




8. Orsolini L, Tomasetti C, Valchera A *et al.* An update of safety of clinically used atypical antipsychotics. *Expert Opin. Drug Saf.* 2016; **15**: 1329–1347.

Hiroyuki Fujiyama, MD Hiroko Sugawara, MD, PhD  Teppei Kanno, MD Kazuhiro Kawahara, MD  Hibiki Tanaka, MD, PhD Ryuji Fukuhara, MD, PhD Shuken Boku, MD, PhD and Minoru Takebayashi, MD, PhD 
 Department of Neuropsychiatry, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan
 Email: mtakebayashi@kumamoto-u.ac.jp

Received 23 May 2020; revised 17 August 2020; accepted 29 August 2020.

public hospitals, and 25 private hospitals). According to the recommendations of the GL, a total of eight QI (Table S1) were evaluated based on the survey of the treatments and prescriptions at discharge for patients with MDD during the first year (2016–2018) in the participating hospitals. The data were collected by the EGUIDE project members. In this survey, we recorded all types and dosages of psychotropic drugs, including antidepressants, antipsychotics, mood stabilizers, and benzodiazepines. The use of modified electroconvulsive therapy (mECT) and cognitive behavioral therapy were also recorded. The ethics committees of the National Center of Neurology and Psychiatry and each participating university/hospital/clinic approved the entire study protocol. Written informed consent was obtained from all participants (psychiatrists who treated the inpatients). The treated inpatients could see the purpose and procedures of the study on websites and could refuse to participate freely (opt-out).

This survey involved a sample of 1283 patients who had been diagnosed with MDD at discharge (Table S2). Values of each QI in all subjects and in each hospital are presented in Table S3. In this study, only 60.2% of patients received antidepressant monotherapy, with a large institutional difference from less than 20% to 100% (Fig. 1). A previous report already confirmed that antidepressant polypharmacy prevailed in Japan,¹ while this is the first report showing a large institutional difference. The proportion of patients who received no prescription of anxiolytics or hypnotics was only 25.1%, which is consistent with the study showing long-term benzodiazepine use despite the recent clinical guidelines in Japan.⁴ Although combination therapy with antidepressants and benzodiazepines may be more effective than therapy with antidepressants alone in the early phase, these effects may not be maintained in the acute or continuous phase.⁵ Thus, long-term benzodiazepine use is not recommended in the GL due to the potential side-effects. The QI values for each hospital type are presented in Table S4. QI-1 was significantly higher in university hospitals than in national/public hospitals, while QI-3, QI-4, QI-5, and QI-6 were significantly higher in university hospitals than in private hospitals. Possible explanations for institutional differences include different instructions from senior psychiatrists regarding prescribing and treatment. Many psychiatry residents included in this study were affiliated with university hospitals and they generally follow the GL rather than prescribing traditions introduced by senior psychiatrists. As regional differences in treatment patterns have been previously reported,^{6, 7} comparisons of QI values between eastern and western Japan are shown in Table S5. There was a significantly higher proportion of patients receiving mECT in eastern Japan (17.6%) compared to that in western Japan (8.4%). Although a compositional difference in hospital type between eastern and western Japan (university: 46.9% vs 37.1%; national/public: 34.7% vs 17.1%; private 18.4% vs 45.7%; χ^2 -test $P = 0.019$) may affect the difference, the difference in the proportion of patients undergoing mECT may stem from different attitudes towards mECT in these regions. The low proportion of patients undergoing mECT treatment in private hospitals (3%) may be because most private hospitals

Unmet needs of patients with major depressive disorder – Findings from the ‘Effectiveness of Guidelines for Dissemination and Education in Psychiatric Treatment (EGUIDE)’ project: A nationwide dissemination, education, and evaluation study

doi:10.1111/pcn.13143

According to past analyses of prescription and treatment patterns for major depressive disorder (MDD), the majority of MDD patients in Japan have not been treated according to the recommended guidelines.¹ In this context, the Japanese Society of Mood Disorders published the ‘Treatment Guidelines for Major Depressive Disorders’ (GL) in 2012, and the ‘Effectiveness of Guidelines for Dissemination and Education in Psychiatric Treatment (EGUIDE)’ project was launched in 2016, which aimed to standardize medical practice using quality indicators (QI) as indices for the quality of medical practice.^{2, 3}

The present study was a cross-sectional, retrospective study conducted in a total of 84 institutions (36 university hospitals, 23 national/

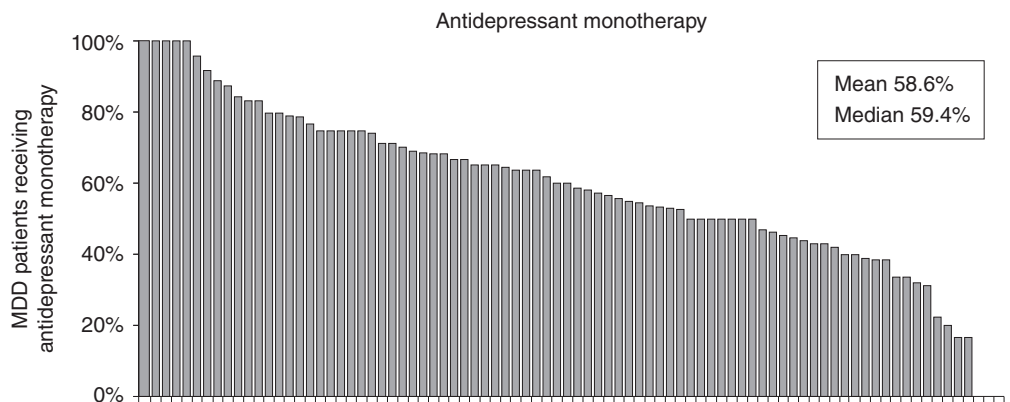


Fig. 1 Proportion of patients with major depressive disorder (MDD) receiving antidepressant monotherapy (quality indicator-1) in 84 hospitals. There is a large difference in the proportion of patients receiving antidepressant monotherapy among the hospitals, ranging from less than 20% to 100%.

do not have the facilities for mECT. The low proportion of patients undergoing cognitive behavioral therapy in all hospitals (1%) may reflect the low level of provision of cognitive behavioral therapy despite its coverage by Japanese health insurance.⁷

This study has several limitations. First, we did not assess depressive symptoms using rating scales. Second, this study may have a selection bias because these 84 hospitals may not reflect the treatment and prescription patterns of all hospitals in Japan. The ratio of antidepressant monotherapy may be affected by not only hospital type but also the patient's background, such as refractory episodes, and the difference in positioning and role of the hospital in the community.

In accordance with the GL, we should strive to reduce antidepressant polypharmacy and long-term use of benzodiazepines in the treatment of MDD in Japan. Based on this baseline survey, we plan to report changes brought by the GL education program. In the future, proper diagnosis and treatment following dissemination of and adherence to the GL will provide suitable circumstances for high-quality research of MDD.^{8–10}

Disclosure statement

The authors declare that they have no conflicts of interest related to this article.

References

- Onishi Y, Hinotsu S, Furukawa TA, Kawakami K. Psychotropic prescription patterns among patients diagnosed with depressive disorder based on claims database in Japan. *Clin. Drug Investig.* 2013; **33**: 597–605.
- Ichihashi K, Hori H, Hasegawa N *et al.* Prescription patterns in patients with schizophrenia in Japan: First-quality indicator data from the survey of “Effectiveness of Guidelines for Dissemination and Education in Psychiatric Treatment (EGUIDE)” project. *Neuropsychopharmacol. Rep.* 2020; **40**: 281–286.
- Takaesu Y, Watanabe K, Numata S *et al.* Improvement of psychiatrists' clinical knowledge of the treatment guidelines for schizophrenia and major depressive disorders using the ‘Effectiveness of Guidelines for Dissemination and Education in Psychiatric Treatment (EGUIDE)’ project: A nationwide dissemination, education, and evaluation study. *Psychiatry Clin. Neurosci.* 2019; **73**: 642–648.
- Takano A, Ono S, Yamana H *et al.* Factors associated with long-term prescription of benzodiazepine: A retrospective cohort study using a health insurance database in Japan. *BMJ Open* 2019; **9**: e029641.
- Ogawa Y, Takeshima N, Hayasaka Y *et al.* Antidepressants plus benzodiazepines for adults with major depression. *Cochrane Database Syst. Rev.* 2019; **6**: CD001026.
- Okumura M, Sameshima T, Awata S *et al.* The present state of electroconvulsive therapy in Japan. *Jpn. J. Gen. Hosp. Psychiatry* 2010; **22**: 105–118.
- Hayashi Y, Yoshinaga N, Sasaki Y *et al.* How was cognitive behavioural therapy for mood disorder implemented in Japan? A retrospective observational study using the nationwide claims database from FY2010 to FY2015. *BMJ Open* 2020; **10**: e033365.
- Inoue T, Sasai K, Kitagawa T, Nishimura A, Inada I. Randomized, double-blind, placebo-controlled study to assess the efficacy and safety of vortioxetine in Japanese patients with major depressive disorder. *Psychiatry Clin. Neurosci.* 2020; **74**: 140–148.
- Akechi T, Kato T, Fujise N *et al.* Why some depressive patients perform suicidal acts and others do not. *Psychiatry Clin. Neurosci.* 2019; **73**: 660–661.
- Sado M, Wada M, Ninomiya A *et al.* Does the rapid response of an antidepressant contribute to better cost-effectiveness? Comparison between mirtazapine and SSRIs for first-line treatment of depression in Japan. *Psychiatry Clin. Neurosci.* 2019; **73**: 400–408.

Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1 The eight quality indicators (QI) used in the present study.

Table S2 Demographic data of patients with major depressive disorder (MDD).

Table S3 Quality indicator (QI) values for patients with major depressive disorder (MDD) in the first year of participation. The QI of each patient ($n = 1283$) is presented. The QI for each hospital ($n = 84$) was also calculated and is presented as the mean \pm SD and the median with interquartile range (IQR).

Table S4 Quality indicator (QI) values for each hospital type in the first year of participation. The QI of five subgroups of the 84 hospitals divided by hospital type (university hospital, national/public hospitals, and private hospitals) are presented as the means \pm SD. QI values in each group were compared with the Kruskal–Wallis test followed by the *post-hoc* test (Dunn test). The significance level was set at two-tailed $P < 6.25 \times 10^{-3}$ because the Bonferroni method was applied. The significance level of the *post-hoc* test was set at $P < 1.7 \times 10^{-2}$. Significant *P*-values are boldfaced and underlined.

Table S5 Quality indicator (QI) values of eastern Japan and western Japan in the first year of participation. The QI of five subgroups of the 84 hospitals divided by region (eastern Japan, western Japan) are presented as the means \pm SD. QI values in each group were compared with the Mann–Whitney *U*-test. The significance level was set at two-tailed $P < 6.25 \times 10^{-3}$ as the Bonferroni method was applied. Significant *P*-values are boldfaced and underlined. There was a significant compositional difference in hospital type between eastern and western Japan (university: 46.9% vs 37.1%; national/public: 34.7% vs 17.1%; private: 18.4% vs 45.7%; χ^2 -test $P = 0.019$).

Hitoshi Iida, MD, PhD,¹ Junichi Iga, MD, PhD,² Naomi Hasegawa, PhD,³ Yuka Yasuda, MD, PhD,⁴ Tomoya Yamamoto, PhD,⁵ Kenichiro Miura, PhD,³ Junya Matsumoto, MD, PhD,³ Atsunobu Murata,³ Kazuyoshi Ogasawara, MD, PhD,⁶ Hisashi Yamada, MD, PhD,⁷ Hikaru Hori, MD, PhD,⁸ Kayo Ichihashi, MD,⁹ Naoki Hashimoto, MD, PhD,¹⁰ Kazutaka Ohi, MD, PhD,¹¹ Norio Yasui-Furukori, MD, PhD,¹² Takashi Tsuboi, MD, PhD,¹³ Toshinori Nakamura, MD,¹⁴ Masahide Usami, MD, PhD,¹⁵ Ryuji Furihata, MD, PhD,¹⁶ Yoshikazu Takaesu, MD, PhD,¹³ Kunihiro Iwamoto, MD, PhD,¹⁷ Nobuhiru Sugiyama, MD, PhD,¹⁸ Taishiro Kishimoto, MD, PhD,¹⁹ Naohisa Tsujino, MD, PhD,²⁰ Hiroki Yamada, MD, PhD,²¹ Akitoyo Hishimoto, MD, PhD,²² Kiyotaka Nemoto, MD, PhD,²³ Kiyokazu Atake, MD, PhD,⁸ Hiroyuki Muraoka, MD, PhD,²⁴ Eiichi Katsumoto, MD,²⁵ Satoru Oishi, MD, PhD,²⁶ Takahiko Inagaki, MD,²⁷ Fumiaki Ito, MD, PhD,²⁸ Yayoi Imamura, MD,¹³ Mikio Kido, MD, PhD,²⁹ Tatsuya Nagasawa, MD, PhD,³⁰ Shusuke Numata, MD, PhD,³¹ Shinichiro Ochi, MD, PhD,² Masaaki Iwata, MD, PhD,³² Hidenaga Yamamori, MD, PhD,³ Junichi Fujita, MD, PhD,²² Toshiaki Onitsuka, MD, PhD,³³ Satoshi Yamamura, MD,³⁴ Manabu Makinodan, MD, PhD,³⁵ Michiko Fujimoto, MD, PhD,³⁶ Yoichiro Takayanagi, MD, PhD,³⁷ Kenji Takezawa, MD, PhD,³⁸ Hiroshi Komatsu, MD, PhD,²⁸ Kentaro Fukumoto, MD, PhD,³⁹ Shinichiro Tamai, MD,⁴⁰ Hirotaka Yamagata, MD, PhD,⁴¹ Chika Kubota, MD, PhD,⁴² Tadasu Horai, MD, PhD,⁴³ Ken Inada, MD, PhD,²⁴ Koichiro Watanabe, MD, PhD,¹³ Hiroaki Kawasaki, MD, PhD,¹ and Ryota Hashimoto, MD, PhD,³

¹Department of Psychiatry, Faculty of Medicine, Fukuoka University, Fukuoka, ²Department of Neuropsychiatry, Molecules and Function, Ehime University Graduate School of Medicine, Ehime, ³Department of Pathology of Mental Diseases, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo, ⁴Medical Corporation Foster, ⁵Department of Pharmacy, Osaka University Hospital, Osaka, ⁶Center for Postgraduate Clinical Training and Career

Development, Nagoya University Hospital, Aichi, ⁷Department of Neuropsychiatry, Hyogo College of Medicine, Hyogo, ⁸Department of Psychiatry, School of Medicine, University of Occupational and Environmental Health, Fukuoka, ⁹Department of Neuropsychiatry, University of Tokyo Hospital, Tokyo, ¹⁰Department of Psychiatry, Hokkaido University Graduate School of Medicine, Hokkaido, ¹¹Department of Psychiatry and Psychotherapy, Gifu University Graduate School of Medicine, Gifu, ¹²Department of Psychiatry, Dokkyo Medical University School of Medicine, Tochigi, ¹³Department of Neuropsychiatry, Kyorin University School of Medicine, Tokyo, ¹⁴Department of Psychiatry, Shinshu University School of Medicine, Nagano, ¹⁵Department of Child and Adolescent Psychiatry, Kohnodai Hospital, National Center for Global Health and Medicine, Chiba, ¹⁶Department of Psychiatry, Nihon University School of Medicine, Tokyo, ¹⁷Department of Psychiatry, Nagoya University Graduate School of Medicine, Aichi, ¹⁸Department of Applied Occupational Therapy, Shinshu University School of Health Sciences, Nagano, ¹⁹Department of Neuropsychiatry, Keio University School of Medicine, ²⁰Department of Neuropsychiatry, School of Medicine, Faculty of Medicine, Toho University, Tokyo, ²¹Department of Psychiatry, Showa University Northern Yokohama Hospital, ²²Department of Psychiatry, Yokohama City University Graduate School of Medicine, Kanagawa, ²³Department of Psychiatry, Faculty of Medicine, University of Tsukuba, Ibaraki, ²⁴Department of Psychiatry, Tokyo Women's Medical University, Tokyo, ²⁵Katsumoto Mental Clinic, Osaka, ²⁶Department of Psychiatry, Kitasato University School of Medicine, Kanagawa, ²⁷Adolescent Mental Health Service, Biwako Hospital, Shiga, ²⁸Department of Psychiatry, Tohoku University Hospital, Miyagi, ²⁹Department of Neuropsychiatry, University of Toyama Graduate School of Medicine and Pharmaceutical Sciences, Toyama, ³⁰Department of Neuropsychiatry, Kanazawa Medical University, Ishikawa, ³¹Department of Psychiatry, Institute of Biomedical Science, Tokushima University Graduate School, Tokushima, ³²Department of Neuropsychiatry, Faculty of Medicine, Tottori University, Tottori, ³³Department of Neuropsychiatry, Graduate School of Medical Sciences, Kyushu University, Fukuoka, ³⁴Suzuka Kosei Hospital, Mie, ³⁵Department of Psychiatry, Nara Medical University School of Medicine, Nara, ³⁶Department of Psychiatry, Osaka University Graduate School of Medicine, Osaka, ³⁷Department of Neuropsychiatry, University of Toyama School of Medicine, Toyama, ³⁸Medical Corporation Matsuzaki Hospital, Toyohashi Mental Care Center, Aichi, ³⁹Department of Neuropsychiatry, Iwate Medical University, Iwate, ⁴⁰Department of Neuropsychiatry, Tokyo Metropolitan Tama Medical Center, Tokyo, ⁴¹Division of Neuropsychiatry, Department of Neuroscience, Yamaguchi University School of Medicine, Yamaguchi, ⁴²Department of Psychiatry, National Center Hospital, National Center of Neurology and Psychiatry, Tokyo, and ⁴³Department of Psychiatry, Kobe University Graduate School of Medicine, Kobe, Japan

Email: ryotahashimoto55@ncnp.go.jp

Received 11 June 2020; revised 19 August 2020; accepted 29 August 2020.

across 35 services. Though important advances have been made in delirium prevention and treatment in the elderly, the application of those findings in adults under 65 years of age is not straightforward. The investigation of delirium incidence in younger adults is fundamental to estimate its relevance.

All data in this prospective cohort study were collected at the University Hospital Zurich, Switzerland, a tertiary care center, in 2014, based on a quality-improvement initiative aiming to improve the detection and management of delirium for all hospitalized patients, the 'Delir-Path'.² This study was approved by the ethics committee of the Canton of Zurich (KEK-ZH-Nr. 2012-0263). A waiver of informed consent was obtained from the committee. Incidence was determined by simple logistic regressions with their respective odds ratios (OR). Please refer to Appendix S1 for more details on the inclusion criteria and the statistical analysis, and to Figure S1 for the flowchart of sample recruitment.

Upon suspicion, trained nursing staff performed the Delirium Observation Screening (DOS) Scale, which reflects DSM-IV criteria. In patients with a DOS score ≥ 3 , presence of delirium was considered, and evaluation by a physician according to the DSM-5 criteria was requested. The contents of nurses' training are described in the supplements. The cut-off score of ≥ 3 was chosen due to the decent sensitivity and specificity, and its high negative predictive value of almost 100% as previously demonstrated.³ Once delirium was documented, it was followed up with DOS three times daily until indication of remission. In the intensive care units (ICU), the Intensive Care Delirium Screening Checklist (ICDSC) was routinely performed three times per day. In patients with an ICDSC score of ≥ 4 , presence of delirium was considered,⁴ and evaluation by a physician was requested.

The overall incidence of delirium in our cohort of adults under 65 years of age was 14.5%. Delirious patients were on average older than non-delirious patients (mean 49 vs 42 years; $P < 0.001$) and were hospitalized considerably longer (mean 17 vs 7 days; $P < 0.001$). Patients developing delirium were often urgent admissions (59% vs 46%; $P < 0.001$, OR 1.7, 95% confidence interval [CI] 1.58–1.86), and came from other hospitals and assisted living rather than from home (76% vs 93%; $P < 0.001$, OR 0.23, CI 0.21–0.26). Their mortality was significantly increased (OR 41.8, CI 32.41–53.98, $P < 0.001$). The need for rehabilitation was much higher in patients who had delirium (23% vs 5%; $P < 0.001$, OR 5.47, CI 5.03–5.95). Across different ICU, the incidence ranged from 64.9% to 84.5% ($P < 0.001$, OR 10.85–32.38; Fig. 1). In medical services, incidence was highest in palliative care (54.0%, OR

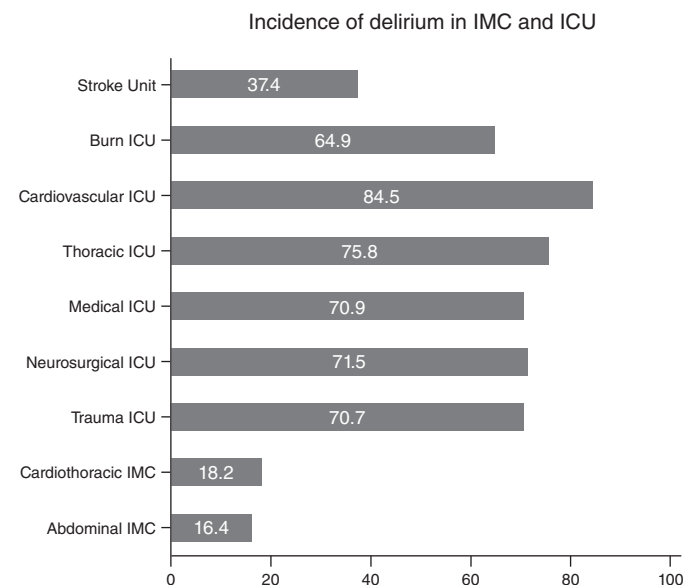


Fig. 1 Bar plots illustrating incidence (%) of delirium across intensive care units (ICU) and intermediate care units (IMC).

Hospital-wide evaluation of delirium incidence in adults under 65 years of age

doi:10.1111/pcn.13155

Delirium is generally perceived as an acute neuropsychiatric condition in the elderly. The incidence in adults under 65 years of age has been largely neglected, although pooled epidemiological data indicate a notable incidence.¹ However, this has not yet been systematically evaluated in a large cohort. Here we show that delirium occurred in about one out of 10 adults under 65 years of age in a comprehensive sample of 18 599 patients