Impact of self-reported comorbidity on physical and mental health status in early symptomatic osteoarthritis: the CHECK (Cohort Hip and Cohort Knee) study

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Abstract

Objective. To describe the relationship between comorbidity (absolute number as well as the presence of specific comorbidities) and pain, physical functioning and mental health status of participants with early symptomatic OA of the hip or knee.

Methods. In the Netherlands, a prospective 10-year follow-up study was initiated by the Dutch Arthritis Association in participants with early symptomatic OA of the hip or knee: CHECK (Cohort Hip and Cohort Knee), which consists of 1002 individuals. At baseline, linear regression analysis was used to determine the influence of comorbidity on the outcome variables: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain, WOMAC physical functioning, Medical Outcomes Study Short Form 36 (SF-36) Physical Component Summary and Mental Component Summary.

Results. Of 979 subjects, 67% reported one or more comorbidities. After controlling for age, gender, social status and severity of radiographic OA (Kellgren and Lawrence score), back disorders have the largest effect on WOMAC pain and physical functioning, and one of the largest effects on physical status of SF-36, besides obesity. Mental status was negatively influenced by the additional presence of duodenal ulcer, thyroid disease, and migraine or chronic headache.

Conclusion. In early stage of OA, the presence of additional problems in the musculoskeletal system and of obesity have a negative effect on pain and physical health status. Also mental status is affected in early symptomatic OA by the presence of specific comorbidities. Comorbidity should be assessed and treated to improve the burden of illness in patients with early symptomatic OA.

Key words: early symptomatic osteoarthritis, comorbidity, pain, physical functioning, mental health status.

Introduction

OA is the most common diagnosis made in elderly patients with knee or hip pain. The prevalence of many other disabling conditions increases with age and (with increasing age) many chronic conditions occur together with OA [1, 2]. OA has a very high rate of comorbidities [1, 3] and patients with OA are significantly more likely to have comorbidity than non-OA patients [4]. In a large representative network of general practices, the Netherlands Information Network of General Practice (LINH), 75% of the OA patients aged ≥ 55 years had one or more comorbidity diseases. Twenty-seven per cent of these patients had
chronic disorders of the neck or back [5]. Combinations of back disorders with OA and hypertension with OA are most reported in absolute values [6, 7]. The consequences of combinations of specific diseases and OA are diverse and not very well known. Previous research in OA patients [1, 8–10] has shown that the number of (co)comorbidities (comorbidity count) is associated with limitations in activities and perceived health. Although the majority of studies on comorbidity have focused on comorbidity count only, it was found that specific (combinations of) chronic diseases have a different influence on physical functioning [8, 9, 11–13]. With regard to mental functioning, it is reported that mental health deteriorates less than physical health with increasing comorbidity and remains relatively high and stable [12, 13]. Other disease characteristics, such as illness duration and disease stage or activity, may be more important for mental health than the type or number of comorbidities [11]. None of the former studies assessed the impact of the presence of specific diseases and complaints of patients in the early stage of OA.

Studying comorbidity in this early phase of OA is important because it influences the burden of illness of OA. Health gain can be achieved by prevention or early recognition and adequate treatment of comorbid diseases, especially in the early stage of OA. Therefore it is necessary to further increase our knowledge of comorbidity in patients with early symptomatic OA. This might enable us to define strategies to prevent a further negative effect on the symptoms of OA. The objective of the present report is to describe the relationship of comorbidity (absolute number as well as the presence of specific comorbidities) with pain, physical and mental health status of participants with early symptomatic OA of knee or hip.

Methods

Study design

For the current cross-sectional evaluation, baseline data of the CHECK (Cohort Hip and Cohort Knee) study were used. The CHECK study is a Dutch prospective 10-year follow-up study, initiated by the Dutch Arthritis Association, to study progression of OA in participants with early symptomatic OA of knee or hip. This multicentre study (10 centres across the Netherlands) was approved by the medical ethical committees of all participating centres, and all participants gave their written informed consent before entering the study. Participants were recruited by general practitioners and through advertisements, articles in local newspapers and on the website. A complete description of the CHECK study has been reported elsewhere [14].

Study population

Individuals were eligible if they had pain or stiffness of the knee or hip, were aged 45–65 years and had not yet consulted their physician for these symptoms, or the first consultation was within 6 months of entry [14]. Exclusion criteria were any non-OA condition that could explain the existing complaints (e.g. other rheumatic disease, previous hip or knee joint replacement, congenital dysplasia, osteochondritis dissecans, IA fractures, septic arthritis, Perthes’ disease, ligament or meniscus damage, plica syndrome, Baker’s cyst). The physicians assessed by protocol a physical examination to exclude any non-OA condition.

Outcome variables

Pain and physical functioning were measured using two subscales of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which is a disease-specific self-report questionnaire with subscales ranging from 0 to 100 and higher scores indicating worse health [15, 16]. The 5-point Likert version of the WOMAC was used. Besides mental health status, physical status (physical functioning) is also measured with the Medical Outcomes Study Short Form 36 (SF-36). This is a generic instrument with eight scales and two summary scores (scales range from 0 to 100, with higher scores indicating a better health status), the Physical Component Summary (PCS) and the Mental Component Summary (MCS) [17]. Country-specific scores have been established to interpret scale scores. Normative data came from a sample from the general Dutch population, aged 18–74 years, mean PCS 49.7 (s.D. 9.3) and mean MCS 52.1 (s.D. 9.6) [18]. Generic and disease-specific instruments measure different dimensions of health status, and the use of both in quality of life studies has been recommended. However, the SF-36 has a higher correlation with comorbidities than the WOMAC [19]. To gain general insight into a patient’s health, and in particular when comorbidity is common, the SF-36 should also be used [19].

Independent variables

Comorbidity has been defined as the existence or occurrence of any distinct additional entity during the clinical course of a patient who has the index disease under study [20, 21]. In the present study, comorbidity is assessed with a self-reported health module of the Central Bureau of Statistics (CBS) in the Netherlands which encompasses 24 chronic diseases [22]. The participants are asked: do you have any other chronic disease or disorder besides your knee or hip complaints? If the participants answer yes, they are asked: would you please mark, if you have or have had in the last 12 months the next disease or disorder? Along with this, height and weight were determined to calculate BMI. Obesity, defined as a BMI ≥30 kg/m², was added as a separate comorbidity. Individual comorbidities were scored and the total number of comorbidities was calculated per participant (comorbidity count).

To assess radiographic OA features, weight-bearing radiographs of the tibio-femoral joint were made in the posterioranterior view with semi-flexed (7–10°) knee, according to Buckland-Wright [23–25]. For the hip, weight-bearing antero-posterior radiographs of the pelvis were made [26, 27]. Radiographs of the posterior-anterior tibio-femoral joint and antero-posterior pelvic
views were scored according to Kellgren and Lawrence [28]. The severity of radiographic OA was defined as the maximum Kellgren and Lawrence (K&L) score assessed in one of the four joints (hips and knees).

Statistical analyses
Baseline characteristics of the total CHECK population and separately for participants with and without comorbidity are presented using descriptive statistics: mean and s.d. or frequency and proportions. Differences in baseline characteristics between participants with and without comorbidity were compared by χ²-tests for dichotomous variables and t-tests for continuous variables.

Linear regression analysis was used to determine the relationship between comorbidity count and outcome variables: WOMAC pain score, WOMAC physical functioning score, SF-36 PCS and SF-36 MCS. All regression models were adjusted for age, gender, social status and severity of radiographic OA.

To analyse the relationship between specific comorbidities and outcome variables, first a univariate regression analysis was performed. For this analysis only those diseases or disorders with a frequency in the CHECK population of >5% or diseases or disorders that were thought to have a large influence on outcome were used. Next, the diseases that had a statistically significant association (P < 0.05) with the outcome in the univariate analyses were all simultaneously added in a linear regression model, after it was checked if two or more diseases were highly correlated (collinearity). If specific diseases were no longer statistically significantly associated with the outcome and/or did not add to the explained variance (R²), they were removed from the model one by one to arrive at a final model. The sample size justifies having a P-value cut-off point of 5% [29]. SPSS version 15 was used for all analyses and P < 0.05 was considered to be statistically significant.

Results
Study population
At baseline 1002 participants were included. For 979 participants, data on comorbidity were present, and these participants were used in the present analysis. Participants with and without complete data on comorbidity did not differ on demographic and clinical variables. The characteristics of the participants of CHECK are presented in Table 1. More than 67% of the total study population reported one or more comorbidity. Disorders of the neck, shoulder, elbow, wrist or hand (23%), hypertension (20%) and back disorders (18%) were most prevalent (Table 2). Remarkably, physical examination of the musculoskeletal system did not show any clear abnormalities underlying self-reported rheumatic diseases. As shown in Table 1, there was a significant difference in WOMAC pain, WOMAC physical functioning, SF-36 PCS and SF-36 MCS between participants with and without comorbidities (all P < 0.001).

Impact of comorbidity count
Figure 1 shows that with an increasing number of comorbidities pain as well as physical functioning deteriorates. Health status (Fig. 2) also deteriorates with an increasing number of comorbidities. Table 3 reports the results of the linear regression analyses with WOMAC pain, WOMAC physical functioning, SF-36 PCS and SF-36 MCS as outcome variables. After controlling for age, gender, social status and K&L score, there was a significant association of the number of comorbidities with the pain and physical function subscales of WOMAC, and PCS and MCS of SF-36. The pain score and physical function score on the WOMAC deteriorate by about 3 and 4 points, respectively, with every (extra) comorbidity: the physical and mental components of the SF-36 deteriorate by about 2 and 1 point, respectively, with every (extra) comorbidity.

Impact of specific comorbidities
Based on results of univariate analyses (Table 4), we selected these items for further analyses in the regression model. The regression model of specific comorbidities (Table 3; controlling for age, gender, social status, K&L score) indicates that back disorders have the greatest effect on WOMAC pain and physical functioning scores and one of the largest effects on physical status of SF-36, besides obesity and neck and upper extremity disorders. The presence of back disorders increases the WOMAC pain score on average by about 7 points, the WOMAC function score by 8 points and the SF-36 PCS score by 4 points. Obesity and the presence of disorders of the neck, shoulder, elbow, wrist and hand also independently negatively associate with scores of pain and physical functioning. Diabetes only negatively associates with physical functioning, not with pain. These diseases do not associate with the mental health status of participants. The mental health status was, however, negatively associated with less frequently occurring duodenal ulcer, thyroid disease and migraine or chronic headache.

Discussion
The objective of the present study was to describe the relationship between comorbidity, pain and the physical and mental health status of participants with early symptomatic OA.

More than 67% of participants suffered from at least one comorbid disease, with disorders of the neck, shoulder, elbow, wrist or hand, hypertension and back disorders being most prevalent. Comparing different studies on self-reported comorbidity different prevalence can be found. These differences can be explained by defining the inclusion and exclusion of diseases in the assessment of comorbidity lists used in individual studies and by differences in the population of interest. Generally the higher the number of possible diseases included in a study, the higher the frequency of comorbidities found [20]. This is apparent for instance in an OA study in which almost all patients (98.6%) suffered from one or more coexistent diseases. In this study, the Cumulative
Illness Rating Scale was used, which consists of 13 domains (organ systems) related to different body systems, also including the presence of diseases of the ear, eye, nose and larynx [8]. In another study, the prevalence of comorbidity in subjects with arthritis (RA or OA) was 44.8%. This study used a list of seven specific chronic diseases: chronic non-specific lung disease, cardiac disease, peripheral atherosclerosis, stroke, diabetes mellitus, malignancies and arthritis (RA or OA) [9]. When comparing the frequency of self-reported comorbidities of the present study with the prevalence of chronic diseases in an age-matched sample of the Dutch population, almost the same frequencies are found [7].

Before studying the impact of specific disease conditions, we first assessed the impact of the number of coexisting diseases (i.e unspecified comorbidity, comorbidity count) in early OA on pain, physical and mental functioning. Participants with more comorbidities reported worse pain, more problems in physical functioning and a worse mental health status as compared with participants without comorbidity. These results confirm earlier research in patients with more advanced OA in which comorbidity was associated with pain, limitations in activities and a poorer physical health status [1, 8].

The influence of specific chronic diseases was assessed by means of linear regression analyses. After adjusting for age, gender and radiographic severity of OA, the presence of disorders of the back, neck, shoulder, wrist or hand or obesity negatively associate with pain and physical functioning. The results were identical when using summed K&L grades instead of the maximum K&L grade. There are possible mechanisms that can explain the influence of the presence of specific comorbidity. Probably, in participants with early OA, coexistent disorders in the musculoskeletal system will aggravate pain and physical functioning, whereas diseases present in the cardiovascular system or pulmonary system will probably not (yet) influence these outcomes. In this concept, obesity is seen as a mechanical loading factor and an inflammatory environment response that also will have a negative influence on the musculoskeletal system. Adipose tissue is now recognized as an organ with the capacity to secrete adipocytokines. These adipocytokines may play an important role in cartilage homeostasis and in

| Characteristic | CHECK all | Early OA without comorbidity | Early OA with comorbidity | P |
|---------------|-----------|-----------------------------|---------------------------|---|
| n             | 979       | 321                         | 658                       |   |
| Age, mean (s.o.), years | 56 (5) | 56 (5) | 56 (5) | 0.961 |
| Female gender, % | 79       | 73                      | 82                      | -0.001 |
| BMI, mean (s.o.), kg/m² | 26 (4) | 25 (2) | 27 (5) | -0.001 |
| Education level, % | 3       | 2                      | 3                      |   |
| Primary school | 70       | 67                      | 72                      | 0.073 |
| Secondary school | 27      | 31                      | 25                      |   |
| High professional education/university | 56 | 56 | 54 |   |
| K&L grade, % | 55       | 33                      | 37                      | 0.190 |
| Grade 0       | 55       | 56                      | 54                      |   |
| Grade 1       | 33       | 29                      | 35                      |   |
| Grade 2       | 11       | 13                      | 10                      |   |
| Grade 3       | 1        | 2                       | 1                       |   |
| WOMAC subscales (range 0–100) | 25.3 (17.1) | 20.8 (15.2) | 27.5 (17.6) | -0.001 |
| Pain, mean (s.o.) | 23.5 (17.1) | 18.5 (15.0) | 26.0 (7.6) | -0.001 |
| Physical function, mean (s.o.) | 45.6 (7.9) | 48.2 (6.6) | 44.4 (8.2) | -0.001 |
| SF-36 subscales (range 0–100), mean (s.o.) | 53.0 (8.6) | 54.4 (7.1) | 52.4 (9.2) | -0.001 |
| PCS            | 53.0 (8.6) | 54.4 (7.1) | 52.4 (9.2) | -0.001 |
| MCS            | 53.0 (8.6) | 54.4 (7.1) | 52.4 (9.2) | -0.001 |
| Comorbidity counts (n=979), n (%) |                       | NA                      | NA                      | NA |
| 0              | 321 (32.8) | NA                      | NA                      | NA |
| 1              | 295 (30.1) | NA                      | NA                      | NA |
| 2              | 188 (19.2) | NA                      | NA                      | NA |
| 3              | 105 (10.7) | NA                      | NA                      | NA |
| 4              | 42 (4.3)   | NA                      | NA                      | NA |
| 5              | 18 (1.8)   | NA                      | NA                      | NA |
| 6              | 7 (0.7)    | NA                      | NA                      | NA |
| 7              | 3 (0.3)    | NA                      | NA                      | NA |

Values are mean (s.o.), except for categorical variables, which are presented as n (%); P-value: χ²-tests for dichotomous variables and t-tests for continuous variables. K&L grade is maximum K&L score of the four joints assessed; WOMAC, with higher score indicating worse health; SF-36 health status survey questionnaire, with higher score indicating a better health status; NA: not applicable.
the modulation of inflammatory processes. However, there is little to support a role of these cytokines in relation to pain [30, 31].

An explanation for the higher pain scores and physical function scores of painful comorbidities in the musculoskeletal system could be the role of central sensitization, suggesting that more than just the receptor area for the painful joint is involved in nociception [31, 32]. Croft et al. [33] also give this explanation for their findings that knee-specific pain and disability, measured with WOMAC, are worse in the presence of pains elsewhere than the knee. Probably the avoidance model, which explains the association between pain, avoidance of activities, muscle strength and activity limitations in participants with early OA, will be reinforced by these painful comorbidities [34]. Other OA studies also showed that low-back pain influences a worsening in WOMAC physical functioning [35, 36]. Back pain can in part be explained by a change in mechanical loading caused by the painful hip or knee joint.

Another explanation for the influence of comorbidity that is described in the literature, but not confirmed in this study, could be that specific combinations of chronic diseases that both influence physical functioning, but through a different mechanism (such as musculoskeletal system and decreased endurance capacity), are perhaps more detrimental than other types of combinations. An

### Table 2

| Comorbidity                                                                 | Prevalence, n (%) |
|----------------------------------------------------------------------------|-------------------|
| Disorders of neck, shoulder, elbow, wrist or handa                          | 222 (22.2)        |
| Hypertensiona                                                               | 198 (19.8)        |
| Back disorders (including slipped disc)a                                    | 172 (17.2)        |
| Obesitya                                                                    | 161 (16.1)        |
| Migraine or chronic headachea                                               | 124 (12.4)        |
| Asthma, chronic bronchitis, pulmonary emphysema or chronic non-specific lung diseasea | 90 (9.1)          |
| Pharyngitis, sinusitis                                                      | 91 (9.0)          |
| Thyroid diseasea                                                            | 53 (5.3)          |
| Prolapsed uterus                                                           | 42 (4.2)          |
| Chronic inflammation of joints (such as RA)                                | 37 (3.7)          |
| Diabetes mellitusa                                                          | 35 (3.5)          |
| Other chronic rheumatic diseases, longer than 3 months                      | 29 (2.9)          |
| Cholelithiasis                                                             | 18 (1.8)          |
| Dizziness with falls                                                        | 17 (1.7)          |
| Chronic urolithiasis                                                       | 16 (1.6)          |
| Peptic ulcer or duodenal ulcera                                             | 14 (1.4)          |
| Severe heart disease or myocardial infarction/strokea                       | 14 (1.4)          |
| Skin disease                                                                | 13 (1.3)          |
| Other, e.g. ear problems, eye problems, bowel disorders, psychological disorders | 276 (27.5)       |

*Comorbidities were used to build the final regression model (Table 3).*
example of such a combination includes arthritis (RA or OA) and cardiac disease; suggested mechanisms are chronic inflammation, but also the use of medication [8, 9, 11]. Initially, in the first analysis, the influence of cardiac diseases was not assessed because of the low prevalence in this population as a consequence of the low mean age (57 years), but when we added this disorder to the final multivariate model, cardiac disease was not associated with any of the outcomes (data not shown). This corresponds with another study, which concluded that there was no significant relationship between cardiac diseases and pain, and limitation in activity [37] in patients with OA. The conflicting results on coexisting disorders in body systems other than the musculoskeletal system in established OA makes it important to test the influence of these disorders in the prospective follow-up of these CHECK participants with very early disease.

We also analysed the influence of comorbidity count and specific diseases on mental functioning; duodenal ulcer, thyroid disease and migraine or chronic headache negatively influenced mental functioning. Contrary to previous research, which shows that mental functioning in patients with arthritis is not influenced by the presence of comorbidity [11], this study suggests that mental health is vulnerable to comorbidities outside the musculoskeletal system during the early stages of the disease.

In the present study, mental health also deteriorated less than physical health with an additional disease. These findings led to the conclusion that among patients with early OA with comorbidity, the focus of the physician should be not only on OA, but also on worsening pain and physical and mental health status due to a second disease. Significant health gain can be achieved by prevention or early recognition and adequate treatment of comorbid diseases [38].

Some limitations of our study should be mentioned before drawing final conclusions. Data on comorbidity and health status were based on subject self-reports, which might be influenced by personal or mood characteristics. Nevertheless, positive correlations have been found between self-reported comorbidity measures and comorbidity from medical record reviews [39].

Second, our study focused on the impact of specific prevalent chronic diseases without taking disease stage and the severity of these diseases into account. Third, the health module of the CBS used in this study did not include psychiatric disorders. Among older adults with OA, the prevalence of depressive symptoms is high and these symptoms may result in limitations in activity and increased pain [40]. The mental health scale of the SF-36 has been shown to be useful in detecting major depression, affective disorders generally, and anxiety disorders [41]. However, after adjusting the final model with pain and functioning as outcomes for mental health, the same results were found. The beta coefficient of the mental health scale was not statistically significant and the explained variance of the outcome variables pain, function and PCS did not change.

Fourth, although significant associations were found, comorbidity count and specific disorders accounted for a small part of the variation in the outcome variables pain, physical functioning and mental health status. The explained variance ranged from 0.03 to 0.013 for comorbidity count and from 0.03 to 0.14 for the coexistence of specific comorbidities in the models with different outcomes. Statistically significant increases in WOMAC pain

SF-36 health status survey questionnaire, with higher score indicating a better health status. PF: physical function; RP: physical role; BP: bodily pain; VT: vitality; SF: social function; RE: emotional role; MH: mental health.

**Fig. 2** Mean SF-36 subscales scores (0–100) in participants with 0, 1, 2, 3 and ≥4 comorbidities.
### Table 3 Results of linear regression model with pain, physical and mental health status as outcome

| Variable                              | B      | P       | 95% CI       | R²   |
|----------------------------------------|--------|---------|--------------|------|
| WOMAC pain                             |        |         |              |      |
| Comorbidity count                      | 2.8    | <0.001  | 2.0, 3.8     | 0.10 |
| Model-specific comorbidities           |        |         |              |      |
| Back disorders (including slipped disc)| 7.4    | <0.001  | 4.7, 10.2    | 0.10 |
| Disorders of neck, shoulder, elbow, wrist or hand | 4.0    | 0.002   | 1.5, 6.6     |      |
| Obesity                                | 4.4    | <0.001  | 1.5, 7.2     |      |
| Adjusted variables                     |        |         |              | 0.05 |
| WOMAC function                         |        |         |              |      |
| Comorbidity count                      | 3.5    | <0.001  | 2.7, 4.2     | 0.13 |
| Model-specific comorbidities           |        |         |              |      |
| Back disorders (including slipped disc)| 7.9    | <0.001  | 5.2, 10.7    | 0.13 |
| Disorders of neck, shoulder, elbow, wrist or hand | 4.4    | 0.001   | 1.9, 6.9     |      |
| Obesity                                | 5.3    | <0.001  | 2.5, 8.1     |      |
| Diabetes mellitus                      | 6.9    | 0.018   | 1.2, 12.5    |      |
| Adjusted variables                     |        |         |              | 0.06 |
| SF-36 PCS                               |        |         |              |      |
| Comorbidity count                      | −1.7   | <0.001  | −2.1, −1.3   | 0.12 |
| Model-specific comorbidities           |        |         |              |      |
| Disorders of neck, shoulder, elbow, wrist or hand | −3.9   | <0.001  | −5.0, −2.7   | 0.15 |
| Back disorders (including slipped disc)| −3.7   | <0.001  | −5.0, −2.5   |      |
| Obesity                                | −2.9   | <0.001  | −4.2, −1.6   |      |
| Diabetes mellitus                      | −2.8   | 0.039   | −5.4, −0.1   |      |
| Adjusted variables                     |        |         |              | 0.04 |
| SF-36 MCS                               |        |         |              |      |
| Comorbidity count                      | −0.8   | <0.001  | −1.2, −0.39  | 0.04 |
| Model-specific comorbidities           |        |         |              |      |
| Duodenal ulcer                         | −5.8   | 0.011   | −10.3, −1.3  | 0.04 |
| Thyroid disease                        | −3.4   | 0.007   | −5.8, −0.9   |      |
| Migraine or chronic headache           | −2.2   | 0.009   | −3.8, −0.5   |      |
| Adjusted variables                     |        |         |              | 0.02 |

Regression coefficients (B) are presented. All models are adjusted for age, gender, social status and K&L score. Adjusted variables: model with adjusted variables only; R²: explained variance. For WOMAC, a higher score implies a worse health status. For SF-36, a higher score implies better health status.

### Table 4 Results of univariate analyses with pain, physical and mental health status as outcome

|                                  | WOMAC pain | WOMAC function | SF-36 PCS | SF-36 MCS |
|----------------------------------|------------|----------------|-----------|-----------|
|                                  | B          | B              | B         | B         |
| Disorders of neck, shoulder, elbow, wrist or hand | 5.4*       | 6.1*           | −4.4*     | −0.2      |
| Hypertension                     | 2.9*       | 3.7*           | −0.98     | −1.4*     |
| Back disorders (including slipped disc) | 8.1*       | 8.6*           | −4.6*     | 0.006     |
| Obesity                          | 6.0*       | 7.2*           | −3.4*     | −0.2      |
| Migraine or chronic headache     | 3.6*       | 5.1*           | −1.0      | −2.9*     |
| Asthma, chronic bronchitis, pulmonary emphysema or chronic non-specific lung disease | 4.4*       | 3.0            | −2.6*     | −1.4      |
| Pharyngitis, sinusitis           | 4.1*       | 5.3*           | −2.6*     | −1.4      |
| Thyroid disease                  | 3.7        | 4.8*           | −2.6*     | −3.5*     |
| Diabetes mellitus                | 4.9        | 9.5*           | −4.3*     | −1.0      |
| Peptic ulcer or duodenal ulcer   | 3.2*       | 8.7            | −2.0      | −6.0*     |
| Severe heart disease or myocardial infarction/stroke | 1.9        | 3.2            | −4.8*     | 0.6       |

Regression coefficients (B) are presented. For WOMAC, a higher score implies a worse health status. For SF-36, a higher score implies better health status. *P < 0.05.
and physical function by comorbidity count or the presence of specific comorbidity are small; for pain, 3 points for comorbidity and 4–7 points for specific comorbidity; and for function, 4 points for comorbidity and 4–8 points for specific comorbidity. These are meaningful differences in this stage of the disease. In the early stage of the disease, small differences are expected that might develop into greater differences in the course of the disease. Fifth, although a significant association between mental health and comorbidity was found, the mean score on the MCS in the present study is >52.1, indicating that mental functioning was almost comparable to the general Dutch population (with a mean age of 47.6 years). Mental summary scores generally increased slightly with age [42].

In conclusion, in the early stage of symptomatic OA, especially (other) disorders in the musculoskeletal system have a negative effect on pain, physical functioning and mental health status. The clinical implications are that to improve the pain and physical health status of participants with early symptomatic OA, not only these complaints have to be treated, but also the additional conditions, especially back, neck, shoulder, elbow, wrist or hand disorders and obesity. Also, mental status can be affected in the early stage of OA by additional comorbidities, especially by the presence of duodenal ulcer, thyroid disease, and migraine or chronic headache. This is a further argument to take comorbidity into account in the management of early OA.

Funding: This study was financially supported by the Dutch Arthritis Association.

Disclosure statement: The authors have declared no conflicts of interest.

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Acknowledgements
The CHECK cohort study was initiated and performed by the Dutch Arthritis Association; Erasmus Medical Center Rotterdam; Kennemer Gasthuis Haarlem; Leiden University Medical Center; Maastricht University Medical Center; Martini Hospital Groningen/Allied Health Care Center for Rheumatology and Rehabilitation Groningen; Medical Spectrum Twente Enschede/Ziekenhuisgroep Twente Almelo; Reade, formerly Jan van Breemen Institute/VU Medical Center Amsterdam; St. Maarten’skliniek Nijmegen; University Medical Center Utrecht and Wilhelmina Hospital Assen.

J.W., P.M.J.W., S.M.A.B.-Z., J.D., J.W.J.B. contributed to the conception and design of this study. J.W. contributed to the analysis of data. P.M.J.W., J.D., K.J.G., M.K., L.D.R. and J.W.J.B. contributed to the interpretation of data. Article drafts were written by J.W. and critically revised by all the authors. The final version of the article was approved by all the authors. J.W. takes responsibility for the integrity of the work as a whole (j.wesseling@umcutrecht.nl).

Rheumatology key messages
- In early OA, additional musculoskeletal diseases have a negative effect on pain and physical functioning.
- Comorbidity should be assessed and treated to improve the burden of illness in early OA.
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