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Body mass index and health-related quality of life of outpatients with knee osteoarthritis: evidence from a cross-sectional study

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Abstract

Purpose To estimate the health-related quality of life (HRQoL) of knee osteoarthritis outpatients in China overall and by body mass index (BMI), and to explore the factors associated with knee osteoarthritis.

Method This was a cross-sectional study in which outpatients with knee osteoarthritis were recruited from three tertiary hospitals in China from June 2020 to May 2021. The EuroQoL five-dimensional instrument was used to measure HRQoL. Descriptive analysis, one-way analysis of variance, and a Tobit regression model were performed.

Results One thousand and eight questionnaires were distributed, and nine hundred and fifty-two participants were included. The mean age was 61.71 years, and 61.03% of the participants were female. The mean health utility was 0.751 (95% CI 0.737, 0.765). The health utility varied significantly according to BMI: underweight = 0.627 (95% CI 0.536, 0.719), normal = 0.764 (95% CI 0.744, 0.784), overweight = 0.755 (95% CI 0.733, 0.776), and obese = 0.728 (95%CI 0.681, 0.776). Additionally, outpatients with knee osteoarthritis who were younger, had received treatment in the past six months, and had a disease duration shorter than 2 years had significantly higher HRQoL scores.

Conclusion The HRQoL of knee osteoarthritis outpatients was considerably impaired and was significantly associated with BMI. These findings emphasize the importance of weight examination and management in outpatients with knee osteoarthritis for healthcare providers. Supplementary data were provided for public health-related policies and health economics studies, contributing to the development of effective management strategies and increasing the breadth of knowledge of HRQoL in outpatients with knee osteoarthritis.

Plain English Summary

There were 595 million people living with osteoarthritis globally in 2020, equal to 7.60% of the global population, with an increase of 132.20% in total cases since 1990. The knee was the most prevalent joint with a prevalence of 21.51% among people aged 40 years and older in China, while the weight has been proven to be an important modifiable risk factor for knee osteoarthritis. Considering the increasing cases of overweight/obesity in China and the great disease burden on individuals and the healthcare system, we estimated the effect of knee osteoarthritis on health and associated factors, health-related quality of life (HRQoL) was measured using health utility and the EQ-VAS scores. A total of 952 participants were included, the average health utility was 0.751, and the average

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EQ-VAS score was 70.37. Participants with a normal BMI were found to have the highest HRQoL, indicating the importance of managing weight in patients with knee osteoarthritis to improve HRQoL. Moreover, age, history of treatment and disease duration have been proven to be associated factors, which provides evidence for public health policymakers and health economic professionals. The findings of the present study increase the breadth of knowledge of HRQoL in individuals with knee osteoarthritis.

Keywords Health-related quality of life, Knee osteoarthritis, Utility, BMI, EQ-5D-5L

Introduction

Osteoarthritis is one of the leading causes of disability and pain worldwide, characterized by joint pain and loss of mobility, imposing a great disease burden on patients and the healthcare system [1]. The World Health Organization (WHO) has designated the period from 2021 to 2030 as the decade of healthy ageing, highlighting the need to improve quality of life and address chronic diseases, such as osteoarthritis [2]. According to a report based on the Global Burden of Disease Study (GBD), there were 595 million people living with osteoarthritis globally in 2020, equal to 7.6% of the global population, with an increase of 132.2% in total cases since 1990 [2]. Osteoarthritis can affect every synovial joint, and the knee is the most frequently affected joint. Among people aged 40 years and older, the prevalence of knee osteoarthritis in China was 21.51% [3]. Osteoarthritis has been responsible for a major source of health expenditure, in the USA, osteoarthritis caused an estimated US$80 billion in 2016, and in Hong Kong, osteoarthritis caused an estimated more than $400 million in medical spending [2].

Osteoarthritis not only increases medical expenditure of the healthcare system, but also seriously impairs patients' health-related quality of life (HRQoL) [4–6]. HRQoL is a multidimensional measure of subjective feelings towards and experiences with health, involving physical, mental and functional health [7]. HRQoL is a widely recognized measure to estimate the effect of diseases especially for chronic diseases on people [8]. Osteoarthritis is responsible for great joint pain, increasing disability and progressive cartilage degeneration in people with osteoarthritis, and significantly affecting HRQoL. The measurement of HRQoL for people with osteoarthritis can provide health care professionals with a better understanding of the disease burden of osteoarthritis [9]. Additionally, the utility estimates are essential input parameters for measuring quality-adjusted life years (QALYs) in economic evaluations, which may vary depending on multiple factors such as population and disease severity [8].

Osteoarthritis places significant disease burdens on both the HRQoL of patients and the increasing medical expenditures in healthcare systems. However, currently, no treatment strategies can cure osteoarthritis completely, modifiable risk factors are important for delaying the onset of osteoarthritis and slowing the progression of osteoarthritis. It has been proven that several possible factors may be associated with the onset and progression of osteoarthritis: age, sex, BMI, genetic factors, behavioral influences, ethnicity, and the environment [6, 10–12]. Among these factors, BMI has been considered to be the main established modifiable risk factor [2, 13, 14]; moreover, approximately half of adults and one-fifth of children are forecast to be overweight or obese in China according to the Chinese criteria, making China the country with the highest number of people with overweight or obesity in the world [15]. Considering the proven association between BMI and osteoarthritis and the increasing cases of overweight and obese in China, reliable estimation of HRQoL for osteoarthritis patients with different BMI levels is necessary to fully understand the disease burden.

Previous studies have estimated the HRQoL of knee osteoarthritis patients using disease-specific instruments, such as the Western Ontario and MacMaster questionnaire (WOMAC) [16–18], the Lysholm knee score [19, 20], the Oxford Knee Score and the Activity and Participation Questionnaire [21, 22], and the Osteoarthritis of Knee and Hip Quality of Life questionnaire (OQKHQOL) [23]. Although these disease-specific instruments have been able to measure changes in disease status for patients with knee osteoarthritis, they are not able to provide the results of health utility scores, which are urgently needed by health-related policies and health economic models. Therefore, in this study, generic instrument was used to report health utility scores for patients with knee osteoarthritis. Meanwhile, although the association has been proven and BMI is supposed to be a modifiable risk factor for osteoarthritis [2, 13, 14], few studies have estimated the extent to which BMI affects the HRQoL of people with knee osteoarthritis [24, 25]. Therefore, the present study aims to estimate the health utility of outpatients with knee osteoarthritis in China by using the EQ-5D-5 L instrument and to explore the factors associated with the HRQoL of outpatients with knee osteoarthritis, with a special emphasis on BMI. The present study can serve as a valuable supplement to previous studies and provide important data for health economics professionals and public health policymakers.

Methods

Study design and participants

This was a cross-sectional study, which was reviewed and approved by the Medical Faculty Ethics Committee of Zhejiang University. Throughout all phases of the research, the confidentiality and the anonymity of the collected data were ensured. Participants' names, contact information and other privacy-related information were not involved in the questionnaire or the face-to-face investigation, and virtual unique codes were assigned to participants during data analysis.

Outpatients with knee osteoarthritis were recruited from three tertiary hospitals in Zhejiang Province from June 2020 to May 2021 (Fig.S1). The eligibility criteria were as follows: (1) outpatients aged 40 years and older; (2) outpatients who were diagnosed with knee osteoarthritis by a physician according to the criteria outlined in the "Osteoarthritis Diagnosis and Treatment Guideline (2018)" established by the Joint Surgery Group of Chinese Orthopaedics Association (Table S2) [26]; (3) outpatients who were not currently pregnant; and (4) outpatients who were conscious, had no cognitive impairment, psychological problems or mental illness, and could express themselves clearly. Outpatients were excluded if they had (1) other serious diseases, such as cardiovascular disease, liver and kidney function impairment, immune deficiency or blood disease, or (2) other bone diseases or injuries that may affect their normal joint function.

Instruments and variable description

The survey was conducted by using a self-designed questionnaire, which was designed according to previous studies and expert consultation [7–9]. The questionnaire was composed of three parts: sociodemographic variables, clinical variables, and a five-level EuroQol five-dimensional instrument (EQ-5D-5 L).

The sociodemographic variables included sex, age, education level, marital status, and healthcare insurance scheme. Age was categorized into three groups: <55, 55–64, and ≥65 years. Education level was categorized into four levels: no formal education, primary school, middle school, and high school and above. Marital status was classified as single (not married or not living in a partnership) or not single (married or living in a partnership). The insurance schemes were divided into four types: no insurance, basic medical insurance for urban employees (UEBMI), basic medical insurance for urban residents (URBMI) and commercial medical insurance.

The clinical variables included BMI, duration of knee osteoarthritis, and history of treatment in the past six months. The cut-off values for BMI in this study were based on the "weight for adults" criterion established by the National Health Commission of China [27]. The participants were classified into four categories based on their BMI values: underweight (BMI < 18.5 kg/m^2), normal weight (18.5 ≤ BMI < 24.0 kg/m^2), overweight (24.0 ≤ BMI < 28.0 kg/m^2) and obese (BMI ≥ 28.0 kg/m^2) [27]. The duration of knee osteoarthritis was divided into three categories: <2 years, 2–5 years, and > 5 years. A history of treatment was a binary variable that referred to whether the outpatient had received any type of treatment in the past six months, including conservative/surgical/medication treatment.

The EQ-5D-5 L instrument was applied in the present study, which is widely used to measure HRQoL, and a Chinese version was used [28–30]. The EQ-5D-5 L comprises two components: the health state descriptive system and the visual analogue scale (EQ-VAS) of 100 mm. In the health state system, a 5-point response scale was applied in the descriptive system, where 1 refers to no problem, 2 refers to a slight problem, 3 refers to a moderate problem, 4 refers to a severe problem, and 5 refers to an extreme problem [30]. The responses to the description were converted into utility index scores through a Chinese general population-based EQ-5D-5 L value set based on the time trade-off (TTO) technique [31]. In the EQ-VAS, participants marked their health on a scale ranging from 0 to 100, where 0 refers to the worst self-reported health state and 100 refers to the best self-reported health state.

Data collection

A face-to-face investigation was conducted. First, the investigators contacted the clinician to review the medical records to confirm the diagnosis of knee osteoarthritis, and then further checked whether the outpatients met the inclusion criteria. Second, if an outpatient met all the inclusion criteria, informed consent was provided to confirm whether the outpatient agreed to participate. Third, for outpatients who met the inclusion criteria and agreed to participate, a face-to-face interview was conducted. Before the investigation, two investigators from the research group were trained based on uniform standards (one was a PhD candidate, and the other was a master's student from our research group at Zhejiang University) to ensure that they fully understood the purpose of the study and the context of the questionnaire. During the investigation, if problems were found, investigators would try to ask the participants again to ensure data integrity and availability. After the investigation, the data were double entered to ensure the accuracy of the database.

Statistical analysis

There were three steps to analyze the data in the present study. First, descriptive statistics were adopted to report the characteristics and HRQoL of knee OA outpatients, and subgroup analysis was conducted to further explore

the data based on demographic and clinical characteristics. The frequencies with percentages were calculated for categorical variables, and the means and 95% confidence intervals (CIs) were calculated for continuous variables. Second, one-way analysis of variance (ANOVA) was applied to compare the health utility and EQ-VAS score according to participant characteristics. Third, a Tobit regression model was adopted to explore the factors that were significantly associated with health utility and the EQ-VAS score. The Tobit model was chosen because the distributions of both health utility and the EQ-VAS score were skewed [31]. Independent variables were chosen based on previous studies, including sex, age, marital status, educational level, insurance scheme, BMI, history of treatment, and duration of knee osteoarthritis [6, 10–12]. A significance level of 0.05 was used. The data were double entered into EpiData 3.1 and analyzed using SPSS 26.0 and Stata/SE 15.1.

Results

Participant characteristics

A total of 1008 questionnaires were distributed, with the exclusion of 42 questionnaires lacking key information and 14 questionnaires having logical problems. As a result, 952 knee osteoarthritis outpatients were included in the present study (Fig.S1). A total of 41 participants were underweight, 467 had a normal BMI, 350 were overweight and 94 were obese. The mean age was 61.71 years (95% CI 61.08, 62.34), with a male proportion of 38.97%. More than half of the participants (50.10%) had an education level of middle school, high school or above. A total of 86.66% of the participants were not single, and more than half of the participants had insurance from the URBMI. Most of the participants (81.62%) reported a duration of knee OA shorter than 5 years (Table 1).

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Health-related quality of life

The most prevalent problem reported by participants with knee osteoarthritis was pain/discomfort (96.11%), followed by impaired activity level (62.50%). The impaired self-care level was the least reported (33.40%). When the participants were divided into different BMI groups, the most serious problem was still pain/discomfort: 92.68% of underweight participants, 96.79% of normal weight participants, 96.29% of overweight participants, and 93.62% of obese participants. The second most serious problems among underweight, normal weight, overweight, and obese participants groups were anxiety/depression (73.17%), usual activity (60.17%), usual activity (63.14%), and usual activity (68.09%), respectively (Fig. 1; Table S1).

The mean health utility of outpatients with knee osteoarthritis was 0.751 (95% CI 0.737, 0.765). The health utility varied significantly between participants with different BMI ($P = 0.002$). The health utility was 0.627 (95% CI 0.536, 0.719) for underweight participants, 0.764 (95% CI 0.744, 0.784) for normal weight participants, 0.755 (95% CI 0.733, 0.776) for overweight participants, and 0.728 (95% CI 0.681, 0.776) for obese participants (Fig. 2; Table 1).

The mean EQ-VAS score for knee osteoarthritis outpatients was 70.37 (95% CI 69.64, 71.09). The EQ-VAS scores were statistically significantly different between participants with different BMI ($P = 0.013$). The score was 67.71 (95% CI 63.28, 72.14) for underweight participants, 71.15 (95% CI 70.18, 72.12) for normal weight participants, 70.43 (95% CI 69.30, 71.57) for overweight participants, and 67.38 (95% CI 64.25,70.52) for obese participants (Table 1).

Factors associated with health-related quality of life

Univariate analysis revealed significant associations between HRQoL (both health utility and EQ-VAS scores) and age, educational level, insurance scheme, BMI, and duration of disease; additionally, associations between health utility and history of treatment and between the EQ-VAS score and marital status were also found. Associations between HRQoL scores and sex were not significant. Participants who were younger, had a higher education level, were covered by UEBMI insurance, or had a normal BMI had greater health utility and EQ-VAS scores (Table 1).

However, the multivariate regression showed that education level and insurance scheme were not significant factors associated with health utility or the EQ-VAS score after adjusting for other variables. The strongest determinant of health utility was BMI. Compared with underweight participants, those with a normal BMI, overweight status, or obesity had greater health utility, while participants with a normal BMI had the highest health utility. In terms of the EQ-VAS score, compared with underweight participants, normal weight and overweight participants had higher EQ-VAS scores, while obese participants had lower EQ-VAS scores. Additionally, compared with participants aged younger than 55 years, those aged older than 65 years had lower EQ-5D utility. Compared with participants who did not receive treatment in the past six years, those who received treatment had greater health utility. Compared with those with a duration shorter than 2 years, those whose duration was longer than 5 years had lower health utility. Compared with participants younger than 55 years, those older than 55 years had lower EQ-VAS scores, compared with those with a duration shorter than 2 years, those whose duration was longer than 5 years had lower EQ-VAS scores (Table 2).

Table 1 Characteristics of knee osteoarthritis outpatients, and health utility and EQ-VAS score stratified by their characteristics

Variables	*N* (%)	Health utility			EQ-VAS score		
		Mean	95%CI	*P*	Mean	95%CI	*P*
Total	952(100)	0.751	[0.737,0.765]		70.37	[69.64,71.09]	
Sex				0.043			0.068
Male	371(38.97)	0.769	[0.748,0.791]		71.21	[69.99,72.44]	
Female	581(61.03)	0.739	[0.721,0.758]		69.83	[68.92,70.73]	
Age (years)				< 0.001			< 0.001
< 55	232(24.37)	0.810	[0.786,0.833]		74.04	[72.69,75.40]	
55–64	315(33.09)	0.766	[0.743,0.788]		70.59	[69.32,71.86]	
≥ 65	405(42.54)	0.706	[0.682,0.730]		68.09	[66.97,69.20]	
Education level				< 0.001			< 0.001
No formal education	158(16.60)	0.710	[0.670,0.751]		68.33	[66.53,70.14]	
Primary school	317(33.30)	0.712	[0.684,0.739]		69.00	[67.79,70.22]	
Middle school	274(28.78)	0.776	[0.754,0.798]		70.40	[68.99,71.81]	
High school and above	203(21.32)	0.811	[0.787,0.834]		74.04	[72.55,75.53]	
Marital status[a]				0.402			0.011
Single	127(13.34)	0.736	[0.696,0.775]		67.95	[65.57,70.34]	
Not single	825(86.66)	0.753	[0.738,0.768]		70.74	[69.98,71.49]	
Insurance				< 0.001			< 0.001
No insurance	45(4.73)	0.728	[0.655,0.801]		70.09	[66.11,74.06]	
UEBMI	266(27.94)	0.810	[0.787,0.832]		73.05	[72.01,74.09]	
URBMI	569(59.77)	0.726	[0.706,0.745]		69.47	[68.47,70.47]	
Commercial medical insurance	72(7.56)	0.749	[0.703,0.794]		67.71	[64.91,70.51]	
History of treatment				0.019			0.615
Untreated	135(14.18)	0.710	[0.668,0.753]		69.91	[68.03,71.78]	
Treated	817(85.82)	0.758	[0.743,0.772]		70.44	[69.65,71.23]	
BMI[b]				0.002			0.013
Underweight	41(4.31)	0.627	[0.536,0.719]		67.71	[63.28,72.14]	
Normal	467(49.05)	0.764	[0.744,0.784]		71.15	[70.18,72.12]	
Overweight	350(36.76)	0.755	[0.733,0.776]		70.43	[69.30,71.57]	
Obese	94(9.87)	0.728	[0.681,0.776]		67.38	[64.25,70.52]	
Duration (years)[c]				< 0.001			< 0.001
< 2	296(31.09)	0.767	[0.743,0.790]		71.78	[70.58,72.98]	
2–5	481(50.53)	0.771	[0.752,0.789]		70.82	[69.86,71.79]	
> 5	175(18.38)	0.670	[0.630,0.711]		66.73	[64.65,68.80]	

BMI body mass index, CI confidence interval; [a]Single refers to not married or not living in a partnership; not single refers to married or living in a partnership; [b]BMI category was defined based on "weight for adults" criterion established by the National Health Commission of China, the cut-off values for BMI: underweight (BMI < 18.5 kg/m^2), normal weight (18.5 ≤ BMI < 24.0 kg/m^2), overweight (24.0 ≤ BMI < 28.0 kg/m^2), and obese (BMI ≥ 28.0 kg/m^2); [c]Duration refers to the time elapsed from the initial diagnosis of knee osteoarthritis to the time of investigation

Discussion

This cross-sectional study estimated the HRQoL and its association with BMI and other potential factors using the EQ-5D-5 L. Furthermore, HRQoL is vital for measuring the impact of knee osteoarthritis on health, and it was represented by both health utility and the EQ-VAS scores in the present study. This study was the first to estimate not only the health utility and EQ-VAS scores for knee osteoarthritis outpatients but also the distribution of HRQoL among individuals with different BMI groups in China. The findings revealed an average health utility of 0.751 for all included knee osteoarthritis outpatients, with participants having a normal BMI exhibiting the highest health utility. Similarly, the average EQ-VAS score was 70.37, with participants having a normal BMI also exhibiting the highest EQ-VAS score.

Outpatients with knee osteoarthritis suffer from considerable impairment in HRQoL. On the one hand, when compared with the normal population, the health utility of the general Chinese population was estimated using the EQ-5D-5 L instrument, with an estimated health utility of 0.927 [32]. This value was much higher than that reported in the present study, emphasizing the critical importance of the management and prevention of knee osteoarthritis. On the other hand, the estimated health utility in our study was higher than that reported in the UK [33]. The National Institute for Health and Care Excellence (NICE) reported health utility values of 0.688, 0.701, and 0.723 for patients with osteoarthritis

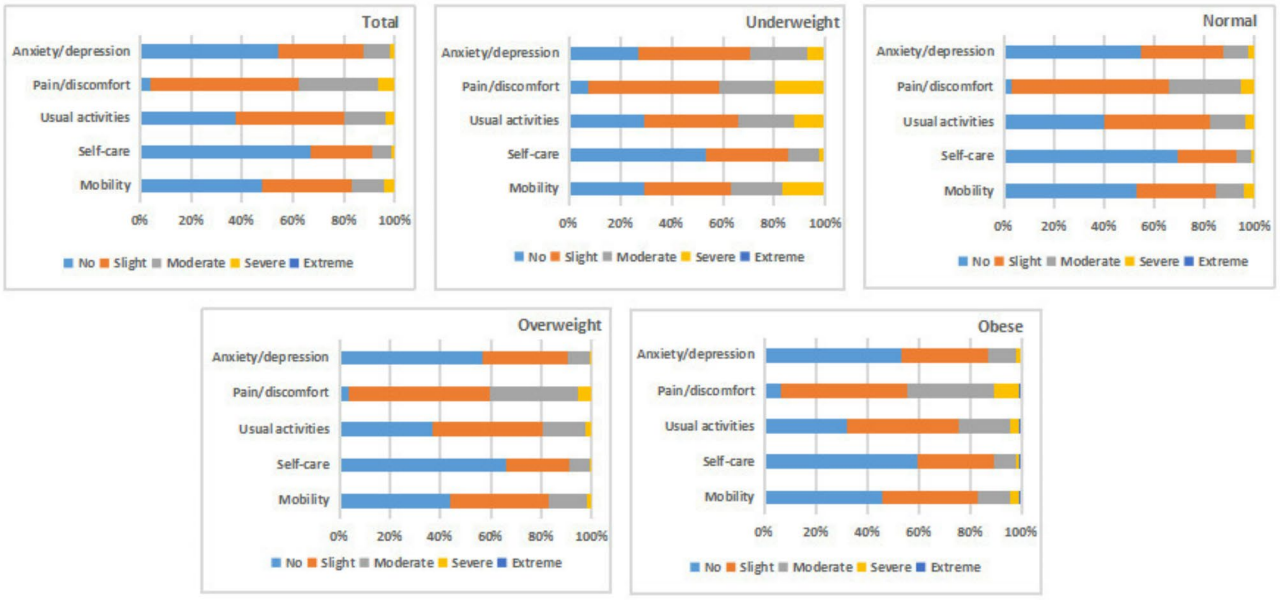

Fig. 1 Distribution of the EQ-5D problems reporting among knee osteoarthritis outpatients

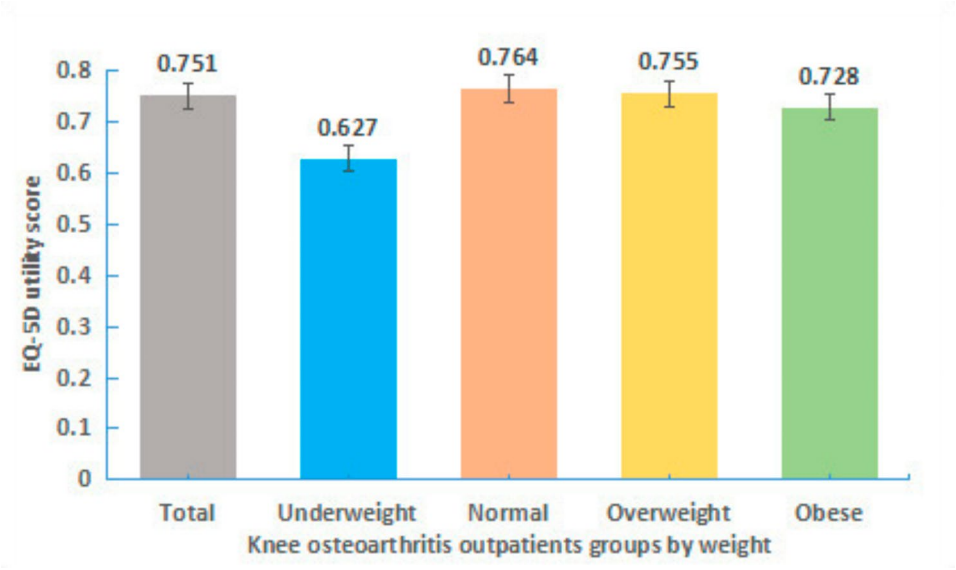

Fig. 2 EQ-5D utility scores of knee osteoarthritis outpatients by weight

who did not take any medications, took paracetamol or took NSAIDs/COX-2 inhibitors, respectively [33]. The cultural difference between China and the UK may contribute non-negligibly to this disparity. All items in the EQ-5D-5 L were subjective, encompassing participants' attitude towards pain and self-care. Compared to participants in the UK, Chinese people have maintained the world's most enduring and successful continuous culture over the past four millennia, with primary beliefs in Taoism, Confucianism, and Buddhism influencing them for thousands of years [34, 35]. For example, within Buddhism beliefs, pain and suffering are viewed as a power, unwanted yet existent, that arises from obstacles in one's past life; within Confucianism, pain is considered an essential element of life. Therefore, it is more likely that Chinese patients will experience pain but also demonstrate resilience in enduring it [35]. Apart from cultural differences, medications were not distinguished in the present study, thus there is a possibility that medication may have influenced participants' attitudes and potentially overestimated people's self-reported health status in the present study.

BMI was indicated to be associated with the HRQoL of participants with knee osteoarthritis in the present study,

Table 2 Association between knee osteoarthritis outpatients' characteristics and EQ-5D utility, EQ-VAS score using a Tobit regression model

Variables	Health utility			EQ-VAS score		
	Coef	95%CI	*P*	Coef	95%CI	*P*
Sex (ref = male)						
Female	-0.017	[-0.044,0.011]	0.245	-0.853	[-2.304,0.598]	0.249
Age, years (ref = < 55)						
55–64	-0.025	[-0.062,0.012]	0.189	-2.400	[-4.322,-0.478]	0.014
≥ 65	-0.066	[-0.104,-0.029]	0.001	-4.235	[-6.196,-2.274]	< 0.001
Education level (ref = no formal education)						
Primary school	-0.016	[-0.057,0.024]	0.433	-0.217	[-2.331,1.897]	0.841
Middle school	0.024	[-0.020,0.068]	0.293	-0.326	[-2.624,1.972]	0.781
High school and above	0.038	[-0.011,0.087]	0.133	2.443	[-0.115,5.001]	0.061
Marital status[a](ref = single)						
Not single	-0.010	[-0.051,0.030]	0.611	1.437	[-0.650,3.524]	0.177
Insurance (ref = no insurance)						
UEBMI	0.038	[-0.031,0.106]	0.279	0.587	[-2.976,4.150]	0.747
URBMI	-0.010	[-0.074,0.054]	0.762	-0.751	[-4.085,2.584]	0.659
Commercial medical insurance	0.006	[-0.072,0.085]	0.873	-2.917	[-7.004,1.169]	0.162
History of treatment (ref = untreated)						
Treated	0.053	[0.015,0.092]	0.007	0.967	[-1.044,2.978]	0.346
BMI[b] (ref = underweight)						
Normal	0.123	[0.056,0.191]	< 0.001	2.736	[-0.777,6.248]	0.127
Overweight	0.112	[0.043,0.180]	0.001	1.785	[-1.788,5.357]	0.327
Obese	0.104	[0.026,0.181]	0.009	-0.417	[-4.451,3.616]	0.839
Duration (ref = < 2)						
2–5	0.009	[-0.021,0.040]	0.550	-0.578	[-2.177,1.020]	0.478
> 5	-0.075	[-0.115,-0.035]	< 0.001	-3.920	[-5.996,-1.843]	< 0.001

Ref reference group, BMI body mass index, CI confidence interval, Coef coefficient; [a]Single refers to not married or not living in a partnership; not single refers to married or living in a partnership

[b]BMI category was defined based on the "weight for adults" criterion established by the National Health Commission of China, the cut-off values for BMI: underweight (BMI < 18.5 kg/m^2), normal weight (18.5 ≤ BMI < 24.0 kg/m^2), overweight (24.0 ≤ BMI < 28.0 kg/m^2), and obese (BMI ≥ 28.0 kg/m^2); [c]Duration refers to the time elapsed from the initial diagnosis of knee osteoarthritis to the time of investigation

and participants with a normal weight had the highest HRQoL scores. The finding that overweight and obese participants had worse HRQoL scores is consistent with previous studies [36–39], which highlights the importance of weight loss for overweight/obese patients with knee osteoarthritis to improve their HRQoL in clinic. It was indicated individuals with an elevated BMI were at a greater risk of experiencing knee pain compared to those with a normal BMI [39]. Body weight represents a potentially modifiable risk factor for the development of knee osteoarthritis, while for obese patients with osteoarthritis, weight loss can help them alleviate symptoms when present [38]. The association between weight and HRQoL among osteoarthritis patients deserves increased attention, and overweight and obese patients with knee osteoarthritis are advised to lose weight to improve their HRQoL, as it has been revealed that 10% weight loss can significantly improve physical HRQoL for overweight or obese patients with knee osteoarthritis [39]. Meanwhile, when compared with participants with a normal BMI, those with an underweight BMI also experienced significantly poorer HRQoL. In the present study, in addition to pain, anxiety/depression was found to be the second most serious problem for underweight participants. However, this was not the case for other participants with different BMI groups, which may explain the poorer HRQoL observed among underweight individuals. Xie's study also found a worse mental HRQoL among underweight participants [7]. They measured the HRQoL of patients with knee osteoarthritis using the 12-item Short Form (SF-12), and underweight participants had worse mean mental component summary (MCS) scores [7]. Additionally, previous studies have reported a U-shaped relationship between anxiety/depression and BMI, with increased levels of anxiety/depression among both underweight and overweight/obese individuals [40, 41]. This finding may partly explain the poorer HRQoL observed among underweight and overweight/obese participants in this study. Meanwhile, the results discussed above focus on statistical differences, and it is also essential to further explore the findings of this study from the perspective of clinical differences. Although there are no validated Minimal Clinically Important Differences (MCIDs) for EQ-5D-5 L health utility values and

EQ-5D-VAS especially for patients with knee osteoarthritis, and significant variations in MCID cut-offs exist due to differences in models and populations [42, 43], there are other relevant studies reporting MCID values of health utility. For example, a 10% improvement was used as an MCID for patients undergoing total knee arthroplasty [44], while another study adopted a threshold of 0.085 for patient undergoing primary knee arthroplasty [45]. Additionally, a threshold of 0.1 was used for patients with rheumatoid arthritis [46]. Therefore, based on the range of MCID thresholds reported in previous studies, the health utility values of patients with a normal BMI, an overweight BMI, and an obese BMI are clinically significantly higher than those of patients with an underweight BMI.

In addition to BMI, potential factors of age, history of treatment and duration of disease were significantly associated with HRQoL for participants with knee osteoarthritis in the present study. A poorer HRQoL was observed among older participants, which is consistent with most studies [7, 9, 47, 48]. Osteoarthritis is a degenerative disease, and it is undeniable that age is recognized as the main influencing factor of osteoarthritis. Symptoms typically onset in middle-aged and elderly individuals, and with increasing age, worsening clinical symptoms may have an impact on the HRQoL of elderly patients. However, Wang's study drew different conclusions on the impact of age on HRQoL, they found that older patients had better HRQoL [49]. They hypothesized that elderly patients who have been suffering from osteoarthritis for a long time may have adapted to the disease, therefore the impact of osteoarthritis on their HRQoL was not as significant as that on younger patients who have had the disease for a shorter duration in their study [49]. History of treatment also significantly affected the HRQoL of participants. Compared with participants who did not receive any treatment in the past six months, participants who received any type of treatment had better HRQoL in the present study, and this finding was partly consistent with two recent studies [7, 50]. Xie's study demonstrated that participants who received any type of treatment had worse physical component summary (PCS) scores, despite having higher MCS [7]. Maybe the fact that all participants included were outpatients with knee osteoarthritis can partly account for this difference. Most of the participants had early-stage knee osteoarthritis and treatments may help reduce the level of pain/anxiety, which in turn benefits patients' HRQoL in the present study. Schepman's study also found that non-pharmacological treatment can predict a higher quality of life [50]. Longer duration of disease negatively affects patients' HRQoL in the present study, which is consistent with the characteristics and progression of knee osteoarthritis. Knee osteoarthritis is a chronic degenerative disease, and longer duration is usually accompanied by more severe symptoms or comorbidities, which may result in worse HRQoL [7].

With the increasing global burden of knee osteoarthritis, effective management of the disease needs to be implemented. In view of the findings of the present study, we suppose the following: First, we highlight the importance of weight examination and management in clinical settings. Patients with a healthy BMI had the highest HRQoL scores, representing a gap and opportunity to improve HRQoL by incorporating dietary guidelines, nutritional education and anxiety relief [51]. Specifically, most studies advised weight loss to improve patients' HRQoL, while weight management for participants with an underweight BMI received less attention. Health intervention strategies should be taken for unhealthy weight patients, which include patients with overweight, obese, and underweight BMI. Second, our study found that age and duration of disease were negatively associated with HRQoL. Since the two factors are non-modifiable, we strongly emphasize that policymakers in the field of public health can prioritize policies aimed at preventing and delaying osteoarthritis progression, in order to alleviate the negative impact of age and duration of disease on HRQoL. Third, the results indicate that participants with a history of treatment in the past six months had better HRQoL, which was partly consistent with existing studies. Therefore, we agree with the treatment principles recommended in the Chinese Osteoarthritis Diagnosis and Treatment Guideline (2018) [26], which suggest that physicians should consider factors such as age, sex, weight, and risk factors, and provide individualized treatment for the patients. Ultimately, since the overall health utility and utility by characteristics were reported for Chinese outpatients with knee osteoarthritis, the results can serve as evidence for future health intervention and cost-effectiveness studies in the field of osteoarthritis management.

Several limitations in the present study should be mentioned. First, the study was conducted in three tertiary hospitals, which may not be truly representative of all patients with knee osteoarthritis in China, thus limiting the generalization of the results, however, the present study can add additional evidence to the existing HRQoL studies for patients with knee osteoarthritis. Second, as this study was a cross-sectional study, only associations could be estimated, and the causes of the difference in HRQoL could not be inferred from the present findings. Therefore, a longitudinal study that includes all of the hospital care systems in China is needed in the future to reach a solid conclusion on the associations found in the present study. Third, almost half of the participants were without formal education or had attended only primary school, and possible misunderstandings may have

existed, which could have biased the responses. Training courses were conducted for the investigators to explain the items to the participants in an easily understandable and accurate way.

Conclusion

The HRQoL of outpatients with knee osteoarthritis was considerably impaired according to our findings, which implied that improved management is important to prevent the rapid progression of knee osteoarthritis. BMI is a modifiable risk factor for knee osteoarthritis, and our findings also revealed a higher HRQoL in outpatients with a normal BMI. The management of weight in overweight/obese outpatients with knee osteoarthritis is vital. We estimated the health utility and EQ-VAS score for outpatients with knee osteoarthritis overall and by BMI class, which could be used in future public health-related policies and economic studies to increase the breadth of knowledge of HRQoL in outpatients with knee osteoarthritis. The factors associated with knee osteoarthritis found in the present study can also guide efforts to improve the HRQoL of outpatients with knee osteoarthritis in the clinic.

Supplementary Information

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Supplementary Material 1

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Author contributions
Author contributions X.S., K.L. and H.D. conducted the investigation; X.S., X.Z., S.G. and H.D. discussed and wrote the methodology; H.D. supervised the entire investigation and writing; X.S and X.Z. wrote the original draft; W.Y., X.Z. and H.D. reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Data availability
All of the principal data were included in the results in the present study. Additional materials with further details can be obtained from the corresponding author.

Declarations

Ethics approval
The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the institutional review board of Zhejiang University School of Public Health (20180923).

Consent to participate
Informed consent was obtained from all participants included in the present study.

Consent to publish
This manuscript didn't contain any individual person's data in any form.

Competing interests
The authors declare no competing interests.

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