

**Table 1** Baseline characteristics of participants classified by the presence or absence of OPLL

	Total (N=1,562)			Men (N=524)			Women (N=1,038)		
	OPLL (-) N=1,532	OPLL (+) N=30	<i>p</i>	OPLL (-) N=507	OPLL (+) N=17	<i>p</i>	OPLL (-) N=1,025	N=1,025 N=13	<i>p</i>
Age distribution (prevalence, %)									
30 years and younger	43	0 (0.0)		12	0 (0.0)		31	0 (0.0)	
40–49 years	141	1 (0.7)		39	0 (0.0)		102	1 (1.0)	
50–59 years	291	7 (2.4)	0.729	92	3 (3.2)	0.604	199	4 (2.0)	0.787
60–69 years	449	9 (2.0)		142	4 (2.7)		307	5 (1.6)	
70–79 years	468	11 (2.3)		175	9 (4.9)		293	2 (0.7)	
80 years and older	140	2 (1.4)		47	1 (2.1)		93	1 (1.1)	
Age (years), mean (SD)	62.9 (12.1)	67.0 (9.3)	0.3495	66.0 (11.7)	70.7 (8.0)	0.0990	64.4 (12.2)	62.2 (9.0)	0.5069
Height (cm), mean (SD)	154.9 (9.1)	159.1 (7.5)	0.0132*	163.3 (7.0)	163.9(5.4)	0.7414	150.8 (6.9)	152.8 (4.6)	0.2945
Weight (kg), mean (SD)	55.0 (10.3)	60.3 (10.1)	0.0053**	61.6 (10.5)	62.7 (8.2)	0.6759	51.7 (8.5)	57.1 (11.7)	0.0219*
BMI (kg/m <sup>2</sup> ), mean (SD)	22.8 (3.2)	23.8 (3.4)	0.1135	23.0 (3.1)	23.3 (2.1)	0.7434	22.7 (3.3)	24.4 (4.6)	0.0671
Residing in the coastal area (%)	49.4	53.3	0.671	46.4	58.8	0.311	50.9	46.2	0.732
Current smoking habit (regularly, ≥1/month) (%)	12.9	23.3	0.095	31.1	41.2	0.377	3.8	0.0	0.472
Current alcohol consumption (regularly, ≥1/month) (%)	39.1	43.3	0.637	66.1	64.7	0.907	25.8	15.4	0.395
Total cholesterol (mg/dL), mean (SD)	208.8 (34.5)	209.6 (36.2)	0.8954	198.6 (34.1)	204.4 (33.5)	0.4874	213.8 (33.6)	216.4 (39.8)	0.7840
Uric acid (mg/dL), mean (SD)	4.84 (1.30)	5.24 (1.21)	0.0943	5.71 (1.26)	5.71 (1.03)	0.9867	4.42 (1.09)	4.65 (1.21)	0.4528
HbA1c (Japan Diabetes Society) (%), mean (SD)	5.17 (0.70)	5.38 (0.79)	0.1124	5.20 (0.79)	5.44 (0.95)	0.2162	5.16 (0.64)	5.29 (0.56)	0.4595
Serum levels of iPTH (pg/mL), mean (SD)	41.2 (34.4)	41.2 (14.2)	0.9952	42.6 (54.4)	41.1 (13.9)	0.9083	40.5 (17.4)	41.3 (15.1)	0.8748
Serum levels of PINP (µg/L), mean (SD)	57.9 (27.0)	52.6 (29.9)	0.2915	47.5 (22.0)	42.6 (14.9)	0.3619	63.1 (27.8)	65.8 (39.2)	0.7301
Urinary levels of β-CTX (µg/mmol Cr), mean (SD)	187.2 (121.3)	150.4 (79.1)	0.0985	128.4 (78.7)	119.8 (58.3)	0.6529	216.2 (128.0)	190.5 (86.8)	0.4693
Plasma levels of pentosidine (µg/mL), mean (SD)	0.058 (0.037)	0.085 (0.140)	0.0005***	0.061 (0.048)	0.102 (0.184)	0.0042**	0.057 (0.030)	0.062 (0.037)	0.5012
BMD of the lumbar spine L2-4 (g/cm <sup>2</sup> ), mean (SD)	0.925 (0.205)	1.084 (0.205)	<0.0001***	1.038 (0.203)	1.176 (0.176)	0.0058**	0.868 (0.181)	0.965 (0.181)	0.0575
BMD of the femoral neck (g/cm <sup>2</sup> ), mean (SD)	0.667 (0.137)	0.747 (0.134)	0.0016**	0.739 (0.132)	0.797 (0.110)	0.0727	0.631 (0.124)	0.681 (0.139)	0.1558
Presence of LS (KL grade≥2) (%)	61.8	83.3	0.016*	76.1	100.0	0.022*	54.7	61.5	0.624
Presence of KOA (KL grade≥2) (%)	49.5	56.7	0.440	41.4	41.2	0.986	53.6	76.9	0.093
Presence of DISH (%)	9.4	33.3	<0.001***	0.7	52.9	0.002**	3.8	7.7	0.469

OPLL ossification of posterior longitudinal ligament, SD standard deviation, BMI body mass index, HbA1c haemoglobin A1c, iPTH intact parathyroid hormone, PINP N-terminal propeptide of type I procollagen, β-CTX β-isomerised C-terminal cross-linking telopeptide of type I collagen, BMD bone mineral density, LS lumbar spondylosis, KOA knee osteoarthritis, KL grade Kellgren–Lawrence grade, DISH diffuse idiopathic skeletal hyperostosis, OPLL(-) absence of OPLL, OPLL(+) presence of OPLL

\**p*<0.05; \*\**p*<0.01; \*\*\**p*<0.001

**Table 2** Odds ratios of potential factors associated with the presence of OPLL vs. the absence of OPLL

Explanatory variables	Reference	OR	95 % CI	<i>p</i>
Age (years)	+1 year	1.03	0.98–1.07	0.269
Gender	0 = men, 1 = women	1.30	0.39–4.34	0.666
Height (cm)	+1 cm	1.04	0.96–1.12	0.352
Weight (kg)	+1 kg	1.00	0.96–1.05	0.909
Pentosidine ( $\mu\text{g}/\text{mL}$ )	+0.01 $\mu\text{g}/\text{mL}$	1.05	1.00–1.09	0.038*
BMD (femoral neck) ( $\text{g}/\text{cm}^2$ )	+1 SD	1.55	1.04–2.33	0.033*
Presence of LS (KL grade $\geq$ 2)	0 = no, 1 = yes	1.94	0.67–5.61	0.219
Presence of DISH	0 = no, 1 = yes	2.78	1.11–6.92	0.029*

Logistic regression analysis was performed using the status of OPLL as the objective variable (0 = absence, 1 = presence), and the abovementioned factors were correspondingly adjusted

*OPLL* ossification of posterior longitudinal ligament, *BMD* bone mineral density, *LS* lumbar spondylosis, *KL grade* Kellgren–Lawrence grade, *DISH* diffuse idiopathic skeletal hyperostosis, *SD* standard deviation, *OR* odds ratios, *95 % CI* 95 % confidence interval

\* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$

association of plasma pentosidine levels and DISH weakened (plasma pentosidine +0.01  $\mu\text{g}/\text{mL}$ , 1.04, 0.997–1.087,  $p = 0.069$ ; presence of DISH 2.37, 0.94–6.00,  $p = 0.069$ ).

#### New occurrence or progression of OPLL

During the three study years, 1,380 individuals (88.3 %; 466 men, 914 women) among the 1,562 subjects at baseline returned for follow-up, and their radiographs were available for observation. Among the 30 individuals with radiographic cervical OPLL at baseline, 25 (83.3 %; 14 men and 11 women) participated in the second survey.

The remaining 1,355 individuals who did not have cervical OPLL at baseline and who participated in the initial and second surveys were regarded as members of the population at risk for the occurrence of OPLL. Among them, only one woman was diagnosed with newly developed radiographic OPLL (incidence 2.46/10,000 per year).

At follow-up, the mean length (in millimetres, SD) and width (in millimetres, SD) of the maximum region of ossification among the 25 individuals with OPLL was 28.7 (16.1) and 3.5 (1.5) mm, respectively. Since the mean values of length and width of the maximum region of ossification of these 25 subjects were 27.0 (16.2) and 3.0 (1.5) mm at the baseline, respectively, both the length and width of the maximum region of ossification increased, although a significant difference was not observed.

To clarify the risk factors associated with this increase in the length and width of the ossification, we performed multivariate regression analysis using the rate of change in these parameters as objective variables and the explanatory variables as those used in the logistic regression analysis, namely height (in centimetres), weight (in kilograms), plasma pentosidine levels (+1  $\mu\text{g}/\text{mL}$ ), BMD of the femoral neck (+1 SD), presence of LS based on the KL grade (0 = KL grade 0 or 1, 1 = KL grade $\geq$ 2)

and DISH (0 = absence, 1 = presence). Adjustments for age (years) and gender (0 = men, 1 = women) were made. However, none of the abovementioned variables was found to be significantly associated with the rate of changes in the length or width.

#### Discussion

In the present population-based study, we clarified the prevalence of radiographic OPLL in the general Japanese population, and we found that it is significantly associated with high plasma pentosidine levels, high BMD and the presence of DISH. The 3-year follow-up study also showed that new cases were very rare, and the length and width of the maximum region of ossification among the subjects with OPLL tended to increase.

The prevalence of OPLL in Japan has been reported to be 1.9 to 4.3 % among individuals aged 30 years and older [1, 15–17]. In other Asian countries, such as in Korea [18, 19] and Taiwan [20], a similar prevalence was reported, but it was lower in Western countries [21], suggesting that ethnic and/or genetic factor(s) could be associated with the onset of OPLL. In the present study, the prevalence of OPLL was found to be 1.9 %. This is consistent with the value found in previous reports. However, it is difficult to clearly distinguish localised-type OPLL from osteophytic changes, and we included two individuals with localised-type OPLL in the OPLL group. Thus, we may have overestimated the presence of radiographic OPLL. If we exclude individuals with localised-type OPLL from the OPLL group, the prevalence of the OPLL in the present study is 1.8 %.

With regard to the gender difference in OPLL prevalence, the prevalence was previously reported to be three times higher in men than in women [22]. We found that men are 2.5 times more likely to have OPLL than women (men 3.2 %, women

1.3 %), which is consistent with results reported previously among Japanese subjects. In contrast, symptomatic OPLL was reported to be usually observed in the sixth decade of life [22], although we were unable to find a significant association between age and the presence of OPLL. This might be explained by the fact that previous studies on the characteristics of OPLL were performed on the subjects with symptomatic OPLL, i.e. they had been clinically diagnosed with OPLL, while our subjects had radiographic OPLL that had not been clinically diagnosed. If the OPLL in our subjects progresses in the future, the peak age at which the symptoms could be expressed may be their 60s.

With regard to the comorbidities of OPLL, several reports have indicated that obesity and DM might be associated with OPLL [5, 6]. In the present study, the values of BMI tended to be higher in the group with OPLL than in that without OPLL, although this difference was not significant. A similar pattern was found in the values of HbA1c, and this finding could be explained by previous findings that the extent of ossification was significantly associated with the fasting serum insulin level but not with the fasting glucose level or the HbA1c level [23]. However, in the ROAD study, since all subjects could not be requested to fast, we could not confirm the association between fasting serum insulin levels and OPLL.

With regard to the association between biochemical markers of bone turnover and OPLL, Matsui et al. showed that the levels of the bone markers serum procollagen type I carboxyl-terminal peptide and intact osteocalcin were higher in patients with OPLL than in normal subjects [24]. This suggested that OPLL was associated with biochemical markers of bone turnover. In the present study, to evaluate the role of bone metabolism in OPLL, we compared the serum levels of iPTH and PINP as bone formation markers and the urinary levels of  $\beta$ -CTX between the groups with and without OPLL. However, we could not find significant differences between the groups.

Instead, the plasma pentosidine levels of the OPLL group were found to be significantly higher than those of the group without OPLL. This tendency remained after potential associated factors were adjusted for. Pentosidine is an advanced glycation end product, products generated by the sequential nonenzymatic glycosylation of protein amino groups [25] that accumulate in various tissues including kidney and coronary arteries, resulting in the development of diabetic vascular complications [26]. The concentrations of pentosidine in cortical and trabecular bone are reported to be adversely associated with bone strength [27–29]. Yamamoto et al. [30] found that serum pentosidine levels were positively associated with the presence of vertebral fractures in postmenopausal women with type 2 diabetes. Renal insufficiency was reported to be a dominant determinant of serum pentosidine levels [31] because of which serum pentosidine levels are increased in patients with chronic renal failure [32, 33]. However, no report has shown the association between pentosidine levels and the

presence of OPLL. On the basis of the abovementioned reports, we performed multivariate logistic regression analysis using the same explanatory factors we had used in the analysis shown in Table 2, along with the estimated glomerular filtration rate. We found that the plasma pentosidine levels were still significantly related to the presence of OPLL (OR, 1.05; 95 % CI, 1.00–1.09;  $p=0.042$ ). We speculate that the levels of pentosidine might be associated with ectopic ossification, such as vascular calcification in patients with renal dysfunction, or the presence of OPLL, directly or indirectly, although the currently available information is inadequate to prove this hypothesis. One reason for the inadequacy of the information obtained in this study could be that we did not evaluate genetic factors in the present study. Further investigations are needed to clarify whether the observed relationship between pentosidine levels and OPLL remains after analysis of other possible confounders, including genetic factors.

In addition to the biochemical markers, high BMDs have been observed in patients with OPLL [24, 34, 35]. However, Morio et al. reported that the BMD was lower in patients with advanced OPLL [36], suggesting that the disuse atrophy may result during advanced-stage OPLL. Our results also showed that subjects with OPLL had higher BMDs. However, the subjects in the present study all had radiographically determined OPLL but few clinical symptoms, so their condition may not have been in the advanced stage. Therefore, based solely on the results of the present study, we were unable to discuss the association between BMD and advanced-stage OPLL.

Several reports have shown that the coexistence of OPLL and DISH is quite common [4, 7, 8]. The pathogenesis of DISH and OPLL has been speculated to be similar, although the details remain unclear. For example, Havelka et al. analysed intron 6 (–4) polymorphisms in the COL 11 A2 gene in Czech patients with DISH and Japanese patients with OPLL, but they found no agreement between the data of subjects with DISH and OPLL [37]. Additional studies with a broader spectrum of genotyping and a larger cohort of patients may clarify the presence or absence of genetic relations between DISH and OPLL.

Few studies have been reported regarding the incidence of OPLL in the general population because OPLL is relatively rare and based on ethnicity, as noted. Using data collected in a pilot study in the corporation of 360 Japanese hospitals [3], Tsuyama described the incidence of OPLL and found that 2,142 patients were treated in these hospitals and the estimated incidence of OPLL was 19 patients per million persons of the total population [3]. In the present study, only one new case of OPLL was detected, so we could not accurately estimate the incidence of OPLL and compare our results to those of previous reports. In order to confirm the incidence of OPLL, we need to follow this cohort for a longer time.

Several studies have investigated the course of OPLL. Chiba et al. use computer-assisted measurement to examine OPLL

progression, and they found that the rate of OPLL progression was 56.5 % over 2 years, and this rate was most common in younger patients with continuous- and mixed-type OPLL [38]. Murakami et al. followed the case of a 67-year-old man who had had cervical OPLL for more than 26 years, and they found that the rate of OPLL progression was 2.2, 8.8 and 2.0 mm/year from 1–4, 4–8 and 8–10 years after the first visit, respectively [39]. However, to our knowledge, no study has reported the progression of radiographically defined OPLL in the general population. In the present study, we found that both the length and width of the maximum region of ossification increased during the 3 years of the study, although it was not a significant change. A previous report [39] found no evidence of OPLL progression after 10 years. We must carefully examine whether or not radiographically defined OPLL progresses to clinical OPLL.

This study has several limitations. First, although the ROAD study includes a large number of participants, these participants may not truly be representative of the general population. To address this, we compared the anthropometric measurements and the frequencies of smoking and alcohol consumption between the study participants and the general Japanese population. No significant differences were found, with the exception that male ROAD study participants aged 70–74 years were significantly smaller in terms of body structure than men from the overall Japanese population ( $p < 0.05$ ) [10]. This difference should be considered when evaluating potential risk factors for men aged 70–74 years; factors such as body build, particularly weight, are known to be associated with metabolic risk factors and KOA. Therefore, our results may have underestimated the prevalence of these conditions. Second, the total number of subjects with confirmed OPLL was very small, which might make the results somewhat less credible. In the present study, we used logistic regression analysis to adjust for gender differences. When the total number of the objective variable, namely OPLL cases, is small, using the multivariate model to adjust for gender differences may be more useful than using a gender-specific analysis. This is because the total number of cases in a gender-specific analysis will be even smaller, which reduces the statistical power. Although the significant associations between OPLL and the plasma levels of pentosidine and between OPLL and DISH were observed only in men in the simple comparative analysis, the pentosidine levels and DISH remained significant factors associated with the presence of OPLL even in the logistic regression analysis with adjustments for gender. We interpreted this result to mean that the female sex might dilute the strength of the association between OPLL and DISH, but the tendency in both genders remained significant.

To clarify the effect of sex differences in the interaction among OPLL, pentosidine levels and DISH, the logistic regression analysis was performed in men and women separately

(Supplementary Table 1). In this logistic regression analysis, the presence of OPLL was significantly associated with the pentosidine levels and femoral neck BMD in men, but the association of OPLL with the presence of DISH was diluted to a marginal association ( $p=0.080$ ). Further, since all male patients with DISH had radiographic LS, we could not evaluate the association between OPLL and LS. In women, the associations among OPLL, pentosidine levels and DISH were not significant. Although these results may indicate that the significant associated factors were observed only in men, they may even be skewed by the small number of female cases. Under these circumstances, it is difficult to distinguish which model should be used, i.e. logistic regression analysis or the multivariate model. It may be necessary to first include an adequate number of OPLL cases before this can be decided. To compensate for these limitations, we decided to include the urban cohort of the ROAD study in the OPLL survey. Thus, more participants will be included in the third ROAD survey planned from 2012 to 2013, and further detailed investigation regarding the risk factors for the presence, occurrence or exacerbation of OPLL may be possible.

In summary, the present study clarified that the prevalence of radiographic cervical OPLL in 1,562 individuals was 1.9 %, which was significantly higher in men than in women ( $p=0.007$ ), but no association with age was observed. In logistic regression analysis, OPLL showed a significant association with the femoral neck BMD, presence of DISH and plasma pentosidine levels. Only one new case of radiographic OPLL was detected, but OPLL progressed in all affected subjects.

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**Conflicts of interest** None.

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# Incidence of certified need of care in the long-term care insurance system and its risk factors in the elderly of Japanese population-based cohorts: The ROAD study

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**Aim:** To examine the incidence of certified need of care in the national long-term care insurance (LTCI) system, and to determine its risk factors in the elderly of Japanese population-based cohorts of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study.

**Methods:** Of the 3040 participants in the baseline examination of the ROAD study, we enrolled 1773 (699 men, 1074 women) aged 65 years or older who were not certified as in need of care level elderly at baseline. Participants were followed for incident certification of need of care in the LTCI system. Associated factors in the baseline examination with occurrence were determined by multivariate Cox proportional hazards regression analysis. Muscle dysfunction was defined in accordance with the European Working Group on Sarcopenia in Older People algorithm for screening sarcopenia.

**Results:** A total of 54 men and 115 women were certified as in need of care level elderly during the average 4.0-year follow up. The incidence was 2.0 and 2.5 per 100 person-years in men and women, respectively. Identified risk factors were region, age, body mass index <18.5 or ≥27.5 kg/m<sup>2</sup>, grip strength, knee extension torque, usual gait speed, chair stand time and muscle dysfunction.

**Conclusions:** Both underweight and obesity, as well as low muscle strength and physical ability, are risk factors for certification of need of care. Considering muscle dysfunction is a risk factor for occurrence, screened individuals are recommended to receive early intervention programs regardless of muscle volume. *Geriatr Gerontol Int* 2014; 14: 695–701.

**Keywords:** activities of daily living, certification of need of care (*youkaigo-nintei*), disability, long-term care insurance system, prospective cohort study.

## Introduction

Japan is a super-aged society experiencing an unprecedented aging of the population. The proportion of the population aged 65 years or older was 23% in 2010, and

is expected to reach 30.1% in 2024 and 39% in 2051.<sup>1</sup> This leads to an increasing proportion of disabled elderly requiring support or long-term care, imposing enormous economic and social burdens on the country. The Japanese Government started the national long-term care insurance (LTCI) system in 2000 based on the Long-Term Care Insurance Act.<sup>2</sup> The aim was to certify need of care level elderly, and to provide suitable care services according to the level of care required (seven levels, including requiring support [levels 1 and 2] and requiring long-term care [levels 1–5]). The total number of certified in need of care level elderly was reported to be 5 million in 2011.<sup>2</sup>

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Certification of need of care in the national LTCI system is an important outcome in Japan, not only because of its massive social and economic burdens, but also because it is urgently required to reduce its risk and decrease the number of disabled elderly requiring care in their activities of daily living (ADL). For establishment of an evidence-based prevention strategy, it is critically important to accumulate epidemiological evidence including the incidence of certified need of care and identification of risk factors. However, there have been no studies to clarify the incidence of certified need of care in the LTCI system or its risk factors using large-scale, population-based cohorts.

In 2005, we started a large-scale, population-based cohort study entitled the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study with a total of 3040 participants, which aims to elucidate the environmental and genetic backgrounds of musculoskeletal diseases.<sup>3,4</sup> The present study investigated the incidence of certified need of care in the national LTCI system, and determined its risk factors using a database from the ROAD study.

## Methods

### Participants

The present analysis was based on data collected from cohorts established in 2005 for the ROAD study. Details of the cohorts have been reported elsewhere.<sup>3,4</sup> Briefly, we created a baseline database from 2005–2007, which included clinical and genetic information on 3040 residents of Japan (1061 men, 1979 women). Participants were recruited from resident registration listings in three communities, namely, an urban region in Itabashi, Tokyo, and rural regions in Hidakagawa and Taiji, Wakayama. Participants in the urban region in Itabashi were recruited from those of a cohort study,<sup>5</sup> in which participants were randomly drawn from the register database of Itabashi ward residents, with a response rate of 75.6% in the group aged >60 years. Participants in the rural regions in Hidakagawa and Taiji were recruited from resident registration lists, with response rates of 68.4% and 29.3%, respectively, in the groups aged >60 years. Inclusion criteria were the ability to: (i) walk to the survey site; (ii) report data; and (iii) understand and sign an informed consent form. For the present study, we enrolled 1773 participants (699 men, 1074 women; mean age 75.4 years) aged 65 years or older who were not certified as need of care level elderly in the national LTCI system at baseline. All participants provided written informed consent, and the study was carried out with approval from the ethics committees of the University of Tokyo and the Tokyo Metropolitan Institute of Gerontology.

### Baseline procedures

Participants completed an interviewer-administered questionnaire containing 400 items that included lifestyle information, such as smoking habits, alcohol consumption and physical activity. At baseline, anthropometric measurements, including height and weight, were taken, and body mass index (BMI; weight [kg]/height<sup>2</sup> [m<sup>2</sup>]) was estimated based on the measured height and weight. Underweight was defined as BMI <18.5 and obesity as BMI ≥27.5, according to the 2004 consensus statement from the WHO regarding appropriate BMI for Asian populations.<sup>6</sup> Grip strength was measured on bilateral sides using a handgrip dynamometer (TOEI LIGHT, Saitama, Japan); the higher measurement was recorded. Isometric peak knee extension torque was measured at a knee flexion angle of 90° using a dynamometer (GT-30; OG GIKEN, Okayama, Japan) twice in participants from the urban regional cohort (Itabashi, Tokyo); the higher measurement was recorded. The time taken to walk 6 m at usual walking speed in a hallway was recorded, and usual gait speed was calculated. Skeletal muscle dysfunction was defined as usual gait speed ≤0.8 m/s or grip strength <30 kg in men and <20 kg in women, according to the algorithm for screening sarcopenia recommended by the European Working Group on Sarcopenia in Older People (EWGSOP).<sup>7,8</sup> The time taken for five consecutive chair rises without the use of hands was recorded in the rural regional cohorts (Hidakagawa and Taiji, Wakayama). Hands were folded in front of the chest with feet flat on the floor. Timing began with the command “Go”, and ended when the buttocks contacted the chair on the fifth landing.

### Certification of need of care in the LTCI system

The nationally uniform criteria for long-term care need certification was established objectively by the Japanese Government, and certification of need of care level elderly is determined based on evaluation results by the Certification Committee for Long-term Care Need in municipalities in accordance with basic guidelines formulated by the Government. The process of eligibility for certification of need of care in the LTCI system was described in detail by Chen *et al.*<sup>9</sup> An elderly person who requires help with ADL or the caregiver contacts the municipal Government to request official certification of care needs. After the application, a trained official visits the home to assess the current physical status of the elderly person, including the presence or absence of muscle weakness or joint contracture of limbs, and difficulties in sitting-up, standing-up, maintaining sitting or standing position, transferring from one place to another, standing on one leg, walking, bathing, dressing, and other ADL. Mental status, including dementia, is also assessed. These data are analyzed to calculate a



**Table 1** Baseline characteristics of population at risk for certified need of care in the long-term care insurance system

	Entire cohort		Urban cohort		Rural cohort	
	Men	Women	Men	Women	Men	Women
No. participants	699	1,074	333	486	366	588
Age (years)	75.6 (5.1)	75.2 (5.3)	77.5 (3.7)	77.3 (3.8)	73.8 (5.5) <sup>†</sup>	73.5 (5.8) <sup>†</sup>
Height (cm)	160.9 (6.0)	147.9 (6.0)*	161.0 (5.8)	148.2 (5.4)*	160.8 (6.2)	147.7 (6.5)*
Weight (kg)	59.4 (9.1)	50.0 (8.3)*	59.4 (8.2)	49.8 (7.8)*	59.4 (9.9)	50.1 (8.8)*
BMI (kg/m <sup>2</sup> )	22.9 (2.9)	22.8 (3.4)	22.9 (2.7)	22.7 (3.3)	22.9 (3.1)	22.9 (3.5)
BMI <18.5 (%)	6.2	8.0	6.1	7.9	6.3	8.0
BMI ≥27.5 (%)	5.7	9.3**	3.9	8.5**	7.4	9.9
Grip strength (kg)	30.4 (6.8)	19.4 (4.9)*	28.6 (6.1)	18.2 (4.1)*	31.9 (7.0) <sup>†</sup>	20.3 (5.2)* <sup>†</sup>
Knee extension torque (kgm)	–	–	79.6 (27.2)	54.8 (17.0)*	–	–
Usual gait speed (m/s)	1.17 (0.31)	1.10 (0.33)*	1.27 (0.24)	1.22 (0.24)*	1.08 (0.34) <sup>†</sup>	1.00 (0.36)* <sup>†</sup>
Chair stand time (s)	–	–	–	–	10.8 (3.7)	12.2 (5.4)*
Muscle dysfunction (%) <sup>§</sup>	48.7	56.0**	52.6	60.0**	45.2	52.6** <sup>‡</sup>
Smoking (%)	21.0	3.2**	19.2	3.0**	22.6	3.4**
Alcohol consumption (%)	61.2	23.0**	61.0	28.8**	61.3	18.4** <sup>‡</sup>

Except where indicated otherwise, values are mean (SD). \* $P < 0.05$  versus men in the corresponding group of the same cohort by unpaired Student's  $t$ -test. \*\* $P < 0.05$  versus men in the corresponding group of the same cohort by  $\chi^2$ -test. <sup>†</sup> $P < 0.05$  versus urban cohort in the corresponding group of the same sex by unpaired Student's  $t$ -test. <sup>‡</sup> $P < 0.05$  versus urban cohort in the corresponding group of the same sex by  $\chi^2$ -test. <sup>§</sup>Muscle dysfunction was defined as usual gait speed  $\leq 0.8$  m/s or grip strength  $< 30$  kg in men and  $< 20$  kg in women. BMI, body mass index; LTCI, long-term care insurance system.

standardized score for determination of the level of care needs (certified support, levels 1–2; or long-term care, levels 1–5). In addition, the primary physician of the applicant assesses physical and mental status, including information on diseases causing ADL disability and the extent of disabilities caused by them. Finally, the Certification Committee for Long-term Care Need reviews the data and determines the certification and its level.

### Follow up and definition of incident certified need of care

After the baseline ROAD survey, participants who were not certified as need of care level elderly at baseline were followed for incident certification of need of care in the LTCI system. Incident certified need of care was defined as the incident certified 7 level, including requiring support (levels 1–2) and requiring long-term care (levels 1–5). Information on the presence or absence of certification of need of care and its date of occurrence were collected by the resident registration listings in three communities every year up to 2010, and were used for analyses in the present study.

### Statistical analysis

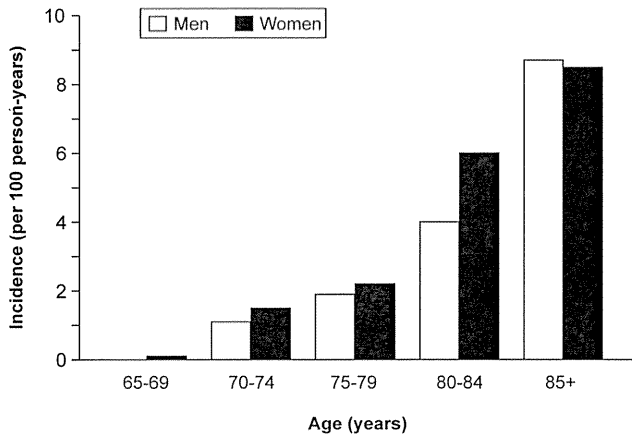
All statistical analyses were carried out using STATA statistical software (STATA, College Station, TX, USA).

Differences in the values of the parameters between two groups were tested for significance using the non-paired Student's  $t$ -test and  $\chi^2$ -test. Factors associated with occurrence of certified need of care were determined using Cox proportional hazards regression analysis; hazard ratios (HR) and 95% confidence intervals (CI) were determined after adjusting for region, age, sex, and BMI.

### Results

Of the 1773 participants who were not certified as in need of care level elderly at baseline, information on certification of need of care could be obtained in 1760 (99.3%) during the average 4.0-year follow up. A total of 54 men and 115 women were certified as in need of care level elderly in the national LTCI system; whereas, 1591 remained uncertified during the follow-up period. A total of 126 participants died, and eight moved away.

Table 1 shows the baseline characteristics of the population at risk for occurrence of certified need of care in the LTCI system. Although BMI was not significantly different between men and women in the entire, urban or rural cohorts, prevalence of obesity (BMI  $\geq 27.5$ ) was significantly higher in women than in men in the entire and urban cohorts. The prevalence of underweight was higher in women than in men in the entire,



**Figure 1** Incidence of certified need of care in the long-term care insurance system in men and women in each age stratum.

urban and rural cohorts; however, there was no significant difference. The prevalence of skeletal muscle dysfunction, determined by gait speed and grip strength, was significantly higher in women than in men in the entire, urban and rural cohorts.

Figure 1 shows sex- and age-distributions of the incidence of certified need of care in the LTCI system. Incidence was 2.3/100 person-years in the overall population of the entire cohort, and 2.0/100 person-years in men and 2.5/100 person-years in women. The incidence was very low in the age-stratum of 65–69 years, whereas, it tended to be markedly higher in the age-strata of 80 years and older in both sexes.

We then determined the risk factors for occurrence of certified need of care in the LTCI system. First, analysis was carried out using region, age, sex and BMI as explanatory variables in the Cox proportional hazards regression model (upper part of Table 2). Rural region and age were found to be risk factors for occurrence of certified need of care in the overall population. Sex and BMI were not significantly different. To further investigate the association between BMI and occurrence, we categorized BMI into three groups. Both underweight (BMI <18.5) and obesity (BMI ≥27.5) were found to be risk factors for occurrence of certified need of care, showing a U-shaped association. As for muscle strength and physical performance, handgrip strength, knee extension torque, usual gait speed, chair stand time and muscle dysfunction were found to be significantly associated with occurrence of certified need of care (lower part of Table 2). We carried out the same analyses in men and women separately (Table 2), and found results similar to those of the overall population.

## Discussion

The present study investigated the incidence of certified need of care in the national LTCI system, and

**Table 2** Hazard ratios and 95% confidence intervals for occurrence of certified need of care in the long-term care insurance system

	Overall population		Men		Women	
	Crude HR (95% CI)	Adjusted HR (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI)
Region (rural vs urban)	1.15 (0.83–1.59)	1.61 (1.17–2.24) <sup>b</sup>	1.13 (0.65–1.96)	1.64 (0.94–2.86) <sup>b</sup>	1.15 (0.77–1.72)	1.59 (1.07–2.38) <sup>b</sup>
Age (+1 year)	1.17 (1.13–1.20)	1.17 (1.14–1.21) <sup>c</sup>	1.19 (1.12–1.26)	1.19 (1.13–1.26) <sup>b</sup>	1.16 (1.12–1.20)	1.16 (1.12–1.21) <sup>b</sup>
Sex (women vs men)	1.25 (0.90–1.74)	1.24 (0.89–1.73) <sup>d</sup>	–	–	–	–
BMI (+1 kg/m <sup>2</sup> )	0.98 (0.93–1.03)	1.01 (0.96–1.06) <sup>e</sup>	0.93 (0.84–1.02)	0.96 (0.88–1.06) <sup>f</sup>	1.00 (0.94–1.06)	1.02 (0.97–1.08) <sup>f</sup>
≥18.5 or <27.5	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
BMI <18.5	2.10 (1.31–3.38)	1.77 (1.10–2.84) <sup>e</sup>	2.43 (1.09–5.40)	1.69 (0.75–3.82) <sup>f</sup>	1.93 (1.07–3.48)	1.79 (0.99–3.22) <sup>f</sup>
BMI ≥27.5	1.82 (1.13–2.93)	2.12 (1.32–3.43) <sup>e</sup>	1.39 (0.50–3.87)	1.91 (0.68–5.38) <sup>f</sup>	1.92 (1.12–3.29)	2.18 (1.27–3.75) <sup>f</sup>
Grip strength (+1 kg)	0.93 (0.91–0.95)	0.94 (0.91–0.97) <sup>f</sup>	0.91 (0.87–0.95)	0.94 (0.89–0.99) <sup>f</sup>	0.89 (0.85–0.92)	0.94 (0.89–0.98) <sup>f</sup>
Knee extension torque (+1 kgm)	0.97 (0.96–0.99)	0.97 (0.96–0.99) <sup>f</sup>	0.97 (0.95–0.99)	0.97 (0.95–0.99) <sup>f</sup>	0.97 (0.95–0.99)	0.97 (0.95–1.00) <sup>f</sup>
Usual gait speed (+0.1 m/s)	0.80 (0.77–0.85)	0.84 (0.79–0.90) <sup>f</sup>	0.81 (0.74–0.88)	0.83 (0.74–0.92) <sup>f</sup>	0.80 (0.76–0.85)	0.85 (0.78–0.92) <sup>f</sup>
Chair stand time (+1 s)	1.09 (1.07–1.12)	1.06 (1.03–1.10) <sup>f</sup>	1.18 (1.10–1.27)	1.11 (1.03–1.21) <sup>f</sup>	1.09 (1.06–1.11)	1.06 (1.02–1.09) <sup>f</sup>
Muscle dysfunction (yes vs no) <sup>a</sup>	2.91 (2.02–4.19)	1.71 (1.16–2.52) <sup>f</sup>	2.60 (1.45–4.68)	1.68 (0.91–3.09) <sup>f</sup>	3.07 (1.92–4.92)	1.72 (1.04–2.85) <sup>f</sup>
Smoking (yes vs no)	0.98 (0.58–1.68)	1.39 (0.79–2.43) <sup>f</sup>	1.18 (0.62–2.26)	1.54 (0.79–3.01) <sup>f</sup>	0.95 (0.30–2.99)	1.09 (0.35–3.47) <sup>f</sup>
Alcohol consumption (yes vs no)	0.71 (0.50–0.99)	0.83 (0.58–1.21) <sup>f</sup>	0.78 (0.45–1.35)	0.93 (0.53–1.61) <sup>f</sup>	0.70 (0.42–1.16)	0.76 (0.46–1.27) <sup>f</sup>

<sup>a</sup>Muscle dysfunction was defined as usual gait speed ≤0.8 m/s or grip strength <30 kg in men and <20 kg in women. <sup>b</sup>Adjusted for age, sex and body mass index (BMI). <sup>c</sup>Adjusted for region, sex and BMI. <sup>d</sup>Adjusted for region, age and BMI. <sup>e</sup>Adjusted for region, age, sex and BMI. <sup>f</sup>Adjusted for region and BMI. <sup>g</sup>Adjusted for region and BMI. <sup>h</sup>Adjusted for region and BMI. <sup>i</sup>Adjusted for region and age. <sup>j</sup>Adjusted for region, age and BMI. Urban region and men were used as references. CI, confidence interval; HR, hazard ratio.

determined its risk factors using Japanese population-based cohorts. Identified risk factors were region, age, underweight, obesity, handgrip strength, knee extension torque, usual gait speed, chair stand time and muscle dysfunction (determined by the EWGSOP algorithm for screening sarcopenia).

In the present study, we could not obtain information on causes of certified need of care in the LTCI system. Therefore, we could not analyze the direct association of each causing condition with such factors as anthropometric and physical performance measurements. The Government of Japan reported that the top five leading causes of certified need of care were cerebral stroke, dementia, asthenia as a result of older age, joint disease and fall-related fracture, comprising 71.6% of all causes in 2010.<sup>10</sup> Based on these data, most of the causes of incident certification in the present study are inferred to be among the top five leading conditions.

Both low and high BMI were found to be risk factors for occurrence of certified need of care, showing an overall U-shaped association. This U-shaped association is similar to that between BMI and risk of death.<sup>11,12</sup> The association between risk of death from cardiovascular disease and other causes, and BMI was reported to be U-shaped in East Asians,<sup>11</sup> whereas the risk of all-cause mortality versus BMI was also found to have a U-shaped association in Western European and North American populations.<sup>12</sup> High BMI is an established risk factor for chronic diseases, including hypertension, dyslipidemia and diabetes mellitus, which increase the risk of cerebral stroke.<sup>13</sup> High BMI is also a major risk factor for knee osteoarthritis,<sup>14-17</sup> which can cause ADL disability in the elderly.<sup>18</sup> In contrast, low BMI is an established risk factor for osteoporosis and related fracture.<sup>19</sup> It also might relate to asthenia, a condition of loss or lack of bodily strength as a result of chronic wasting disease. Underweight as a result of malnutrition or sarcopenia is suggested to be included in this category.

Other identified risk factors were handgrip strength, knee extension torque, usual gait speed, chair stand time and muscle dysfunction (determined by the EWGSOP algorithm for screening sarcopenia). Previous studies have reported that low muscle strength and physical performance were predictors of subsequent ADL disability in the elderly.<sup>20-23</sup> The results of the present study are consistent with these previous reports. As many of the performance tests used in the present study are easy to carry out and evaluate, they can be utilized for screening elderly persons at high risk of certified need of care in the LTCI system. Those who were classified as having muscle dysfunction in the present study were at high risk of sarcopenia as well as certified need of care, regardless of muscle volume. Therefore, elderly persons screened by the EWGSOP algorithm are recommended to receive early interven-

tion programs for prevention of ADL disability and subsequent deterioration leading to certified need of care.

The Japanese Orthopedic Association proposed the concept of "locomotive syndrome" in 2007 for the promotion of preventive health care of locomotive organs.<sup>24-26</sup> Locomotive syndrome refers to conditions under which the elderly have been receiving support or long-term care, or high-risk conditions under which they might soon require support or long-term care, that are caused by musculoskeletal disorders.<sup>24-26</sup> Functional declines in locomotive organs, including muscle strength, walking speed and balancing ability, usually progress slowly and gradually. As such, it might be difficult for people to recognize this decline in their daily life. Therefore, it is of particular importance to raise awareness of the growing risk caused by these disorders, and to take action to improve and maintain the health of locomotive organs. Population approaches, including promotion of the concept of locomotive syndrome to both younger and older generations, are important, in addition to high-risk approaches, including identifying those at risk for certified need of care and practicing intervention programs to reduce the risk of certified need of care.

There were some limitations in the present study. As we could not obtain information on causing conditions, we could not determine the risk factors for occurrence of certified need of care with respect to each causing condition. Additional studies are necessary to identify those direct associations. In the present study, the rural region was at higher risk of incident certified need of care compared with the urban region. The reasons for this could include differences in available public and private transportation or delivery services regarding meals and commodities for the elderly. In addition to these, the threshold between certified and non-certified elderly might be different among municipalities, which could lead to regional differences. Although the Certification Committee for Long-term Care Need in each municipality determines certification in accordance with guidelines formulated by the Government, the Committee also has to consider assessment by the applicant's primary physician and objective evaluation results regarding physical and mental status, which could affect the threshold of certification. Another limitation was health bias. Participants at baseline in the present study were those who could walk to the survey site, and could understand and sign an informed consent form. As those who could not were not included in the analyses, the study participants do not truly represent the general population due to health bias. Therefore, incidence of certified need of care was most likely underestimated, which should be taken into consideration when generalizing the results of the present study.

In conclusion, the present study revealed the incidence of certified need of care in the national LTCI

system, and determined its risk factors using Japanese population-based cohorts. Both underweight and obesity were found to be risk factors for certified need of care, suggesting that maintenance of intermediate BMI is important for prevention. Low muscle strength and physical ability were also shown to be risk factors for certified need of care. Physical performance measures identified as predictors can be used as screening tools to identify high-risk individuals. Considering muscle dysfunction, screened by the EWGSOP algorithm, was a risk factor for occurrence, screened individuals are recommended to receive early intervention programs regardless of muscle volume. Further studies are necessary to develop intervention programs and to test their effectiveness, along with accumulation of epidemiological evidence, to prevent certified need of care and reduce the social and economic burdens associated with this condition.

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## Disclosure statement

The authors declare no conflict of interest.

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# Association of physical activities of daily living with the incidence of certified need of care in the long-term care insurance system of Japan: the ROAD study

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## Abstract

**Background** The present study aimed to investigate association of physical activities of daily living with the incidence of certified need of care in the national long-term care insurance (LTCI) system in elderly Japanese population-based cohorts.

**Methods** Of the 3,040 participants in the baseline examination, we enrolled 1,773 (699 men, 1,074 women) aged 65 years or older who were not certified as in need of care-level elderly at baseline. Participants were followed during an average of 4.0 years for incident certification of need of care in the LTCI system. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used assess function. Associated factors in the baseline examination with the occurrence were determined by multivariate Cox proportional hazards regression analysis. Receiver operating characteristic curve analysis was performed to evaluate cut-off values for discriminating between the occurrence and the non-occurrence group.

**Results** All 17 items in the WOMAC function domain were significantly associated with the occurrence of certified need of care in the overall population. Cut-off values of the WOMAC function score that maximized the sum of sensitivity and specificity were around 4–6 in the overall population, in men, and in women. Multivariate Cox hazards regression analysis revealed that a WOMAC function score  $\geq 4$  was significantly associated with occurrence with the highest hazard ratio (HR) for occurrence after adjusting for confounders in the overall population (HR [95 % confidence interval (CI)] 2.54 [1.76–3.67]) and in women [HR (95 % CI) 3.13 (1.95–5.02)]. A WOMAC function score  $\geq 5$  was significantly associated with the highest HR for occurrence in men [HR (95 % CI) 1.88 (1.03–3.43)].

**Conclusions** Physical dysfunction in daily living is a predictor of the occurrence of certified need of care. Elderly men with a WOMAC function score  $\geq 5$  and women with a score  $\geq 4$  should undergo early intervention programs to prevent subsequent deterioration.

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## Introduction

Japan is a super-aged society experiencing an unprecedented aging of the population. The proportion of the population aged 65 years or older was 23 % in 2010, and is expected to reach 30.1 % in 2024 and 39 % in 2051 [1]. This leads to an increasing proportion of disabled elderly requiring support or long-term care, imposing enormous economic and social burdens on the country. The Japanese Government started the national long-term care insurance (LTCI) system in 2000 based on the Long-Term Care Insurance Act [2]. The aim was to certify need of care-level elderly and to provide suitable care services according to the level of care required [7 levels, including requiring support (levels 1 and 2) and requiring long-term care (levels 1–5)]. The total number of certified need of care-level elderly was reported to be 5 million in 2011 [2]. Certification of need of care in the national LTCI system is an important outcome in Japan not only because of its massive social and economic burdens, but also because it is urgently necessary to reduce risk and decrease the number of disabled elderly requiring care in their activities of daily living (ADLs). It is critically important to accumulate epidemiologic evidence, including identification of predictors, to establish evidence-based prevention strategies. However, no studies have determined the association of physical ADLs with the incidence of certified need of care in the national LTCI system using large-scale, population-based cohorts. The objective of the present study was to investigate the association of physical ADLs with the incidence of certified need of care in the national LTCI system and determine its predictors in elderly participants of large-scale, population-based cohorts of the research on osteoarthritis/osteoporosis against disability (ROAD) study.

## Subjects and methods

### Participants

The analysis was based on data collected from cohorts established in 2005 for the ROAD study. Details of the cohorts have been reported elsewhere [3, 4]. Briefly, a baseline database was created from 2005 to 2007, which included clinical and genetic information on 3,040 residents of Japan (1,061 men, 1,979 women). Participants were recruited from resident registration listings in three communities, namely, an urban region in Itabashi, Tokyo, and rural regions in Hidakagawa and Taiji, Wakayama. Participants in the urban region in Itabashi were recruited from those of a cohort study [5] in which the participants were randomly drawn from the register database of Itabashi

ward residents, with a response rate in the age group >60 years of 75.6 %. Participants in the rural regions in Hidakagawa and Taiji were recruited from resident registration lists, with response rates in the groups aged >60 years of 68.4 and 29.3 %, respectively. Inclusion criteria were the ability to (1) walk to the survey site, (2) report data, and (3) understand and sign an informed consent form. For the present study, we enrolled 1,773 participants (699 men, 1,074 women; mean age 75.4 years) aged 65 years or older who were not certified as in need of care-level elderly in the national LTCI system at baseline. All participants provided written informed consent, and the study was conducted with approval from the ethics committees of the participating institutions.

### Baseline procedures

Participants completed an interviewer-administered questionnaire containing 400 items that included lifestyle information, such as smoking habits, alcohol consumption, and physical activity. At baseline, anthropometric measurements, including height and weight, were taken, and body mass index (BMI) [weight (kg)/height<sup>2</sup> (m<sup>2</sup>)] was estimated based on the measured height and weight.

### Assessment of physical ADLs

We used the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for assessment of physical ADLs. The WOMAC is a health status instrument, consisting of three domains: pain, stiffness, and physical function. We used the WOMAC function domain to evaluate physical ADLs. It consisted of 17 items: assessing difficulties in descending stairs, ascending stairs, rising from sitting, standing, bending to floor, walking on a flat surface, getting in/out of car/bus, going shopping, putting on socks/stockings, rising from bed, taking off socks/stockings, lying in bed, getting into/out of bath, sitting, getting on/off toilet, heavy domestic duties, and light domestic duties. Each item in the domain is graded on either a 5-point Likert scale (scores of 0–4) or a 100-mm visual analog scale [6, 7]. In the present study, we used the Likert scale (version LK 3.0). Items were rated from 0 to 4; 0, no difficulty; 1, mild difficulty; 2, moderate difficulty; 3, severe difficulty; 4, extreme difficulty. The domain score ranges from 0 to 68. Japanese versions of the WOMAC have been validated [8].

### Certification of need of care in the LTCI system

The nationally uniform criteria for long-term care need certification was established objectively by the Japanese Government, and certification of need of care-level elderly

is determined based on evaluation results by the Certification Committee for Long-term Care Need in municipalities in accordance with basic guidelines formulated by the Government. The process of eligibility for certification of need of care in the LTCI system was described in detail by Chen et al. [9]. An elderly person who requires help with ADLs or the caregiver contacts the municipal government to request official certification of care needs. After the application, a trained official visits the home to assess the current physical status of the elderly person, including presence or absence of muscle weakness or joint contracture of limbs, and difficulties in sitting-up, standing-up, maintaining sitting or standing position, transferring from one place to another, standing on one leg, walking, bathing, dressing, and other ADLs. Mental status, including dementia, also is assessed. These data are analyzed to calculate a standardized score for determination of the level of care needs (certified support, levels 1–2; or long-term care, levels 1–5). In addition, the primary physician of the applicant assesses physical and mental status, including information on diseases causing ADL disability and the extent of disabilities caused by them. Finally, the Certification Committee for Long-term Care Need reviews the data and determines the certification and its level.

Follow-up and definition of incident certified need of care

After the baseline ROAD survey, participants who were not certified as in need of care-level elderly at baseline were followed for incident certification of need of care in the LTCI system. Incident certified need of care was defined as the incident certified 7 levels, including requiring support (levels 1–2) and requiring long-term care (levels 1–5). Information on the presence or absence of certification of need of care and its date of occurrence were collected by the resident registration listings in three communities every year up to 2010, and were used for analyses in the present study.

Statistical analysis

All statistical analyses were performed using STATA statistical software (STATA, College Station, TX, USA). Differences in values of the parameters between the two groups were tested for significance using the unpaired Student’s *t* test, the Mann–Whitney’s *U* test, and Chi-square test. We used receiver operating characteristic (ROC) curve analysis to determine a cut-off value of the WOMAC function score for discriminating two distinct groups: an occurrence and a non-occurrence group of certified need of care. Cut-off values were determined that maximized the sum of sensitivity and specificity. Factors

associated with the occurrence of certified need of care were determined using Cox proportional hazards regression analysis; hazard ratios (HRs) and 95 % confidence intervals (CIs) were determined after adjusting for region, age, sex, and BMI. Smoking habit and alcohol consumption were not included as confounders because they were not significantly associated with the incidence of certified need of care.

Results

Of the 1,773 participants who were not certified as in need of care-level elderly at baseline, information on

**Table 1** Baseline characteristics of population at risk for the certified need of care in the LTCI system

	Men	Women
No. of subjects	699	1,074
Age (years)	75.6 (5.1)	75.2 (5.3)
Height (cm)	160.9 (6.0)	147.9 (6.0) <sup>b</sup>
Weight (kg)	59.4 (9.1)	50.0 (8.3) <sup>b</sup>
BMI (kg/m <sup>2</sup> )	22.9 (2.9)	22.8 (3.4)
Smoking (%)	21.0	3.2 <sup>c</sup>
Alcohol consumption, %	61.2	23.0 <sup>c</sup>
WOMAC function domain		
Descending stairs, pts <sup>a</sup>	0 (0, 0, 1, 1)	0 (0, 0, 1, 2) <sup>d</sup>
Ascending stairs, pts <sup>a</sup>	0 (0, 0, 1, 1)	0 (0, 0, 1, 2)
Rising from sitting, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 1, 1) <sup>d</sup>
Standing, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 1, 1) <sup>d</sup>
Bending to floor, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 1, 1)
Walking on a flat surface, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 0, 1)
Getting in/out of car/bus, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 1, 1) <sup>d</sup>
Going shopping, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 0, 1) <sup>d</sup>
Putting on socks/stockings, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 0, 1) <sup>d</sup>
Rising from bed, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 0, 1) <sup>d</sup>
Taking off socks/stockings, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 0, 1) <sup>d</sup>
Lying in bed, pts <sup>a</sup>	0 (0, 0, 0, 0)	0 (0, 0, 0, 1) <sup>d</sup>
Getting into/out of bath, pts <sup>a</sup>	0 (0, 0, 0, 0)	0 (0, 0, 0, 1) <sup>d</sup>
Sitting, pts <sup>a</sup>	0 (0, 0, 0, 0)	0 (0, 0, 0, 0) <sup>d</sup>
Getting on/off toilet, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 1, 2) <sup>d</sup>
Heavy domestic duties, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 0, 1) <sup>d</sup>
Light domestic duties, pts <sup>a</sup>	0 (0, 0, 0, 1)	0 (0, 0, 0, 1) <sup>d</sup>
Total, pts <sup>a</sup>	1 (0, 0, 5, 12)	2 (0, 0, 8, 17) <sup>d</sup>

Except where indicated otherwise, values are mean (SD)  
 LTCI long-term care insurance system, BMI body mass index, WOMAC the Western Ontario and McMaster Universities Arthritis Index  
<sup>a</sup> Median (10, 25, 75, and 90 percentile)  
<sup>b</sup> *P* < 0.05 vs men by unpaired Student’s *t* test  
<sup>c</sup> *P* < 0.05 vs men by Chi-square test  
<sup>d</sup> *P* < 0.05 vs men by Mann–Whitney *U* test



**Table 2** Association of physical activities of daily living with the occurrence of certified need of care in the LTCI system

Physical activity	Overall population		Men		Women	
	HR (95 % CI)	<i>P</i> value	HR (95 % CI)	<i>P</i> value	HR (95 % CI)	<i>P</i> value
Descending stairs, pts	1.47 (1.26, 1.72)	<0.001	1.29 (0.96, 1.74)	0.089	1.56 (1.30, 1.87)	<0.001
Ascending stairs, pts	1.47 (1.25, 1.73)	<0.001	1.29 (0.93, 1.77)	0.123	1.55 (1.29, 1.86)	<0.001
Rising from sitting, pts	1.58 (1.34, 1.88)	<0.001	1.38 (0.95, 1.99)	0.092	1.67 (1.37, 2.03)	<0.001
Standing, pts	1.64 (1.41, 1.91)	<0.001	1.39 (1.02, 1.90)	0.037	1.73 (1.45, 2.06)	<0.001
Bending to floor, pts	1.57 (1.32, 1.85)	<0.001	1.61 (1.15, 2.27)	0.006	1.57 (1.29, 1.90)	<0.001
Walking on a flat surface, pts	1.57 (1.30, 1.90)	<0.001	1.25 (0.88, 1.77)	0.22	1.78 (1.41, 2.23)	<0.001
Getting in/out of car/bus, pts	1.76 (1.47, 2.10)	<0.001	1.60 (1.14, 2.26)	0.007	1.85 (1.50, 2.29)	<0.001
Going shopping, pts	1.72 (1.46, 2.03)	<0.001	1.55 (1.14, 2.11)	0.005	1.81 (1.48, 2.21)	<0.001
Putting on socks/stockings, pts	1.60 (1.33, 1.92)	<0.001	1.41 (0.98, 2.03)	0.065	1.71 (1.37, 2.12)	<0.001
Rising from bed, pts	1.68 (1.40, 2.03)	<0.001	1.41 (0.98, 2.02)	0.066	1.83 (1.47, 2.29)	<0.001
Taking off socks/stockings, pts	1.64 (1.37, 1.98)	<0.001	1.48 (1.01, 2.16)	0.046	1.72 (1.39, 2.13)	<0.001
Lying in bed, pts	1.82 (1.44, 2.30)	<0.001	1.96 (1.13, 3.40)	0.017	1.79 (1.38, 2.32)	<0.001
Getting into/out of bath, pts	1.71 (1.43, 2.04)	<0.001	1.64 (1.15, 2.33)	0.006	1.75 (1.43, 2.15)	<0.001
Sitting, pts	2.21 (1.73, 2.82)	<0.001	1.92 (1.14, 3.22)	0.014	2.32 (1.75, 3.06)	<0.001
Getting on/off toilet, pts	1.87 (1.52, 2.29)	<0.001	1.51 (1.00, 2.27)	0.05	2.09 (1.63, 2.68)	<0.001
Heavy domestic duties, pts	1.27 (1.09, 1.49)	0.003	1.20 (0.89, 1.62)	0.238	1.33 (1.10, 1.60)	0.003
Light domestic duties, pts	1.68 (1.41, 2.01)	<0.001	1.49 (1.07, 2.07)	0.019	1.80 (1.45, 2.24)	<0.001

Hazard ratios (HRs) and 95 % confidence intervals (CIs) were determined by Cox proportional hazards regression analysis after adjusting for age, sex, body mass index, and region in the overall population, and after adjusting for age, body mass index, and region in men and in women, respectively

LTCI long-term care insurance system

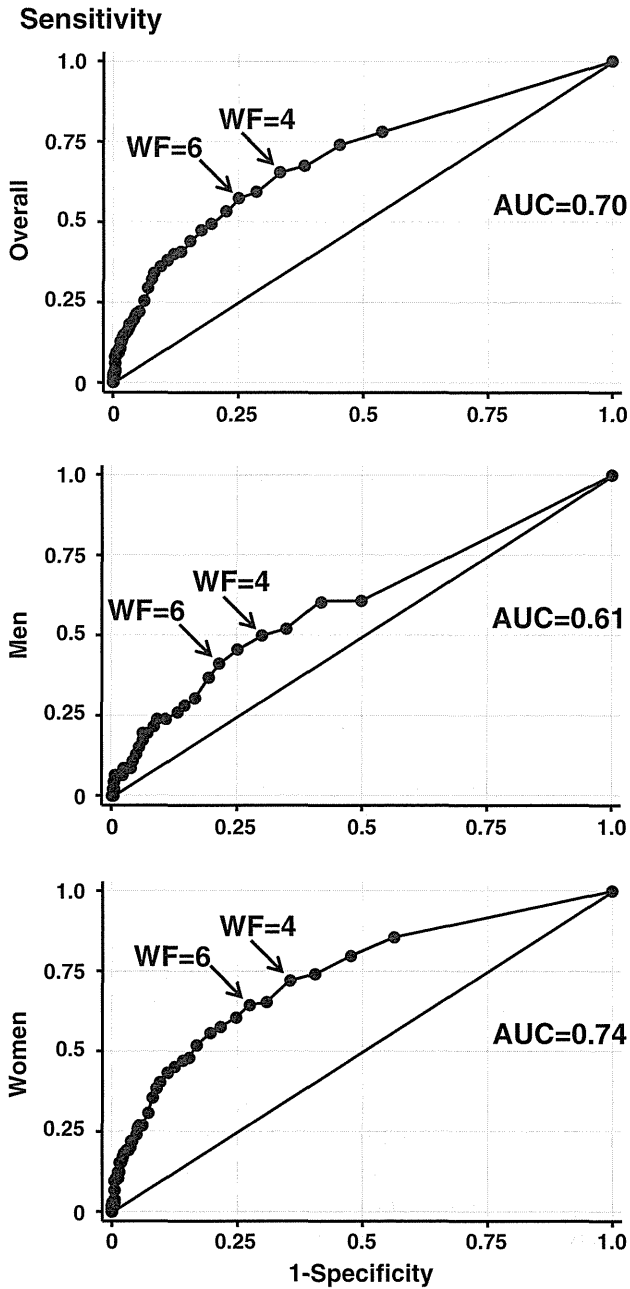
certification of need of care could be obtained in 1,760 (99.3 %) during the average 4.0-year follow-up. Fifty-four men and 115 women were certified as in need of care-level elderly in the national LTCI system, whereas, 1,591 remained uncertified during the follow-up period. The average period for the certification was 2.3 years. Among the above 54 men and 115 women, those who were certified as requiring long-term care level 1, 2, 3, 4, and 5 were 7, 9, 2, 4, 3 men, and 12, 17, 9, 4, 4 women, respectively. One hundred and twenty-six participants died and eight moved away. Incidence of certified need of care in the LTCI system was 2.3/100 person-years in the overall population, and 2.0/100 person-years in men and 2.5/100 person-years in women. Table 1 shows the baseline characteristics of the population at risk for occurrence of certified need of care in the LTCI system. The score of each item in the WOMAC function domain was significantly higher in women than in men in almost all items.

We then investigated association of each item in the WOMAC function domain with the occurrence of certified need of care in the LTCI system (Table 2). All 17 items in the WOMAC function domain were significantly associated with the occurrence of the certified need of care in the overall population and in women. In men, standing, bending to floor, getting in/out of car/bus, going shopping,

taking off socks/stockings, lying in bed, getting into/out of bath, sitting, and light domestic duties were significantly associated with the occurrence of certified need of care, whereas other ADLs were not. In addition, the value of HR for each item in the association was higher in women than in men in 15 of 17 items.

Next we determined cut-off values of total score of the WOMAC function domain for discriminating two groups: an occurrence and a non-occurrence group of certified need of care using ROC curve analysis. The area under ROC curve was 0.70 in the overall population, 0.61 in men, and 0.74 in women (Fig. 1). The cut-off value of the WOMAC function score that maximized the sum of sensitivity and specificity was 6, 5, and 6 in the overall population, in men, and in women, respectively. In addition, the sensitivity/specificity was 57.3/75.0 % in the overall population, 45.7/75.0 % in men, and 64.4/72.6 % in women, respectively (Table 3). Furthermore, the cut-off value by which the sum was the second largest was 4 in the overall population, 4 in men, and 4 in women, and the sensitivity/specificity was 65.3/66.7 % in the overall population, 50.0/70.0 % in men, and 72.1/64.5 % in women, respectively (Table 3).

Because ROC curve analysis is a univariate analysis, we performed multivariate Cox hazards regression analysis to determine the cut-off value of the WOMAC function score for best discriminating between an occurrence and a non-



**Fig. 1** Receiver operating characteristic (ROC) curve analysis for discriminating the occurrence group of certified need of care in the overall population, in men, and in women. *AUC* area under ROC curve, *WF* WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) function score

occurrence group of certified need of care after adjusting for age, sex, BMI, and region (Table 4). The group with WOMAC function score  $\geq 4$  was significantly associated with the occurrence of certified need of care compared with the group with the score  $< 4$  with the highest HR in the overall population [HR 2.54, 95 % CI (1.76–3.67)] and in women [HR 3.13, 95 % CI (1.95–5.02)]. In men, the group with WOMAC function score  $\geq 5$  was significantly

**Table 3** Sensitivity and specificity of the occurrence of certified need of care determined by the cut-off point of the WOMAC function score

Cut-off point	Overall population			Men			Women		
	Sensitivity (%)	Specificity (%)	Sensitivity + specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity + specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity + specificity (%)
WF = 4pts	65.3	66.7	132.0	50.0	70.0	120.0	72.1	64.5	136.6
WF = 5pts	59.3	71.4	130.7	45.7	75.0	120.7	65.4	69.2	134.6
WF = 6pts	57.3	75.0	132.3	41.3	78.6	119.9	64.4	72.6	137.0

WOMAC the Western Ontario and McMaster Universities Arthritis Index, *WF* WOMAC function score

**Table 4** Association of groups divided by the WOMAC function score with the occurrence of certified need of care in the LTCI system

	Overall population		Men		Women	
	HR (95 % CI)	<i>P</i> value	HR (95 % CI)	<i>P</i> value	HR (95 % CI)	<i>P</i> value
WF $\geq$ 4 pts vs WF < 4 pts	2.54 (1.76, 3.67)	<0.001	1.85 (1.01, 3.39)	0.045	3.13 (1.95, 5.02)	<0.001
WF $\geq$ 5 pts vs WF < 5 pts	2.35 (1.64, 3.36)	<0.001	1.88 (1.03, 3.43)	0.040	2.71 (1.73, 4.27)	<0.001
WF $\geq$ 6 pts vs WF < 6 pts	2.50 (1.75, 3.58)	<0.001	1.84 (1.00, 3.39)	0.051	3.03 (1.93, 4.76)	<0.001

Hazard ratios (HRs) and 95 % confidence intervals (CIs) were determined by Cox proportional hazards regression analysis after adjusting for age, sex, body mass index, and region in the overall population, and after adjusting for age, body mass index, and region in men and in women, respectively

WOMAC the Western Ontario and McMaster Universities Arthritis Index, LTCI long-term care insurance system, WF WOMAC function score

**Table 5** Association of the WOMAC function score with the occurrence of different certified need of care levels in the LTCI system

Outcome variable	Overall population		Men		Women	
	HR (95 % CI)	<i>P</i> value	HR (95 % CI)	<i>P</i> value	HR (95 % CI)	<i>P</i> value
RSL1–2 and RCL 1–5	1.05 (1.03, 1.06)	<0.001	1.03 (1.01, 1.06)	0.008	1.05 (1.04, 1.07)	<0.001
RCL 1–5	1.05 (1.03, 1.07)	<0.001	1.04 (1.00, 1.07)	0.046	1.06 (1.03, 1.08)	<0.001
RCL 2–5	1.06 (1.04, 1.08)	<0.001	1.04 (1.01, 1.08)	0.015	1.06 (1.04, 1.09)	<0.001
RCL 3–5	1.05 (1.03, 1.08)	<0.001	1.05 (0.99, 1.10)	0.099	1.06 (1.02, 1.09)	0.001
RCL 4–5	1.04 (1.00, 1.08)	0.048	1.02 (0.95, 1.10)	0.501	1.05 (1.00, 1.10)	0.057
RCL 5	1.01 (0.93, 1.09)	0.830	0.99 (0.82, 1.20)	0.945	1.01 (0.93, 1.11)	0.780

Hazard ratios (HRs) and 95 % confidence intervals (CIs) were determined by Cox proportional hazards regression analysis after adjusting for age, sex, body mass index, and region in the overall population, and after adjusting for age, body mass index, and region in men and in women, respectively

WOMAC the Western Ontario and McMaster Universities Arthritis Index, LTCI long-term care insurance system, RSL requiring support level, RCL requiring long-term care level

associated with the occurrence of certified need of care compared with the group with a score of <5 with the highest HR [HR 1.88, 95 % CI (1.03–3.43)].

Furthermore, we examined association of the WOMAC function domain with the occurrence of different certified need of care levels in the LTCI system (Table 5). When the outcome variable of the occurrence was defined as requiring support level (RSL) 1–2 and requiring long-term care level (RCL) 1–5, RCL 1–5, and RCL 2–5, there were significant associations in the overall population, in men, and in women, respectively. When the outcome variable of the occurrence was defined as RCL 3–5, there were significant associations in the overall population and in women. When the outcome variable of the occurrence was defined as RCL 4–5, there was significant association in the overall population.

## Discussion

The present study determined association of physical ADLs with the incidence of certified need of care in the national LTCI system in elderly participants of Japanese population-based cohorts. All 17 items in the WOMAC function

domain were significantly associated with the occurrence of certified need of care in the overall population. ROC curve analysis showed that cut-off values of the WOMAC function score of around 4–6 maximized the sum of sensitivity and specificity of the occurrence of certified need of care. Furthermore, multivariate Cox hazards regression analysis revealed that the group with WOMAC function score  $\geq$ 4 was significantly associated with the occurrence of certified need of care with the highest HR after adjusting for confounders in the overall population and in women, while the group with WOMAC function score  $\geq$ 5 was significantly associated with the highest HR in men.

In the present study, we could not obtain information on causes of certified need of care in the LTCI system. Therefore, we could not analyze the direct association of each causing condition with the WOMAC function domain. The Government of Japan reported that the top five leading causes of certified need of care were cerebral stroke (21.5 %), dementia (15.3 %), asthenia as a result of older age (13.7 %), joint disease (10.9 %) and fall-related fracture (10.2 %), comprising 71.6 % of all causes in 2010 [10]. Based on these data, most of the causes of incident certification in the present study are inferred to be among the top five leading conditions. Although we could not

know the exact percentage of each causing condition, joint disease and fall-related fracture are inferred to represent approximately 20 % in total causes of incident certification in the present study, and cerebral stroke, dementia, and asthenia as a result of older age are inferred to represent approximately 50 % in total causes of incident certification.

The Government of Japan also reported that the percentage of joint disease and fall-related fracture was 16.7 % for the cause of RCL 1–5 [10]. Furthermore, it was 17.6, 19.8, 14.8, 17.4, and 9.8 % for the cause of RCL 1, 2, 3, 4, and 5, respectively [10]. Although we could not know the exact percentage of joint disease and fall-related fracture for the cause of each RCL in the present study, the percentage for the cause of RCL 1–4 is inferred to be approximately 15 % or more based on the data of the Government of Japan, which may be the reason why the WOMAC domain was significantly associated with the occurrence of certified need of care including RCLs 1–4 in the overall population.

The WOMAC physical function domain assesses difficulties in ADLs, including going up/down stairs, getting in/out of a car and bath, shopping, and household duties. Therefore, results of the present study indicate that the severity of physical dysfunction in ADLs predicts subsequent deterioration in ADLs, leading to the occurrence of certified need of care. Previous studies reported that low physical function was a predictor of subsequent ADL disability in the elderly [11, 12]. Although no previous studies have investigated the association of physical ADLs with the incidence of certified need of care in the national LTCI system in large-scale population-based cohorts, those previous findings are consistent with the present results in that low physical activity predicted subsequent deterioration in ADLs.

All 17 items in the WOMAC domain were significantly associated with the occurrence of certified need of care in women. On the other hand, 9 of 17 items were significantly associated with the occurrence of certified need of care in men. In addition, the HR for each item in the association was higher in women than in men for 15 of 17 items. The sex difference identified in this association may be due to the difference in the prevalence of knee osteoarthritis between the sexes. Muraki et al. [13] reported that prevalence of radiographic knee osteoarthritis determined by the Kellgren–Lawrence grade  $\geq 2$  was 47.0 % in men and 70.2 % in women, respectively, in subjects aged 60 years and older in Japanese population-based cohorts. Therefore, women are more likely than men to be affected by knee osteoarthritis and have difficulties in physical function of the lower extremities, leading to higher scores on the WOMAC function scale. Another reason for the sex differences may be the weaker muscle strength in women; muscle strength in men is higher than that in women in all decades of life [14], which may obscure the association in

men, as muscle strength has been reported to be inversely associated with the WOMAC domains [15].

Functional declines in locomotive organs including physical ADLs usually progress slowly and gradually. As such, it may be difficult for people to recognize this decline in their daily life. Therefore, it is of particular importance to raise awareness of the growing risk caused by such disorders, and to take action to improve and maintain the health of the locomotive organs. The Japanese Orthopaedic Association proposed the concept of “locomotive syndrome” in 2007 for the promotion of preventive healthcare of the locomotive organs [16–18]. Locomotive syndrome refers to conditions under which the elderly have been receiving support or long-term care, or high-risk conditions under which they may soon require support or long-term care, that are caused by musculoskeletal disorders [16–18]. Population approaches, including promotion of the concept of locomotive syndrome to both younger and older generations, are important, in addition to high-risk approaches, including identifying those at risk for certified need of care and practicing intervention programs to reduce the risk of certified need of care.

Because the WOMAC function scale is a self-assessment questionnaire that is easy to conduct and evaluate, it can be used to screen elderly persons at high risk of certified need of care in the LTCI system. Multivariate Cox hazards regression analysis showed that a WOMAC function score of 5 in men and 4 in women best discriminated between the occurrence and the non-occurrence group of certified need of care in this study population. Elderly men with a WOMAC function score  $\geq 5$  had a 1.88-fold higher risk of occurrence of certified need of care compared with elderly men with a score  $< 5$ . Elderly women with a WOMAC function score  $\geq 4$  had a 3.13-fold higher risk of occurrence of certified need of care compared with elderly women with a score  $< 4$ . Elderly persons screened by these cut-off values should receive early intervention for the prevention of subsequent deterioration in ADLs that could lead to certified need of care. Further studies, along with the accumulation of epidemiologic evidence, are necessary to develop intervention programs that are safe and effective for elderly subjects who are at high risk of certified need of care.

There are some limitations in the present study. First, we could not obtain information on causes of certified need of care in the LTCI system. Therefore, we could not analyze the direct association of each causing condition with measured factors, and could not determine the risk factors for occurrence of certified need of care with respect to each causing condition. The Japanese government reported that the top five leading causes of certified need of care were cerebral stroke, dementia, asthenia, osteoarthritis, and fall-related fracture, comprising 71.6 % of all causes in 2010 [10]. Based on these data, most of the causes of incident certification in the present