REAP What have we achieved?

Brief History of REAP Study
Past 15 years

Naotaka Shinfuku, Fukoka, Japan

Tan Chay Hoon, Singapore
Research on Asian Prescription Pattern (REAP)

- International Collaborative Research on Psychotropic Drug Prescription in Asian Countries
- The long lasting and the largest international collaboration in research in the field of psychiatry in Asia
  - Started in 2001 and still continuing
  - Supported by more than 60 psychiatric centers in 15 countries in Asia.
Six large scale multinational surveys

• 1. Six surveys on prescription pattern of psychotropic drugs in Asia.

• 2. Four surveys on the use of psychoactive drugs for schizophrenic patients in Asia.

• Two surveys on the Use of anti-depressants in Asia. In 2004 and 2013.

• Review and Analysis of over 10,000 prescriptions over 15 years.
Six REAP Surveys

- Year and the number of countries
  - First Survey: 2001, AP 1, Six countries
  - Second Survey: 2004, AP 2, Six countries
  - Third Survey: 2004, AD 1, Five countries
  - Fifth Survey: 2013, AD 2, Ten countries
  - Sixth Survey: 2016, AP 4, Fifteen countries

  China, Korea, Japan, Hong Kong, Taiwan, Singapore, India, Malaysia, Thailand, Indonesia, Sri Lanka, Vietnam, Myanmar, Bangladesh and Pakistan.
Beginning

• The collaborative research in psychiatry between Kobe University International Center for Medical Research (ICMR) and National Singapore University School of Medicine (SNU).

• First supported by Japan Society for Promotion of Science (JSPS)

• Singapore National University hosted the Seminar on Neuro-psycho-pharmacology in December 1999 at SNU.
Interesting findings

• The difference on the use of psychotropic drugs in Asian countries participated in the Congress.

• What prescription pattern do they have in neighboring Asian countries?

• Simple clinical question.
Preparation of research protocole

• Preparation of an unified research protocole and questionnaire in 2000.
• Agreement of definition of the terms and diagnostic criteria to be used among different countries.
• Agreement and fine tuning of the questionnaire to be used.
• Recruitements of researchers from East Asia.
Objectives

1. Prescribing patterns
   To study prescription habits of psychotropic drugs and their changes.

2. Drug utilization
   To analyze factors affecting prescription habits of psychiatrists.

3. Prescribing behavior
   To evaluate the impact of prescription habits in each of the participating centers & physician.

4. To suggest ways to improve prescription habits of psychotropic drugs in Asia.
First AP Survey in 2001

- Survey (1st to 31st July 2001) at 6 countries.
- Data entry (Data were sent from participating countries to Kobe coordinating center)
- 5th Investigator's meeting in Singapore in October 2001 to evaluate the data.
- Data from China, Korea, Japan, Taiwan, Hong Kong and Singapore were accepted for final computation.
China, Hong Kong, Korea, Japan, Singapore and Taiwan participated.
Presentation of the data

- 6th investigator's meeting in Kobe (February 9th 2002), ICMR Kobe University School of Medicine.
- Reports from each participating countries.
- China, Hong Kong, Indonesia, Japan, Korea, Malaysia, Singapore, Taiwan etc.
- Publication of the Proceeding of REAP
REAP 2001 Survey Summary

• Prescription pattern differs greatly country by country
• China uses clozapine as the first choice
• Japan has a tendency of poly-pharmacy and a prescription of the high dosage
• Singapore favors the use of depot
• Prescription habits might be influenced the licensing policy and cost rather than scientific data.
WPA Yokohama 2002

• In 2002, Japan Society of Psychiatry and Neurology organized the World Congress of Psychiatry in Yokohama.

• It was the first WPA Congress in Asia and attended by more than 6,000 participants from all over the world.

• REAP organized the Symposium at WPA which attracted attention of many participants and media.
12th World Congress of Psychiatry
Yokohama Japan August 2002
Publications

• More than 10 original papers in International and domestic journals based on REAP AP-1
• China undertook a nation wide prescription survey using REAP methodology and questionnaire (Si Tienmei)
Presentation at several international conferences

- 2002 August 12th WPA World Congress Yokohama
- 2004 October 18th WCSP (Social Psychiatry) Kobe
- 2005 CINP Regional Meeting in Beijing
- 2006 12th PRCP (Pacific Rim College) in Taipei
- 2006 REAP Mtg in Kaoshiung
- 2007 WPA Regional Meeting in Seoul
- 2007 WPA Regional Meeting in Shanghai
- 2008 August 11th ASEAN Conference in Bangkok
- 2008 13th PRCP Tokyo
- 2009 November, 2nd WCAP in Taipei.
WPA Regional Meeting in Shanghai, September 2007
REAP AP 2 in 2004
Follow up survey Anti-psychotic drugs

- To review the change since 2001.
- Used the same research protocol
- 25 hospitals and 203 psychiatrists participated from 6 countries and areas
- China (504 cases), Hong Kong (100), Japan (583), Korea (412), Singapore (91) and Taiwan (446).
- In total 2138 cases collected as valid entry.
Mean Doses of Antipsychotics

( in CPZ equivalent means )

$p$-value $< 0.05$
REAP AD 1  REAP on anti-depressants

Survey carried out in 2004.

- The major change from REAP AP was to use anti-depressants as inclusion criteria
  - Inclusion criteria: 56 anti-depressants listed at ATC-DDD (WHO Center Oslo)
- Five countries/regions have agreed to participate. China, Korea, Japan, Taiwan and Singapore.
Results-Overall

- Total 1,898 samples from 20 teaching hospitals and major psychiatric institutions in East Asia:
  - China: 537
  - Japan: 609
  - Korea: 293
  - Singapore: 72
  - Taiwan: 387

- Total 1,898 samples
Diagnosis by ICD-10

- F3: 1,170 (61.6%)
- non-F3: 728 (38.4%)

(N=1,898)
Japanese exception

• Japan had very limited choice.
• Fluoxetine, sertraline, citalopram, venlafaxine were not available in Japan at the time of the survey in 2004.
• This made a sharp contrast with Korea where all of the above anti-depressants were prescribed.
• Government regulation to approve new drug is strict in Japan.

• The above situation has changed recently.
Survey in 2008

• From 2004 to 2008, several new anti psychotropic drugs entered into clinical world in Asia.
• It was considered useful to undertake the third follow up survey in 2008.
• 2008 Thailand, Malaysia and India joined
• In total 9 countries and regions participated in the survey in 2008.
Research on Asian Psychotropics prescription study, REAP.
REAP AP 2008

• REAP AP 3 survey was completed in October 2008

• Overall, 2,226 outpatients were recruited from 50 psychiatric centers of 9 countries: China, Korea, Japan, Taiwan, Hong Kong, Singapore, Thailand, Malaysia, and India.

• The first report on REAP 2008 was made by Ms Yang Shu Yu at the 2nd World Congress of Asian Psychiatry (WCAP) held at Taipei in November 2009.
REAP AP in 2008-2009

- Publish in international and domestic journals.
- Propose REAP Symposium at WPA International Meeting, Beijing Sept 2010.
- REAP 2008 included data from Malaysia, Thailand and India.
- Compare with other Regions.
- Pharmaco-economical analysis.
## Study subjects and sites

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<td><strong>514</strong></td>
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<td>31</td>
<td>12</td>
<td>4</td>
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<tr>
<td>Singapore</td>
<td>300</td>
<td>91</td>
<td>100</td>
<td>4</td>
<td>10</td>
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<td>311</td>
<td>446</td>
<td>499</td>
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<td>Malaysia</td>
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<tr>
<td>Thailand</td>
<td>39</td>
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<td></td>
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<td>4</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>2399</strong></td>
<td><strong>2136</strong></td>
<td><strong>2226</strong></td>
<td><strong>144</strong></td>
<td><strong>204</strong></td>
<td><strong>180</strong></td>
<td><strong>31</strong></td>
<td><strong>25</strong></td>
<td><strong>34</strong></td>
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</table>
Comparison of Antipsychotics Used

*FGAs

*SGAs

*LONG-ACTING

*p-value < 0.05
Doses of Antipsychotics (in CPZ equivalent median*)

LAs: long-acting antipsychotics; FGAs: first-generation antipsychotics; SGAs: second-generation antipsychotics.

Mean(SD), median: 597.5 (536.4), 450.0mg
Mean Doses of Antipsychotics
（in CPZ equivalent means*）

*p-value < 0.05
Reported adverse events (focus on antipsychotics)

* indicates p value < 0.001

- Over sedation
- Cardiovascular
- Metabolic
- Endocrinological
- Autonomic
- Movement

%
Taipei with colleagues Nov 2009
Contribution by young members

- From 2011, Dr Xiang Yu Tao, Hong Kong, published more than 15 papers based on the data from REAP surveys.
  - Sex differences in the use
  - Use of anti-cholinergic drugs
  - Tardive dyskinesia
  - Clozapine use
  - ECT use
Presentation at several international conferences

• 2002 August 12th WPA World Congress Yokohama
• 2004 October 18th WCSP (Social Psychiatry) Kobe
• CINP Regional Meeting in Beijing
• 2006 12th PRCP (Pacific Rim College) in Taipei
• 2006 REAP Mtg in Kaosiung
• 2007 WPA Regional Meeting in Seoul
• 2007 WPA Regional Meeting in Shanghai
• 2008 August 11th ASEAN Conference in Bangkok
• 2008 13th PRCP Tokyo
• 2009 November, 2nd WCAP in Taipei.
• 2011 March, 12th International Congress of Psychiatric Epidemiology, Kaohsiung.
The 2nd World Congress of Asian Psychiatry

November 7 - 10, 2009 (Saturday-Tuesday)
Taipei, Taiwan
Taipei International Convention Center

Website: www.2ndwcap.org.tw
E-mail Address: 2ndwcap@mail.hato.com.tw

Hosted by:
Taiwanese Society of Psychiatry
http://www.sop.org.tw
REAP members meeting at PRCP September 2012 Seoul
4th World Congress of Asian Psychiatry, Bangkok, August 2013.
REAP Symposium
Prof Tan Chay Hoon
## Average dose of medications used

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg/day)</th>
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<tr>
<td>Escitalopram</td>
<td>11.57</td>
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<tr>
<td>Sertraline</td>
<td>80.33</td>
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<tr>
<td>Fluoxetine</td>
<td>34.23</td>
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<tr>
<td>Paroxetine</td>
<td>26.74</td>
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<tr>
<td>Imipramine</td>
<td>78.85</td>
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<tr>
<td>Amitriptyline</td>
<td>41.99</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>20.71</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>53.64</td>
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</tbody>
</table>
REAP Symposium
Dr Chee, Malaysia
3rd AsCINP, Beijing 2013 Sept
3rd AsCINP, Beijing 2013 Sept
REAP members with Prof Sartorius
The 3rd AsCINP, Beijing 2013 Sept REAP Symposium
REAP-AD 2013

• Cross-sectional, Drug-centered survey

• Date of the survey: the first March 2013

• Participating countries and area: 10 countries China, Hong Kong, Korea, Japan, Taiwan, Singapore, Malaysia, Thailand, India, Indonesia
Methods

• Inclusion criteria

Patients who are receiving antidepressant medications (62 agents classified as antidepressants in ATC-DDDs) on the day of survey.

not limited to the diagnosis of ‘depression’
REAP AD-2

• Data collected, March to May 2013.
• Analysis completed, July 2013
• In total, 2,320 cases from 10 countries
• 40 centers
• 215 psychiatrists
• China (350), Indonesia (269), Hong Kong (81), Japan (246), Korea (259), Singapore (135), Taiwan (199), India (309), Malaysia (161) and Thailand (311).
Young member from Korea

- Adjunctive Antipsychotic Prescriptions for Outpatients with Depressive Disorders in Asia: The Research on Asian Psychotropic Prescription Patterns for Antidepressants (REAP-AD) Study.

- Park SC, Shinfuku N, Maramis MM, Lee MS, Park YC.

Young psychiatrist from Singapore NIMH

- Factors Associated With Antidepressant Dosing in Asia: Findings From the Research on Asian Psychotropic Prescription Study.
Young member from India

- Prescription pattern of antidepressants in five tertiary care psychiatric centres of India.
5th World Congress of Asian Psychiatry

- From 3 to 6th March 2015
- Fukuoka Kyusyu University
- AFPA President: Prof Pichet Thailand
- Congress President: Shigenobu Kanba
- Chairman: Scientific Program Committee
  Prof N Sartorius (Geneva)

- http://afpa.asia/
5th World Congress of Asian Psychiatry
3-6 March 2015, Fukuoka Japan
REAP group 5WCAP Fukuoka
REAP Dinner, November 2015
Taipei
REAP AP 4 Survey in 2016

- Protocol and questionnaire were prepared to undertake the follow up survey of previous surveys of REAP.
- The duration was from March to June 2016.
- Many centers experienced the hardships to get the approval from the Internal Review Board (IRB).
- Members were asked to get the informed consent from the participating patients.
15 countries and areas joined
Including 5 new countries

• 15 countries participated
• East Asia (5) . China, Korea, Japan, Hong Kong, Taiwan
• South East Asia (6) Singapore, Malaysia, Thailand, Indonesia, Vietnam, Myanmar.
• South Asia (3) Bangladesh, India, Sri Lanka
• West Asia (1) Pakistan.
• They were asked to complete the questionnaire
REAP AP 4 Results

• 3,742 cases were collected from 61 leading psychiatric centers of 15 countries in Asia.
• East Asia : China (160), Korea( 131), Japan( 229), Hong Kong (31), Taiwan( 404)
• South East Asia : Singapore (171), Thailand (322), Malaysia( 305), Indonesia ( 561), Vietnam(274), Myanmar (164)
• South Asia : India ( 479), Bangladesh (99), Sri Lanka (97), Pakistan (299)
REAP Data Review Meeting
September 2016, Taipei
40th Anniversary of Chang Gung Memorial Hospital International Symposium on Psychiatry Nov.2.2016.Kaohsiung Taiwan
17th Pacific Rim College of Psychiatrists Scientific Meeting (PRCP) Nov.3-5, 2016, Kaohsiung Taiwan

Opening Ceremony

Welcome from the Congress Host
Professor Mian-Yoon Chong
Dr. Shi-Ku Lin, Taipei on Antipsychotic polypharmacy: good or bad?
REAP Symposium speakers and chairpersons at PRCP
Important lessons we have learned

• It is possible to organize a large scale international collaborative research without a big research fund.

• For the management, it is important to encourage and help young members to present at international congress and to write papers.

• Senior members should give constructive advises and encouragements to young members when necessary.
Key elements to continue REAP

- Both senior and junior psychiatrists in Asia find it fruitful and enjoyable to join REAP.
- It is nice to meet friends coming from different countries.
- It is much more enjoyable to meet and dine together with friends.
Technical aspects

• Very simple research protocol.
• Well structured questionnaire.
• Use of internet for communication.
• Friendship formed through collaboration for long years.
• Wise advice by senior members.
• Fortunate to have many talented young psychiatrists as members.
What we have achieved.

- More than 60 papers accepted by reputed international journals.
- REAP organized more than 30 symposium at major International congress.
- Formed the research networks among Asian psychiatrists.
What we might have possibly achieved.

- Promotion of research minds among young Asian psychiatrists.
- Data from REAP might have contributed to improve the prescription behaviors of psychiatrists in Asia.
- Building up friendship and trust beyond national borders.
Our hope

• We are proud that we have formed a good research network among Asian psychiatrists.
• We hope this network will continue.
• There are so many areas in Asian psychiatry to be researched by Asian psychiatrists together.
• Young members may wish to identify areas for mutual interest and organize international collaborative studies.
Sphinx - Research Questions
Thanks

We extend our thanks to all Asian colleagues and advisers who have supported REAP surveys over the past 15 years.

The presentation was made at the 17th Scientific Meeting of Pacific Rim College of Psychiatrists
3-5 November 2016, Kaohsiung Taiwan