

ORIGINAL ARTICLE

# Validation of screening questionnaires for evaluation of knee osteoarthritis prevalence in the general population of Singapore

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## Abstract

**Background:** The prevalence of symptomatic knee osteoarthritis (KOA) in Singapore is unknown. We aimed to: (i) validate questionnaires to screen for symptomatic KOA; and (ii) estimate the prevalence of symptomatic KOA in Singapore using the validated algorithms.

**Methods:** Subjects aged  $\geq 50$  years were evaluated for symptomatic KOA based on American College of Rheumatology clinical and radiographic criteria in a rheumatology clinic, and completed three sets of adapted screening questionnaires. The better performing screening questionnaire with adequate sensitivity and specificity was administered to a nationally representative sample of survey subjects ( $n = 3364$ ) to estimate the weighted prevalence of symptomatic KOA in Singapore.

**Results:** Out of 146 subjects evaluated in the clinic, 45 had symptomatic KOA. A screening algorithm which consisted of three KOA symptoms or one symptom plus physician-diagnosed KOA produced high specificity (0.95, 95% confidence intervals [CI]: 0.88–0.98) but low sensitivity (0.44, 95% CI: 0.30–0.60). Replacing the term 'KOA' with 'physician-diagnosed ageing-related knee problem' improved the sensitivity (0.62, 95% CI: 0.47–0.76) without significantly compromising the specificity (0.87, 95% CI: 0.79–0.93). The prevalence of symptomatic KOA weighted to the Singapore population distribution were 4.7% and 11%, using the most conservative and more liberal algorithms, respectively. There was a sharp rise in prevalence after age of 40. The weighted prevalence of KOA was higher in women and among Indian and Malay than Chinese.

**Conclusion:** Our study adapted and validated questionnaires to the local context to screen for symptomatic KOA. We estimated the prevalence of symptomatic KOA in Singapore utilizing the better-performing algorithms.

**Key words:** symptomatic knee osteoarthritis, screening, epidemiology, prevalence.

## BACKGROUND

Knee osteoarthritis (KOA) is the most common form of arthritis, and is one of the leading causes of disability

among non-institutionalized adults.<sup>1</sup> The burden of KOA has been rising in the past two decades with increasing prevalence of obesity and aging populations.<sup>2</sup> Singapore is one of the fastest aging populations in Asia<sup>3</sup> and the economic burden and public consequences of KOA<sup>4,5</sup> are expected to rise. However, the prevalence of KOA in Singapore is unknown. The closest crude estimate from National Health Surveillance Survey (NHSS) 2007 based on self-reported diagnosis

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of arthritis in general was 10%.<sup>6</sup> The prevalence of KOA seems to differ in different ethnic groups. For instance, KOA was reported to be more prevalent among Chinese than Caucasian populations.<sup>7</sup> Thus, in Singapore, a multiethnic Asian country with a Chinese majority (74.1%),<sup>3</sup> the prevalence of KOA may be higher.

The prevalence estimate of KOA may vary depending on the classification criteria used. The most accepted way of classifying KOA consists of a combination of radiographic and clinical criteria, namely the American College of Rheumatology (ACR) classification criteria for KOA.<sup>8</sup> However, the implementation of both clinical and radiological evaluation to confirm KOA is complex, expensive, and difficult to perform in large-scale population-based studies. For epidemiology studies, prevalence evaluation using a specifically designed screening questionnaire is a less costly and more feasible approach. The goal of the screening questionnaire is to yield a high diagnostic rate of symptomatic KOA (high specificity), without missing a substantial number of patients with symptomatic KOA (high sensitivity). Prior studies have investigated the efficiency of several screening questionnaires for KOA. Questionnaires based on self-reported symptoms were found to be insensitive and nonspecific.<sup>9</sup> Newer studies in European countries using questionnaires that combined self-reported diagnosis, symptoms and disability were proven to be valid for symptomatic KOA screening and helpful in estimating the prevalence of KOA.<sup>10–13</sup> Yet, extrapolating the results of Western studies to the Asian context would be limited by sociocultural differences, such as knowledge of diagnosis and perception of symptoms among different cultures. Therefore, the aims of our study were: (i) to validate questionnaires to screen for symptomatic KOA in the general population of Singapore; and then (ii) to administrate the validated questionnaires to a nationally representative cohort from the National Health Surveillance Survey (NHSS) 2013 to estimate the prevalence of symptomatic KOA in Singapore.

## METHODS

### Screening questionnaires

Three sets of screening questionnaires for KOA were sourced from the literature<sup>9,10,12</sup> and adapted to the local context. In Singapore, English is the common spoken language, while Mandarin is often used among elderly Chinese.<sup>3</sup> As more than 80% of Singaporeans are literate in English and 71% are literate in two or more languages,<sup>3</sup> at least 98% of the population in

Singapore could be included in our studies with questionnaires available in both English and Chinese. The screening questionnaires were translated from the sourced English version to Chinese following standard guidelines.<sup>14</sup> In brief, two bilingual translators proficient in both English and Chinese independently translated the screening questionnaires from English to Chinese, and then developed a reconciled version. Another two independent bilingual translators back-translated the Chinese version into English and reconciled differences. The final Chinese version was adapted with further refinements via a panel review comparing the original source and back-translated versions.

The three sets of KOA screening questionnaires after adaptation to the local sociocultural context in Singapore (named Instrument 1 to Instrument 3) and their case-defining algorithms are shown in Table S1. For example, one of the question items in the original questionnaires included the term 'doctor'. In Singapore, seeing Traditional Chinese Medicine (TCM) practitioners is common practice, so to distinguish TCM practitioners from Western trained doctors, the term 'doctor (Western trained)' was utilized in our screening questionnaires. Another adaptation to Instrument 3<sup>12</sup> was made to replace the term 'rheumatologist' with 'doctor (Western trained)'. This was because there were only 34 rheumatologists across the country at the time of the study, and the majority of the general population were not familiar with the term 'rheumatologist'. Lastly, our study utilized an alternative question to replace 'KOA' diagnostic terms in all three screening questionnaires. The term 'KOA' was foreign to most of the Singapore general population as doctors usually conveyed the diagnosis as an 'aging-related problem' or a 'wear and tear problem'. We asked an additional question: 'Has a doctor (Western trained) ever told you that your knee problem is related to aging?' (Table S1). We evaluated the sensitivity and specificity of the three questionnaires compared to the ACR classification criteria for KOA. We also analyzed the effects of the additional question when used in place of the 'KOA' diagnostic terms in each questionnaire.

### Validation of screening questionnaires study

Subjects aged 50 years and above were recruited from a community elderly center in Singapore from June to October 2012 via pamphlets and advertisements. A total of 150 interested subjects who signed up were given an initial telephone interview with one of the screening questionnaires (Instrument 3) (Table 1). We excluded four subjects who could not understand either

**Table 1** Algorithm of the screening instrument selected to administer in the nationally representative cohort

Instrument 3 <sup>†</sup>	Algorithm 1:	(yes) to any one of Q1 to Q4
Q1. During the past 4 weeks, have you had knee pain on most days? (yes/no)	Algorithm 2:	(yes) to any two of Q1 to Q3 AND
Q2. During the past 4 weeks, have you had knee pain while climbing down stairs or walking down slopes? (yes/no)		(yes) to Q4
Q3. During the past 4 weeks, have you had swelling in one or both knees? (yes/no)	Algorithm 3:	(yes) to Q1 and Q2 and Q3, OR
Q4. Do you have knee osteoarthritis? (If you do, was the diagnosis made by a Western trained doctor?) (yes/no)		(yes) to any one of Q1 to Q3 AND (yes) to Q4

<sup>†</sup>Adapted from Roux *et al.*<sup>12</sup>

English or Chinese, or were unable to give an informed consent. We invited 146 eligible patients to attend an outpatient rheumatology clinic in Singapore General Hospital; approximately half of the subjects answered positive to any one out of four question items, and half of those answered negative to all four items in Instrument 3.

During the clinic visit, subjects provided sociodemographic data. They were evaluated for their comorbidities with the Charlson comorbidity index,<sup>15</sup> and for the knee symptoms using the Knee injury and Osteoarthritis Outcome Score (KOOS).<sup>16</sup> The KOOS consists of five subscales, namely pain, symptoms, function in daily living, function in sport and recreation, and knee-related quality of life. Each subscale is reported as a normalized score with 100 indicating no symptom and 0 indicating extreme symptoms. Study subjects self-administered either the English or Chinese version of the three questionnaires according to their preference and main spoken language (Table 1). To minimize the learning effect, the three screening questionnaires were presented in a random sequence.

One rheumatologist (YYL) blinded to the answers of the screening questionnaires, performed physical examinations. Body weight and height were measured. Subjects had standard standing and weight-bearing anteroposterior and lateral view radiographs and skyline view radiographs of both knees. The diagnosis of symptomatic KOA was ascertained based on the ACR combined clinical and radiographic criteria,<sup>8</sup> where radiographic criteria were taken as Kellgren–Lawrence (KL) grade of >2 in at least one knee.<sup>17</sup> One musculoskeletal radiologist (SBW) blinded to the clinical features of patients read and scored the radiographs.

The study protocol was approved by the SingHealth Centralized Institutional Review Board (CIRB) (2012/143/E), and all subjects signed an informed consent prior to the study.

## NHSS 2013 follow-up study

The NHSS 2013 was a cross-sectional survey on a representative but disproportionate sample (under-sampling of Chinese and over-sampling of Malays, Indians and other races) of non-institutionalized Singapore residents aged 18 years and above. It was planned, coordinated and undertaken by Singapore Ministry of Health (MOH) while its outsourced survey fieldwork was conducted between November 2012 and October 2013.

A follow-up study was jointly conducted by Singapore General Hospital and Singapore Ministry of Health in November 2014 that recruited a subset of consented subjects (aged ≥18 years old) from the NHSS 2013 survey who provided telephone numbers at the time of interview. We invited the selected subjects to complete the adapted screening questionnaire, Instrument 3 (Table 1) together with the additional question item (Table 1) by mail. If no response was received after 4 weeks, we contacted the subjects by telephone to complete the questionnaire. The study protocol for NHSS 2013 follow-up study was approved by SingHealth CIRB (2014/907/E).

## Statistical analysis

The performances of screening questionnaires were evaluated based on the sensitivity and specificity with 95% confidence intervals (CIs). Sensitivity was defined as the proportion of symptomatic KOA cases that screened positive, and specificity as proportion of non-symptomatic KOA subjects who screened negative. We evaluated the performance of three screening questionnaires (Instruments 1, 2 and 3; Table 1). Instrument 3 was analyzed by testing three different case-defining algorithms (Table 1). In algorithm 1, a KOA case was defined for positive answers to any one of the question items from Q1 to Q4. In algorithm 2, KOA was defined for positive response to any two of KOA symptoms

(Q1–Q3) plus physician-diagnosed KOA (Q4). In algorithm 3, KOA was defined for positive response to all three KOA symptoms (Q1–Q3), or any one symptom (Q1–Q3) plus physician-diagnosed KOA (Q4). In addition, in all instruments and algorithms, we repeated the analysis of performance by replacing the item of self-reported physician-diagnosed KOA diagnosis with the additional question: ‘Has a doctor (Western trained) ever told you that your knee problem is related to ageing?’ Lastly, the performance of the additional question as a lone question item in a screening questionnaire was also analyzed.

The unweighted prevalence of KOA in NHSS 2013 follow-up cohort was tabulated using the most promising algorithms of Instrument 3. Confidence limits were estimated using the Wilson binomial approximation.<sup>18</sup> We estimated the weighted prevalence of symptomatic KOA weighted to the population distribution by accounting for the proportion of subjects who provided telephone numbers and also weighted to the gender, age and ethnic distribution profiles of the final respondents.

Statistical analyses were performed using the IBM SPSS Statistical Package, version 21.0. (Armonk, NY, USA).

## RESULTS

### Validation screening questionnaires study

There were 146 subjects recruited, of which 76 subjects responded positive to any of the four question items and 70 subjects answered negative to all items in Instrument 3. Forty-five subjects fulfilled the ACR clinical and radiographic criteria for symptomatic KOA. Subjects with symptomatic KOA had significantly higher body mass index (BMI). There were trends in symptomatic KOA subjects to have concurrent symptomatic hand OA, as well as more comorbidities. Subjects with symptomatic KOA had poorer KOOS scores in all the subscales (Table 2). Table 3 illustrates the performance of all the screening questionnaires and their algorithms. The most sensitive questionnaire to screen for symptomatic KOA was Instrument 3 algorithm 1 with a sensitivity of 0.93 (95% CI: 0.81–0.98). However, this algorithm lacked specificity (0.50, 95% CI: 0.39–0.60). Algorithm 3 of Instrument 3, which consisted of three KOA symptoms, or one symptom plus physician-diagnosed KOA, yielded a higher specificity (0.95, 95% CI: 0.86–0.97), but a lower sensitivity (0.44, 95% CI: 0.30–0.60). In algorithm 3A of Instrument 3, we

**Table 2** Sociodemographic characteristics of subjects participating in screening questionnaire validation

	Non-symptomatic KOA ( <i>n</i> = 101)	Symptomatic KOA ( <i>n</i> = 45)	<i>P</i>
<b>Demographic</b>			
Age, years <sup>†</sup>	60.8 ± 4.8	59.5 ± 5.8	NS
Female (%)	70.3	82.2	NS
Ethnicity (% Chinese)	98	88.9	0.29
<b>Educational level (%)</b>			
No formal education	8.9	8.8	
Primary	26.7	33.3	
Secondary and above	64.4	57.8	NS
Body mass index, kg/m <sup>2†</sup>	23.6 ± 3.3	26.3 ± 4.7	<0.0001
Presence of OA hand (%)	21.8	27.3	NS
Charlson comorbidity index <sup>†</sup>	0.50 ± 0.89	0.53 ± 1.01	NS
<b>Knee radiography grading (%)</b>			
KL 0	35.6	0	
KL 1	59.4	0	
KL 2	5.0	57.8	
KL 3	0	24.4	
KL 4	0	17.8	NS
Total knee replacement ( <i>n</i> )	0	1	–
<b>KOOS scores, (0–100)<sup>†</sup></b>			
Symptoms and stiffness	88.2 ± 10.8	68.9 ± 21.1	<0.0001
Pain	90.0 ± 11.1	74.6 ± 17.1	0.008
Daily activity	92.8 ± 9.6	80.2 ± 16.4	0.001
Sport and recreation	83.4 ± 18.2	57.0 ± 31.4	<0.0001
Quality of life	78.5 ± 18.1	55.6 ± 22.8	<0.0001

KL, Kellgren–Lawrence grade of radiographic knee osteoarthritis; KOOS, Knee injury and Osteoarthritis Outcome Score; KOA, knee osteoarthritis; OA, osteoarthritis; NS, not significant.

<sup>†</sup>Mean ± SD.

replaced the term ‘KOA’ (Q4) with the additional question ‘physician-diagnosed aging-related knee problem’; the sensitivity (0.62, 95% CI: 0.47–0.76) improved without significantly compromising the specificity (0.87, 95% CI: 0.79–0.93) (Table 3).

**Table 3** Performance of knee osteoarthritis screening questionnaires

Screening questionnaires	Sensitivity (95% CI)	Specificity (95% CI)
Instrument 1	0.20 (0.10–0.35)	0.98 (0.92–1.00)
Instrument 1A <sup>†</sup>	0.51 (0.36–0.66)	0.91 (0.83–0.96)
Instrument 2	0.38 (0.24–0.53)	0.85 (0.76–0.91)
Instrument 2A <sup>†</sup>	0.42 (0.28–0.58)	0.84 (0.75–0.90)
Instrument 3		
Algorithm 1	0.93 (0.81–0.98)	0.50 (0.39–0.60)
Algorithm 1A <sup>†</sup>	0.96 (0.84–0.99)	0.47 (0.37–0.57)
Algorithm 2	0.31 (0.19–0.47)	0.93 (0.86–0.97)
Algorithm 2A <sup>†</sup>	0.53 (0.38–0.68)	0.88 (0.80–0.93)
Algorithm 3	0.44 (0.30–0.60)	0.95 (0.88–0.98)
Algorithm 3A <sup>†</sup>	0.62 (0.47–0.76)	0.87 (0.79–0.93)
Self-reported diagnosis of KOA by a Western trained doctor	0.27 (0.15–0.42)	0.95 (0.88–0.98)
Alternative question <sup>‡</sup>	0.58 (0.42–0.72)	0.84 (0.75–0.90)

KOA, knee osteoarthritis.

<sup>†</sup>Alternative question replaced Q1 (in Instrument 1), Q2 (in Instrument 2) and Q4 (in Instrument 3).

<sup>‡</sup>Alternative question was "Has a doctor (Western trained) ever told you that your knee problem is related to ageing?"

### Unweighted and weighted prevalence of symptomatic KOA from NHSS 2013 follow-up study

The 4633 subjects (48.1%, out of 9361 subjects in NHSS 2013) who provided telephone numbers were recruited to the NHSS 2013 follow-up study. The demographic characteristics of participants included in this follow-up study were not significantly different from those who were not (data not shown). There were a further 76 subjects who were excluded from the study, as their information was incomplete either on address, addressee or telephone number. Invitation letters for participation with an enclosed screening questionnaire, Instrument 3 and the additional question (Table 1) were sent to 4557 subjects; 3364 (73.8%) subjects responded and completed the screening questionnaire. Specifically, 2459 and 905 responses were returned by mail and completed by telephone interview, respectively. The characteristics of respondents were not significantly different from that of the original NHSS 2013 cohort (data not shown).

Table 4 outlines the unweighted prevalence of symptomatic KOA using the NHSS 2013 follow-up cohort, and the prevalence weighted to the distribution of the general population of Singapore. The weighted prevalence of symptomatic KOA was 4.7% using the

conservative algorithm (Model 1, algorithm 3 of Instrument 3) and was more than double (11%) using the more liberal algorithm (Model 2, algorithm 3 of Instrument 3A). Symptomatic KOA was more prevalent in women than in men consistently across all age groups and ethnicities (Table S2). The prevalence of symptomatic KOA increased with age, and ranged from 3.3% to 8.6% for ages  $\geq 60$  years as compared to 9.5% to 19.7% for ages 18–59 years. Across different ethnic groups, symptomatic KOA was more prevalent among Indians, followed by Malays and Chinese.

### DISCUSSION

In this study, we adapted and validated screening questionnaires for identification of symptomatic KOA in Singapore. Instrument 3 algorithm 1 was found to be the most sensitive questionnaire, but not adequately specific. It would be a useful tool for screening appropriate subjects to enter into a clinical trial, in which a second-step confirmation with physical examination and radiographic evaluation is necessary. Questionnaires that include items enquiring upon the physician's diagnosis of KOA were more specific, but less sensitive. Algorithm 3 and 3A derived from Instrument 3, which consisted of three KOA symptoms or one KOA symptom together with physician's diagnosis yielded a higher sensitivity, without losing the specificity. We utilized this questionnaire in a nationally representative cohort, and estimated the prevalence of symptomatic KOA weighted to the general population distribution of Singapore to be 4.7% using the most conservative algorithm. The weighted prevalence of symptomatic KOA was substantially higher (11%) when using an algorithm that substituted 'physician-diagnosed KOA' with 'physician-diagnosed aging-related knee problem'. The prevalence of symptomatic KOA was higher among women and it increased with age. Using either algorithm, the prevalence of symptomatic KOA rose sharply after the age of 40, illustrating that symptomatic KOA starts affecting adults in their middle age. Across the different ethnic groups, symptomatic KOA was more prevalent among Indians, followed by Malays and Chinese.

Knowledge of KOA prevalence in a country is crucial in the evaluation of KOA-related healthcare needs, specifically for the planning and optimization of healthcare resource allocation. The estimate of KOA prevalence may vary, depending on the classification criteria used. In epidemiology studies of KOA, radiographic criteria have been commonly used to estimate

	Unweighted prevalence, % (95% CI)			Weighted prevalence, %	
	n	Model 1 <sup>†</sup>	Model 2 <sup>‡</sup>	Model 1 <sup>†</sup>	Model 2 <sup>‡</sup>
Overall	3364	5.8 (5.1–6.6)	14.3 (13.2–15.5)	4.7	11.0
By gender					
Female	1822	7.1 (6.0–8.4)	17.5 (15.8–19.3)	5.6	13.1
Male	1542	4.2 (3.3–5.3)	10.5 (9.1–12.1)	3.7	8.8
By age groups					
18–29 years	424	0.7 (0.2–2.1)	2.4 (1.3–4.3)	0.8	1.6
30–39 years	465	1.3 (0.6–2.8)	7.5 (5.5–10.3)	0.6	5.7
40–49 years	828	4.3 (3.2–6.0)	12.1 (10.0–14.5)	4.4	9.7
50–59 years	830	7.5 (5.9–9.5)	18.3 (15.8–21.1)	6.4	15.7
60–69 years	527	9.5 (7.3–12.3)	21.3 (18.0–24.9)	8.7	18.4
≥70 years	290	13.1 (9.7–17.5)	24.8 (20.2–30.1)	10.8	21.5
By age categories					
<60 years	2547	4.2 (3.5–5.1)	11.7 (10.5–13.0)	3.3	8.6
≥60 years	817	10.8 (8.8–13.1)	22.5 (19.8–25.5)	9.5	19.7
By ethnicity and age groups					
Chinese					
Total	1989	5.1 (4.2–6.1)	10.9 (9.6–12.3)	4.3	9.3
<40 years	450	0.9 (0.3–2.3)	2.9 (1.7–4.9)	0.7	2.6
40–59 years	967	4.7 (3.5–6.2)	10.5 (8.7–12.5)	4.9	10.5
≥60 years	572	9.1 (7.0–11.7)	17.8 (14.9–21.9)	8.4	16.7
Malay					
Total	746	5.2 (3.8–7.1)	18.5 (15.9–21.4)	4.8	17.7
<40 years	243	0.8 (0.2–3.0)	6.6 (4.1–10.4)	0.5	5.9
40–59 years	381	5.8 (3.8–8.6)	22.6 (18.7–27.0)	5.3	20.8
≥60 years	122	12.3 (7.6–19.3)	29.5 (22.1–38.1)	12.0	33.6
Indian					
Total	456	10.1 (7.6–13.2)	23.0 (19.4–27.1)	9.2	20.3
<40 years	147	2.0 (0.7–5.8)	9.5 (5.8–15.4)	1.2	9.1
40–59 years	222	12.2 (8.5–17.1)	25.2 (20.0–31.3)	11.5	23.9
≥60 years	87	18.4 (11.6–27.8)	40.2 (30.6–50.7)	19.6	35.5

<sup>†</sup>Model 1 = algorithm 3 of Instrument 3, sensitivity 0.44, specificity 0.95 for symptomatic knee osteoarthritis.

<sup>‡</sup>Model 2 = algorithm 3A of Instrument 3, sensitivity 0.62 and specificity 0.87 for symptomatic knee osteoarthritis.

national prevalence.<sup>7,19,20</sup> However, the discordance between radiographic and clinical features of KOA may lead to inaccurate prevalence estimates of KOA that are symptomatic.<sup>21–24</sup> On the other hand, utilizing clinical criteria alone may overestimate KOA prevalence.<sup>24,25</sup> Current recommendation advocates for the use of both clinical and radiographic criteria,<sup>26</sup> but its implementation would be costly and impractical for large-scale epidemiology studies.<sup>9</sup> An alternative tool to estimate the national KOA prevalence for public health purposes would be a screening questionnaire.

Prior studies have attempted to validate screening questionnaires that combine symptoms, physical limitation and self-reported diagnosis of KOA. These

**Table 4** Prevalence of symptomatic knee osteoarthritis in NHSS follow-up study, Singapore ( $n = 3364$ )

questionnaires demonstrated reasonable diagnostic performance.<sup>10,12,13</sup> They were utilized to distinguish KOA from other inflammatory arthritides<sup>27</sup> and to estimate the prevalence of KOA in the general population.<sup>13</sup> In this study, after the initial validation exercise, we selected the screening questionnaire adapted from Roux *et al.* (Instrument 3) to estimate the prevalence of symptomatic KOA in the general population of Singapore. The original screening questionnaire for KOA by Roux *et al.*<sup>12</sup> utilized a two-stage approach, starting with administration of a screening questionnaire by telephone, followed by ascertainment of diagnosis by clinical and radiographic evaluation in subjects who screened positive. The overall two-step procedure

resulted in a sensitivity of 0.87 and specificity of 0.92 for detecting KOA. A subsequent study applied the two-step procedure, including a full evaluation of 3707 subjects in a clinic, and estimated the prevalence of KOA in France to be 9%.<sup>13</sup> Despite the accurate estimate produced by this method, it was rather costly to replicate on a larger scale and therefore has limited application in subsequent KOA epidemiology studies for evaluation of the burden of illness of KOA in the population. Another study in Spain has investigated a one-step approach utilizing a questionnaire with its set of algorithms to screen for KOA (Instrument 2).<sup>10</sup> Although the method was highly sensitive, none of the algorithms was adequately specific to be implemented as a screening tool. Our present study has shown that a screening questionnaire with the particular algorithms could be utilized in epidemiology studies with a high specificity and adequate sensitivity as a one-step procedure to screen for KOA (Instrument 3, algorithms 3 and 3A).

In the present study, we demonstrated that the inclusion of an item enquiring about physician-diagnosed KOA increased the sensitivity but reduced the specificity of algorithms. The relatively lower sensitivity of the algorithms was likely attributed to the fact that the general population is unfamiliar with the term 'KOA'. The diagnosis of KOA is usually conveyed by most doctors as 'aging-related problem' or 'wear and tear problem' in both primary and secondary healthcare settings in Singapore. Compared to similar studies in Western countries, the single screening question that enquires about 'physician-diagnosed KOA' generally yielded sensitivities in the range of 0.80–0.90,<sup>9,10,12,28</sup> as compared to a sensitivity of only 0.27 (95% CI: 0.15–0.42) in the current study. Replacing 'physician-diagnosed KOA' with 'physician-diagnosed aging-related knee problem' increased the sensitivity of our screening questionnaires. The unfamiliarity of the general population with the term KOA was also seen in our validation cohort for the screening questionnaire. Out of the 45 cases of KOA ascertained by the ACR criteria, only 33.3% of subjects responded positively to the question enquiring about physician-diagnosed KOA, while a higher proportion (57.8%) answered positively to the additional question enquiring about physician-diagnosed aging-related knee problem.

The suboptimal sensitivity of our best screening questionnaire could be attributed to several other factors. Firstly, KOA is a very slowly progressive disease and its sporadic symptoms may deter patients from seeking medical attention.<sup>29</sup> Second, our screening

questionnaire could only be considered a diagnosis by a Western trained doctor; however, seeking alternative medicine is common in Singapore. Many of the patients with KOA might have sought care from Traditional Malay, Indian or Chinese Medicine practitioners.<sup>30</sup> Taken together, the low sensitivity of our screening questionnaire may result in underestimation of the true prevalence of symptomatic KOA in the population, especially when using the most conservative algorithm (Instrument 3, algorithm 3). Using the more liberal model (Instrument 3, algorithm 3A), with a slightly lower specificity of 0.87, the estimated prevalence of symptomatic KOA may be closer to the true prevalence. This is consistent with the higher prevalence of both radiographic and symptomatic KOA among Chinese in the Beijing OA study (symptomatic KOA in men 5.6% and 15.0% for women) compared to the US Framingham cohort (prevalence ratio 1.43 [95% CI: 1.16–1.75]).<sup>7</sup>

The prevalence of symptomatic KOA in Singapore is unknown despite its high disease burden.<sup>2,4,5</sup> To the best of our knowledge, our study was the first to validate screening questionnaires for symptomatic KOA in Asia. The burden of KOA in Singapore was previously estimated based on self-reported chronic joint pain or physician-diagnosed arthritis in the NHSS 2007.<sup>6</sup> The prevalence of chronic joint pain or physician-diagnosed arthritis from the NHSS 2007, without specifying the site of arthritis, was 10.1%; it increased with age and was 19.8% among elderly aged 60–69 years.<sup>6</sup> The estimated prevalences of symptomatic KOA from this study were therefore comparable to the previous study, although likely to be underestimated as limited by the poor sensitivities of the screening questionnaires. In addition, we showed that the prevalence of symptomatic KOA increases with age, and we noted a sharp increase in prevalence from age 40 and above. Further, the prevalence of symptomatic KOA was found to differ across ethnic groups. Symptomatic KOA was more prevalent among Indians, followed by Malays and Chinese. This difference could be attributed to the higher prevalence of obesity among Indians and Malays.<sup>31</sup>

The strengths of our study include the use of combined clinical and radiographic evaluation as the standard for KOA case ascertainment during the validation exercise. In addition, the present validation studies also evaluated carefully the word choices as it has been shown that prevalence estimate may change with minor wording changes in the questionnaires.<sup>32</sup> Lastly, the validated screening questionnaires in our study (Instrument 3, algorithms 3 and 3A) had an improved

sensitivity and high specificity to identify KOA cases, as compared to the screening methods used in previous studies in Singapore.<sup>6</sup> There are a few limitations in our study. First, subjects in the validation screening questionnaire study were members of a community center, who were elderly aged  $\geq 50$  years old and predominantly Chinese. This may limit the generalizability of the screening questionnaire results to the younger age groups and other ethnicities. Nevertheless, the middle-aged and older population present a major public concern because KOA prevalence rises sharply after middle age.<sup>2</sup> The second limitation was the relatively low sensitivity of the best-performing screening questionnaire, as compared to the one in Western studies<sup>9,10,12</sup> for the reasons outlined earlier. The suboptimal sensitivity may lead to underestimation of the prevalence of symptomatic KOA. We did not evaluate the utility of this screening questionnaire in distinguishing KOA from other inflammatory arthritides of the knee in the current study, although this utility has been demonstrated previously by Morvan *et al.*<sup>27</sup> Given the relatively low prevalence of inflammatory arthritis (0.37% in Southeast Asia) in the general population compared to KOA,<sup>33</sup> the impact of such mis-classification on the KOA prevalence estimation is expected to be low.

In conclusion, our study adapted and validated screening questionnaires to the local sociocultural context for symptomatic KOA screening in the general population of Singapore. For a one-step evaluation in population-based studies, two screening algorithms had improved sensitivities and reasonable specificities to estimate the prevalence of symptomatic KOA. The weighted prevalences of symptomatic KOA were 4.7% and 11%, respectively, using the most conservative and the more liberal algorithms. The prevalence of symptomatic KOA increased sharply after the age of 40 years, and was higher in women than that in men. Symptomatic KOA was more prevalent among Indians followed by Malays and Chinese.

## **ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

The study protocol of validation of screening questionnaires was approved by the SingHealth Centralized Institutional Review Board (CIRB) (2012/143/E), and all subjects signed an informed consent prior to the study. The study protocol for NHSS 2013 follow-up study was approved by SingHealth CIRB (2014/907/E). A waiver of re-consent was granted.

## **CONSENT FOR PUBLICATION**

Not applicable.

## **AVAILABILITY OF DATA AND MATERIAL**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## **COMPETING INTERESTS**

None. All authors have declared no conflict of interest.

## **FUNDING**

This project was supported by the Singapore General Hospital Grant 2012 (SRG#13/2012) and 2014 (SRG-S/11/2014). The principal investigator (YYL) was supported by the Singapore General Hospital Center Grant (GGKATYLEUNG) and the National Medical Research Council, Singapore (NMRC/HSRG/0061/2016). The sponsors had no role in study design, in the collection, analysis and interpretation of data, in the writing of the report or in the decision to submit the article for publication.

## **AUTHORS CONTRIBUTIONS**

YYL, SM and JT conceptualized and designed the study. YYL, SBW, CML and IS acquired the data. YYL, SM analyzed the data. All authors interpreted the data. All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. YYL had full access to all of the data in the study and takes responsibility for the integrity of the work as a whole.

## **ACKNOWLEDGEMENTS**

The authors appreciate the support from Dr. Carol Tan, Mr. Firman Firdaus Loo and Mr. Peter Chou of the Nice Organization in administering the screening questionnaires, and from Ms. Tan Hwee Kheng of the NTUC Elder Care in recruiting patients. We would like to thank Mr. Cheung Chun Chung, Ms. Connie Tse Kwan Yi, Ms. Lee Wan Pin, Ms. Chua Ming Boon and Mr. Lewis Wong for their assistance in translating the screening questionnaires. We also thank Ms. Serene Ong of Duke NUS Medical School for editorial help.



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### Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

**Table S1.** Knee osteoarthritis screening questionnaires.

**Table S2.** Prevalence of symptomatic knee osteoarthritis stratified by gender in NHSS follow-up study, Singapore ( $n = 3364$ ).