

鴉片類藥物成癮治療在 臺灣之臨床經驗與現況

唐心北

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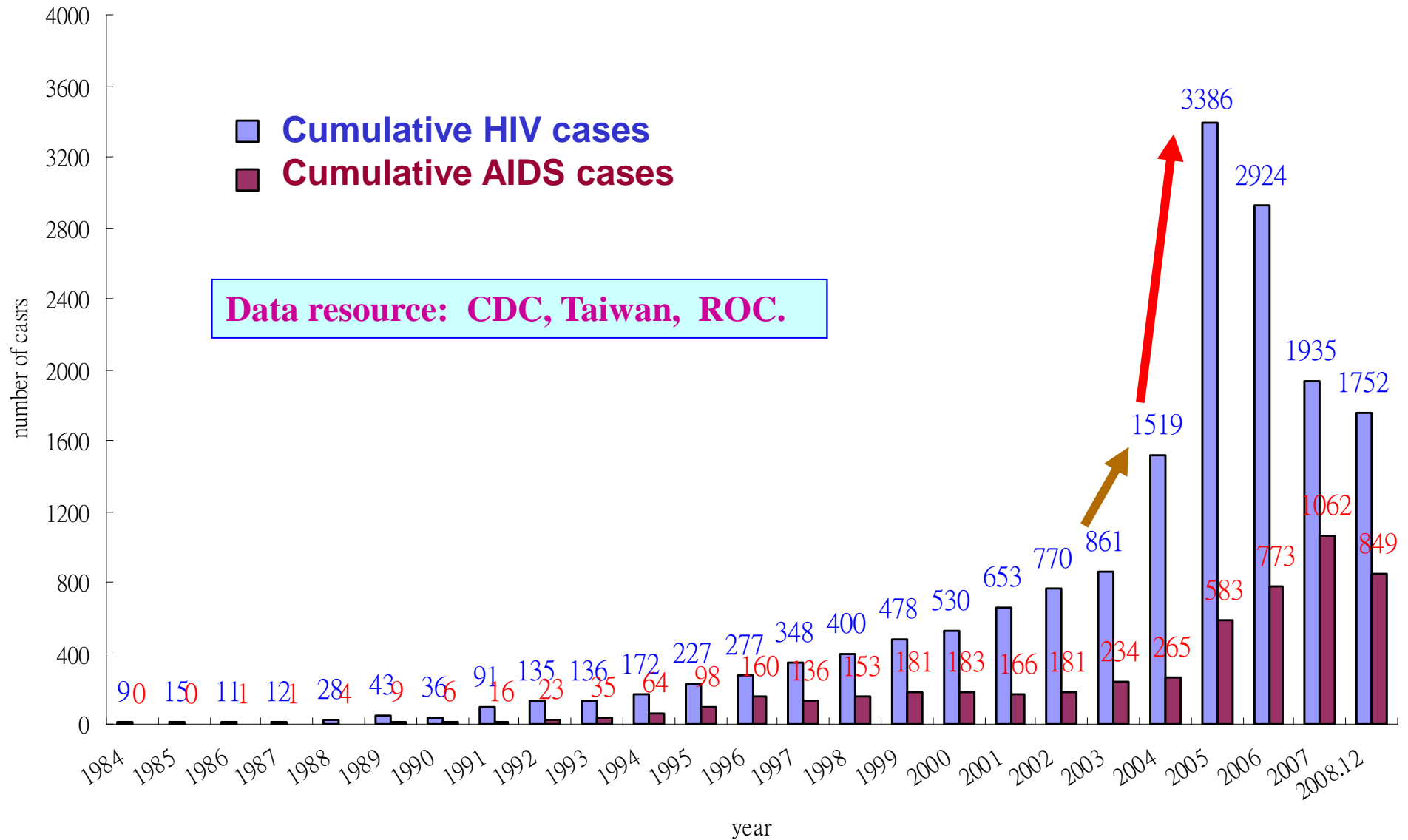
Nov. 1992, Orlando, FL. USA.



Harm Reduction Program and Opiate Substitution Therapy in Taiwan

THE EMERGE OF HIV EPIDEMICS

Reported Cases of HIV/AIDS by Year of Diagnosis in Taiwan, 1984-2008



Inclusion criteria

- **Opioid dependence (by DSM-IV-TR)**
- **At least 20 year-old**
- **Normal intelligent function to understand the contract**
- **Agree to sign the contract (included the personal data and fingerprint)**

Priority Rules

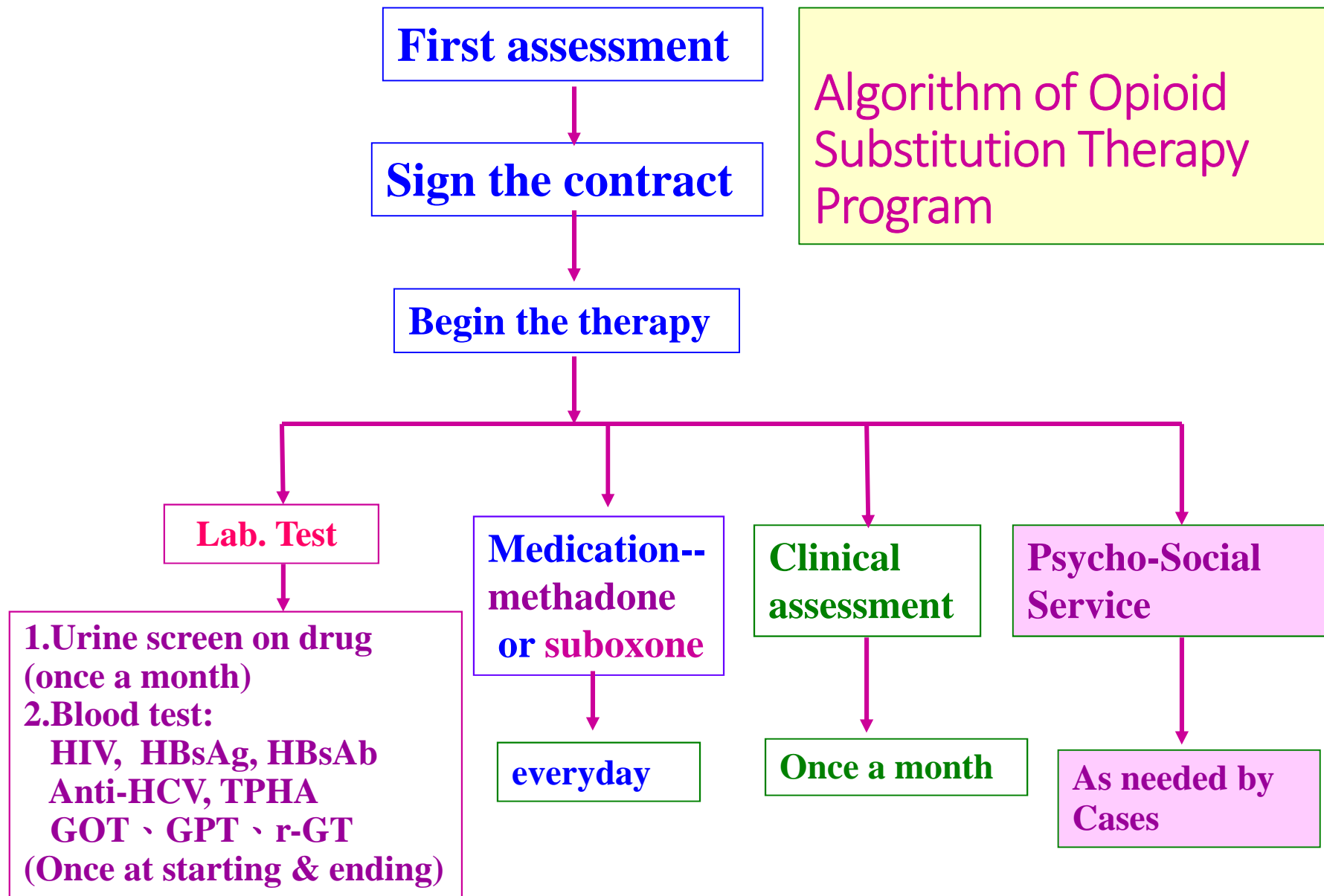
- Long-term injected drug use and syringe sharing behavior.
- Infected with HIV, Hepatitis B or C, pulmonary TB, or Syphilis.
- Committal history but relapse.
- Abstinent therapy history in the hospital with D.O.H. assignment.

Exclusion Criteria

- **Major psychotic disorders, and under hospitalization.**
- **Antisocial personality disorder or behavior.**
- **Severe physical illness, such as liver cirrhosis.**

Early Termination

- **Death.**
- **Commitment, especial the drug-dealer, or violation of the rules, violent behaviors toward the staffs or others, during the treatment process.**
- **Incarceration due to other crimes.**
- **Admission for more than 1 week due to the physical illness.**
- **Refused to engage the treatment program.**



Service Content

Outpatient Service

- At least one clinic every weekday.

Medication Service

- Service Time -- Everyday, no off.
- The weekday
- Weekend and holiday

Psycho-Social Service--as needed

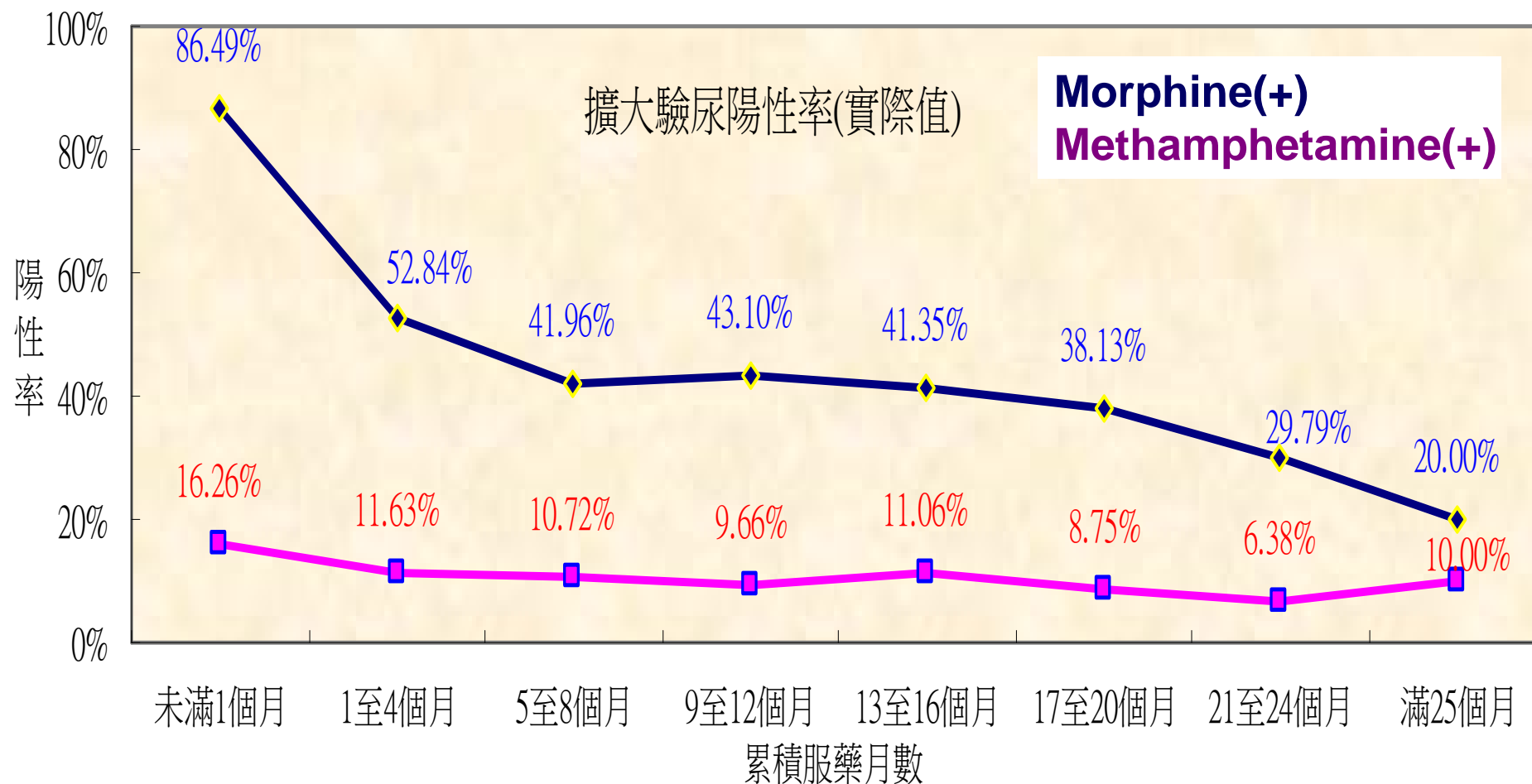
- Case Management
- Group Psychotherapy
- Family Support Group
- Vocational Counseling

Outcome survey

Did you use heroin during the last 30 days ?
If yes, how many times during the last 30 days ?

	2007/4/14-15	2007/7/28-29	2007/10/20-21
No	61.21%	59.84%	56.44%
Yes	38.79%	40.16%	43.56%
1 ~ 2 times	84.48%	76.49%	70.45%
3 ~ 4 times	12.07%	19.60%	20.45%
≥ 5 times	3.45%	3.91%	4.55%

Opioid- & Meth- Positive urine specimens decreased by time on MMT



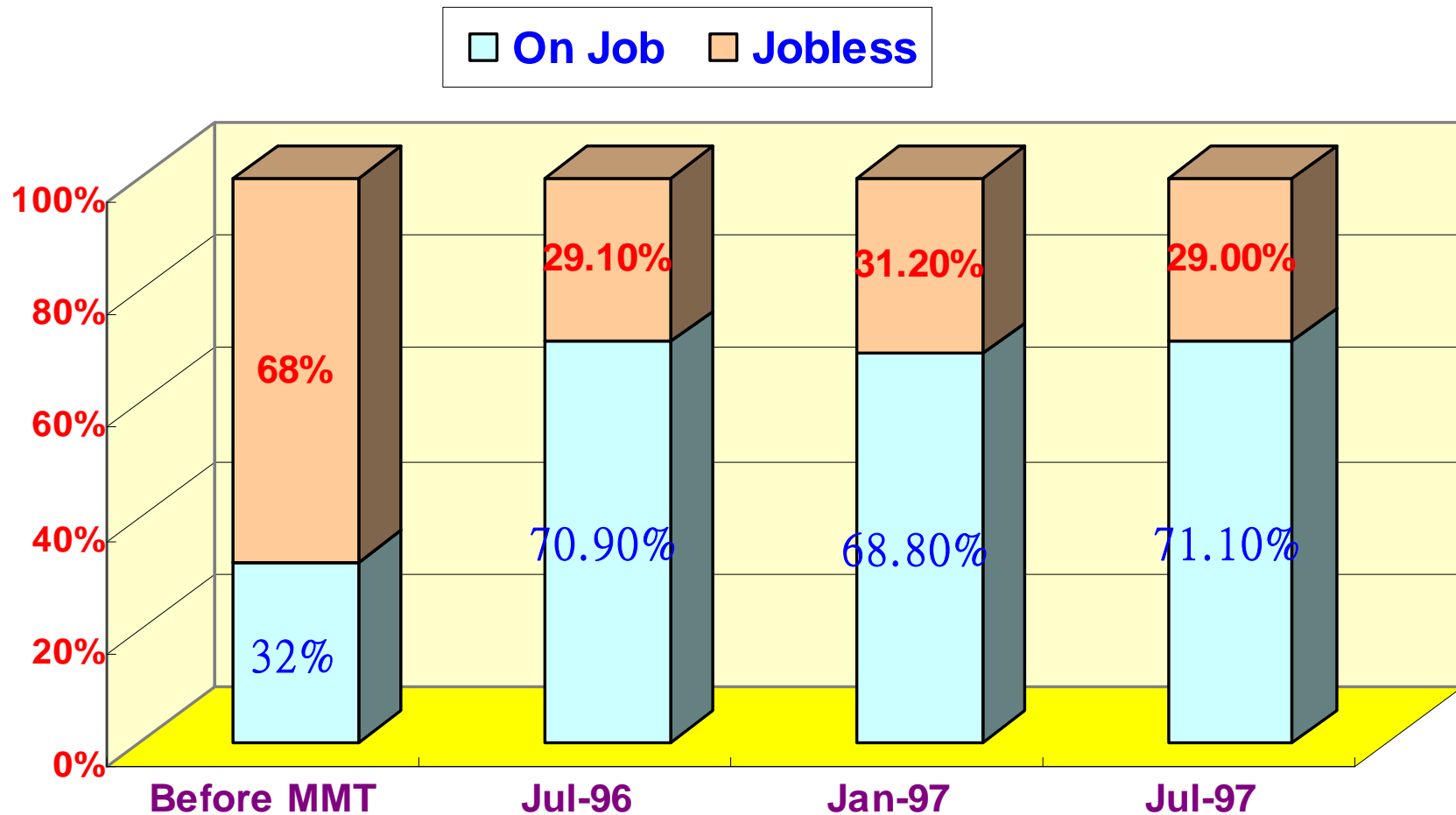
Tang, et al. 2009.

Outcome survey

How much the improvement over these areas after you enrolled into MMT ?

	Very much	Much	Some	Nil
Physical Condition	45.16%	31.45%	16.13%	7.26%
Occupation	41.67%	28.33%	15.83%	14.17%
Emotional controlling	36.89%	41.80%	15.57%	5.74%
Family Relation	52.46%	34.43%	9.02%	4.10%
Interpersonal Relation	39.67%	39.67%	14.05%	6.61%

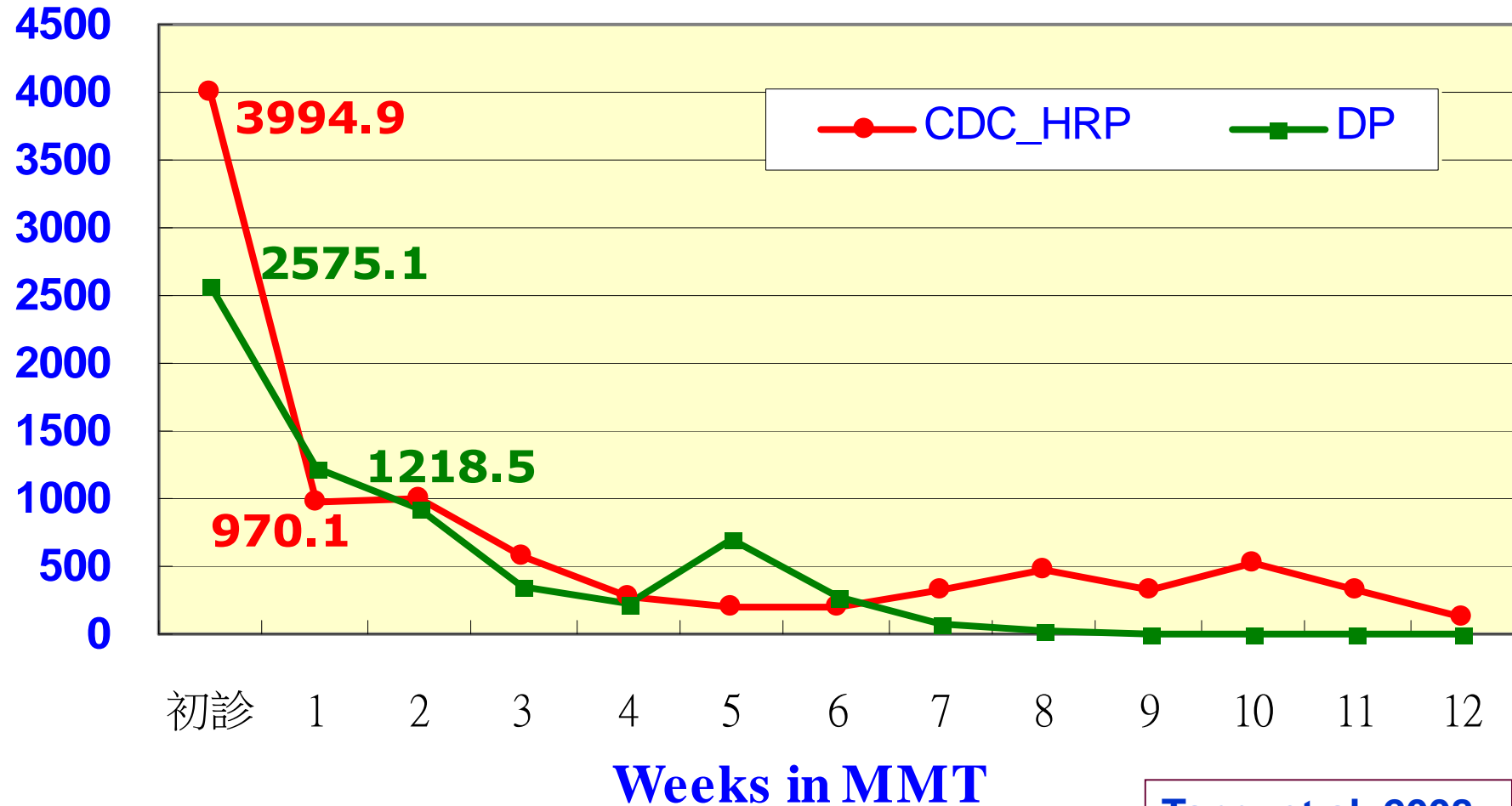
Employment Status of addicts improved after received MMT



Tang, et al. 2009.

Daily cost on Heroin using Decreased after enrolled into MMT

(\$NT/day)



Tang, et al. 2008.

The reductions in monetary cost and gains in productivity with methadone maintenance treatment: One year follow-up

The average annual total cost was approximately US\$26,485 (1.43 GDP per capita in 2010) at baseline, and **decreased by 59.3%** to US\$10,784 (0.58 GDP) at follow-up. The **mean number of months of unemployment dropped** from 6.03 to 2.79, the **mean income increased** to exceed the basic salary, but only reached 45.3% of the national average monthly earnings. The participants '**mental health improved**', but their QOL scores did not increase significantly.

Chih Yin Hsiao Kao Chin Chen, Lan-Ting Lee, Hsin Chun Tsai, Wei Hung Chang, I Hui Lee, Po See Chen, Ru-Band Lu, Yen Kuang Yang. 2015.

WHO-QoL Score Before vs After MMT for One year

完成治療一年者之生活品質前後測比較

N=130	初診First visit	結案One-year	<i>p</i>
生理健康 Physical component	44.6±16.8	63.4±14.5	0.000
心理健康 Psychological component	53.8±16.6	55.1±16.9	0.565
社會關係 Social component	47.7±17.2	57.8±15.8	0.000
環境 Environmental component	49.0±15.5	58.6±15.4	0.000
整體 Overall	5.92±1.41	6.48±1.27	0.004

Improvement of quality of life in methadone treatment patients in northern Taiwan: a follow-up study

Table 3 Quality-of-life (QoL) scores and cost per QoL point in the four domains at the 6-month assessment (n = 285)

	Baseline score <i>M (SD)</i>	6-month score <i>M (SD)</i>	QoL gained	Cost per QoL point
Physical	58.53(15.51)	60.13(14.68)	1.6	368.7
Psychological	49.89(16.64)	53.19(17.15)	3.3 ^{***}	178.7
Social Relations	54.71(18.13)	55.77(17.05)	1.06	556.5
Environmental	52.92(16.97)	55.42(16.20)	2.5 ^{**}	235.9

Note. Repeated measures analyses of variance of baseline and 6-month follow-up were performed to control for age, education, gender, age at first heroin use, methadone dose and days in MMT before study. Cost per QoL point = Total MMT cost/Incremental QoL gain. MMT cost was \$1179.70 in 2009. For the 6-month calculation, \$589.85 (1179.7/2) was used.

p* < .05. *p* < .01.

Chou et al. BMC Psychiatry 2013, 13:190
<http://www.biomedcentral.com/1471-244X/13/190>

Effects of education on harm-reduction programmes

*Shu-Yu Lyu, Lien-Wen Su, *Yi-Ming Arthur Chen Lancet 2011*

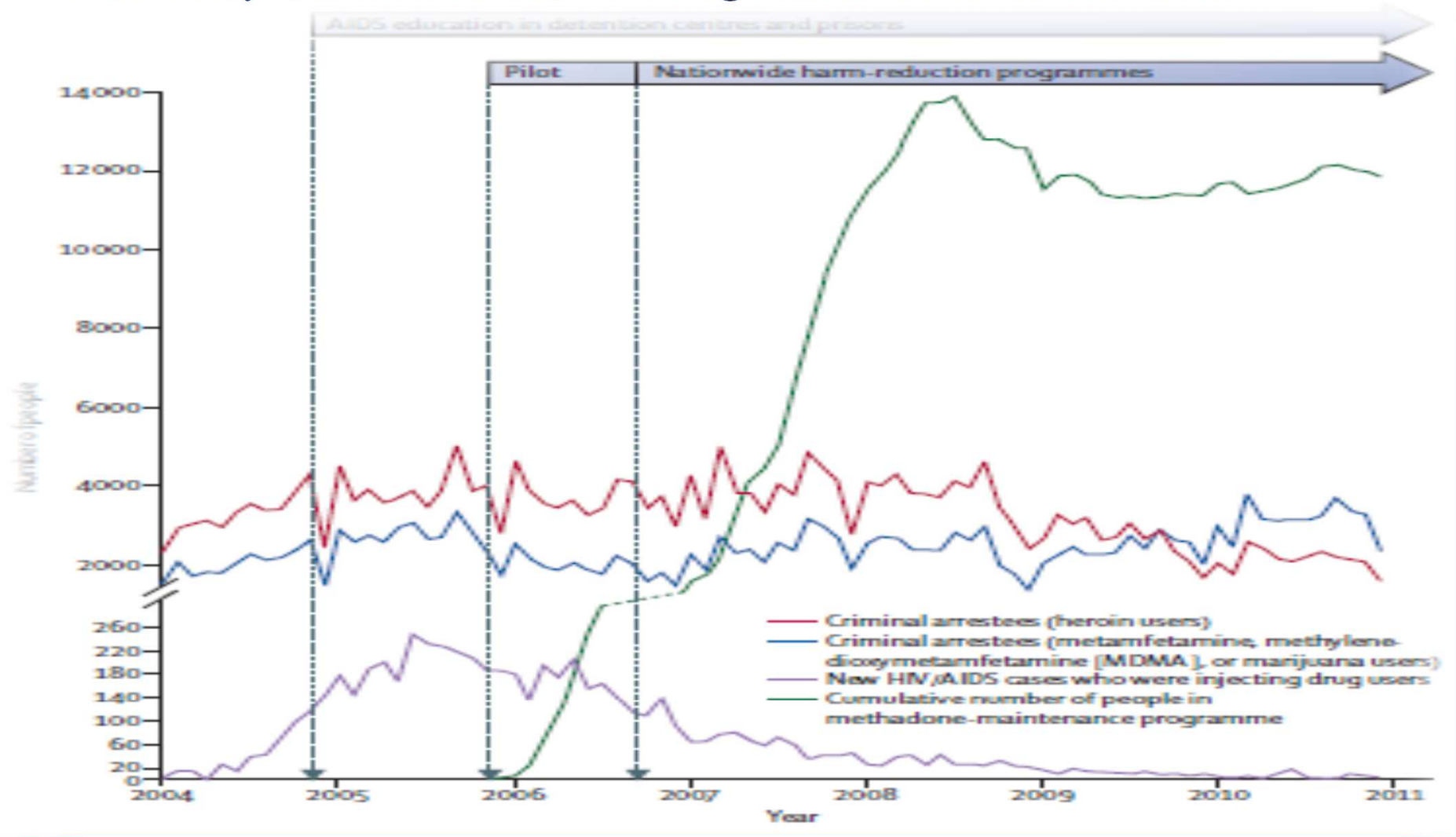


Figure: Effectiveness of AIDS education and harm-reduction programmes in Taiwan

Data on new HIV-1-infected injecting drug users and cumulative numbers of patients enrolled in methadone-maintenance clinics are from Taiwan Centers for Disease Control.⁷ Data for schedule-I criminal arrestees (heroin users) and schedule-II criminal arrestees (metamfetamine, methylenedioxyamfetamine [MDMA], or marijuana users) are from Taiwan's Ministry of Justice.⁸ A pilot programme was done in two cities

Current status of substance abuse and HIV in Taiwan

Wen-Jing Yu, Wen-Ing Tsay, Jih-Heng Li.

J of Food and Drug Analysis, 21, (2013) S 27-32.

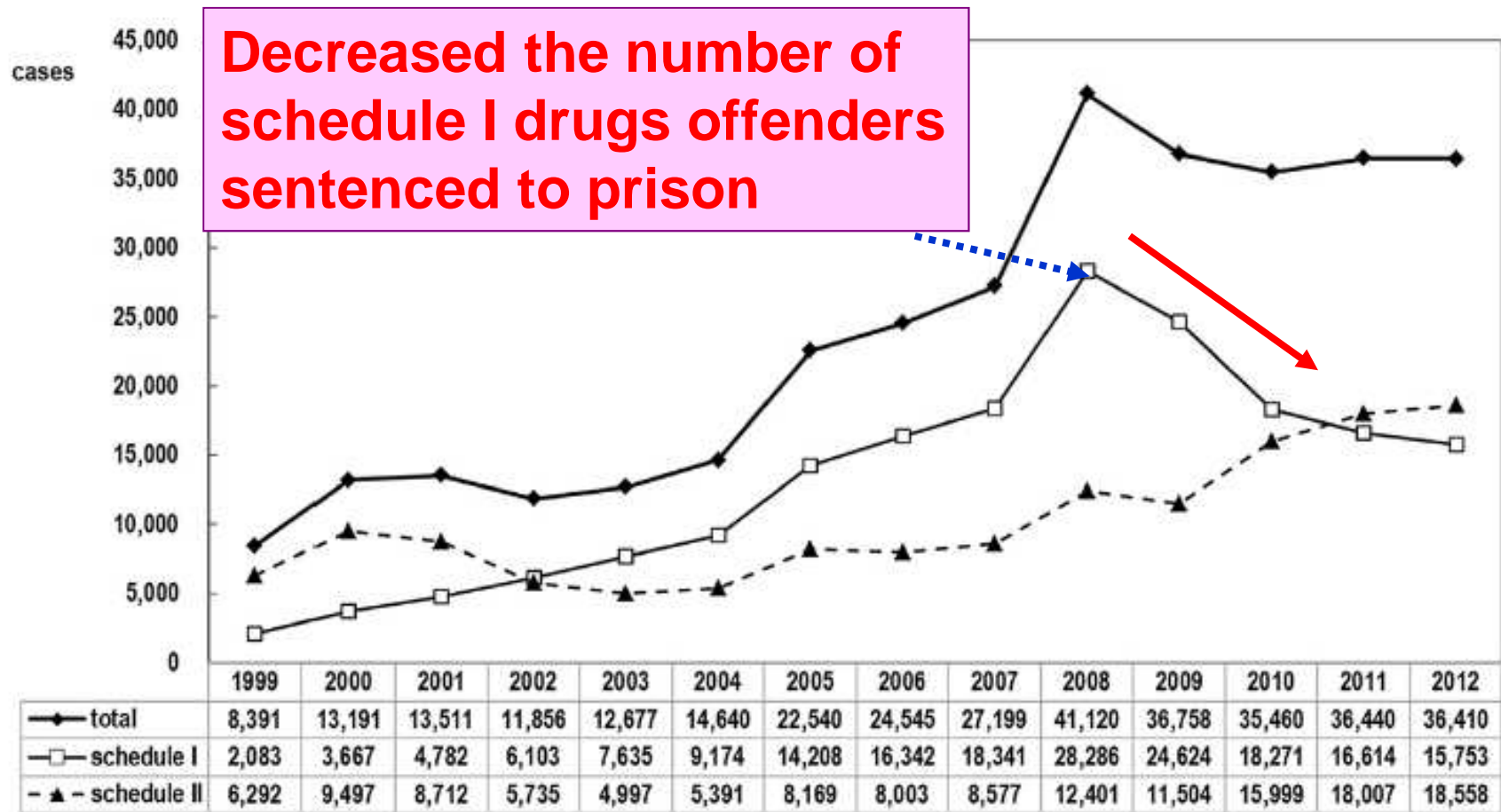
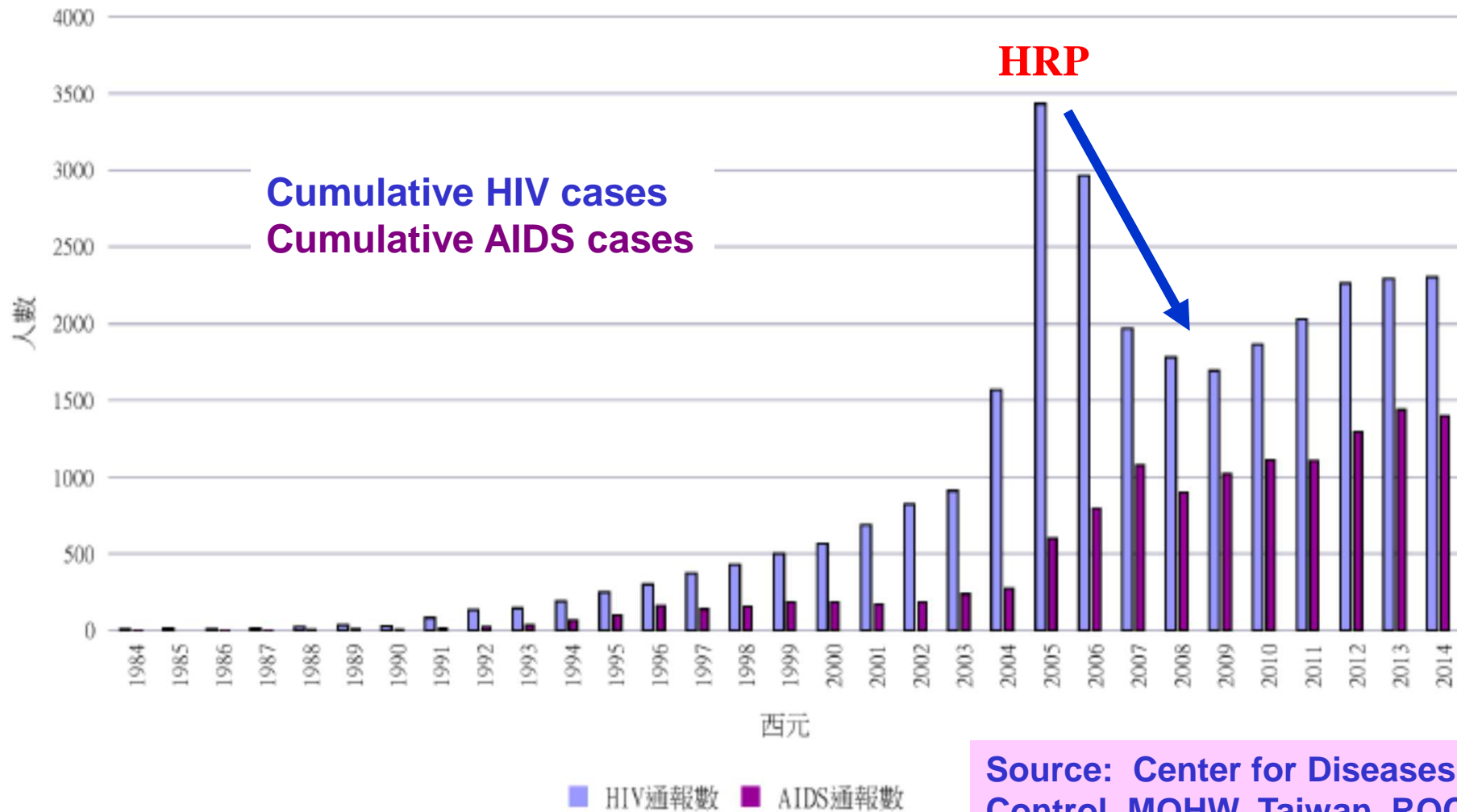


Fig. 5 – Number of schedule I & II drug offenders sentenced to prison in Taiwan from 1999 through 2012. Heroin and methamphetamine were the most commonly abused schedule I and II drugs, respectively.

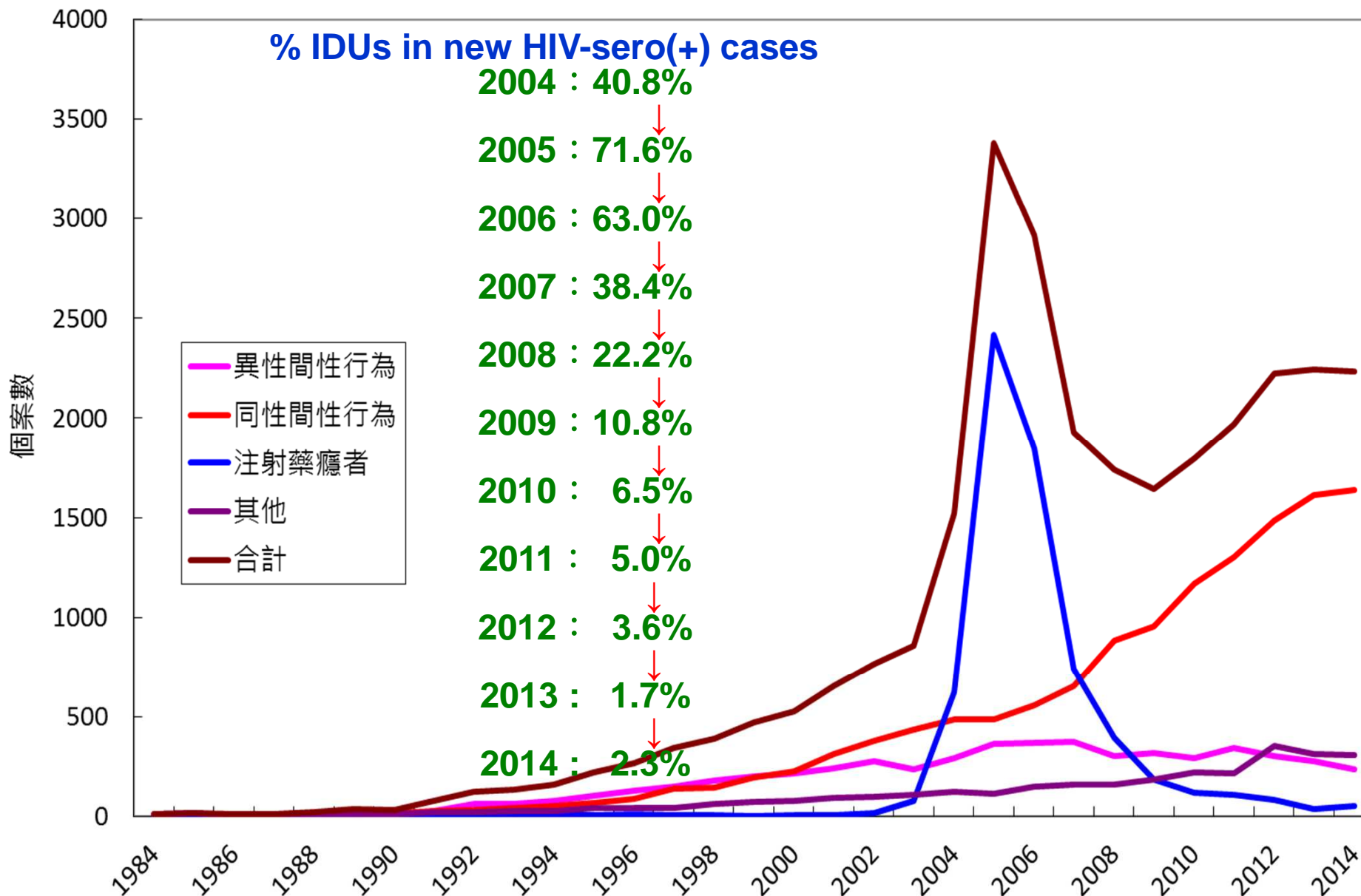
Reported Cases of HIV/AIDS in Taiwan 1984-2014

本國籍感染人類免疫缺乏病毒者趨勢圖
1984年至2014年12月(依診斷日分析)



Source: Center for Diseases Control, MOHW, Taiwan, ROC.

Risk factors of HIV Infection via IDU declined in Taiwan



Harm reduction policy in Taiwan: toward a comprehensive understanding of its making and effects

Jia-shin Chen . Harm Reduction Journal (2016) 13:11.

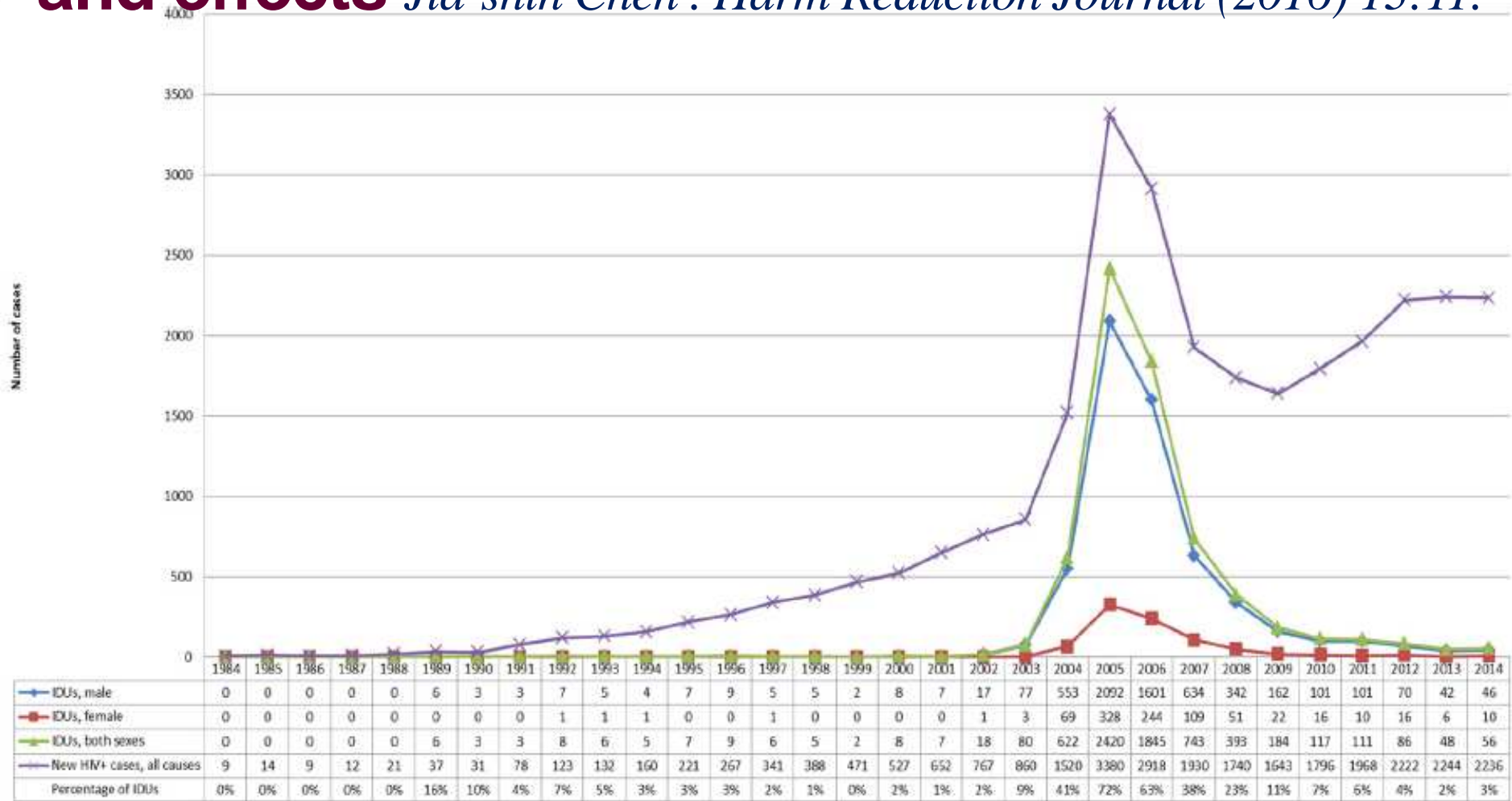
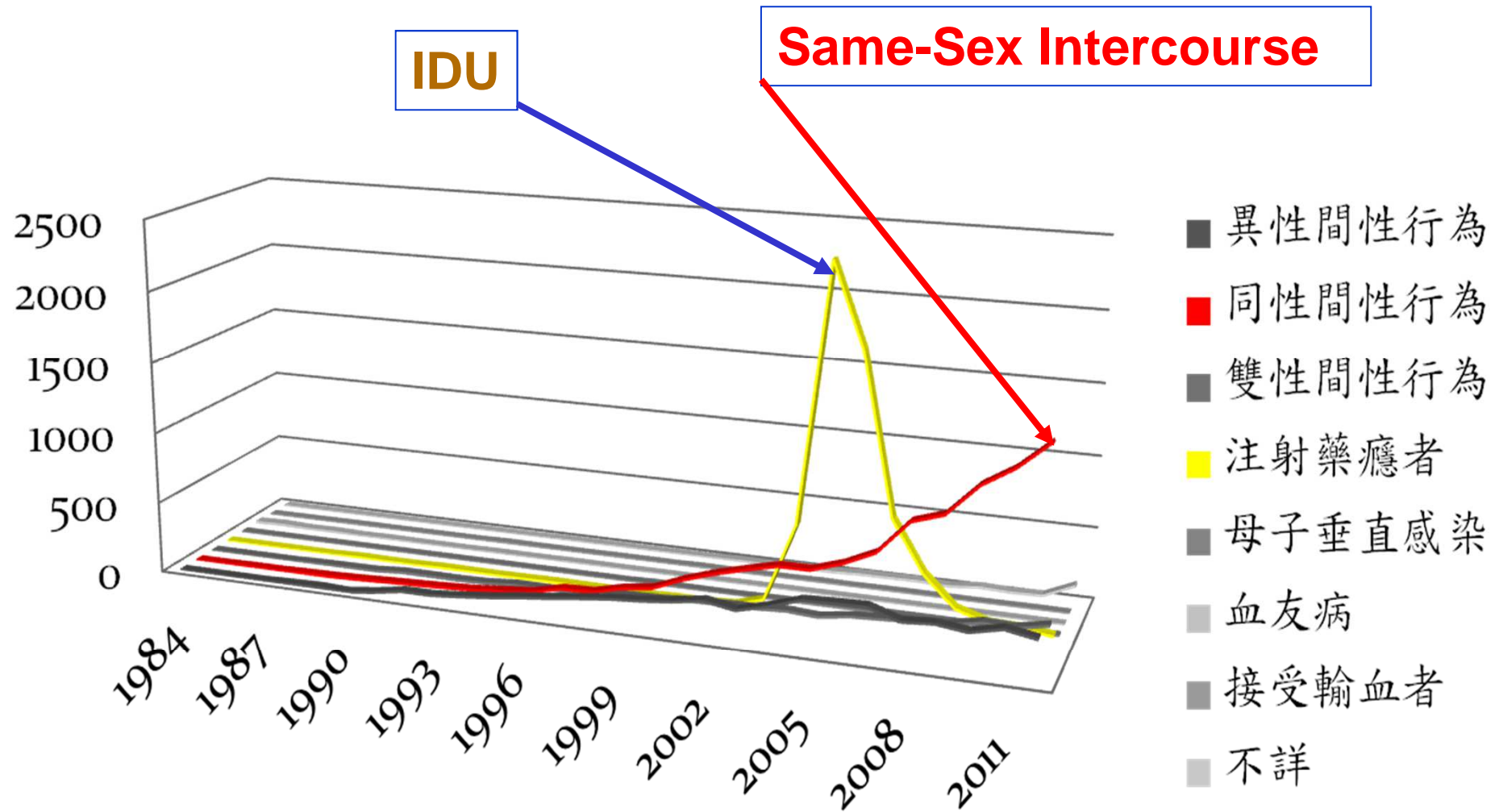


Fig. 1 Reported number of HIV-positive injection drug users, 1984-2014. Note that the new HIV cases from all causes (*purple line*) increase in 2009 while the number representing new HIV-positive drug users (*green line*) keeps declining (adopted from TCDC [22])

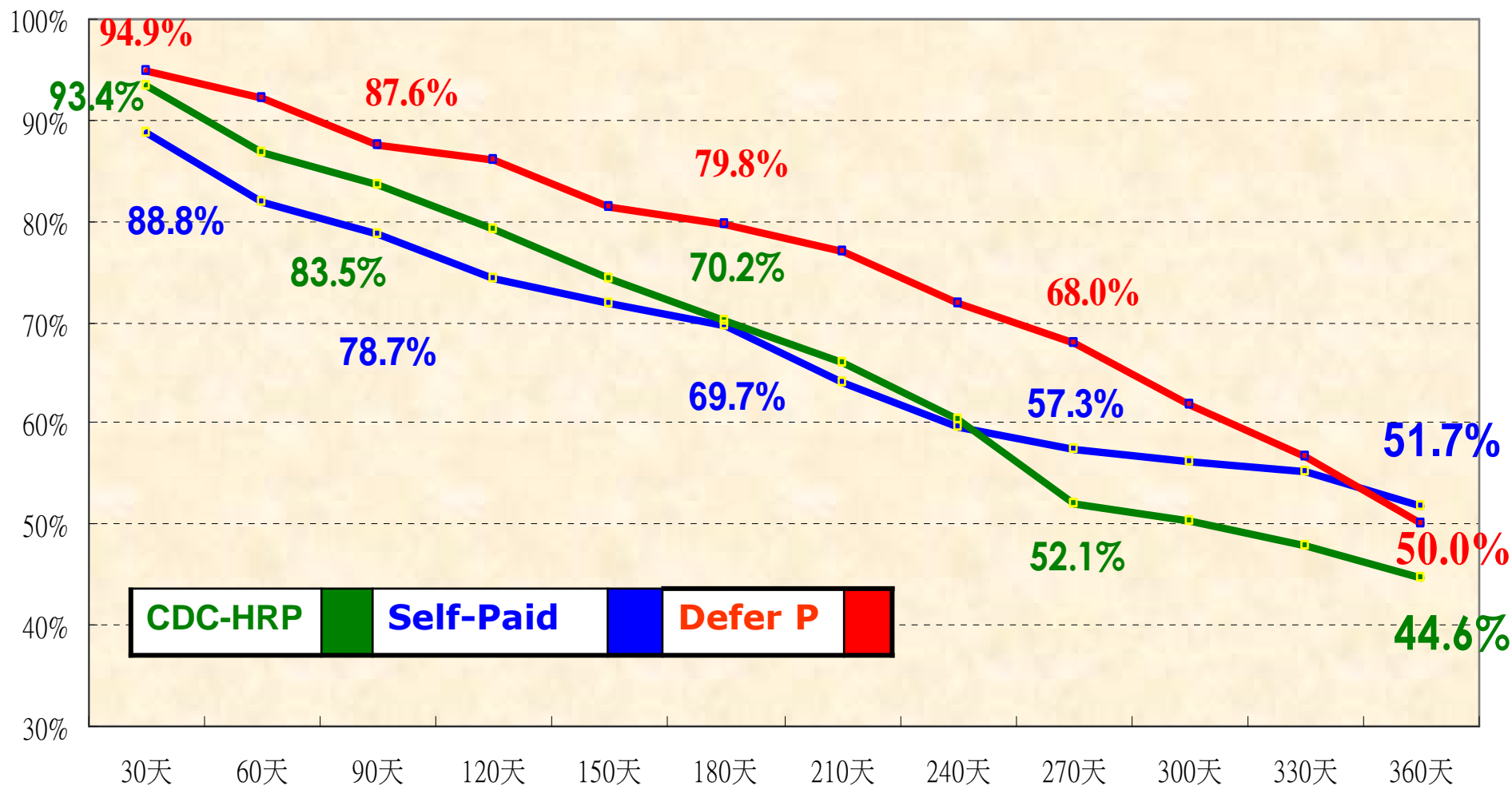
Risk factors of HIV Infection in Taiwan



Data resource: CDC, MOHW, Taiwan, ROC.

Retention Rate -- by Status

Deferred prosecution increased the retention rate !



P.S. Excluded on Suboxone, Re-enrolled, Transferred cases.

Tang, et al. 2009.

Mortality among a cohort of drug users after their release from prison: an evaluation of the effectiveness of a harm reduction program in Taiwan

Table 3 Crude mortality rates among individuals during methadone maintenance therapy (MMT) attendance, after MMT dropout and non-enrollees.

<i>Classification</i>	<i>Deaths</i>	<i>Person-years (pyrs)</i>	<i>Mortality rate (deaths per 100 pyrs)</i>	<i>(95% confidence interval)</i>
During MMT attendance	3	1244.6	0.24	(0.08–0.74)
Not during MMT attendance				
Non-enrollees	111	4289.3	2.6	(2.1–3.1)
After MMT dropout (in community)	27	384.8	7.0	(4.8–10.2)
After MMT dropout (re-incarceration)	1	334.4	0.3	(0.04–2.1)
Total	142	6253.1	2.3	(1.9–2.7)

Yen-Fang Huang, & Hsu-Sung Kuo, et al., *Addiction*, 106, 1437–1445

Higher methadone doses are associated with lower mortality in patients of opioid dependence in Taiwan.

Among all of the 33,549 recruited patients, the crude mortality rate was 134.78/10,000 person-years, and the standardized mortality ratio was 4.68. A dose–response relationship of higher- vs. lower-dosage groups on the risk of mortality risk was observed (adjusted HR = 0.68, $P = 0.016$). In further subgrouping analysis, this trend was more significant in HIV positive patients, in subgroup of patients who continuously staying in MMT, and in subgroup of patients who re-enter MMT.

Ding-Lieh Liao, Pau-Chung Chen, Chia-Hsiang Chen, Chia-Jung Hsieh, Yen-Fang Huang, Wen-Yi Shih, Joseph J.S. Cheng, 2013

Moving toward Personalized Medicine in the Methadone Maintenance Treatment Program: A Pilot Study on the Evaluation of Treatment Responses in Taiwan

The results demonstrated that **the methadone maintenance dose, *CYP2B6* 785G allele, and *ABCB1* 2677T allele have positive effects on the methadone plasma concentration.** In contrast, **patients with HCV co-infection, alcohol problems, and psychiatric diseases may have a negative response to treatment.** Thus, a comprehensive evaluation of treatment responses in the MMTP should include not only genetic polymorphisms in methadone metabolism and transporter proteins, but also concomitant diseases, MDIs, and poly-substance use.

H-Y Lee, J-H Li, Y-L Sheu & H-P Tang. 2013.

Pharmacogenomics study in a Taiwan methadone maintenance cohort

In this study, 366 patients who had taken methadone continually in the previous 7 days were examined. The **SNPs on CYP2B6** were associated with **plasma S-methadone concentration**; **SNPs on CYP3A4** were associated with **withdrawal symptoms and side effects**; and **SNPs on CYP2C19** were associated with **methadone dose**. SNPs in the genes encoding the **morphine phase II metabolic enzyme, UGT2B7**, were associated with **withdrawal symptom scores**. In pharmacodynamic genes, the **SNPs on OPRM1** were associated with **insomnia and change in libido side effects**.

Sheng-Chang Wang, Hsiao-Hui Tsou, Ing-Kang Ho, Keh-Ming Lin, & Yu-Li Liu.
J Food Drug Anal. 2013 December ; 21(4): S62–S68.

Challenges of MMTP in Taiwan

- ✓ 污名或標籤化(Stigmatization)
 - No Prison-based MMT
- ✓ 可近性不足(insufficiency of accessibility)
 - 服務點不多 (Availability of service)
 - 外展點 Out-reach delivery points
- ✓ 流用 (diversion)
- ✓ 藥物交互作用 (drug-drug interaction)
- ✓ 心理社會治療不足 (insufficiency of psycho-social intervention)
- ✓ 費用 (fee)
- ✓ 法律規範 (regulation)

毒販專找戒毒者推銷 病患不堪報警抓人

高雄市刑警大隊接獲檢舉，民眾因為想戒毒，所以到醫院尋求「美沙冬」替代療法，但是有毒販專找這些想要戒毒者推銷毒品，以致有些人一直無法擺脫毒品控制。

警方循線跟監逮捕葉姓毒販，以及正和他進行毒品交易的兩名男女，向葉姓毒販買毒的兩人也都正在接受美沙冬替代療法。警方調查，主嫌葉男有毒品前科，佯裝到醫院喝美沙冬戒毒，規避警方查緝，夥同2名均有毒品前科的藥腳，上醫院與戒治者「博感情」。葉男打出「首購免費」，引誘戒治者吸毒，以後非買不可，造成戒治者戒毒不成，反深陷毒海難自拔。

警方於訊後將全案依違反毒品危害防制條例移送偵辦，並報請檢察官向法院聲請羈押葉男獲准，同時將針對在醫院附近販毒給戒治者的類似案件，擴大掃蕩毒品犯罪。

中央通訊社, 2012/6/24

中廣新聞網, 2012/6/25

自由時報, 2012/6/25

感冒藥拿成美沙冬 粗心母害5歲兒毒死

彰化5歲男童母親本身有吸毒前科，去年3月，她把男友送的「美沙冬」及兒子的感冒藥都放在冰箱，卻在拿感冒藥餵食時，不小心拿成了美沙冬，讓男童喝下，結果隔天早上6點多，男童因呼吸衰竭與中毒性休克死亡，男童母親被依過失致死罪起訴。

另外，提供藥物的男子，也就是男童母親的男友，違反藥事法，轉讓禁藥罪嫌，求刑4年。

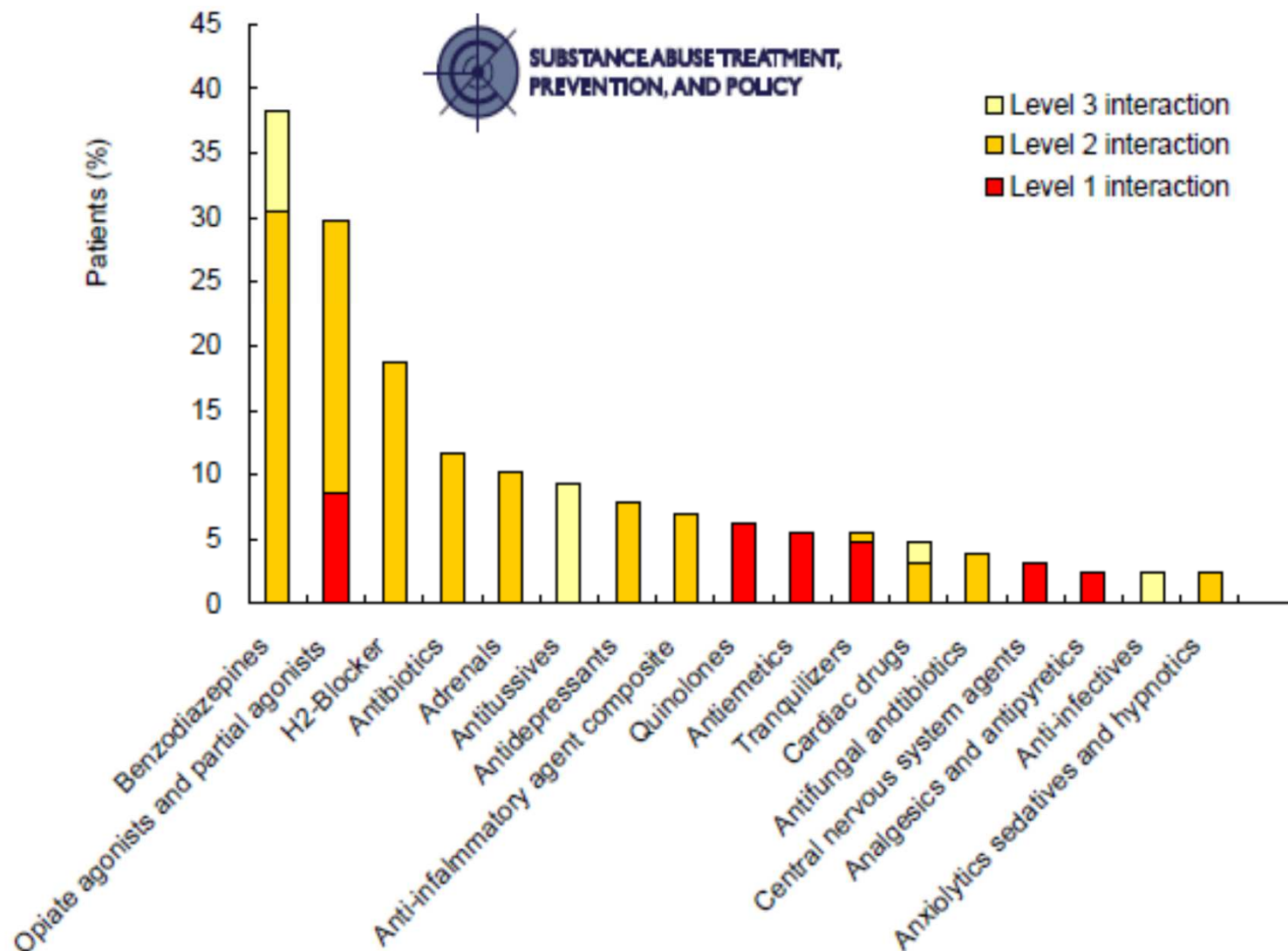
毒犯到醫院接受戒癮治療過程，必須在醫護人員監視下，按時服用美沙冬，毒犯是怎麼把美沙冬挾帶出醫院，還轉送給男童母親？也成了檢方調查重點。

Survey of methadone-drug interactions among patients of methadone maintenance treatment program in Taiwan

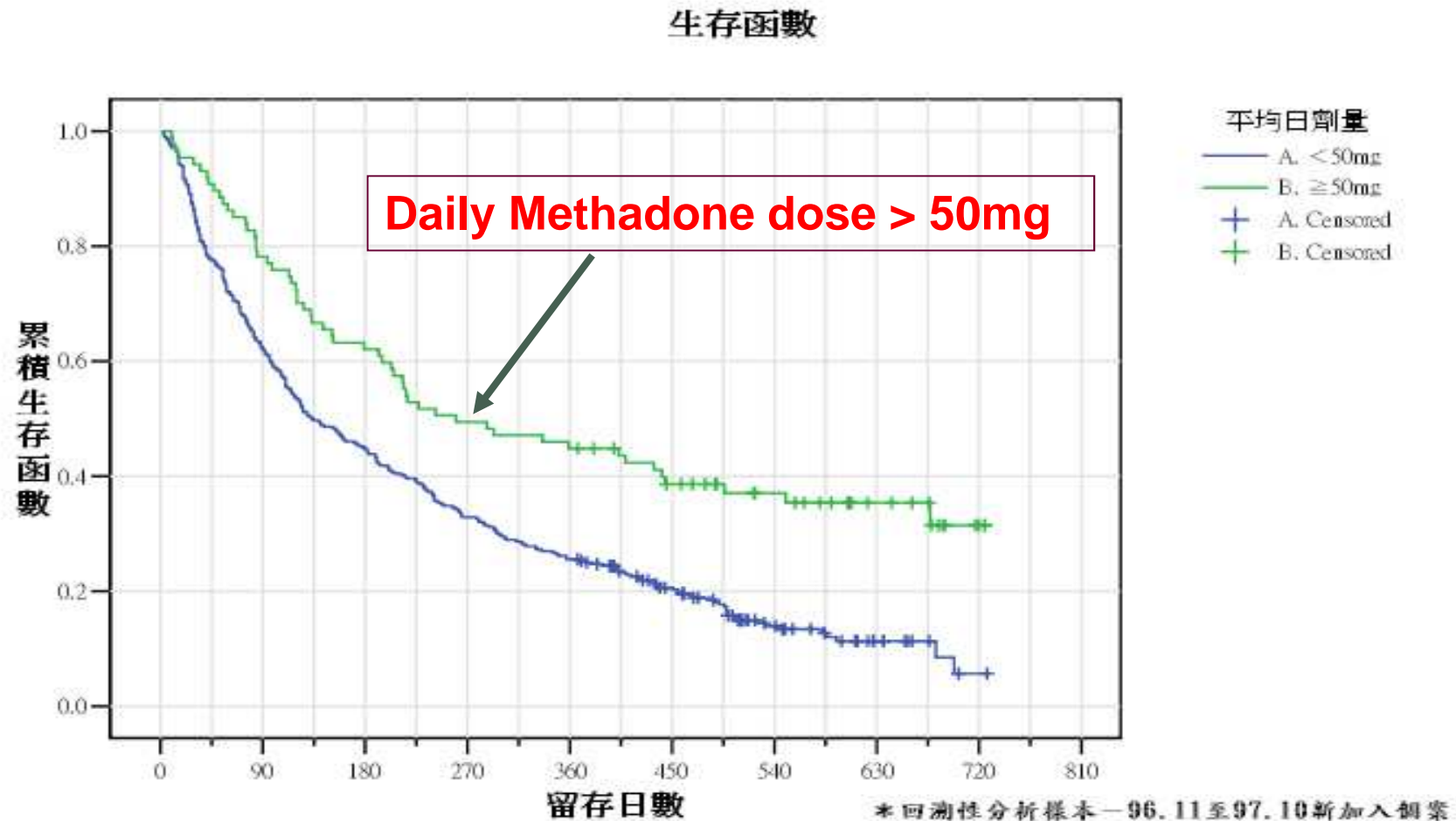
H-Y Lee, J-H Li, L-T Wu, J-S Wu, C-F Yen & H-P Tang.

Substance Abuse Treatment, Prevention, and Policy 2012, 7:11

鴉片類治療藥物之交互作用

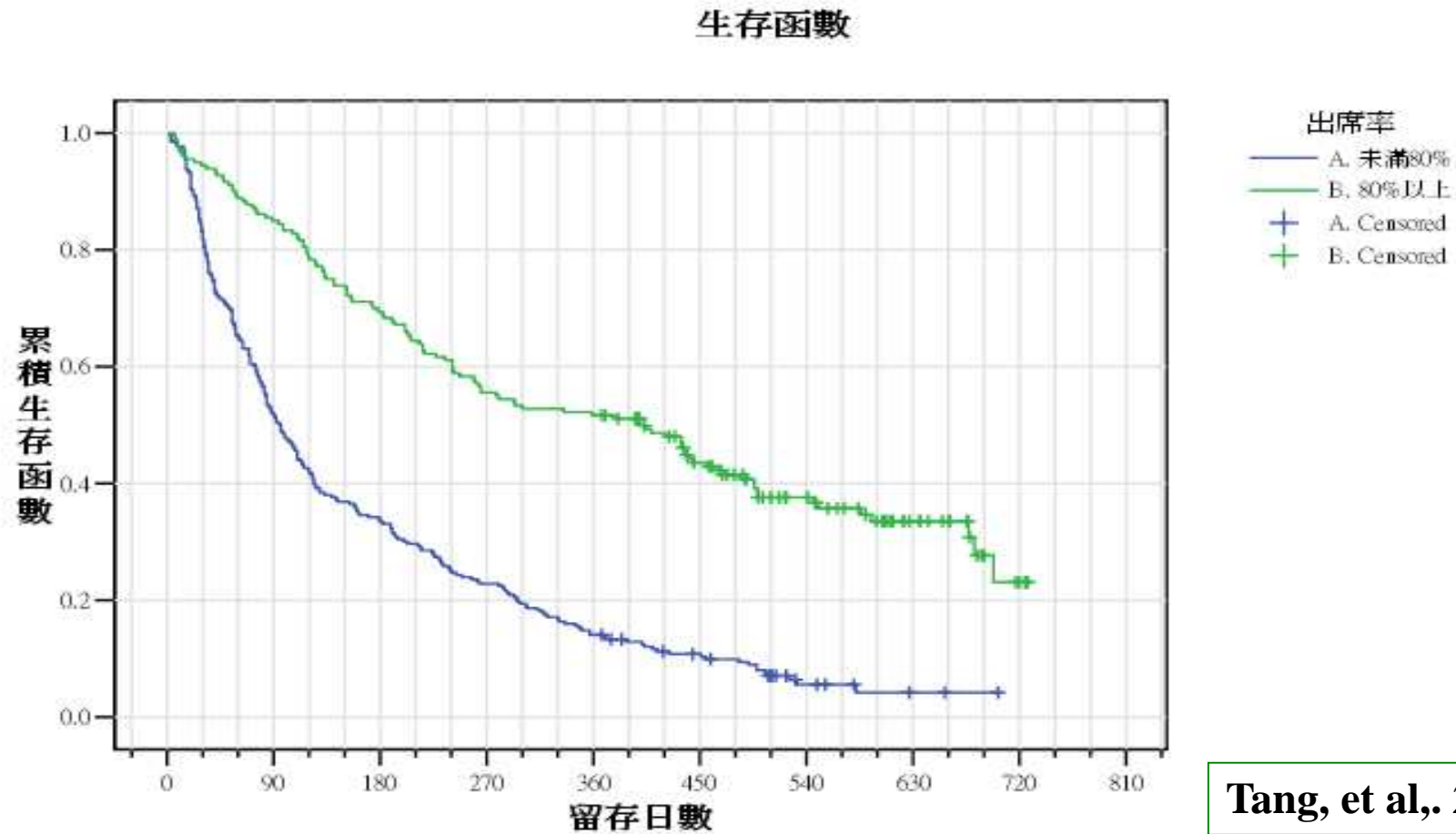


The Association between Daily Dose of Methadone and Retention rate



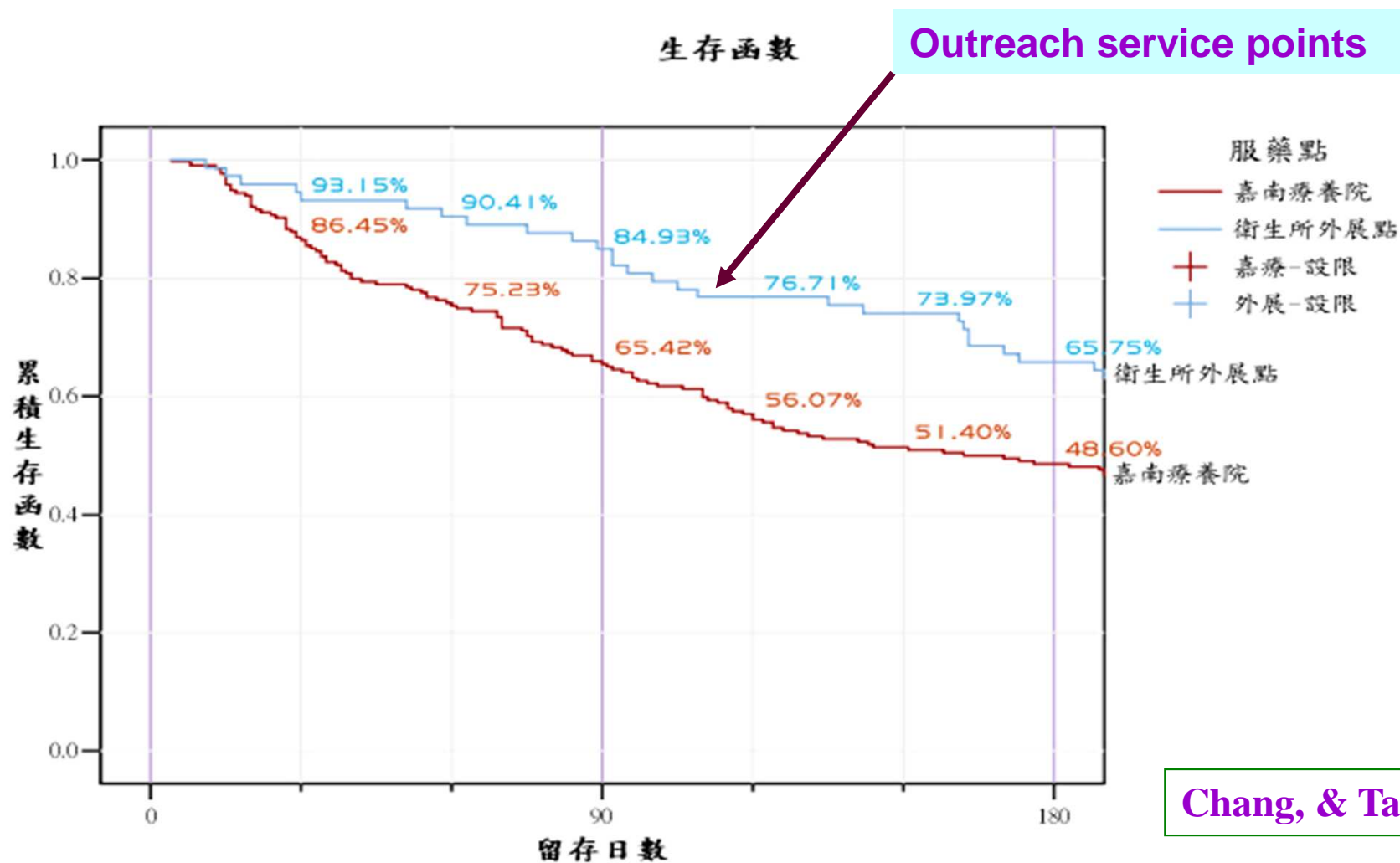
Tang, et al., 2010.

The Association between Attendance rate and Retention rate



Tang, et al., 2010.

Retention rates between Central Hospital and Outreach service points



Service points of MMT at Tainan City

- 替代治療機構
- 衛福部新營醫院
- 行政院退輔會臺中榮總永康分院
- 衛福部嘉南療養院
- 國立成功大學醫學院附設醫院
- 衛福部臺南醫院
- 奇美醫院台南分院

- 外展給藥服務點
- 佳里區衛生所
- 東山區衛生所
- 七股區衛生所
- 官田區衛生所
- 玉井區衛生所
- 善化區衛生所
- 將軍區衛生所
- 關廟區衛生所

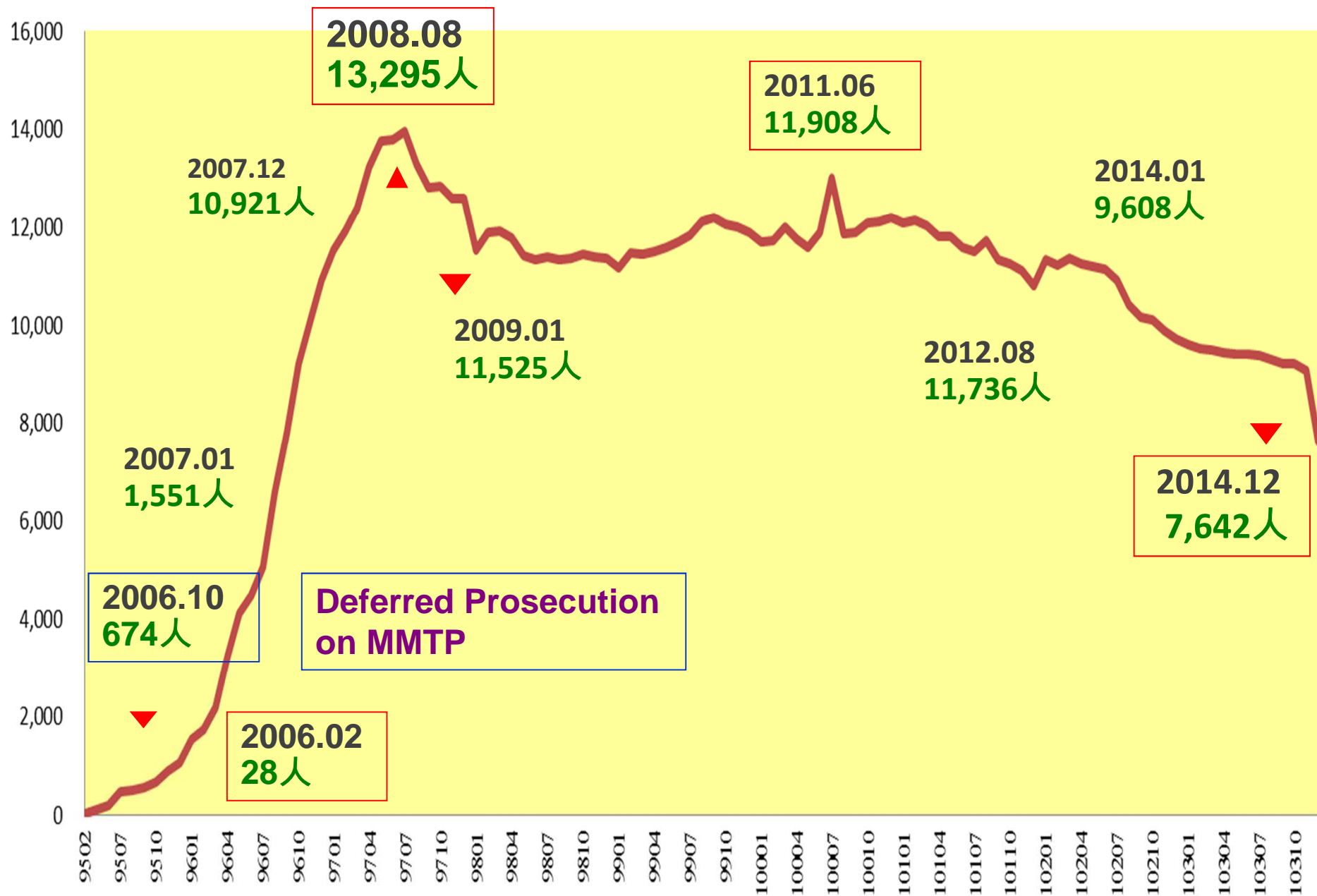


Background information on 128 newly admitted participants and hazard ratios from a Cox multivariate regression analysis on treatment dropout within the 18-month prospective follow-up period.

The Cox regression performed on the 90 patients not incarcerated during the follow-up period indicated that being female, HCV positive, living a longer distance from the clinic, and receiving treatment in New Taipei City, respectively, were associated with shorter durations of MMT.

Lin CK, Hung CC, Peng CY, Chao E, Lee TSH (2015) Factors Associated with Methadone Treatment Duration: A Cox Regression Analysis. PLoS ONE 10(4): e0123687.
doi:10.1371/journal.pone.0123687

The Numbers of Patients On MMT at Taiwan, 2006.02 – 2014.12



Buprenorphine HCL/ Naloxone

適應症：鴉片類成癮的治療

妊娠等級：C

管制藥品等級：在臺灣列為第三級管制藥品。

分別以美沙冬和丁基原啡因
為海洛因成癮者減害替代治療
之成效分析

**The Comparison of Treatment Effect between
Methadone and Buprenorphine as the
Substitution Therapy for Opiate Addicts--the
Duration of 1 Year**

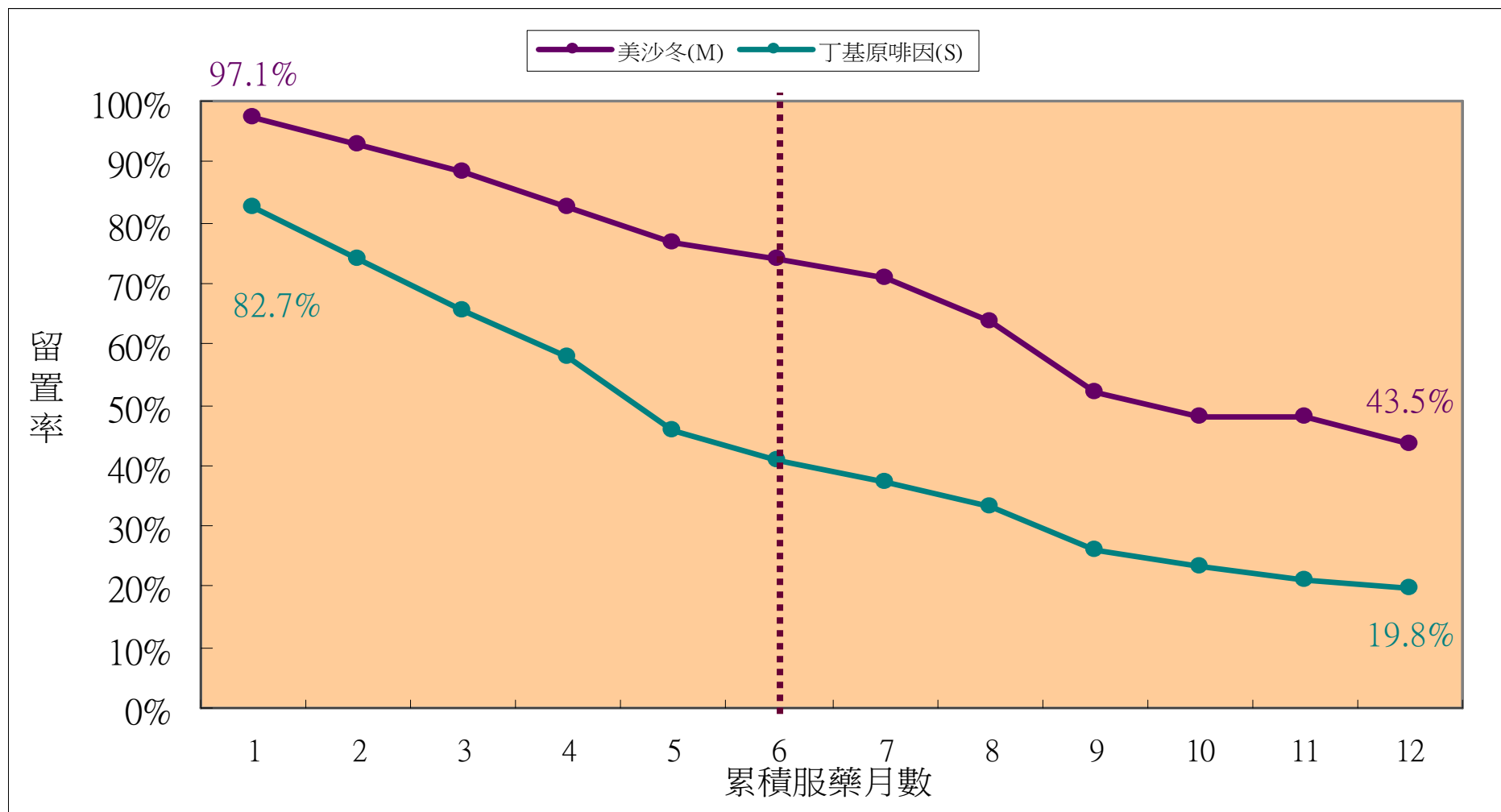
江明澤、張耿嘉、張達人、簡以嘉、唐心北、
李文光、林玖瑩、賴清薰

本研究經費：行政院衛生署管制藥品管理局委託研究計畫DOH96-NNB-1032

本研究通過行政院衛生署嘉南療養院人體試驗委員會之審查JMH-96-01

留置率分析

Treatment Retention among Patients Randomized to Buprenorphine/Naloxone Compared to Methadone in Jia-Nan Mental Hospital



Treatment Retention among Patients Randomized to Buprenorphine/Naloxone Compared to Methadone in A Multi-site Trial

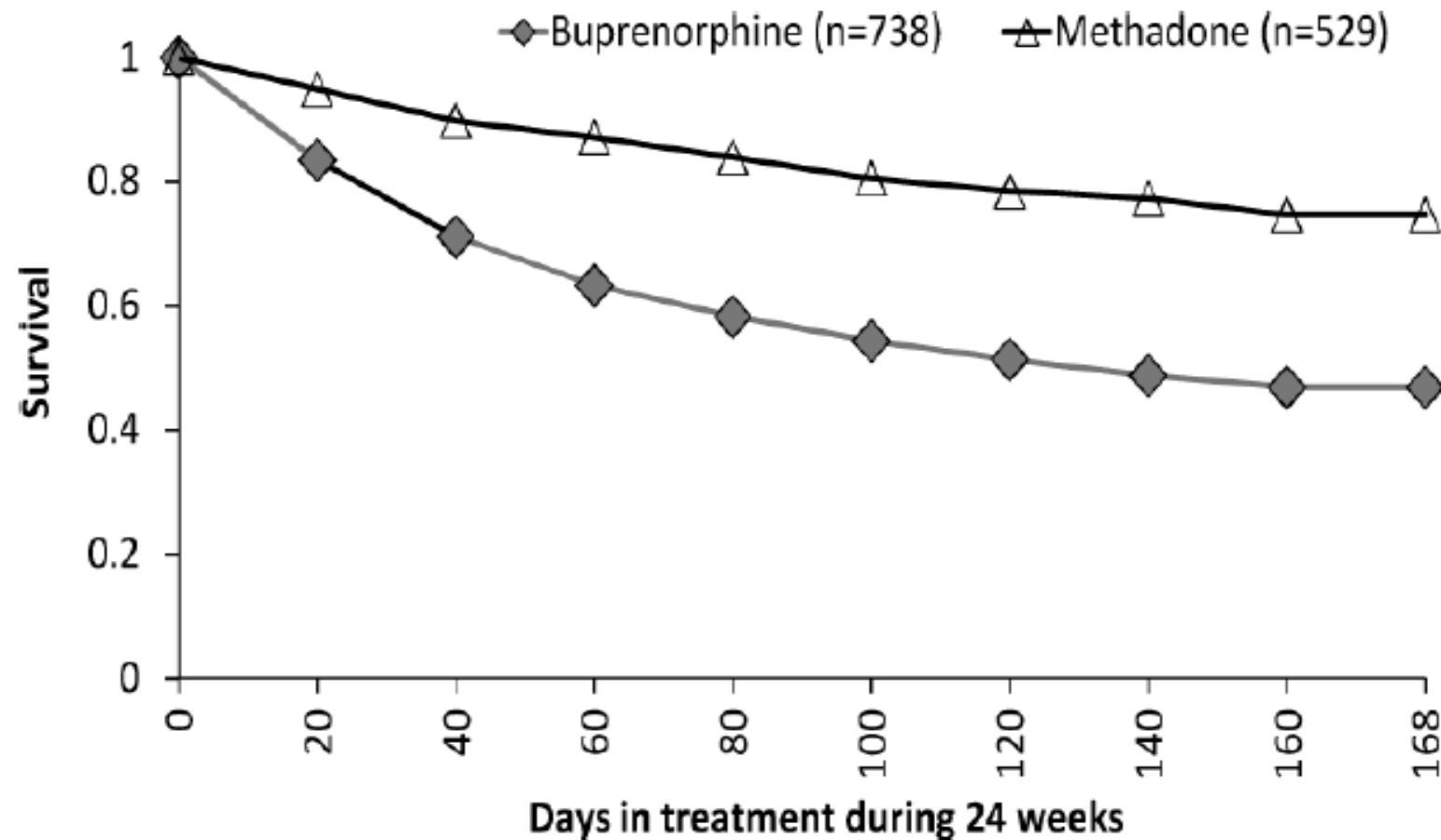
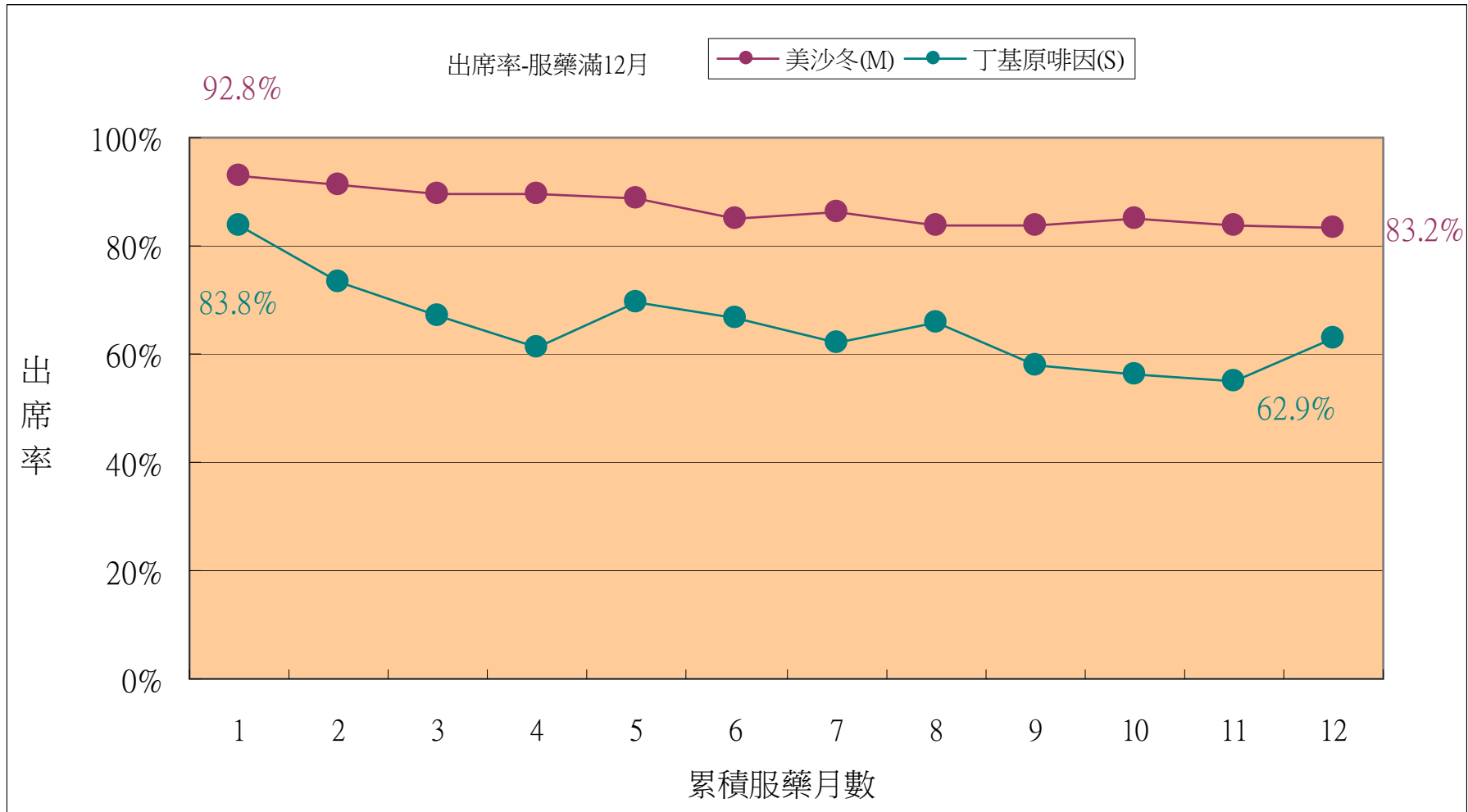


Figure 1.
Survival Curves for Buprenorphine Versus Methadone

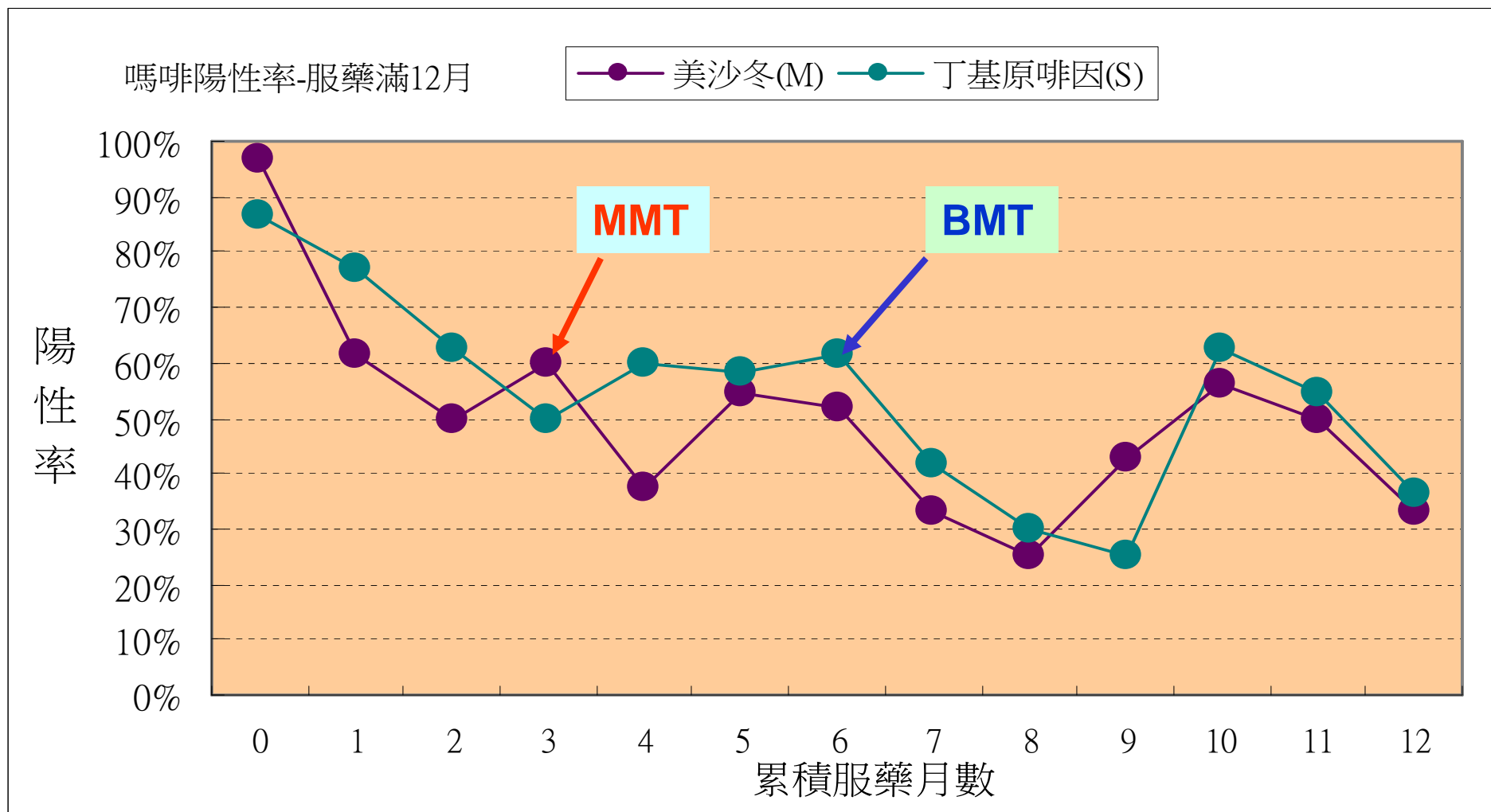
Yih-Ing Hser, et al., *Addiction*.
2014 Jan; 109(1): 79–87.

出席率-服藥滿12月



嗎啡陽性率-服藥滿12月

Urine Morphine Positive rate by time on MMT vs BMT



生活品質 (WHO-QoL)

滿意程度/分數	第二次問卷		
	MMT(美沙冬) (n=26)	BMT丁基原啡因 (n=9)	p-value
健康相關生活品質	66.58	65.89	0.805
健康相關生活品質(海洛因成癮前)	72.23	80.89	0.469
身體健康	61.42	72.78	0.172
心理健康	66.54	71.00	0.544
獨立程度 Independent level	68.81	83.33	0.032
社會關係	70.38	75.56	0.459
環境	71.46	76.25	0.541
宗教信仰或信念	70.88	76.67	0.58

分別以美沙冬和丁基原啡因為藥癮戒治替代療法之成本效益分析研究

Comparing the cost-effectiveness of methadone maintenance therapy(MMT) and buprenorphine maintenance therapy(BMT) for the management of opioid-dependent individuals

In a scheme of 6 months of methadone or buprenorphine maintenance therapy, costs per subject amounted to NT\$ 31,950 with methadone and NT\$ 49,604 with buprenorphine. Subjects receiving methadone and buprenorphine achieved an abstinence rate 18.7% and 14.7% respectively. Incremental cost-effectiveness(增加成本效益比) of methadone maintenance as compared with suboxone treatment was NT\$ 441,350 per abstinence rate.

陳建坊、簡以嘉、唐心北、李文光、江明澤、譚秀芬、司彥翔. 2009.

1. 服藥六個月之各項成本統計分析表：

服藥六個月	methadone (n=123)	suboxone (n=34)
直接成本		
藥品成本	3,748 (1,518)	20,686 (7,319)
藥品給予成本 (掛號費、調劑費等)	748 (329)	717 (273)
醫療相關成本 (診察費、檢驗費等)	13,662 (4,325)	15,991 (4,137)
間接成本		
藥物不良反應之醫療成本	539 (707)	545 (780)
交通費	13,253 (7,289)	11,663 (8,225)
總成本	31,950 (9,466)	49,604 (13,723)

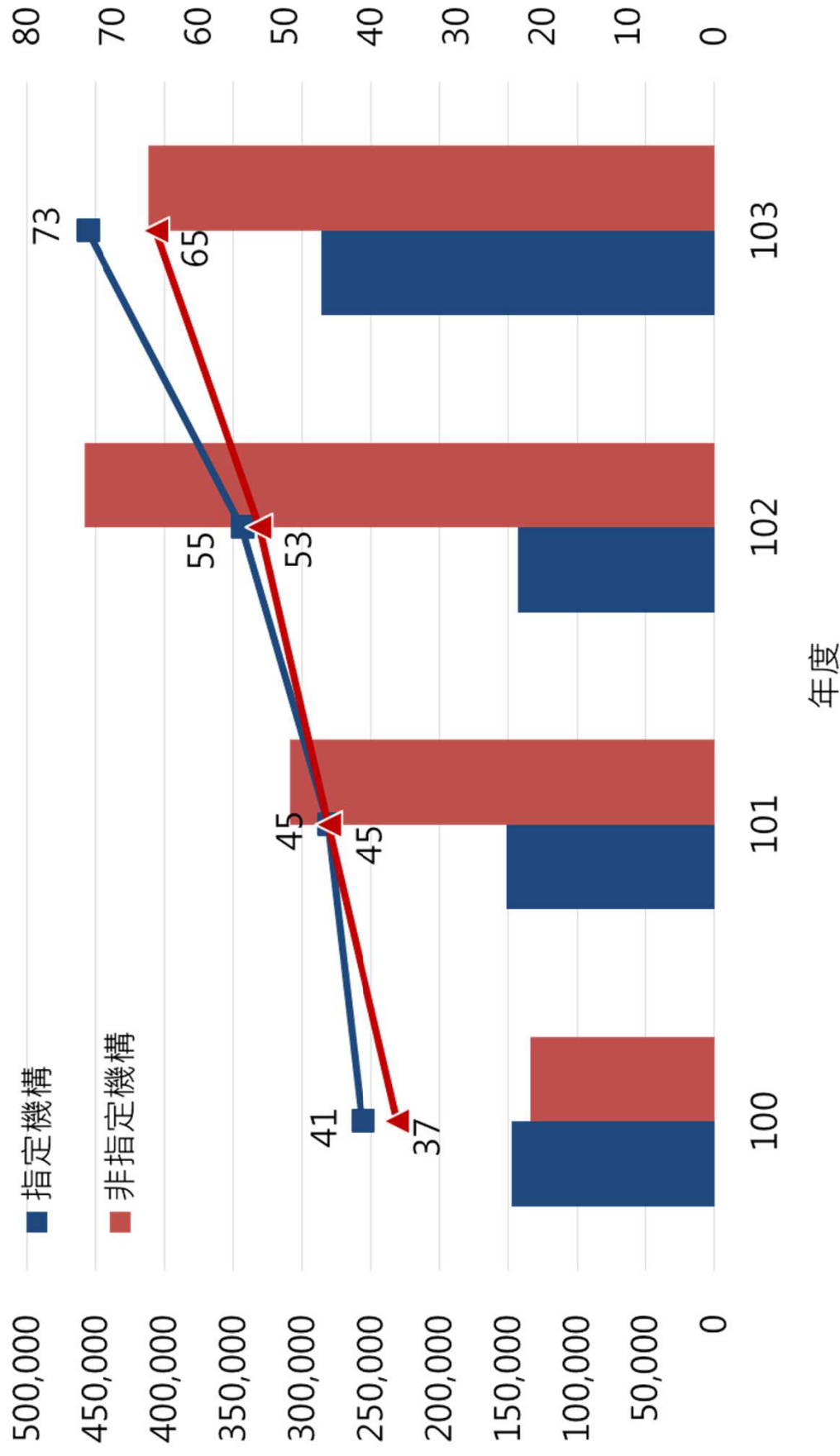
※表格數據之表示方式為：平均值(標準差)

陳建坊、簡以嘉、唐心北、李文光、江明澤、譚秀芬、司彥翔. 2009.

Challenges of BMTP in Taiwan

- ✓ 不當使用與流用 (Mis-use and diversion)
 - 未依照臨床指引
 - 遵醫囑性不佳 (poor compliance)
- ✓ 缺乏具體評估與紀錄 (insufficiency of assessment and record)
- ✓ 缺乏個案管理 (Lack of case management)
- ✓ 心理社會治療不足 (insufficiency of psycho-social intervention)
- ✓ 費用 (fee)

100-103年全國丁基原啡因使用量(顆)趨勢



這款醫生！診所內賣毒 還供「宅配」服務

高雄一名家醫科醫師，涉嫌未經看診，也沒開立處方簽，就販售FM2和一粒眠給病患，且如果病患不能前來看病，他還可以透過超商宅配，更扯的是，這名醫師被逮時，居然還說這是替毒癮病患戒毒的一種取代療程。進診所不是看病，而是買藥，買的還是管制藥品，像是丁基原咖啡因舌下錠、FM2，還有海洛因抵癮藥包，一包100元到150元不等，吸引不少毒犯上門，怕被抓，還有人透過宅配，隔空就可取藥。

TVBS, 2014/03/12



衛生福利部105年5月10日衛部 心字第1051760805號函

疾病管制署今(105)年度疫情調查指出，有新通報之愛滋感染藥癮者反應可輕易於社區購買到丁基原啡因之舌下錠，作為短期解癮，而未正規定期服用；對美沙冬替代治療持負向觀感，認為美沙冬戒斷症狀與戒斷時間比海洛因更痛苦更久，且有個案表示無法忍受副作用等情事。

Buprenorphine/Naloxone的擴大使用

- 訓練一般科醫師：
 - 如何評估篩選病患進入Buprenorphine/Naloxone治療
 - 轉介
 - 協同照護
- 訓練完成證明文件
- 申請購用Buprenorphine/Naloxone
- 稽核使用狀況
 - 病歷記載
 - 三級管制藥品查核
- 加強個案管理、衛教、追蹤.....

Key Points of Successful Induction on Buprenorphine/Naloxone

- ✓ **Careful Evaluation**
 - ✓ **Drugs history**
 - ✓ **Current frequency, route & dose of opioid substance**
 - ✓ **Last dose & Time**
- ✓ **Education about Buprenorphine/Naloxone**
- ✓ **Discussion about the treatment plan**
- ✓ **Monitoring daily for 3-7 days after first dose of Buprenorphine/Naloxone**

Key Points of Successful Induction on Buprenorphine/Naloxone

- ✓ **Evaluation at each visit**
 - ✓ **Physical condition—opioid withdrawal symptoms, side effects of Buprenorphine/Naloxone,**
 - ✓ **Re-use of opioid substance**
 - ✓ **Compliance**
 - ✓ **Urine toxicology**
- ✓ **Family involvement**

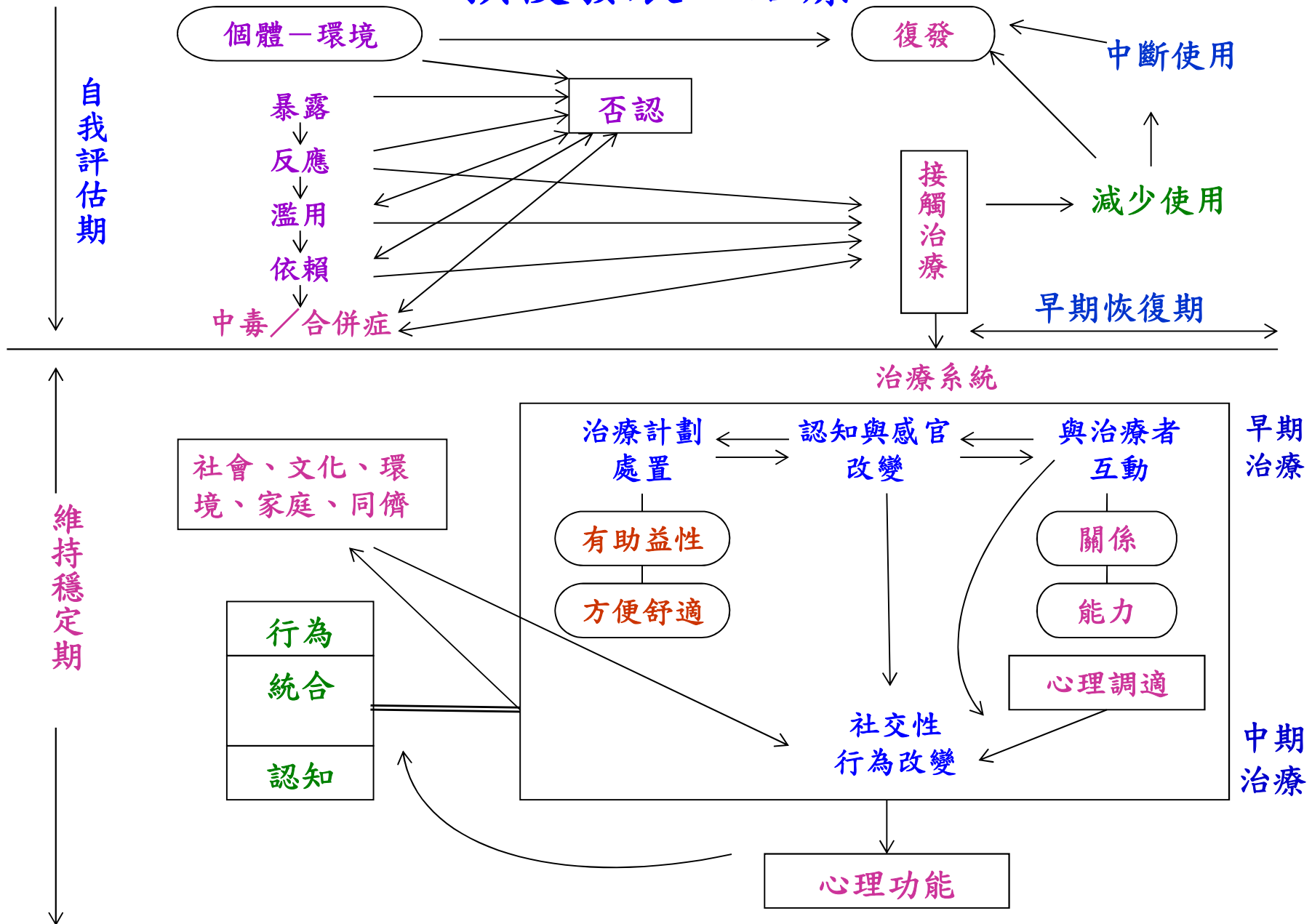
替代治療未來發展

- ❖ 健康促進概念與實踐
- ❖ 特殊族群的照護
 - ❖ HIV帶原者
 - ❖ 女性
 - ❖ 孕婦
 - ❖ 精神疾病共病者
 - ❖ 老人
 - ❖ 青少年
- ❖ 心理社會治療的必要性

替代治療未來發展

- ❖ 給藥點的擴充—法律規範的調整
 - ❖ 監所內
 - ❖ 巡迴醫療模式
 - ❖ 異地服藥制度的建立(traveling system)
- ❖ 品質提升
 - ❖ 出席率與留存率
 - ❖ 尿液篩檢
 - ❖ 生活品質與角色功能之改善
 - ❖ 認證與評鑑制度

物質使用問題之整合性模式 預後發展—治療



Thanks for Your Attention

