Depression in Taiwan

From past, present to future

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Epidemiology

Clinical pharmacological practice pattern

Brain imaging and Neuromodulation

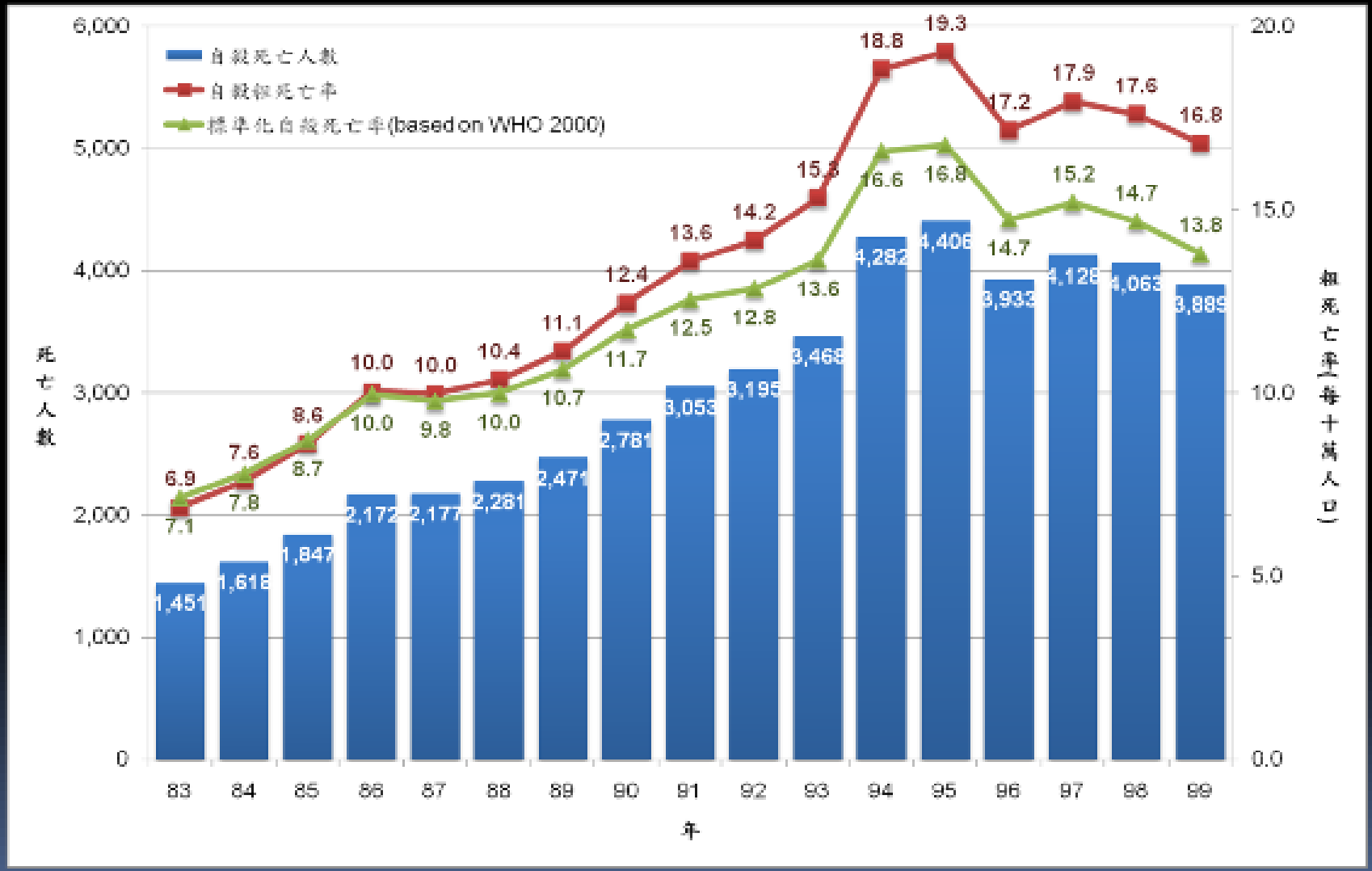
Epidemiological studies of depression in Taiwan

- 1980s: lifetime prevalence of major depression 1.1% by DIS (Hwu, & Weissman 1996), *lower end* of the spectrum worldwide
- 1990s: one-month prevalence 5.9% of major depression and 15.3% of depressive neurosis in the *elderly* by GMS, (Chong et al 2001)
  - *Risk factor: widows with low educational levels (urban area) and among those with physical illness*
- 2003-2005: a nationally representative sample survey: lower lifetime prevalence (1.2%) of major depression by WMH-CIDI (Liao & Lee, 2011)
  - *Risk factors:* divorced, widowed, age <=40 and females, rural residents were lower risk for MDD
  - Only *1/3 MDD* sought help, despite loss *twice* the No of workdays vs. US sample (*cultural stoicism*, high tolerance)

- Data from
- Taiwan Suicide Prevention Center
- 2011, 10,04

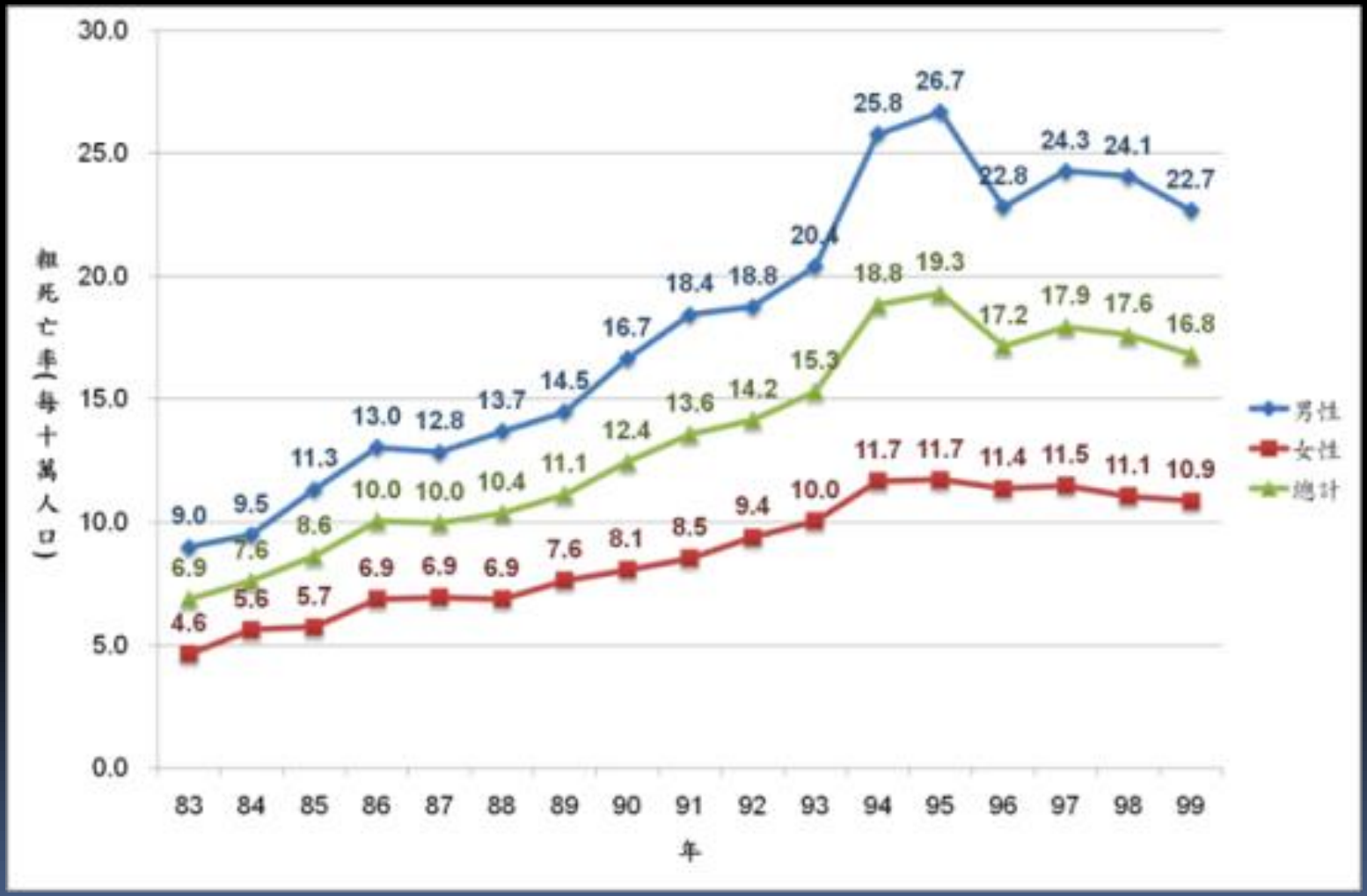
Suicide Update in Taiwan

Suicide mortality rate from 1994 through 2010



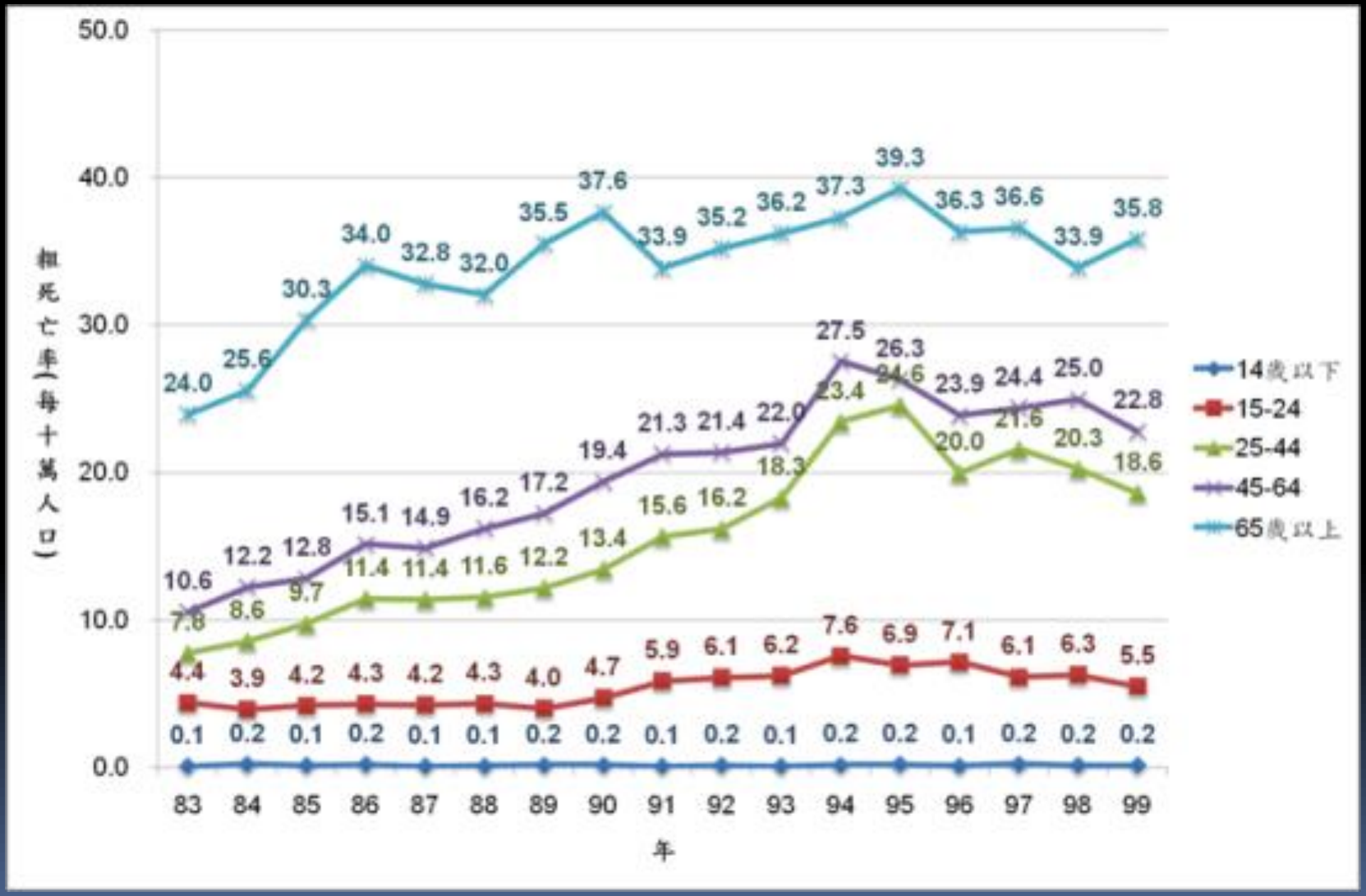
TSPC

Suicide mortality rate by gender (1994 to 2010)



TSPC

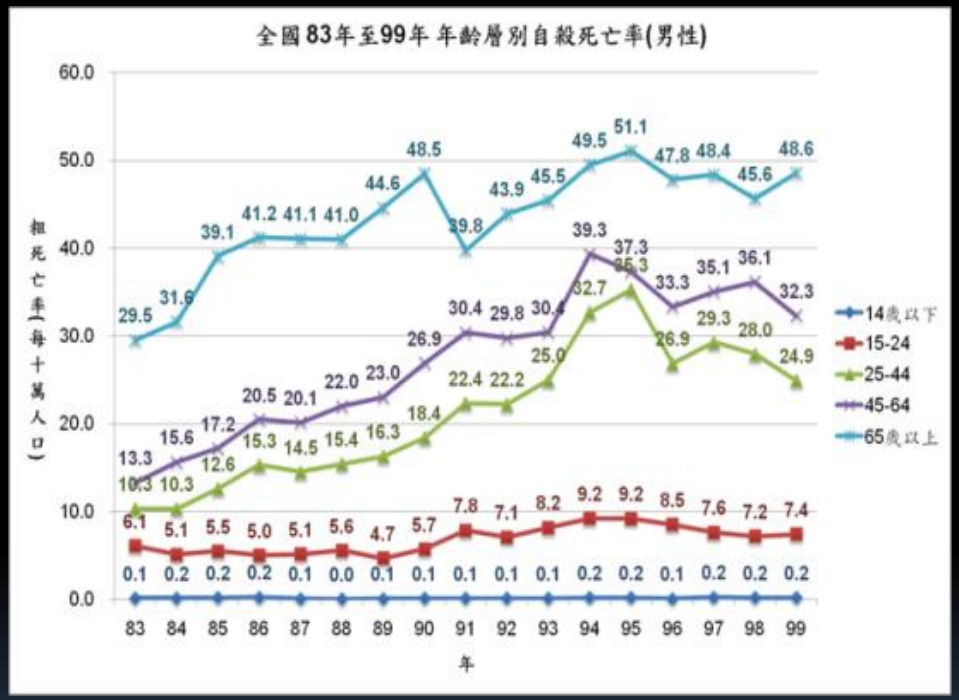
Suicide mortality rate by age levels (1994 to 2010)



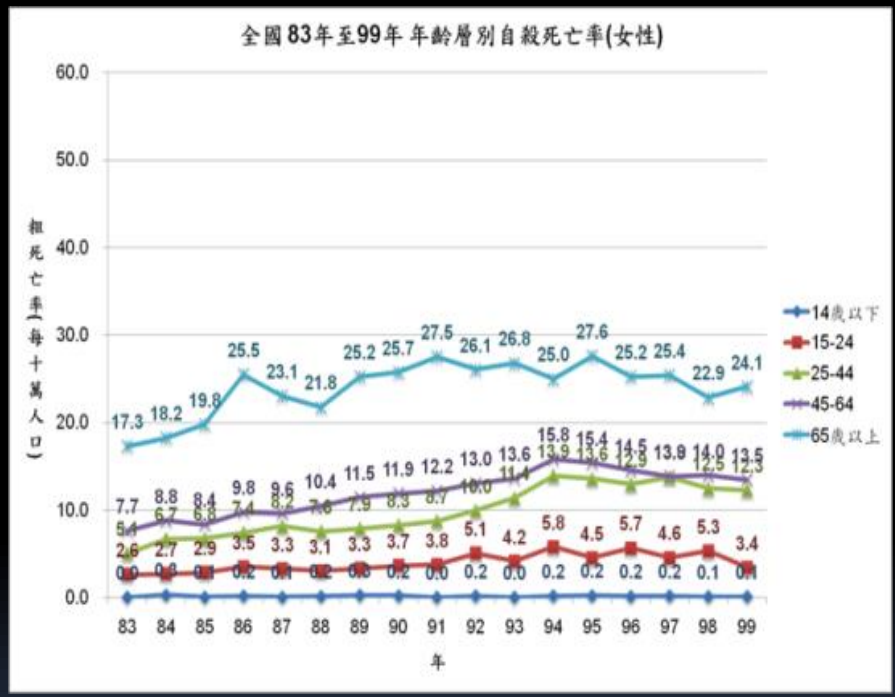
TSPC

Suicide mortality rate by age level (1994 to 2010)

Male

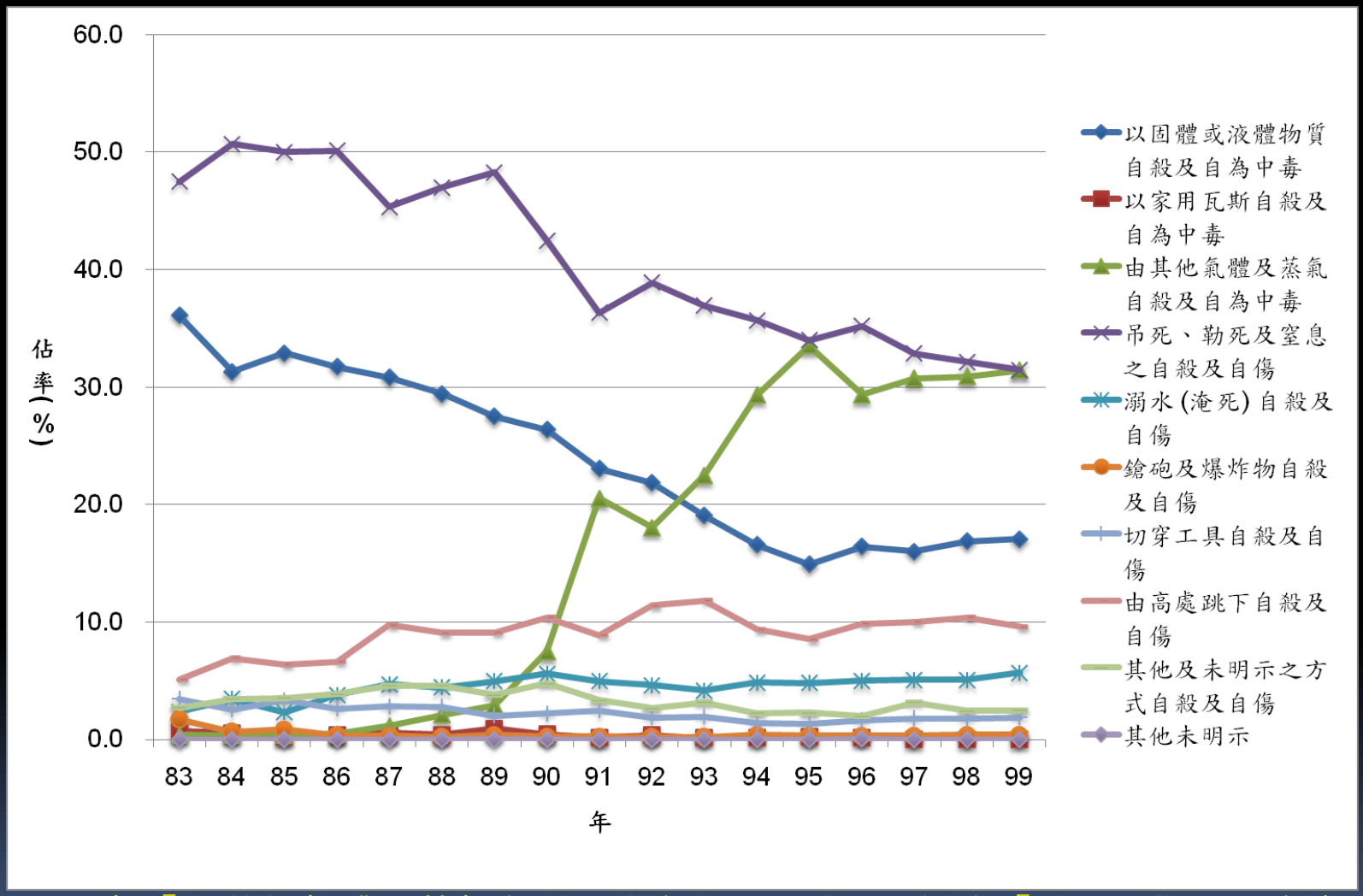


Female



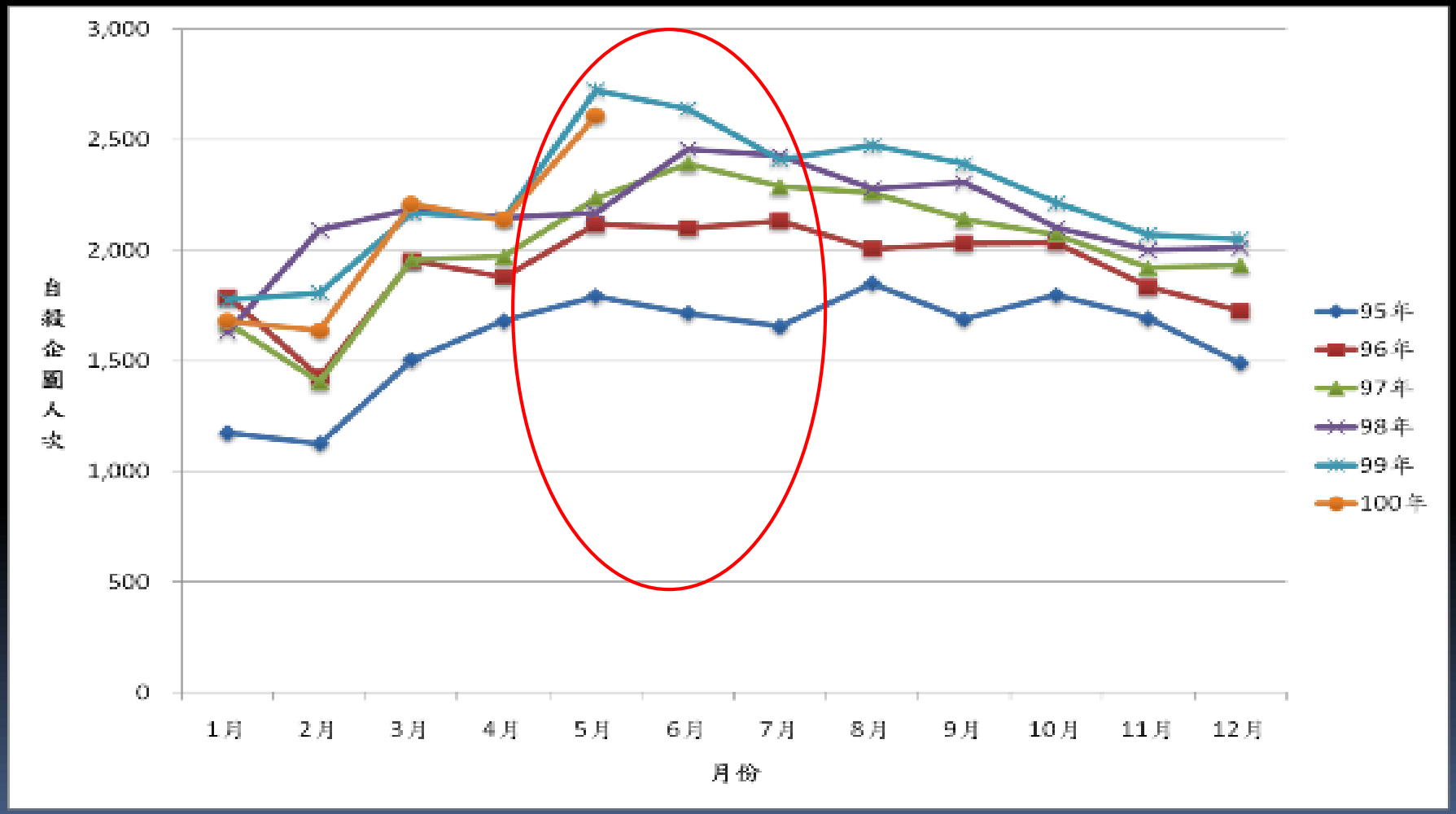
TSPC

「由其他氣體及蒸氣自殺」自90年起明顯增加



99年「由其他氣體及蒸氣自殺」佔率(31.42%)，已近與「吊死、勒死及窒息」(31.47%)並列第一位，持續將燒炭自殺列為重要防治措施。

Increasing the reported number of suicidal people across 2006 to 2011



TSPC

Mass media effects

Andrew Cheng "book: Media and suicide"

- May, 2005, a famous TV / movie star Mr. Ni who hung himself on the tree
  - Reported continuously for 17 days with 1.5 pages of newpapers daily for the details of suicide methods and his family
  - TV reported this event hourly for the initial few days
  - He was recognized by mass media as a 'hero'
  - Induced increased suicide rate subsequently by imitation
- This inappropriate report then was requested to have self-regulation by adhering the rules set by the government, Administrative Yuan

Increased awareness of depression in Taiwan

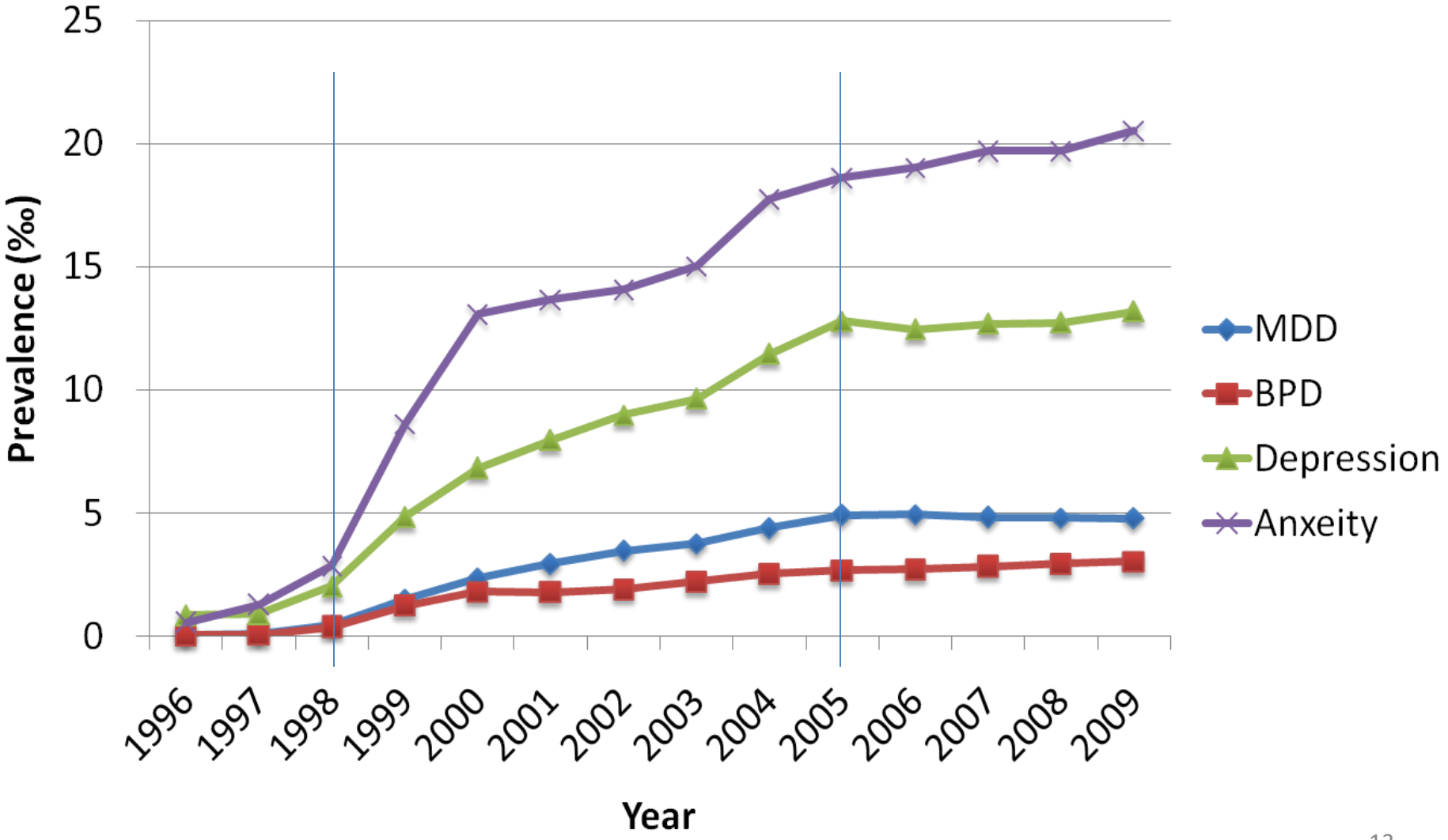
- From *neuroasthenia* to depression took a long way
- From *social stigma* to *cultural stoicism*
- The effect of urbanization with increase of divorced rate and other traumatic events

- There is *much room for improvement* in raising the Taiwanese public's awareness about MDD and encouraging their *willingness* to seek professional help. The following organizations were established :

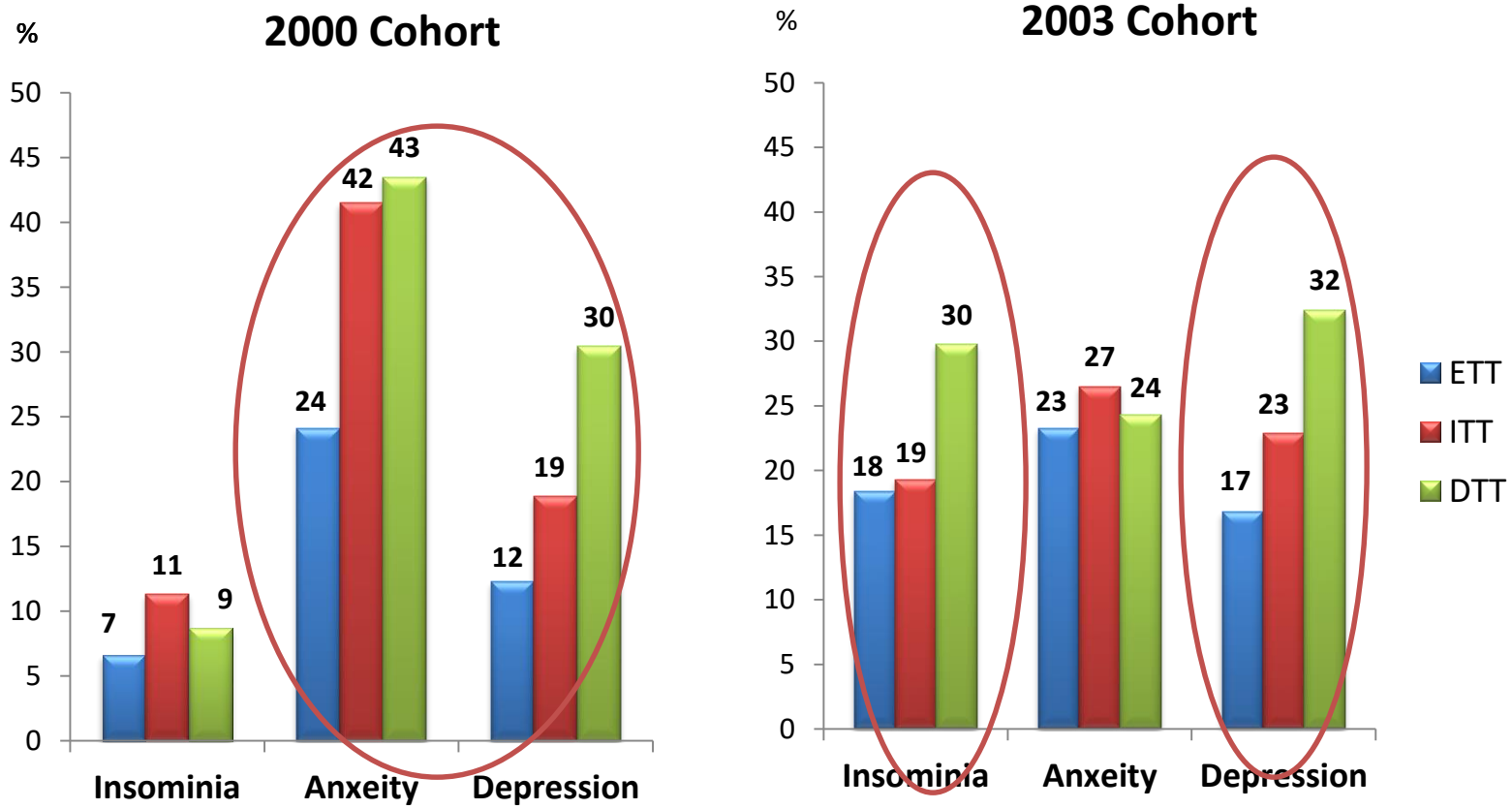
  - 2002: Taiwan Association Against Depression (TAAD)
  - 2005: Taiwan Suicide Prevention Center (TSPC)
  - Suicide mortality rate went down from 19.3 to 16.8 persons/100,000

Prevalence of mood disorders

1996 to 2009



Less severe mood disorders preceded the diagnosis of MDD (within two years)

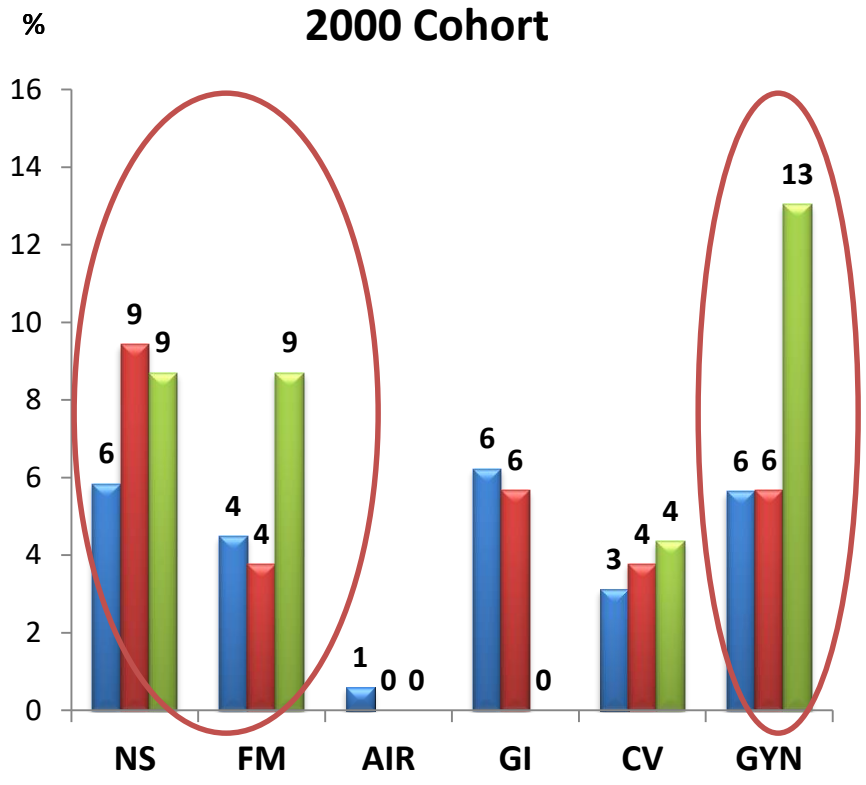


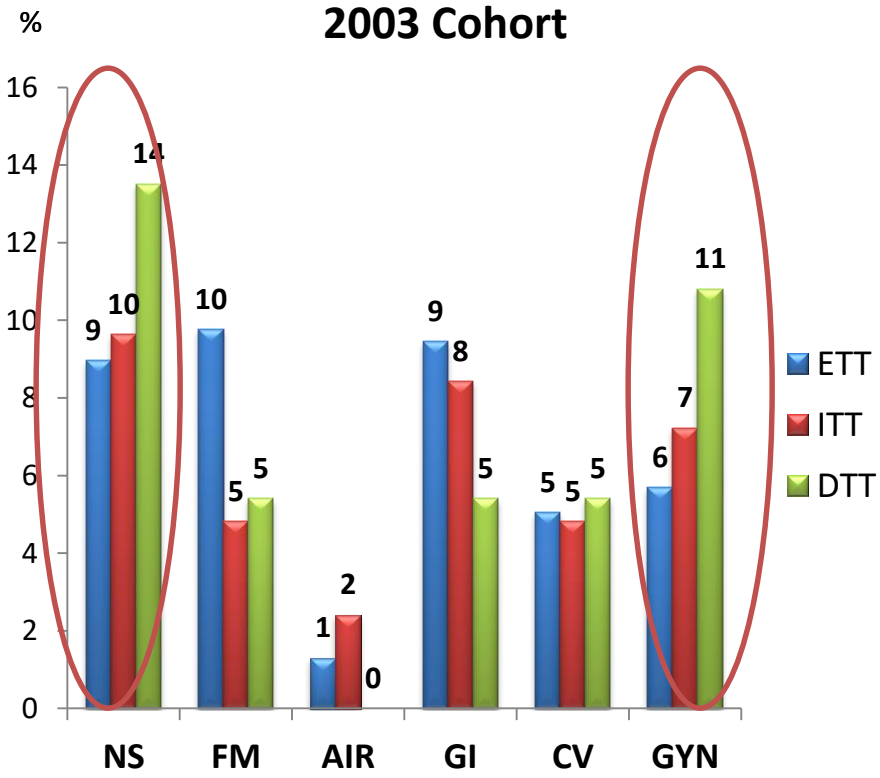
ETT: easy to treat (no change of any given ATD)

ITT: intermediate level of difficult to treat (change once after an adequate ATD trial)

DTT: difficult to treat (change over two times after an adequate ATD trial)

Visits of non-psychiatric clinic
Before MDD diagnosed at psychiatry clinic





ETT: easy to treat (no change of any given ATD)
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Outpatient Practice and antidepressant Utilization in Taiwan 2000 -2009

Tung-Ping Su TVGH

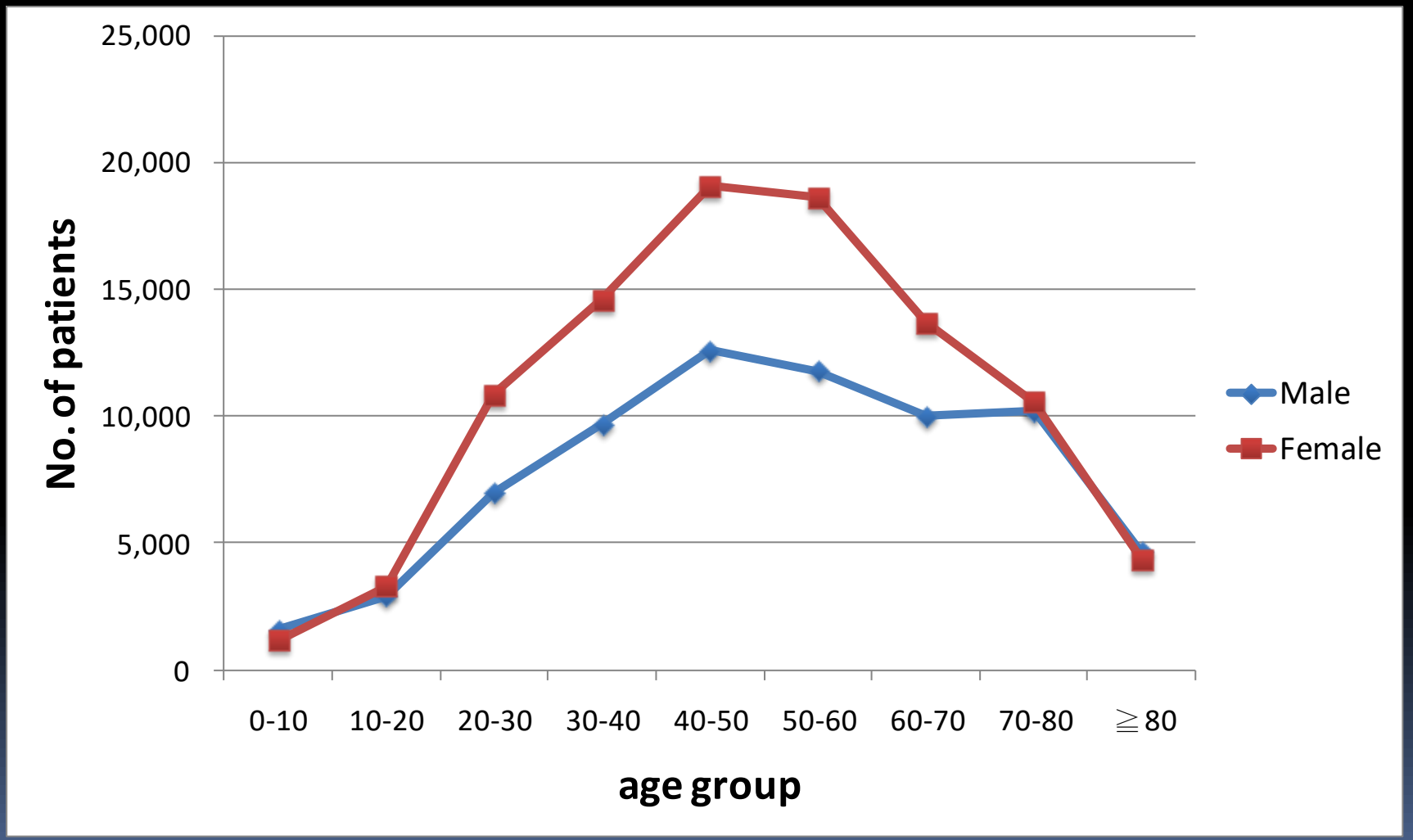
Data Source

- National Health Insurance program covering 96-99% of 2.3 million people in Taiwan
- National Health Insurance data collected from 2000-2009, based on 2005 one million sampling set
- All prescriptions included antidepressants from 2000-2009 were 1,673,345 in total
  - Antidepressant:

    ATC code of Drug : **N06A**

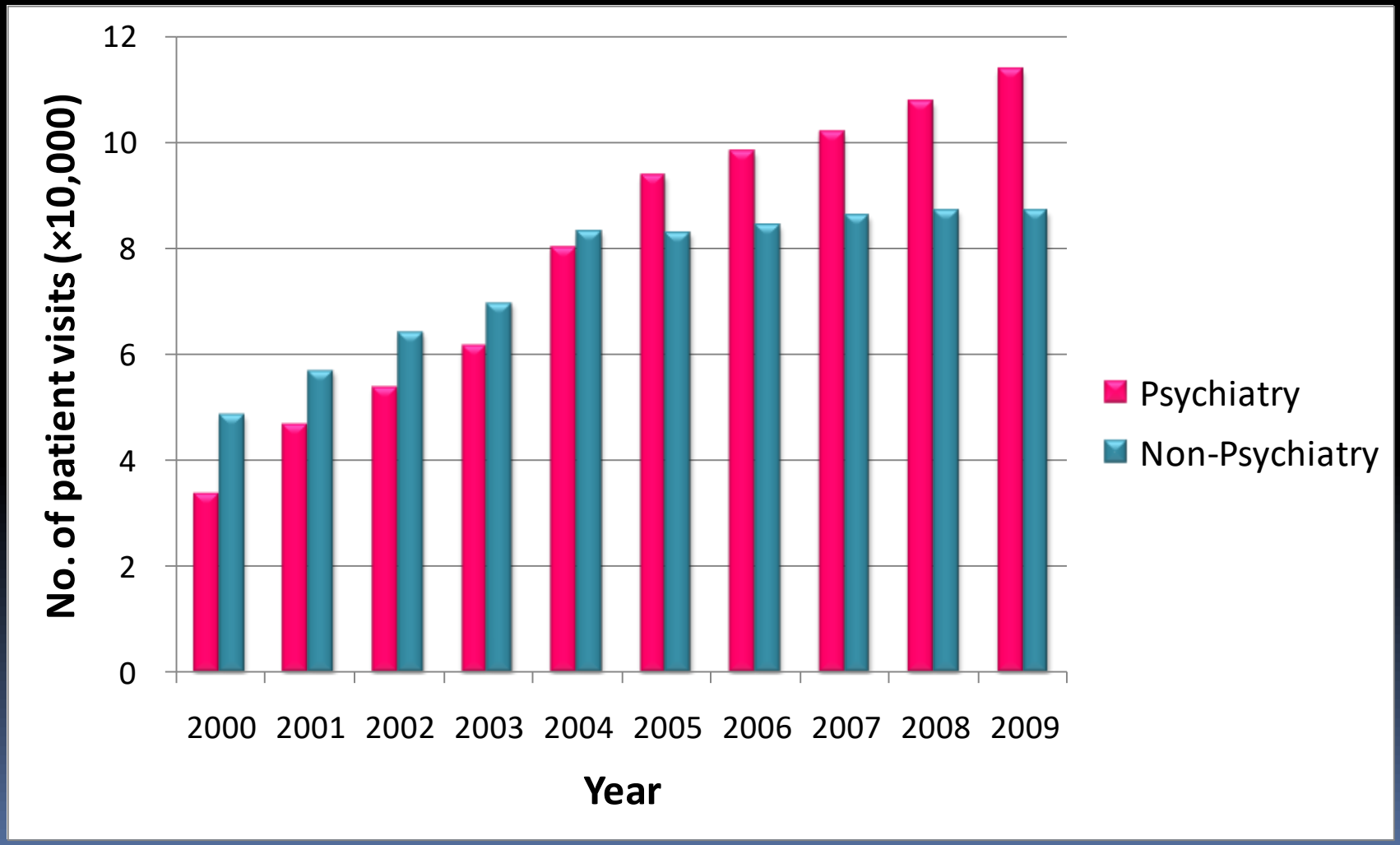
    168 drugs, 19 subclasses

No. of patients by age, gender



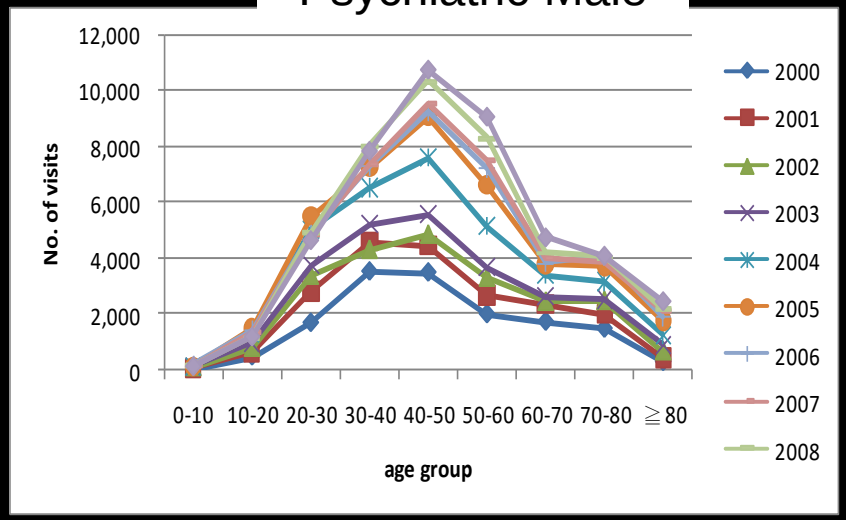
No. of outpatient visits with antidepressant prescription: 2000-2009

Psychiatry vs. Non-psychiatry

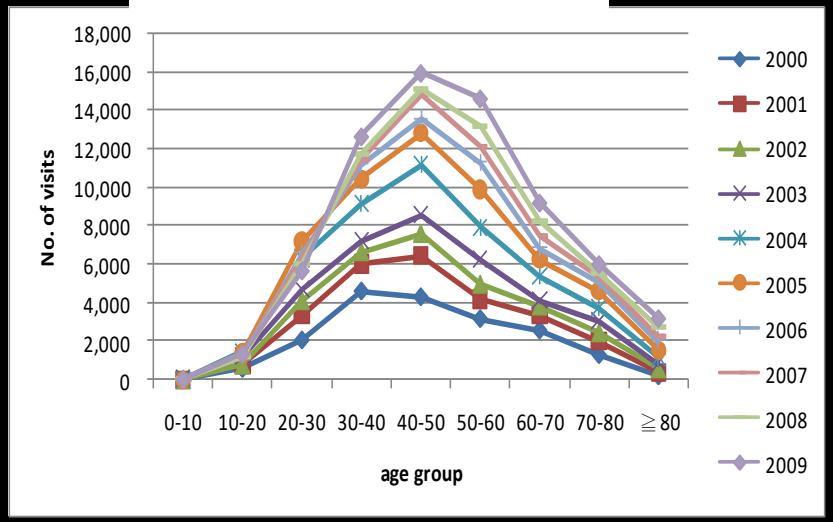


Outpatient visit with ATD prescriptions by age

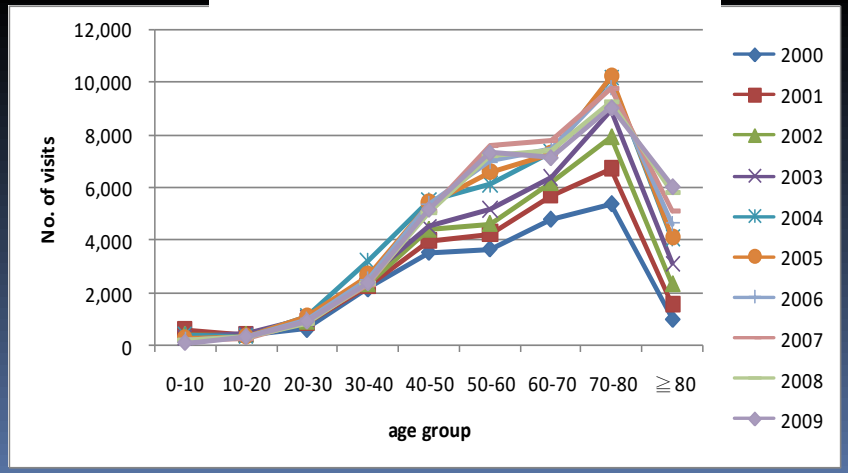
Psychiatric Male



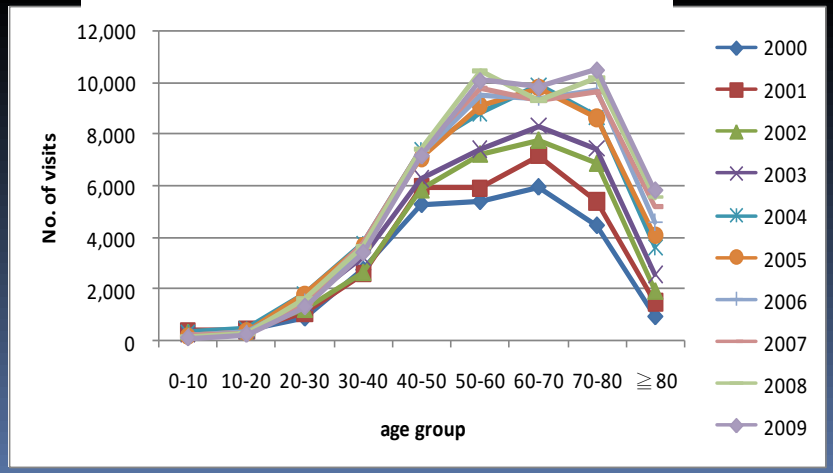
Psychiatric Female



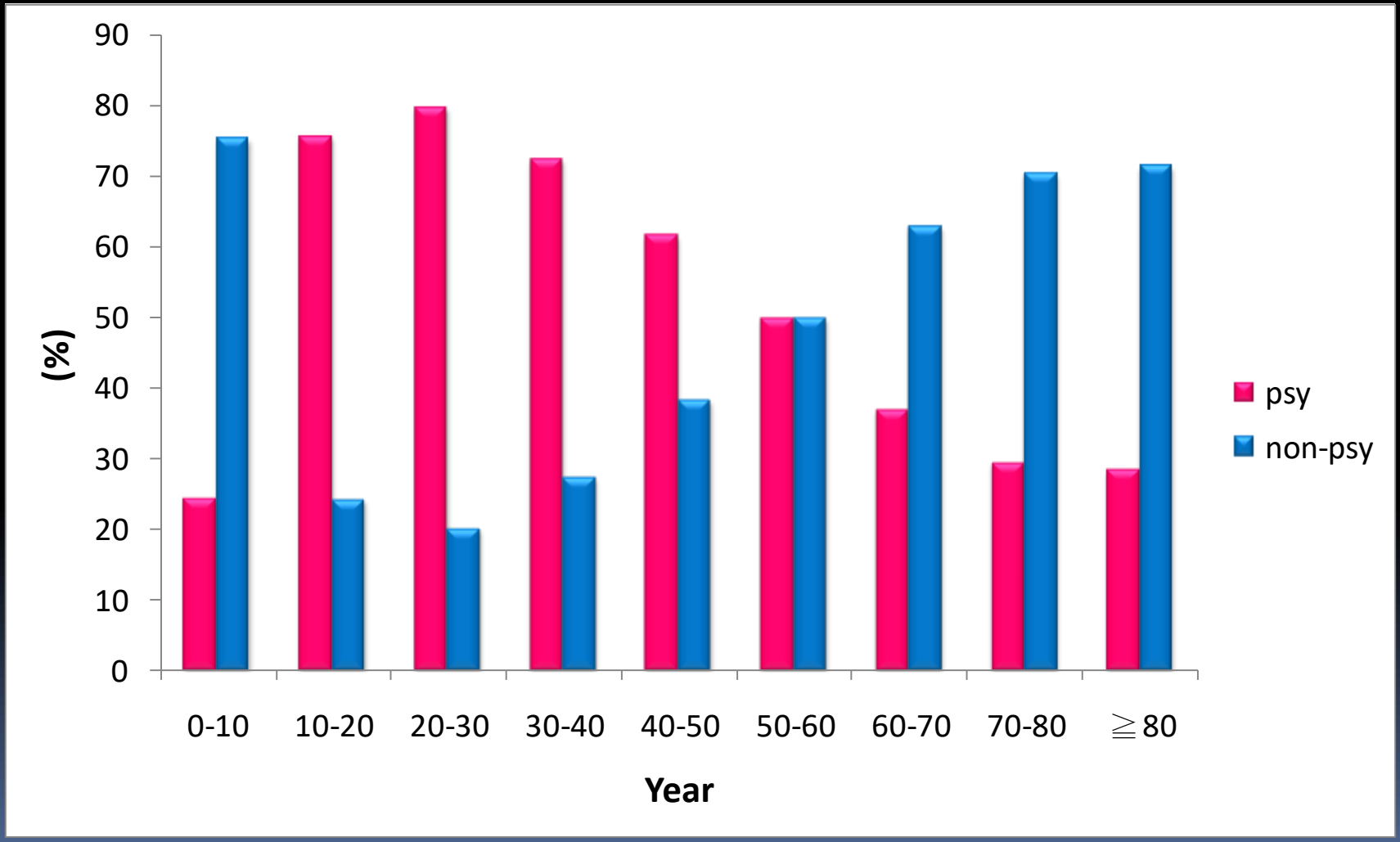
Non- Psychiatric Male



Non- Psychiatric Female



Prevalence of patients utilizing antidepressant
with age distribution:
Psychiatry vs. Nonpsychiatry (2009)

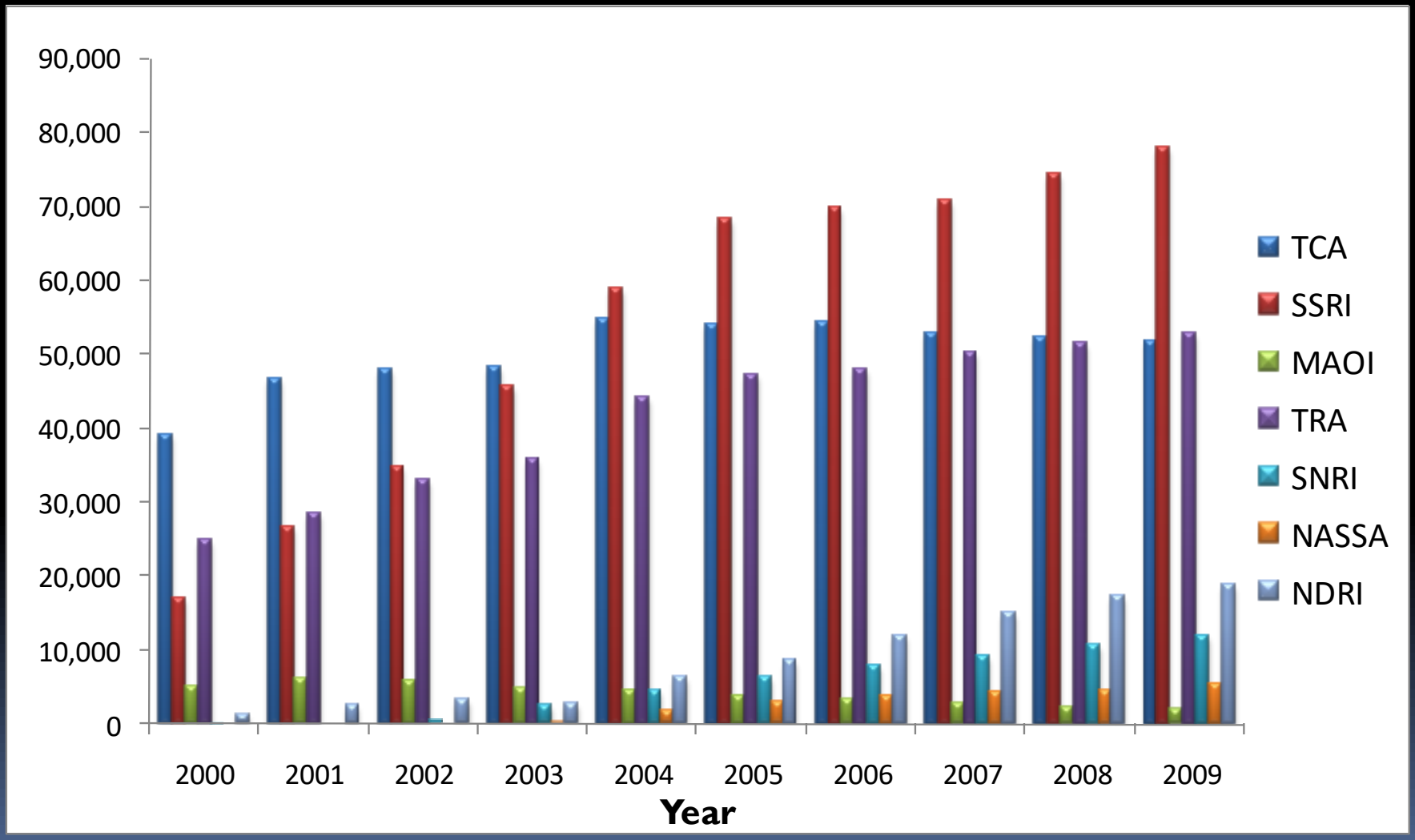


Number of prescribed antidepressants from 2000-2009

Number of Antidepressants	Psychiatric outpatient prescriptions	%	Non-psychiatric outpatient Prescriptions	%	total prescriptions	%
1	705,147	88.99	724,425	96.45	1,429,572	92.62
2	85,624	10.81	24,880	3.31	110,504	7.16
3	1,582	0.20	1,680	0.22	3,262	0.21
4	34	0.00	99	0.00	133	0.01
5	0	0.00	1	0.00	1	0.00

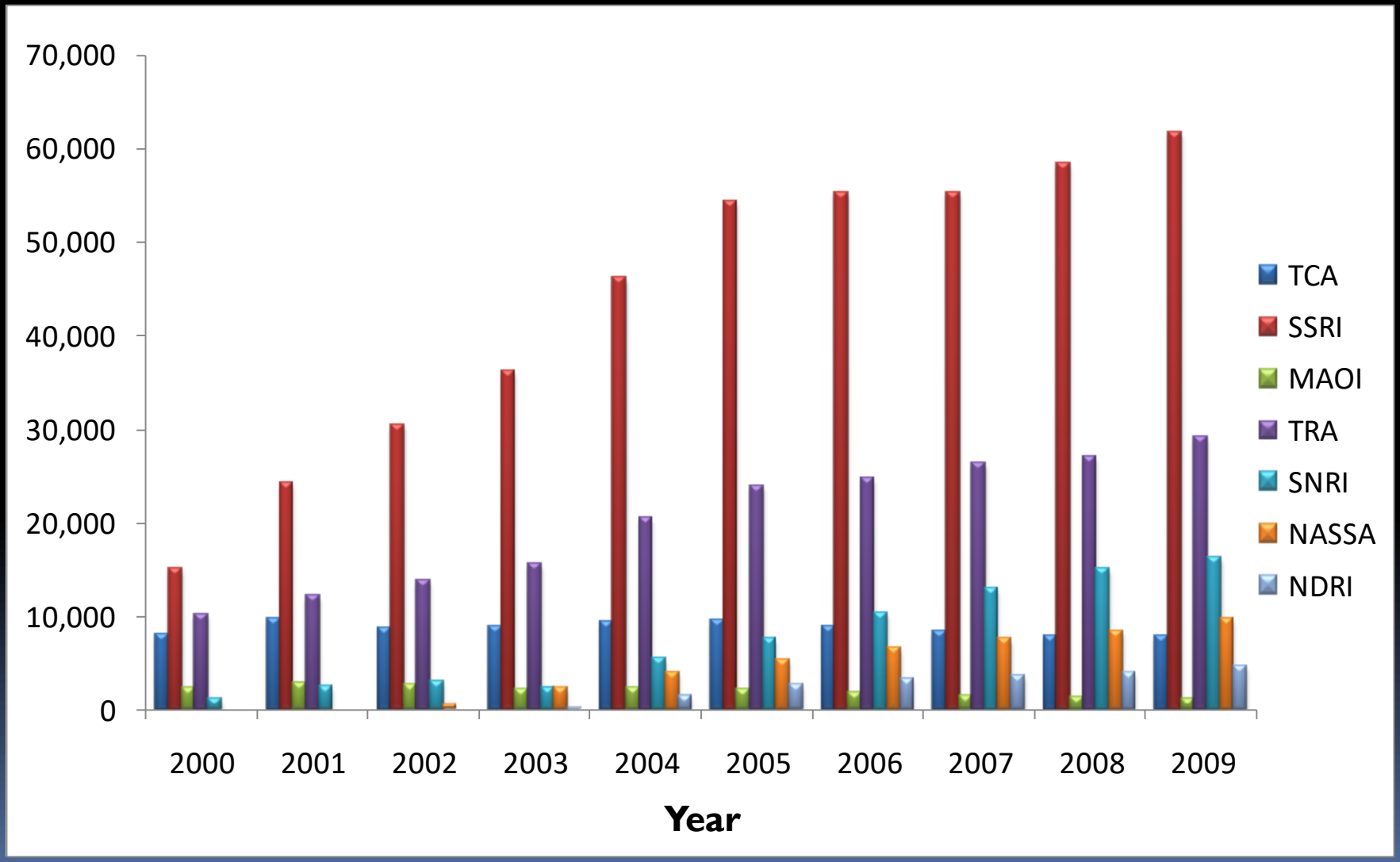
Prescription, DDD and Cost of Antidepressants (2000 – 2009)

Prescription of antidepressants in Taiwan
2000-2009

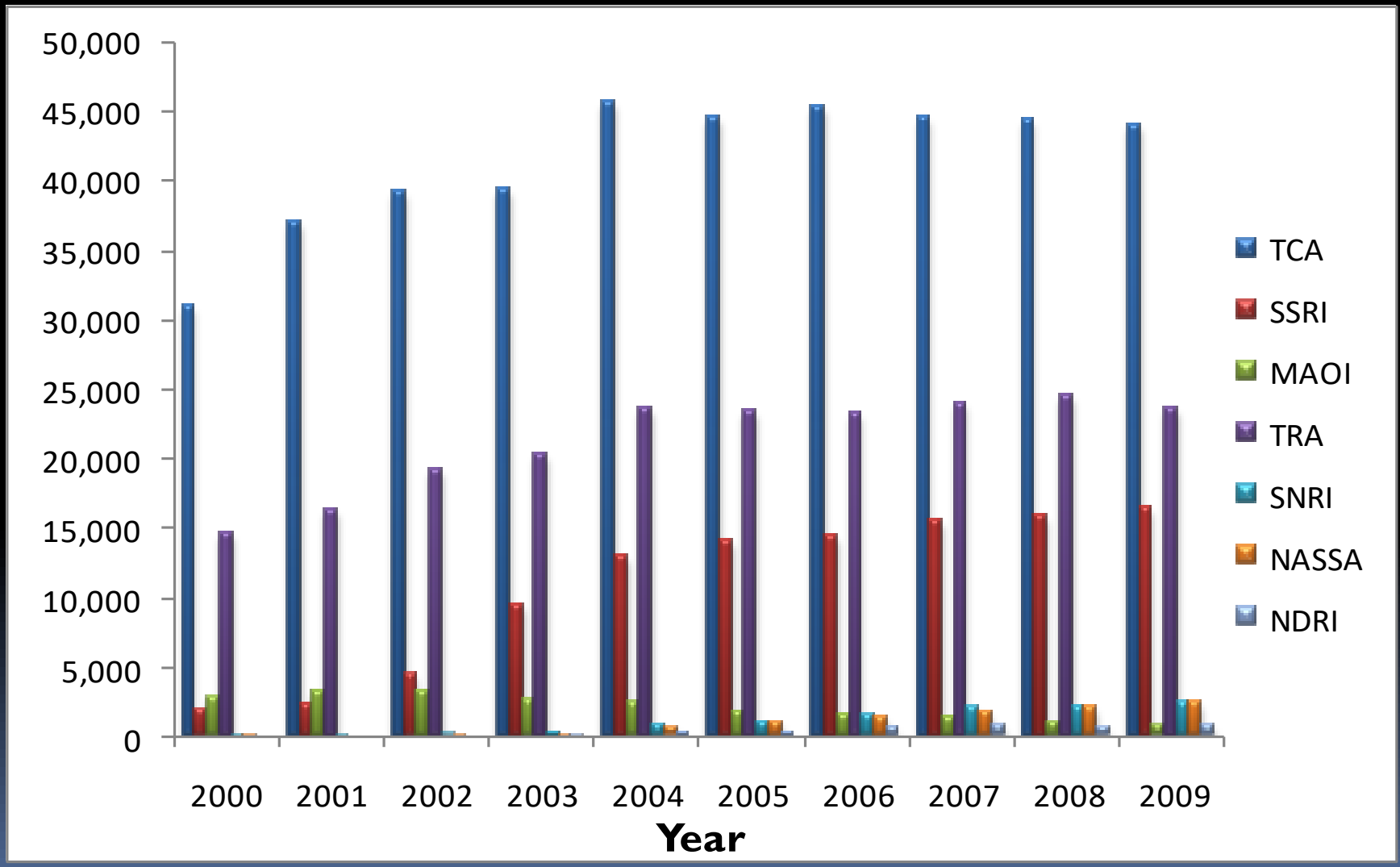


Prescription of antidepressants in Taiwan

Psychiatric outpatients (2000-2009)

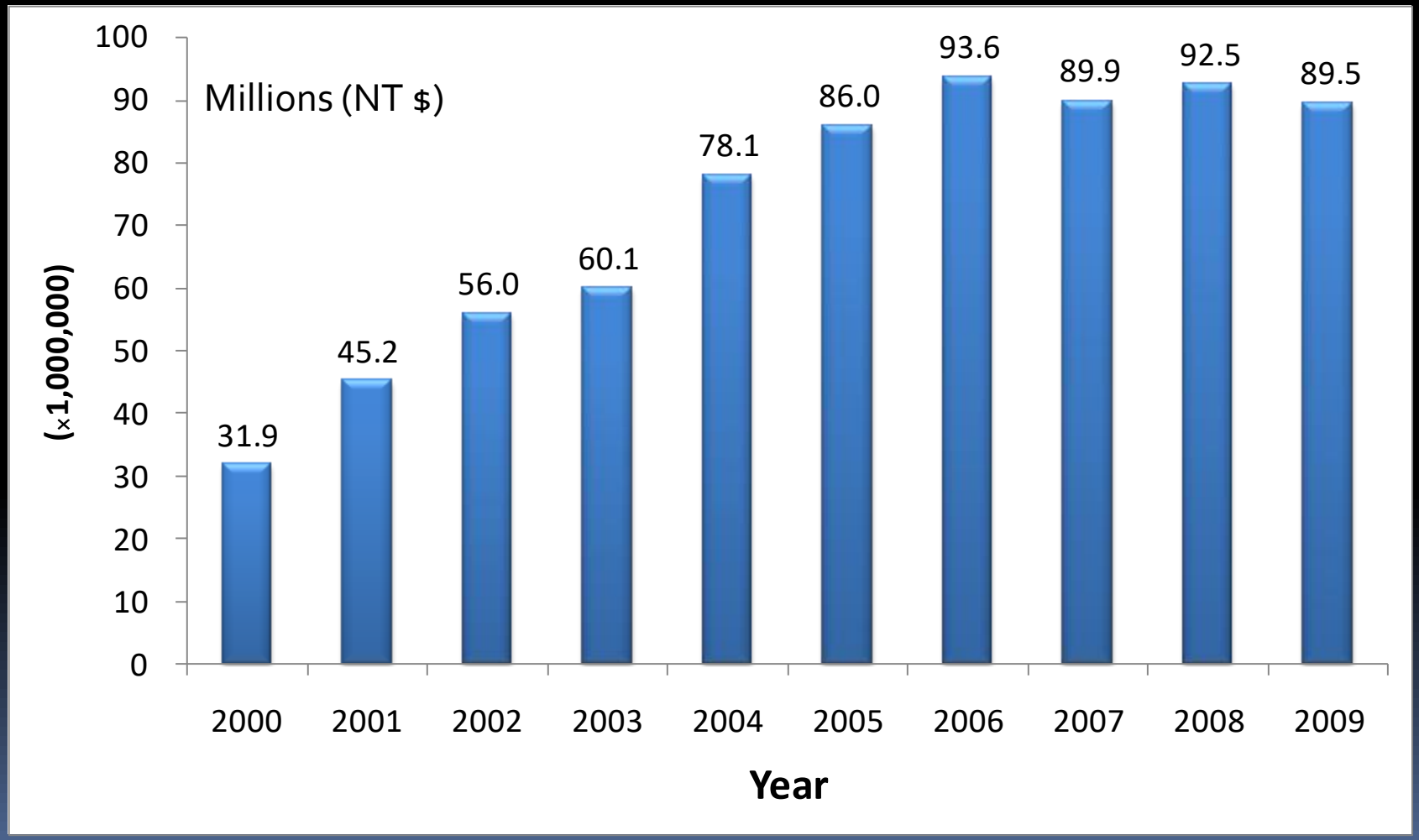


Prescription of antidepressants in Taiwan:
Non-Psychiatric outpatients (2000-2009)

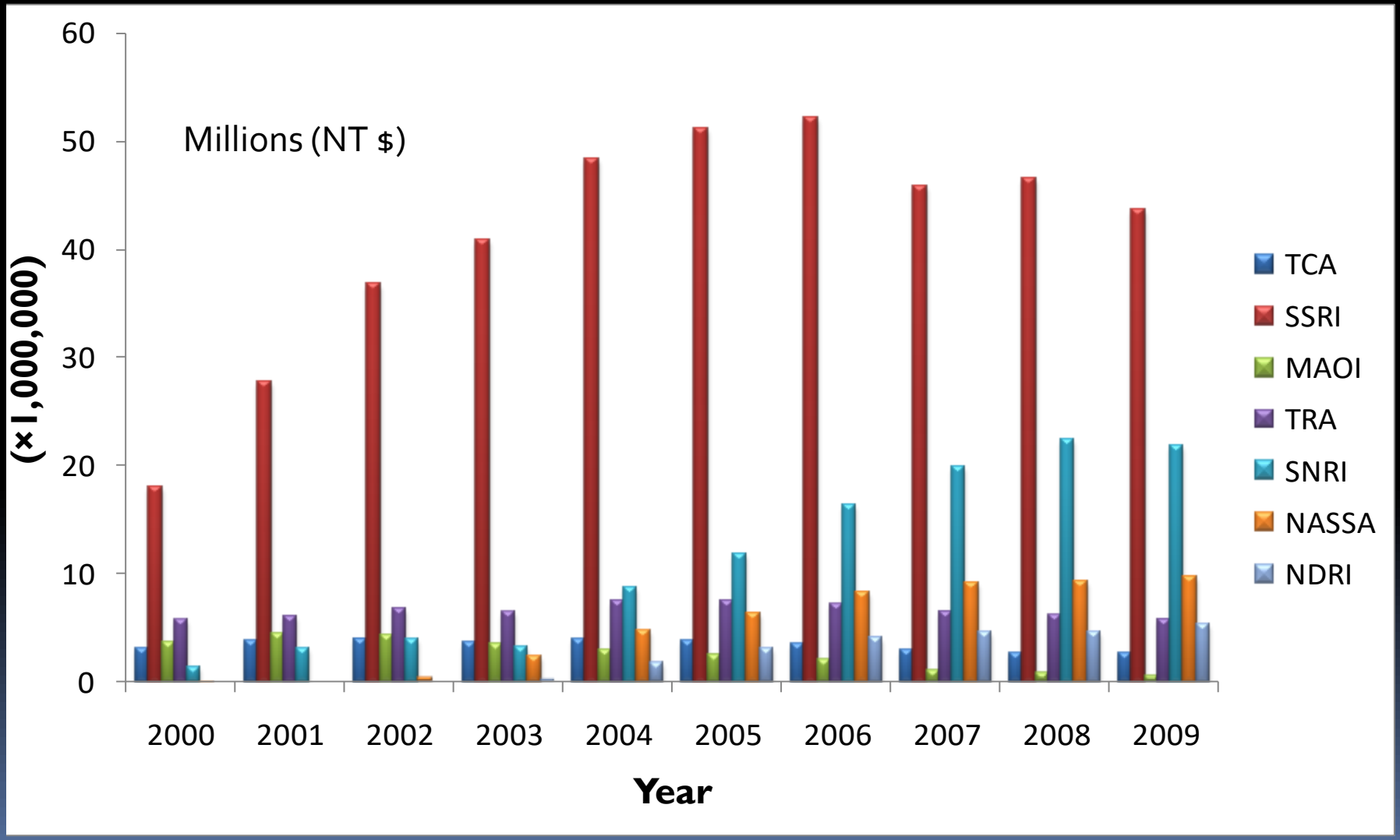


Total cost of antidepressant use in Taiwan 2000-2009

Psychiatry vs. non-psychiatry ratio= 4 : 1

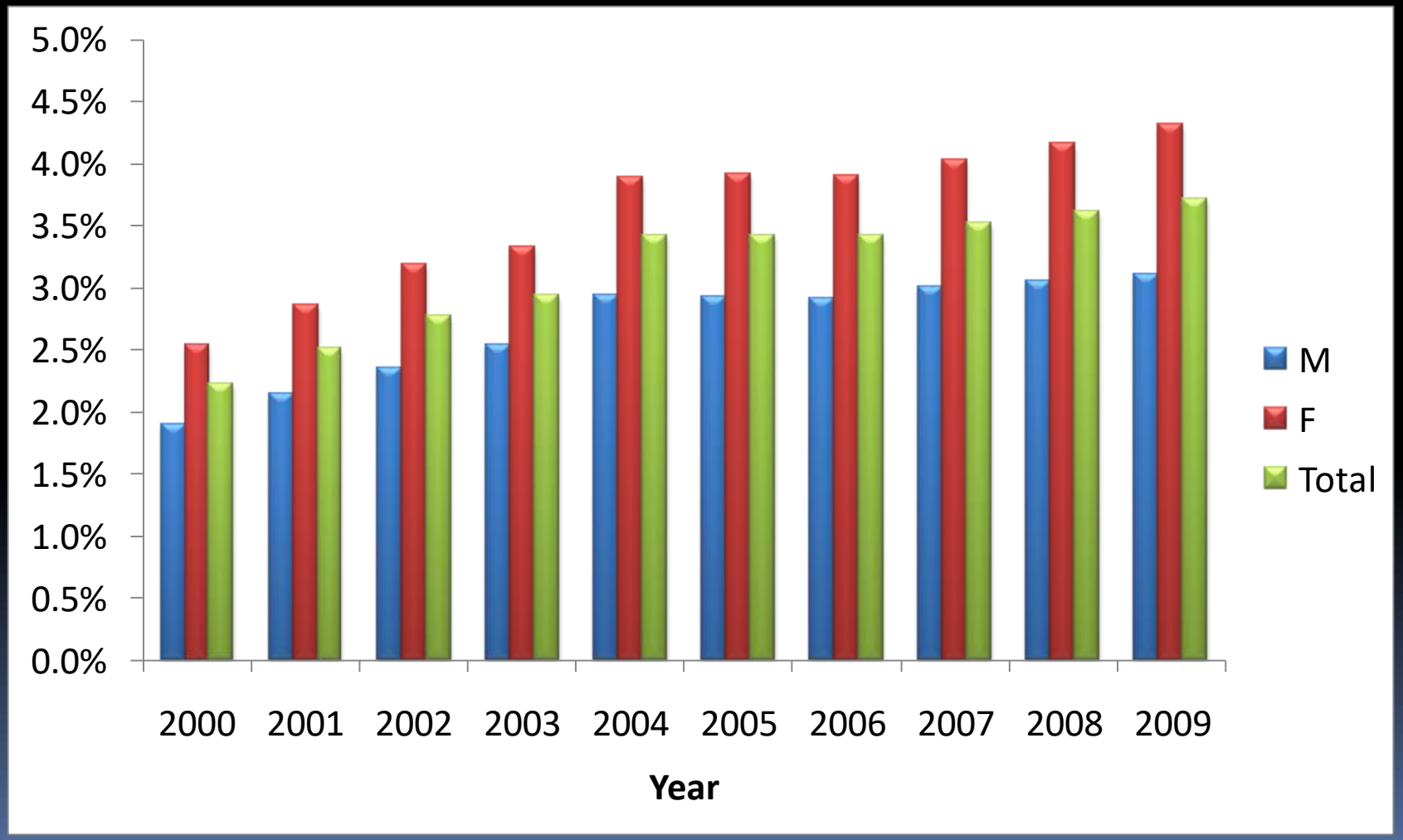


Comparison of total cost of different antidepressant use (2000 – 2009)



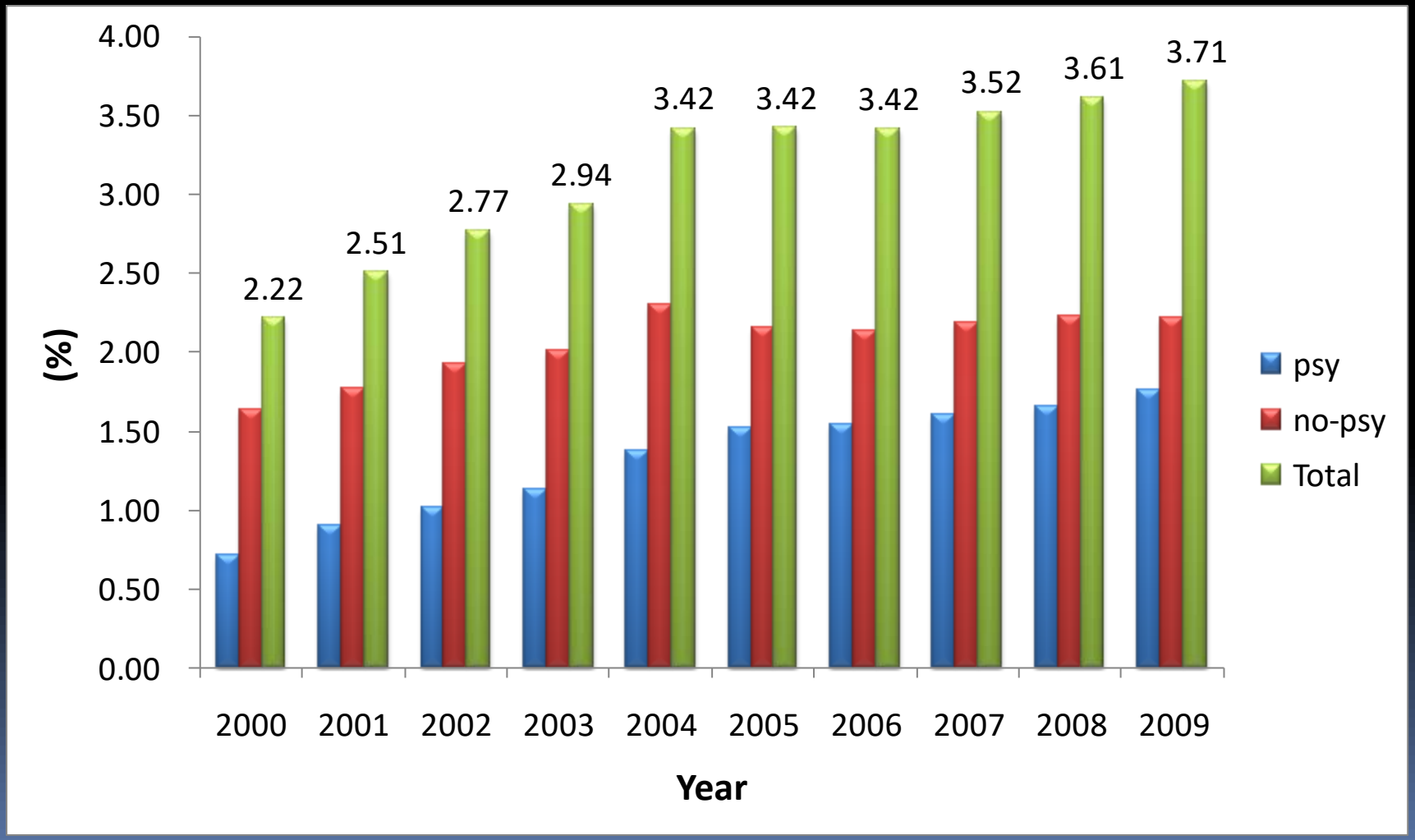
Prevalence of Antidepressant utilization (2000 – 2009)

Prevalence of antidepressant utilization
by gender (2000-2009)
Female more use than male



Prevalence of patients utilizing antidepressants,
Psychiatry vs. non-psychiatry (2000-2009)

Non-psychiatry more use than Psychiatry



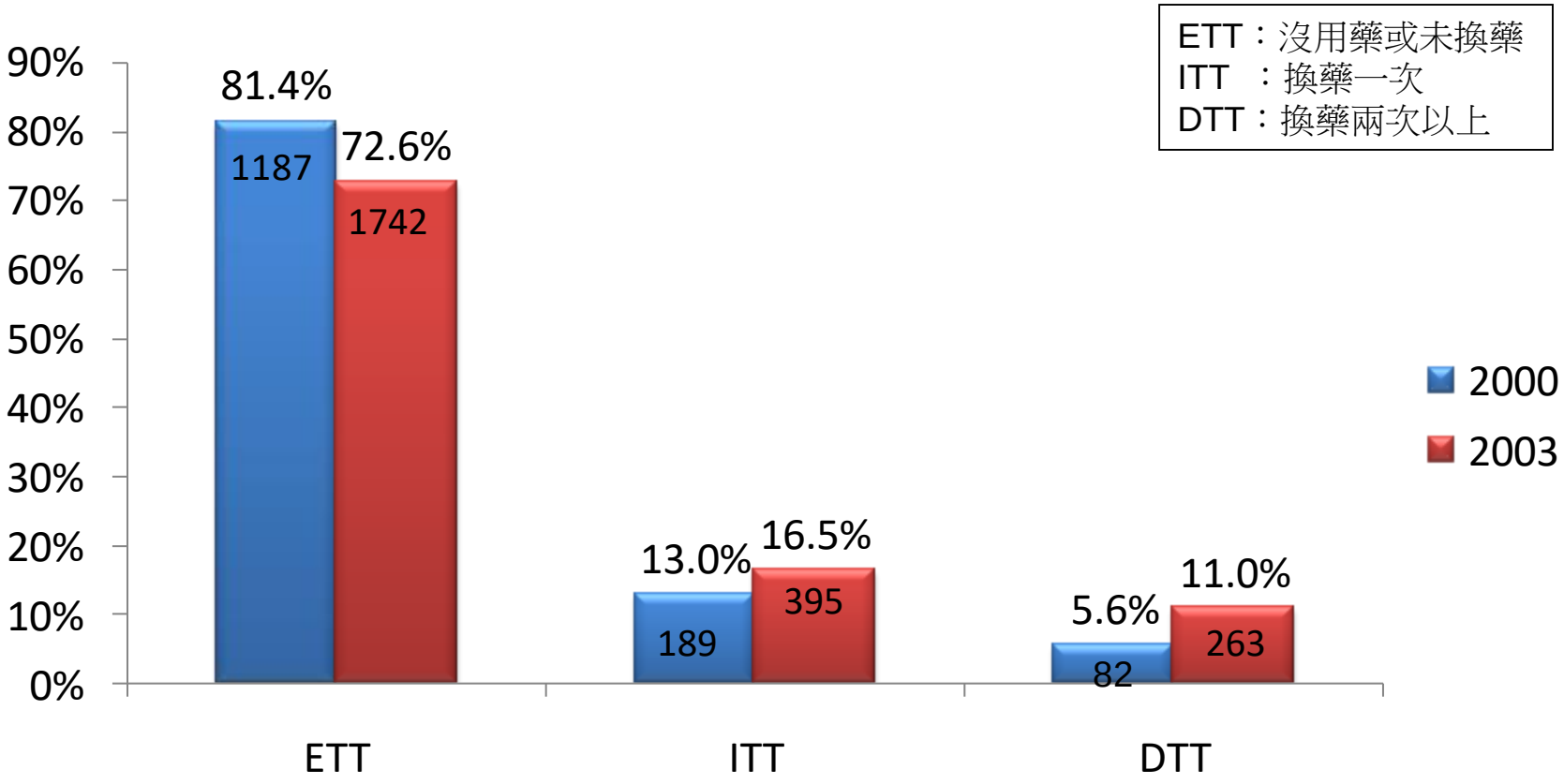
Change diagnosis

from

Depression to

Bipolar disorder

Distribution of different severity level of major depression in cohort 2000 and cohort 2003



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ITT: intermediate level of difficult to treat (change once after an adequate antidepressant trial)

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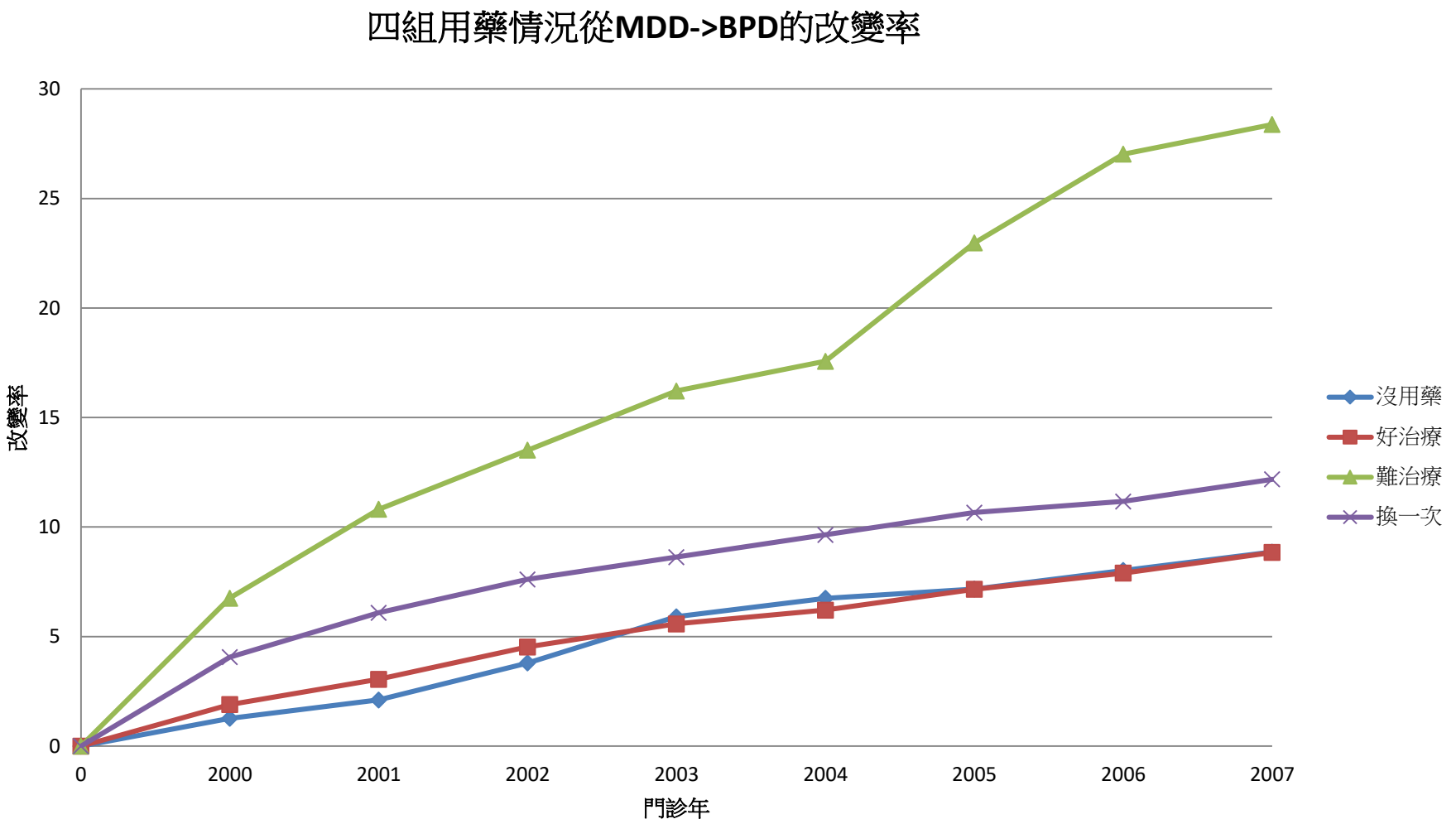
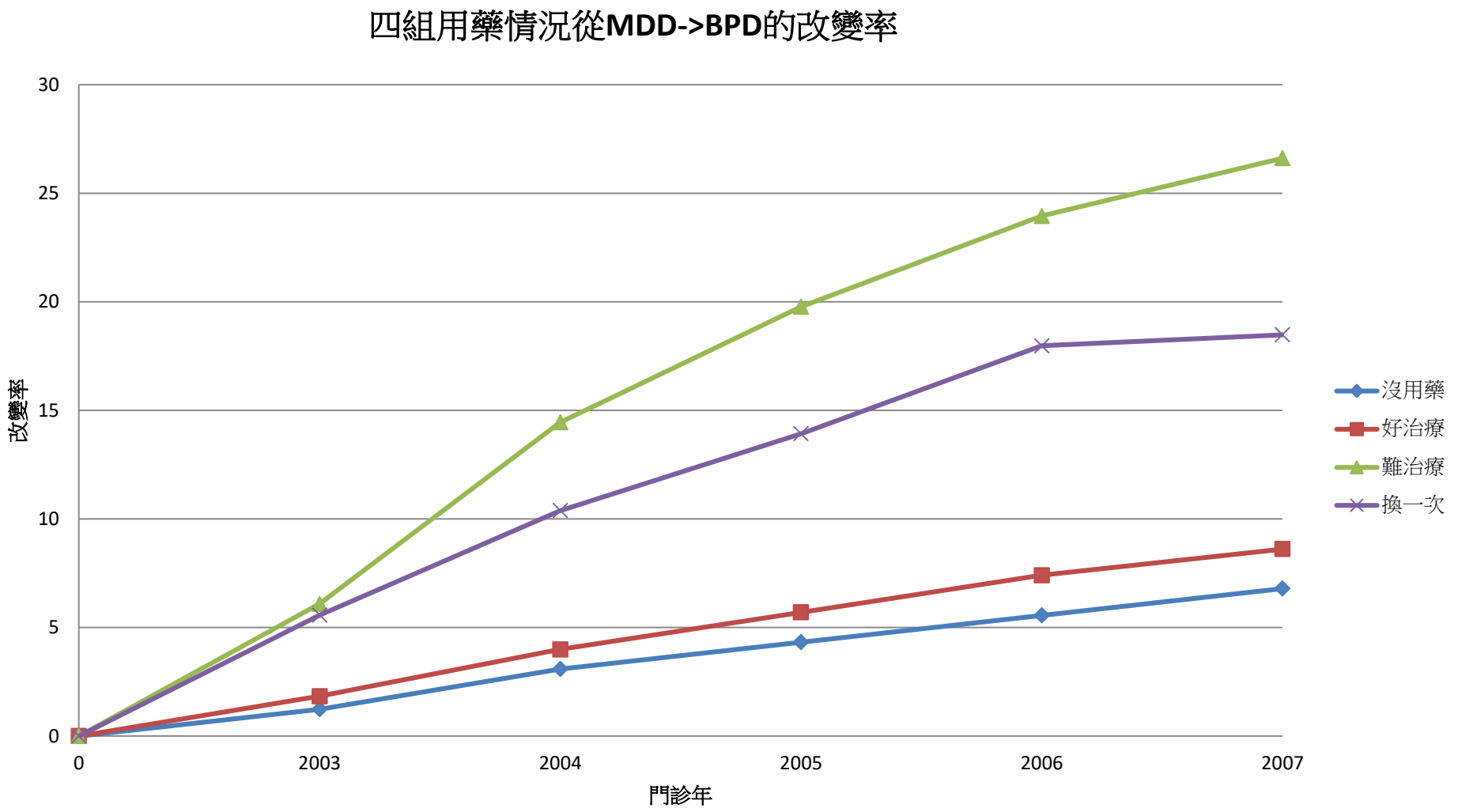
Switching rates over time (Cohort 2000)



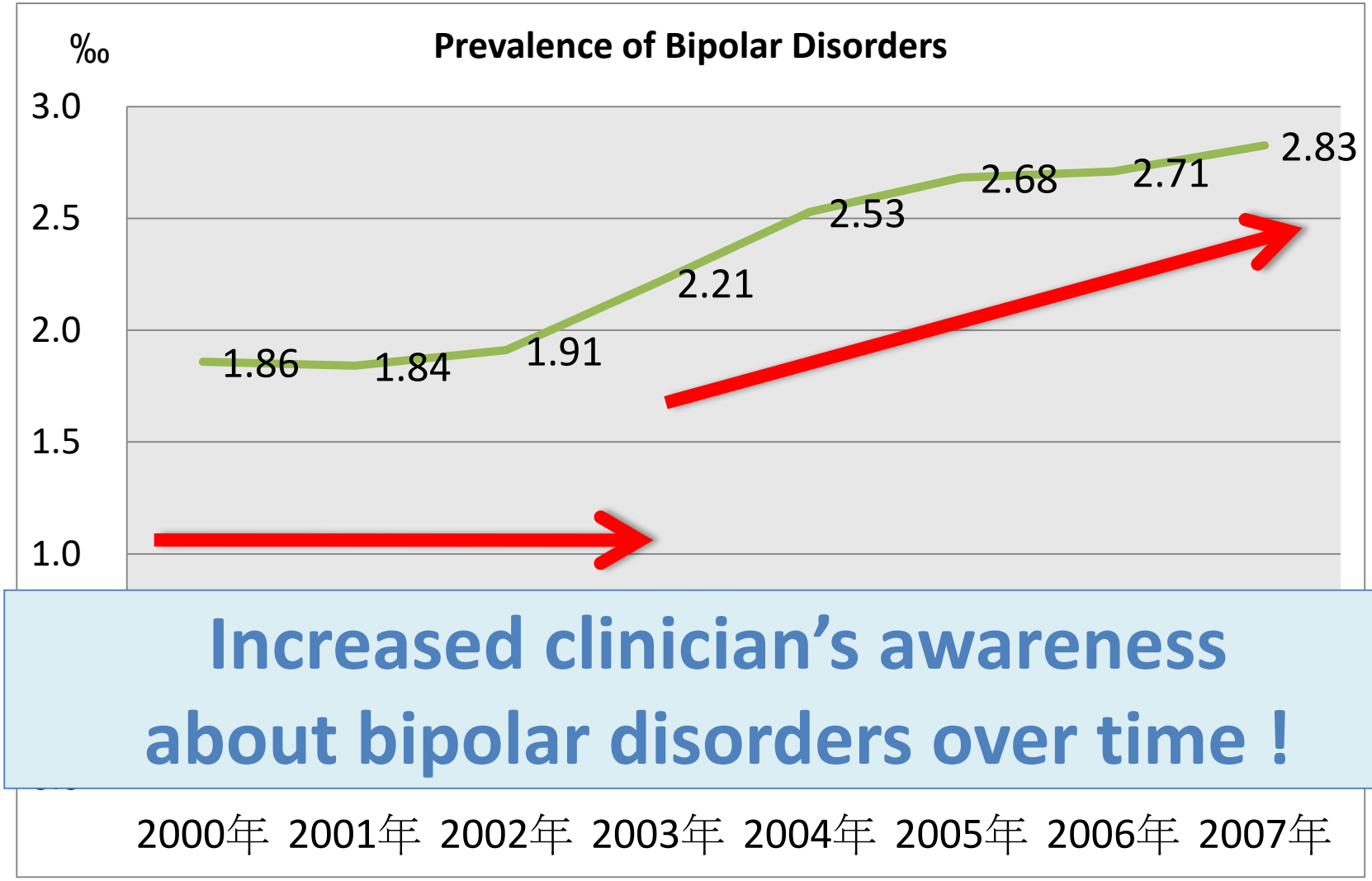
Switch to possible BPD I = 13.7% (hospitalization >= 2 times)
Switch to possible BPD II = 86.3% (hospitalization < 2 times)

Switching rates over time (Cohort 2003)



Switch to possible BPD I = 6.7% (hospitalization >= 2 times)
Switch to possible BPD II = 93.3% (hospitalization < 2 times)

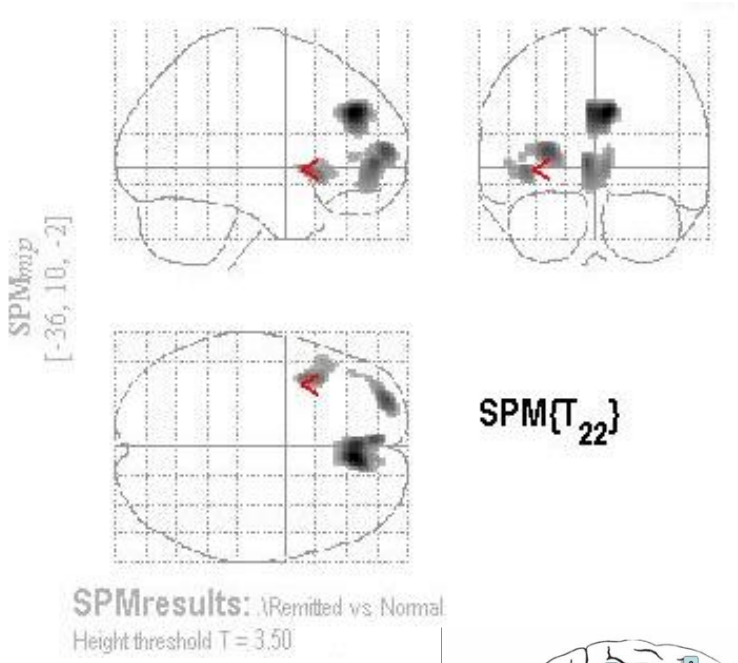
Prevalence rates of bipolar disorder

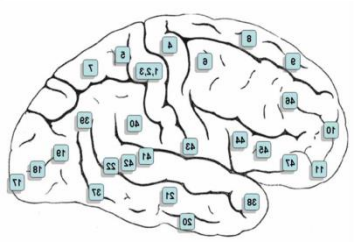


Increased clinician's awareness about bipolar disorders over time !

Remitting MDD vs. Normal_ hypometabolism

Two sample t-test :
K=200 voxels
Cluster-level, Pcorrected<0.001

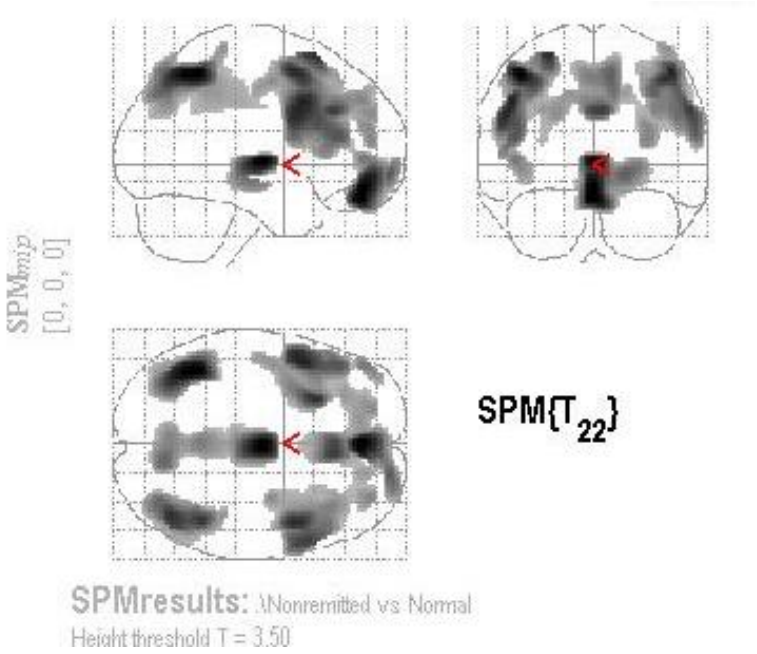




Z-score	Brain area	Coordinate Atlas
5.76	**Right** Cerebrum, **Medial Frontal Gyrus**, BA 9, Range=3	8,42,32
3.92	**Left** Cerebrum, **Middle Frontal Gyrus**, BA 9/10, Range=1	-28,58,10
3.89	**Left** Cerebrum, **Medial Frontal Gyrus**, BA 10, Range=0	-4,52,2
3.73	**Left** Cerebrum, **Sub-lobar, Insula**, BA 13, Range=0	-40,16,-2

Non-remitting MDD vs. Normal_ hypometabolism

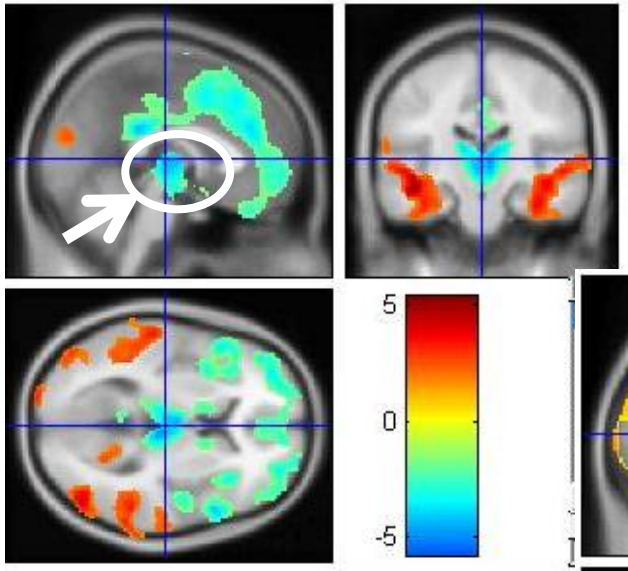
Two sample t-test :
K=200 voxels
Cluster-level, Pcorrected<0.001



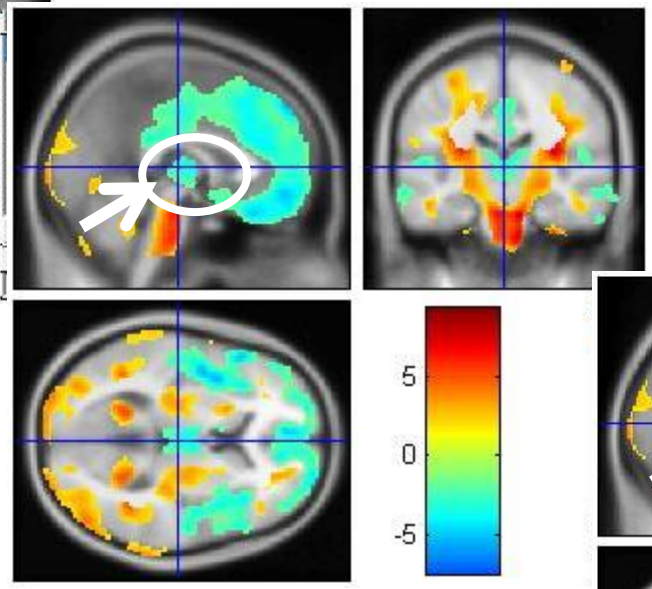
Z-score	Brain area	Coordinate Atlas
4.78	**Left** Cerebrum, **Orbital Frontal Gyrus**, BA 11, Range=2	0,44,-20
4.77	**Left** Cerebrum, **Inferior Parietal Gyrus**, BA 40, Range=0 (fusiform)	-42,-54,52
4.76	**Right** Cerebrum, **Sub-lobar thalamus,** Range=1	2,-12,2
4.48	**Left** Cerebrum, **Middle Frontal Gyrus**, BA 8, Range=2	-48,12,36
4.38	**Right** Cerebrum, **Superior parietal lobe**, BA 40, Range=0	42,-66,50
3.95	**Right** Cerebrum, **Parietal lobe**, **Precuneus**, BA 7, Range=2	10,-70,52

Remitted Medication-Resistant Depressive ~= BD

Very similar based on visual inspection !!!!!

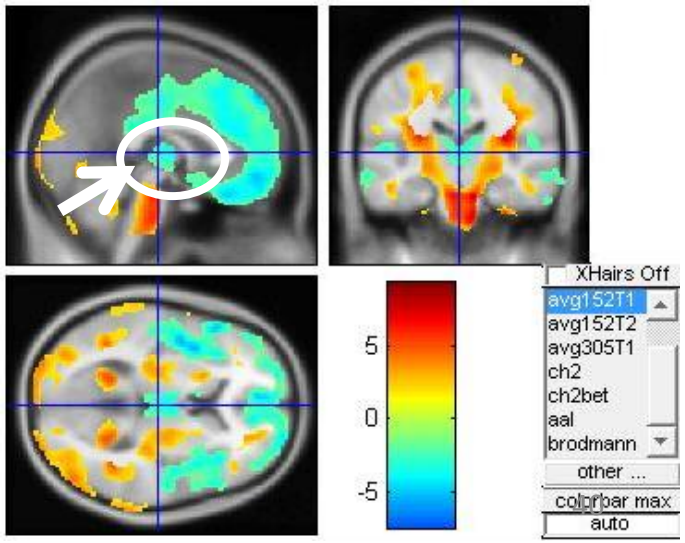


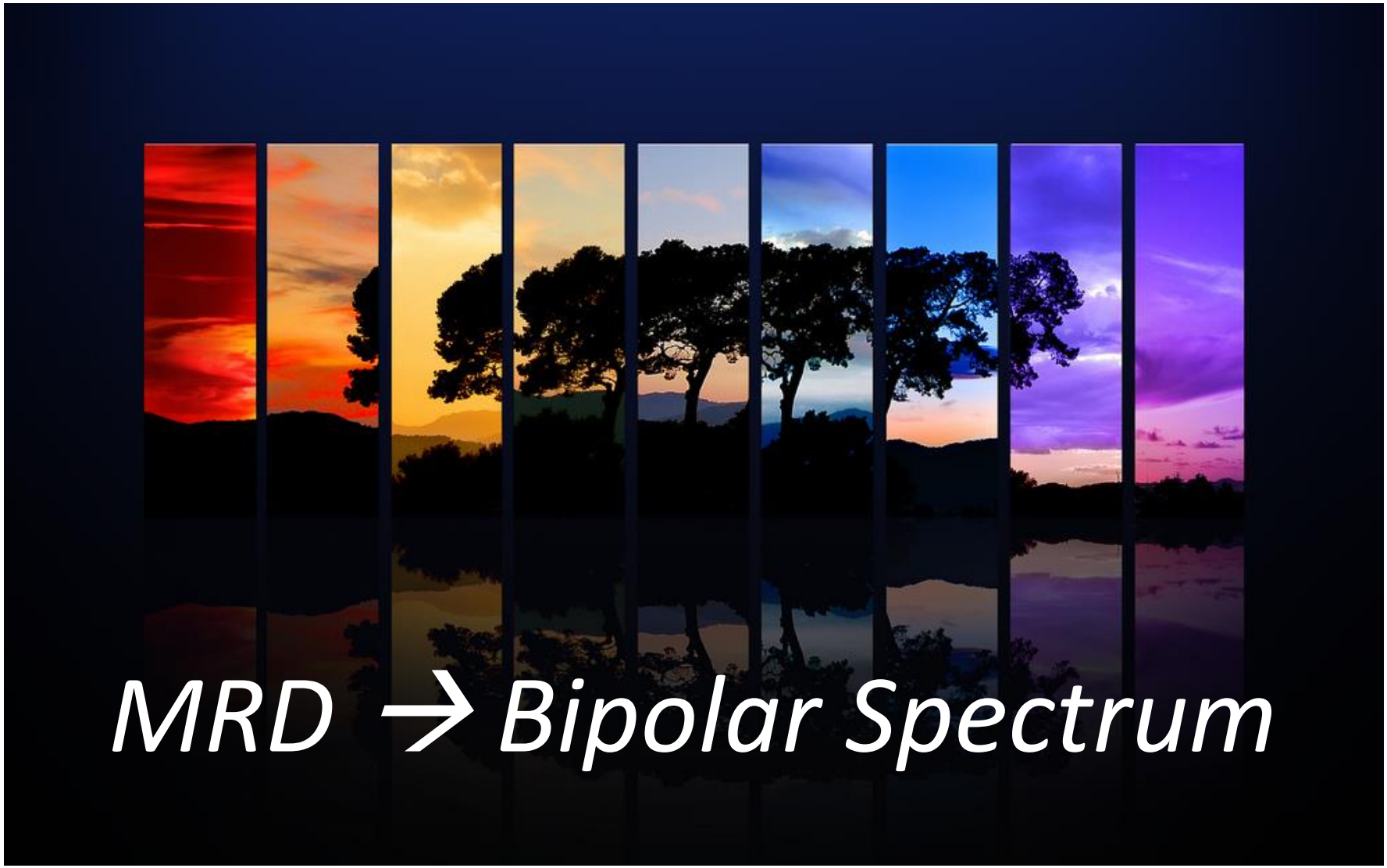
BD1$_{Remitted}$



BD2$_{Remitted}$

MRD$_{Remitted}$




MRD → Bipolar Spectrum

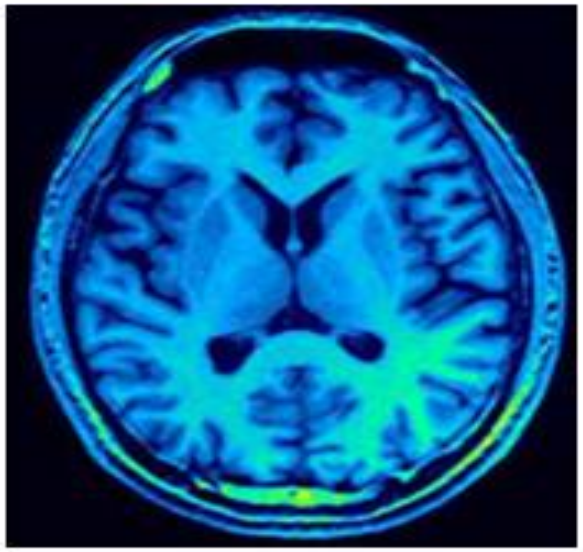
Neuromodulation

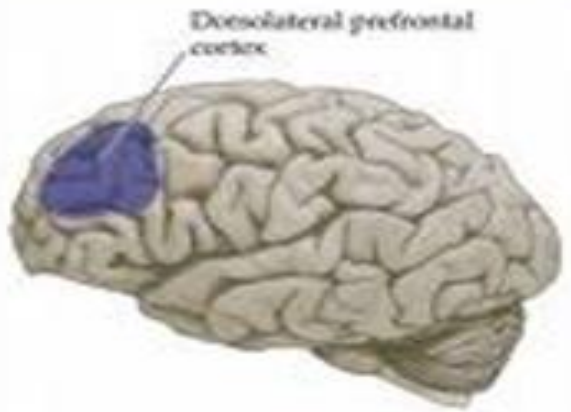
rTMS

Repetitive transcranial magnetic stimulation

DBS *in the future*

Deep brain stimulation

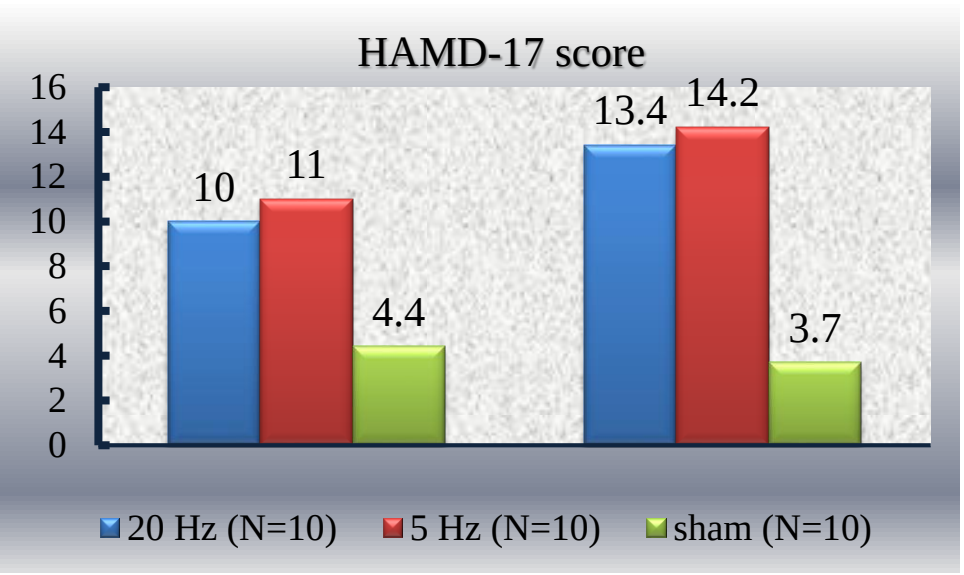




MRI-navigated to

Left Dorsolateral PFC

Improvement of HAMD-17 score & response rate with 2-week active VS. sham rTMS



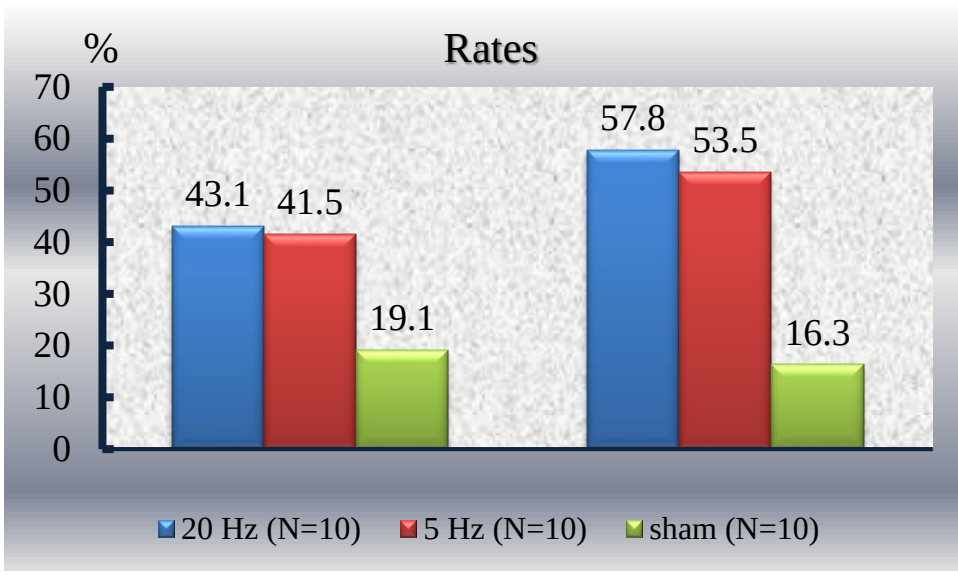


Table 2. Scores on the Clinical Rating Scales of 3 rTMS Groups Over Time[a]

	Baseline			Week 1			End of Treatment			ANOVA-R Group × Time	
	Active			Active			Active				
Rating Scale	20 Hz (N = 10)	5 Hz (N = 10)	Sham (N = 10)	20 Hz (N = 10)	5 Hz (N = 10)	Sham (N = 10)	20 Hz (N = 10)	5 Hz (N = 10)	Sham (N = 10)	F[b]	p
HAM-D	23.2 (7.5)	26.5 (5.2)	22.7 (4.7)	13.2 (5.6)	15.5 (6.4)	18.3 (6.7)	9.8 (7.1)	12.3 (7.7)	19.0 (7.7)	4.8	< .01
BDI	28.0 (9.1)	33.9 (7.6)	33.4 (9.6)	22.1 (8.7)	24.0 (10.5)	27.9 (13.7)	12.8 (6.7)	19.7 (12.3)	28.7 (15.1)	3.5	.01
CGI-S	4.5 (0.7)	4.7 (0.8)	4.7 (0.48)	3.2 (0.8)	3.5 (0.7)	4.0 (0.9)	2.8 (1.1)	2.7 (1.2)	3.6 (1.1)	1.2	NS
HAM-A	16.5 (7.1)	20.6 (3.5)	18.8 (3.9)	12.0 (5.2)	12.6 (6.3)	14.6 (5.5)	11.1 (10.8)	10.7 (7.1)	12.8 (4.6)	1.2	NS

[a]Only subjects who completed the entire study are included. Data are given as mean (SD).
[b]df = 4,54.
Abbreviations: ANOVA-R = repeated measures analysis of variance, BDI = Beck Depression Inventory, CGI-S = Clinical Global Impressions-Severity of Illness, HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression, NS = not significant, rTMS = repetitive transcranial magnetic stimulation.

(Su et al., Journal of Clinical Psychiatry, 2005)

rTMS in refractory depression

- Not every rTMS paradigm is equally effective
  - Most effective:
    - **High**-frequency (>=5 Hz)
    - Over **left** dorsolateral prefrontal cortex (**DLPFC**)

Fitzgerald, P.B., Daskalakis, Z.J., The effects of repetitive transcranial magnetic stimulation in the treatment of depression. Expert Rev Med Devices 2011: 8, 85-95.

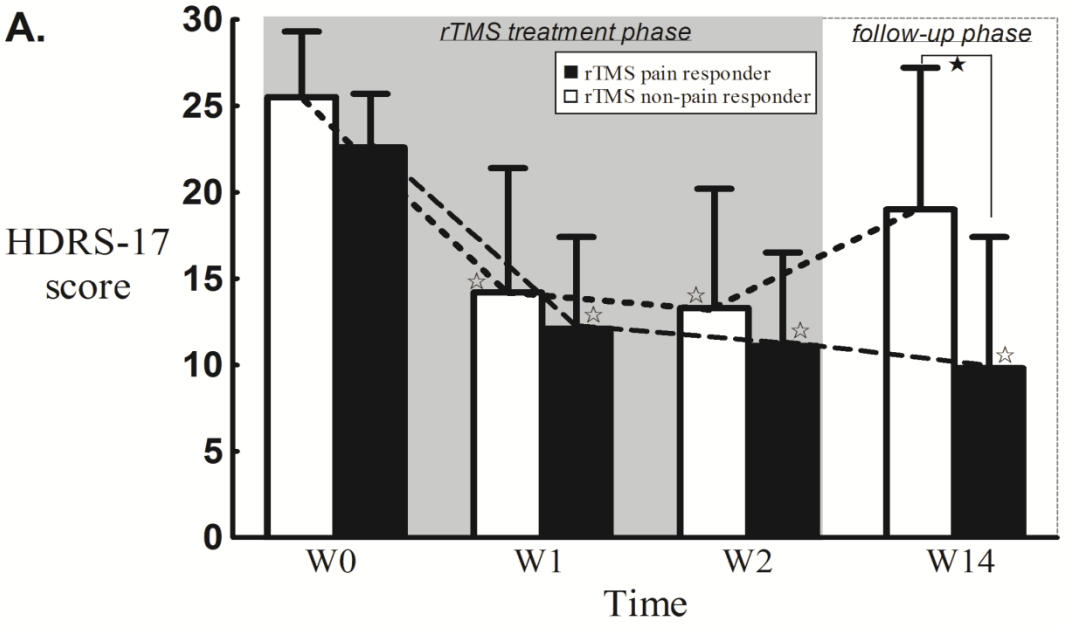
Repetitive Transcranial Magnetic Stimulation

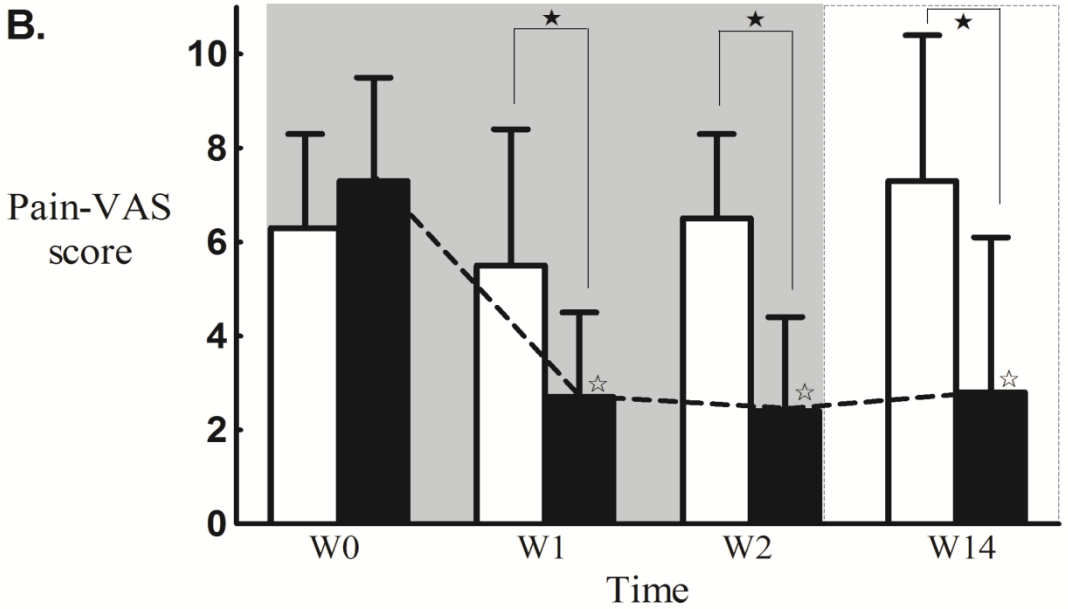
rTMS

Antidepressant effects

Left prefrontal rTMS

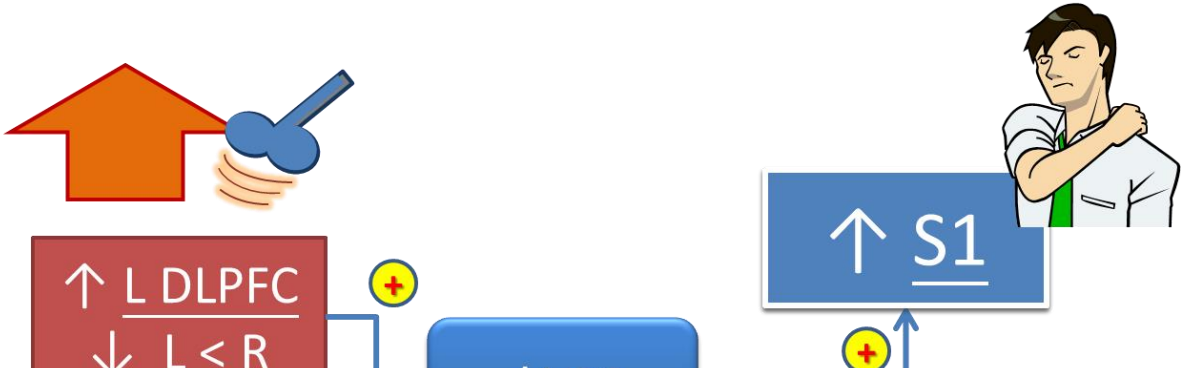
Analgesic effects





Cheng-Ta Li, Tung-Ping Su and Jen-Chuen Hsieh et al., Pain (under review)

Dissociable rTMS mechanisms on pain and depression:
a combined PET, MEG and TMS study



↑ L DLPFC
↓ L < R

dACC

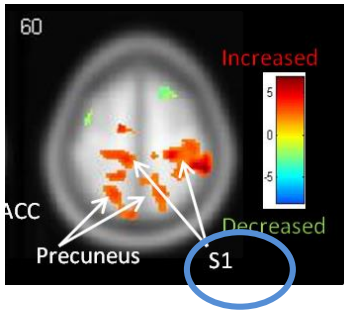
↑ S1

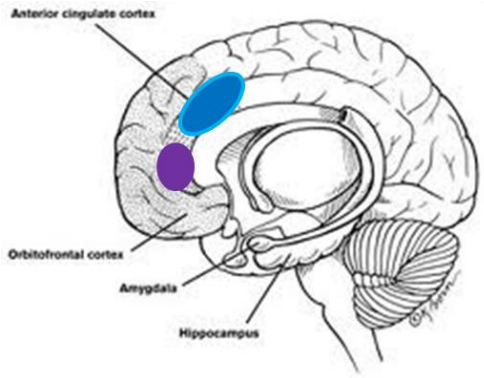
rACC

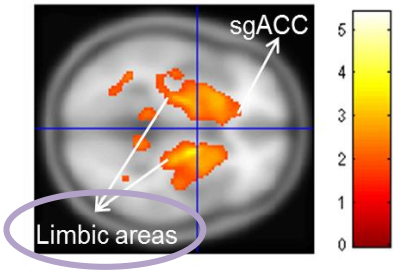
Thalamus

Midbrain

Limbic/paralimbic hyperactivity







1. CT Li and Tung-Ping Su* et al., Journal of Affective Disorders, 2010
2. Cheng-Ta Li, Tung-Ping Su*, Li-Fen Chen and Jen-Chuen Hsieh* et al., (paper in submission)

Future target

- Continued to reduce suicide rate
- Integrated research in mood disorders
  - Epidemiology, brain imaging, and molecular genetics (e.g., pharmacogenetics)
  - Biomarkers (classifer) for bipolar and unipolar depression
- Clinical trial for novel antidepressants
- Development of neuromodulation techniques
  - rTMS / tDCS (transcranil direct current stimulation)
  - DBS (deep brain stimulation)
- Education for mood disorders to reduce stigma

Thank you
for your attention