| Article category                                                                                 |
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| Original article                                                                                 |
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| Title                                                                                            |
| Diagnostic difficulties and factors affecting diagnosis in acutely ill elderly Japanese patients |
| living at home                                                                                   |
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| Conflicts of interest                                                                            |
| The authors have no conflicts of interest directly relevant to the content of this article.      |
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| Running title                                                                                    |
| Diagnosis of acutely ill elderly patients at home                                                |
|                                                                                                  |
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#### **Abstract**

Background: Home visits by primary care physicians to elderly patients in Japan have increased as part of a government initiative to relieve pressure on acute care hospitals. However, there is evidence of discrepancies between diagnoses in the primary care and hospital settings.

Methods: We conducted a retrospective cross-sectional study using two years of medical records from a primary care center to investigate diagnostic accuracy of acutely ill elderly patients in the primary care setting, and reasons for emergency hospital admissions. We analyzed data from all cases where extra home visits were needed due to acute illness, and used inferential statistics to compare initial diagnosis with final diagnosis and analyze the factors affecting diagnostic accuracy.

Results: We analyzed 591 cases (mean age of patients: 85 years). The most common reasons for emergency hospitalization were respiratory, gastrointestinal, or cardiovascular diseases. There was a significant difference in initial diagnostic accuracy between respiratory diseases, gastrointestinal diseases, and other conditions (p=0.005); an accurate diagnosis was likely for respiratory diseases but unlikely for gastrointestinal diseases. Polypharmacy ( $\geq$ 8 medications) was associated with low diagnostic accuracy on multivariable logistic regression analysis (odds ratio, 0.24; 95% confidence interval, 0.06-0.67; p=0.006).

Conclusion: Primary care providers should note subtle symptoms and the number of

medications taken, provide follow-up, and consider gastrointestinal diseases when making a diagnosis following acute changes in an elderly patient.

# Keywords

Acute illness, diagnosis, elderly, polypharmacy, primary care

## 1. Introduction

The dramatic increase of the aged population is a pressing problem in Japan; the number of people aged 75 or over is expected to reach 22 million by 2025, accounting for 25% of the population. The Japanese government has promoted various long-term-care services, including home visits rather than inpatient admissions, to cope with this growing pressure on medical resources.<sup>2</sup> In the Japanese health insurance system, physicians visit elderly patients in their own homes or residential care twice monthly. If patients have more significant needs, urgent consultations or emergency hospital admissions can be arranged. As morbidity and mortality from infections, adverse effects of drugs, and other complications are greater in the elderly,<sup>3, 4</sup> physicians must often make prompt diagnoses when visiting elderly patients to manage their conditions appropriately.<sup>3</sup> However, deciding whether to admit patients can be difficult due to the limited diagnostic tools available during a home visit.<sup>5</sup> Functional disability, polypharmacy, lowered immunity, and other physiological decline<sup>5</sup> leading to comorbidities<sup>6-8</sup> may amplify the difficulty. However, as hospitalization is also a known risk factor for functional decline<sup>4, 5</sup> and other health problems in the elderly,<sup>9-11</sup> unnecessary hospitalization should be avoided.

Pretest probability is important in clinical decision making.<sup>12</sup> Irrespective of the medical setting, information on incidence and prevalence of a disease and consideration of the risk factors are essential to improve diagnostic accuracy.<sup>13</sup> We conducted a retrospective survey

using the medical records of elderly patients hospitalized as emergencies, and considered the clinical significance of our findings.

#### 2. Materials and Methods

The study was performed in a clinic providing primary-care home visits in a rural area of Okayama, Japan. The clinic was an outpatient family-medicine training center with three to six doctors, including family medicine residents. We reviewed medical records of patients receiving routine medical care in their own homes or care homes who were admitted to hospital as emergencies due to acute illness between January 1, 2011 and December 31, 2012. We defined emergency hospitalization as admission to the hospital within four days after additional home visits by primary-care physicians.

We collected and analyzed data on age, sex, number of medications taken, physician's clinical experience, number of days between home visit and hospitalization, proportion of patients who returned home three months after admission to the hospital, whether patients lived alone or with family members, place of residence (own home or care home), activities of daily living (ADL), level of care needed according to the Japanese long-term-care insurance system, <sup>1, 14</sup> Charlson Comorbidity Index (CCI), <sup>15</sup> updated CCI, <sup>16</sup> catheterization (gastrostomy and/or urinary catheter), nutritional status (last serum albumin level in the six months prior to hospitalization), initial diagnosis, final diagnosis, history of pneumonia, hospitalization within the previous year, history of gastrointestinal disease (peptic ulcer disease, biliary calculus, or hepatitis), and history of cardiovascular disease (cerebrovascular disease, congestive heart failure, myocardial infarction, or peripheral vascular disease). The level of care-need was

classified as levels 1-5, from no care required to constant support needed, based on expert evaluations of the patient's mental and physical status. According to previous studies<sup>17, 18</sup>, we further categorized the care-need levels into three groups: low-level (less than care level), middle-level (care-need level 1-2), high-level (care-need level 3-5). Need for greater support corresponded with a higher care-need level, lower ADL index, and lower cognitive function.

In all patients, the initial diagnosis was defined as the diagnosis recorded in the medical records following a home visit, after taking a medical history and performing a physical examination, simple blood tests (complete blood count [CBC], C-reactive protein [CRP] and blood glucose levels), urine analysis, and electrocardiogram. The final diagnosis was defined as the diagnosis made in secondary or tertiary medical facilities. Diagnoses were classified according to the International Classification of Diseases, 10<sup>th</sup> Revision (ICD-10); the initial diagnosis was considered accurate when the initial and final diagnoses were the same, or when the same differential diagnoses were included in both initial and final diagnoses. Diagnostic accuracy in this study was assessed by three physicians, each of whom had more than 10 years of clinical experience, including a fellow from the Japanese Society of Internal Medicine and a certified diplomate from the American Board of Family Medicine.

Student's t-test, the Wilcoxon rank-sum test, the chi-square test, and the Cochran-Armitage test for trend were used to analyze parametric, non-parametric, categorical, and discrete variables, respectively. The level of significance (p) was <0.05 for all tests. Statistical analysis

was carried out using JMP® Pro12 software (SAS Institute Inc., Cary, NC, USA).

The study was advertised on the Shimane University and primary care websites. All participants were presumed to consent unless they contacted the study group to opt out. As the study was retrospective, the requirement for written informed consent was waived by the Shimane University Institutional Committee on Ethics, which approved the study design.

#### 3. Results

No patient opted out of the study. We found that 125.5 patients per month lived at home or in care homes and had difficulty visiting medical surgeries. A total of 591 encounters (25 encounters/month) were extra domiciliary visits. A total of eight primary-care physicians took part in the study. In total, 81 encounters (68 patients, 3.4 cases/month) resulted in patients' admission to the hospital within four days of the initial home visit. Patients ranged from 57 to 101 years old (mean age: 85±8.5 years). The interval between the physician's visit and hospital admission was recorded as "same day" (n=35), "next day" (n=24), "two days later" (n=3), "three days later" (n=18), or "four days later" (n=1). Cases where the final diagnosis was not known (n=4) were excluded, leaving 77 of 81 cases eligible for this study. This number included multiple admissions of the same patient. As there was no significant difference in diagnostic accuracy on first admission and subsequent admissions for patients with multiple admissions (60% versus 54%; p=1.00), all emergency admissions were analyzed as independent events. Thirty percent (23/77) of the patients returned home three months after emergency hospitalization.

Primary reasons for emergency admission were pneumonia (n=28) followed by calculus of bile duct with cholangitis (n=5), and acute appendicitis (n=3) (Table 1). Initial diagnostic accuracy was 80% (24/30) for respiratory and 33.3% (6/18) for gastrointestinal diseases. Poor diagnostic accuracy of the latter was significantly higher in the older age group (p=0.03).

There was a slight but non-significant association between low ADL index and poor diagnostic accuracy (p=0.14). No association was observed with other variables, such as sex, dementia, history of gastrointestinal disease, history of cardiovascular disease, nutritional state, or indwelling catheter.

Table 2 shows the characteristics relating to initial diagnostic accuracy. The number of medications taken was associated with significantly low initial diagnostic accuracy (p=0.013for trend); the median value was nine in the incorrect and six in the correct diagnosis groups. Significantly low initial diagnostic accuracy was found with patients taking eight or more medications (43% diagnostic accuracy with ≥8 medications, versus 74% in <8 medications; p=0.006). We did not observe any association between the number of medications ( $\geq 8$ medications) and updated CCI score, but there was a significant positive association with history of cardiovascular disease (p<0.001). There was a significant difference in diagnostic accuracy between respiratory and gastrointestinal diseases, and other diagnoses. On home visits, respiratory diseases were more likely to be diagnosed than were gastrointestinal diseases. The number of medications included long-term medications, and excluded non-prescription analgesic drugs and eye drops, as the actual dosage for these was unknown. Table 3 shows the factors associated with initial diagnostic accuracy on multivariable logistic regression analysis. We found a significant association between patients taking eight or more medications and low initial diagnostic accuracy. This result remains even when we

included history of pneumonia and admissions over the last year, diabetes mellitus, malignancies, dementia, living alone, living in a residential care home, and history of gastrointestinal and cardiovascular diseases.

### 4. Discussion

When selecting variables, we focused on CCI, ADL, dementia, number of medications taken (≥8 medications), and the physician's clinical experience. The CCI is an index of comorbidities used to estimate one-year mortality. We used the updated CCI, which was developed according to new medical advances. Following previous studies, we categorized cases into four groups: 0, 1, 2, ≥3. 16, 19 A higher risk of fever has been noted in people with a low ADL index, such as wheelchair users or those who are bedridden, than in the ambulatory population. Poor cognition may increase communication difficulties and obscure signs of infection. Polypharmacy is reported to be associated with a decline in cognitive capacity or functional ability, using three groups: non-polypharmacy (0-5 medications), polypharmacy (6-9 medications) and excessive polypharmacy (≥10 medications). We followed this categorization in our study. An association has also been found between clinical performance of physicians and their length of time in practice or age. 23

Respiratory diseases, skin and soft tissue infections, and urinary tract infections have been reported as the leading causes of fever in elderly patients living at home.<sup>3,20</sup> We did not limit our study to new cases of fever, and found that most emergency admissions due to fever were for respiratory diseases (39%) followed by gastrointestinal diseases (26%). This discrepancy may be because skin, soft tissue, and urinary tract infections could be treated in an outpatient setting by oral or intravenous antibiotics, whereas gastrointestinal diseases such as

cholecystitis, cholelithiasis, or appendicitis require inpatient treatment. Another study<sup>24</sup> noted biliary tract disease as the most common reason for intra-abdominal surgery in the elderly, with the incidence of cholelithiasis more than 50% in patients over 70 years old. This may have accounted for differences in frequency of diagnoses.

In our study, gastrointestinal diseases had the lowest diagnostic accuracy. Crombie, 25 Hampton<sup>26</sup> and Sandler<sup>27</sup> reported that taking a history and conducting a physical examination contributed to 73-91% of the final diagnosis; another study<sup>28</sup> reported that simple investigations such as blood or urine tests, electrocardiograms, and radiography contributed to 81% of the final diagnosis. Our study indicated these factors had a 62% diagnostic value. The likely reason for this difference is the influence of factors such as the older age of patients and their backgrounds, difficulty in assessing patients' symptoms outside the surgery, doctors' level of experience, high mismatch rate in the emergency department,<sup>29</sup> and a wider range of diseases in our study. Diagnostic accuracy of abdominal conditions is reported to be lower in the elderly, <sup>22</sup> and as high as 40% of elderly patients with acute abdominal conditions have been reported as misdiagnosed.<sup>22, 28</sup> Poor diagnostic accuracy of gastrointestinal diseases in this study was highly associated with older age, and there was an association, albeit non-significant, with low ADL index.

Diagnostic errors have been categorized as no-fault errors (masked or unusual presentation of disease or patient-related errors); system-related errors (technical failure, equipment

problems, and organizational flaws); and cognitive errors (faulty knowledge, data gathering, and faulty synthesis).<sup>30</sup> In our study, one patient with appendicitis presented with only low-grade fever, a reported slight alteration in behavior, no abdominal pain or change in appetite, and normal gait. This shows that examination of elderly patients can result in inevitable no-fault errors because of masked or unusual presentation of symptoms, particularly within a primary-care setting. Acute appendicitis is reported to have an atypical presentation in the elderly<sup>31</sup> and is initially misdiagnosed in 40-50% of the elderly patients.<sup>24,31</sup>

Our study also revealed that it became more difficult to reach an early, accurate diagnosis in elderly patients who were taking eight or more medications, even though they were more severely ill. There was a significant association between taking eight or more medications and history of cardiovascular disease, since these patients tend to take more medications, which are usually difficult to reduce because of their importance in disease control. Although history of cardiovascular diseases was not directly related to poor diagnostic accuracy in our study, these patients take more medications, which may mask other conditions. "Taking eight or more medications" had a greater impact on accurate diagnosis than any other comorbidity in the patient's medical history. A study of polypharmacy noted that taking five or more medications decreased the diagnostic accuracy of tests for identifying frailty in older people.<sup>32</sup>

Our study has several limitations. First, it was a retrospective study using medical records.

Secondly, the quality of the medical records depended on each physician, and there is a possibility that physicians did not record information that they considered irrelevant. Thirdly, data for alternative medicines or over-the-counter drugs were not appropriately documented and were likely underestimated. Finally, this study was conducted on a relatively small number of patients at one medical facility. As the initial diagnoses in this study were made by only eight doctors at a single clinic, albeit representative of similar primary care clinics in Japan, caution should be exercised in extrapolating our results. Furthermore, although the number of medications was analyzed, their type was not evaluated.

In conclusion, it can be extremely challenging for primary care physicians to diagnose acute early-stage illnesses in the elderly, particularly during home visits. Respiratory diseases, followed by gastrointestinal diseases, were the main reasons for emergency hospital admissions in the elderly patients living at home and unable to visit medical facilities. Low initial diagnostic accuracy was associated with taking eight or more medications, possibly because signs of the disease were either masked or unusual. The number of medications was largely dependent on past history of cardiovascular diseases. We recommend that primary care physicians pay close attention to subtle symptoms and offer prudent follow-up, consider the possibility of gastrointestinal diseases, and take into account polypharmacy and history of cardiovascular disease when forming a diagnosis involving an acute change in an elderly patient.

## **Funding/support statement**

The Department of General Medicine, Faculty of Medicine Shimane University is an endowment department, supported by Ohda City.

## Acknowledgments

The authors would like to thank Professor Kristina Sundquist and Professor Jan Sundquist from the Center for Primary Health Care Research, Department of Clinical Sciences, Lund University for help in interpreting the results of this study.

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identifying frailty in community-dwelling older people: a systematic review. *Age Ageing*. 2015;44:148-152.

Table 1 Main reasons for emergency admission, classified according to ICD-10 (n=77)

| T. C.1:                 | ]     | Main reasons for emergency admission   |     |
|-------------------------|-------|----------------------------------------|-----|
| Type of disease         | Code  | Final diagnosis                        | — n |
| Endocrine, metabolic    | F97.5 | TT 1.1.                                | 1   |
| disorder                | E87.5 | Hyperkalemia                           | 1   |
|                         | F05.1 | Delirium superimposed on dementia      | 1   |
| Psychiatric and nervous | F19   | Other psychoactive substance-related   | 1   |
| diseases                | F19   | disorders                              | 1   |
|                         | G06.0 | Intracranial abscess                   | 1   |
|                         | I50   | Heart failure                          | 3   |
|                         | I21   | Acute myocardial infarction            | 1   |
|                         | I63   | Cerebral infarction                    | 1   |
| Cardiovascular system   | I61.9 | Nontraumatic intracerebral hemorrhage  | 1   |
|                         | I26.9 | Pulmonary embolism                     | 1   |
|                         | I73   | Peripheral vascular disease            | 1   |
|                         | J18   | Pneumonia                              | 28  |
| Respiratory system      | 1440  | Chronic obstructive pulmonary disease  | 2   |
|                         | J44.0 | with acute lower respiratory infection | 2   |

|                         | K80.3 | Calculus of bile duct with cholangitis    | 5 |
|-------------------------|-------|-------------------------------------------|---|
|                         | K85.1 | Biliary acute pancreatitis                | 2 |
|                         | K81.0 | Acute cholecystitis                       | 2 |
|                         | K35   | Acute appendicitis                        | 3 |
| Contraintentinal avatam | K40   | Inguinal hernia                           | 1 |
| Gastrointestinal system | K44   | Diaphragmatic hernia                      | 1 |
|                         | K26.0 | Duodenal ulcer                            | 1 |
|                         | K65.0 | Acute peritonitis                         | 1 |
|                         | K52   | Noninfective gastroenteritis and colitis  | 1 |
|                         | A09   | Infectious gastroenteritis and colitis    | 1 |
|                         | B02.8 | Herpes zoster with other complications    | 1 |
| Skin                    | L89   | Decubitus ulcer and pressure area         | 1 |
|                         | L88   | Pyoderma gangrenosum                      | 1 |
| Musculoskeletal system  | M11.2 | Chondrocalcinosis, elbow                  | 1 |
| Urogenital system       | N71   | Inflammatory disease of uterus            | 1 |
|                         | N10   | Acute pyelonephritis                      | 1 |
|                         | S32.0 | Fracture of unspecified lumbar vertebra   | 1 |
| Damage                  | S22.0 | Fracture of thoracic vertebra             | 1 |
|                         | S70.9 | Unspecified superficial injury of hip and | 1 |

|        | _             | thigh                                    |    |
|--------|---------------|------------------------------------------|----|
|        | G <b>72</b> 0 | Fracture of unspecified part of neck of  | 2  |
|        | S72.0         | femur                                    | 2  |
|        | T02.1         | Fracture of lumbar and thoracic vertebra | 1  |
|        | C22.0         | Liver cell carcinoma (rupture)           | 1  |
|        | C18           | Malignant neoplasm of colon              | 1  |
| Others | R56.8         | Unspecified convulsions                  | 1  |
|        | R50.9         | Fever, unspecified                       | 1  |
|        | Z43.1         | Attention to gastrostomy                 | 1  |
| Total  |               |                                          | 77 |

ICD-10 = International Classification of Diseases 10th Revision, 2014

Table 2 Characteristics of incorrect and correct diagnoses at initial medical examination (n=77)

|                                                            | Initial diagno     | Initial diagnostic accuracy |                      |  |
|------------------------------------------------------------|--------------------|-----------------------------|----------------------|--|
| X7 : 11                                                    | Incorrect          | Correct                     |                      |  |
| Variable                                                   | diagnosis          | diagnosis                   |                      |  |
|                                                            | n <sup>i</sup> =29 | n°=48                       |                      |  |
|                                                            | Mean $\pm$ SD      | $Mean \pm SD$               | P-value <sup>a</sup> |  |
| Age                                                        | $85.6 \pm 7.1$     | $84.3 \pm 7.1$              | 0.48                 |  |
| Physician's clinical experience (years)                    | $9.8 \pm 6.6$      | $7.6 \pm 4.9$               | 0.17                 |  |
| Albumin (g/dL) (n <sup>i</sup> =23 vs. n <sup>c</sup> =42) | $3.44 \pm 0.5$     | $3.39 \pm 0.5$              | 0.46                 |  |
|                                                            | n                  | n                           | $P$ -value $^b$      |  |
| Sex (female)                                               | 18                 | 21                          | 0.11                 |  |
| Final diagnosis:                                           |                    |                             |                      |  |
| Respiratory system                                         | 6                  | 24                          | 0.005*               |  |
| Gastrointestinal system                                    | 12                 | 6                           |                      |  |
| Others                                                     | 11                 | 18                          |                      |  |
| Diabetes mellitus                                          | 7                  | 4                           | 0.05                 |  |
| Malignancy                                                 | 5                  | 7                           | 0.75                 |  |

| Dementia                                                        | 13 | 29  | 0.18   |
|-----------------------------------------------------------------|----|-----|--------|
| History of pneumonia in the last year                           | 7  | 14  | 0.63   |
| History of admission over the last year                         | 19 | 24  | 0.18   |
| History of digestive disease                                    | 6  | 10  | 0.98   |
| History of circulatory disease                                  | 21 | 24  | 0.06   |
| Number of medications:                                          |    |     |        |
| Non-polypharmacy                                                | 7  | 20  | 0.013* |
| Polypharmacy                                                    | 10 | 21  |        |
| Excessive polypharmacy                                          | 12 | 7   |        |
| Returning home ratio at 3 months after                          | 0  | 1.5 | 0.20   |
| admission to hospital                                           | 8  | 15  | 0.29   |
| Patients living alone                                           | 6  | 7   | 0.48   |
| Patients living in residential care                             | 3  | 7   | 0.69   |
| ADL (wheelchair users or bedridden)                             | 10 | 22  | 0.32   |
| Level of care need (n <sup>i</sup> =28 vs. n <sup>c</sup> =45): |    |     |        |
| Low-level                                                       | 5  | 3   | 0.28   |
| Middle-level                                                    | 8  | 15  |        |
| High-level                                                      | 15 | 27  |        |
| Gastrostomy                                                     | 5  | 5   | 0.39   |

| Urinary catheter | 4  | 6  | 0.87 |
|------------------|----|----|------|
| Updated CCI:     |    |    |      |
| 0                | 3  | 2  | 0.73 |
| 1                | 0  | 2  |      |
| 2                | 6  | 18 |      |
| 3 or more        | 20 | 26 |      |

<sup>&</sup>lt;sup>a</sup> Wilcoxon rank-sum test

ADL = activities of daily living; SD = standard deviation; CCI = Charlson comorbidity index

<sup>&</sup>lt;sup>b</sup> Differences between groups were assessed using the Chi-square test. Number of medications, level of care-need, and updated CCI were analyzed using the Cochran-Armitage test for trend in proportion

<sup>&</sup>lt;sup>i</sup> incorrect diagnosis; <sup>c</sup> correct diagnosis

<sup>\*</sup> P < 0.05

Table 3 Factors associated with initial diagnostic accuracy on multivariable logistic regression analysis (n=77)

|                                 | Model           | 1       | Model 2          |         |  |
|---------------------------------|-----------------|---------|------------------|---------|--|
| Variable                        | OR (95% CI)     | P-value | OR (95% CI)      | P-value |  |
| 0.98                            |                 |         | 0.98             | 0.61    |  |
| Age (per 1 year) <sup>a</sup>   | (0.90-1.08)     | 0.71    | 0.71 (0.89-1.07) |         |  |
| g (2 1)                         | 0.48            | 0.10    | 0.36             |         |  |
| Sex (female)                    | (0.15-1.43)     | 0.18    | (0.09-1.18)      | 0.09    |  |
| Number of medications           | 0.24            | 0.005#  | 0.22             | 0.002*  |  |
| (≥8 drugs)                      | (0.06-0.67)     | 0.006*  | (0.07-0.61)      | 0.003*  |  |
| Physician's clinical            | 0.93            | 0.00    | 0.92             | 0.06    |  |
| experience (years) <sup>a</sup> | (0.84-1.02)     | 0.09    | (0.83-1.01)      | 0.06    |  |
| V. 1. 100                       | 0.94            | 0.66    | 0.94             | 0.62    |  |
| Updated CCI                     | (0.71-1.26)     | 0.66    | (0.71-1.25)      | 0.63    |  |
| ADL (wheelchair users           | 1.1 (0.27.2.22) | 0.05    |                  |         |  |
| or bedridden)                   | 1.1 (0.36-3.33) | 0.85    |                  |         |  |
| Catheterization                 |                 |         | 0.34             | 0.16    |  |
| (gastrostomy and/or             |                 |         | (0.06-1.59)      | 0.16    |  |

urinary catheter)

<sup>a</sup> Per 1-year increase

ADL = activities of daily living; CI = confidence interval; OR = odds ratio; CCI =

Charlson comorbidity index

\* P < 0.01