Health Inequalities Among Elderly Type 2 Diabetes Mellitus Patients in Japan

Peng Jiang, MS,1 Akira Babazono, MS, MD, PhD,1 and Takako Fujita, MPH1,2

Abstract

The influence of socioeconomic status (SES) on health inequalities has received much attention worldwide. This study examined the effect of SES on the following older type 2 diabetes mellitus patient health outcomes: oral hypoglycemic agent (OHA) medication adherence (proportion of days covered, PDC), risk of hospitalization for diabetic macrovascular complications, and in-hospital death. A retrospective cohort design using 2013–2016 claims data was used. Subjects were 58,349 diabetes patients aged >74 years in 2013. Age, sex, residential area, and comorbidities were controlled for. Logistic regression was conducted to assess the effects of income on PDC; survival analysis was used to assess the effects on hospitalization and in-hospital death. Regressions were conducted separately by sex. Compared with the lowest income group, adjusted PDC odds ratios for medium- and high-income males, respectively, were 1.35 (95% CI: 1.27–1.43) and 1.41 (95% CI: 1.30–1.54); females: 1.17 (95% CI: 1.11–1.23) and 1.24 (95% CI: 1.13–1.35). Adjusted hazard ratios (AHRs) for male hospitalization were 0.88 (95% CI: 0.80–0.96) and 0.88 (95% CI: 0.79–0.99); females: 1.00 (95% CI: 0.93–1.07) and 0.95 (95% CI: 0.83–1.08). AHRs for male in-hospital death were 0.83 (95% CI: 0.75–0.91) and 0.62 (95% CI: 0.54–0.70); females: 0.94 (95% CI: 0.87–1.02) and 0.77 (95% CI: 0.65–0.92). Results revealed sex-specific health inequalities among older Japanese diabetes patients. Subjects with worse SES had significantly poorer OHA medication adherence (both sexes), higher hospitalization risk for diabetes complications (males), and higher in-hospital death risk (both sexes).

Keywords: health inequality, diabetes mellitus, adherence, hospitalization, in-hospital death

Introduction

The relationship between socioeconomic status (SES) and health outcomes is a critical problem in social epidemiology.1 Some empirical studies have demonstrated an association between shorter life expectancy and SES-related health inequalities.

The population of Japan has one of the longest life expectancies in the world, and the increasingly aged population is a major problem. According to an estimate by the Japan Ministry of Internal Affairs and Communications Statistics Bureau, by May 1, 2018, there were 35.3 million (28.4%), 17.7 million (14.3%), and 5.6 million (4.5%) people older than ages 65, 75, and 85 years, respectively, in Japan.2 A National Health and Nutrition Survey conducted by the Japanese Ministry of Health, Labour and Welfare (MHLW) in 2016 showed that diabetes occurs frequently among the older population and has a substantial effect on quality of life (QOL); moreover, up to 10 million people are likely to have diabetes mellitus (DM), about 12.1% of the overall population of Japan.3 In addition, the proportion of both male and female DM patients older than age 60 years has been increasing.3

The incidence of diabetes complications is more frequent in older people.3 A combination of diabetes complications and frailty substantially affect the QOL of aging populations. The risk of developing diabetic macrovascular disease, including ischemic heart disease (IHD), stroke, and peripheral arterial disease (PAD), is higher in patients with diabetes than in patients without diabetes.4,5
Thus, daily control of blood sugar is important for older DM patients. Good medication adherence to oral hypoglycemic agents (OHAs) may reduce hospitalization for diabetic macrovascular complications. However, the aforementioned MHLW survey found that about 75% of people who are strongly suspected to have DM received medical treatment in Japan, and the proportion was higher for males than for females. Some studies have shown that nonadherence to OHAs may lead to subsequent hospitalization.

Although a consensus is lacking, many studies have demonstrated that SES has a large impact on health outcomes in the older population. However, the effect of SES on medication adherence and diabetic macrovascular complications in DM patients in Japan is still unclear. Many Western studies suggest that differences between the sexes affect the association between SES and diabetes. However, only a few Asian studies have investigated the effect of sex on this association.

Therefore, the study objective was to evaluate the effect of SES on older patients’ medication adherence to OHAs and hospital admission for diabetic macrovascular complications by sex. The effects of SES on inpatient mortality also were assessed as a secondary outcome.

Methods

Data

This study used a retrospective cohort design. A health care claims database and master database for Fukuoka Prefecture Wide-Area Association of Latter-Stage Elderly Healthcare was used to obtain data for the period April 1, 2013, to March 31, 2016. The database is a component of Japan’s social insurance system. People aged 75 years and older and those aged between 65 and 74 years are recognized by the Association as having a designated level of disability and are allowed to participate in this insurance plan. This health care claims database includes detailed data on diagnosis and treatment, such as International Classification of Diseases, 10th Revision (ICD-10) data, diagnosis date, drug prescriptions, and details of medical procedures. The master database includes information such as enrollee’s demographic variables, and dates of enrollment and withdrawal. Most of this health care-insured population has sustainable long-term eligibility once they are enrolled; therefore, few study subjects were lost to follow-up because of moving to other prefectures or for other reasons. Most of these databases are computer administered and have a high penetration rate (98.6% as at April 2015). One reason for this is that the Japanese Health Insurance Claims Review & Reimbursement services are responsible for quality control of computer-administered claims databases.

The Institutional Review Board of Kyushu University (Clinical Bioethics Committee of the Graduate School of Healthcare Sciences, Kyushu University) approved this study.

Definition of study subjects

First, patients with diabetes were defined as individuals who were diagnosed with diabetes (ICD-10 codes E10–E14) and prescribed oral antidiabetic agents or insulin in fiscal year 2013. Drugs were identified using the Japanese version of the National Health Insurance Drug List. Then, subjects younger than age 75 years were excluded from the study population because individuals younger than age 75 can only be enrolled in the health insurance plan if they have a disability; the inclusion of such individuals may have biased health outcomes data, as disability may affect hospital visits. Additionally, only patients prescribed OHAs in fiscal years 2014, 2015, and 2016 were included. Patients prescribed insulin also were excluded from the study, as detailed information about insulin treatment was not included in the administrative claims data, meaning that the ultimate subjects were type 2 diabetes patients.

Definition of variables

OHA adherence was assessed using proportion of days covered (PDC) instead of medication possession ratio because of potential problems with overestimation and data availability with the latter. The denominator of OHA PDC was the number of days from April 1, 2014, until hospitalization admission for macrovascular complications or death. The numerator was the number of days covered by OHA prescription during the observation period. A PDC <80% was defined as nonadherence; this cutoff value has been used in many studies on chronic disease.

The primary event was defined as hospitalization for diabetic macrovascular complications using ICD-10, including IHD, stroke, and PAD, as shown in Table 1. Number of days from beginning of observation until admission also were calculated. The secondary event was defined as hospital mortality; for this, the period from beginning of observation until hospital death was calculated.

Income group was used as the SES indicator because no detailed income data were available. Based on the insurance policy, the income group for each enrollee was determined by their income level, reflecting each enrollee’s SES. The income group was divided into 3 groups according to the insurance policy: lowest, medium, and highest income groups. The lowest income and medium-income groups had a co-payment of 10%. The highest-income group, who had a co-payment of 30%, was defined as those whose incomes were comparable to the current workforce. Age was categorized into 3 groups: 75–79 years, 80–84 years, and 85 years or older. The Charlson comorbidity index (CCI) for all conditions and ICD-10 codes were used to assess medical complications, except for mild diabetes and diabetes with complications. CCI was categorized into 3 groups: 0–2, and 3–4, or ≥5. Residential area also was adjusted for in the regression model, using the Japan Secondary Healthcare Area, which divides Fukuoka Prefecture into 13 subareas. Furthermore, other lifestyle-related diseases (hypertension [I10] and hyperlipidemia [E78.0–78.5]) also were controlled for as confounding factors using ICD-10 codes from medical claims data during the study period.

Statistical analysis

Patient characteristics were described by frequency counts and proportions for categorical variables, and Pearson χ² tests were conducted to analyze categorical variables by sex.

A multivariate logistic regression model was used to assess the effect of income on OHA PDC, because PDC is a binary variable. Adjusted odds ratios (AORs) and 95% confidence
intervals (95% CIs) were estimated for different income groups. In this model, residential area, age, CCI, hypertension, and hyperlipidemia were set as independent variables. For hospitalization of macrovascular disease and hospital mortality, a survival model was used to estimate the effect of SES. Time from beginning of observation to first incidence of admission for macrovascular hospitalization was analyzed as the time-to-event. The diagnosis date recorded in the electronic health record, or the censoring at the final event if the events were not observed, was used as the end point. Kaplan-Meier survival curves were produced, and the log-rank test and the Cox proportional hazard model were used to estimate hazard ratios and 95% CIs. In the Cox proportional hazard model, residential area, age group, CCI, hypertension, and hyperlipidemia were adjusted as covariates. For all models, the significance level was set at $P < 0.05$, and data extraction and analyses were conducted using Microsoft SQL Server 2014 (Microsoft Corporation, Redmond, WA) and Stata Statistical Software, release 14 (StataCorp LLC, College Station, TX).

### Results

#### Descriptive statistics

A total of 58,349 patients were identified, and 54.2% were female. Table 1 shows subject characteristics by sex. The median ages for males and females were 80 years and 81 years, respectively. Significantly more males than females had high incomes. Significantly more females than males had hypertension and hyperlipidemia, but the CCI of females was lower. For outcome variables, the medium PDC values for males and females were 90.2% and 89.4%, respectively, and the proportion of subjects with PDC $>$ 80 was slightly but significantly higher in males than in females.

#### Results for OHA PDC

For males, compared with subjects with the lowest incomes, the AOR for subjects with medium incomes was 1.35 (95% CI: 1.27–1.43, $P < 0.01$) and the AOR of those with the highest incomes was 1.41 (95% CI: 1.30–1.54, $P < 0.01$).

| Category                  | Total | Female | Male   | P    |
|---------------------------|-------|--------|--------|------|
| **Age (years)**           |       |        |        |      |
| 75–79                     | 25,955| 12,572 | 13,383 | 0.000|
| 80–84                     | 18,626| 9865   | 8761   |      |
| ≥85                       | 13,768| 9128   | 4640   |      |
| **Income**                |       |        |        |      |
| low                       | 17,145| 12,599 | 4546   | 0.000|
| medium                    | 34,342| 16,481 | 17,861 |      |
| high                      | 6862  | 2485   | 4377   |      |
| **Charlson comorbidity index** |       |        |        |      |
| 0/2                       | 9122  | 6036   | 3086   | 0.000|
| 3/4                       | 15,247| 8734   | 6513   |      |
| ≥5                        | 33,980| 16,795 | 17,185 |      |
| **Region**                |       |        |        |      |
| Fukuoka/Itoshima          | 14,037| 7482   | 6555   | 0.000|
| Kasuya                    | 2433  | 1281   | 1152   |      |
| Munagata                  | 1714  | 929    | 785    |      |
| Chikushit                 | 3690  | 1872   | 1818   |      |
| Asakura                   | 1285  | 691    | 594    |      |
| Kurume                    | 5492  | 3064   | 2428   |      |
| Yame/Chikugo              | 1863  | 994    | 869    |      |
| Ariake                    | 3558  | 2005   | 1553   |      |
| Idsuka                    | 2775  | 1621   | 1154   |      |
| Nogata                    | 1750  | 959    | 791    |      |
| Tagawa                    | 2097  | 1172   | 925    |      |
| Kitakyushu                | 14,988| 8063   | 6925   |      |
| Keichiku                  | 2667  | 1432   | 1235   |      |
| **Hypertension**          |       |        |        |      |
| No                        | 7912  | 3696   | 4216   | 0.000|
| Yes                       | 50,437| 27,869 | 22,568 |      |
| **Hyperlipidemia**        |       |        |        |      |
| No                        | 20,031| 9378   | 10,653 | 0.000|
| Yes                       | 38,318| 22,187 | 16,131 |      |
| **Proportion of days covered** |     |        |        |      |
| ≤80%                      | 24,107| 13,182 | 10,925 | 0.017|
| >80%                      | 34,242| 18,383 | 15,859 |      |
| **Acute myocardial infarction** |    |        |        |      |
| No                        | 57,916| 31,348 | 26,568 | 0.095|
| Yes                       | 433   | 217    | 216    |      |
| **Ischemic heart disease** |       |        |        |      |
| No                        | 55,252| 30,070 | 25,182 | 0.000|
| Yes                       | 3097  | 1495   | 1602   |      |
| **Hemorrhagic stroke**    |       |        |        |      |
| No                        | 56,522| 30,608 | 25,914 | 0.135|
| Yes                       | 1827  | 957    | 870    |      |
| **Ischemic stroke**       |       |        |        |      |
| No                        | 55,980| 30,441 | 25,539 | 0.000|
| Yes                       | 2369  | 1124   | 1245   |      |
| **Peripheral arterial disease** |    |        |        |      |
| No                        | 57,378| 31,107 | 26,271 | 0.000|
| Yes                       | 971   | 458    | 513    |      |
| **Inpatient death**       |       |        |        |      |
| No                        | 52,822| 28,962 | 23,860 | 0.000|
| Yes                       | 5527  | 2603   | 2924   |      |
For females, compared with subjects with the lowest incomes, the AOR of subjects with medium incomes was 1.17 (95% CI: 1.11–1.23, \(P<0.01\)) and the AOR of subjects with the highest incomes was 1.24 (95% CI: 1.13–1.35, \(P<0.01\)). The magnitude of the effect of income among males was obviously greater than among females.

Results of the survival analysis for hospitalization and in-hospital death

For macrovascular hospitalizations among males, the \(P\) value of the log-rank test for different income categories was 0.05 (\(\chi^2 = 5.97\)). The Cox model indicated that, compared with those with the lowest incomes, the adjusted hazard ratio (AHR) of subjects with medium incomes was 0.88 (95% CI: 0.80–0.96, \(P<0.01\)) and the AHR of subjects with the highest incomes was 0.88 (95% CI: 0.79–0.99, \(P=0.03\)). However, there were no significant differences in AHR among females within different income groups. The \(P\) value of the log-rank test was 0.55 (\(\chi^2 = 1.20\)). Compared with those with the lowest incomes, the AHR of females with medium incomes was 1.00 (95% CI: 0.93–1.07, \(P=0.98\)), and the AHR of females with the highest incomes was 0.95 (95% CI: 0.83–1.08, \(P=0.44\)). Kaplan-Meier curves for macrovascular hospitalizations among different income groups are shown in Figure 1 and Figure 2.

For the in-hospital death event, the \(P\) value of the log-rank test for males in different income categories was smaller than 0.01 (\(\chi^2 = 43.97\)). Compared with subjects with the lowest incomes, the AHR of males with medium incomes was 0.83 (95% CI: 0.75–0.91, \(P<0.01\)) and the AHR of males with the highest incomes was 0.62 (95% CI: 0.54–0.70, \(P<0.01\)). For females, the \(P\) value of the log-rank test was smaller than 0.01 (\(\chi^2 = 30.89\)). Compared with those with the lowest incomes, the AHR of female subjects with medium incomes was 0.94 (95% CI: 0.87–1.02, \(P=0.15\)), which suggested that there was no significant between-group difference for in-hospital death hazard. The AHR of females with the highest incomes was 0.77 (95% CI: 0.65–0.92, \(P<0.01\)). Kaplan-Meier curves for in-hospital death among different income groups are shown in Figure 3 and Figure 4.

Discussion

SES determines 3 major aspects of health: health care, environmental exposure, and health behavior. Findings from this study showed that lower income level, which is an important indicator of poorer SES, had a significantly negative effect on older DM patients’ health outcomes of OHA medication adherence, hospitalization for diabetic macrovascular complications, and, ultimately, in-hospital mortality.

OHA medication adherence is a measure of patient health behavior. This study found that although males had slightly better adherence than females, both sexes exhibited a significant decrease in PDC according to lower income level, indicating that worse SES had a significantly negative effect.
on older DM patients’ OHA medication adherence. These results are consistent with many previous findings.\textsuperscript{17–19} Nonadherence can be caused by the burden of increased expenditure.\textsuperscript{14} Moreover, the odds ratios in this study showed that the adherence decrease for males was greater than for females, indicating that there might be a correlation between SES and sex when discussing health disparities.

Many previous studies have demonstrated income inequality in hospitalization\textsuperscript{20} not only in DM patients but also in the general population.\textsuperscript{21,22} The present findings are consistent with those of previous studies. This study found that older male DM patients with medium and lowest incomes were at significantly greater risk of hospitalization for diabetic macrovascular complications than those at the highest income level. The trend was similar for females; however, there was a significant difference in hospitalization risk only for subjects with the lowest and the highest incomes, which was consistent with the results of the log-rank test.

Several previous studies have reported that better medication adherence is associated with the lowest hospitalization rates among patients with DM and other lifestyle-related diseases.\textsuperscript{23} There is also evidence that lower adherence to DM medication is associated with higher risk of subsequent hospitalization.\textsuperscript{24} Several studies have demonstrated an association between poor OHA adherence and metabolic control.\textsuperscript{24} In addition, glucose control is important for vascular outcome management in DM patients. One recent meta-analysis suggested that lowering glucose is important to prevent long-term microvascular complications in adults with type 2 diabetes.\textsuperscript{25} Given the link between poor adherence and lower SES, there may be an association between OHA medication adherence and macrovascular hospitalization.

Regardless of the risk of in-hospital death, many studies have suggested that lower income is associated with a higher risk of in-hospital mortality.\textsuperscript{26,27} Present study findings show that both male and female older DM patients with higher incomes had significantly reduced inpatient death. However, the effect of income level on in-hospital death may be multifactorial. SES factors such as housing conditions, poor nutrition, and lack of access to preventive services may have negative effects on health in low-SES populations.\textsuperscript{28} Although these populations tend to have higher rates of chronic diseases and other comorbidities, they have poorer baseline health status than high SES populations.\textsuperscript{29,30} As a result, multifaceted dimensions of poor SES may combine to have a negative effect on disparities for in-hospital deaths.

In this study, age, residential area, and comorbidities were adjusted for to examine the effect of SES. Age was found to be significantly associated with OHA nonadherence, hospitalization admission, and in-hospital death in both males and females, indicating that older DM patients had worse OHA medication adherence. However, previous research has failed to show a consistent association between age and nonadherence in DM patients. Some studies have found no association\textsuperscript{31,32} whereas others show that medication adherence improves with age.\textsuperscript{33} Although previous studies have shown the same association between age and nonadherence as was found in the present study,\textsuperscript{34} especially for older DM patients, nonadherence may be associated with aging because of higher prevalence of cognitive impairment in older individuals.\textsuperscript{35,36} One recent study suggests that cognitive impairment may decrease medication adherence in older chronic disease patients without dementia.\textsuperscript{37}

Regarding the effect of comorbidities, both male and female subjects showed a trend for higher CCI to be associated with nonadherence and a higher risk of hospitalization and in-hospital death. Subjects with higher CCI scores may have been prescribed more medication than those with lower CCI scores. Some studies have suggested that prescribing and dispensing patterns may contribute to the accumulation of unwanted and unused medications,\textsuperscript{38} and that polypharmacy may be linked to a higher risk of nonadherence\textsuperscript{39,40}; however, data about polypharmacy were not available in the study. Additionally, in this study DM patients with hypertension or hyperlipidemia had better adherence than those without these conditions.

Limitations

SES is usually conceptualized in terms of multidimensional indicators, such as income, education level, occupation, and housing conditions. However, only income was examined in this study because of data availability. This study emphasized lower medication adherence as the main factor that led to poorer diabetes outcomes in the lower SES group; however, other factors may matter, such as nutrition and exercise management. Nevertheless, the information was not available. Another limitation is that although almost all residents in Fukuoka Prefecture were included, individuals from countries other than Japan were not included; therefore, the data may not be generalizable to other populations and ethnic groups. Furthermore, the study used a retrospective design and data from a claims database, which did not include information about DM severity (although diabetes complications were assessed using CCI). In claims databases, input and coding errors also are possible, although these are likely to be random errors with little influence on the statistical inferences drawn.

Additional prospective studies involving diverse ethnic groups and multidimensional SES indicators are required to obtain higher quality evidence of health disparities among older DM patients.

Conclusion

There are health inequalities among older DM patients in Japan. The present study showed that worse SES was associated with significantly poorer OHA medication adherence for both sexes, higher risks of hospitalization for diabetic macrovascular complications for males, and higher risk of in-hospital death for both sexes. The authors suggest that lower OHA medication adherence related to lower income may increase the risk of hospitalization for diabetic macrovascular and in-hospital mortality. This effect is sex-specific; that is, low-SES males had significantly greater morbidity and hospital mortality, whereas low-SES females only showed significantly greater hospital mortality. Therefore, insurer strategies that motivate beneficiaries with DM to improve medication adherence may be effective in reducing the risk of hospitalization for diabetic macrovascular complications and in-hospital mortality, thus reducing unnecessary medical expenditure.
Acknowledgments

We thank the Fukuoka Prefecture Association of Latter-Stage Elderly Healthcare for provision of the health care claims database. We thank Diane Williams, PhD, from Edanz Group for editing a draft of this manuscript.

Author Disclosure Statement

The authors declare that there are no conflicts of interest.

Funding Information

No funding was received for this article.

References

1. Marmot M. Income inequality, social environment, and inequalities in health. J Policy Anal Manage 2001;20:156–159.
2. Ministry of Internal Affairs and Communications, Statistics Bureau of Japan. Population estimates monthly report. 2018. https://www.stat.go.jp/english/data/jinsui/2.html Accessed September 20, 2019.
3. Ministry of Health Labour and Welfare. National Health and Nutrition Survey, 2016. https://www.mhlw.go.jp/file/04-Houdouhappyou-10904750-Kenkoukyoku-Gantaisaku kenkouzoushinka/kekkagaiyou_7.pdf Accessed October 10, 2019.
4. Haffner SM, Lehto S, Pöyrälä K, Laakso M. Mortality from ischemic heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 1998;339:229–234.
5. Iso H, Imano H, Kitamura A, et al. Type 2 diabetes and risk of non-embolic ischemic stroke in Japanese men and women. Diabetologia 2004;47:2137–2144.
6. Nishi T, Babazono A, Maeda T. Risk of hospitalization for diabetic macrovascular complications and in-hospital mortality with irregular physician visits using propensity score matching. J Diabetes Investig 2014;5:428–434.
7. Lau DT, Nau DP. Oral antihyperglycemic medication non-adherence and subsequent hospitalization among individuals with type 2 diabetes. Diabetes Care 2004;27:2149–2153.
8. Kowall B1, Rathmann W, Strassburger K, Meisinger C, Holle R, Mielck A. Socioeconomic status is not associated with type 2 diabetes incidence in an elderly population in Germany: KORA S4/F4 cohort study. J Epidemiol Community Health 2011;65:606–612.
9. Rathmann W1, Haastert B, Icks A, et al. Sex differences in the associations of socioeconomic status with undiagnosed diabetes mellitus and impaired glucose tolerance in the elderly population: the KORA Survey 2000. Eur J Public Health 2005;15:627–633.
10. Robbins JM1, Vaccarino V, Zhang H, Kasl SV. Socioeconomic status and type 2 diabetes in African American and non-Hispanic white women and men: evidence from the Third National Health and Nutrition Examination Survey. Am J Public Health 2001;91:76–83.
11. Tang M, Chen Y, Krewski D. Gender-related differences in the association between socioeconomic status and self-reported diabetes. Int J Epidemiol 2003;32:381–385.
12. Nagamine Y, Kondo N, Yokobayashi K, et al. Socioeconomic disparity in the prevalence of objectively evaluated diabetes among older Japanese adults: JAGES cross-sectional data in 2010. J Epidemiol 2019;29:295–301.
13. Lee DS, Kim YJ, Han HR. Sex differences in the association between socio-economic status and type 2 diabetes: data from the 2005 Korean National Health and Nutritional Examination Survey (KNHANES). Public Health 2013;127:554–560.
14. Duncan JC, Rogers R. Medication compliance in patients with chronic schizophrenia: implications for the community management of mentally disordered offenders. J Forensic Sci 1998;43:1133–1137.
15. Gary TL, Crum RM, Cooper-Patrick L, Ford D, Brancati FL. Depressive symptoms and metabolic control in African-Americans with type 2 diabetes. Diabetes Care 2000;23:23–29.
16. Kaganimimori S, Gaine A, Nasermoaddeli A. Socioeconomic status and health in the Japanese population. Soc Sci Med 2009;68:2152–2160.
17. Breitscheidel L, Stamenitis S, Dipple FW, Schöffski O. Economic impact of compliance to treatment with anti-diabetes medication in type 2 diabetes mellitus: a review paper. J Med Econ 2010;13:8–15.
18. Hansen RA, Farley JF, Droeger M, Maciejewski ML. A retrospective cohort study of economic outcomes and adherence to monotherapy with metformin, pioglitazone, or a sulfonylurea among patients with type 2 diabetes mellitus in the United States from 2003 to 2005. Clin Ther 2010;32:1308–1319.
19. Nishi T, Babazono A, Maeda T. Association between income levels and irregular physician visits after a health checkup, and its consequent effect on glycemic control among employees: a retrospective propensity score-matched cohort study. J Diabetes Investig 2019;10:1372–1381.
20. Huang CJ, Lin CH, Hsieh HM, et al. A longitudinal study of healthcare utilisation and expenditure in people with type 2 diabetes mellitus with and without major depressive disorder. Gen Hosp Psychiatry 2019;57:50–58.
21. Dewan P, Rørth R, Jhund PS, et al. Income inequality and outcomes in heart failure: a global between-country analysis. JACC Heart Fail 2019;7:336–346.
22. Rosengren A, Smyth A, Rangarajan S, et al. Socioeconomic status and risk of cardiovascular disease in 20 low-income, middle-income, and high-income countries: the Prospective Urban Rural Epidemiologic (PURE) study. Lancet Glob Health 2019;7:e748–e760.
23. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Med Care 2005;43:521–530.
24. Schectman JM, Nadkarni MM, Voss JD. The association between diabetes metabolic control and drug adherence in an indigent population. Diabetes Care 2002;25:1015–1021.
25. Zoungas S, Arima H, Gerstein HC, et al. Effects of intensive glucose control on microvascular outcomes in patients with type 2 diabetes: a meta-analysis of individual participant data from randomised controlled trials. Lancet Diabetes Endocrinol 2017;5:431–437.
26. Rush B, Wiskar K, Celi LA, et al. Association of household income level and in-hospital mortality in patients with sepsis: a nationwide retrospective cohort analysis. J Intensive Care Med 2018;33:551–556.
27. Armenia SJ, Pentakota SR, Merchant AM. Socioeconomic factors and mortality in emergency general surgery: trends over a 20-year period. J Surg Res 2017;212:178–186.
28. Baker MG, Barnard LT, Kvalsvig A. Increasing incidence of serious infectious diseases and inequalities in New
Zealand: a national epidemiological study. Lancet 2012; 379:1112–1119.
29. Murray CJ, Kulkarni SC, Michaud C, et al. Eight Americas: investigating mortality disparities across races, counties, and race-counties in the United States. PLoS Med 2006;3: e260.
30. Esper AM, Moss M, Lewis CA, Nisbet R, Mannino DM, Martin GS. The role of infection and comorbidity: factors that influence disparities in sepsis. Crit Care Med 2006;34: 2576–2582.
31. Abebe SM, Berhane Y, Worku A. Barriers to diabetes medication adherence in North West Ethiopia. Springerplus 2014;3:195.
32. Waari G, Mutai J, Gikunju J. Medication adherence and factors associated with poor adherence among type 2 diabetes mellitus patients on follow-up at Kenyatta National Hospital, Kenya. Pan Afr Med J 2018;29:82.
33. Rwegerera GM. Adherence to anti-diabetic drugs among patients with type 2 diabetes mellitus at Muhimbili National Hospital, Dar es Salaam, Tanzania- a cross-sectional study. Pan Afr Med J 2014;17:252.
34. García-Pérez LE, Álvarez M, Dilla T, Gil-Guillén V, Orozco-Beltrán D. Adherence to therapies in patients with type 2 diabetes. Diabetes Ther 2013;4:175–194.
35. Borah B, Sacco P, Zarotsky V. Predictors of adherence among Alzheimer’s disease patients receiving oral therapy. Curr Med Res Opin 2010;26:1957–1965.
36. Poon I, Lal LS, Ford ME, Braun UK. Racial/ethnic disparities in medication use among veterans with hypertension and dementia: a national cohort study. Ann Pharmacother 2009; 43:185–193.
37. Cho MH, Shin DW, Chang SA, et al. Association between cognitive impairment and poor antihypertensive medication adherence in elderly hypertensive patients without dementia. Sci Rep 2018;8:11688.
38. Wieczorkiewicz SM, Kassamali Z, Danziger LH. Behind closed doors: medication storage and disposal in the home. Ann Pharmacother 2013;47:482–489.
39. Kaur G. Polypharmacy: the past, present and the future. J Adv Pharm Technol Res 2013;4:224–225.
40. Schuh JL, Hewuse AJ. The cost of unused medications. Fed Pract 2015;32:14–18.

Address correspondence to:
Peng Jiang, MS
Department of Health Care Administration and Management
Graduate School of Medical Sciences
Kyushu University
3-1-1 Maidashi
Fukuoka 812-8582
Japan

E-mail: jiang21peng@163.com