Reference curves for the Australian/Canadian Hand Osteoarthritis Index (AUSCAN) in the middle-aged Dutch population

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ABSTRACT

Objectives. To establish reference curves of the Australian/Canadian Hand Osteoarthritis Index (AUSCAN), a widely used questionnaire assessing hand complaints.

Methods. Analyses were performed in a population-based sample, the Netherlands Epidemiology of Obesity study (n=6,671, aged 45-65 years). Factors associated with AUSCAN scores were analysed with ordered logistic regression, since AUSCAN data were zero-inflated, dividing AUSCAN into three categories (0 vs. 1-5 vs. >5). Age- and sex-specific reference curves for the AUSCAN (range 0-60, higher is worse) were developed using quantile regression in conjunction with fractional polynomials. Observed scores in relevant subgroups were compared to the reference curves.

Results. Median age was 56 (interquartile range (IQR) 50-61), 56% were women and 12% had hand osteoarthritis according to American College of Rheumatology criteria. AUSCAN scores were low (median 1, IQR 0-4). Reference curves where higher for women, and moderately increased with age: 95% percentiles for AUSCAN in men and women were respectively 5.0 and 12.3 points for a 45-year-old, and 15.2 and 33.6 points for a 65-year-old individual. Additional associated factors included hand osteoarthritis, inflammatory rheumatic diseases, fibromyalgia, socio-economic status, and BMI. Median AUSCAN pain subscale scores of women with hand osteoarthritis lay between the 75th and 90th centiles of the general population.

Conclusions. AUSCAN scores in the middle-aged Dutch population were overall low and higher in women than in men. AUSCAN reference curves could serve as benchmark in research and clinical practice settings. However, the AUSCAN does not measure hand complaints specific for hand osteoarthritis.

Keywords: Hand osteoarthritis, outcomes research, epidemiology

KEY MESSAGES

- Australian/Canadian Hand Osteoarthritis Index age- and sex-specific reference curves in a middle-aged population are presented.
- Presented Australian/Canadian Hand Osteoarthritis Index reference curves could serve as benchmark in research and clinical practice.

INTRODUCTION

Hand complaints are frequent in the general population[1]. Hand osteoarthritis (OA) is a common cause of hand complaints such as pain and functional disability[2]. Current treatment strategies for hand OA aim to alleviate symptoms, although their efficacy is limited[3]. Clinical trials aiming for disease modification have been conducted recently, or are still on-going[3].

Assessment of patient-reported outcomes is important to evaluate treatment. The Australian/Canadian Hand Osteoarthritis Index (AUSCAN) is a widely used instrument, recognised by both Osteoarthritis Research Society International (OARSI) and Outcome Measures in Rheumatology Clinical Trials (OMERACT) as a valid and reliable outcome in clinical trials for hand OA[4-6]. The interpretation of patient-reported outcomes like the AUSCAN however, depends on the availability of benchmarks, such as the patient acceptable symptom state (PASS). Recently, a PASS for the AUSCAN was established in a multinational sample of patients with OA[7]. A disadvantage of the PASS is that it is a cut-off value, which is not adjusted for age and sex. Population-based normative values can also serve as benchmarks. Previously, age- and sex-specific normative values for the AUSCAN were developed in an Australian population-based cohort[8]. Limitations of this study, however, were the limited availability of information on other characteristics of the studied population, and the definition of normative values solely based on descriptive analysis of observed scores.

The objective of this study was to investigate factors associated with AUSCAN scores in the middle-aged Dutch population, such as sex, body mass index (BMI), socio-economic status (SES), and presence of hand OA or other (inflammatory) rheumatic diseases, and to establish reference curves for the AUSCAN taking associated factors in account.

METHODS

Study design and study population

The Netherlands Epidemiology of Obesity (NEO) study is a population-based cohort. Detailed information about study design and data collection are described elsewhere[9]. Men and women aged between 45 and 65 years with a self-reported BMI ≥27 kg/m^2 living in the greater area of Leiden (The Netherlands) were eligible to participate, resulting in 5,000 participants. Additionally, all inhabitants aged between 45 and 65 years from one municipality (Leiderdorp) were invited, irrespective of their BMI, resulting in 1,671 additional participants, and allowing a reference distribution of BMI. The present study is a cross-sectional analysis of baseline measurements of the NEO study. The study was approved by the medical ethics committee of the Leiden University Medical Center (LUMC) and all participants gave written informed consent.

Data collection

All participants completed questionnaires on demographic and clinical data and visited the study centre for baseline measurements including physical examination.

Questionnaires included standardised questions on ethnicity (self-identification in eight categories, which we grouped into white (reference) and other), education (the highest form of education from which the participant had graduated, which we grouped into poorly (none, primary school or lower

vocational education; reference) versus highly educated), income (monthly net personal income, divided into seven categories ranging from less than €500 to more than €3,000), the presence of self-reported rheumatic diseases (i.e., rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), gout, fibromyalgia, psoriatic arthritis, and ankylosing spondylitis), and self-reported hand pain and stiffness on most days of the prior month (present or absent). The AUSCAN was completed on a 5-point Likert scale, with a total score ranging from 0 to 60, and scores from the three subscales pain, stiffness and function ranging from 0 to 20, 4 and 36 respectively (higher scores are worse). Physical examination of the hands was performed by trained research nurses, assessing bony and soft swellings, deformities and pain on palpation in the distal interphalangeal (DIP), proximal interphalangeal (PIP), metacarpophalangeal, and first carpometacarpal (CMC-1) joints. Primary hand OA was defined as fulfilment of the American College of Rheumatology criteria for hand OA, without a concurrent inflammatory rheumatic disease (RA, SLE, gout, psoriatic arthritis or ankylosing spondylitis)[10]. "Pre-hand OA" was defined as having hand pain, and at least two bony swellings or deformities in the DIP, PIP, or CMC-1 joints, without being classified as having primary hand OA or reporting an inflammatory rheumatic disease.

Statistical analyses

In the NEO study there is an oversampling of persons with a BMI ≥27 kg/m^2. To correctly represent distributions and associations in the general population[11], adjustments for the oversampling of individuals with a BMI ≥27 kg/m^2 were made. This was done by weighting individuals towards the BMI distribution of participants from the Leiderdorp municipality[12], whose BMI distribution was similar to that of the general Dutch population[13]. All results were based on weighted analyses, using probability weights in Stata. Consequently, results apply to a population-based study without oversampling.

Ordered logistic regression analyses were performed to examine factors associated with increasing AUSCAN scores. For this purpose, three categories of AUSCAN total (0 versus 1-5 versus >5) and each subscale (0 versus 1-2 versus >2 for pain and function, and 0 versus 1 versus >1 for stiffness) were created. Cut-offs for AUSCAN categories were chosen in a way that the upper two categories were approximately equal in size, and that the cut-off values of the subscales added up to the cut-off value of the total score. Ordered logistic regression was chosen, because AUSCAN data were heavily zero-inflated (reflecting absence of hand complaints in most individuals). Participants with missing data of all AUSCAN subscales or physical examination were excluded from these analyses. Analyses were stratified by sex. Associations were expressed as odds ratios (ORs) with 95% confidence intervals (CIs), representing the OR of being in the highest compared to the middle or lowest AUSCAN category for a unit change in the determinant.

Age- and sex-specific reference curves were developed for the AUSCAN total and its subscales, except the stiffness subscale, because it is a single question. The curves were developed similar to the approach used for development of short form-36 population norms and children's growth curves, using data from all participants, i.e. not excluding those with hand complaints. We applied a commonly used method to derive reference curves, based on fractional polynomials described by Royston and Wright[14]. Since a parametric approach was not possible in our zero-inflated data, reference curves were derived using quantile regression in conjunction with fractional polynomials. This allows quantiles to be estimated as a smooth function of covariates without imposing parametric distributional assumptions, allowing to construct reference curves on data that do not meet the assumptions of normality, linearity, and constant variance[15 16]. The application of fractional polynomials provides the possibility to account for a curved relationship between the independent (i.e., age) and the dependent variable (i.e., AUSCAN score). The 75^{th}, 90^{th}, 95^{th}, 97.5^{th} and 99^{th} centiles were derived. Powers for the fractional polynomial models were taken from a predefined set (S = {-2, -1, -0.5, 0, 0.5, 1, 2, 3}). Simple functions were preferred; more complicated functions were accepted only if the fit was substantially improved. Adjustments for other covariates

assessed in the regression analyses were only made if deemed necessary, to improve feasibility in practical application. The goodness of fit of the regression line of the simple function was inspected visually first. If it was judged that the line did not fit the data well, fit of the regression line of the more complicated function was visually inspected and the deviance of both models was compared (estimated as $n_{obs}*log(\sum_{adev} / \sum_{rdev})$, where n_{obs} is the number of observations, $\sum_{adev}$ is the sum of absolute deviations and $\sum_{rdev}$ is the sum of raw deviations). Only when the fit of the more complicated model was both visually and statistically significantly better ($p<0.05$), was the complex model adapted. The final percentile curves were compared with observed (unweighted) values of the AUSCAN in subgroups hypothesised to have high AUSCAN scores (e.g., individuals with primary hand OA).

Items from the questionnaire driving high scores were explored. Therefore, in the subgroup of participants with high pain or function subscale scores, defined as a score >2 for that subscale, histograms of the proportion of participants that scored positive on each item were made, as well as histograms of the proportion of participants with each possible score (0, 1, 2, 3 or 4) on each item. An item was flagged as a driver of high scores when the proportion of participants with a positive score on that item was higher, or the distribution of the participants' scores within that item was more skewed towards high scores than on the other items.

Data were analysed using Stata V14, StataCorp LP, Texas.

RESULTS

Population characteristics

After exclusion of individuals with missing data on all AUSCAN subscales (n=14) and physical examination (n=14), data from 6,643 participants were analysed. Table 1 shows the participants' characteristics. Median age was 56 years (interquartile range (IQR) 50 to 61), and 56% were women.

Primary hand OA was present in 6% of men and 16% of women, and its prevalence increased with increasing age (2.4% in individuals aged 44 to 48 year, up to 16.3% in the age group 61 to 66). Median AUSCAN scores were low in both men and women, although scores were higher in women and increased slightly with age (median (IQR) 0 (0-2) in the age group 44-48 years, up to 1 (0-6.4) in the age group 61-66). However, even in the highest age category, AUSCAN scores remained low.

Associations with AUSCAN scores

We assessed associations of factors that were hypothesised to be related with AUSCAN scores in men and women with univariable followed by multivariable ordered logistic regression analyses (Table 2). Regression analyses in the three subscales of the AUSCAN yielded similar results (not shown). Associated factors were age, presence of primary hand OA, presence of self-reported inflammatory rheumatic diseases or fibromyalgia, "pre-hand OA", education (as proxy for SES), and BMI. These associations were similar in men and women, although after correction for rheumatic diseases, BMI in men and education in women were no longer associated with AUSCAN.

Reference curves

Age- and sex-specific AUSCAN reference curves and associated percentiles are presented in Figures 1A-F and Table 3. No additional covariates were deemed essential to be taken into account for development of the curves. Most curves were derived using the simplest fractional polynomial function (i.e., a first degree fractional polynomial, introducing only one power in the function of the regression line), except the 99th percentile of the AUSCAN pain subscale in men, which was fitted with a second degree fractional polynomial (introducing two powers in the function of the regression line). The function of the regression line for each percentile, an estimation example and a table with regression coefficients are published as online supplementary files (Supplementary text 1

and Table S1). Reference curves for women were generally higher than those for men. For instance, the 95% percentiles for AUSCAN in men were 5.0 and 15.2 points for a 45- and a 65-year-old respectively, whereas for women these were 12.3 and 33.6 points. Although AUSCAN scores moderately increased with age in both sexes, maximum scores were not reached and the score plateaued at 40.

Subgroup specific AUSCAN scores relative to reference curves

In Figure 2A and 2B reference curves of AUSCAN pain are plotted over boxplots of observed AUSCAN scores of women with primary hand OA and self-reported fibromyalgia respectively. The median AUSCAN pain score of women with primary hand OA lay between the 75th and 90th percentile curves of the general population. Scores of women with self-reported fibromyalgia were even higher (between the 90th and 95th percentiles). Moreover, AUSCAN pain scores of women with primary hand OA did not seem to increase markedly with age. A similar figure of women with inflammatory rheumatic diseases showed comparable results as the figure with primary hand OA (not shown).

Items driving high AUSCAN scores

In participants with a high pain subscale (>2), especially the items assessing pain during activities (grabbing, lifting, turning and squeezing objects) were scored positive by many (88-96%). For the function subscale the most important items appraised difficulty with opening jars and grabbing large or heavy objects (94% and 83% scored these items positive), and to a lesser extent difficulty in carrying objects with one hand and squeezing a cloth (62% and 63% with positive score). Results for men and women were similar (not shown).

DISCUSSION

In this study we developed age- and sex-specific reference curves for the AUSCAN in the middle-aged Dutch population. Overall, AUSCAN scores were low, and women reported more hand complaints than men. This gender difference is in part explained by a higher prevalence of hand OA in women. Besides, it is possible that women report hand complaints more readily than men do[17]. Furthermore, many participants had a score of zero, and the percentile curves plateaued at a score of 40 on the AUSCAN total. This might indicate that there is a lack of items assessing mild symptoms or relatively easy tasks. We saw that mainly squeezing and turning motions led to pain and functional limitation, and perhaps other items only depart from normal in extreme situations (e.g., end-stage disease of hand OA).

Previously described normative values in an Australian population-based sample also showed increasing hand complaints with increasing age and similar differences between men and women[8]. However, AUSCAN scores reported in that cohort did not clearly plateau and were overall higher than what we observed. This may be explained by cultural differences, as previous studies have highlighted important differences across countries in the assessment of patient-reported outcomes[18], or the occurrence of selection bias in the Australian study (i.e., individuals with more complaints might have been more inclined to return the mailed questionnaire). A different percentage of participants with hand OA or other rheumatic diseases could also explain the discrepancies, but this information is not available for the Australian cohort. Moreover, the authors applied different statistical analyses, using empirical centiles based on descriptive analysis to define normative values for different age categories. Empirical centiles can be biased in small samples, and estimates are known to be inefficient and have large variance[19]. Reference curves for outcome measures are preferably developed using regression models, adjusting for important factors (e.g., age), as has been done for the well-known and extensively used growth curves[14 20].

An important limitation of our study is the age range of included participants, limiting the age range for which reference curves could be developed. However, the included age range is the most relevant, since it is the timeframe in which the prevalence of symptomatic as well as radiological hand OA steeply increases and as a consequence it can be expected that the prevalence of hand complaints increases too[21 22]. Besides, we used self-reported data on other rheumatic diseases than hand OA, without validating these in medical records, although a recent review suggested that the accuracy of self-reported RA is acceptable for large-scale studies[23]. Furthermore, the low prevalence of rheumatic diseases sometimes led to excessively large ORs and corresponding CIs, such as for fibromyalgia, resulting in an inaccurate estimate of the true size of the association between AUSCAN and these diseases. Finally, a disadvantage of the AUSCAN is that it is not freely available (copyrighted), but nevertheless it was used for this study since it is the most widely used hand-specific questionnaire with evidence of good metric properties[24].

An important strength of the NEO study is its large sample size and the availability of extensive demographic and clinical data with few missing data. Another strength of our study was the solid methodology used for the statistical analysis, based on the methodology used for the development of pediatric growth curves by the World Health Organization[20]. Since a parametric approach was not possible, we adopted a modified approach (i.e., quantile regression in conjunction with fractional polynomials). A similar method was used previously to develop reference curves for radiographic damage in RA patients[16]. Quantile regression is robust and flexible, and an important advantage is that it allows age to remain a continuous variable[25]. The latter enables the computation of a value for the reference curve for every year of age, and it makes the charts easier to use, because the x-axis is in years rather than in age categories. A drawback, however, is that this approach lacks an explicit formula to convert measurements into quantiles and z-scores, and that the produced curves may be irregular near the extremes[25].

These reference curves can serve as a useful benchmark in hand OA in both research and clinical practice settings. By plotting the AUSCAN score of an individual on the chart, their measurement can be expressed as a centile. These charts can be used to compare AUSCAN scores across different populations (see figure 2), compare scores of the same population at different occasions, or to detect aberrant individual scores[26]. It is also possible to plot a sequence of measurements over time of an individual in the same chart. A person whose 'individual curve' tracks along the same centile over time, develops hand complaints expected according to their increase in age. Yet if their 'individual curve' 'crosses' centiles up or down, that person may develop complaints faster or slower than average. One has to be cautious with the latter interpretation, however, since our analyses were performed cross-sectionally and therefore do not contain information on the variability between individuals in the increase in AUSCAN over time[26]. Cross-sectional curves that are interpreted in a longitudinal manner (i.e., following an individual over time), can especially be misleading when the rate of change is high, for example growth during infancy or puberty, because a mean cross-sectional curve partly smooths out this peak growth[27]. However, the increase of AUSCAN over time is only moderate and it is unlikely that variations between individuals in slope of AUSCAN over time are pronounced. Therefore, we believe that these reference curves can also be applied in the follow-up of individuals over time, as long as results are interpreted with caution.

The strong associations of AUSCAN with many other factors besides primary hand OA underline that this instrument does not measure hand OA specific complaints. This should be kept in mind when using the AUSCAN. AUSCAN pain scores of individuals with self-reported fibromyalgia were even higher than those of participants with primary hand OA. Since we also know that fibromyalgia-like symptoms are prevalent in hand OA patients, this finding stresses the difficulties and complexity in recognizing the origin of complaints in hand OA patients[28]. Furthermore, our study provides more evidence that the burden of disease in patients with hand OA is at least similar to that of RA patients, since both subgroups had equally high AUSCAN scores[29].

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COMPETING INTERESTS

None.

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FIGURE LEGENDS

Figure 1. *Age- and sex-specific reference curves for AUSCAN total, AUSCAN pain and AUSCAN function in men (A, C, E) and women (B, D, F).*

Figure 2. *Reference curves for AUSCAN pain plotted over boxplots of the observed (unweighted) values of the AUSCAN scores of women with primary hand OA (A) and self-reported fibromyalgia (B).*

Each box represents the IQR, with the median represented by a horizontal line within the box. Whiskers represent the smallest and largest value within 1.5 IQR, and dots depict outliers.

Table 1. Characteristics of the study population, stratified by sex.

	Men	**Women**
Prevalence, %	44	56
Age, years	57 (51-62)	56 (50-61)
Ethnicity, % Caucasian	95.1	94.7
Education, % high	48.1	44.4
Income*, %		
- **Less than €500 up to €1500**	11.2	52.9
- **€1500 up to €2500**	38.9	27.0
- **€2500 or more**	39.7	5.4
- **Unknown**	10.2	14.7
BMI, kg/m^2	26.4 (24.4-28.7)	25.1 (22.4-28.0)
Fulfilling ACR criteria for hand OA [10], %	6.3	18.0
Primary hand OA†, %	5.5	16.3
"Pre-hand OA"‡, %	3.3	7.9
Self-reported inflammatory rheumatic disease, %	4.6	3.9
- **Rheumatoid arthritis**	1.2	2.4
- **SLE**	0.1	0.1
- **Psoriatic arthritis**	0.1	0.2
- **Gout**	2.8	1.0
- **Ankylosing spondylitis**	0.4	0.2
Self-reported fibromyalgia, %	0.3	3.0
AUSCAN total score (range 0-60)	0 (0-1)	2 (0-8)
AUSCAN pain subscale (range 0-20)	0 (0-0)	0 (0-2)
AUSCAN stiffness subscale (range 0-4)	0 (0-0)	0 (0-1)
AUSCAN function subscale (range 0-36)	0 (0-0)	1 (0-5)

Results are based on weighted analyses of the study population (n=6643). Medians (interquartile range) are reported unless otherwise specified.

*Net monthly personal income. †Defined as fulfilment of the ACR criteria for hand OA, without a concurrent inflammatory rheumatic disease (RA, SLE, gout, PsA, or AS). ‡Defined as the presence of hand pain in combination with at least two bony swellings or deformities in the DIPs, PIPs, or first CMC joints, and not being classified as having primary hand OA or reporting a concurrent inflammatory rheumatic disease.

ACR, American College of Rheumatology; AS, ankylosing spondylitis; AUSCAN, Australian/Canadian Hand Osteoarthritis Index; BMI, body mass index; CMC, carpometacarpal; DIP, distal interphalangeal; OA, osteoarthritis; PIP, proximal interphalangeal; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

Table 2. Factors associated with AUSCAN total scores, stratified by sex.

	Univariable OLR (OR (95% CI))		Multivariable OLR (OR (95% CI))	
	Men	**Women**	**Men**	**Women**
Age (years)	1.03 (1.01 to 1.05)	1.07 (1.05 to 1.08)	1.02 (1.00 to 1.04)	1.04 (1.02 to 1.06)
Education (high vs other)	0.75 (0.61 to 0.93)	0.76 (0.63 to 0.91)	0.79 (0.62 to 1.00)	0.95 (0.77 to 1.17)
BMI (kg/m^2)	1.03 (1.00 to 1.05)	1.04 (1.02 to 1.05)	0.99 (0.96 to 1.02)	1.01 (1.00 to 1.03)
Primary hand OA	14.11 (9.42 to 21.14)	9.55 (7.09 to 12.87)	18.37 (11.94 to 28.27)	12.37 (8.92 to 17.15)
"Pre-hand OA"	9.81 (6.10 to 15.75)	5.51 (3.72 to 8.17)	15.39 (9.24 to 25.62)	9.64 (6.28 to 14.81)
Inflammatory rheumatic disease*	2.44 (1.55 to 3.85)	4.78 (2.95 to 7.74)	3.15 (1.85 to 5.37)	8.78 (5.22 to 14.78)
Fibromyalgia	246.76 (29.84 to 2040.97)	20.13 (9.73 to 41.64)	228.00 (23.64 to 2198.82)	13.67 (6.23 to 30.00)

Results are based on weighted analyses of the study population.

*Including RA, SLE, gout, PsA or AS.

AS, ankylosing spondylitis; AUSCAN, Australian/Canadian Hand Osteoarthritis Index; BMI, body mass index; CI, confidence interval; OA, osteoarthritis; OLR, ordered logistic regression; OR, odds ratio; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

Table 3. Calculated age- and sex-specific percentiles for AUSCAN total, AUSCAN pain and AUSCAN function.

		Percentiles									
		Men					Women				
Measure	**Age**	**75th**	**90th**	**95th**	**97.5th**	**99th**	**75th**	**90th**	**95th**	**97.5th**	**99th**
AUSCAN total	45	0.9	3.4	5.0	11.0	17.9	1.9	6.1	15.2	23.4	39.3
	50	1.0	3.9	9.6	15.9	22.3	5.6	15.1	23.1	32.3	39.8
	55	1.1	4.6	11.1	18.1	25.6	8.5	20.4	27.8	35.3	40.0
	60	1.5	5.7	11.8	19.4	28.4	10.9	24.2	31.0	36.8	40.1
	65	2.1	7.0	12.3	20.3	30.9	13.0	27.1	33.6	37.7	40.1
AUSCAN pain	45	0	1.7	5.0	5.0	7.5	0	2.0	7.2	8.6	12.2
	50	0	1.8	5.0	7.4	11.8	1.3	6.0	9.6	11.0	13.0
	55	0	2.2	5.0	7.8	11.8	2.5	7.7	10.4	11.8	13.8
	60	0	2.9	5.0	8.0	10.7	3.8	8.8	10.8	12.2	14.7
	65	0	4.0	5.0	8.0	9.3	5.0	9.5	11.1	12.4	15.5
AUSCAN function	45	0	1.8	3.0	5.4	10.2	1.3	3.5	7.0	14.0	22.8
	50	0.1	2.0	5.0	7.6	13.5	3.8	9.0	14.0	19.3	24.4
	55	0.2	2.3	5.7	9.3	16.0	5.3	12.3	17.1	21.6	25.0
	60	0.6	3.0	6.0	10.7	18.1	6.4	14.6	18.9	23.0	25.3
	65	1.1	4.0	6.2	12.0	20.0	7.2	16.4	20.2	24.0	25.4

Results are based on weighted analyses of the study population.

AUSCAN, Australian/Canadian Hand Osteoarthritis Index.

Supplementary files

Online supplementary text 1.

Regression function of the reference curves

The function of the regression line of each percentile curve is the following:

$$\boldsymbol{Y^Q = \beta_0^Q + \beta_1^Q \cdot X_1}$$

with $\mathbf{Y^Q}$ AUSCAN at Q^{th} percentile
$\boldsymbol{\beta_0^Q}$ Intercept at Q^{th} percentile
$\boldsymbol{\beta_1^Q}$ Regression coefficient of X_1 at Q^{th} percentile
$\mathbf{X_1}$ Age variable, which is calculated as follows:

$$\mathbf{X_1} = \left(\frac{\boldsymbol{age - 40}}{\mathbf{10}}\right)^{\boldsymbol{FP}} - \boldsymbol{sf}$$

with **FP** Fractional polynomial power, taken from a predefined set: *S* = {-2, -1, -0.5, 0, 0.5, 1, 2, 3}, where X^0 denotes ln(X)
sf Scaling factor, which is calculated as follows:

$$\boldsymbol{sf} = \left(\frac{\overline{\boldsymbol{Y}}}{\boldsymbol{i}}\right)^{\boldsymbol{FP}}$$

with $\overline{\boldsymbol{Y}}$ Mean AUSCAN
i Estimated by STATA depending on possible values of **X** and **Y**
FP Fractional polynomial power

If the independent variable in regression analyses with fractional polynomials is too large or too small, the reported results of the analysis may be difficult to interpret. That is why age was scaled before adding it to the regression equation (by subtracting 40 and subsequently dividing by 10) in order to ensure its magnitude was neither too large nor too small.

The value of **i** is calculated automatically by the statistical package for scaling purposes of the regression coefficient. The scaling factor **sf** is provided in the output of the regression analysis.

<u>Example: What is the AUSCAN total in a 60 year old man at the 97.5th percentile?</u>

$\boldsymbol{\beta_0^Q}$ = 18.44
$\boldsymbol{\beta_1^Q}$ = -11.90
FP = -0.5
sf = 0.79

$$\boldsymbol{Y^Q = \beta_0^Q + \beta_1^Q \cdot \left(\left(\frac{age-40}{10}\right)^{FP} - sf\right)}$$
$$\boldsymbol{Y^{75th}} = 18.44 + -11.90 \cdot \left(\left(\frac{60-40}{10}\right)^{-0.5} - 0.79\right)$$
$$\boldsymbol{Y^{75th}} \approx 19.4$$

Supplementary table S1. Intercepts, regression coefficients with 95% confidence interval, fractional polynomial powers and scaling factor for each of the quantile regression curves.

		Men				***Women***			
	Percentile	**β_0**	**β_1 (95% CI)**	**FP**	**sf**	**β_0**	**β_1 (95% CI)**	**FP**	**sf**
AUSCAN total	75th	1.20	0.08 (0.03 to 0.13)	3	4.11	8.79	12.65 (9.63 to 15.67)	0.5	1.25
	90th	4.81	0.60 (0.02 to 1.17)	2	2.56	20.87	13.07 (9.03 to 17.11)	0	0.44
	95th	11.30	-4.58 (-9.02 to -0.14)	-1	0.62	28.15	11.43 (6.12 to 16.74)	0	0.44
	97.5th	18.44	-11.90 (-28.01 to 4.20)	-0.5	0.79	35.53	-8.93 (-18.23 to 0.38)	-1	0.64
	99th	26.30	14.88 (-7.40 to 37.16)	0.5	1.27	40.01	-0.55 (-13.63 to 12.54)	-1	0.64
AUSCAN pain	75th	*	*	*	*	2.65	2.50 (1.83 to 3.17)	1	1.56
	90th	2.28	0.15 (0.02 to 0.27)	3	4.11	7.90	-9.62 (-13.66 to -5.58)	-0.5	0.80
	95th	5.00	0.00 (-1.75 to 1.75)	-1	0.62	10.49	-2.45 (-4.42 to -0.49)	-1	0.64
	97.5th	7.86	-0.79 (-1.74 to 0.15)	-2	0.39	11.87	-2.38 (-4.40 to -0.36)	-1	0.64
	99th	11.65	2.34 (-3.39 to 8.07) -5.50 (-12.61 to 1.60)†	0 0†	0.47 0.22†	13.93	1.67 (-0.01 to 3.35)	1	1.56
AUSCAN function	75th	0.29	0.07 (0.03 to 0.12)	3	4.11	5.43	3.64 (3.00 to 4.28)	0	0.44
	90th	2.39	0.14 (0.03 to 0.25)	3	4.11	12.55	8.00 (5.66 to 10.33)	0	0.44
	95th	5.75	-2.00 (-3.53 to -0.47)	-1	0.62	17.37	-16.94 (-24.30 to -9.58)	-0.5	0.80
	97.5th	9.62	7.54 (-0.50 to 15.58)	0.5	1.27	21.85	-12.79 (-25.54 to -0.04)	-0.5	0.80
	99th	16.48	11.16 (-1.15 to 23.47)	0.5	1.27	25.04	-1.64 (-8.11 to 4.84)	-1	0.64

*Values could not be estimated because the AUSCAN pain values in this percentile are not higher than zero.
†The 99th percentile curve of AUSCAN pain for men was estimated with a second degree fractional polynomial function, which means that a second regression coefficient ($\beta_{1a}{}^{Q}$) with a corresponding polynomial (FP_b) was added to the regression function to improve model fit ($Y^Q = \beta_0^Q + \beta_{1a}^Q \cdot X_{1a} + \beta_{1b}^Q \cdot X_{1b}$). The age variable corresponding to the second regression coefficient is calculated as follows:$X_{1b} = \left(\left(\frac{age-40}{10}\right)^{FP_b} \cdot \ln\left(\frac{age-40}{10}\right)\right) - sf_{1b}$.
AUSCAN, Australian/Canadian Hand Osteoarthritis Index; CI, confidence interval; FP, fractional polynomial power; sf, scaling factor; β_0, intercept; β_1, regression coefficient.

Figure 1 (colour – online version)

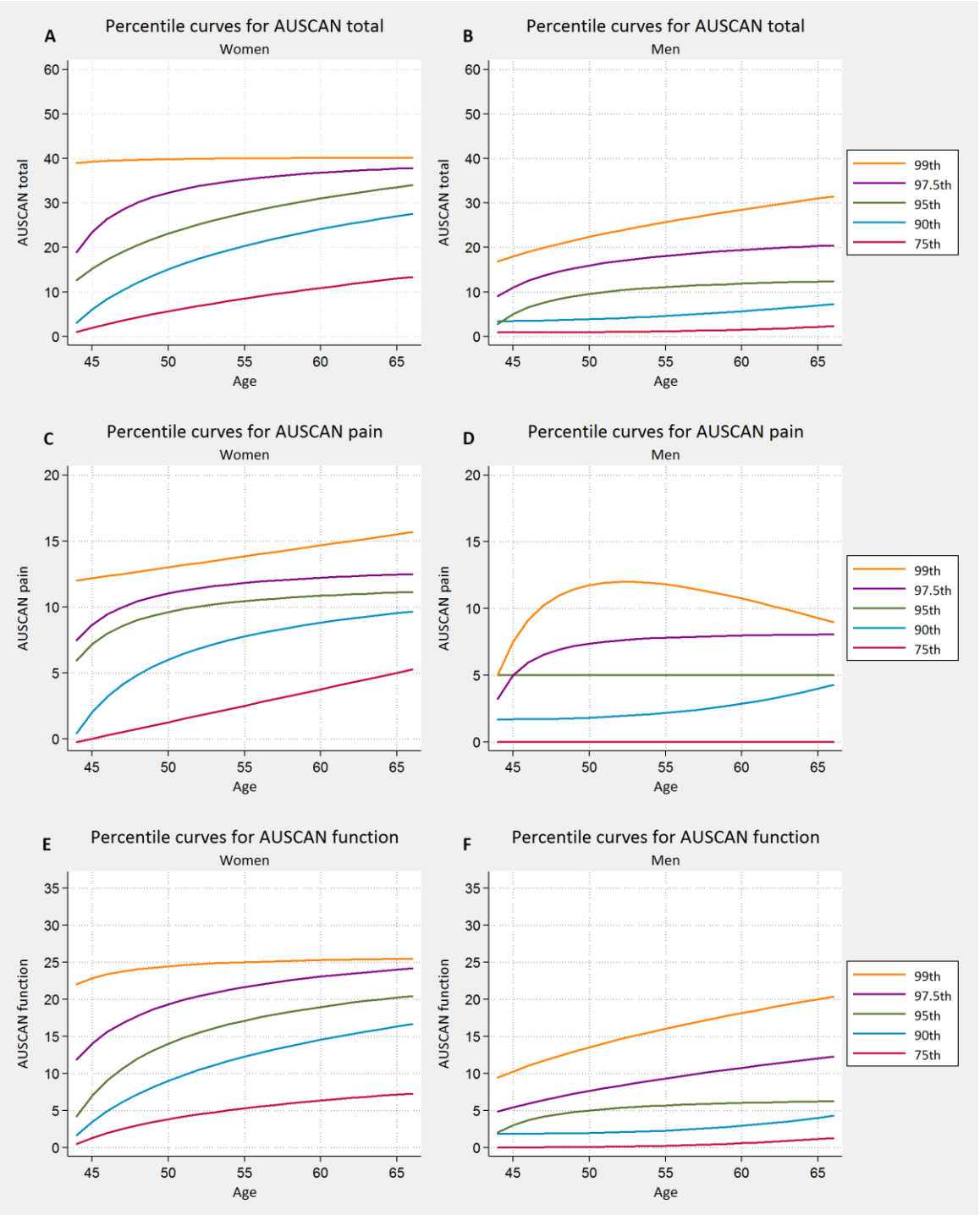

Figure 1 (grey scale – printed version)

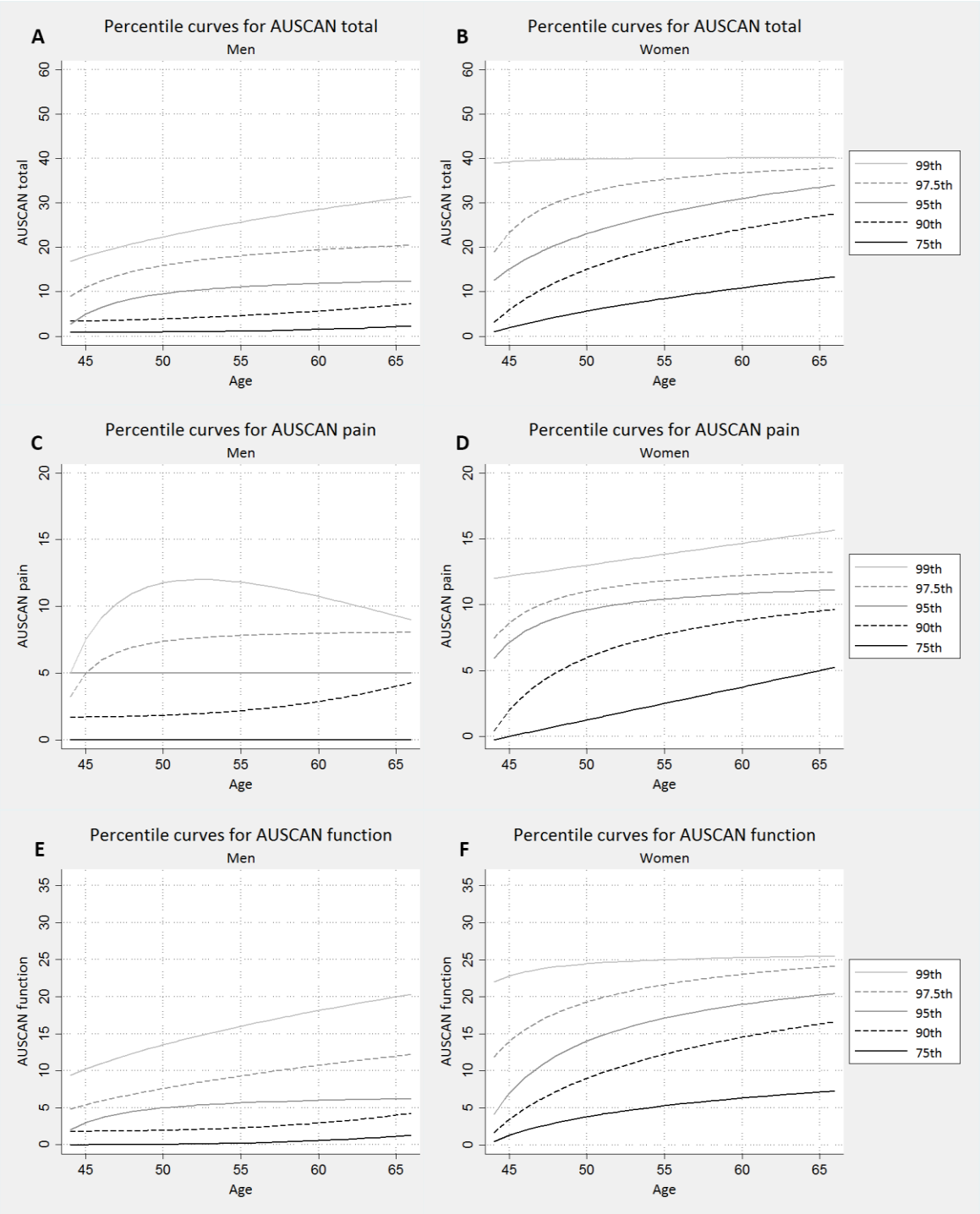

Figure 2 (colour – online version)

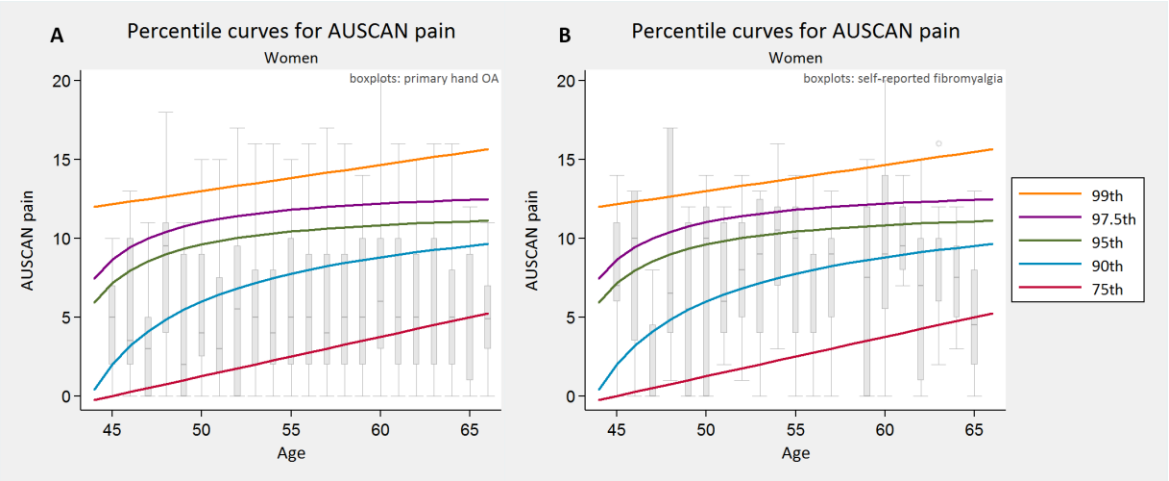

Figure 2 (grey scale – printed version)