation in CNS.	[76], [77]
Parkinson's disease	NIH-AARP diet and health cohort study	1,113/ 306,895	Moderate risk, AUD activates cytochrome P450 2E1 and causes dopamine toxicity with the aggregation of α-synuclein in neuronal tissue.	[78], [79]
Amyotrophic lateral sclerosis (ALS)	Population-based case-control study	1557/2922	No influence, inconsistent risk.	[80], [81]
Generalized dementia	Ginkgo evaluation of memory study	512/3021	Considerable evidence, evidence of marked white matter disturbances, and alteration of glucose metabolism with decreasing neuronal density and volume decreases may be responsible factors for dementia in AUD	[82], [83]
Huntington's disease	Small study (42 subjects at johns-Hopkins hospitals)	***	Alcohol abuse has a strong effect on onset of motor symptoms in Huntington's disease, concurrent with depression syndromes.	[84], [85]
Multiple sclerosis	Population based cohort study	About 450/500000	Considerable evidence of elevated risk on concurrent alcohol abuse with cigarette smoking, heavy alcohol consumption may cause inflammatory demyelination and axonal degeneration.	[81], [84]

Note: *** no data available.

Alzheimer's disease

Parkinson's disease

Amyotrophic lateral sclerosis

General dementia

Huntington's disease

Multiple sclerosis

Table 2. The association between lifestyle modification and neurodegeneration in AUD.

Lifestyle and etiological factors	Risk assessment in AUD for developing neurodegeneration.	Protective strategy	References
Age	The brain is highly susceptible to induced neurodegeneration in old age (>65) with a history of chronic alcoholism.	Alcohol abstinence with antioxidants supplements can reduce the aging or degenerative process.	[4], [143], [82]
Genetic susceptibility	ApoE 4 genotype is a strong risk factor for developing AD. Moderate and heavy alcohol consumption during old age causes dementia with a major decline in learning ability among ApoE4 allele carriers.	Lower risk of developing dementia among ApoE 2 allele carriers.	[77], [144]
Smoking	Concurrent heavy smoking with alcohol drinking increases the incidence of dementia, AD.	Control drinking and smoking risk with vitamin A, C supplementation to decrease the risk of dementia	[145], [146]
Substance misuse	Cocaine use associated with AUD to facilitates neurodegeneration.	Stop drug use and add nutritional supplements	[147], [148]
Comorbid conditions	Cardiovascular disease, liver cirrhosis, stroke, traumatic brain injury can exaggerate the alcohol effects on the CNS.	Alcohol abstinence with treatment and control of the comorbid condition.	[149], [150]
Hypertension and hypercholesteremia	High blood pressure and high lipidemia have a relation with AUD to develop neurodegeneration in the elderly.	Reduce cholesterol and BP by controlling alcohol consumption	[149], [151]

Nutritional hypothesis	Alcohol interferes with vitamin absorption in the body and causes nutritional (thiamine, folate) deficiency which induces CNS degeneration	Choline, folate, Vitamin A, C, B1, B6 supplementation can postpone the alcohol-related degeneration.	[77], [152]
Physical exercise	Less physical activity enhances the chance to develop dementia in AUD	Aerobic and anaerobic exercise triggers the body's enzymatic antioxidants production and prevents neurodegeneration.	[124], [153]
Psychosocial status	Less education, depression, work complexity enhances neurotoxicity in AUD.	Increased mental activity and social networking, cognitive training, and education can help to prevent dementia.	[154], [149]

7. The potential therapeutic approach to prevent neurodegeneration

7.1. Reducing ROS by antioxidant and anti-inflammatory therapy

7.2. Pharmacological and lifestyle modifications

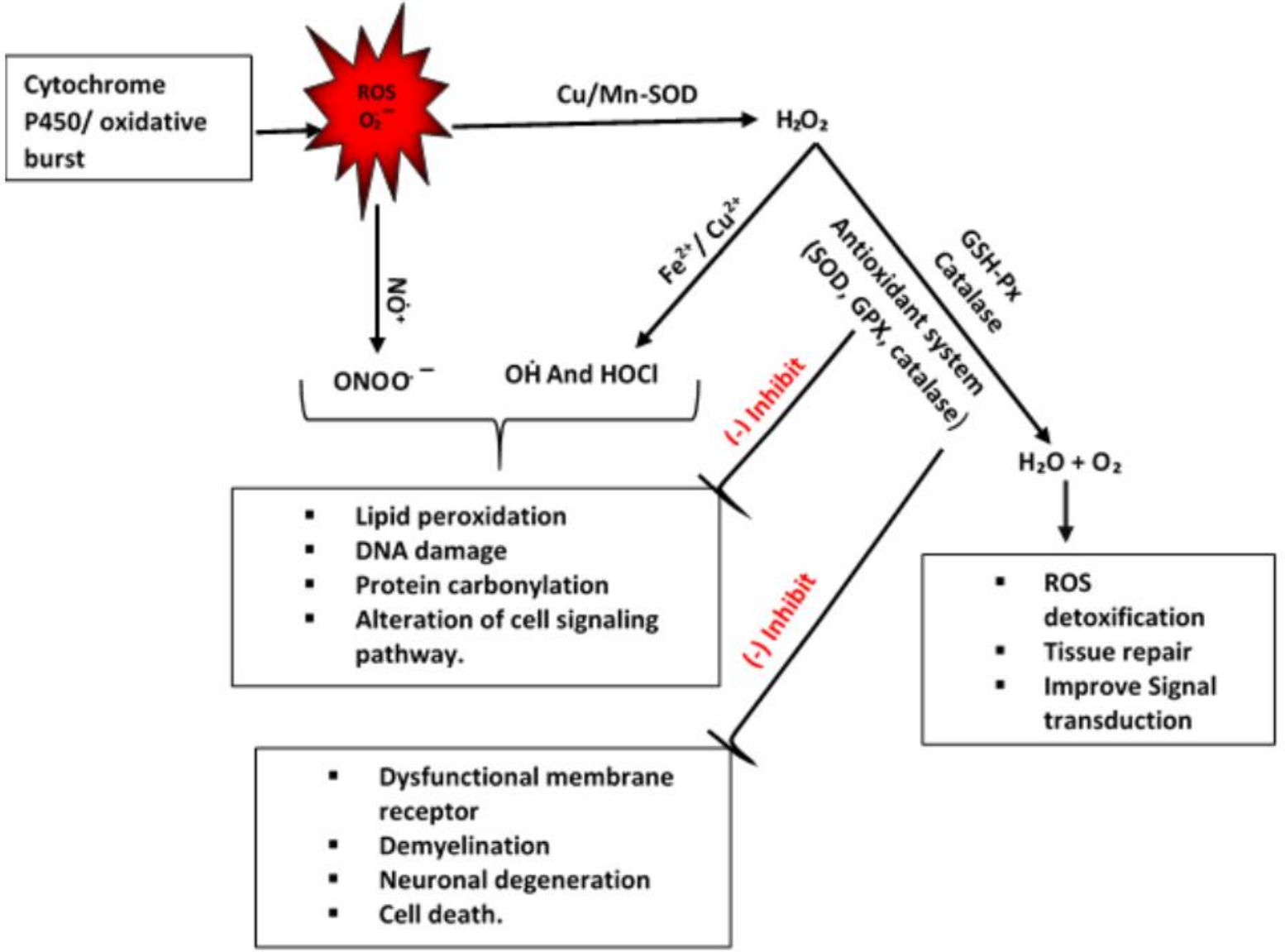


Figure 2. Alcohol-induced oxidative response which enhances the formation of certain free radicals (H_2O_2, $OH^{\cdot}$, and HOCl), causes cell damage and neuronal degeneration. However, increased expression of the antioxidant system can inhibit the process of cellular dysfunction and trigger the tissue repair system.

7.2. Pharmacological and lifestyle modifications

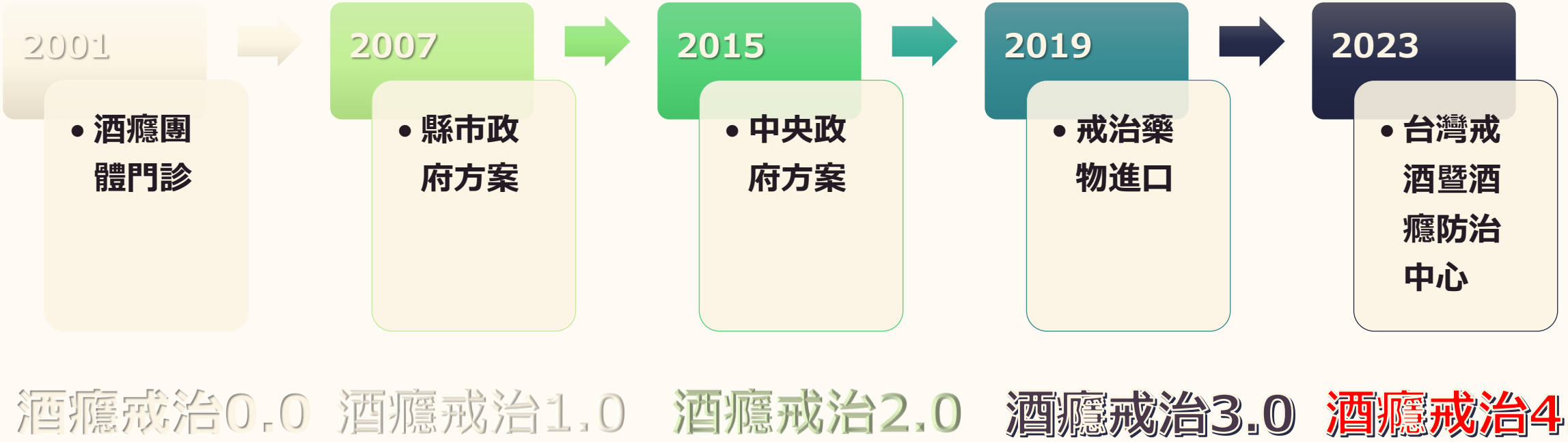
Currently, only five FDA-approved drugs are available to diminish the progression of neurodegenerative conditions. Four of them donepezil, rivastigmine, galantamine, tacrine, are based on acetylcholinesterase inhibition, and one of them, memantine, is an NMDA receptor antagonist [119]. Cognitive-behavioral therapy in conjunction with pharmacological options is developing interest as a treatment regime to enhance alcohol abstinence along with relapse prevention. The therapeutic agent, disulfiram was discovered for the treatment of alcohol dependence that blocks the conversion of acetaldehyde to acetic acid irreversibly results in accumulates the intermediate toxic product to develop an aversion to alcohol rather than proceed neurochemical actions of alcohol [127]. The adverse effect of disulfiram is outrageous over the clinical success towards preventing alcohol relapse. Anti-craving agents acamprosate and naltrexone are emerging concepts to control drinking.

Naltrexon

Naltrexone is an opioid receptor antagonist, found to be more effective to prevent relapse and maintain abstinence that reduces the rewarding effect of alcohol by generating fewer withdrawal effects [127,128]. Acamprosate enhance the tolerance of alcohol withdrawal symptom by stabilizing the activity of N-methyl-D-aspartate (NMDA)-mediated glutamatergic excitation during early abstinence. However, their full clinical success has not been established and it depends on the administration, target, and severity of the disease.

Acamprosate

馬偕酒癮戒治五階段的發展



歷年馬偕紀念醫院與政府的「酒」合作

- 酒癮戒治處遇服務方案。台北縣衛生局（2007~2009）
- 飲酒減量醫療戒治服務計畫。新北市(台北縣)衛生局（2010~2020）
- 特殊境遇族群心理衛生服務：臺北市酒癮戒治服務計畫。台北市衛生局（2011~2013; 2016-2020)
- 建構問題性飲酒與癮者醫療處置 及社會復健服務模式計畫。衛生福利部(2015~2020)
- 問題性飲酒與酒癮者成癮醫療及社會復健轉銜服務模式深耕計畫。衛生福利部(2021~2024)
- 酒癮防治中心建置試辦計畫。衛生福利部(2023~2024)

引進BRENDA模式 與政府密切合作

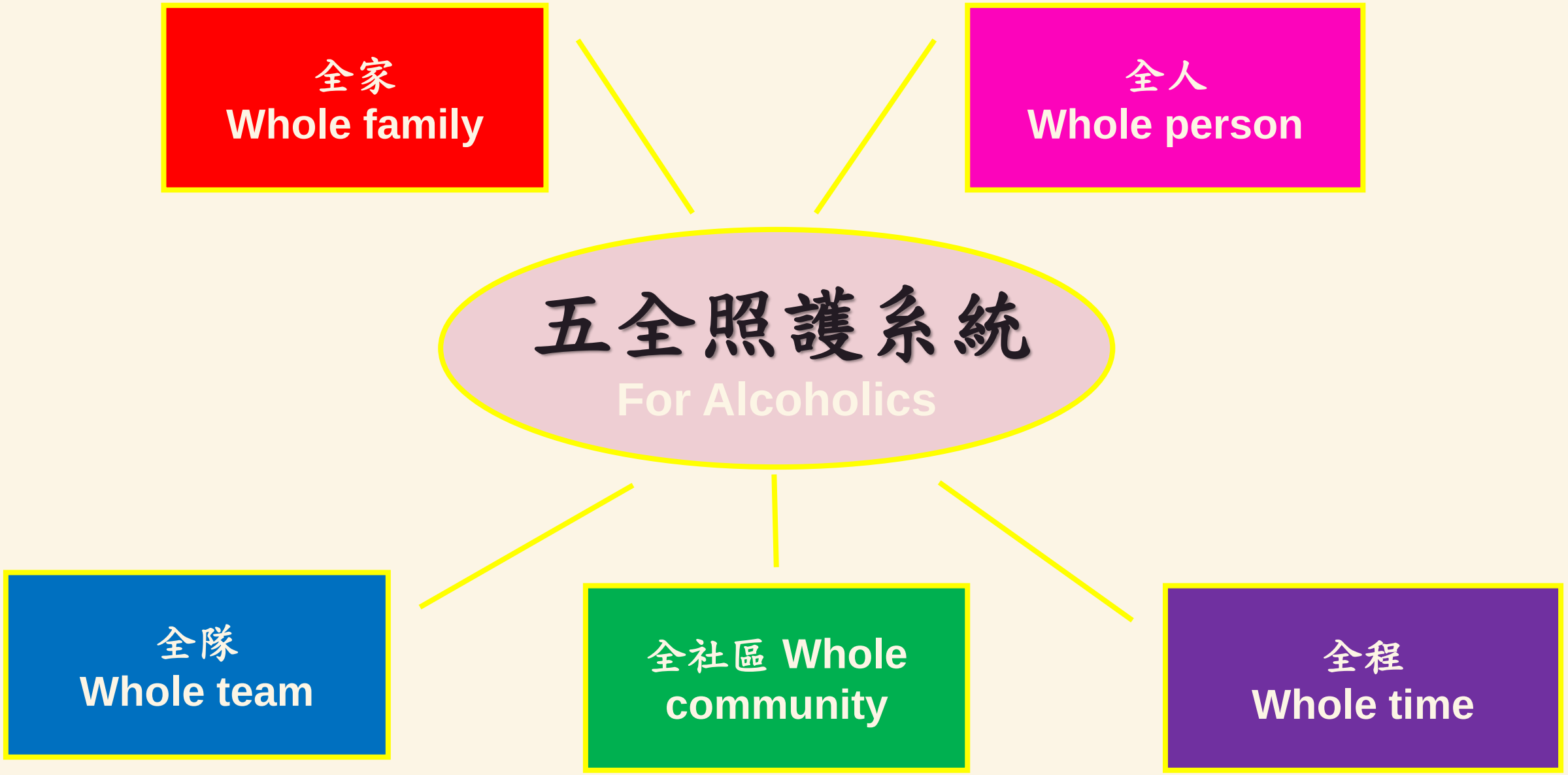
酒癮戒治1.0

馬偕自殺防治中心第2座

SNQ

IASP

World Health Organization

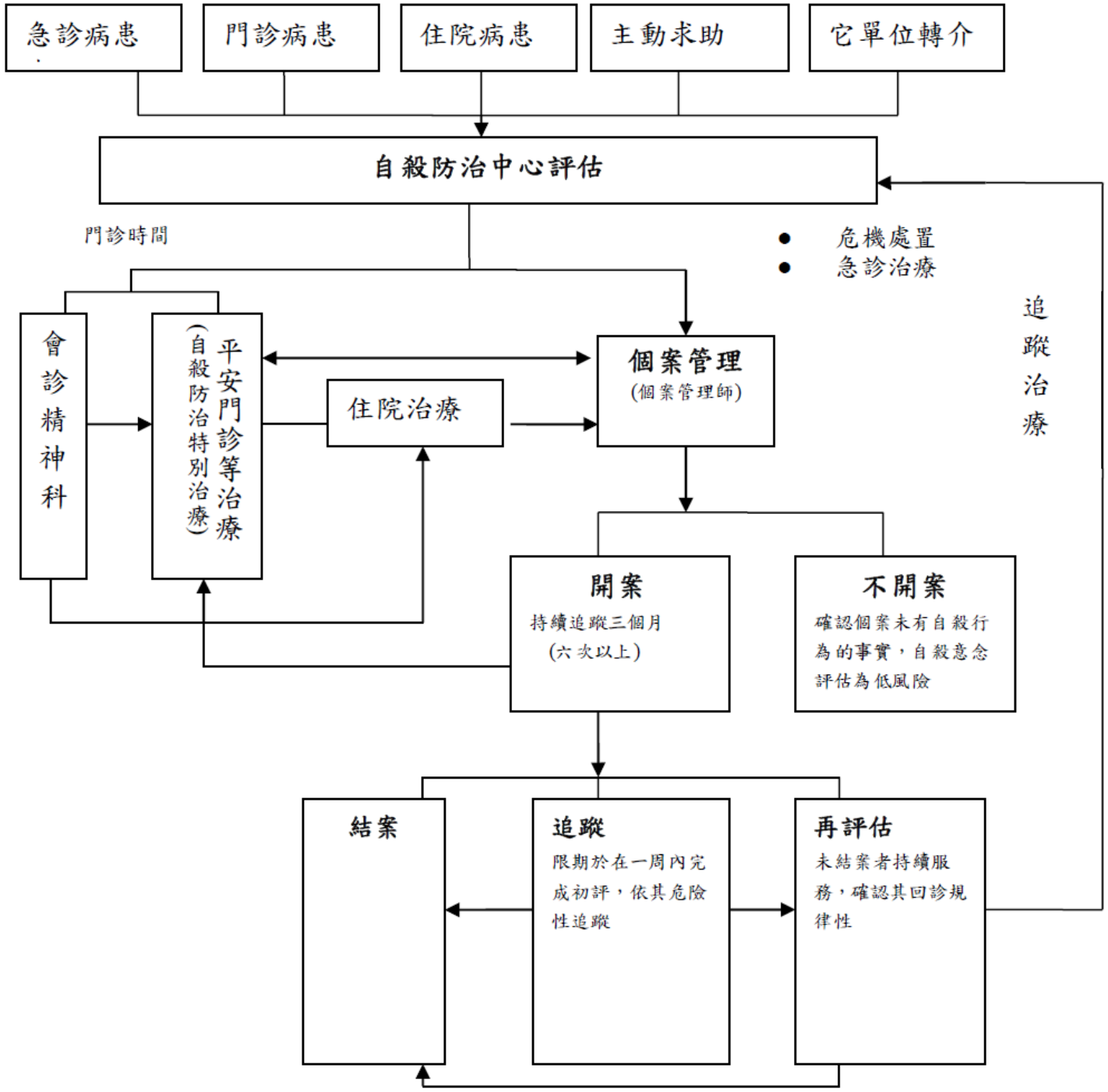

全家
Whole family
全人
Whole person
五全照護系統
For Alcoholics
全隊
Whole team
全社區 Whole community
全程
Whole time

BRENDA

- B :生理、心理和社會(Biopsychosocial)功能評估。
- R : 向病人告知(Report)評估結果。
- E :以同理心(Empathy)了解病人的問題。
- N:協助病人確認其需求(Needs)。
- D: 直接(Direct)建議病人如何達成需求。
- A :評估(Assess)病人對直接建議的反應，必要時調整建議，以達到最好的效果。

Volpicelli, JR.; Pettinati, HM.; McLellan, AT., et al. Combining medication and psychosocial treatments for addictions: The BRENDA approach. New York: The Guilford Press; 2001.

馬偕酒癮院外收案流程


急診病患
門診病患
住院病患
主動求助
它單位轉介
自殺防治中心評估
門診時間
危機處置
急診治療
追蹤治療
會診精神科
平安門診等治療
(自殺防治特別治療)
住院治療
個案管理
(個案管理師)
開案
持續追蹤三個月
(六次以上)
不開案
確認個案未有自殺行為的事實，自殺意念評估為低風險
結案
追蹤
限期於在一周內完成初評，依其危險性追蹤
再評估
未結案者持續服務，確認其回診規律性

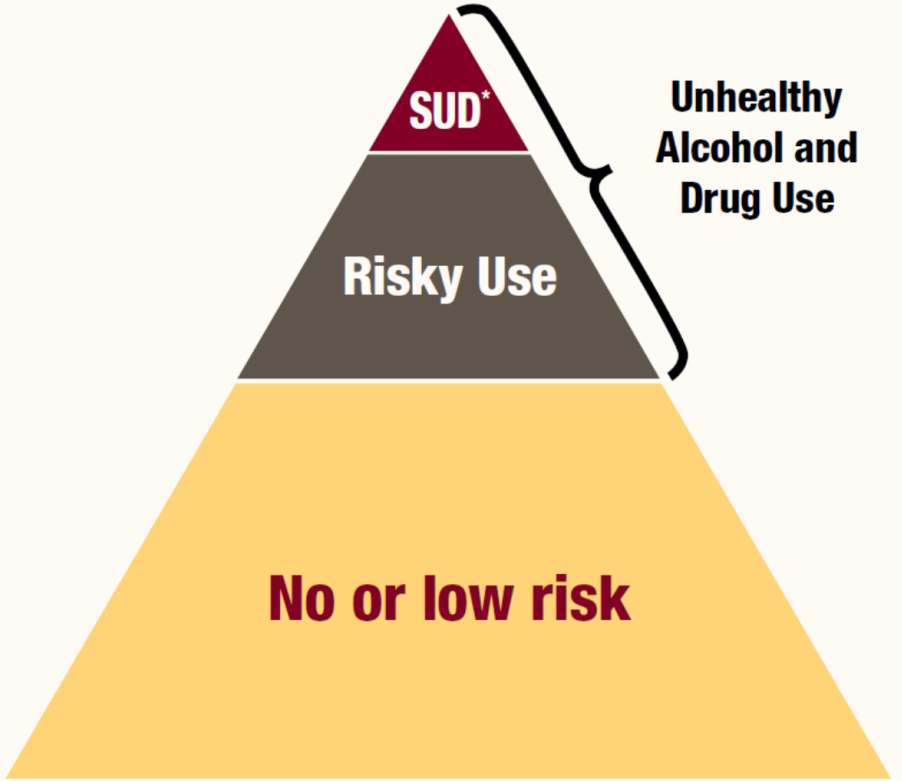
衛福部建構問題性飲酒與酒癮者之醫療處置及社會復健服務模式計畫

酒癮戒治2.0

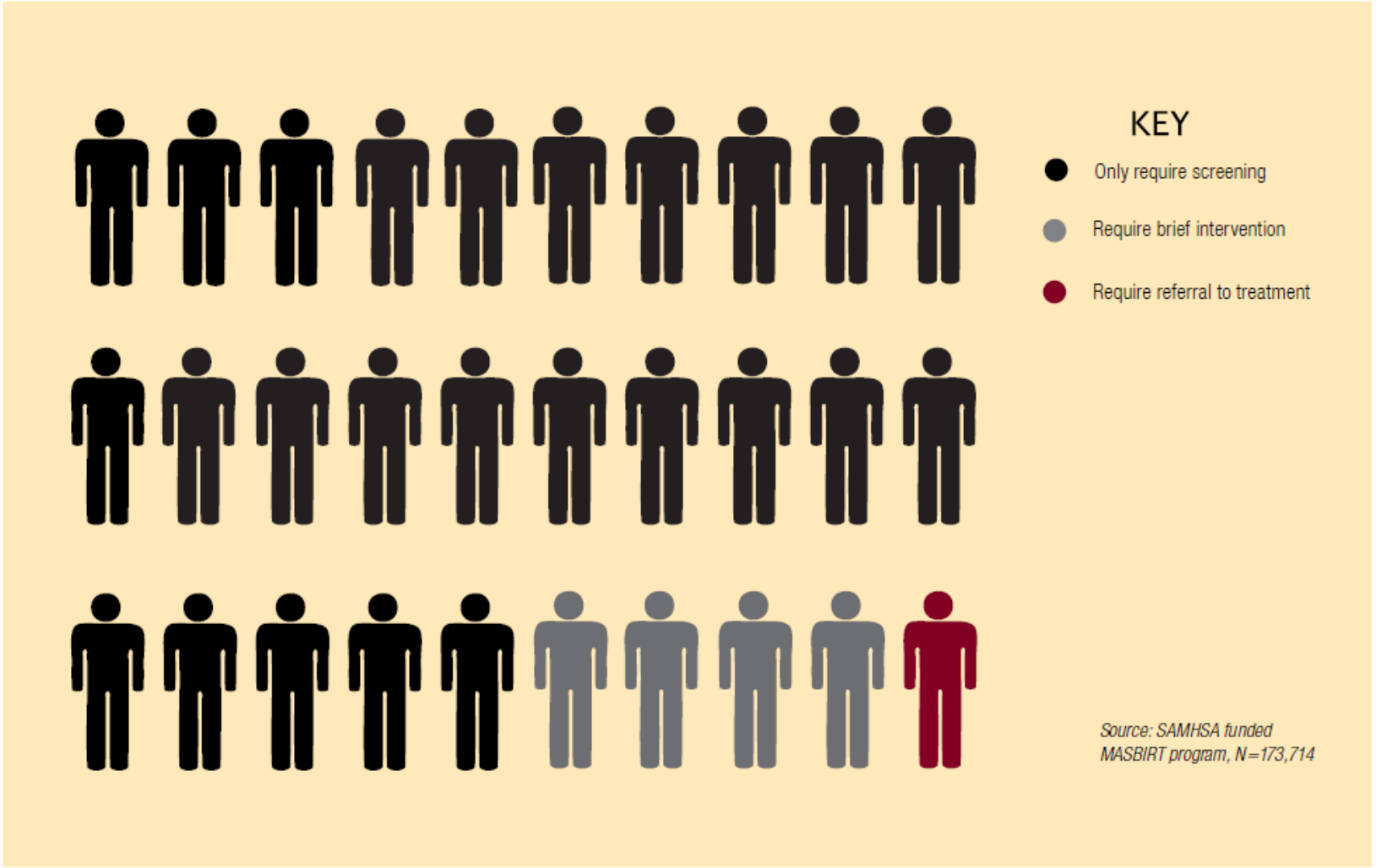
SBIRT

SBIRT components are:

- Universal, annual **Screening (S)** identifies unhealthy use. 75-85% of patients will screen negative. For those who screen positive, further assessment is needed to determine level of risk.
- **Brief Intervention (BI)** provides feedback about unhealthy substance use. It also focuses on education, increasing patient insight and awareness about risks related to unhealthy substance use, and enhances motivation toward healthy behavioral change.
- **Referral** to **Treatment (RT)** helps facilitate access to addiction assessment and treatment. A referral is usually indicated for only about 5% of people screened.



*Substance Use Disorders


KEY
Only require screening
Require brief intervention
Require referral to treatment
Source: SAMHSA funded
MASBIRT program, N=173,714

SBIRT


酒精知識諮詢關懷櫃檯
減害飲酒健康久久，終結酒駕幸福長久
「建構問題性飲酒與酒癮者篩檢及
社會復健服務模式計畫」
減害飲酒諮詢
評估與轉介治療
話:0800-551-099
點至3點
酒精知識諮詢關懷櫃檯
中央通訊社
THE CENTRAL NEWS AGENCY


酒精知識諮詢關懷櫃檯
減害飲酒健康久久，終結酒駕幸福長久
「建構問題性飲酒與酒癮者篩檢及
社會復健服務模式計畫」
服務項目:
酒精知識衛教 / 減害飲酒諮詢
酒精使用疾患評估與轉介治療
減害飲酒專線電話:0800-551-099
服務時間:每週三下午1點至3點

精神醫學部

專業人員	人數
專任主治醫師	21人
住院醫師(R1-R5)	10人
專任臨床心理師	8人
專任諮商心理師	4人
專任社會工作師	6人
專任職能治療師	6人
專任專科/臨床護理師	6人
約聘就業服務員+行銷	8人
約聘方案助理(老精+藥酒癮)	4人
護理師	>40人
全職實習心理師(臨床)	7人

自殺防治中心

專業人員	人數
專任臨床心理師	1人
專任諮商心理師	2人
專任社會工作師	1人
專任護理師	2人
特約諮商心理師(酒癮)	5人
特約社會工作師(酒癮)	2人
約聘關懷訪視員	6人
約聘方案助理(酒癮+AAAPC)	2+1人
全職實習心理師(臨床/諮商)	5人

板橋監理站攜手馬偕
酒精知識諮詢關懷櫃檯

*編制在精神醫學部的諮商心理師，服務安寧療護、癌症照護、失智症照護等業務。

馬偕紀念醫院總院(台北院區+淡水院區)

馬偕酒癮戒治團隊

醫師團隊	職級
方俊凱副教授	資深主治醫師
劉珣瑛教授	資深主治醫師(兒童青少年心智科)
徐堅棋助理教授	精神醫學部主任
林承儒博士候選人	老年精神科主任/SPC主任
孫藝文	資深主治醫師(老年精神科)
李朝雄副教授	資深主治醫師(一般精神暨身心科)
吳書儀副教授	一般精神暨身心科主任
黃郁心助理教授	兒童青少年心智科主任
林　穎博士候選人	資深主治醫師(老年精神科)
胡敬和	主治醫師(社區暨成癮防治科)
林辰翰	主治醫師(社區暨成癮防治科)

護心社團隊	職系	編制
林家華	護理師	自殺防治中心正編
施寶雯	諮商心理師	自殺防治中心特約
葉子菁	諮商心理師	自殺防治中心特約
游心慈	諮商心理師	Taiwan AAAPC約聘
買詠諫	諮商心理師	Taiwan AAAPC約聘
黃予岑	諮商心理師	自殺防治中心特約
徐瑋婷	諮商心理師	自殺防治中心特約
陳昱融	諮商心理師	自殺防治中心特約
林瓊珠	社會工作師	自殺防治中心特約
周書尹	社會工作師	自殺防治中心特約

Japanese Journal of Radiology (2020) 38:809–820
https://doi.org/10.1007/s11604-020-00989-3

INVITED REVIEW

Comprehensive review of Wernicke encephalopathy: pathophysiology, clinical symptoms and imaging findings

Yoshiaki Ota[1,2] · Aristides A. Capizzano[1] · Toshio Moritani[1] · Shotaro Naganawa[1] · Ryo Kurokawa[3] · Ashok Srinivasan[1]

Received: 9 April 2020 / Accepted: 29 April 2020 / Published online: 10 May 2020

Abstract

Wernicke's encephalopathy (WE) is a severe and life-threatening illness resulting from vitamin B1 (thiamine) deficiency. The prevalence of WE has been estimated from 0.4 to 2.8%. If not treated properly, severe neurologic disorders such as Korsakoff psychosis and even death may occur. The classical triad of clinical symptoms (abnormal mental state, ataxia, and ophthalmoplegia) is found in only 16–33% of patients on initial examination. The originally described underlying condition of WE is alcoholism, but it accounts for about 50% of causes of WE. Nonalcoholic patients are also affected by WE and likely to present symptoms and radiological imaging findings different from patients with alcoholism, which further complicates the diagnosis of WE. Being familiar with predisposing causes, symptoms and radiological imaging findings of WE is important for radiologists and clinicians when making the diagnosis to start immediate treatment. This review discusses pathophysiologies, underlying causes, clinical symptoms, imaging findings and their mimics.

Keywords Wernicke encephalopathy · Thiamine · Cytotoxic and vasogenic edema · MRI · Complications

Thiamine is a key vitamin in the maintenance of membrane integrity and osmotic gradients across cell membranes and is stored in body tissues predominantly as thiamine diphosphate (TDP). TDP participates in energy production as an essential cofactor for several enzymes in the TCA cycle and pentose phosphate pathways [5, 6]. The TCA cycle is a metabolic pathway that represents a key part of aerobic respiration. It involves a series of chemical reactions occurring in the mitochondria, which leads to the oxidation of acetate derived from carbohydrates, fatty acids, and amino acids into carbon dioxide, producing chemical energy in the form of adenosine triphosphate (ATP). The pentose phosphate pathway, a cytosolic process, generates pentoses, which are essential for the nucleic acid synthesis and the reduced form of nicotinamide adenine dinucleotide phosphate (NADPH), which is necessary for several anabolic processes. NADPH also helps to scavenge free radicals during oxidative stress [5, 6].

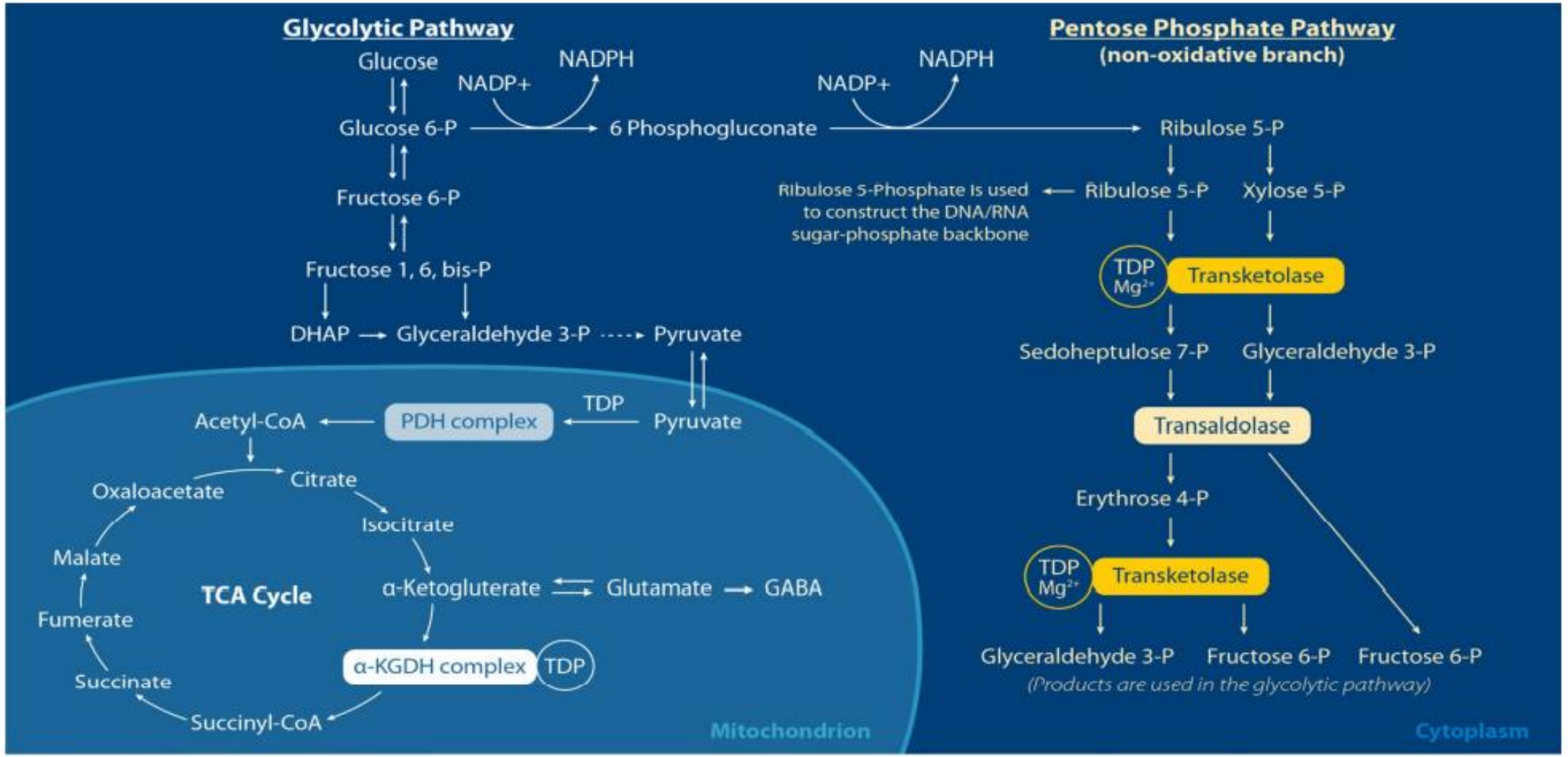


Fig. 1 Metabolic pathway related to thiamine

Fig. 2 Cytotoxic edema and vasogenic edema

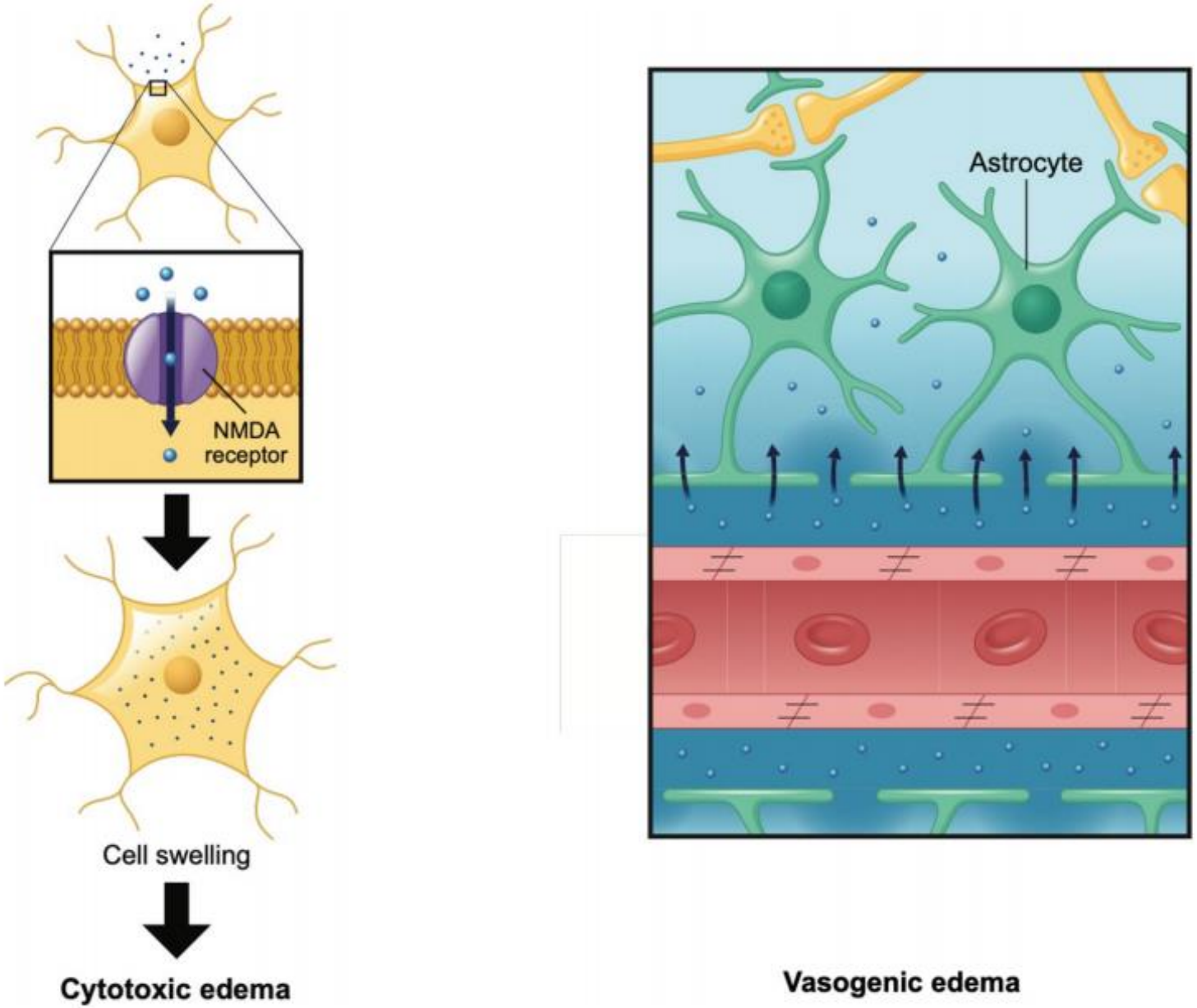
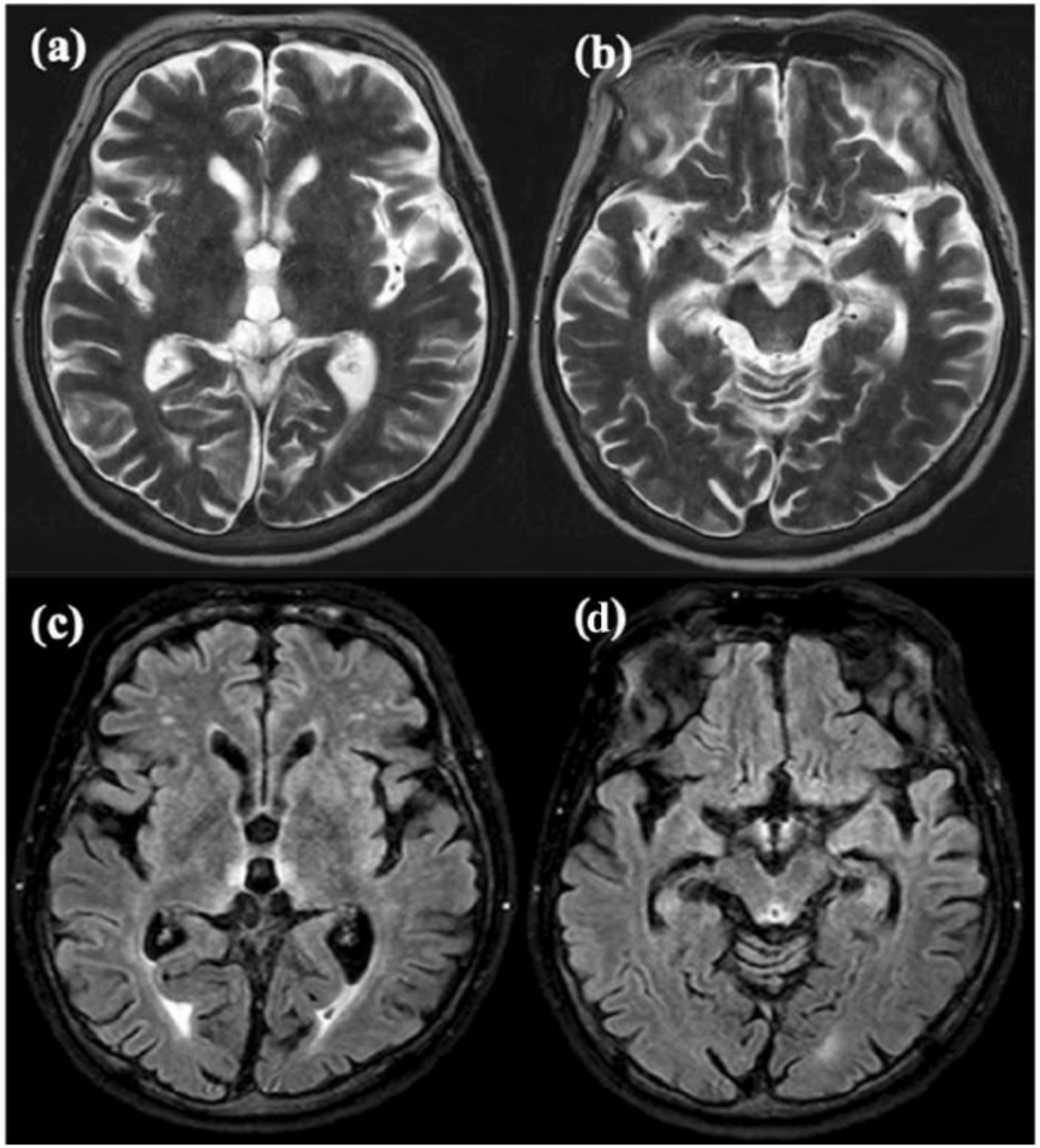


Table 1 Underlying conditions and diseases of Wernicke encephalopathy

Causes	Mechanisms of thiamine deficiency
Alcoholism	Low uptake of thiamine Low thiamine absorption rate at the mucosal level Impaired thiamine utilization
GI procedure/starvation	Low uptake of thiamine
Hyperemesis gravidarum	Low uptake of thiamine Increased demands of pregnancy and depleted thiamine stores Loss of thiamine
Chemotherapy	Low uptake of thiamine Decreased thiamine availability Inactivation of thiamine or enzymes of the intermediate carbohydrate metabolism Cachexia
Hyperthyroidism	Raised thiamine metabolism
Infectious and inflammatory diseases	Low uptake of thiamine Raised thiamine metabolism Inhibition of intestinal thiamine uptake
Genetic diseases	Inactivation of thiamine transporter



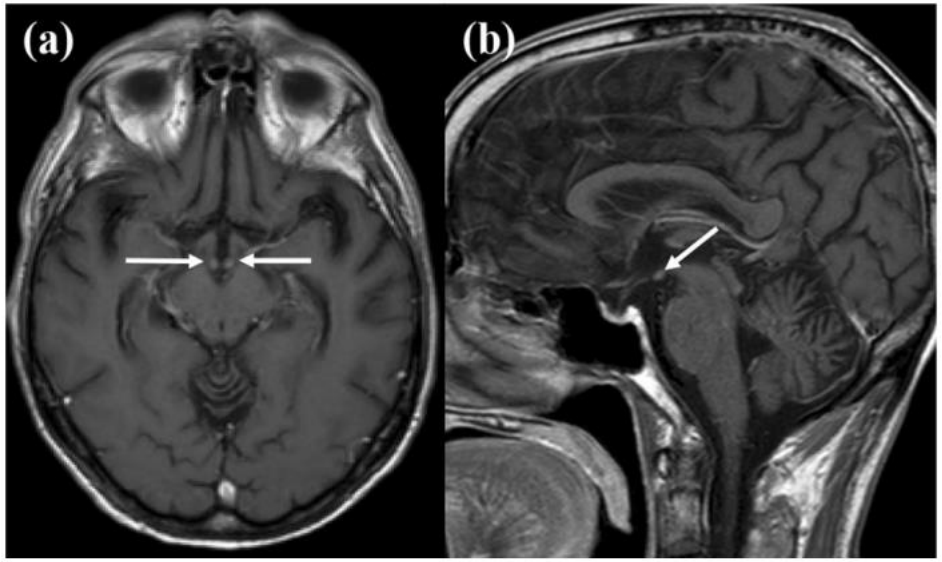


Fig. 7 Wernicke encephalopathy in Diabetic Ketoacidosis. A 54-year-old alcoholic patient with hyperglycemia, diabetes and ketoacidosis presented with mental status changes. **a**, **b** Symmetric abnormal enhancement in the mammillary bodies are demonstrated (arrows). FLAIR images show no signal intensity alteration (not shown)

Fig. 3 Typical MRI findings of Wernicke Encephalopathy. A 55-year-old alcoholic man presented with a 2-day history of confusion, ataxia and nystagmus. **a**, **b** T2-weighted images show bilateral and symmetric hyperintensity in the medial thalami, hypothalamus, mammillary bodies, periaqueductal area, and tectal plate. **c**, **d** FLAIR images demonstrate hyperintensity in the same lesions more conspicuously than T2-weighted images

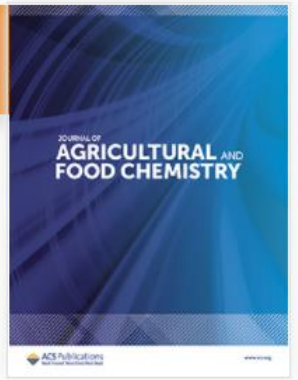
Anti-inflammatory Effects of the Roots of *Alpinia pricei* Hayata and Its Phenolic Compounds

Yu-Shan Yu†, Chin-Lin Hsu‡, and Gow-Chin Yen*†

Hide Author Information

† Department of Food Science and Biotechnology, National Chung Hsing University, 250 Kuokuang Road, Taichung 40227, Taiwan
‡ School of Nutrition, Chung Shan Medical University, Number 110, Section 1, Jianguo North Road, Taichung 40201, Taiwan

*To whom correspondence should be addressed. Telephone: 886-4-22879755. Fax: 886-4-22854378. E-mail: gcyen@nchu.edu.tw



Journal of Agricultural and Food Chemistry

Cite this: *J. Agric. Food Chem.* 2009, 57, 17, 7673–

Abstract

Alpinia pricei Hayata is cultivated throughout Asia and is an endemic plant in Taiwan. The leaf and root of this plant are used for traditional wrapping of food and as a cooking substitute for fresh ginger. The aim of this work was to study the *in vitro* anti-inflammatory effects of ethanol extracts from *A. pricei* Hayata (EEAP) and its phenolic compounds. High-performance liquid chromatography (HPLC) profiling indicated that EEAP contained caffeic acid, chlorogenic acid, ferulic acid, *p*-hydroxybenzoic acid, rutin, apigenin, curcumin and pinocembrin. EEAP and its phenolic compounds, apigenin, curcumin, and pinocembrin, inhibited lipopolysaccharide (LPS)-stimulated nitric oxide (NO) and prostaglandin E_2 (PGE_2) production in RAW 264.7 cells. Furthermore, EEAP, apigenin, curcumin, and pinocembrin decreased LPS-mediated induction of protein and mRNA expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in RAW 264.7 cells. In addition, EEAP and its major active compound pinocembrin inhibited LPS-induced nuclear translocation of nuclear factor-κB (NF-κB) and NF-κB-mediated reporter gene expression. EEAP and pinocembrin also significantly inhibited LPS-induced intracellular reactive oxygen species (ROS) production in RAW 264.7 cells. When these results are taken together, they indicate that EEAP and pinocembrin suppressed LPS-induced NO and PGE_2 production by inhibition of NF-κB nuclear translocation and ROS generation.

Taylor & Francis
Taylor & Francis Group

Journal of Enzyme Inhibition and Medicinal Chemistry

ISSN: 1475-6366 (Print) 1475-6374 (Online) Journal homepage: https://www.tandfonline.com/loi/ienz20

Curcumin inhibits TNFα-induced lectin-like oxidised LDL receptor-1 (LOX-1) expression and suppresses the inflammatory response in human umbilical vein endothelial cells (HUVECs) by an antioxidant mechanism

Hye-Sook Lee, Min-Ja Lee, Hyuck Kim, Sung-Kyu Choi, Jai-Eun Kim, Hyung-In Moon & Won-Hwan Park

To cite this article: Hye-Sook Lee, Min-Ja Lee, Hyuck Kim, Sung-Kyu Choi, Jai-Eun Kim, Hyung-In Moon & Won-Hwan Park (2010) Curcumin inhibits TNFα-induced lectin-like oxidised LDL receptor-1 (LOX-1) expression and suppresses the inflammatory response in human umbilical vein endothelial cells (HUVECs) by an antioxidant mechanism, Journal of Enzyme Inhibition and Medicinal Chemistry, 25:5, 720-729, DOI: 10.3109/14756360903555274

To link to this article: https://doi.org/10.3109/14756360903555274

Abstract

In this study, the anti-oxidative activities of 70% **ethanol** extract from Curcuma aromatica Salisb. (CAS) and **curcumin** (CUR) were studied. The CAS extracts and CUR were both found to have a potent scavenging activity against the reactive **species** tested, as well as an inhibitory effect on LDL oxidation. Cultured human umbilical vein endothelial cells (HUVECs) were stimulated with tumour necrosis factor alpha (TNFalpha), expression of intracellular reactive oxygen **species** (**ROS**), nitric oxide (NO), endothelial nitric oxide synthase (eNOS), lectin-like oxidised LDL receptor-1 (LOX-1), adhesion molecules, inhibitory kappa Balpha (IkappaBalpha) and nuclear factor kappa B (NFkappaB) were measured. In HUVECs stimulated with TNFalpha, CUR significantly suppressed expression of the intracellular **ROS**, LOX-1 and adhesion molecules, degradation of IkappaBalpha and translocation of NFkappaB, while inducing production of NO by phosphorylation of eNOS ($p < 0.05$). In conclusion, CAS and CUR may modulate lipoprotein composition and attenuate oxidative stress by elevated antioxidant processes.

日台
喝酒
文化
差異

日本心理腫瘤醫學會JPOS晚宴之後

喝酒當晚睡前

喝酒隔天早上

MAYO CLINIC

Evidenced-Based Pharmacotherapies for Alcohol Use Disorder: Clinical Pearls

Jeremiah Fairbanks, DO; Audrey Umbreit, PharmD, RPh; Bhanu Prakash Kolla, MD; Victor M. Karpyak, MD, PhD; Terry D. Schneekloth, MD; Larissa L. Loukianova, MD, PhD; and Shirshendu Sinha, MBBS, MD

Abstract

Pathologic alcohol use affects more than 2 billion people and accounts for nearly 6% of all deaths worldwide. There are three medications approved for the treatment of alcohol use disorder by the US Food and Drug Administration (FDA): disulfiram, naltrexone (oral and long-acting injectable), and acamprosate. Of growing interest is the use of anticonvulsants for the treatment of alcohol use disorder, although currently none are FDA approved for this indication. Baclofen, a γ-aminobutyric acid B receptor agonist used for spasticity and pain, received temporary approval for alcohol use disorder in France. Despite effective pharmacotherapies, less than 9% of patients who undergo any form of alcohol use disorder treatment receive pharmacotherapies. Current evidence does not support the use of pharmacogenetic testing for treatment individualization. The objective of this review is to provide knowledge on practice parameters for evidenced-based pharmacologic treatment approaches in patients with alcohol use disorder.

 ■ Mayo Clin Proc. 2020;■■(■):1-14

From the Department of Family Medicine and Community Health, University of Minnesota, Mankato (J.F.); Department of Pharmacy, Mayo Clinic Health System, Southwest Minnesota Region and Mayo Clinic College of Medicine and Science, Mankato (A.U.); Department of Psychiatry and Psychology, Mayo Clinic College of Medicine and Science, Rochester, MN (B.P.K., V.M.K., T.D.S., L.L.L., S.S.); and the Department of Psychiatry and Psychology, Mayo Clinic College of Medicine and Science, Scottsdale, AZ (T.D.S.).

Acamprosate

Naltexone

Disulfam

Topiramate

Baclofen

TABLE 3. Comparison of Medications for Alcohol Use Disorder[a]

Medication	Precautions	Additional indications	Approximate monthly cost[b]
FDA-approved pharmacotherapy			
Acamprosate	Renal impairment		$270/180 tablets
	Hypercalcemia		
Naltrexone	Liver disease	Opioid use disorder	$108/30 tablets
	Active opioid use	Binge-eating disorder (in combination with bupropion)[c]	$1,366/IM injection
Disulfiram	Liver disease	Stimulant abuse[c]	$104/30 tablets
	Active alcohol use		
	Psychosis		
	Cardiovascular disease		
Non-FDA–approved pharmacotherapy			
Nalmefene	Active opioid use		Not available in the United States
	Liver disease		
	Renal impairment		
Gabapentin	Renal impairment	Peripheral neuropathy	$150/90 tablets
	Potential for abuse	Seizure disorder	
		Restless leg syndrome	
		Anxiety[c]	
		Cannabis use disorder[c]	
		Alcohol withdrawal[c]	
Topiramate	Liver disease	Migraine prophylaxis	$151/60 tablets
	Renal impairment	Seizure disorder	
	Pregnancy (may cause fetal harm)	Binge-eating disorder[c]	
Baclofen	Renal impairment	Muscle spasm	$96/90 tablets
Ondansetron	QTc prolongation	Nausea	$204/50-mL bottle (solution required for appropriate dose)
	Serotonin syndrome		

[a]FDA = US Food and Drug Administration; IM = intramuscular.

[c]Denotes off-label use.

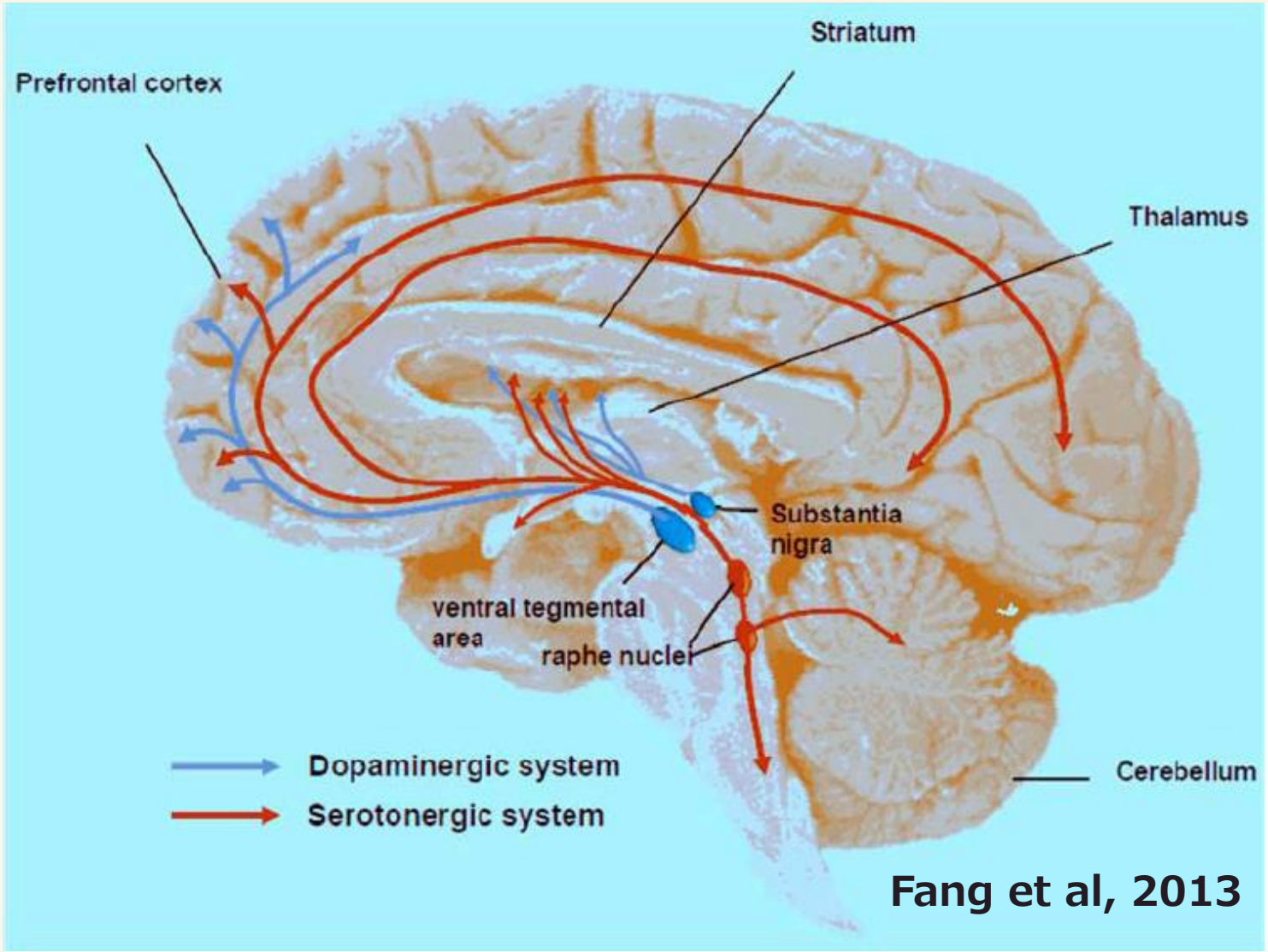
[b]Cost derived from average cash prices, excluding insurance coverage, as available on goodrx.com as of February 21, 2019.

PERSONALIZED MEDICINE

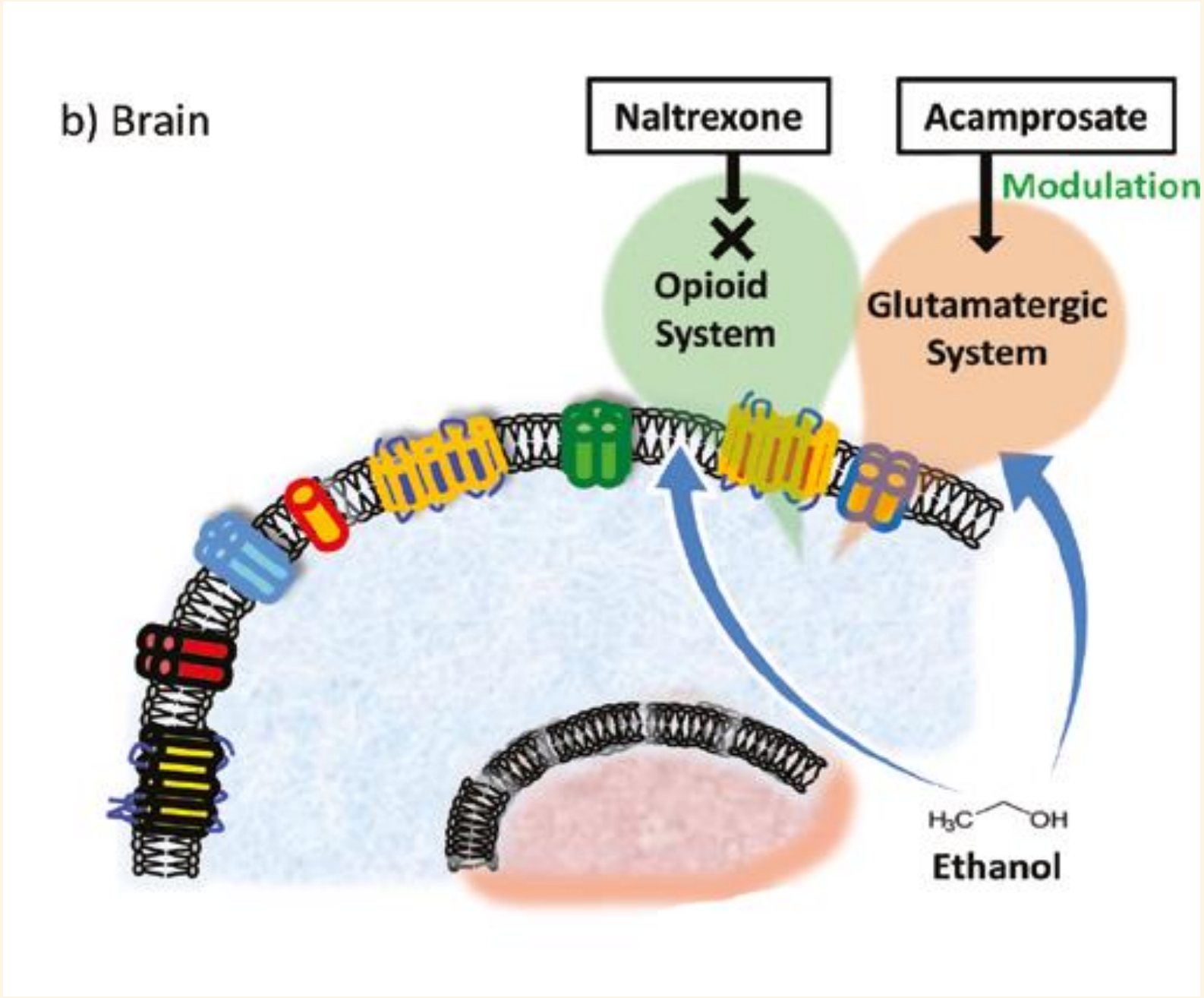
Pharmacogenomics is the study of how genetic factors affect individual drug response and represents an emerging approach in treatment of AUD. Although current evidence is insufficient to support broad implementation of personalized medicine for AUD, genetic variation has been shown to influence the response to several AUD medications. Naltrexone has been the most widely studied to date and has the most promising results with more than 20 replicated trials.[89] A specific polymorphism, A118G (rs1799971) in the μ-opioid receptor gene OPRM1, has been associated with naltrexone response. Patients with the OPRM1 118G allele appear to have a better treatment response compared with carriers of the 118A allele, making it a likely indicator for personalized naltrexone treatment.[90,91] These findings seem to be most promising in patients with East Asian ancestry, although other ethnic populations have also shown correlation.[91] However, two recent trials which attempted to replicate these findings were unsuccessful, making the role of OPRM1 genetics in predicting naltrexone response unclear.[14,92] Other AUD medications, including disulfiram, acamprosate, topiramate, nalmefene, and ondansetron, have fewer pharmacogenetics studies at this time.

Mayo Clin Proc. ■ XXX 2020;■■(■):1-14 ■ https://doi.org/10.1016/j.mayocp.2020.01.030
www.mayoclinicproceedings.org

基因檢測沒有帶來令人滿意的結果！



- 物質濫用或依賴在腦部的假說，是以mesolimbic dopaminergic pathway為最終的常見路徑。
- 酒精、鴉片、興奮劑、大麻、BZD、致幻覺劑、尼古丁，均影響mesolimbic dopaminergic system。



衛生福利部　函

機關地址：11558 台北市南港區忠孝東路六段488號
傳　　真：(02)3322-9526
聯絡人及電話：許寶文(02)2787-7675
電子郵件信箱：xav5611@fda.gov.tw

106
臺北市大安區信義路三段149號15樓

受文者：美時化學製藥股份有限公司

發文日期：中華民國107年9月18日
發文字號：衛授食字第1070022699號
速別：普通件
密等及解密條件或保密期限：
附件：藥品分配表

主旨：有關貴會為協助醫療機構順利遂行酒癮戒治服務用，協助各醫療院所集體申請並委託由美時化學製藥協助專案進口一案，經核，復如說明段，請查照。

說明：

一、復貴會107年6月20日癮字第10700000005號函。

二、本案本部原則同意專案進口藥品如下，藥品分配表如附件（簽審文件編號：DHS00000735624，項次：001-002，單位：TAB）。

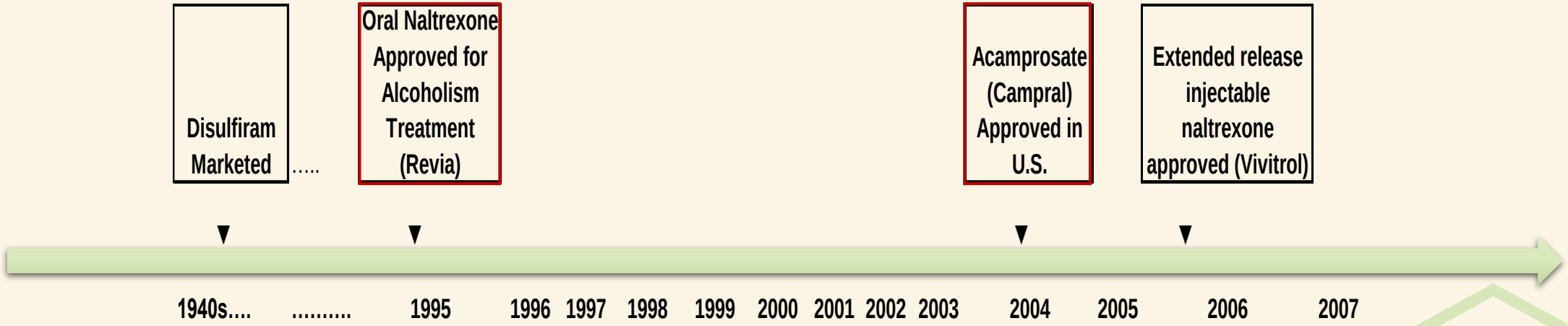
(一)項次：001，印度Glenmark Pharmaceuticals Ltd.製造之「Alcohout 333mg Delayed-Release Tablets (Acamprosate Calcium 333mg/tablet)」共812,880顆。

(二)項次：002，印度Intas Pharmaceuticals Ltd.製造之「Notholic 50mg Film-coated Tablets (Naltrexone hydrochloride 50mg/tablet)」共403,920顆。

三、該產品尚未經衛生福利部核准上市，請貴會詳實控管產品流向，每半年將藥品使用分配情形送本署備查，並提醒案內各醫療院所加強對藥品之不良反應監視及通報，若經發現，請立即通知全國藥物不良反應通報中心，以保障病人權益。

台印合作

Alcoholism Medications Approval Time Line



衛生福利部
Ministry of Health and Welfare

其實，早就知道了！

Addiction Biology (September 2005) 10, 289–292

RESEARCH ARTICLE

A double-blind, placebo-controlled study of naltrexone in the treatment of alcohol dependence in Taiwan

黃名琪

陳喬琪

MING-CHYI HUANG,[1,2] CHUN-HSIN CHEN,[2,3] JENG-MING YU[1] & CHIAO-CHICY CHEN[1,2]

[1]Department of Adult Psychiatry, Taipei City Psychiatric Center, [2]Department of Psychiatry, School of Medicine, Taipei Medical University, and [3]Department of Psychiatry, Taipei Medical University-Wan Fang Hospital, Taipei, Taiwan

Abstract

The aim of this study was to investigate the effectiveness of naltrexone in Taiwanese Han males with alcohol dependence. In conjunction with limited supportive psychotherapy, 40 alcoholic patients, who met Diagnostic and Statistical Manual version III revised (DSM-III-R) criteria for alcohol dependence, were assigned to a randomized double-blind, placebo-controlled trial of naltrexone hydrochloride (50 mg/day) for 14 weeks following alcohol detoxification. Among recruited patients, 45% (n = 9/20) of the naltrexone-treated subjects and 35% (n = 7/20) of the placebo-treated subjects dropped out (p = 0.374). The relapse rates between the two groups were not significant (p = 0.671). Subjects taking naltrexone reported less alcohol craving compared with placebo-treated subjects. In support of previous reports, the present results suggest that naltrexone may be safe and effective in craving reduction in alcohol-dependent subjects.

結果有希望，卻不是太理想！

Table 1. *Sociodemographic characteristics, drinking history and baseline data in the naltrexone and placebo treatment groups*

	Naltrexone $n=20$ (%)	Placebo $n=20$ (%)	p-value
Age (years old)	38.1 ± 5.8	42.9 ± 9.3	0.158
Education			
<9 years	12 (60.0)	12 (60.0)	
⩾9 years	8 (40.0)	8 (40.0)	0.626
Socioeconomic status			
I–III	3 (15.0)	2 (10.0)	
IV–V	17 (85.0)	18 (90.0)	0.500
Marital status			
Single	4 (20.0)	6 (30.0)	
Married	14 (70.0)	12 (60.0)	
Divorced	2 (10.0)	0 (0.0)	
Others	0 (0.0)	2 (10.0)	0.285
Age of first drinking (years old)	18.2 ± 3.3	20.3 ± 7.4	0.413
Age of first time drunk (years old)	18.5 ± 3.3	21.1 ± 7.5	0.326
Age of habitual drinking (years old)	27.5 ± 6.7	26.3 ± 7.1	0.686
Baseline alcohol craving score	5.6 ± 2.6	6.9 ± 2.2	0.311

其實
還是不錯的

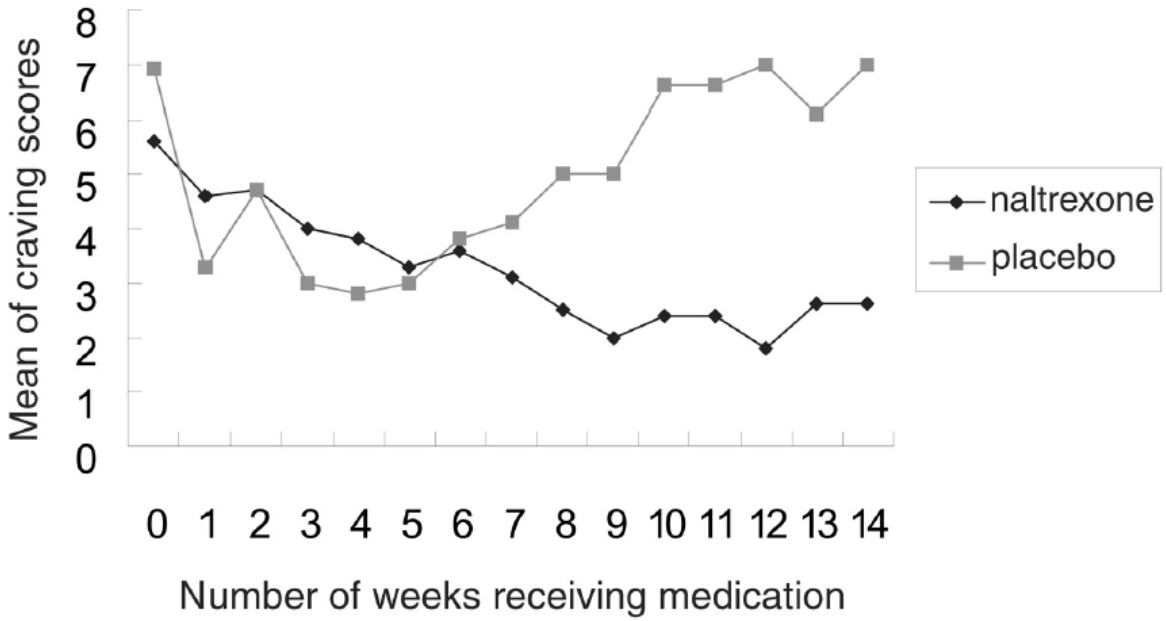


Figure 1. *Craving score for the naltrexone and placebo-controlled groups across the 14 weeks of the study.*

Alcohol & Alcoholism Vol. 39, No. 6, pp. 542–547
Advance Access publication 29 September 2004

doi:10.1093/alcalc/agh093

COMBINED THERAPY: WHAT DOES ACAMPROSATE AND NALTREXONE COMBINATION TELL US?

FALK KIEFER* and KLAUS WIEDEMANN

Department of Psychiatry, University Hospital of Hamburg, Hamburg, Germany

(*Received* 9 *June* 2004; *first review notified* 28 *July* 2004; *in revised form* 8 *August* 2004; *accepted* 8 *August* 2004)

Abstract — Aims: Relapse prevention treatment with both acamprosate and naltrexone has been shown to be efficacious in the treatment of alcoholism. Whereas both compounds act pharmacologically differently, there is up to now only limited evidence as to whether combined treatment is efficacious and pharmacologically safe. It remains to be answered whether data justify the combination of both drugs in clinical practice. **Methods:** Review of the three pre-clinical and four clinical studies that have been published to date on either combined tolerability or efficacy. **Results:** Data available up to now show no occurrence of severe adverse events during combined treatment. Diarrhoea and nausea were shown to be the most significant side-effects. Whereas pre-clinical studies regarding efficacy of combined treatment are not yet conclusive, clinical data show the superiority of combined treatment compared with both placebo and acamprosate monotherapy. The synergistic effect of combined treatment remained after 12 weeks of drug-free follow-up. **Conclusions:** The combination of acamprosate with naltrexone in a clinical sample seems to be efficacious and safe. Numerous alcohol dependent patients could benefit, particularly those that responded insufficiently on monotherapeutic treatment with either acamprosate or naltrexone.

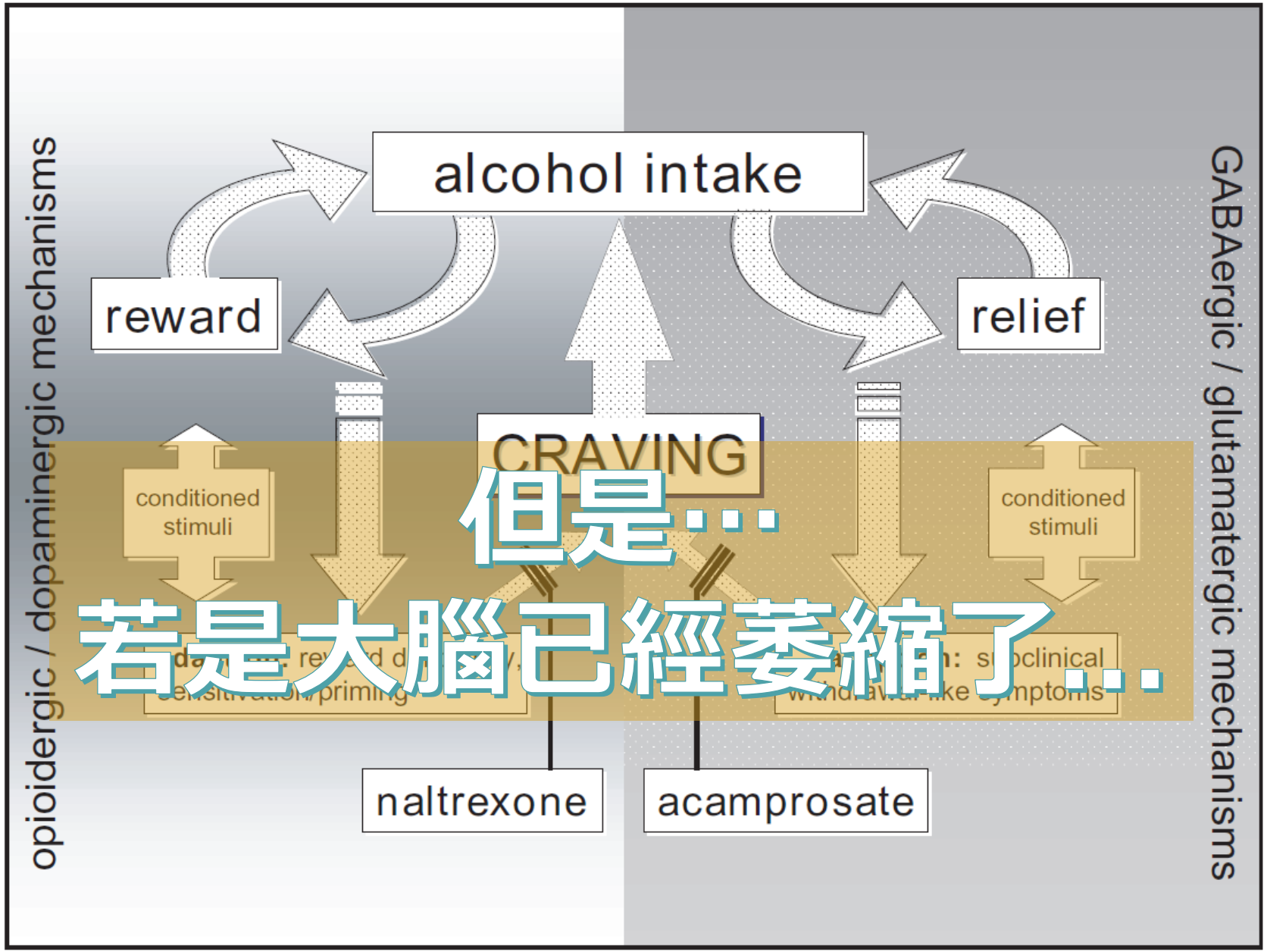


Figure 1. Dynamics of alcohol craving and consumption, indicating proposed neurophysiological mechanisms and possible points of impact of naltrexone and acamprosate.

酒癮戒治3.0

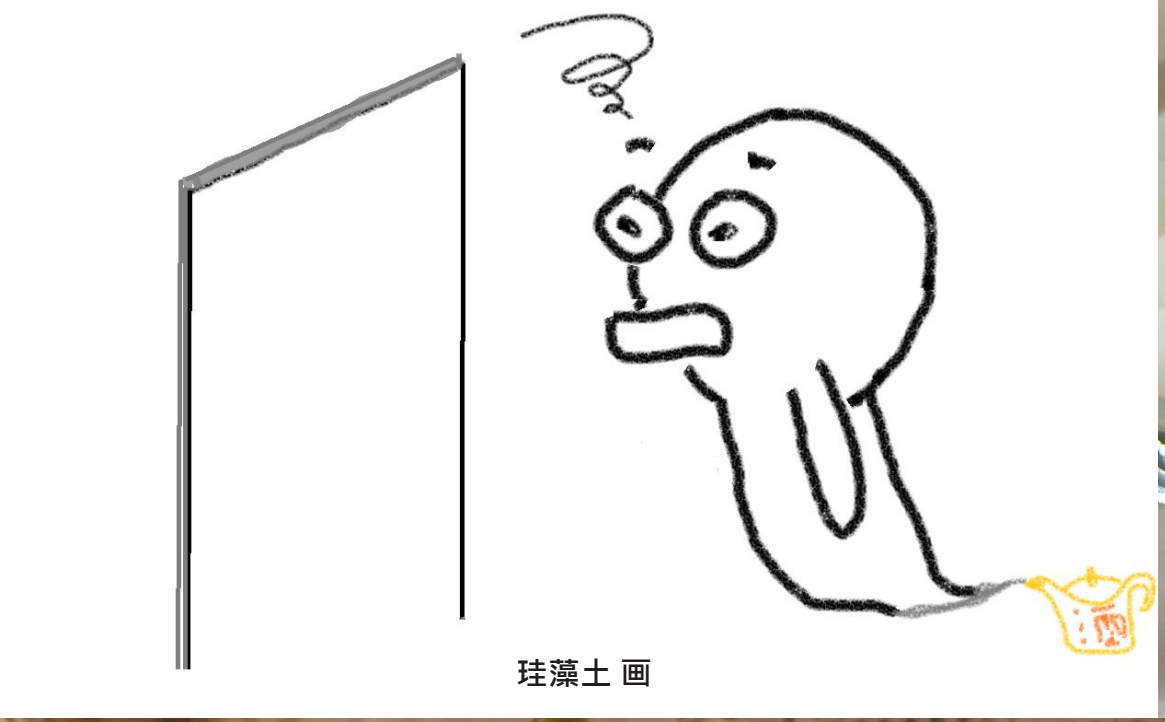
蘋果即時

新藥專案進口 37間機構可使用

更新時間： 2019/06/12 05:00

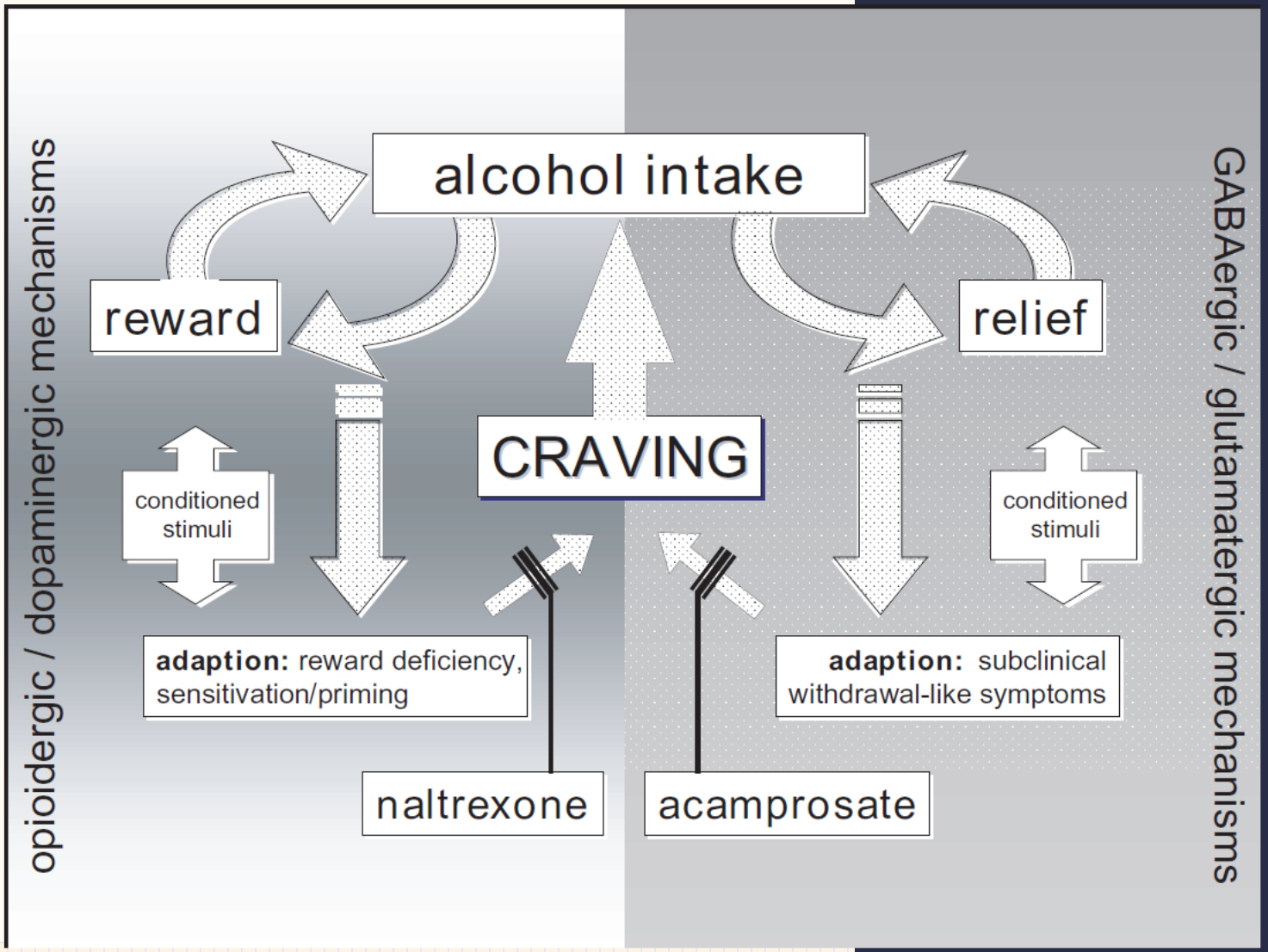
目前美國食品藥物管理局（FDA）已核准Naltrexone「納曲酮」、Acamprosate「阿坎酸」及Disulfiram（Antabuse）等三種藥物對酒癮治療具實證醫學療效，但以往國內成癮醫療界一直苦無上述藥物可用。黃三原表示，台灣成癮學會自去年委請廠商協助，以專案進口模式向衛福部食藥署提出兩種酒癮治療藥物。目前衛福部已准許37間醫療機構使用專案進口Naltrexone「納曲酮」及Acamprosate「阿坎酸」兩項口服藥物，供酒精使用障礙症患者選擇。

酒癮治療大致可分為「中毒治療」、「預防戒斷治療」、及「維持清醒及對抗酒精渴求治療」。黃三原強調，在酒癮的治療過程中，雖在酒精中毒與戒斷譫妄屬危險致命期，患者只要經成癮專業醫師治療多數皆能安全恢復。黃三原最怕是酒癮個案不斷地迴轉門式復發，因此，成癮學會委請專案進口的Naltrexone「納曲酮」及Acamprosate「阿坎酸」，這兩種藥物主要目的在於減低酒癮的興奮感，及對抗對酒的慾望，進而減少喝酒量與次數達到延長及維持不再酗酒之療效。



珪藻土 画

李白
究竟是死於撈月的意外
還是
AUD引起的腦病變+意外？



個人經驗

- 依照實證與仿單
  1. 確認肝腎功能
  2. 以6個月為目標
- 依照戒治動機
  1. 先確定全戒除或減量
  2. 確認肝腎功能
  3. 以長期使用為目標
     - 先Acamprosate後Naltrexone
     - 直接Naltrexone

SDM的精神與病人家屬一同決定

【會員限定】抗炎運動》搖呼拉圈、吃好油 甩19公斤　阻斷發炎——消除健檢紅字

直到一趟旅程才驚覺這樣很不健康，起心動念後，開始利用自己專長規劃減肥。兩年前生酮飲食正流行，試了幾周發現不可行，要我不吃澱粉完全不可能，使用的椰子油又是飽和脂肪酸，讓自己健康非常不好。後來，我修正為「類生酮」減肥法，因為我愛吃美食，因此每周還是會吃一到兩次的適量澱粉，以優質的五穀根莖類為主，例如：地瓜、燕麥等，每個月也會吃兩次麵食，像是拉麵或牛肉麵，這樣就不會讓減肥太悲慘。

油品的選擇，以omega3及6為主，我買了十多種油輪流使用，包括亞麻仁油、苦茶油、南瓜籽油、橄欖油、沙棘果油、酪梨油，不只可以涼拌也能單喝，好的油不只可以抗發炎，還能保護腦細胞。

草屯療養院的PDA for SDM

更多酒癮衛教資訊 可掃下方QR Code

成癮衛教資訊

酒癮衛教宣導

酒精與精神疾病

酒癮戒治介紹

酒癮難戒嗎? 還有哪些方法可戒酒呢?

這問題交給我們草療專業的成癮團隊爲您解答

酒精使用患者應該使用戒酒發泡錠嗎?

酒癮醫病共享決策

此決策適用對象

酒精使用疾患確認檢測(AUDIT) >20分
過去嘗試多種治療方法，效果不好
醫師建議使用戒酒發泡錠

衛生福利部
草屯療養院
Tsaotun Psychiatric Center, Ministry of Health and Welfare
酒精成癮精神科
電話：049-2550800 轉3911或5101
地址：南投縣草屯鎮玉屏路161號

臺北市立聯合醫院的PDA for SDM

醫病共享決策輔助工具(PDA)

臺北市立聯合醫院
醫病共享決策輔助平台

拒絕酒害-酒癮治療的藥物選擇

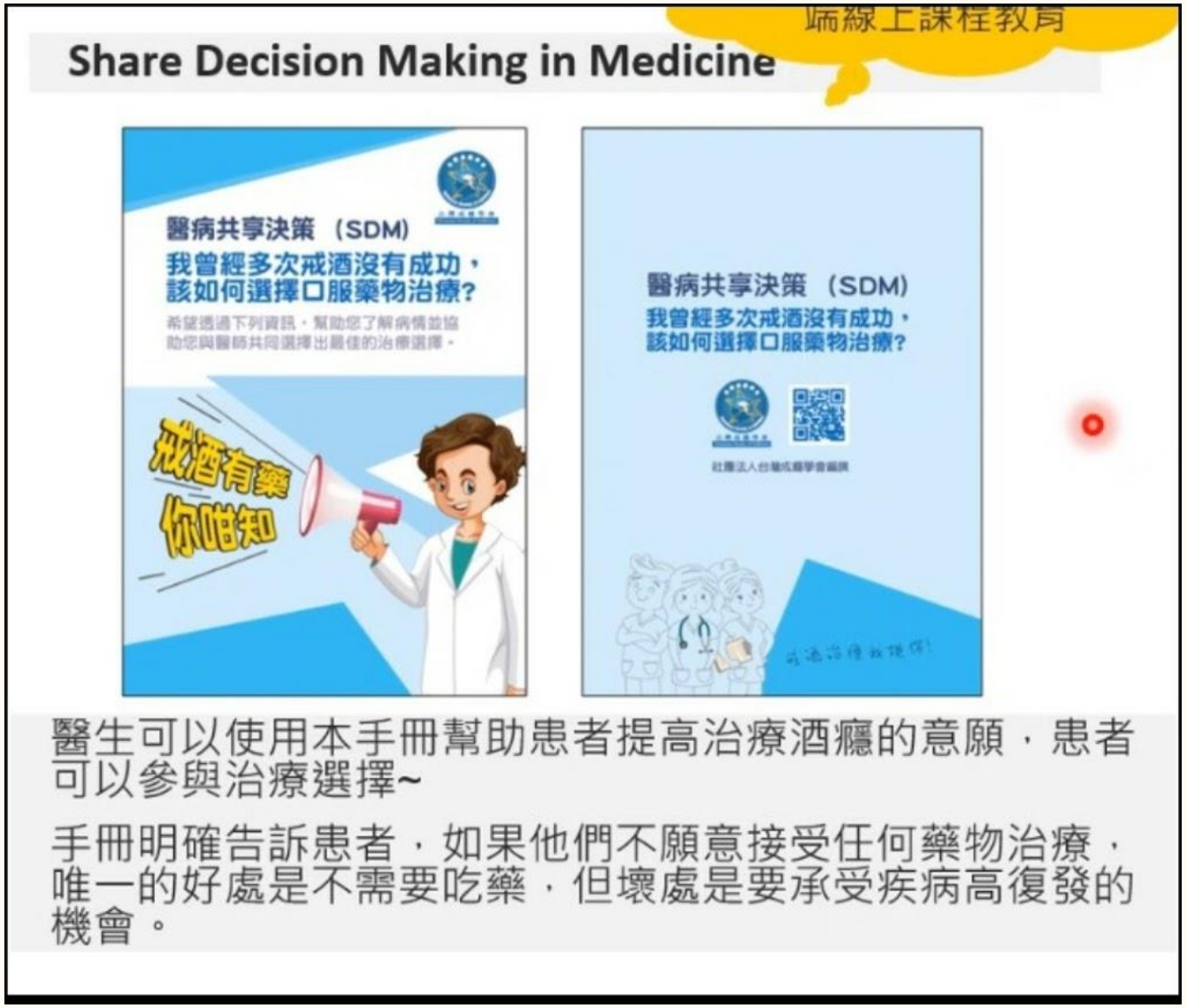
精神與行為

字級：A⁻ A A⁺　分享：

STEP1 前言 | STEP2 比較 | STEP3 考量 | STEP4 了解 | STEP5 決定 | STEP6 提交

前言

台灣成癮防治學會的PDA for SDM



醫生可以使用本手冊幫助患者提高治療酒癮的意願，患者可以參與治療選擇~

手冊明確告訴患者，如果他們不願意接受任何藥物治療，唯一的好處是不需要吃藥，但壞處是要承受疾病高復發的機會。

馬偕紀念醫院的PDA for SDM

PDA負責醫師：陳奕廷

吃藥最多只傷肝，喝酒全身都傷！

萬有都是所賜，藥物也是神的恩典，只要正向使用就好。

2023/6/29

馬偕紀念醫院近三年與院內及院外單位合作連結

積極與院內非精神科病房以及院外單位包含監理站、家防中心等各單位合作，於監理站架設個別諮詢櫃台，並積極出席社政單位之個案討論會議。

院內非精神科病房跨團隊會議

監理站架設諮詢櫃台

新北更生保護會個案討論

東區家庭服務會議宣導減害飲酒轉介

減害飲酒個案服務成效

本院近三年減害飲酒之服務：

① 個案量平均266人

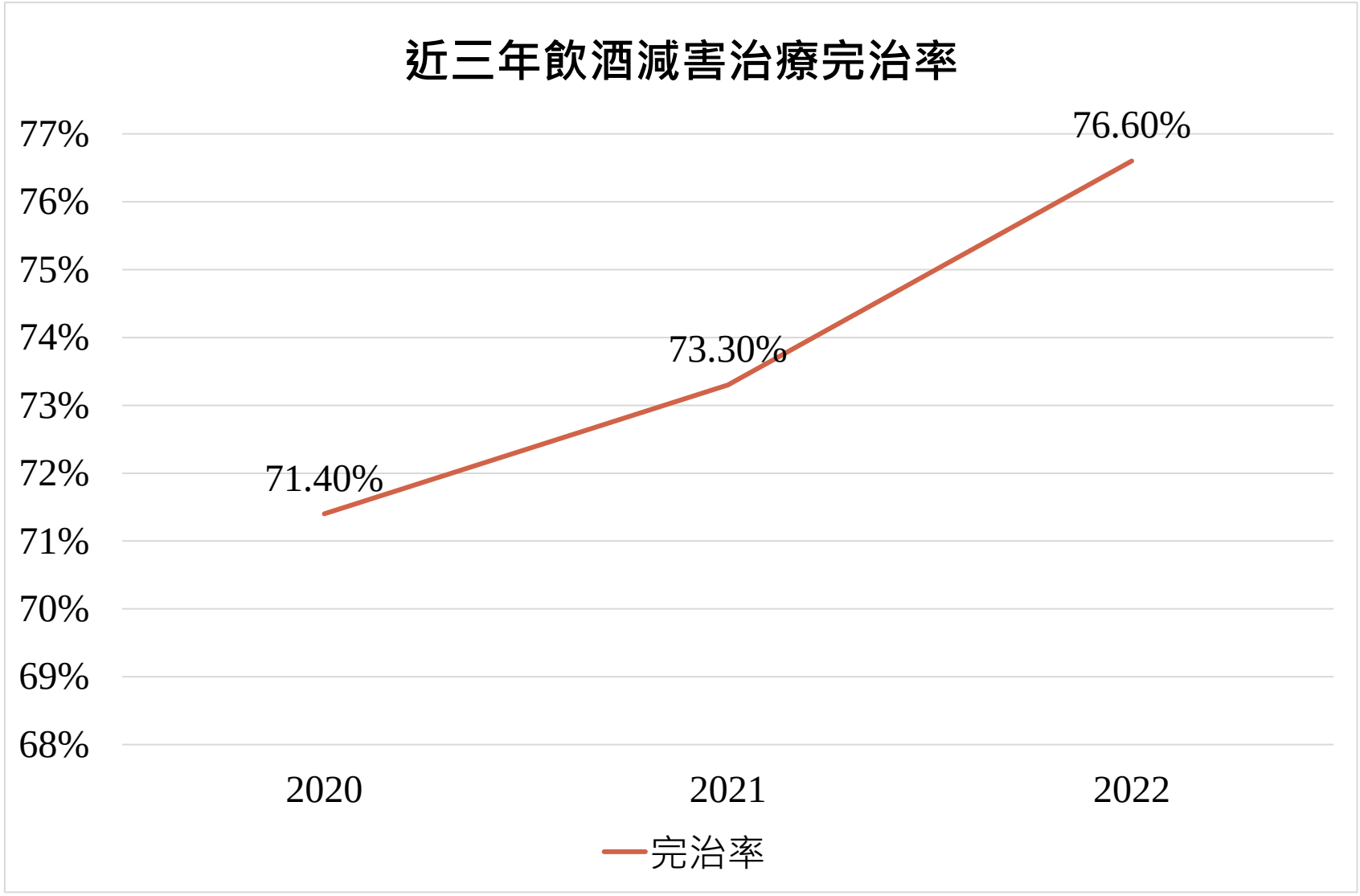
② 平均完治率達73.8%

③ 平均退出率7.3%

遠低於國外統計酒精成癮者的22%治療退出率（Lappan, et al., 2020）。

項目 年度	總服務個案	完治率*1	退出率*2
2020	268	71.4%	7.3%
2021	235	73.3%	6.5%
2022	296	76.6%	8.1%
總平均	**266**	**73.8%**	**7.3%**

*1完治率計算方式：（當年度完成治療人數／當年度結案人數）x100%
*2退出率計算方式：（當年度非不可抗力因素退出治療人數／當年度結案人數）x100%


近三年飲酒減害治療完治率
77%
76%
75%
74%
73%
72%
71%
70%
69%
68%
76.60%
73.30%
71.40%
2020
2021
2022
完治率

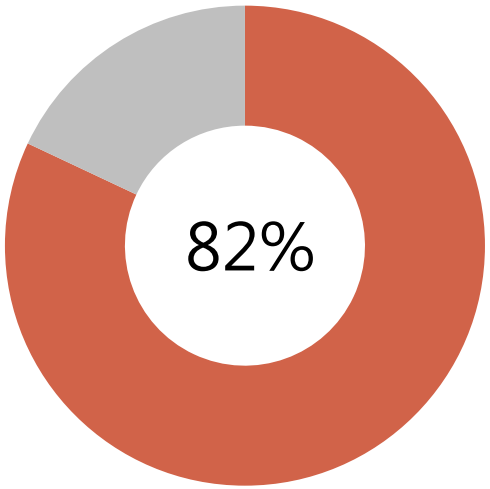
減害飲酒個案服務成效

酒癮個案治療前後成效指標變化（以2022年為例）：

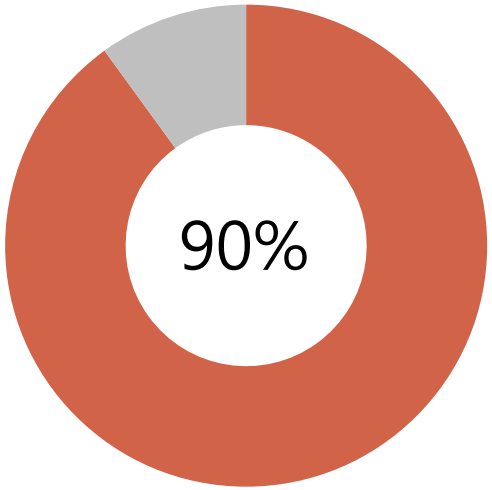
- 當年度結案個案**完治率高達76.60%**，

  其中**近三成個案可以完全停酒超過三個月**。

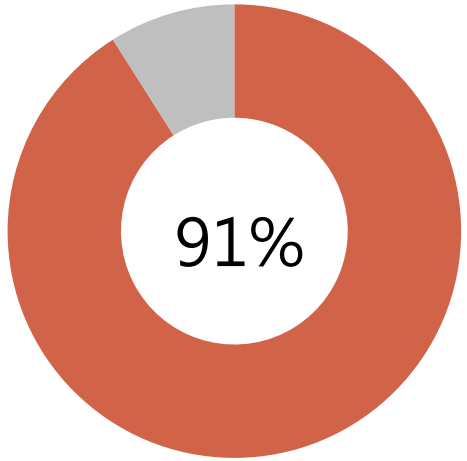
飲酒頻率下降



飲酒量下降



大量飲酒頻率下降
（每次超過6單位）



酒癮戒治4.0

馬偕紀念醫院承接衛福部委辦之酒癮防治中心建置試辦計畫，規劃於112年設立**「台灣戒酒暨酒癮防治中心」（Taiwan AAAPC）**推動酒害知識宣導推廣及專業人力培育。並主責酒癮深耕計畫之管理與效益評估，辦理聯繫會議及成果發表會。

112-113年　15家承作酒癮深耕計畫醫院分佈圖

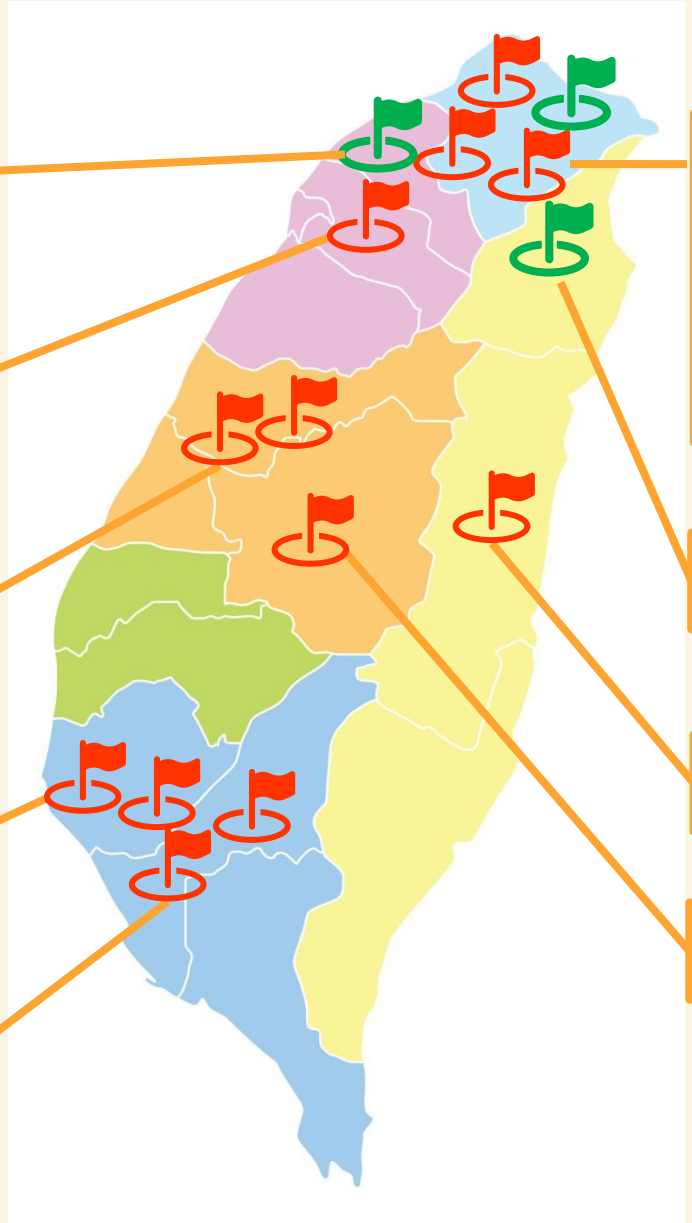
衛生福利部桃園療養院

國軍新竹地區醫院附設民眾診療服務處

中國醫藥大學附設醫院
臺中榮民總醫院

衛生福利部嘉南療養院
奇美醫院

高雄市立凱旋醫院
高醫大附設中和紀念醫院



馬偕紀念醫院
台北慈濟醫院
臺北市立聯合醫院松德院區
國防醫學院三軍總醫院

國立陽明交通大學附設醫院

臺北榮民總醫院玉里分院

衛生福利部草屯療養院

酒癮深耕計畫服務內容

對外辦理業務包含：

① 接受院內外各資源網絡轉介酒癮個案。

② 辦理專業人員教育訓練工作坊。

③ 辦理一般民眾減害癮酒宣導。

提供酒癮個案服務內容，包含：

① 酒癮門診與藥物治療。

② 個別心理治療。

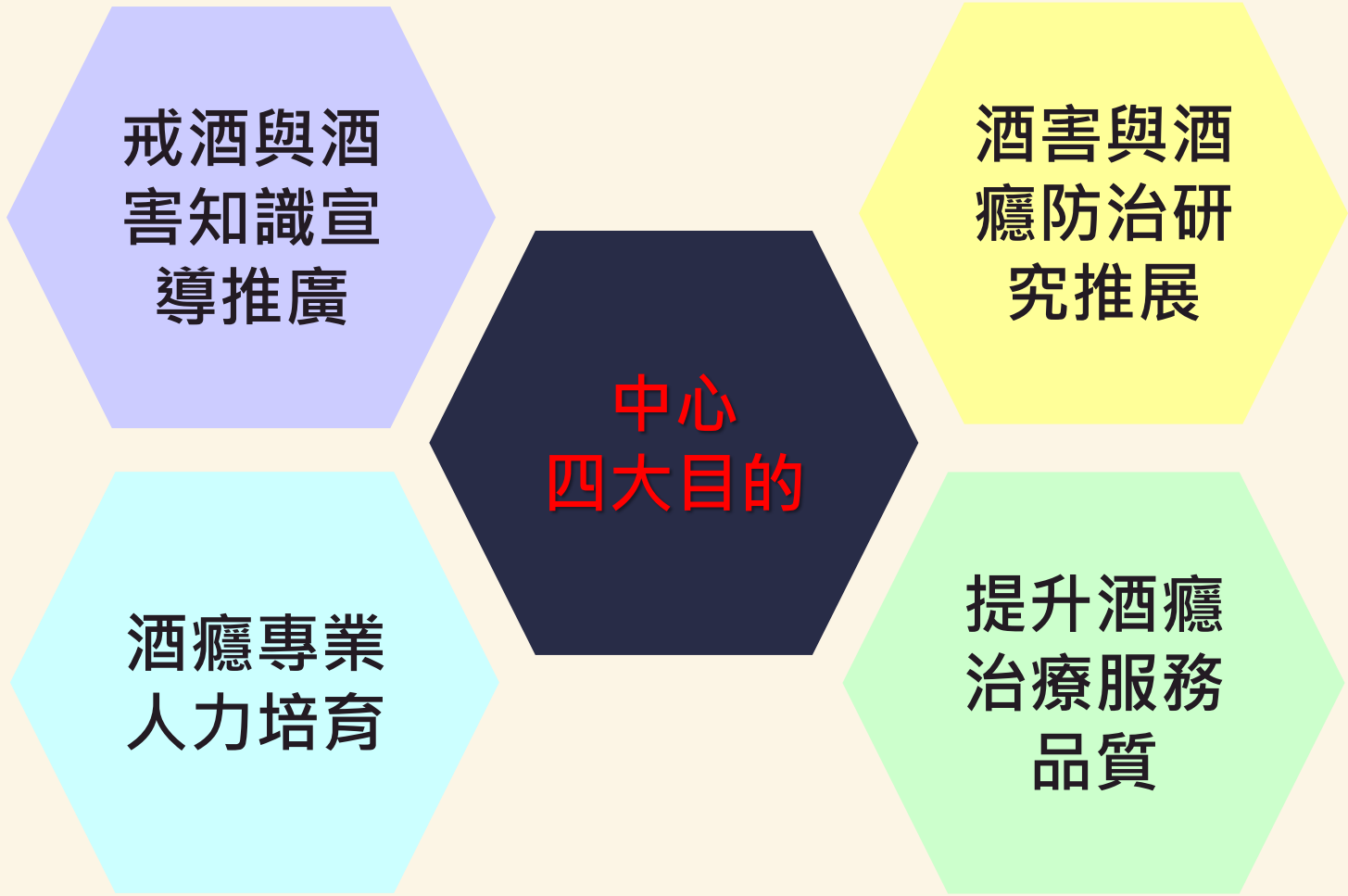
③ 家族 / 伴侶治療。

④ 團體心理治療。

⑤ 外展服務。

⑥ 個案管理。

「台灣戒酒暨酒癮防治中心」四大目標



提高民眾對酒癮與酒害之認識與篩檢。

統計分析數據，推動發展酒癮治療相關研究。

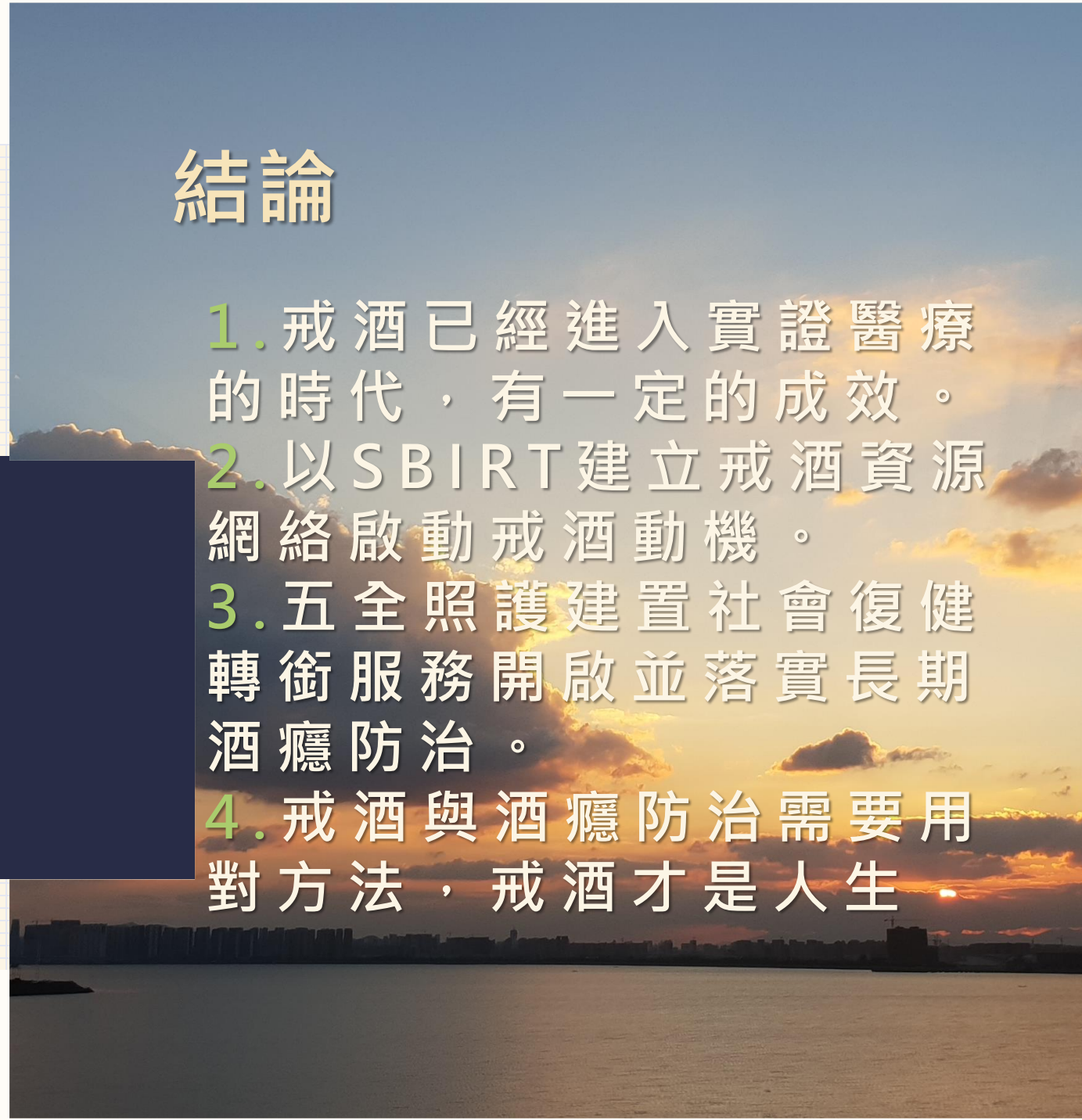
投入專業人才的培訓，精進酒癮治療品質、服務量能。

建立在地化的酒癮治療流程、指標，及治療模式。

預計辦理活動

1. 預計於112年十一月份辦理**「台灣戒酒暨酒害防治中心」開幕記者會**。
2. 每季針對一般民眾辦理
3. 針對專業人員需求，設計並辦理酒癮專業人員教育訓練系列課程。

THANK YOU



結論

1.戒酒已經進入實證醫療的時代，有一定的成效。
2.以SBIRT建立戒酒資源網絡啟動戒酒動機。
3.五全照護建置社會復健轉銜服務開啟並落實長期酒癮防治。
4.戒酒與酒癮防治需要用對方法，戒酒才是人生。