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Ethnic Differences of Prevalence of Knee Pain among Adults in the Community in a Cross- Sectional Study

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Abstract:

Objective: To determine the prevalence of knee pain among three major ethnic groups in Malaysia. By identifying high-risk groups, preventive measures can be targeted at these groups of people.

Methods: A cross sectional survey was carried out in both rural and urban areas in a state in Malaysia. Adults aged 18 years old and above were invited to answer a self-administered questionnaire on pain experienced in the past 6 months. Socio-demographic data and types of pain as well as medications used were captured.

Results: A total of 5056 subjects participated in this study. About 58.2% (n=2926) were female and about 64.3 % (n= 3250) from urban area. Ethnic distribution was Malays 50% (n= 2512), Chinese 41.4% (n=2079), and Indians 8.6% (n=434). 21.1% (n=1069) had knee pain in the past 6 months. More Indians (31.8%) experienced knee pain compared to Malays (24.3%) and Chinese (15%) (p<0.001). Knee pain was also more common in those older than 45 years old (25.5%)

compared to those under 45 years old (19.8%) (p<0.001). Those with higher education (18.7%) had less knee pain than those with lower education (22.1%, p <0.006). Multiple logistic regression showed that there was no difference in the prevalence of knee pain between gender, rural or urban area, and those employed or unemployed. About 68.1% Indians used analgesia for knee pain while use by Malays was 75.4% and Chinese 52.1% (p<0.001). The most common analgesic used for knee pain across the three ethnic groups was topical medicated oil (43.7%).

Conclusion: The prevalence of knee pain in adults was 21.2% and it was more common in the Indian population, older age group and those with lower educational level. Further studies should look into the reasons for these differences.

Introduction:

Knee pain is the most common pain complaint among older individuals and the most common cause is osteoarthritis (OA) of the knees.(1, 2) OA of the knee impacts on quality of life and causes physical disability as well as limitation of function in the elderly.(3, 4) Studies have shown that there are differences in prevalence of knee pain due to OA amongst different ethnic groups.(5-9) About 13.1 % Indian woman had knee pain in COPCORD study compared to Malay female (11.1%) and Chinese female (5.8%).(5) A study in the United States showed that knee pain was disproportionately higher among older African American than the non- Hispanic white groups.(8)

Cultural background, pain threshold, and genetic predisposition may be some of the reasons why knee pain is more common in certain ethnic groups. Importantly, many environmental and lifestyle risk factors are reversible (e.g. obesity, and muscle weakness) or avoidable (e.g. occupational or recreational joint trauma) which has implications for secondary and primary prevention.

The aim of our study is to describe the prevalence of knee pain and use of analgesic medications for knee pain amongst the different ethnic groups in Malaysia. By identifying the high risk groups, it helps health care workers to understand more about patients' experience and beliefs about pain and hence preventive measure can be targeted at these groups of people.

Methods:

A cross sectional survey was carried out in 6 districts in the State of Selangor in Malaysia based on purposive sampling in: four urban districts (Petaling Jaya, Subang, Seri Kembangan, Kampong Medan) and two rural towns in Kuala Langat district (Banting and Jenjarom). The districts were selected based on the ethnic distribution as well as the socio-economic status. Secondary schools were randomly selected and used as a sampling unit to reach out to the adults in the community. The children from the selected schools were given the self- administered questionnaire for their parents or main care-giver aged 18 years and above to complete. Efforts were made to optimize the response rate through reminders and providing incentives to schools which were able to achieve at least 70% response rate. The questionnaires were collected two weeks after distribution. Out of 9,300 questionnaires distributed, 5206 were returned, giving a response rate of 56.0%. However we excluded 150 subjects who did not fall into any of the three ethnic groups, giving a total of 5056 questionnaires for analysis. These findings had summarized in a flow diagram as below.

Fig 1: Flow chart showing method of subjects' selection

The missing data were not addressed as the sample size was big (n= 5056) and we believed that it would not affect the findings of the study. Furthermore we did not have the respondents' contact number as the questionnaire were distributed to the students for them to bring back for their parents or main care-giver aged 18 years and above to complete and bring back to the researcher two weeks later.

The sample size was calculated by using Epi Info 7.0, based on the prevalence of knee pain of 46% in one of country in Asia.(2) The estimated sample size was 4103 with 99 percent power, 95 percent confidence interval (CI), and statistical significant level (α) at 5 percent. The total number of respondents needed was 5128, after taking into account a non-respondent rate of 25 percent.

The researchers designed the self-administered questionnaires based on existing literature and discussion. Socio- demographic data (including age, sex, occupation, education level, location of residency, and ethnicity), types of pain experienced in the past 6 months, and

medications used were captured. All of the data including ethnicity and types of pain were self-declared. The English questionnaires were translated into two other languages (Malay and Chinese) and back-translated. Any discrepancy in translation was discussed and agreed upon by 3 researchers. This was followed by pilot-testing on adults of different ethnicity, mainly Malay, Chinese and Indians, and further revision was made before the survey.

Approval to conduct this study was obtained from the University of Malaya Medical Centre Medical Ethics Committee. We also sought permission from the schools and State Education Department. Written informed consent was taken from all the participants.

Measurement of social class and socioeconomic status are based on the SOC 2010 Volume 3: The National Statistics Socio- economic classification (NS- SEC rebased on the SOC 2010)(10) in which classification was done according to occupation. There were 8 occupational classes:

i) higher managerial, administrative and professional occupations,
ii) lower managerial administrative and professional occupations,
iii) intermediate occupations,
iv) small employers and own account workers
v) lower supervisory and technical occupations,
vi) semi-routine occupations,
vii) routine occupations
viii) never worked and long-term unemployed.

We reclassified these eight classes as into four groups i.e. upper (I &ii), middle (iii &iv) and lower classes (v-vii). The fourth group was the non-employed category which consisted of participants who never worked or were unemployed, students and housewives. These four groups were later classified as categorized (upper, middle and lower class) and not-categorized (never worked, long term unemployed, students and housewives) This is in line with most education research which assessed social class and socio-economic status (SES) based on income, occupation education, and material possessions.(11) We classified the education level as tertiary and non-tertiary (non-schooling, primary and secondary school education). We categorized the subjects into two age groups i.e. less than 45 and equal or greater than 45 years of age in accordance with the age definition used by guidelines for osteoarthritis.(12)

Stratification of rural areas were based on the census from Malaysia 2010 which defined as when the population was less than 10,000 people and having agriculture and natural resources. Urban area as defined as gazette areas with population of 10 000 and more.(13)

The statistical analysis was done using the Statistical Package for Social Sciences (SPSS version 16). Continuous data were described as mean and standard deviation if the distribution is normal. When the data were skewed, median and interquartile range (25-75th percentiles) were used. Categorical data were reported as proportions (percentage) and Chi-square test or Fisher exact tests were used for bivariate analysis. Multivariate logistic regression analysis was used to look for the independent factors associated with knee pain. All variables with the p-value of less than 0.05 in the univariate analyses as well as clinically significant variables were entered into the multivariate logistic regression model. The dependent variable was knee pain (yes or no). The independent variables were age, sex, ethnicity, location, education level and social classes. All analyses were done with 95% confidence intervals (95% CI), and the level of significance was set at $p<0.05$. All data and findings are full available without restriction.

Results:

There was a total of 5056 participants responded to the questionnaire. The median age of the subjects was 40 years (IQR=9). Table 1 shows the demographic profile of the subjects. Just over half were female 58.2% (n=2926) and nearly two thirds 64.3% (n= 3250) lived in an urban area. Ethnic distribution was Malays 50% (n= 2512), Chinese 41.4% (n= 2079), and Indians 8.6% (n=434).

Table 1: Demographic profile of all study subjects (N= 5056)

Variables	Frequency (n, %)	
Sex	Male	2103 (41.8)
	Female	2926 (58.2)
Age groups	<45	3869 (76.6)
	≥45	1181 (23.4)
Location	Urban	3250 (64.3)
	Rural	1806 (35.7)

Ethnicity		2512 (50)
	Chinese	2079 (41.4)
	Indian	434 (8.6)
Education	Tertiary	1612 (32.2)
	Non-tertiary*	3397 (67.8)
Social class	Upper	350 (6.9)
	Middle	929 (18.4)
	Lower	988 (19.6)
	Not-categorized#	2785 (55.1)

* Non-tertiary includes those who are non-schooling, primary school or secondary education

#Non-categorized group consists of those never worked, unemployed, students and housewives(10)

Overall 21.1% (n=1069) had knee pain. Indian population (31.8%, n=138) had the highest prevalence of knee pain, followed by Malays 24.3% (n=610) and Chinese 15% (n=311). Two thirds (67.6%, n= 716) used medications for their knee pain for the past 6 months. Malay (75.4%, n=460) were more likely to use medications than Indians (68.1%, n=94) and Chinese (52.1%, n=162) (p<0.001) in Table 2. Figure 1 shows the medication used which include topical methyl-salicylate ointment (43.7%), paracetamol (12.9%), mefenamic acid (5.3%) and injections (3.8%).

Table 2: Comparison of ethnic groups in using analgesia for knee pain (N=716/1069)

Variables		Knee pain on any analgesia (n= 716/1069), (n, %)		P- value
		Yes	No	
Ethnicity	Malay	460 (75.4)	150 (24.6)	<0.001
	Indian	94 (68.1)	44 (31.9)	
	Chinese	162 (52.1)	149 (47.9)	

Fig 2: Types of analgesics used for knee pain (N=716)

Table 3 compares the socio-demographic variables of those with and without knee pain. Those older than 45 years old had more knee pain compared to their younger counterparts 25.5% (n=301) of those over 45 years versus 19.8% (n=766) in those under 45 years old (p<0.001).

Univariate analysis of other variables showed that lower educational level, those from rural area and those categorized (upper, middle and lower socioeconomic classes) have more knee pain. However, multiple logistic regression (Table 4) showed that only those older (adjusted OR=1.421, p<0.001), being Indians (adjusted OR 2.729, p<0.001) and Malays (adjusted OR= 1.937, p<0.001) compared to the Chinese and those with lower education (adjusted OR= 1.315, p<0.001) were more likely to have knee pain.

Table 3: Association of socio-demographic profile of subjects with and without knee pain (N=5056)

Variables		Knee pain (n, %)		Total	p-value
		Yes (n=1069)	No (n=3987)	(N, 100%)	
Sex	Male	440 (20.9)	1663 (79.1)	2103	<0.73
	Female	624 (21.3)	2302 (78.7)	2926	
Age Group (years)	<45	766 (19.8)	3103 (80.2)	3869	<0.001
	≥45	301 (25.5)	880 (74.5)	1181	
Location	Urban	641 (19.7)	2609 (80.3)	3250	<0.001
	Rural	428 (23.7)	1378 (76.3)	1806	
Ethnicity	Chinese	311 (15.0)	1768 (85.0)	2079	<0.001
	Malay	610 (24.3)	1902 (75.7)	2512	
	Indian	138 (31.8)	296 (68.2)	434	
Education	Tertiary	302 (18.7)	1310 (81.3)	1612	<0.006
	Non-tertiary*	752 (22.1)	2645 (77.9)	3397	
Social class	Categorized@	512 (22.6)	1755 (77.4)	2267	<0.025
	Non-Catogorized#	557 (20)	2228 (80)	2785	

* Non-tertiary including those who are from non-schooling, primary school and secondary school.
@Categorized groups are those who categorized in upper, middle and lower classes(10)
Not- categorized group consists of those never worked, students and housewives(10)

Table 4: Multivariate logistic regression for predictors of knee pain

Variables		Univariate			Multivariate			p value
		OR	95.0% CI		Adjusted OR	95.0% CI		
			Lower	Upper		Lower	Upper	
Age Group	<45 years	1			1			
	≥ 45 years	1.386	1.189	1.615	1.421	1.212	1.665	<0.001
Location	Urban	1			1			
	Rural	1.264	1.1	1.452	1.018	0.876	1.182	<0.819
Ethnicity	Chinese	1			1			
	Malay	1.823	1.567	2.121	1.937	1.642	2.284	<0.001
	Indian	2.65	2.095	3.353	2.729	2.14	3.481	<0.001
Education	Tertiary	1			1			
	Non-Tertiary*	1.233	1.063	1.431	1.315	1.124	1.539	<0.001
Socio Class	Categorized@	1			1			
	Non-Catogorized#	1.167	1.019	1.336	1.062	0.919	1.227	<0.418

* Not tertiary including those who are from non-schooling, primary school and secondary school.
@ Categorized groups are those who categorized in upper, middle and lower classes(10)
# Not- categorized group consists of those never worked, students and housewives(10)

Discussion:

Knee pain is common in the community.(5) We found that nearly a third of the Indian population had knee pain compared to other ethnic groups (AOR= 2.729, p <0.001). This was also seen in the COPCORD survey where 13.1% of the Indian females experienced knee pain as compared to Malay females (11.1%) and Chinese females (5.8%).(5) Local study also showed that prevalence of pain complaints among Indian ethnic group is higher compared to Malay and Chinese in both one public primary care clinics (KK) and general practice clinic (GP) settings.(9) These findings may point to possible genetic factors and cultural background that determine response to pain among Indian populations. Perceptions towards pain threshold is greatly affected by family members, peers, and cultural background. Bone mineral density plays an important role in development of arthritis and sclerosis which was shown in study by Allen et

all.(6) It also shows that forces experienced during walking in certain ethic groups will cause knee OA, for instance, African- Americans were more likely than Caucasians to have valgus thrust during walking which cause more knee OA.

However more studies need to be carried out in order to examine these observations. In our study, Chinese ethnicity had the lowest prevalence of knee pain and this is again consistent with another study which also found a lower prevalence of knee pain amongst Chinese.(5) This could be due to their culturally based response to pain and genetic factors as well as their beliefs in using complementary medicines which are widely available among Chinese populations such as acupuncture and thermal cupping.

Although our study did not specifically determine the cause of the knee pain, we found that in this study, the knee pain was more common in the older age group suggesting that the cause could be OA.(12, 14-16) There was more knee pain amongst those with lower educational level (AOR= 1.315, $p<0.001$) and this could be due to lack of knowledge to assess for health care services and awareness for prevention of knee OA. Besides, it could be due to the type of works undertaken by those without tertiary education whereby more stress may have been placed on their knees due to their strenuous jobs.

This study did not show a female preponderance for knee pain. This could be due to in part to the women in our study being younger as most of them are mothers of school-going children, where OA is not so common. This is in contrast with other studies that showed females have more knee pain than men.(5-7, 14, 15) Our study also did not find any difference in the prevalence of knee pain amongst different social classes (AOR= 1.062, $p<0.418$). However several studies found that socioeconomic status (16) and psychological factors (17, 18) were determinants of knee pain and physical function.(19) COPCORD survey shown housewives (non- categorized socioeconomic class) reported more musculoskeletal pain and this may be related to repetitive household tasks and psychological stresses.(5)

However, we did not look at other confounding factors such as psychosocial factors, BMI (14, 17, 20-22) and menopausal states (23) in experiencing knee pain, these variables have been shown to have an impact on perception of knee pain. Our response rate was 56%, it could be due

to attitude of students who might forget or loss the questionnaire forms and did not pass it to their parents/ main guardians.

In our study there was also no difference in prevalence of knee pain whether one is living in a rural or urban environment. While several other studies found that there was rural-urban difference.(15, 16) The prevalence of knee pain in our rural community (23.7%) was higher than that of a study done in rural South India (17.2%).(14) This could be due to a wide variation in the definition of rural or urban amongst different countries. It also could be due to population who lives in urban setting has more sedentary lifestyles, hence obesity rate is higher and leading to higher prevalence of knee pain.

Among those who had knee pain, Malays instead of Indian tended to use more analgesia. This could be due to more Indian were from rural area and lower socioeconomic classes and hence poor knowledge in getting health care services for their knee pain. The medication most commonly used was a topical agent which has less adverse effects than NSAIDs. This could be because it is cheaper to obtain and are more readily available while NSAIDs require a doctor's prescription. In addition, combination of traditional and western medicines are common practice among patients nowadays.(24) Self-medication is also common among patients in our study, which has also been reported in the COPCORD survey.(5) With the ageing population and increasing number of consultations for knee pain, future studies should try to understand public's perceptions, awareness and knowledge in self-care of knee pain and study the factors that influence patients to seek help.

In summary our study found that Indian population has a higher prevalence of knee pain compared to other ethnic groups. It is important to target this high-risk group so that prevention and appropriate interventions can be provided early. Murphy and colleagues suggested that prevention programs should be offered relatively early in life and to understand the need of health care utilization in diagnosing early knee OA.(14)

Future studies should look at other confounding factors such as other co-morbid conditions, genetic predisposition, psychosocial factors and medical access factors as well as more precise and better assessment tools in diagnosing knee pain in the primary care setting.

Conclusion:

Prevalence of knee pain was more common in the Indian ethnic group. It is also more common in the older age groups and those with lower educational level. The most common medication used for knee pain was topical medicated oil. Further studies need to be carried out to explore the reason of these differences.

Strength and Limitation:

- Sample size is large.
- Comprising sufficient numbers of the different races in Malaysia.
- Not able to attribute the knee pain being entirely due to OA
- We did not collect clinical data in this study
- Absence of height and weight data for BMI calculation.

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Contributorship Statement:

- First author Prof Chia Yook Chin had fulfilled all three of the ICMJE guidelines for authorship which she contributed the conception and design, acquisition of data, or analysis and interpretation of data, she is also drafting the article or revising it critically for important intellectual content; and final approval of the version to be published.
- Second author Dr Beh Hooi Chin also had fulfilled all three of the ICMJE guidelines for authorship as mentioned earlier on.
- Third author Prof Ng Chirk Jenn also had fulfilled all three of the ICJME guidelines for authorship as stated on the previous paragraph.
- Fourth author Prof Teng Cheong Lieng also played an important role in authorship which he also fulfilled all three of the ICMJE guidelines.

- Fifth author Prof Nik Sherina Hanafi also had contributed the conception and design, acquisition of data, or analysis and interpretation of data, she is also drafting the article or revising it critically for important intellectual content; and final approval of the version to be published as per guidelines stated in ICJME guidelines for authorship.
- Sixth author Prof Choo Wan Yuen also had fulfilled all three of the ICMJE guidelines for authorship as mentioned earlier on.
- Seventh author Dr Ching Siew Mooi also had fulfilled all three of the ICMJE guidelines for authorship as mentioned before.

Competing Interests

The authors have declared that no competing interests exist. No additional data available.

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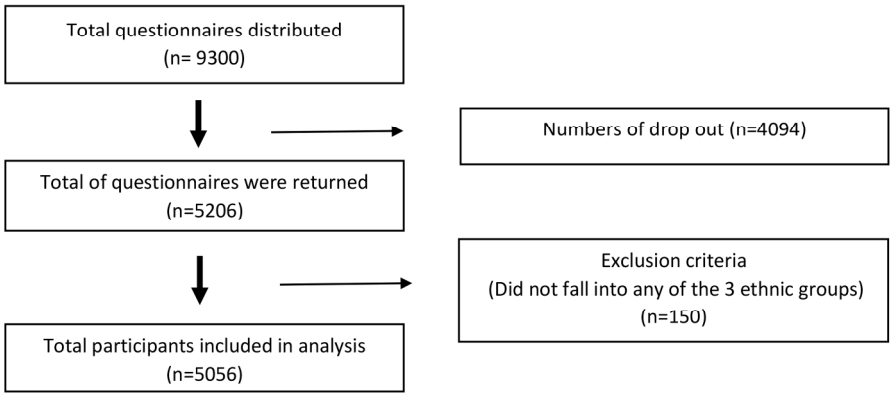

Fig 1: Flow chart showing method of subjects' selection (row 71)
Fig 1: Flow chart showing meth
183x84mm (300 x 300 DPI)

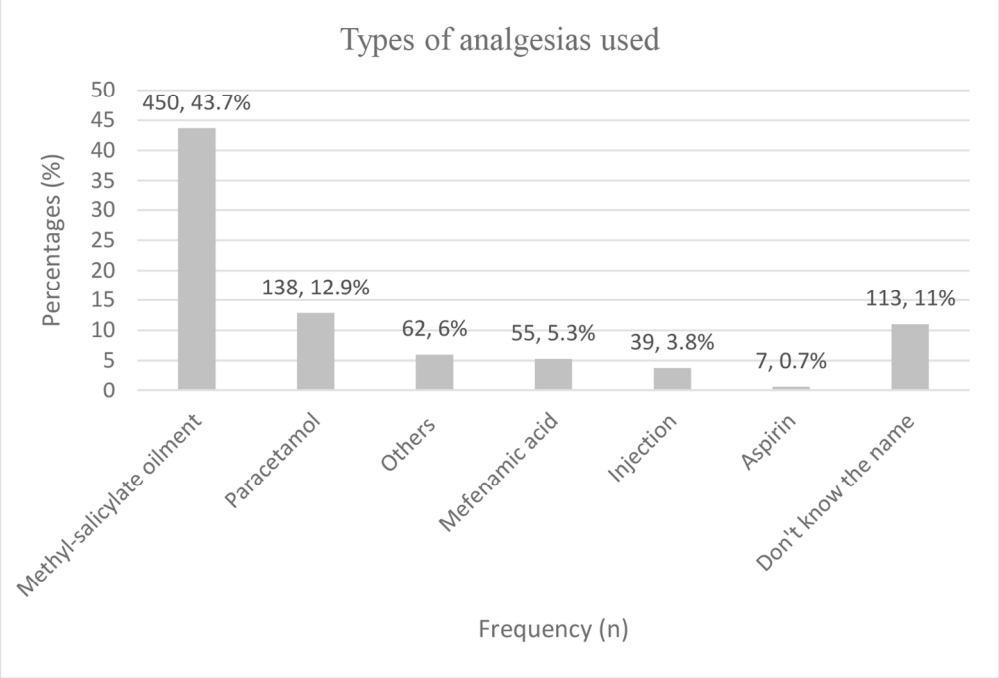

Fig 2: Types of analgesics used for knee pain (row 145)
Fig 2: Types of analgesics use
131x89mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	3,4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-4
Bias	9	Describe any efforts to address potential sources of bias	3-4
Study size	10	Explain how the study size was arrived	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5,8
		(*b*) Describe any methods used to examine subgroups and interactions	5,7,8
		(*c*) Explain how missing data were addressed	3
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Not applicable

		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5,
		(b) Give reasons for non-participation at each stage	9,10
		(c) Consider use of a flow diagram	3
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5,6
		(b) Indicate number of participants with missing data for each variable of interest	3
Outcome data	15*	Report numbers of outcome events or summary measures	6-8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7
		(*b*) Report category boundaries when continuous variables were categorized	4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7,8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	10,11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	5
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Ethnic Differences of Prevalence of Knee Pain Among Adults in the Community in a Cross-Sectional Study

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Ethnic Differences of Prevalence of Knee Pain among Adults in the Community in a Cross- Sectional Study

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Abstract:

Objective: To determine the prevalence of knee pain among three major ethnic groups in Malaysia. By identifying high-risk groups, preventive measures can be targeted at these groups of people.

Design and Setting: A cross sectional survey was carried out in both rural and urban areas in a state in Malaysia. Secondary schools were randomly selected and used as sampling units.

Participants: Adults aged ≥18 years old were invited to answer a self-administered questionnaire on pain experienced in the past 6 months. Out of 9,300 questionnaires distributed, 5206 were returned, 150 subjects who did not fall into the three ethnic groups were excluded, giving a total of 5056 questionnaires for analysis. 58.2% (n=2926) were females. 50% (n= 2512) were Malays, 41.4% (n=2079) were Chinese, and 8.6% (n=434) were Indians.

Results: 21.1% (n=1069) had knee pain in the past 6 months. More Indians (31.8%) experienced knee pain compared to Malays (24.3%) and Chinese (15%) (p<0.001). Odds of Indian females reporting knee pain was two times higher as compared to Malay females. There was an increasing trend in prevalence of knee pain with increasing age (p<0.001). The association between age and knee pain appeared to be stronger in females than males. 68.1% Indians used analgesia for knee pain while 75.4% Malays and 52.1% by Chinese (p<0.001). The most common analgesic used for knee pain across was topical medicated oil (43.7%).

Conclusion: The prevalence of knee pain in adults was more common in the Indian females and older female age group and Chinese males with lowest prevalence of knee pain. Further studies should look into the reasons for these differences.

Strength and Limitations of This Study:

- Sample size is large.
- Comprising sufficient numbers of the different races in Malaysia.
- Not able to attribute the knee pain being entirely due to OA.
- We did not collect the data of other confounding factors such as body mass index (BMI), psychosocial factors, history of trauma, and menopausal status.
- Although we did not do a formal sample size calculation, but our sample size was large and is comparable to another study. (1)

Introduction:

Knee pain is the most common pain complaint among older individuals and the most common cause is osteoarthritis (OA) of the knees.(1, 2) OA of the knee impacts on quality of life and causes physical disability as well as limitation of functions in older individuals.(3, 4) Studies have shown that there are differences in prevalence of knee pain due to OA amongst different ethnic groups.(5-9) In the COPCORD study, 13.1 % Indian females had knee pain compared to Malay females (11.1%) and Chinese females (5.8%).(5) A study in the United States showed that knee pain was disproportionately higher among older African American than the non- Hispanic white groups.(8)

Cultural background, pain threshold, and genetic predisposition may be some of the reasons why knee pain is more common in certain ethnic groups. Importantly, many environmental and lifestyle risk factors are reversible (e.g. obesity, and muscle weakness) or avoidable (e.g. occupational or recreational joint trauma) which has implications for secondary and primary preventions.

The aim of our study is to describe the prevalence of knee pain and use of analgesic medications for knee pain amongst the different ethnic groups in Malaysia as well as the interaction and association of socio-demographic to the prevalence of knee pain. By identifying the high risk groups, it helps health care workers to understand more about patients' experience and beliefs about pain and hence preventive measures can be targeted at these groups of people.

Methods:

A cross sectional survey was carried out in 6 districts in the State of Selangor in Malaysia based on purposive sampling in four urban districts (Petaling Jaya, Subang, Seri Kembangan, Kampong Medan) and two rural towns in Kuala Langat district (Banting and Jenjarom). The districts were selected based on the

ethnic distribution as well as the socio-economic status. Secondary schools within these districts were randomly selected and used as a sampling unit to reach out to the adults in the community. The children from the selected schools were given the self- administered questionnaire for their parents or main care-giver aged 18 years and above to complete. Efforts were made to optimize the response rate through reminders and providing incentives to schools which were able to achieve at least 70% response rate. The questionnaires were collected two weeks after distribution. Out of 9,300 questionnaires distributed, 5206 were returned, giving a response rate of 56.0%. However we excluded 150 subjects who did not fall into any of the three ethnic groups, giving a total of 5056 questionnaires for analysis. The findings are summarized in Figure 1.

Fig 1: Flow chart shows the flow of selection of participants

We did not address the issue of non-respondents as the sample size was large (n= 5056) and we believe that it would not affect the findings of the study. Furthermore we did not have the non- respondents' contact number as the questionnaire were distributed to the students for them to bring home to their parents or main care-giver aged 18 years and above to complete and bring back to the researcher two weeks later.

The researchers designed the self-administered questionnaires based on existing literature and discussion. Socio- demographic data (including age, sex, occupation, education level, location of residency, and ethnicity), types of pain experienced in the past 6 months, and medications used were captured. All of the data including ethnicity and types of pain were self-declared. The English questionnaires were translated into two other languages (Malay and Chinese) and back-translated. Any discrepancy in translation was discussed and agreed upon by 3 researchers. This was followed by pilot-testing on adults of different ethnicity, mainly Malay, Chinese and Indians, and further revision was made before the survey.

Approval to conduct this study was obtained from the University of Malaya Medical Centre Medical Ethics Committee. We also obtained permission from the schools and State Education Department. Written informed consent was taken from all the participants.

We classified the occupation based on employment status either 'yes' or 'no' for the data analyses, educational level as primary and non-formal, secondary and tertiary. And we also categorized the subjects into three main age groups which were ≤ 30 years old, 31-40 years old and >40 years old.

Stratification of rural areas were based on the census from Malaysia 2010 which defined as when the population was less than 10,000 people and having agriculture and natural resources. Urban area as defined as gazette areas with population of 10 000 and more.(10)

Data analysis

Categorical data were reported in proportions (percentage). Continuous data were described as mean and standard deviation if the distribution is Gaussian. Chi-square analyses were used to determine

significant group differences with knee pain prevalence. Binary logistic regression analyses examined the relationship between ethnicity and knee pain controlling for other socio-demographic variables. Crude and adjusted odds ratio (OR) and 95% confidence interval (95% CI) are presented. Significance was set at an alpha level of 0.05. All analyses were performed using SPSS Version 16.0.

The multivariate analyses were first performed using all combined data. A hierarchical regression strategy was used in which the independent variables were forced into the equation: (I) ethnicity alone (Model 1); (II) the main effects of all independent variables (Model 2); and finally (III) main effects including all possible 2 way- interactions terms with ethnicity (Model 3) to determine the presence of interaction effect. The 2 way- interactions between (I) ethnicity and gender; and (II) gender and age were statistically significant. Subsequent regression analyses were therefore stratified by gender. In gender specific regression analyses, a similar hierarchical approach was adopted. Because none of the 2-ways interaction terms were found to be significant in these models, only the results of the main effects were presented in the final model for each gender. All data and findings are fully available without restriction.

Results:

A total of 5056 participants responded to the questionnaire. The mean age of participants was 38.5 (SD ± 8.95) with males (Mean age= 40.6, SD ± 9.2) being slightly older than females (Mean age= 36.9, SD± 8.46). Table 1 shows the overall socio-demographic distribution of participants and their association with knee pain. The majority of respondents were Malays (50%) followed by Chinese (41.4%) and Indian (8.6%). The sample was mostly females, from urban residence, had secondary and higher education level and being employed.

The overall prevalence of knee pain among all respondents was 21.2%. The prevalence of knee pain differed significantly with age, ethnicity, urban-rural area and educational level. (See Table 1).

Table 1. Respondent characteristics by prevalence of knee pain (N=5056)

Characteristics	Overall	Knee pain, N (%)		p value
		Yes	No	
Ethnicity				<0.001
Malay	2512 (50.0)	610 (24.3)	1902 (75.7)	
Chinese	2079 (41.4)	311 (15.0)	1768 (85.0)	
Indian	434 (8.6)	138 (31.8)	296 (68.2)	
Age (years)				<0.001
<30	846 (16.8)	129 (15.2)	717 (84.8)	
31-40	1936 (38.3)	392 (20.2)	1544 (79.8)	
>40	2268 (44.9)	546 (24.1)	1722 (75.9)	
Gender				0.730
Male	2103 (41.8)	440 (20.9)	1663 (79.1)	
Female	2926 (58.2)	624 (21.3)	2302 (78.7)	
Residence				<0.001
Urban	3250 (64.3)	641 (19.7)	2609 (80.3)	
Rural	1806 (35.7)	428 (23.7)	1378 (76.3)	
Education				0.022

Tertiary	766 (32.2)	302 (18.7)	1310 (81.3)	
Secondary	2631 (52.5)	580 (22.0)	2051 (78.0)	
Primary or non-formal	1612 (15.3)	172 (22.5)	594 (77.5)	
Employment status				0.485
Yes	3208 (69.9)	683 (21.3)	2525 (78.7)	
No	1382 (31.1)	307 (22.2)	1075 (77.8)	

Overall 21.1% (n=1069) had knee pain. Indian population (31.8%, n=138) had the highest prevalence of knee pain, followed by Malays 24.3% (n=610) and Chinese 15% (n=311). Two thirds (67.6%, n= 716) used medications for their knee pain in the past 6 months. Malay (75.4%, n=460) were more likely to use medications than Indians (68.1%, n=94) and Chinese (52.1%, n=162) (p<0.001) in Table 2. Figure 2 shows the medications used which include topical methyl-salicylate ointment (43.7%), paracetamol (12.9%), mefenamic acid (5.3%) and injections (3.8%).

Table 2: Comparison of ethnic groups in using analgesia for knee pain (N=716/1069)

Characteristics	Knee pain on analgesia, N (%)		p value
	Yes	No	
Ethnicity			<0.001
Malay	460 (75.4)	150 (24.6)	
Chinese	162 (52.1)	149 (47.9)	
Indian	94 (68.1)	44 (31.9)	

Fig 2: Types of analgesics used for knee pain (N=716)

Subgroup analyses by gender suggest that the overall prevalence of knee pain significantly increased with age among women (p<0.001) but not among men (p=0.102) (Figure 3). In stratified analysis by ethnicity, there is no significant difference found between gender and knee pain except among the Indians. Indian females reported significantly higher knee pain than Indian males. An increasing prevalence of knee pain with increasing age (p<0.001) was observed among the Malays and Chinese but not among those of Indian ethnicity (Table 3).

Fig 3: Prevalence of knee pain by gender and age group

Table 3. Ethnic distribution of knee pain by gender and age group

Ethnic	Prevalence (%)						
	Gender			Age (in years)			
	Male	Female	*p value	≤ 30	31-40	> 40	**p value
Malay	24.8	23.7	0.543	17.9	21.7	29.0	**<0.001**
Chinese	13.9	15.7	0.304	11.0	13.8	17.4	**0.004**
Indian	22.9	39.4	**<0.001**	31.0	34.1	29.9	0.683

p- value derived comparing * gender (or **age group) difference in each ethnic category

In multivariate analysis (Table 4), the unadjusted odds ratios (Model 1) suggest that ethnicity, age, residence and education level were associated with knee pain. Gender and employment status of respondents did not have an influence on knee pain. However, gender became statistically significant after adjustment for other confounding variables. The main effect model (Model 2) showed that compared to males, the odds of reporting knee pain among females were higher by 23%. The odds of knee pain were 49% lower among the Chinese and 42% higher among the Indians compared to Malays. Compared to age <30 years group, the odds of reporting knee pain were higher among those above 40 years group (AOR = 1.60, 95% CI 1.26-2.02). When all possible 2 way-interaction terms were added in the regression analysis, the association between knee pain with ethnicity, gender and age group was diminished (Model 3). There was significant effect modification between knee pain and ethnicity by gender. Similarly, there was age by gender interaction.

Subsequent gender specific multivariate analyses (Table 5) suggest Chinese males reported significantly less knee pain than Malay males. Chinese females also reported significantly less knee pain (AOR 0.54; 95% CI 0.43-0.68), whilst the odds of Indian females reporting knee pain were twice higher compared to Malay females. The association between age and knee pain appeared to be stronger in females than in males. The odds of reporting knee pain were twice higher among older females (>40 years above) compared to younger females. Lower education level (primary or lower) was associated with knee pain in males but this was not observed in females.

Table 4. Unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95% CI) of knee pain by socio-economic factors

Associated factor	Unadjusted odds ratio	Adjusted odds ratio	
	Model 1	Model 2	Model 3
Gender			
Male (Ref)			
Female	1.03 (0.89-1.18)	**1.23 (1.04-1.45)**	0.69 (0.44-1.11)
Ethnicity			
Malay (Ref)			
Chinese	**0.55 (0.47-0.64)**	**0.51 (0.43-0.61)**	**0.31 (0.14-0.68)**
Indian	**1.45 (1.17-1.81)**	**1.42 (1.12-1.78)**	1.46 (0.55-3.91)
Age (years)			
≤30 (Ref)			
31-40	**1.41 (1.14-1.75)**	1.19 (0.94-1.51)	1.10 (0.69-1.75)
>40	**1.76 (1.43-2.18)**	**1.60 (1.26-2.02)**	1.26 (0.81-1.96)

Residence			
Urban (Ref)			
Rural	**0.79 (0.69 - 0.91)**	0.99 (0.85-1.16)	0.92 (0.76-1.12)
Education			
Tertiary (Ref)			
Secondary	**1.26 (1.02-1.55)**	**1.37 (1.07 -1.75)**	**1.47 (1.03 -2.11)**
Primary or non-formal	**1.23 (1.05 - 1.43)**	**1.23 (1.04-1.45)**	**1.33 (1.07-1.66)**
Employment status			
No (Ref)			
Yes	1.06 (0.91-1.23)	0.99 (0.83-1.18)	0.87 (0.68-1.11)
Race*Gender			
Chinese*Female	-	-	**1.22 (0.83-1.79)**
Indian*Female	-	-	**2.09 (1.21 -3.60)**
Gender*Age group			
Female*Age group (31-40)	-	-	1.24 (0.75-2.07)
Female*Age group (>40)	-	-	**1.96 (1.21-3.17)**

Model 1: adjusted for other factors shown in the table
Model 2: adjusted for other factors
Model 3: adjusted for all possible 2 way-interactions terms with ethnicity. Only interaction terms that were significant were presented

Table 5. Unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95% CI) of knee pain by socio-economic factors stratified by gender

Associated factor	Male		Female	
	Unadjusted odds ratio	Adjusted odd ratio	Unadjusted odds ratio	Adjusted odd ratio
Ethnicity				
Malay (Ref)				
Chinese	**0.49 (0.38-0.63)**	**0.47 (0.36-0.63)**	**0.59 (0.49-0.73)**	**0.54 (0.43-0.68)**
Indian	0.90 (0.63-1.28)	0.91 (0.63-1.31)	2.09 (1.56-2.80)	**2.02 (1.48-2.76)**
Age (years)				
≤30 (Ref)				
31-40	1.37 (0.94-1.99)	1.13 (0.74-1.73)	1.43 (1.10-1.87)	1.32(0.98-1.77)
>40	**1.45 (1.03-2.05)**	1.20 (0.81-1.76)	2.10 (1.60-2.76)	**2.11(1.55-2.87)**
Residence				
Urban (Ref)				
Rural	**0.78 (0.63-0.96)**	0.76 (0.49-1.16)	0.82 (0.69-1.00)	0.94 (0.77-1.16)
Education				
Tertiary (Ref)				
Secondary	1.18 (0.85-1.64)	1.36 (0.92-2.01)	0.87 (0.68-1.11)	1.28 (0.93-1.77)
Primary or non-formal	0.85 (0.59-1.21)	**1.42 (1.11-1.82)**	0.77(0.59-1.00)	1.12(0.89-1.41)
Employment status				
No (Ref)				
Yes	1.17 (0.79-1.73)	0.76 (0.49-1.16)	1.01 (0.84-1.22)	1.03 (0.84-1.27)

Models were adjusted for other factors shown in the table

Discussion:

Knee pain is a common medical complaint in the community. We found that nearly a third of the Indian population had knee pain compared to other ethnic groups (p <0.001) especially Indian females who reported knee pain two times higher compared to Malay females (AOR 2.02, 95% CI 1.48-2.76). This was also seen in the COPCORD survey where 13.1% of the Indian females experienced knee pain as compared to Malay females (11.1%) and Chinese females (5.8%).(5, 11) One of the studies done locally also showed

that prevalence of pain complaints among Indian ethnic group is higher compared to Malay and Chinese in both one public primary care clinics (KK) and general practice clinic (GP) settings.(9) These findings may point to possible genetic factors and cultural background that determine response to pain among Indian populations. Perception towards pain threshold is greatly affected by family members, peers, and cultural background. Bone mineral density played an important role in development of arthritis and sclerosis which was shown in a study by Allen et all.(6) It also showed that forces experienced during walking in certain ethnic groups will caused knee OA, for instance, African- Americans were more likely than Caucasians to have valgus thrust during walking which cause more knee OA.

However more studies need to be carried out in order to examine these observations. In our study, Chinese ethnicity especially males (AOR 0.47, 95% CI 0.36-0.63) had the lowest prevalence of knee pain and this was again consistent with another study which also found a lower prevalence of knee pain amongst Chinese.(5) This could be due to their culturally based response to pain and genetic factors as well as their beliefs in using complementary medicines which are widely available among Chinese populations such as acupuncture and thermal cupping.

Although our study did not specifically determine the cause of the knee pain, we found that knee pain was more common in the older age group suggesting that the cause could be OA.(12-15) And specifically, we found that the odds of knee pain were two times higher among older females compared to younger females (AOR 2.11, 95% CI 1.55-2.87).

There was more knee pain amongst those with lower educational level especially males who were in primary and non- formal education level and this could be due to lack of awareness and knowledge about access to health care services and for prevention of knee OA. Besides, it could be due to the types of works undertaken by those without tertiary education whereby more stress may have been placed on their knees due to their strenuous jobs and hence causing more knee pain in this particular population.

Our study showed that gender became statistically significant only after adjustment for other confounding variables. The main effect model (Model 2) showed that compared to males, the odds of reporting knee pain among females were higher by 23% (95% CI 1.04-1.45). Females' pain threshold was lower as compared to males found in one of the studies by Cepeda et al.(16) A meta-analysis showed that gender stereotypes played an important role in pain sensitivity and pain threshold. (16, 17)

Our study did not find any significant difference in the prevalence of knee pain amongst employment status despite after adjustment for other confounding variables or stratified it according to gender. However several studies found that socioeconomic status(14) and psychological factors(18, 19) were determinants of knee pain and physical function.(20) The COPCORD survey showed that housewives (unemployed) reported more musculoskeletal pain and this may be related to repetitive household tasks and psychological

stresses.(5) In our study there was also no difference in prevalence of knee pain to whether one was living in a rural or urban environment. However, other studies found that there were more complaints of musculoskeletal symptoms in socially deprived areas.(21) The prevalence of knee pain in our rural community (23.7%) was higher than that of a study done in rural South India (17.2%).(22) This could be due to a wide variation in the definition of rural or urban amongst different countries.

However, we did not collect the data of looking at other confounding factors such as psychosocial factors, BMI(13, 18, 23-25) and menopausal states(11, 26) in experiencing knee pain and these variables have been shown to have an impact on perception of knee pain.

Among those who had knee pain, although Indians had more knee pain, it was the Malays instead of Indians who used more analgesia. This could be because more Indians were from rural area and from lower socioeconomic classes and hence poor knowledge in getting health care services for their knee pain. The medication most commonly used was a topical agent. This could be because it was cheaper to obtain and are more readily available as over the counter medications while NSAIDs required a doctor's prescription. With an ageing population and increasing number of consultations for knee pain, future studies should try to understand public perceptions, awareness and knowledge in self-care of knee pain and study the factors that influence patients to seek help.

In summary our study found that Indian females had a higher prevalence of knee pain compared to other ethnic groups. It is important to target this high-risk group so that prevention and appropriate interventions can be provided early. Murphy and colleagues suggested that prevention programmes should be offered relatively early in life and to understand the need of health care utilization in diagnosing early knee OA.(13)

Future studies should look at other confounding factors such as other co-morbid conditions, genetic predisposition, psychosocial factors and medical access factors as well as more precise and better assessment tools in diagnosing knee pain in the primary care setting.

Conclusion:

Prevalence of knee pain was more common in the Indian ethnic group especially among Indian females. It was also more common in the female older age groups and lowest prevalence of knee pain among Chinese males. The most common medication used for knee pain was topical medicated oil. Further studies need to be carried out to explore the reasons of these differences.

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Contributorship Statement:

- First author Prof Chia Yook Chin had fulfilled all three of the ICMJE guidelines for authorship which she contributed the conception and design, acquisition of data, or analysis and interpretation of data, she is also drafting the article or revising it critically for important intellectual content; and final approval of the version to be published.
- Second author Dr Beh Hooi Chin also had fulfilled all three of the ICMJE guidelines for authorship as mentioned earlier on.
- Third author Prof Ng Chirk Jenn also had fulfilled all three of the ICJME guidelines for authorship as stated on the previous paragraph.
- Fourth author Prof Teng Cheong Lieng also played an important role in authorship which he also fulfilled all three of the ICMJE guidelines.
- Fifth author Prof Nik Sherina Hanafi also had contributed the conception and design, acquisition of data, or analysis and interpretation of data, she is also drafting the article or revising it critically for important intellectual content; and final approval of the version to be published as per guidelines stated in ICJME guidelines for authorship.
- Sixth author Prof Choo Wan Yuen also had fulfilled all three of the ICMJE guidelines for authorship as mentioned earlier on.
- Seventh author Dr Ching Siew Mooi also had fulfilled all three of the ICMJE guidelines for authorship as mentioned before.

Competing Interests

The authors have declared that no competing interests exist. All data and the findings described in our manuscript are fully available, readily to be shared without restriction and from the time of publication. No additional data available.

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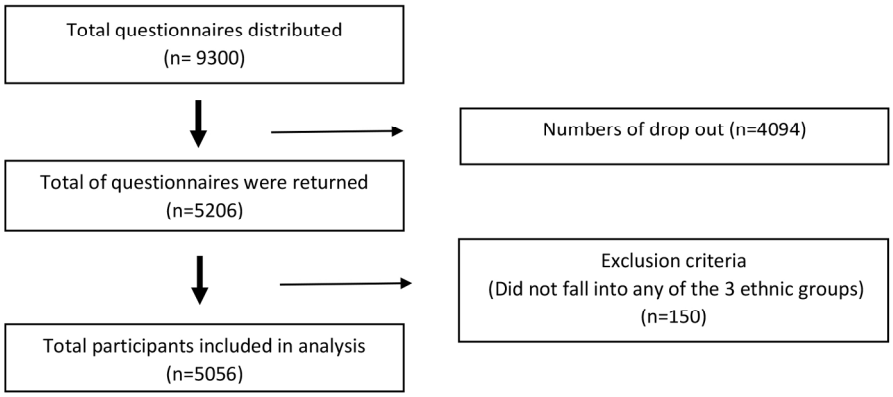

Fig 1 Flow chart shows the flow of selection of participants (Line 73)
Fig 1: Flow chart shows the fl
173x79mm (300 x 300 DPI)

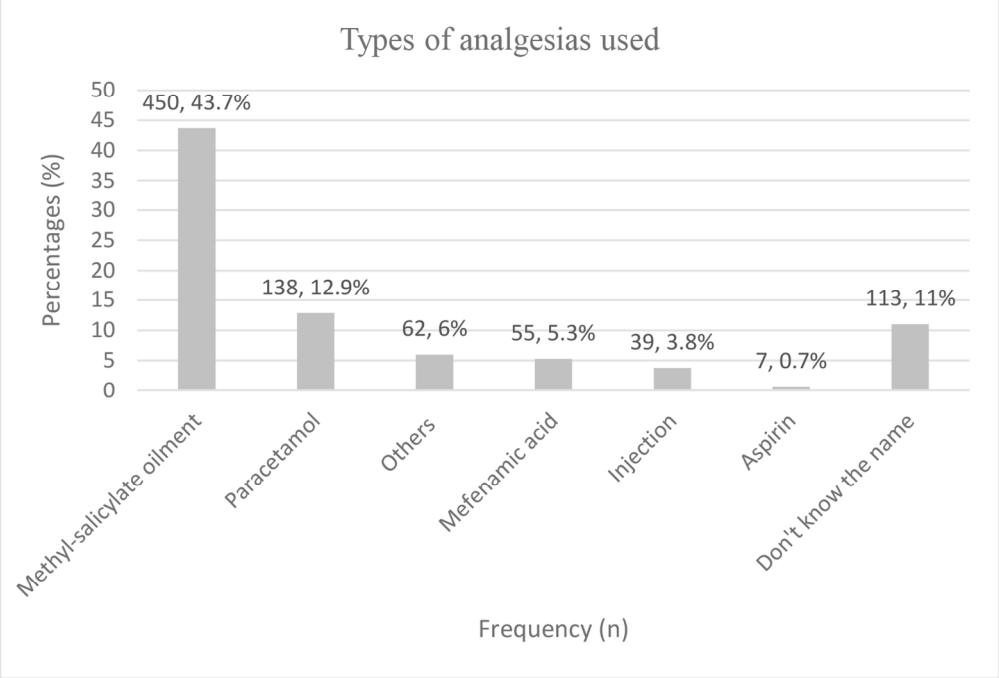

Fig 2 Types of analgesics used for knee pain (N=716) (Line 132)
Fig 2 Types of analgesics used
131x89mm (300 x 300 DPI)

Fig 3: Prevalence of knee pain by gender and age group

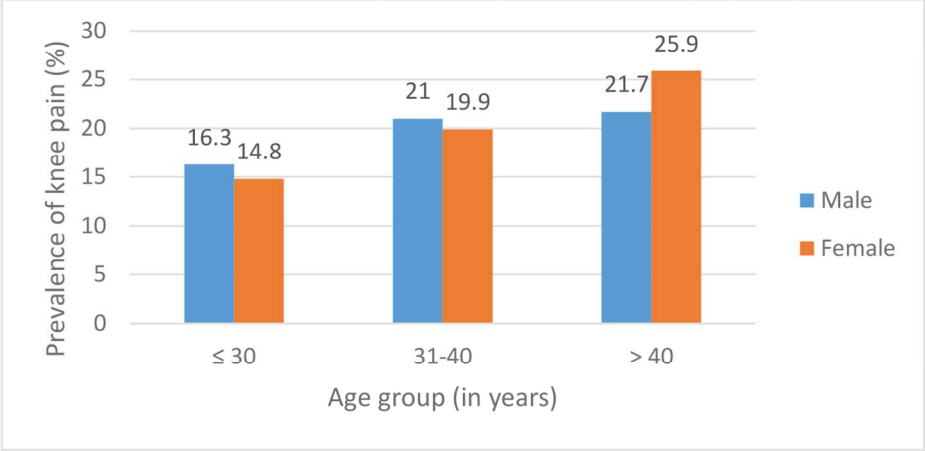

Fig 3 Prevalence of knee pain by gender and age group (Line 139)
Fig 3 Prevalence of knee pain
124x64mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2-3
Objectives	3	State specific objectives, including any prespecified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	2-4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	3-4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	2-3
Study size	10	Explain how the study size was arrived	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4-5
		(*b*) Describe any methods used to examine subgroups and interactions	4-5
		(*c*) Explain how missing data were addressed	2-3
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Not applicable

		(*e*) Describe any sensitivity analyses	Not applicable
Results			5-8
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	3 (Fig 1), 4-5
		(b) Give reasons for non-participation at each stage	3
		(c) Consider use of a flow diagram	3 (Fig 1)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5-8
		(b) Indicate number of participants with missing data for each variable of interest	5 (Table 1)
Outcome data	15*	Report numbers of outcome events or summary measures	4-5
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5 (Table 4,5)
		(*b*) Report category boundaries when continuous variables were categorized	3
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	2
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	5-7
Generalisability	21	Discuss the generalisability (external validity) of the study results	2,7
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	7

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Ethnic Differences in the Prevalence of Knee Pain amongst Adults of a Community in a Cross-Sectional Study

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Words count: 3883 words

Abstract:

Objective: To determine the prevalence of knee pain among three major ethnic groups in Malaysia. By identifying high-risk groups, preventive measures can be targeted at these population.

Design and Setting: A cross-sectional survey was carried out in both rural and urban areas in a state in Malaysia. Secondary schools were randomly selected and used as sampling units.

Participants: Adults aged ⩾18 years old were invited to answer a self-administered questionnaire on pain experienced over the previous 6 months. Out of 9,300 questionnaires distributed, 5206 were returned and 150 subjects that did not fall into the three ethnic groups were excluded, yielding a total of 5056 questionnaires for analysis. 58.2% (n=2926) were females. 50% (n= 2512) were Malays, 41.4% (n=2079) were Chinese, and 8.6% (n=434) were Indians.

Results: 21.1% (n=1069) had knee pain in the previous 6 months. More Indians (31.8%) experienced knee pain compared to Malays (24.3%) and Chinese (15%) (p<0.001). The odds of Indian females reporting knee pain was twofold higher compared to Malay females. There was a rising trend in the prevalence of knee pain with increasing age (p<0.001). The association between age and knee pain appeared to be stronger in females than males. 68.1% of Indians used analgesia for knee pain while 75.4% of Malays and 52.1% of Chinese did so (p<0.001). The most common analgesic used for knee pain across all groups was topical medicated oil (43.7%).

Conclusion: The prevalence of knee pain in adults was more common in Indian females and older female age groups and Chinese males had the lowest prevalence of knee pain. Further studies should investigate the reasons for these differences.

Strengths and Limitations of this Study:

- Sample size was large and comprised of sufficient numbers of the different ethnicity groups in Malaysia.
- Population were parents with children and might be different for non-parents.
- We were unable to attribute knee pain being entirely due to OA.
- We did not collect data on other confounding factors such as body mass index (BMI), psychosocial factors, history of trauma, and menopausal status.
- Although we did not perform a formal sample size calculation, our sample size was large and it was comparable to another study. (1)

Introduction:

Knee pain is the most common pain complaint among older individuals and the most frequent cause of osteoarthritis (OA) of the knees.(1, 2) OA of the knee impacts on quality of life and causes physical disability as well as limitations in functioning in older individuals.(3, 4) Studies have shown that there are differences in the prevalence of knee pain based on OA amongst different ethnic groups.(5-9) In the COPCORD study, 13.1 % Indian females had knee pain compared to 11.1% of Malay females and 5.8% of Chinese females (5.8%).(5) A study in the United States showed that knee pain was disproportionately higher among older African Americans than non- Hispanic white groups.(8)

Cultural background, pain threshold, and genetic predisposition may be some of the reasons why knee pain is more common in certain ethnic groups. Importantly, many environmental and lifestyle risk factors are reversible (e.g, obesity, muscle weakness) or avoidable (e.g, occupational or recreational joint trauma) which has implications for primary and secondary preventions.

The aim of our study was to describe the prevalence of knee pain and use of analgesic medications for knee pain amongst different ethnic groups in Malaysia as well as the interaction and association of socio-demographic information to the prevalence of knee pain. Identifying the high-risk groups would assist health care workers in understanding patients' experiences with and beliefs on pain, and hence preventive measures could be targeted to these groups of people.

Methods:

A cross-sectional survey was carried out in 6 districts in the State of Selangor in Malaysia based on purposive sampling in four urban districts (Petaling Jaya, Subang, Seri Kembangan, Kampong Medan) and

two rural towns in Kuala Langat district (Banting and Jenjarom). The districts were selected based on ethnic distribution as well as socio-economic status. Secondary schools within these districts were randomly selected and used as sampling units to reach out to the adults in the community. The children from the selected schools were provided with self- administered questionnaires for their parents or main care-givers aged 18 years and above to complete. Efforts were made to optimize the response rate through reminders and providing incentives to schools which were able to achieve an at least 70% response rate. The questionnaires were collected two weeks after distribution. Out of 9,300 questionnaires distributed, 5206 were returned, yielding a response rate of 56.0%. However, we excluded 150 subjects that were not part of any of the three key ethnic groups (Chinese, Malays and Indians), leaving a total of 5056 questionnaires for analysis. The findings are summarized in Figure 1.

Figure 1: Flow chart showing the selection of participants

We did not address the issue of non-respondents as the sample size was large (n= 5056) and we believed that it would not affect the findings of the study. Furthermore we did not have the non- respondents' contact numbers as the questionnaires were distributed to the students for them to bring home to their parents or main care-givers.

The researchers designed the self-administered questionnaires based on the existing literature and discussion. Socio- demographic data (including age, sex, occupation, education level, location of residency, and ethnicity), types of pain experienced over the previous 6 months, and medications used were captured. All of the data, including ethnicity and types of pain were self-declared. The English questionnaires were translated into two other languages (Malay and Chinese) and then back-translated. Any discrepancy in translation was discussed and agreed upon by 3 researchers. This was followed by pilot-testing on adults of different ethnicities, mainly Malay, Chinese and Indians, and further revisions were made before the survey was distributed.

Approval to conduct this study was obtained from the University of Malaya Medical Centre Medical Ethics Committee. We also were given permission from the schools and State Education Department. Written informed consent was acquired from all the participants.

We classified occupation based on employment status, either 'yes' or 'no' for the data analyses, and educational level as primary and non-formal, secondary and tertiary. We also categorized the subjects into three main age groups, being $\leqslant$ 30 years old, 31-40 years old and >40 years old.

Stratification of rural areas was based on the census from Malaysia in 2010 that defined as rural areas as having populations less than 10,000 people and featuring agriculture and natural resources. Urban areas were defined as gazette areas with populations of 10,000 and more.(10)

Data analysis

Categorical data were reported in proportions (percentage). Continuous data were described as means and standard deviations if the distribution were Gaussian. Chi-square analyses were employed to

determine significant group differences with knee pain prevalence. Binary logistic regression analyses examined the relationship between ethnicity and knee pain controlling for other socio-demographic variables. Crude and adjusted-odds ratios (OR) and 95% confidence intervals (95% CI) are presented. Significance was set at an alpha level of 0.05. All analyses were performed using SPSS Version 16.0.

Multivariate analyses were first performed using all combined data. A hierarchical regression strategy was used in which the independent variables were forced into the equation: (I) ethnicity alone (Model 1); (II) the main effects of all independent variables (Model 2); and finally (III) main effects including all possible 2 way- interactions terms with ethnicity (Model 3) to determine the presence of interaction effect. The 2 way- interactions between (I) ethnicity and gender; and (II) gender and age were statistically significant. Subsequent regression analyses were therefore stratified by gender. With the gender specific regression analyses, a similar hierarchical approach was applied. As none of the 2-way interaction terms were found to be significant in these models, only the results of the main effects were presented in the final model for each gender. All data and findings are fully available without restriction.

Results:

A total of 5056 participants responded to the questionnaire. The mean age of the participants was 38.5 (SD ± 8.95) with males (mean age= 40.6, SD ± 9.2) being slightly older than females (mean age= 36.9, SD ± 8.46). Table 1 shows the overall socio-demographic distribution of participants and their association with knee pain. The majority of respondents were Malays (50%) followed by Chinese (41.4%) and Indians (8.6%). The sample was mostly females, from urban residences, had secondary and higher education levels and being employed.

The overall prevalence of knee pain among all respondents was 21.2%. The prevalence of knee pain differed significantly with age, ethnicity, urban-rural area and educational level. (See Table 1).

Table 1. Respondents' characteristics by prevalence of knee pain (N=5056)

Characteristics	Overall	Knee pain, N (%)		p-value
		Yes	No	
Ethnicity				<0.001
Malay	2512 (50.0)	610 (24.3)	1902 (75.7)	
Chinese	2079 (41.4)	311 (15.0)	1768 (85.0)	
Indian	434 (8.6)	138 (31.8)	296 (68.2)	
Age (years)				<0.001
<30	846 (16.8)	129 (15.2)	717 (84.8)	
31-40	1936 (38.3)	392 (20.2)	1544 (79.8)	
>40	2268 (44.9)	546 (24.1)	1722 (75.9)	
Gender				0.730
Male	2103 (41.8)	440 (20.9)	1663 (79.1)	
Female	2926 (58.2)	624 (21.3)	2302 (78.7)	
Residence				<0.001
Urban	3250 (64.3)	641 (19.7)	2609 (80.3)	
Rural	1806 (35.7)	428 (23.7)	1378 (76.3)	
Education				0.022
Tertiary	766 (32.2)	302 (18.7)	1310 (81.3)	
Secondary	2631 (52.5)	580 (22.0)	2051 (78.0)	

Primary or non-formal	1612 (15.3)	172 (22.5)	594 (77.5)	
Employment status				0.485
Yes	3208 (69.9)	683 (21.3)	2525 (78.7)	
No	1382 (31.1)	307 (22.2)	1075 (77.8)	

Overall 21.1% (n=1069) of respondents had knee pain. The Indian population (31.8%, n=138) had the highest prevalence of knee pain, followed by Malays at 24.3% (n=610) and Chinese at 15% (n=311). Two-thirds (67.6%, n= 716) used medications for their knee pain over the previous 6 months. Malays (75.4%, n=460) were more likely to use medications than Indians (68.1%, n=94) and the Chinese (52.1%, n=162) (p<0.001), just as depicted in Table 2. Figure 2 list the medications used which included topical methyl-salicylate ointment (43.7%), paracetamol (12.9%), mefenamic acid (5.3%), and injections (3.8%).

Table 2: Comparison of ethnic groups using analgesia for knee pain (N=716/1069)

Characteristics	Knee pain on analgesia, N (%)		p-value
	Yes	No	
Ethnicity			<0.001
Malay	460 (75.4)	150 (24.6)	
Chinese	162 (52.1)	149 (47.9)	
Indian	94 (68.1)	44 (31.9)	

Figure 2: Types of analgesics used for knee pain (N=716)

Subgroup analyses by gender suggested that the overall prevalence of knee pain significantly increased with age among women (p<0.001) but not among men (p=0.102) (Figure 3). With the stratified analysis by ethnicity, there was no significant difference found between gender and knee pain except among Indians. Indian females reported significantly higher levels of knee pain than Indian males. An increasing prevalence of knee pain with increasing age (p<0.001) was observed among the Malays and Chinese but not among those of Indian ethnicity (Table 3).

Figure 3: Prevalence of knee pain by gender and age group

Table 3. Ethnic distribution of knee pain by gender and age group

Ethnic	Prevalence (%)						
	Gender			Age (in years)			
	Male	Female	*p value	⩽ 30	31-40	> 40	**p-value
Malay	24.8	23.7	0.543	17.9	21.7	29.0	**<0.001**
Chinese	13.9	15.7	0.304	11.0	13.8	17.4	**0.004**
Indian	22.9	39.4	**<0.001**	31.0	34.1	29.9	0.683

p- value derived from comparing * gender (or **age group) difference in each ethnic category

In multivariate analysis (Table 4), the unadjusted OR (Model 1) indicated that ethnicity, age, residence and education level were associated with knee pain. Gender and employment status of the respondents did not have an influence on knee pain. However, gender became statistically significant after adjusting for other confounding variables. The main effect model (Model 2) demonstrated that compared to males, the odds of reporting knee pain among females were higher by 23%. The odds of knee pain were 49% lower among the Chinese and 42% greater among Indians compared to Malays. Versus the aged <30 years group, the odds of reporting knee pain were higher among those above 40 years group (AOR = 1.60, 95% CI = 1.26-2.02). When all possible 2 way-interaction terms were added in the regression analysis, the association between knee pain with ethnicity, gender and age group was diminished (Model 3). There was significant effect modification between knee pain and ethnicity by gender. Similarly, there was age by gender interaction.

Subsequent gender specific multivariate analyses (Table 5) suggested that Chinese males reported significantly less knee pain than Malay males. Chinese females were less likely to report knee pain (AOR 0.54; 95% CI= 0.43-0.68), whilst the odds of Indian females reporting knee pain were twice as high compared to Malay females. The association between age and knee pain appeared to be stronger in females than in males. The odds of reporting knee pain were two-fold higher among older females (>40 years above) compared to younger females. Lower education level (primary or lower) was associated with knee pain in males but this was not observed in females.

Table 4. Unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95% CI) of knee pain by socio-economic factors

Associated factor	Unadjusted odds ratio	Adjusted odds ratio	
	Model 1	**Model 2**	**Model 3**
Gender			
Male (Ref)			
Female	1.03 (0.89-1.18)	**1.23 (1.04-1.45)**	0.69 (0.44-1.11)
Ethnicity			
Malay (Ref)			
Chinese	**0.55 (0.47-0.64)**	**0.51 (0.43-0.61)**	**0.31 (0.14-0.68)**
Indian	**1.45 (1.17-1.81)**	**1.42 (1.12-1.78)**	1.46 (0.55-3.91)
Age (years)			
≤30 (Ref)			
31-40	**1.41 (1.14-1.75)**	1.19 (0.94-1.51)	1.10 (0.69-1.75)
>40	**1.76 (1.43-2.18)**	**1.60 (1.26-2.02)**	1.26 (0.81-1.96)
Residence			
Urban (Ref)			
Rural	**0.79 (0.69 - 0.91)**	0.99 (0.85-1.16)	0.92 (0.76-1.12)
Education			
Tertiary (Ref)			
Secondary	**1.26 (1.02-1.55)**	**1.37 (1.07 -1.75)**	**1.47 (1.03 -2.11)**
Primary or non-formal	**1.23 (1.05 - 1.43)**	**1.23 (1.04-1.45)**	**1.33 (1.07-1.66)**
Employment status			

No (Ref)			
Yes	1.06 (0.91-1.23)	0.99 (0.83-1.18)	0.87 (0.68-1.11)
Ethnicity*Gender			
Chinese*Female	-	-	**1.22 (0.83-1.79)**
Indian*Female	-	-	**2.09 (1.21 -3.60)**
Gender*Age group			
Female*Age group (31-40)	-	-	1.24 (0.75-2.07)
Female*Age group (>40)	-	-	**1.96 (1.21-3.17)**

Model 1: adjusted for other factors shown in the table
Model 2: adjusted for other factors
Model 3: adjusted for all possible 2 way-interactions terms with ethnicity. Only interaction terms that were significant are presented

Table 5. Unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95% CI) of knee pain by socio-economic factors stratified by gender

Associated factor	Male		Female	
	Unadjusted odds ratio	Adjusted odd ratio	Unadjusted odds ratio	Adjusted odd ratio
Ethnicity				
Malay (Ref)				
Chinese	**0.49 (0.38-0.63)**	**0.47 (0.36-0.63)**	**0.59 (0.49-0.73)**	**0.54 (0.43-0.68)**
Indian	0.90 (0.63-1.28)	0.91 (0.63-1.31)	2.09 (1.56-2.80)	**2.02 (1.48-2.76)**
Age (years)				
≤30 (Ref)				
31-40	1.37 (0.94-1.99)	1.13 (0.74-1.73)	1.43 (1.10-1.87)	1.32(0.98-1.77)
>40	**1.45 (1.03-2.05)**	1.20 (0.81-1.76)	2.10 (1.60-2.76)	**2.11(1.55-2.87)**
Residence				
Urban (Ref)				
Rural	**0.78 (0.63-0.96)**	0.76 (0.49-1.16)	0.82 (0.69-1.00)	0.94 (0.77-1.16)
Education				
Tertiary (Ref)				
Secondary	1.18 (0.85-1.64)	1.36 (0.92-2.01)	0.87 (0.68-1.11)	1.28 (0.93-1.77)
Primary or non-formal	0.85 (0.59-1.21)	**1.42 (1.11-1.82)**	0.77(0.59-1.00)	1.12(0.89-1.41)
Employment status				
No (Ref)				
Yes	1.17 (0.79-1.73)	0.76 (0.49-1.16)	1.01 (0.84-1.22)	1.03 (0.84-1.27)

Models were adjusted for other factors shown in the table

Discussion:

Knee pain is a common medical complaint in the community. We found that nearly a third of the Indian population had knee pain compared to other ethnic groups (p <0.001), especially Indian females who reported knee pain two-fold more compared to Malay females (AOR 2.02, 95% CI= 1.48-2.76). This was also seen in the COPCORD survey where 13.1% of Indian females experienced knee pain versus Malay females (11.1%) and Chinese females (5.8%).(5, 11) Another local study conducted also showed that prevalence of pain complaints among the Indian ethnic group was greater compared to Malay and Chinese in both public primary care clinics (KK) and general practice clinic (GP) settings.(9) These findings may point to possible genetic factors and cultural backgrounds determining response to pain among Indian populations. Perceptions towards pain threshold are greatly affected by family members, peers, and cultural background. Bone mineral density plays an important role in the development of arthritis and sclerosis, as evidence in a

work by Allen et all.(6) They also showed that forces experienced during walking by certain ethnic groups will cause knee OA. For instance, African- Americans were more likely than Caucasians to have valgus thrust during walking, causing more knee OA.

Yet, more research need to be carried out to examine these observations more closely. In our study, the Chinese ethnicity especially Chinese males (AOR 0.47, 95% CI = 0.36-0.63) had the lowest prevalence of knee pain and this was again consistent with another study which also found a lower prevalence of knee pain amongst the Chinese.(5) This could be due to their culturally-based response to pain and genetic factors as well as their beliefs in using complementary medicines widely available among Chinese populations such as acupuncture and thermal cupping.

Although our study did not specifically determine the cause of knee pain, we found that knee pain was more common in older age groups suggesting that the etiology could be OA.(12-15)As well, in particular, we observed that the odds of knee pain were two times higher among older females compared to younger females (AOR 2.11, 95% CI 1.55-2.87).

There was more knee pain amongst those with lower educational levels, especially males with primary and non- formal education levels and this could be due to lack of awareness and knowledge about access to health care services for prevention of knee OA. Besides, it may arise from the types of works undertaken by those without tertiary education whereby more stress may have been placed on their knees because of their strenuous jobs, hence causing more knee pain in this particular population.

Our study demonstrated that gender became statistically significant only after adjustment for other confounding variables. The main effect model (Model 2) showed that compared to males, the odds of reporting knee pain among females were higher by 23% (95% CI= 1.04-1.45). Females' pain thresholds were determined to be lower than that of males in one of the studies by Cepeda et al.(16) A meta-analysis showed that gender stereotypes have a significant influence on pain sensitivity and pain threshold. (16, 17)

Our study did not find any significant difference in the prevalence of knee pain with the context of employment status, despite after adjusting for other confounding variables or according to gender. However several studies found that socioeconomic status(14) and psychological factors(18, 19) were determinants of knee pain and physical function.(20) The COPCORD survey showed that housewives (unemployed) reported more musculoskeletal pain and this may be related to repetitive household tasks and psychological stresses.(5) In our study there was also no difference in prevalence of knee pain based on whether one was living in a rural or urban environment. Yet, other studies have found that there are more complaints of musculoskeletal symptoms in socially-deprived areas.(21) The prevalence of knee pain in our rural community (23.7%) was higher than that of a study done in rural South India (17.2%).(22) This may be the results of a wide variation in the definition of rural or urban areas amongst different countries.

Although we did not collect data of looking on other confounding factors such as psychosocial factors, BMI(13, 18, 23-25) and menopausal states(11, 26) with regards to experience knee pain, these variables have been shown to impact perceptions of knee pain.

Among those who had reported having knee pain in our study, though Indians had more knee pain, the Malays were more prone to analgesic use. This could be because more Indians were from rural areas and from lower socioeconomic classes. Hence having poor knowledge with respect to accessing health care services for their knee pain. The medication most commonly used was a topical agent. Possibly because it was cheaper to obtain and more readily available as over the counter medications. NSAIDs require a physician's prescription. With an ageing population and rising number of consultations for knee pain, future studies should attempt to understand public perceptions, awareness and knowledge of self-care of knee pain and investigate the factors that influence patients seeking help.

In summary, our study found that Indian females had a higher prevalence of knee pain compared to other ethnic groups. It is important to target this high-risk group so that prevention and appropriate interventions can be provided early. Murphy and colleagues suggested that prevention programmes should be offered relatively early in life and that there should be dissemination of understanding the need of health care utilization in diagnosing early knee OA within communities.(13)

Future studies should look at other confounding factors such as other co-morbid conditions, genetic predisposition, psychosocial factors and medical access factors as well as more precise assessment for tools in diagnosing knee pain in the primary care setting.

Conclusion:

Prevalence of knee pain was more common in the Indian ethnic group especially among Indian females. It was also more frequently reported in the older female age groups, though was least prevalence among Chinese males. The most common medication used for knee pain was topical medicated oil. Further studies need to be carried out to explore the reasons for these differences.

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Contributorship Statement:

- First author Prof Chia Yook Chin, had fulfilled all three of the ICMJE guidelines for authorship, contributing the conception and design, acquisition of data, or analysis and interpretation of data. She

also drafted the article or revised it critically for important intellectual content, and provided final approval of the version to be published.

- Second author, Dr Beh Hooi Chin, had also fulfilled all three of the ICMJE guidelines for authorship as mentioned earlier.
- Third author Prof Ng Chirk Jenn had also fulfilled all three of the ICJME guidelines for authorship as stated.
- Fourth author Prof Teng Cheong Lieng also played an important role in fulfilling all three of the ICMJE guidelines.
- Fifth author, Prof Nik Sherina Hanafi, had also contributed the conception and design, acquisition of data, or analysis, and interpretation of data. She had drafted the article or revised it critically for important intellectual content, and provided final approval of the version to be published as per guidelines stated in ICJME guidelines for authorship.
- Sixth author, Prof Choo Wan Yuen had also fulfilled all three of the ICMJE guidelines for authorship as mentioned earlier on.
- Seventh author Dr Ching Siew Mooi too fulfilled all three of the ICMJE guidelines for authorship.

Competing Interests

The authors have declared that no competing interests exist. All data and the findings described in our manuscript are fully available, ready to be shared without restriction from the time of publication. No additional data are available.

Data sharing statement

All data and the findings described in our manuscript are fully available, without restriction and from the time of publication. No additional data available.

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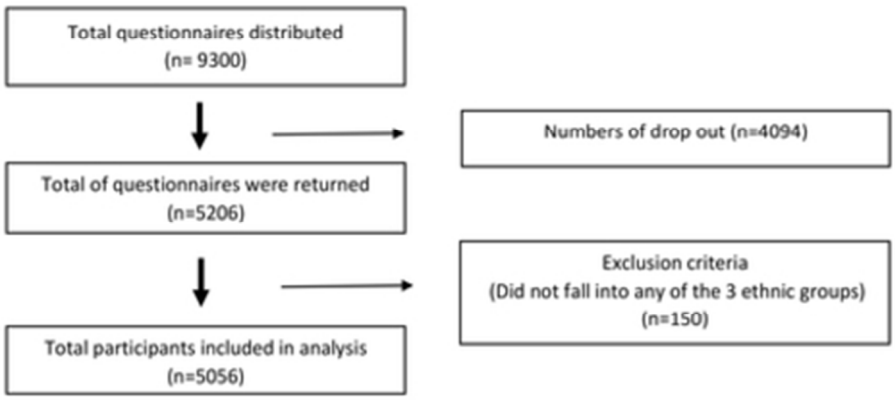

Fig 1 Flow chart showing selection of participants (Line 77)
Line 77
183x83mm (72 x 72 DPI)

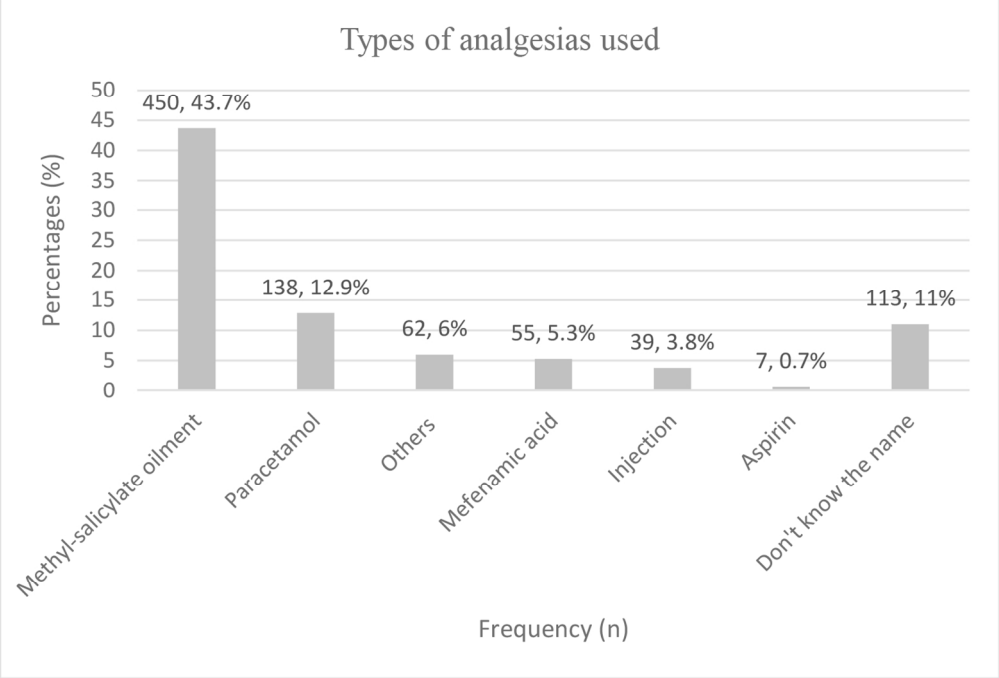

Fig 2 Types of analgesics used for knee pain (Line 137)
Line 137
131x89mm (300 x 300 DPI)

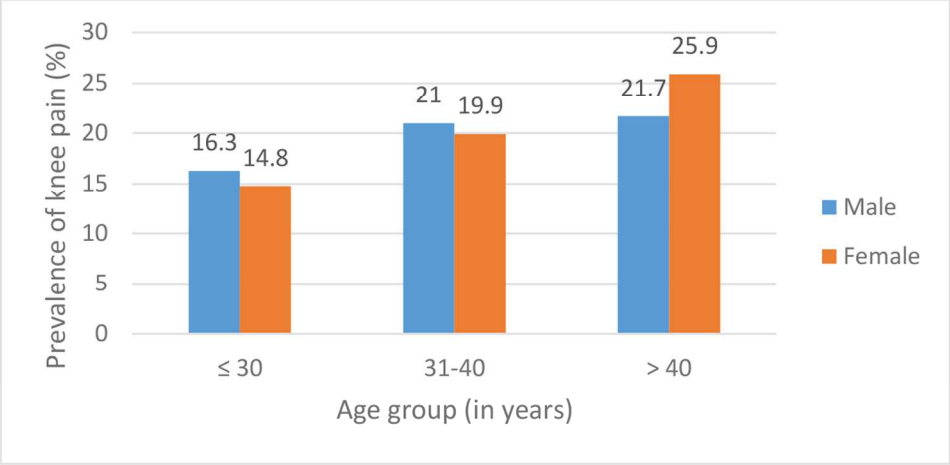

Fig 3 Prevalence of knee pain by gender and age group (Line 144)
Line 144
121x57mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2-3
Objectives	3	State specific objectives, including any prespecified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	2-4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	3-4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	2-3
Study size	10	Explain how the study size was arrived	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4-5
		(*b*) Describe any methods used to examine subgroups and interactions	4-5
		(*c*) Explain how missing data were addressed	2-3
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Not applicable

		(*e*) Describe any sensitivity analyses	Not applicable
Results			5-8
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	3 (Fig 1), 4-5
		(b) Give reasons for non-participation at each stage	3
		(c) Consider use of a flow diagram	3 (Fig 1)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5-8
		(b) Indicate number of participants with missing data for each variable of interest	5 (Table 1)
Outcome data	15*	Report numbers of outcome events or summary measures	4-5
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5 (Table 4,5)
		(*b*) Report category boundaries when continuous variables were categorized	3
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	2
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	5-7
Generalisability	21	Discuss the generalisability (external validity) of the study results	2,7
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	7

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.