Why Japanese psychiatrists are prescribing polypharmacy and high dose psychotropic drugs?
Review of REAP - reasons and trends

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Greeting from Japan
Asia Map

**Geography**
- East Asia
- ASEAN
- South Asia
- Central Asia
- West Asia
REAP

- Research on Asian Psychotropic Prescription pattern (REAP).
- Started in 1999 and continued for 20 years.
- More than 10,000 prescriptions of patients with mental illness in Asia were reviewed.
- More than 400 psychiatrists, 71 leading psychiatric centers from 15 countries in Asia participated.
- Results published by more than 70 peer reviewed journals.
15 countries/areas in Asia
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

- 3,744 cases were collected from 71 leading psychiatric centers of 15 countries in Asia.
- East Asia : China (160), Korea (131), Japan (229), Hong Kong (31), Taiwan (403)
- South East Asia : Singapore (171), Thailand (322), Malaysia (306), Indonesia (581), Vietnam (274), Myanmar (164)
- South Asia : India (479), Bangladesh (99), Sri Lanka (97), Pakistan (298)
REAP-AP4

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Long-Form: BPRS, DIEPSS, Comorbidity, Laboratory
Overviews on the Results from the REAP-AP4 in 2016 and Planning for REAP-BD and REAP-MS 2018

Shih-Ku Lin, Shu-Yu Yang
and Naotaka Shinfuku
17th PRCP Nov 3-5.2016, Kaohsiung Taiwan
Dr Shi-Ku Lin report on the results of REAP AP -4 PDD/DDD and PDL
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## REAP-AP1234

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Polypharmacy and combined medications

- **Polypharmacy**
  - In psychiatry: use of two or more antipsychotic medications

- **Combined therapy**
  - Multiple therapies to treat a single disease

- **Combined medications**
  - In the treatment of schizophrenia: additional use of mood stabilizer, antidepressants, anxiolytics and hypnotics besides antipsychotics

- **Psychotropic drug loading**
  - Sum of each psychotropic drug prescribed daily dose divided by its defined daily dose (DDD)
  - In the five categories of antipsychotics, mood stabilizers, antidepressants, anxiolytics and hypnotics
Figure 1. Comparison of psychotropic drug loading between countries.
REAP 2016 summary

• Comparison of psychotropic drug loading between 15 countries.
• Japan is still the highest for both psychotropic drug loading and anti-psychotic drug loading.
• Comparison of polypharmacy rates from the REAP-AP1 to REAP-AP4
• Japan showed the gradual decreasing trend of polypharmacy from 2001, 2004, 2008 and 2016
• However, the rate of polypharmacy was the highest in Japan in 2016.
Queries by Dr. Sim Kang

• We are looking at some analyses in 2016 AP data.

• In Japan, the doses of aripiprazole can be given up to 48 mg, and risperidone up to 27 mg, quetiapine up to 2100 mg in exceptional cases as we see this in the 2016 REAP data.

• Is this your impression as well?
My reply: Reality and guideline in Japan

- As you note, these doses can be possible in Japan.
- However, according to the guideline, the maximum doses are set as:
  - 1. aripiprazole up to 30 mg. (48 mg)
  - 2. risperidone up to 12mg (27mg)
  - 3. quetiapine up to 750mg (2100 mg)
Why high dose in Japan?

The reason is not simple.

• A number of socio-economical-cultural factors

- It was almost the first time for Japanese psychiatrists to get to know the extremely high dose prescription of antipsychotics and psychotropic drugs in Japan comparing to those in other Asian countries.
- Also, it was the first time to know the high rate of polypharmacy in Japan.
Mean Doses of Antipsychotics

(in CPZ equivalent means)

\[ p\text{-value} < 0.05 \]
6 REAP Surveys

- From 2001 to 2016, REAP carried out six international collaborative surveys.
- First Survey: 2001, AP 1 (6 countries)
- Second Survey: 2004, AP 2 (6 countries)
- Third Survey: 2004, AD 1 (5 countries)
- Fourth Survey: 2008, AP 3 (9 countries)
- Fifth Survey: 2013, AD 2 (10 countries)
- Sixth Survey: 2016, AP 4 (15 countries)
Impacts of REAP

- To see outside world is the best education.
- REAP has showed to Japanese psychiatrists over 20 years
  - Extreme polypharmacy in Japan.
  - Extreme high dose prescription.
- Compare to other Asian countries
- Based on the data using the same research protocol. No excuse.
Polypharmacy in Japan

- Japan is still the highest for both psychotropic drug loading and anti-psychotic drug loading in 2016.
- Comparison of polypharmacy rates from the REAP-AP1 to REAP-AP4
- Japan showed the gradual decreasing trend of polypharmacy from 2001, 2004, 2008 and 2016
REAP any impacts in Japan?

- Do findings of research influence practices?
- Polypharmacy and prescribing high dose of psychotropic drugs are on decline in Japan.
- Continuous decrease of the mean dose of prescribed psychotropic drugs and antipsychotics in Japan from 2001 to 2016.
Comparison of polypharmacy rates from the REAP-AP1 to REAP-AP4.
Polypharmacy is world wide

- Schizophrenia Research 2012
- Gallego et al
- 147 research papers published from 1970 to 2009.
- Polypharmacy rate of each region was 15% in North America, 32% in Asia, 23% in Europe and 16% in Oceania. In the past 20 years, the polypharmacy decreased in Asia.
Polypharmacy: International Comparison

(Gallego JA et al. 2012 Schizophrenia Res.)
Discussion

• Why polypharmacy and high dose prescription in Japan?
• Recent regulation to frame the polypharmacy and high dose prescription in Japan?
• Has REAP influenced?
Reasons for high dose prescription and polypharmacy in Japan.

• 1. Mental health service system
• 2. Objective of prescription.
• 3. National insurance system
• 4. Doctor’s right to prescribe
• 5. Multiple doctors for a patient
• 6. Doctor’s culture
• 7. Patient’s culture
• 8. Lack of training for pharmacotherapy
1) Mental Health service system

- Unique mental health service system
- Hospital centered psychiatric services
- More than 1,600 psychiatric hospitals and more than 300,000 psychiatric beds.
- Many patients stay for far long period.
- Around 100,000 patients stay more than 10 years.
- Long stay patients tend to receive high dose.
2) Objectives for prescription

- Long stay patients
- Poor incentive for rehabilitation by families and hospitals.
- Sedation becomes the priority.
- Each time a patient demonstrates psychotic symptom, the dose of drugs is added.
- In the long run, a patient receives high dose.
3) National insurance system

- In 1961, National Medical Insurance system started covering/subsidying all medical cost.
- All kinds of medical activities including cost of prescription drugs are covered.
- System basically pays for each prescribed drug to hospital/clinic.
- This system encourages financially the high dose prescription and polypharmacy.
- If a doctor prescribes heavier dose and many drugs, he may get bigger reimbursement.
4). Doctor’s right to prescribe

- The right of medical doctor to prescribe drugs to patient is protected by law.
- It was only a recent development that pharmacy and hospital/clinic have been separated.
- For the whole system, there exist very weak checking system to prevent high dose prescription and poly-pharmacy.
5) Multiple doctors for a patient

- Most of long stay patients have received may drugs for different complains from different doctors, such as psychotic symptoms, depressive mood, insomnia, irritability etc.
- Long stay patients tend to receive high dose prescription and poly pharmacy.
- It is easy to increase the drug but hard to decrease drug.
6) Doctor’s culture

- For a young doctor, it is not polite to delete the prescribed drug by his senior doctor.
- When young doctor wants to change the prescription, only way was to add new drug.
- This Japanese culture of respect for seniority may result in the high dose prescription and polypharmacy in the long run.
7) Patients culture

• Japanese patients like to receive many drugs.
• In traditional herbal medicine, multiple drugs increase the potency and efficacy.
• Many Japanese people believe drugs are good and many drugs are better.
• This tradition allows physicians to prescribe high dose and polypharmacy.
8) Lack of training for pharmacotherapy

- REAP surveys showed the poor recognition of side effects by Asian psychiatrists.
- Japan was not the exception for poor recognition of side effect of high dose prescription and polypharmacy.
- The dangers of high dose prescription and polypharmacy have not been sufficiently trained among Japanese psychiatrists.
Recent Changes

• There are so many factors which decide the prescription habits of clinicians.
• Recently, Ministry of Health (MOHL) has introduced several financial measure to prevent polypharmacy in psychiatry.
• 2010 Team established to reduce polypharmacy
• 2012, 2014, 2016 Limitation on the number of psychototropic drugs
• 2015 Separation of medical and dispensary services
No more words but money talks.

- Guidelines were not effective.
- Training of doctors were not effective.
- Only money will be effective.
- Ministry of Health and Welfare have introduced a few changes in payment system to frame the polypharmacy.
- But not for the high dose prescription.
MOHWL issued the regulation to limit the polypharmacy in 2010

- The regulation to reduce polypharmacy came in the context of suicide prevention.
- Ministry of Health, Welfare and Labor (MOHWL) established the team to prevent suicide and depression in 2010.
- They found 60% of persons under psychiatric treatment who completed suicide used the high dose psychototropic drugs before the acts.
Regulation in 2012

• Survey by MOHWL in 2010
• 19.8% of patients consulted at psychiatric clinics and hospitals receive more than 3 kinds of anxiolytics and hypnotics.
• Combined use of 3 anxiolytics and hypnotics reaches 25.8mg Eq-diazepam.
• Reduction of payments to the prescription of more than 3 anxiolytics and hypnotics
Regulation to limit the overuse of anxiolytics and hypnotics

- This guidelines in 2012 specifically limited the number of anxiolytics and hypnotics.
- In 2014, the target was enlarged to cover anti-psychotics and depressant prescribed to a patient.
- The guideline used the national health insurance system to discourage the polypharmacy.
Separation of medical and dispensary practice

• Another measure was a separation of medical and dispensary practice in 2015. Before, hospitals and clinics dispenses medicine for treating patients.

• Dispensary belonged to hospital and clinic. System guaranteed to pay more to a doctor who prescribe more drugs.
Revised regulation in 2014

- Enlargement of the control
- Reduction of reimbursement for a prescription of
  - More than 3 anxiolytics
  - More than 3 Hypnotics
  - More than 4 Antidepressants
  - More than 4 Antipsychotics
- Objection by JSNP and some exceptions were agreed
Pharmacists as gate keeper

- MOHWL separated medical practice and drug dispensation to prohibit such abuse of national insurance scheme.
- MOHWEL issued the guideline to utilize pharmacists as gate keeper against polypharmacy
- September 2016, Japan Society of Psychopharmacology was established.
Re-revised regulation in 2016

• In 2016, the regulation was strengthened to limit the use of anti-psychotics and antidepressants to two.

• Reduced reimbursement for
  More than 3 Antidepressants
  More than 3 Antipsychotics

Psychiatric institutions have to report the cases of polypharmacy to MOHWEL every three months.
Concerted measures for the reduction of polypharmacy

• Training of psychiatrists
• Strengthen the role of pharmacists as gatekeeper
• The guideline used the national health insurance system to penalize the polypharmacy.
• No reimbursement will be made for the drug prescribed over the fixed number.
Conclusion 1

• Wide range strategies are needed to improve prescription in Japan.
• REAP surveys taught us science played a limited role in the real decision process of psychotropic prescription.
  - National mental health policy
  - Financing system for drug prescription
  - Low recognition of side effects, etc
Conclusion 2

- Hospital based national mental health policy and mental health financing systems have been the biggest obstacles to reduce polypharmacy in Japan.
- The development of mental health services in communities away from hospital will be the prerequisite.
- Training and education of psychiatrists are needed to the reduction of polypharmacy.
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, especially in Japan.
• Building up friendship and trust beyond national borders.
Thanks for your kind attention