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Generalised Joint Hypermobility and knee joint hypermobility - prevalence, knee joint symptoms and health-related quality of life in the Danish adult population

Tina Junge1,2, Peter Henriksen1,2, Sebrina Hansen1, Lasse Østengaard1, Yvonne M. Golightly3,4,5,6, Birgit Juul-Kristensen1

1Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, DK
2Health Sciences Research Centre, University College Lillebaelt, Odense, DK
3Department of Epidemiology, University of North Carolina, Chapel Hill, North Carolina, USA
4Thurston Arthritis Research Center, University of North Carolina, Chapel Hill, North Carolina, USA
5Injury Prevention Research Center, University of North Carolina, Chapel Hill, North Carolina, USA
6Division of Physical Therapy, University of North Carolina, Chapel Hill, North Carolina, USA

Correspondence about the manuscript and reprints to:
T. Junge, FoF, IoB, University of Southern Denmark,
Campsuvej 55, 5230 Odense M, Denmark
Aim
Several biomechanical factors, such as knee joint hypermobility, are suggested to play a role in the etiology of knee joint symptoms and knee osteoarthritis. Nevertheless, the prevalence or consequences of knee joint hypermobility (KJH) solely or included in the classification of Generalized Joint Hypermobility (GJHk) is unknown for a general population. Therefore, the objectives were to report the prevalence of self-reported GJHk and KJH, as well as the association of these conditions to knee joint symptoms, severity and duration of symptoms, and health related quality of life (HRQoL) in the Danish adult population.

Method
This study is a cross-sectional population-based survey of 2056 Danish adults. Respondents received online questionnaires of GJHk and KJH, knee joint symptoms, the severity and duration of these, as well as HRQoL.

Results
Total response rate was 49% (n=1006). The prevalence of self-reported GJHk and KJH was 13% and 23%, mostly representing women. More than half of the respondents with GJHk and KJH had knee joint symptoms. The odds for reporting knee joint symptoms, severity of knee joint symptoms and duration of knee joint symptoms were twice as high for respondents with GJHk and KJH. Respondents with GJHk and KJH reported lower HRQoL.

Conclusion
GJHk and KJH were frequently reported in the Danish adult population, mostly in women. Respondents with GJHk and KJH were two times more likely to report knee joint related symptoms such as pain, reduced performance of usual activity and lower HRQoL. The impact of these conditions on HRQoL is comparable with knee osteoarthritis.

Key words
Generalized Joint Hypermobility, Knee Joint, Pain, Quality of Life

"Knee hypermobility affects women"
Introduction

Musculoskeletal disorders, including osteoarthritis (OA), are some of the most burdensome medical conditions in the western countries, both to the individual and society. One of the most affected body regions is the knee joint, with reports of pain, decreased physical function and reduced Health Related Quality of Life (HRQoL). The lifetime risk of symptomatic knee OA in at least one knee is remarkably high, being nearly 1 in 2 in the adult population in the United States.

Several biomechanical factors are suggested to play a role in the etiology of knee OA, knee joint symptoms and/or pain, including knee joint laxity and knee joint hypermobility. Knee joint laxity is typically defined as an excessive displacement or rotation of the tibia with respect to the femur, whereas joint hypermobility is an exaggerated ability to exceed the joint beyond the normal range of motion. The exact relationship between knee joint laxity and knee joint hypermobility is not known, but both conditions are found to be associated with severe knee injuries, such as rupture of the anterior cruciate ligament (ACL), which again is strongly associated with knee OA.

Knee joint hypermobility may be included in the classification of Generalized Joint Hypermobility (GJH), which is a hereditary condition. GJH is most often evaluated by the Beighton test (BT) nine point scoring system, assessing hypermobility bilaterally of the first and fifth fingers, elbows and knees as well as forward bending with straight knees. The prevalence of GJH varies from 2-57% between studies, depending on the criteria used and the population studied. Most population studies reporting prevalence of GJH include study samples from specific sport settings, ethnic areas, age groups, or patient groups. Among 46,000 adults, already in contact with the health care system, the prevalence of GJH was found to be 18%, using a 5-part questionnaire for identifying hypermobility. However, the prevalence of self-reported knee joint hypermobility solely or included in the classification of GJH within the general adult population is not known.

In laboratory studies, adults with GJH including knee joint hypermobility report more knee-related pain and lower knee-related quality of life than adults without GJH. Also, individuals with GJH and knee joint hypermobility have shown altered neuromuscular strategies during daily functions that involve the knee, e.g. gait and jumping. Malalignment of the knee joint due to reduced passive stability may affect knee joint load distribution adversely and consequently lead to knee joint pain, reduced activities of daily living and HRQoL. However, the associations between these plausible
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consequences for daily life and self-reported knee joint hypermobility solely or included in the classification of GJH in a general adult population have not previously been reported.

Therefore, the aims of this study were to 1) report the prevalence of self-reported knee joint hypermobility solely and knee joint hypermobility when included in the classification of GJH in a general population of adults, and 2) study the association between self-reported knee joint hypermobility and knee joint symptoms, duration of symptoms, activities of daily living and HRQoL.

Methods
Design
The current study is a cross-sectional population-based one-phase survey of GJH conducted at the University of Southern Denmark. The study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines 19, and executed according to the guidelines of The Regional Committees on Health Research Ethics for Southern Denmark 20. The invited participants were informed that participation was optional and would be regarded as declaration of consent. The study was approved by the Danish Data Protection Agency (J.no.2014-41-3211).

Population
The inclusion criteria were Danish adult citizens between 25 to 65 years and with permanent residency in Denmark. Eligible participants were randomly selected from a governmental institution, the Danish Civil Registration System, a population-based database, executed by a governmental institution, Statens Serum Institute, thereby minimizing risk of sampling bias. Names and home addresses of the participants were provided from the data extraction. Letters of invitation to participate in the current study contained information about the study, including an internet link with a personal code to an online questionnaire, hosted by SurveyXact 21 and instructions on how to fill out the online questionnaire 22. The letters of invitation were sent out in January 2015. Non-responders were sent a first reminder after three weeks and a second reminder after an additional three weeks. In total, 2072 letters of invitation were sent out.

Questionnaires

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The online questionnaire was designed to identify 1) hypermobility, 2) musculoskeletal symptoms 3) HRQoL and 4) demographics, using predominantly validated questionnaires.

**Hypermobility**

Information about self-reported GJH was collected using the five-part questionnaire developed by Hakim and Grahame (5PQ)\(^\text{13}\). All five questions were dichotomous (yes/no) combined to a minimum score of zero and a maximum score of five. GJH status was determined by a cut-point of at least two positive answers, which has been shown to yield the highest sensitivity (84 %) and specificity (89 %)\(^\text{13}\). A Danish translated and cross-culturally adjusted version has been developed, and approved by the principal author of the 5PQ\(^\text{13}\).

The questions were: Q1) ‘Can you now (or could you ever) place your hands flat on the floor without bending your knees?’, Q2) ‘Can you now (or could you ever) bend your thumb to touch your forearm?’, Q3) ‘As a child did you amuse your friends by contorting your body into strange shapes or could you do the splits?’, Q4) ‘As a child or teenager did your shoulder or kneecap dislocate on more than one occasion?’, and Q5) ‘Do you consider your self double-jointed?’. Responses to all questions were ‘yes’ or ‘no’.

For prevalence of self-reported KJH, a supplementary question was added to the 5-PQ, corresponding to Q6) ‘Can you hyperextend one or both your knees?’ Respondents who answered ‘yes’ to this question, were classified as GJHk, provided they were classified as GJH. Respondents with solely unilateral or bilateral KJH were classified as having KJH. Respondents not classified with GJHk or KJH, were categorized as not joint hypermobile (NJH).

**Musculoskeletal symptoms outcome**

For information about presence, severity and duration of musculoskeletal symptoms, the general part of the Standardized Nordic Questionnaire (SNQ) was included\(^\text{23}\). In the SNQ, the body is divided into regions, including the knee region, and a body chart next to the questions illustrates these different body regions.

1) Respondents answered ‘yes’ or ‘no’ to whether they had had any presence of musculoskeletal symptoms (pain, ache, discomfort), in one or both knees, within the latest 12 months.

2) If the respondents provided an affirmative answer, they were asked specifically whether their symptoms had prevented them from performing their usual activities (at home/outside their home),
allowing a dichotomous answer (yes/no) regarding one aspect of the severity of their knee joint symptoms.

3) Also, the respondents were asked for how many days they had had this disorder (0 days/1-7 days/8-30 days/31-90 days/more than 90 days). To describe the duration of knee joint symptoms per year, duration was collapsed into the following groups: 0 days/1-30 days/31-90 days/above 90 days.

**Health-related quality of life (HRQoL) outcome**

For information about HRQoL, the EuroQoL-5D-5L (EQ-5D-5L), consisting of two parts, was included 24, 25.

4) The first part of the questionnaire includes a descriptive system with five dimensions concerning: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, including the newest version with five levels, shown to have the lowest ceiling effect 26. The five dimensions indicate perceived health status at the present day and is answered by the options: 1) no problems, 2) slight problems, 3) moderate problems, 4) severe problems, and 5) extreme problems. The Index calculator of the EuroQol research foundation was used to get a total index score of the HRQoL, ranging from one to below null 27. A score of one indicates that the respondents perceive their health at the best possible state, while a score below null indicates a state of health that is worse than death, and where null is the reference score of death. In patients with shoulder instability problems, EQ-5D-5L has been found to have satisfactory psychometrics properties 28, 29.

5) The second part in EQ-5D-5L includes the EuroQol visual analogue scale (VAS), where the respondents mark their perceived health at the present day on the VAS scale, ranging from ‘Best imaginable health state’ to ‘Worst imaginable health state’. EuroQol VAS ranges from 0-100, where a score of 100 equals the best possible health, and null equals the worst possible health.

Questions of demographics included sex, age, height and weight.

**Statistical analyses**
Outcome measures were tested for normality (Shapiro Wilk, histogram distributions), and found to be normally distributed. Descriptive statistics displaying medians with interquartile range (IQR) for continuous data and percentages with standard deviations for categorical data were used to present demographic data. Group differences in demographics on respondents with or without GJHs or KJH were tested with Wilcoxon rank-sum (Mann-Whitney U-test) for continuous data, and with Chi-square or Fisher’s exact test for categorical data.

Exposure was GJHk or KJH, with the referent category of NJH being respondents without GJHk or KJH. Outcome variables were knee joint symptoms described by 1) the presence, 2) the severity and 3) the duration of knee joint symptoms, as well as HRQoL described as 4) perceived health status at the present day cumulating five dimensions of EQ-5D-5L and 5) perceived health at the present day by VAS score.

Tests for associations of GJHk or KJH and knee joint symptoms, in addition to the first and second part of the EQ-5D-5L, were performed separately using multiple logistic and linear regression analyses for continuous and categorical outcomes, respectively, adjusting for sex and age. Statistical assumptions for performing logistic and linear regression models were fulfilled.

Sample size calculation was based on an estimated prevalence of musculoskeletal trouble in the general adult population in Denmark, corresponding to approximately 15% 30, and an estimated prevalence of musculoskeletal trouble in adults with GJH of 30% 31. The prevalence of GJH was set to a ratio of 1:6, which equals 17%. A two-sample proportion Chi-square test, with significance level of 5% and power of 80% in a two-sided test, revealed that 518 respondents were required to detect a significant difference in musculoskeletal symptoms between those with GJHk or KJH and NJH. Due to an expected response rate of 28% 12, the current survey was sent out to four times as many participants as estimated, corresponding to 2072 participants.

A p-value of 0.05 or less was considered statistically significant. All statistical analyses were conducted in STATA version 13, StataCorp. 2013.

Results

Due to 16 invalid addresses, a total of 2056 persons were invited to participate and 1006 persons responded, resulting in a response rate of 49%, of which 989 (98%) respondents filled out the entire
questionnaire (Figure 1). The total response rate was 48%, with response rates of 25% and 41% after the initial letter and first reminder, respectively. Reasons for non-participation included decline to participate, self-reported physical impairments, lack of computer or internet, incomplete data, undelivered letters, and non-responding for unknown reasons. Fourteen (1.4%) participants declined to participate, 16 (1.6%) persons were unable to participate, and 18 (1.8%) non-response letters were returned to sender. Data collection period ranged from January to June 2015.

In total of the surveyed population, 13% (130) respondents were classified as self-reported GJHk, mostly representing women (80%). KJH was reported by 23% (223), with 77% of this group being women. Those with self-reported GJHk and KJH were significantly younger than those without these conditions (Table 1). The control group consisted of 636 respondents not classified with self-reported hypermobility.

A higher proportion of respondents with GJHk (56%) and respondents with KJH (53%) reported knee joint symptoms compared to those without hypermobility (42%; Table 2). The duration of knee joint symptoms was longer for those with self-reported GJHk and KJH compared to those without hypermobility, with approximately 15% of both GJHk and KJH respondents versus 7.5% of those without either condition experiencing long-lasting symptoms for more than 90 days. Almost one third of the participants with GJHk and KJH reported knee joint symptoms to prevent them from performing usual activities at home and/or outside the home (Table 2).

The odds of having knee joint symptoms, such as pain, were twice as high for respondents with GJHk (2.03, CI:1.38-2.98) and KJH (1.98, CI:1.44-2.71) versus those without self-reported hypermobility, adjusted for sex and age (Table 3). Compared to those without self-reported hypermobility, the odds for reporting reduced activity due to knee joint symptoms were more than twice as high (2.58, CI:1.76-3.78) in respondents with self-reported KJH, and more than three times higher (3.02, CI:1.95-4.68) in respondents with self-reported GJHk than in controls (Table 3). The odds for experiencing knee joint symptoms during longer periods corresponding to more than 90 days were more than twice as high in respondents with self-reported GJHk (2.09, CI: 1.42-3.06) and almost twice as high in self-reported KJH (1.95, CI:1.43-2.67) compared to those without self-reported hypermobility (Table 3). The explained variance was low (< 5%) for all analyses.
Approximately 1% of the observed effect of was explained by age.

A negative association was found between self-reported GJHk ($\beta=-0.236$, SE=0.068, $p=0.001$) and self-reported KJH ($\beta=-0.286$, SE=0.083, $p=0.001$) and the total index score of the five dimensions regarding perceived health status at the present day. Also, a negative association was seen between self-reported GJHk ($\beta=-0.001$, SE=0.0006, $p=0.002$) and self-reported KJH ($\beta=-0.002$, SE=0.001, $p=0.003$) and the EuroQol VAS, marking the perceived health at the present day.

**Discussion**

Knee joint hypermobility was frequently reported in the current general Danish adult population, especially in women. More than half of the respondents with self-reported GJHk and KJH had knee joint symptoms. The odds were twice as high for the groups with self-reported GJHk and KJH for experiencing knee joint symptoms, being prevented from usual activities due to knee joint symptoms and having knee joint symptoms during longer periods. Respondents with self-reported GJHk and KJH reported lower HRQoL.

The prevalence of GJH is related to the sex \(^{11,13}\), which was confirmed in the current study, with overweight women reporting hypermobility, also knee joint hypermobility. The finding of the current study lies within the interval of earlier prevalence rates of 2-57% \(^{11,13}\); the large interval may be due to different settings and criteria.

To our knowledge, no previous studies have reported prevalence of self-reported GJHk or KJH in a general population. Since knee joint hypermobility was not addressed by the 5PQ, a specific question was developed. Therefore, the current prevalence represents self-reported status of GJH including KJH, and KJH solely, in a normal, adult population, adding information to the extent and impact of these conditions in the general population. In a clinical study of young adults (18-34 years) undergoing ACL reconstruction, knee joint hypermobility of the non-injured knee was clinically measured and registered frequently in both patients with ACL injury (79%, $n=133$), and also in controls without knee joint symptoms (37%, $n=24$) \(^{32}\).

Knee joint symptoms and the association with GJH and/or KJH are frequently addressed in sport-specific populations. A positive association between GJH (with or without KJH) and knee injuries

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was reported in a recent systematic review with meta-analyses, where sport participants (9-39 years) with GJH at BT $\geq$4/9 points had five times higher risk of knee injuries, especially during contact sport activities in high school, college and all levels of sport. In a prospective case-control study of 1558 female high school and collegiate soccer and basketball players, a positive measure of knee joint hyperextension increased the odds of ACL-injured status 5-fold (95% CI, 1.24–18.44). In a case-control study of ACL reconstruction in adults, ACL injuries were more frequent in patients with GJH at BT $\geq$6/9 points and knee joint hypermobility in the contralateral, uninjured knee. Similar, female soccer players (14-39 years) with GJH at BT $\geq$4/9 points had more than 5 times higher odds for injuries, primarily knee injuries, in a prospective cohort study registering injuries resulting in time-loss from practice and/or matches. Also, GJH and knee joint laxity increased the risk of ACL injuries in military cadets by 2.8 and 2.6 times, respectively. In contrast, no such associations were found between knee injuries and GJH in female, adult soccer players at BT $\geq$4/9 points in a prospective cohort study, using weekly text messages for time-loss injuries and exposure in training and matches.

Overall, there seems to be a positive association between knee joint symptoms, presented as knee injuries, and clinically measured GJHk or KJH, similar to the findings of the current study of knee joint symptoms with self-reported status of hypermobility.

In a recent systematic review with meta-analysis, higher levels of disability with respect to performance or capacity measures, were found with increasing levels of pain for groups with GJH and symptomatic GJH, often called Hypermobility Syndrome (HMS), not stratified in groups with knee joint hypermobility. Nevertheless, it seems plausible, that disability or reduced activity in individuals with GJHk and KJH, as seen in the current study, may be caused by pain in the knee. From a functional perspective, individuals with GJHk and KJH present with increased joint compression during walking and in dynamic balance tasks, reasonably caused by the decreased passive knee joint stability. Increased knee joint load, as seen with kinematic changes and in individuals with knee joint hypermobility, is associated with a higher risk of knee OA, which again is associated with reduced quality of life. Future studies should elucidate both underlying biomechanical mechanisms as well as the impact on function and quality of life in individuals with GJHk and KJH.

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Hypermobility, especially in terms of symptomatic GJH, is known to be associated with chronic pain and similarly, in a population-based survey, respondents with GJH reported significantly more chronic widespread pain (18.5%) than controls (16%)\textsuperscript{12}. Most studies are not registering region specific pain, but in a laboratory study, a significantly higher percentage of adults with GJH reported presence of knee joint symptoms such as pain and OA compared with controls \textsuperscript{17}. The latter is in line with findings of the current study, with respondents with GJHk or KJH having two times higher odds for reporting knee joint symptoms, including long-lasting pain.

To our knowledge, no previous studies have estimated overall HRQoL among individuals with GJH, but it seems reasonable to compare the current results with those of other conditions like knee OA, HMS, Ehlers-Danlos syndrome hypermobile type and rheumatoid arthritis. Similar to the present survey, individuals with knee OA, HMS and Ehlers-Danlos syndrome had lower HRQoL compared to healthy controls \textsuperscript{31, 43, 44}. However, some studies have shown that GJH was associated with anxiety/depression \textsuperscript{45} and lower functional capacity \textsuperscript{46}, which is comparable with the anxiety/depression and usual activity dimensions in EQ-5D. Similarly, one study found that individuals with GJHk reported lower knee-related quality of life \textsuperscript{17}, but no studies have estimated overall HRQoL in this group.

Moreover, individuals with rheumatoid arthritis reported a EuroQol Index score of 0.721 \textsuperscript{47}, which is similar to current values for the group of GJHk (score of 0.80). This finding is noteworthy, since rheumatoid arthritis is considered a serious long-term disease with dominant joint pain and poor outcomes \textsuperscript{48}. This indicates that GJHk may affect the HRQoL similar to more recognized musculoskeletal conditions.

The strengths of the current study are the large sample size, the high response rate as well as the random selection of respondents. The random selection minimizes selection bias, although no drop out analysis was performed. Equally, errors during data collection process are diminished by use of electronic data collection. According to Statistics Denmark, 92% of the Danish population have access to the internet and 87% are online every day, why this sample is likely to representative of general population \textsuperscript{49}. Furthermore, information bias was minimized by using predominantly validated and reliable questionnaires.
One of the limitations of the current study is that recall bias may be introduced by the recall period (ever) in the 5PQ, because those with current joint problems or poorer HRQoL may be more inclined to recall past joint problems, like hypermobility, than those without these conditions; the size of this recall bias is not known. Moreover, differential misclassification of individuals with GJHk or KJH may occur due to the non-validated question to identify knee hypermobility, however, the magnitude of this bias also is unknown.

Generally, cross-sectional design is limited in providing evidence of the temporal relationship between exposure and outcomes, while causal relationships are better tested in prospective cohort studies, however, they are often time consuming and expensive. Therefore, data from the current population may also include and reflect knee joint status in sport participants with knee joint laxity due to previous ACL injury, but no information of previous knee injury, sport participation or level of physical activity was collected. The association of knee joint laxity and knee joint hypermobility is still not known.

Conclusion
Self-reported knee joint hypermobility with or without Generalized joint hypermobility is common among the general, Danish adult population with a prevalence of 13% and 23%, respectively. Respondents with self-reported GJHk and KJH were two times more likely to report knee joint related symptoms such as pain and reduced performance of usual activity. Both self-reported GJHk and KJH were associated with lower HRQoL, and the impact of these conditions on HRQoL is comparable with those having knee OA.

References


Figure legends

Figure 1. Flowchart of inclusion and exclusion of respondents

Knee hypermobility affects women
Figure 1

Sample size
\( n = 2072 \)

Not included in the study due to invalid addresses
\( n = 16 \)

Subjects invited
\( n = 2056 (100\%) \)

No internet, PC or laptop \( n = 1 \)
Unable to participate due to PH \( n = 1 \)
Declined to participate \( n = 1 \)

Respondents before reminder 1
\( n = 510 (25\%) \)

No internet, PC or laptop \( n = 7 \)
Unable to participate due to PH \( n = 2 \)
Declined to participate \( n = 7 \)
Returned letters \( n = 9 \)

Reminder 1
\( n = 1543 \)

Respondents before reminder 2
\( n = 845 (41\%) \)

No internet, PC or laptop \( n = 3 \)
Unable to participate due to PH \( n = 2 \)
Declined to participate \( n = 6 \)
Returned letters \( n = 9 \)

Reminder 2
\( n = 1183 \)

Total number of respondents
\( n = 1006 (49\%) \)

Incomplete dataset
\( n = 17 \)

Complete dataset
\( n = 989 (48\%) \)

Categorised as GJHk
\( n = 130 (13\%) \)

Categorised as KJH
\( n = 223 (23\%) \)

Categorised as NJH
\( n = 636 (64\%) \)

PH= physical health (contacted by partner or the court due to; severe Alzheimer, death, brain cancer and cerebral palsy)
GJHk = Generalised Joint Hypermobility including knee joint hypermobility
KJH= Knee Joint Hypermobility
NJH= Not Joint Hypermobile
Table 1. Demographics of respondents not being joint hypermobile (NJH), respondents with Generalised Joint Hypermobility including knee hypermobility (GJHk) and respondents with Knee Joint Hypermobility (KJH). Group differences between NJH and GJHk, and NJH and KJH are illustrated by the p-values.

<table>
<thead>
<tr>
<th></th>
<th>All (n=989)</th>
<th>NJH (n=636)</th>
<th>GJHk (n=130)</th>
<th>p-value</th>
<th>KJH (n=223)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women, % (no.)</td>
<td>56 (565)</td>
<td>50 (393)</td>
<td>80 (104)</td>
<td>&lt;0.001*</td>
<td>77 (172)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Age, (years) Mean (SD)</td>
<td>48 (10.7)</td>
<td>48.5 (10.6)</td>
<td>46 (11.2)</td>
<td>0.02*</td>
<td>46.2 (11.2)</td>
<td>0.003*</td>
</tr>
<tr>
<td>BMI, (Kg/m²) Mean (SD)</td>
<td>26.2 (7.2)</td>
<td>26.3 (7.8)</td>
<td>25.6 (4.6)</td>
<td>0.33</td>
<td>25.7 (4.5)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

*Indicates a p-value <0.05.
Table 2. Self-reported knee joint symptoms, severity and duration in respondents not being joint hypermobile (NJH), respondents with Generalised Joint Hypermobility including knee hypermobility (GJHk) and respondents with Knee Joint Hypermobility (KJH). Group differences between NJH and GJHk, and NJH and KJH are illustrated by the p-values.

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<th>p-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee joint symptoms % (no.)</td>
<td>42 (419)</td>
<td>47 (300)</td>
<td>56.1 (73)</td>
<td>53.3 (119)</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Severity of knee joint symptoms % (no.)</td>
<td>16.7 (165)</td>
<td>16.6 (106)</td>
<td>30.7 (40)</td>
<td>26.4 (59)</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Duration of knee joint symptoms % (no.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-30 days</td>
<td>25.0 (252)</td>
<td>24.0 (186)</td>
<td>29.2 (38)</td>
<td>29.6 (66)</td>
<td>0.03*</td>
<td>0.002*</td>
</tr>
<tr>
<td>31-90 days</td>
<td>7.4 (75)</td>
<td>7.1 (55)</td>
<td>10.7 (14)</td>
<td>9.1 (20)</td>
<td>0.05*</td>
<td>0.09</td>
</tr>
<tr>
<td>&gt;90 days</td>
<td>9.1 (92)</td>
<td>7.5 (59)</td>
<td>16.1 (21)</td>
<td>14.8 (33)</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*Indicates a p-value <0.05.