

STUDY PROTOCOL

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# Analysis of the evidence-practice gap to facilitate proper medical care for the elderly: investigation, using databases, of utilization measures for National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB)

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## Abstract

As Japan becomes a super-aging society, presentation of the best ways to provide medical care for the elderly, and the direction of that care, are important national issues. Elderly people have multi-morbidity with numerous medical conditions and use many medical resources for complex treatment patterns. This increases the likelihood of inappropriate medical practices and an evidence-practice gap. The present study aimed to: derive findings that are applicable to policy from an elucidation of the actual state of medical care for the elderly; establish a foundation for the utilization of National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB), and present measures for the utilization of existing databases in parallel with NDB validation.

Cross-sectional and retrospective cohort studies were conducted using the NDB built by the Ministry of Health, Labor and Welfare of Japan, private health insurance claims databases, and the Kyoto University Hospital database (including related hospitals). Medical practices (drug prescription, interventional procedures, testing) related to four issues—potential inappropriate medication, cancer therapy, chronic kidney disease treatment, and end-of-life care—will be described. The relationships between these issues and clinical outcomes (death, initiation of dialysis and other adverse events) will be evaluated, if possible.

**Keywords:** Claims data, Database, Elderly, Evidence-practice gap, Validation

## Background

As Japan becomes a super-aged society, the question of how medical care for the elderly is provided and the direction of that care are important national issues. Elderly people are physically frail and consequently often have multi-morbidity [1, 2], and thus, treatment patterns are often complex [3–5]. As a result, cases of polypharmacy in

elderly people are not uncommon in clinical practice [6]. Treatment guidelines have been created with the aim of avoiding this kind of potentially inappropriate medical care, but those recommendations are not always properly implemented in clinical practice. The problem of when evidence from clinical research and treatment guidelines is not utilized in practice is called an evidence-practice gap [7]. In the USA, there are reports on the state of evidence-based health care [8] and proposals for narrowing the gap in actual clinical practice [9–11].

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In Japan, the computerization of health and medical information is progressing, and large databases have been established. The utilization of these databases is an important issue. Since the mid-2000s, private companies have created databases of health insurance society claims that are used for research purposes [12, 13]. At the national level, National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) has been constructed together with enforcement of the “Act on Assurance of Medical Care for Elderly People” of 2008. Since 2011, the NDB has been used secondarily for research purposes.

These databases are the quantitative information to measure the actual state of medical environment. There are few research papers which reported the actual situation of medical care in elderly based on a large-scale of data in Japan [14, 15], however, none of the papers which discuss about evidence-practice gap in elderly in super-aging society based on large-scale of data as NDB can be found currently.

In this study, we validate NDB in the onsite research center at Kyoto University Hospital, settled by the Ministry of Health, Labor and Welfare of Japan, to elucidate the actual state of medical care for the elderly and actual situation of evidence-practice gap. Research procedures are shown as follows.

First, we validate and estimate reliability of NDB using a database of the Kyoto University Hospital (including associated hospitals database), and private health insurance claims databases. Additionally, we compare the characteristic points of each database through validation and show the guidance for choosing the database depend on specific purpose.

Secondly, we elucidate how medical care for the elderly is provided in a super-aging society in Japan. To elucidate, the following three examples are settling: 1. potential inappropriate medication (PIM), 2. cancer treatment, 3. chronic kidney disease (CKD) treatment. PIM was chosen because improper use of medicine and medicine interaction caused by multiple drug administration cause adverse events and impair quality of life (QOL) of the elderly. We will conduct research that will contribute to safe medication for the elderly. The reason for choosing cancer treatment is that cancer is the disease of the main topic even in the world [16] and it is the leading cause of death in Japan, too [17]. The reason for choosing CKD treatment is one of the major complications of lifestyle-related diseases, and if it can delay progress by early intervention, and it will lead to improvement of QOL.

We will select databases which suit for elucidating the actual situation of these three examples based on selection guidelines by validation of NDB.

Third, through finding aspects, we will discuss the evidence-practice gap. Also, we will assess the examples in the view of medical economics, because Japan will enter the super-aged society ahead of the world, the elderly population will continue to increase [18] and medical costs will be expected to increase. We will clarify the current situation of medical costs and lead to the creation of solutions.

For “PIM”, we will clarify the status of drug prescriptions that should be limited in elderly people and polypharmacy, and show findings that will serve to alert medical practitioners to this. In “Cancer treatment”, we will check the implementation status of treatment recommendation guidelines, which will contribute to normalization of proper treatment and elimination of disparities, and to develop a system for the provision of novel cancer care. For “CKD treatment,” we will clarify the implementation status of existing treatment quality indices, provide information that will contribute to efforts to prevent increasing severity by the insurer, and assess the effects on health care costs.

Then, comprehensively considering the findings through efforts related to the three examples above, we will focus on “Medical care provided to end-of-life elderly patients”, because QOL of elderly patients is that concerns not only elderly patients but also medical state in super-aging society as a whole. We will show the actual palliative care and other end-of-life care that is currently provided, and build a foundation for social discussion of the kind of medical care that is desirable for elderly people.

Finally, from the above, we will elucidate the current state of evidence-practice gap from the perspectives of both under- and over-treatment in the super-aging society of Japan, and analyze medical economically, together with presentation of ways to provide medical care in the future and directions for this care in aspect of epidemiology.

## Methods

### Materials

In Japan, all citizens are generally covered with public health insurance [19] as a whole.

In this study, the research questions will be analyzed using the data in the NDB, which holds billing information on more than 95% of the all current health insurance treatments under public health insurance system, Kyoto University Hospital databases including associated hospitals databases (CyberOncology<sup>®</sup>, p-Retriever<sup>®</sup>), and private databases shown as Fig. 1. NDB is a health insurance claims information and specific medical checkups information database. CyberOncology<sup>®</sup> is an in-hospital registry including insurance claims, test information, medical record, and clinical outcome information, that highly accurate analyses are possible. p-Retriever<sup>®</sup> is a database management system, including insurance claims and test information, which is possible to analyze













Purpose of use	Data	Level of information accuracy	Scale of information
Resolve issues to facilitate utilization	 Health insurance claim information and specific medical check information database (NDB)	Low  <ul style="list-style-type: none"> <li>Information accuracy unknown</li> <li>Existence of "insurance claim disease name"</li> <li>No verification of accuracy of information on bed number, clinical dept., etc.</li> <li>Almost no data cleaning done</li> </ul>	Large  <ul style="list-style-type: none"> <li>Very high exhaustiveness</li> </ul>
NDB validation + original use	 Private databases (Japan Medical Data Center etc.)	 <ul style="list-style-type: none"> <li>Included information is mainly insurance claim information and the same as the NDB (some DPC included)</li> <li>Data cleaning is done and analyses are easy.</li> </ul>	 <ul style="list-style-type: none"> <li>Consists of data from specific institutions, and data bias is inevitable.</li> <li>There are also databases on scales of hundreds of thousands to tens of millions of units.</li> </ul>
	 P-retriever® (Database management system)	 <ul style="list-style-type: none"> <li>In addition to information included in insurance claims, <b>test information</b> are also included. Wide range of analyses is possible.</li> </ul>	 <ul style="list-style-type: none"> <li>Consists of data from some medical institutions only (Kyoto University Hospital and cooperative medical institutions), and data bias is inevitable.</li> </ul>
	 CyberOncology® (In-hospital cancer registry)	 <ul style="list-style-type: none"> <li>In addition to information included in insurance claims <b>test, medical record, and clinical outcome information</b> are also included. Highly accurate analyses are possible.</li> </ul> High	 <ul style="list-style-type: none"> <li>Consists of data from one medical institution only (Kyoto University Hospital), and data bias is inevitable</li> </ul> Small

Fig. 1 Characteristics of the data used in this study

highly in wide range. Data that are suitable for achieving the aims of this study will be extracted from NDB. Both the NDB and private data consist mainly of health insurance claims, including basic patient information such as sex and age plus things such as the number of insurance points, the name of the illness or injury, medical practice information, and drug administration and prescription information. Information that is not included in health insurance claims data will be assessed in detail with complementary use of Kyoto University Hospital databases.

**Study structure**

This study is planned and implemented by a steering committee consisting of individuals from the Kyoto University Graduate School of Medicine, Kyoto University Hospital, and Division of Medical Information Technology and Administration Planning in Kyoto University Hospital.

**Schedule**

The study was prepared in 2014 and began in April 2015 and will continue until March 2017 (Fig. 2). The first fiscal year (2015) is centered on accumulating previous findings on the research questions, developing database systems, systemic review of validation studies, tentative analysis of the databases, and establishing an operational structure, environment, and regulations for the NDB onsite research center. In the second fiscal year (2016), analysis of the particulars of the NDB and other databases will be conducted and the direction for policy application will be investigated.

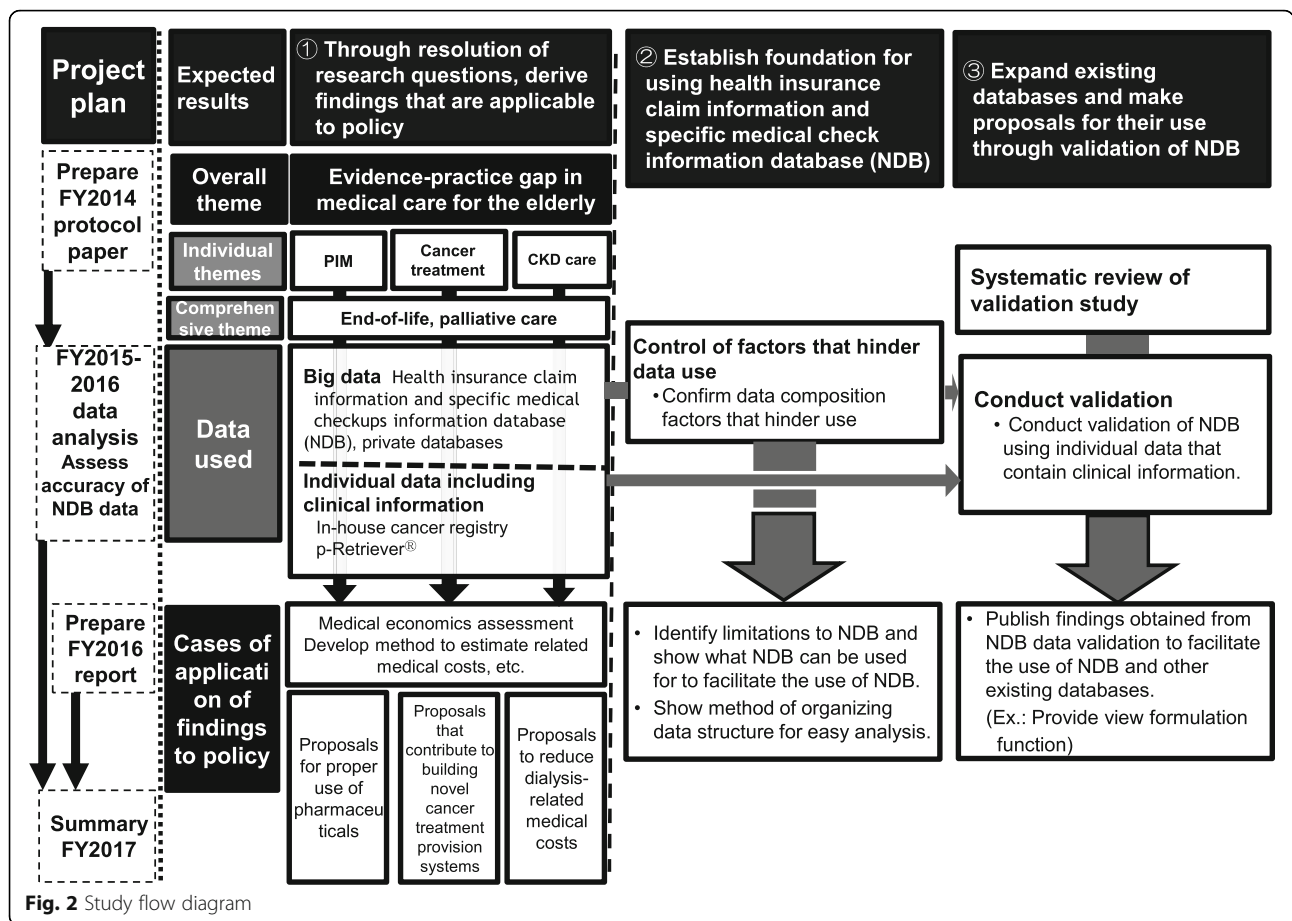
**Instruments**

**Methods for validation**

In secondary use of medical data, validation studies are recommended to assess the accuracy of definitions of things such as exposure and outcomes used in the study. Validation refers to comparison of the validity of information included in the data in question with other highly reliable information sources in secondary use when performing an investigation. Health insurance claims do not include test results, and the name of the disease does not necessarily reflect the patient's medical diagnosis due to insurance claims needs. Thus, caution is needed in analysis for research purposes since the "insurance claims disease name" is included. Health care data included in hospital databases includes test values, and since a more detailed picture of the patient can be obtained, the two need to be compared in validation as a reference to assess the validity of the health insurance claims disease name. Prior to the actual validation study in this study, a systematic review will be conducted of existing research on the validation of health insurance claims data.

**Three examples to elucidate the actual state of medical care for the elderly**

To elucidate the actual state of medical care for the elderly, this study has the three examples which are (1) potential inappropriate medication (PIM), (2) cancer treatment, (3) chronic kidney disease (CKD)treatment. The current state



of each example will be clarified below mentioned specified criteria based on NDB. After all, through all findings, the evidence-practice gap for elderly will be discussed and assessed medical economically.

**PIM**

**Elucidation of actual state of medical care for PIM**

The evidence to clarify the state of evidence-practice gap is STOPP (Screening Tool of Older person’s Potentially inappropriate Prescriptions) list of the Japan Geriatrics Society guidelines and the Japanese version of the Beers criteria [20–23]. We will specify drugs that are preferably avoided in elderly people following STOPP list and Beers criteria through NDB, based on the frequency of use of these drugs (number of prescriptions, dosage, concomitant medications including polypharmacy, etc.), incidence of new administration, related factors and association with adverse events (verification centered on diseases included in the Charlson Comorbidity Index). These findings will be analyzed by strata including sex, age, comorbidities, and place of treatment.

**Medical economics assessments** Database of the patients aged 70 will be focused on as that is when the individual payment rate increases from 30% to 10 or 20%, depends on the income, and the effect of the change in the individual payment rate on medical consultations and prescription behavior is analyzed.

**Cancer treatment**

**Elucidation of actual state of medical care for cancer treatment**

Since cancer is the leading cause of death in Japan [17], we focus on the actual medical state of cancer treatment. In the 5 major cancer disease in Japan (breast, colon and rectum, stomach, lung, liver), we will choose 3 kinds of cancer (stomach [24], colon and rectum [25], liver [26]). Checking the implementation status of treatment recommendation guidelines of 3 kinds of cancer [24–26] as criteria, following points will be elucidated; treatment patterns (operative procedure, anti-cancer agent prescription), implementation of standard treatment, occurrence of adverse events, treatment patterns that lead to better treatment efficacy and fewer adverse events, and medical costs analyzed by strata for age, presence of comorbidity, region, hospital function,

and hospital size. The Kyoto University Hospital database, CyberOncology®, which consists of treatment information which is not included in health insurance claims will be used for validation.

**Medical economics assessments** In a medical economics assessment, a regression analysis is conducted to see how much of the variation in medical costs can be explained by age, sex, and treatment pattern.

#### **CKD treatment**

**Elucidation of actual state of medical care for CKD treatment** In Japan, Statistically, the total number of patients with CKD is about 240,000 and the number of dialysis patients is 320,000, approximately 70% of dialysis patients occupied by over 65 years in 2015 [27]. Based on 11 different quality indices named Quality Indicators for Chronic Kidney Disease self-developed between 2010 and 2013 [28], we will choose seven different quality indices [ use of Renin-Angiotensin System (RAS) inhibitors, serum creatinine measurements in patients using RAS inhibitors, serum potassium measurements in patients using RAS inhibitors, fluid replacement in patients undergoing contrast-enhanced computerized tomography (CT), avoidance of regular use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), implementation of nutritional counseling, implementation of urinalysis [28–30] ] obtained from health insurance claims information will be measured. Treatment quality and associations with the start of dialysis treatment will be investigated longitudinally. Health insurance claims information at hospitals associated with Kyoto University that have introduced p-Retriever®, which can extract health insurance claims and test values, will be used for validation.

**Medical economics assessment** In a medical economics assessment, the effects of differences in treatment quality on patient symptoms are modeled and the effect of treatment quality on cost-effectiveness is evaluated.

#### **Medical care given to end-of-life elderly patients**

**Elucidation of actual state of medical care given to end-of-life elderly patients** Through NDB and private database, we will focus on the data of elderly of more than 65 years old [31, 32], and going backward from death from one month to one year, and clarified the content, frequency, and cost of medical care provided in the end-of-life stage. Prescriptions and implementation status are examined from the perspectives of both under- and over-treatment, particularly cardiopulmonary resuscitation, gastric fistula, blood transfusion, dementia medications, antihypertensive medication, cholesterol-lowering drugs, hypoglycemic

agents, osteoporosis drugs, anticancer agents, and palliative care. In health insurance claims, there is an “outcome” column, but it is not always filled in. When death as an outcome cannot be ascertained, the operational definition of a judgment of “death” in health insurance data from the suspension of treatment that had been continued up to that point is investigated. In parallel with an understanding of the end-of-life period retroactively from death, the actual medical behaviors above are determined with elderly people divided into age cohorts.

**Medical Economics Assessment** In a medical economics assessment, the medical care and the associated costs are investigated by region, by the type of care (hospital or home care), and by the type of disease (cancer, stroke, ischemic heart disease and dementia etc.).

#### **Strengths/Limitations**

The NDB contains exhaustive data including information on nearly all health insurance claims. However, the state of insurance claims information, such as disease name and other factors, do not reflect actual clinical status of patients. A number of previous studies have indicated that validation is a common issue worldwide when using databases, but there are almost no reports from Japan. The significance of this study is in raising the validity of findings obtained by carrying out validation studies, and in the suggestions it provides for precautions and further potential uses of health insurance claims information and specific medical checkups information and the NDB, in which such data is accumulated. At the same time, the study is limited by the fact that the NDB itself cannot be linked to other data, accordingly, the NDB cannot be directly validated, and comparisons with other health care information, such as insurance claims information and test values, must be done within limited groups, such as several medical institutions.

#### **Abbreviations**

BIDAME: Big Data Analysis of Medical care for the Elderly in Kyoto; CKD: Chronic kidney disease; CT: Computerized tomography; NDB: National Database of Health Insurance Claims and Specific Health Checkups of Japan; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; PIM: Potential inappropriate medication; QOL: Quality of life; RAS: Renin-Angiotensin System; STOPP: Screening Tool of Older person's Potentially inappropriate Prescriptions

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#### **Availability of data and material**

Not applicable.

**Authors' contributions**

TN contribute to make a plan of this research and general management of this research to carry out. YI will contribute for systematic review and carry out the economic assessment, YO will carry out to analyze data and discuss for cancer treatment, GK will contribute to manage progress strategy and make a structure of database setting to analyze, TK will make a structure of environment for database setting, RG will also contribute the economic assessment, ST will carry out systematic review and analyze for PIM, HT will also contribute systematic review, SF will manage of analysis for CKD, SF will contribute for systematic review and data analysis for CKD, MM will manage to analyze database and discuss for cancer treatment, MY will manage to analyze data base and discuss for CKD, YY will manage of analysis for PIM, and all other BiDAME members will join systematic review, management of research progress, setting up the technical environment to analyze database and contribute to analyze database for the medical care given to end-of-life elderly patients. All authors read and approved the final manuscript.

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**Competing interests**

The authors declare that they have no competing interests. Declarations of COI from each researcher are managed by Kyoto University.

**Consent for publication**

The Kyoto University Hospital databases (CyberOncology®, p-Retriever®) extract data within the Kyoto University Hospital from special servers through secure connections and create data sets for analysis that exclude information that could identify individuals (medical chart no. etc.). We also present the opt-out consent statement for the patients.

The NDB consists of unlinkable anonymized data, and individuals cannot be identified.

The private databases provided to researchers is unlinkable anonymized data sets, too.

**Ethics approval and consent to participate**

This study complies with the Helsinki Declaration and the "Ethical guidelines for medical and health research involving human subjects" of the Ministry of Education, Culture, Sports, Science and Technology, and the Ministry of Health, Labor and Welfare of Japan. This study has been reviewed and approved by a Ministry of Health, Labor and Welfare panel of experts and approved by the Kyoto University medical ethics committee (reference number: R0307).

The NDB consists of unlinkable anonymized data, and individuals cannot be identified. The Kyoto University Hospital databases (CyberOncology®, p-Retriever®) extract data within the Kyoto University Hospital from special servers through secure connections and create data sets for analysis that exclude information that could identify individuals (medical chart no. etc.). The private databases provided to researchers is unlinkable anonymized data sets that also cannot be combined at the company managing them.

The "Guidelines for the provision of National Database of Health Insurance Claims and specific Health Checkups of Japan" are followed in using NDB, and care is exercised so that aggregation items consisting of fewer than 10 patients are not used so that individuals are not identified [33, 34]. The data obtained in this study were not used for purposes other than this study and data sharing not applicable.

This study is an observational study using existing data, and matters of advantage or disadvantage to research participants, or that cause new invasion or adverse events to research participants, do not apply.

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**References**

- Fortin M, Lapointe L, Hudon C, Vanasse A, Ntutu AL, Maltais D. Multimorbidity and quality of life in primary care: a systematic review. *Health Qual Life Outcomes*. 2004;2:51.
- Metsemakers JF, Höppener P, Knottnerus JA, Kocken RJ, Limonard CB. Computerized health information in The Netherlands: a registration network of family practices. *Br J Gen Pract*. 1992;42(356):102–6.
- Dong HJ, Wresle E, Marcusson J. Multimorbidity patterns of and use of health services by Swedish 85-year-olds: an exploratory study. *BMC Geriatr*. 2013;13:120. doi:10.1186/1471-2318-13-120.
- Holzhausen M, Fuchs J, Busch M, Ernst A, Six-Merker J, Knopf H, Hapke U, Gaertner B, Kurzawe-Seitz I, Dietzel R, Schodel N, Welke J, Wiskott J, Wetzstein M, Martus P, Scheidt-Nave C. Operationalizing multimorbidity and autonomy for health services research in aging populations—the OMAHA study. *BMC Health Serv Res*. 2011;11:47. doi:10.1186/1472-6963-11-47.
- Schäfer I, Hansen H, Schön G, Maier W, Höfels S, Altiner A, Fuchs A, et al. The German MultiCare-study: patterns of multimorbidity in primary health care - protocol of a prospective cohort study. *BMC Health Serv Res*. 2009;9:145. doi:10.1186/1472-6963-9-145.
- Wise J. Polypharmacy: a necessary evil. *BMJ*. 2013;347:f7033. doi:10.1136/bmj.f7033.
- Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. *Lancet*. 2003;362(9391):1225–30.
- McGlynn EA, Asch SM, Adams J, Keesey J, Hicks J, DeCristofaro A, Kerr EA. The quality of health care delivered to adults in the United States. *N Engl J Med*. 2003;348(26):2635–45.
- Elliott JH, Turner T, Clavisi O, Thomas J, Higgins JP, Mavergames C, Gruen RL. Living systematic reviews: an emerging opportunity to narrow the evidence-practice gap. *PLoS Med*. 2014;11(2):e1001603. doi:10.1371/journal.pmed.1001603. eCollection 2014.
- Zwarenstein M, Hux JE, Kelsall D, Paterson M, Grimshaw J, Davis D, Laupacis A, Evans M, Austin PC, Slaughter PM, Shiller SK, Croxford R, Tu K. The Ontario printed educational message (OPEM) trial to narrow the evidence-practice gap with respect to prescribing practices of general and family physicians: a cluster randomized controlled trial, targeting the care of individuals with diabetes and hypertension in Ontario, Canada. *Implement Sci*. 2007;2:37.
- Holloway RG, Benesch C, Rush SR. Stroke prevention: narrowing the evidence-practice gap. *Neurology*. 2000;54(10):1899–906.
- Nakaoka S, Ishizaki T, Urushihara H, Satoh T, Ikeda S, Morikawa K, Nakayama T. Echocardiography for the detection of valvulopathy associated with the use of ergot-derived dopamine agonists in patients with Parkinson's disease. *Intern Med*. 2011;50(7):687–94. Epub 2011 Apr 1.
- Kirigaya D, Nakayama T, Ishizaki T, Ikeda S, Satoh T. Management and treatment of osteoporosis in patients receiving long-term glucocorticoid treatment: current status of adherence to clinical guidelines and related factors. *Intern Med*. 2011;50(22):2793–800. Epub 2011 Nov 15.
- Fukawa T. Inpatient expenditure of the descendent elderly in Japan. *BJMMR*. 2016;15(10):1–10.

15. Ooba N, Setoguchi S, Ando T, Sato T, Yamaguchi T, et al. Claims-based definition of death in Japanese claims database: validity and implications. *PLoS One*. 2013;8(5):e66116. doi:10.1371/journal.pone.0066116.
16. Bekelman JE, Halpern SD, Blankart CR, Bynum JP, Cohen J, Fowler R, et al. Comparison of site of death, health care utilization, and hospital expenditures for patients dying with cancer in 7 developed countries. *JAMA*. 2016;315(3):272–83.
17. Ministry of Health, Labour and Welfare Home Page. [http://www.mhlw.go.jp/toukei/saikin/hw/jinkou/kakutei15/dl/02\\_kek.pdf](http://www.mhlw.go.jp/toukei/saikin/hw/jinkou/kakutei15/dl/02_kek.pdf). Accessed 12 Jan 2017.
18. Ministry of Health, Labour and Welfare Home Page 2015 Edition. Labour and Welfare Report. Consideration of a depopulating society. Towards a society where people can live in peace and realize of their hope. Summary. <http://www.mhlw.go.jp/english/wp/wp-hw9/dl/summary.pdf>. Accessed 12 Jan 2017.
19. Ministry of Health, Labour and Welfare Home Page. <http://www.mhlw.go.jp/file/06-Seisakujouhou-12400000-Hokenkyoku/0000072791.pdf>. Accessed 11 Jan 2017.
20. American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2012;60(4):616–31. doi:10.1111/j.1532-5415.2012.03923.x.
21. Imai H, Fick DM, Waller JL, Maclean JR. Physician characteristics associated with prescription of inappropriate medications using Beers criteria. *Geriatr Gerontol Int*. 2007;7(4):380–7.
22. Imai I, Beers MH, Ficks DM, Niwata S, Otaki K. Koureisya ni okeru futekisetu na yakuzai syoho no kijun: Beers criteria no nihon ban no kaihatsu. *J Japan Med Assoc*. 2008;137(1):84–91.
23. Kojima T, Mizukami K, Tomita N, Arai H, Ohru T, Eto M, et al. Screening tool for older person's appropriate prescriptions in Japanese: report of the Japan Geriatrics Society working group on "Guidelines for medical treatment and its safety in the elderly". *Geriatr Gerontol Int*. 2016;16:983–1001.
24. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver.4). *Gastric Cancer*. 2017;20:1–19. doi:10.1007/s10120-016-0622-4.
25. Watanabe T, Itabashi M, Shimada Y, Tanaka S, Ito Y, Ajioka Y, et al. Japanese Society for Cancer of the Colon and Rectum. Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2014 for treatment of colorectal cancer. *Int J Clin Oncol*. 2015;20:207–39.
26. The Japan Society of Hepatology. Clinical Practice Guidelines for Hepatocellular Carcinoma 2013. [http://www.jsh.or.jp/English/guidelines\\_en/Guidelines\\_for\\_hepatocellular\\_carcinoma\\_2013](http://www.jsh.or.jp/English/guidelines_en/Guidelines_for_hepatocellular_carcinoma_2013). Accessed 10 Jan 2017.
27. The Japanese Society of Dialysis Therapy Home Page. <http://docs.jsdt.or.jp/overview/index.html>. Accessed 11 Jan 2017.
28. Fukuma S, Shimizu S, Niihata K, Sada K, Yanagita M, Hatta T, et al. Development of quality indicators for care of chronic kidney disease in the primary care setting using electronic health data: a RAND-modified Delphi method. *Clin Exp Nephrol*. (Published online: 04 May 2016). doi:10.1007/s10157-016-1274-8.
29. Fukuhara S. Kousei roudou kagaku kenkyuhoi hojyokin Rinsyo ekigaku kiban seibikenkyu jigyo: Rinsyo ekigaku kenkyu ni katuyou kanou nashinryo jyouhou platte form kouchiku ni kansuru kenkyu. *Kenkyuseika houkokusyo* (Heisei 20nendo-Heisei 22 nendo). 2011.
30. The RAND / UCLA Appropriateness Method User's Manual. Hayashino Y(translation). Kyoto, Department of Healthcare Epidemiology, Kyoto University Graduate School of Medicine, School of Public Health. 2010.
31. Ministry of Health, Labour and Welfare Home Page e-health net. <https://www.e-healthnet.mhlw.go.jp/information/dictionary/alcohol/ya-032.html>. Accessed 11 Jan 2017.
32. Act on Assurance of Medical Care for Elderly People. Roujin hoken ho. Law number: Act No.80 of 1982. <http://roppou.aichi-u.ac.jp/joubun/s57-80.htm>.
33. Guidelines for the Provision of National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) (2015, April revised). [http://www.mhlw.go.jp/file/05-Shingikai-12401000-Hokenkyoku-Soumuka/000064238\\_3.pdf](http://www.mhlw.go.jp/file/05-Shingikai-12401000-Hokenkyoku-Soumuka/000064238_3.pdf). Accessed 15 July 2016.
34. Pharmaceuticals and Medical Devices Agency 2014. Iryo jouho database wo motiita iyakuhiin no anzensei hyouka niokeru yakuzai ekigaku kenkyu no jissshi ni kansuru guideline.

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