Public healthcare attendance associates with enhanced conventional and non-conventional atherosclerotic cardiovascular disease risk burdens in established rheumatoid arthritis

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Abstract

Objective

To assess whether public healthcare attendance associates with altered atherosclerotic cardiovascular disease risk in established rheumatoid arthritis (RA).

Methods

We determined disparities in major conventional (hypertension, dyslipidemia, smoking and diabetes), other conventional (underweight, obesity, metabolic syndrome, chronic kidney disease, alcohol use, tension, depression and body height) and non-conventional (current and cumulative inflammation markers) cardiovascular risk factors between 424 consecutive public and 202 private healthcare patients in mixed regression models.

Results

Eighty-one percent of public healthcare patients were black (67%) or caucasian (14%) and 83% of private healthcare cases were caucasian. Seventy percent of the patients had ≥1 major conventional risk factor. After adjustment for age, gender, ethnic origin and statin use when appropriate, public healthcare attendance associated with the prevalence of hypertension (odds ratio (OR) [95%CI]=1.72 [1.03, 2.85]), having ≥1 major conventional risk factor (OR [95%CI]=1.83 [1.09, 3.07]) and an increased mean (SD) number of such risk factors (p=0.03), metabolic syndrome frequency (OR [95%CI]=1.90 [1.07, 3.40]), alcohol use (OR [95%CI]=0.07 [0.03, 0.18]), shorter stature (p<0.0001), higher tension (p=0.02) and depression score (p<0.0001) and higher inflammatory markers including the disease activity score in 28 joints (p=0.005), C-reactive protein concentration (p=0.0006), Health Assessment Questionnaire disability index (p<0.0001), and number of deformed joints (p<0.0001). In sensitivity analyses performed in caucasian Africans, public healthcare attendance associated with increased frequencies of each major conventional risk factor (OR=2.06 to 3.69) and higher other conventional and non-conventional mediated cardiovascular risk.

Conclusion

Public healthcare patients with established RA experience markedly enhanced conventional and non-conventional cardiovascular risk burdens.

Key words

Atherosclerotic cardiovascular disease risk, public healthcare attendance, socioeconomic disadvantage, rheumatoid arthritis.

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Introduction

The risk for atherosclerotic cardiovascular disease (CVD) is markedly exacerbated in subjects that have developed rheumatoid arthritis (RA) (1-12). Reported evidence indicates that both traditional cardiovascular risk factors and high-grade inflammation (1-12) along with genetic components (13, 14) predict CVD in patients with RA.

In non-RA subjects, the major conventional risk factors of hypertension, dyslipidemia, smoking and diabetes are responsible for the bulk of CVD (15, 16). Socioeconomic deprivation further enhances prevalent and incident coronary heart disease at least 50% through increased psychosocial stress, more atherogenic conventional cardiovascular risk profiles and adverse factors acting early in life as estimated by a shortened body height (17, 18). In RA, socioeconomic disadvantage has substantial unfavorable effects on disease activity and severity, mortality and treatment characteristics (19-29). However, to our knowledge, its impact on CVD risk has not been investigated.

Very recently, Sokka and colleagues (29) showed that in 6004 RA patients enrolled in the Quantitative Standard Monitoring of Patients with Rheumatoid Arthritis (QUEST-RA) cohort from 71 sites in 25 different countries, the gross domestic product of their resident country explained as much as 61% of the variation in the disease activity score (DAS) in 28 joints (29). Previously used parameters in published studies aimed at evaluating the effect of socioeconomic status on disease outcomes in patients with RA included educational level, personal income, area of residence and public healthcare attendance (19-28). The determination of which of these characteristics is preferable in the context of RA is not expected to be helpful as the solution to most would be by increasing access to resources in disadvantaged patients (26). We previously reported that public healthcare attendance strongly associates with enhanced physical disability in patients with RA (30). The use of public healthcare attendance as a marker of socioeconomic disadvantage is particularly pertinent in a setting like ours. Indeed, although South Africa is considered a middle income country in terms of its economy, due to its historical apartheid system that discriminated against non-caucasians and ended in 1994 together with subsequent macroeconomic policies fostering growth rather than redistribution (31), this country is currently one the most unequal societies in the world with a Gini coefficient of 0.77 (the closer to 1, the greater the inequality) (31, 32). Less than 15% of the population are members of private sector medical schemes and consistently seek help in the private healthcare sector (31, 33). The availability of resources is markedly restricted in the public healthcare sector with 60 to 70% of doctors working in the private sector and an annual expenditure per head of R1300 (€120; $170) to R1500 (€135; $195) and R9500 (€855; $1230) in those that are and those that are not members of private sector medical schemes, respectively (31).

We recently initiated a study on atherogenesis in African populations with RA (34). In the current investigation, we analysed the data that were obtained to date with the aim to test the hypothesis that public healthcare attendance as an indicator of disadvantaged circumstances of life associates with an enhanced atherosclerotic CVD risk burden in patients with established RA independent of demographic characteristics.

Patients and methods

Participants

We invited 626 consecutive patients that met the American College of Rheumatology criteria for RA (35) and had previously taken disease modifying agents to participate. None refused and 424 and 202 patients were enrolled at the Charlotte Maxeke Johannesburg Academic Hospital (public healthcare) and at the Milpark Hospital (private healthcare), respectively. Public healthcare patients were mostly black (66.5%) or caucasian (14.4%) whereas the predominant ethnic origin in private healthcare was caucasian (83.2%) (Table I). Public healthcare patients were more often women (p=0.04; Table II). In all patients, the mean (SD) disease duration was 9.1 (2.4) years and, at

the time of the study, disease modifying agents, non-steroidal anti-inflammatory agents, prednisone (mean (SD) dose = 4.7 (1.8) mg/day) and statins were prescribed in 97.8, 18.4, 4.8 and 6.1% of cases, respectively. None of these characteristics differed between private and public healthcare patients. However, cyclooxygenase 2 inhibitors and tumor necrosis factor-alpha blockers were only used in private healthcare patients (n=19 and n=6, respectively) and antihypertensive agents were more often employed in public healthcare patients (50.9 versus 33.7%; odds ratios (OR) [95% CI]=2.05 [1.44, 2.90]). The study was approved by the Ethics Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand. Written informed consent was obtained from each patient.

Assessments

The recorded cardiovascular risk factor profiles are presented in Tables II and III and Figure 1. All the patients had fasted for at least 8 hours prior to blood sampling. Hypertension was diagnosed in patients with a blood pressure of >140 mmHg systolic or/and >90 mmHg diastolic or/and when antihypertensives were prescribed, and dyslipidemia when the atherogenic index (total cholesterol÷HDL cholesterol ratio) was >4 (15, 36). The proatherogenic non-HDL cholesterol concentrations were calculated by subtracting HDL cholesterol from total cholesterol concentrations (36). We assessed current smoking status and patients with a fasting plasma glucose of ≥7 mmol/l or in whom glucose lowering agents were prescribed were diagnosed with diabetes. Patients with a body mass index (BMI) of <20 kg/m^2 were considered to be underweight (37). We used the recently reported RA-specific BMI threshold (≥28 kg/m^2) (38) in identifying cases with generalised obesity. Patients were classified as having the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) defined metabolic syndrome (MetS) using the ethnicity-specific criteria as recently updated by the American Heart Association and National Heart, Lung and Blood Institute (39). The glomerular filtration rate (GFR) was estimated by the Modification of Diet in Renal Disease (MDRD) equation and chronic kidney disease (CKD) was diagnosed when the GFR was <60 ml/min (40). We assessed alcohol consumption (41) (protective cardiovascular risk factor) and depression and tension were evaluated using the Arthritis Impact Measurement Scales (AIMS) (42). Body height was recorded as a cardiovascular risk factor that originates in environmental and genetic factors acting early in life (17). The evaluated RA characteristics as potential cardiovascular risk factors included C-reactive protein concentrations, the disease activity score in 28 joints (DAS28), the Health Assessment Questionnaire disability index (HAQ-DI) and the number of deformed joints.

Data management and analysis

We grouped the cardiovascular risk factors into 3 categories: (1) major conventional cardiovascular risk factors comprising the modifiable risk factors that are the most established role players in atherogenesis in the non-RA subjects and, accordingly, form the basis of risk assessment in current guidelines on cardiovascular disease prevention in the population at large (15, 16); (2) other conventional cardiovascular risk factors including underweight, generalised obesity, the MetS, alcohol use, CKD, depression and anxiety and body height and (3) non-conventional cardiovascular risk factors consisting of markers of current (DAS28, C-reactive protein, HAQ-DI) and cumulative inflammation (HAQ-DI and number of deformed joints). Except for alcohol use, obesity and body height, each of the risk factors that were assessed in the current investigation were previously documented to increase atherosclerotic CVD risk in not only the general population but also in patients with RA (1-12, 43, 44). Although glucocorticoid therapy, non steroidal anti-inflammatory agents and disease modifying agents can modify cardiovascular risk and disease, the previously reported (30) and ongoing inconsistent supply of these medications in our public healthcare sector precluded making a reliable assessment of the association of healthcare setting with use of these agents.

Dichotomous variables are expressed as proportions or percentages and continuous variables as mean (SD). Non-normally distributed characteristics were logarithmically transformed prior to statistical analysis and for these variables geometric means (SD) are given. Differences in means and proportions between public and private healthcare patients were first assessed by Student *t*-tests and in univariate logistic regression models, respectively. The associations of public healthcare attendance with cardiovascular risk factor profiles were subsequently investigated in multivariable logistic and linear regression models as appropriate and with consistent adjustment for age and gender and black as well as caucasian ethnic groupings since the latter characteristics differed by healthcare sector (Table I). Statin use was further adjusted for upon assessing the association of public healthcare attendance with lipid values. Finally, the relation of public healthcare attendance to metabolic cardiovascular risk was investigated by employing the NCEP ATPIII criteria definitions (39).

In order to further evaluate the relationship between public healthcare attendance and cardiovascular risk independent of ethnicity, we performed sensitivity analyses using the data obtained in caucasian patients. Caucasian cases were sufficiently represented (n>50) in both the private or public healthcare sector to allow for meaningful multivariable analysis.

Statistical computations were made using the GB Stat™ program (Dynamic Microsystems, Inc., Silverspring, Maryland, USA). Significance was set at $p<0.05$.

Results

The relation of public healthcare attendance to atherosclerotic cardiovascular risk in patients with rheumatoid arthritis

Table II shows that 70% of patients had one or more major conventional risk factor. Hypertension was by far the most prevalent conventional risk factor (60%) whereas dyslipidemia, current smoking and diabetes were identified

Table I. Public and private healthcare rheumatoid arthritis patients by ethnicity.

Ethnic group	Private n (%)	Public n (%)	*p*-value
Black	9 (4.5)	282 (66.5)	<0.0001
White	168 (83.2)	61 (14.4)	<0.0001
Asian	16 (7.8)	47 (11.1)	0.3
Mixed	9 (4.5)	34 (8)	0.1

in 19, 11 and 10% of patients, respectively. The 11% of subjects that used tobacco smoked 11(2) cigarettes daily and in the 15% that consumed alcohol, the daily intake was 0.9 (0.3) units.

In univariate analysis (columns 3-5 in Table II), public healthcare attendance associated with more prevalent hypertension (odds ratio (OR) [95% CI]=1.86 [1.33, 2.62]), lower smoking rate (OR [95% CI]=0.58 [0.35, 0.95]) and a tendency (p=0.057) to an increased frequency of diabetes (OR [95% CI]=1.87 [0.98, 3.51]). These disparities translated in an increased likelihood of having one or more major conventional risk factors (OR=1.58 [1.11, 2.26]) in public healthcare pa-

Table II. Association of public healthcare attendance with atherosclerotic cardiovascular disease risk profiles in 626 patients with rheumatoid arthritis.

Characteristics	All, % (n=626)	Private, % (n=202)	Public, % (n=424)	OR* [95% CI]	OR† [95% CI]
Female gender	84.5	80.2	86.6	1.59 [1.02, 2.48]	–
Major conventional CV risk factors					
Hypertension	59.8	49.5	64.8	***1.86 [1.33, 2.62]***	***1.72 [1.03, 2.85]***
T chol÷HDL chol>4	19.1	17.3	20.0	1.18 [0.76, 1.82]	1.36 [0.75, 2.46]
Smoking	11.4	15.3	9.5	***0.58 [0.35, 0.95]***	1.74 [0.92, 3.30]
Diabetes	9.8	6.4	11.5	1.86 [0.98, 3.51]	1.50 [0.62, 3.62]
≥1 major CV risk factor	69.9	62.4	72.4	***1.58 [1.11, 2.26]***	***1.83 [1.09, 3.07]***
Other conventional CV risk factors					
BMI<20 kg/m^2	9.9	9.9	10.0	0.97 [0.55, 1.71]	1.11 [0.53, 2.35]
BMI≥28 kg/m^2	39.6	25.7	46.4	***2.37 [1.63, 3.42]***	1.51 [0.91, 2.50]
Metabolic syndrome	25.4	15.8	30.0	***2.27 [1.48, 3.50]***	***1.90 [1.07, 3.40]***
MDRD GFR<60 ml/min	7.2	7.0	7.3	0.95 [0.49, 1.85]	1.36 [0.55, 3.35]
Alcohol use	14.7	42.1	1.7	***0.02 [0.01, 0.05]***	***0.07 [0.03, 0.18]***
Non conventional CV risk factors	76.7	78.2	75.9	0.71 [0.48, 1.06]	0.67 [0.39, 1.14]
Rheumatoid factor positive					
Continuous variables	**All, % mean (SD)**	**Private, % mean (SD)**	**Public, % mean (SD)**	***p*-value***	***p*-value†**
Age, years	55.9 (11.6)	56.2 (12.1)	55.7 (11.4)	0.6	–
Major conventional CV risk factors					
T chol, mmol/l	4.8 (1.0)	4.9 (1.0)	4.7 (1.1)	0.06	0.2
HDL chol‡, mmol/l	1.50 (1.42)	1.57 (1.34)	1.46 (1.46)	0.008	0.5
T chol÷HDL chol‡	3.1 (1.4)	3.0 (1.3)	3.1 (1.5)	0.2	0.2
LDL chol, mmol/l	2.7 (0.9)	2.8 (0.9)	2.6 (0.9)	0.08	0.5
Non-HDL chol, mmol/l	3.2 (1.0)	3.2 (1.0)	3.2 (1.0)	0.3	0.1
Number of major risk factors	1.0 (0.8)	0.9 (0.8)	1.0 (0.8)	0.1	0.03
Other conventional CV risk factors					
Triglycerides‡, mmol/l	1.1 (1.7)	1.0 (1.6)	1.1 (1.7)	0.0006	<0.0001
AIMS tension	3.8 (1.8)	3.5 (1.9)	3.9 (2.0)	0.02	0.02
AIMS depression	3.2 (2.0)	2.2 (1.6)	3.6 (2.0)	<0.0001	<0.0001
Height, cm	161.5 (10.3)	166.3 (9.3)	159.1 (10.0)	<0.0001	<0.0001
Non conventional CV risk factors					
DAS28	3.0 (1.5)	2.4 (1.4)	3.2 (1.4)	<0.0001	0.005
C-reactive protein‡, mg/l	6.2 (3.6)	3.9 (3.6)	7.8 (3.4)	<0.0001	0.0006
HAQ-DI	0.71 (0.66)	0.48 (0.58)	0.83 (0.66)	<0.0001	<0.0001
Number of deformed joints	8 (9)	5 (8)	10 (9)	<0.0001	<0.0001

Significant (p<0.05) associations between public care attendance and cardiovascular risk factors in logistic regression models are shown in bold italic.
*unadjusted, †adjusted for age, ethnic origin and gender, as well as statin use upon assessment of the association between public healthcare attendance and lipid variables, ‡geometric mean and SD are given in view of non-normal distribution.
OR: odds ratio; CI: confidence interval; CV: cardiovascular; T: total; chol: cholesterol; BMI: body mass index; MDRD: Modification of Diet in Renal Disease; GFR: glomerular filtration rate; AIMS: Arthritis Impact Measurement Scale; DAS: Disease Activity Score; HAQ-DI: Health Assessment Questionnaire disability index.

tients. Further, the other conventional and non conventional risk factors were all either similar or more adverse (HDL cholesterol concentrations, generalised obesity, MetS, alcohol use, triglyceride concentrations, AIMS tension and depression, body height and markers of current and cumulative inflammation) in public compared to private healthcare patients.

When the above-mentioned analyses were repeated (column 6 in Table II) with adjustment for potential confounders, public healthcare attendance associated with the major conventional cardiovascular risk factor of hypertension (OR [95% CI]=1.72 [1.03, 2.85]) and the likelihood of experiencing one or more major conventional cardiovascular risk factors (OR [95% CI]=1.83 [1.09, 3.07]) and a higher mean (SD) number of such risk factors (p=0.03), other conventional risk factors including MetS (OR [95% CI)]=1.90 [1.07, 3.40]), alcohol consumption (OR [95% CI]=0.07 [0.03-0.18]), higher triglyceride concentration (p<0.0001) and AIMS tension (p=0.02) and depression (p<0.0001) and lower body height (p<0.0001) as well as each non-conventional risk factor comprising a higher DAS28 (p=0.005), C-reactive protein concentration (p=0.0006), HAQ-DI (p<0.0001) and number of deformed joints (p<0.0001).

Table III. Association of public healthcare attendance with atherosclerotic cardiovascular disease risk profiles in 229 caucasian patients with rheumatoid arthritis.

Characteristics	Private, % (n=168)	Public, % (n=61)	OR* [95% CI]	OR† [95% CI]
Female gender	79.8	85.2	1.47 [0.66, 3.28]	-
Major conventional CV risk factors				
Hypertension	50.6	65.6	***1.86 [1.01, 3.43]***	***2.06 [1.06, 4.01]***
T chol÷HDL chol>4	14.9	28.3	***2.21 [1.09, 4.48]***	***2.32 [1.06, 5.07]***
Smoking	14.9	26.2	***2.03 [1.00, 4.16]***	***2.20 [1.06, 4.57]***
Diabetes	4.8	15.8	***3.46 [1.26, 9.48]***	***3.69 [1.33, 10.25]***
≥1 major CV risk factor	61.3	83.6	***3.22 [1.52, 6.81]***	***3.65 [1.67, 7.99]***
Other conventional CV risk factors				
BMI<20 kg/m^2	10.1	8.2	0.79 [0.28, 2.26]	0.75 [0.26, 2.16]
BMI≥28 kg/m^2	22.0	42.6	***2.63 [1.40, 4.93]***	***2.88 [1.51, 5.49]***
Metabolic syndrome	9.5	32.8	***4.63 [2.20, 9.78]***	***4.97 [2.31, 10.69]***
MDRD GFR<60 ml/min	7.2	9.8	1.42 [0.51, 3.98]	1.38 [0.48, 4.02]
Alcohol use	47.0	5.0	***0.06 [0.02-0.20]***	***0.06 [0.02-0.19]***
Non conventional CV risk factors	76.2	77.6	0.88 [0.45, 1.73]	0.92 [0.46, 1.81]
Rheumatoid factor positive				

Continuous variables	Private mean (SD)	Public mean (SD)	p-value*	p-value†
Age, years	57.1 (11.8)	57.7 (11.5)	0.7	-
Major conventional CV risk factors				
T chol, mmol/l	4.9 (1.0)	5.2 (1.2)	0.05	0.04
LDL chol, mmol/l	2.8 (0.9)	2.9 (1.1)	0.3	0.2
HDL chol‡, mmol/l	1.61 (1.33)	1.55 (1.38)	0.4	0.4
T chol÷HDL chol‡	3.0 (1.3)	3.3 (1.4)	0.05	0.03
Non-HDL chol, mmol/l	3.2 (1.0)	3.6 (1.2)	0.02	0.01
Number of major risk factors	0.8 (0.8)	1.3 (0.8)	0.0003	<0.0001
Other conventional CV risk factors				
Triglycerides‡, mmol/l	1.0 (1.6)	1.6 (1.8)	<0.0001	<0.0001
AIMS tension	3.5 (1.9)	4.2 (2.2)	0.05	0.03
AIMS depression	2.2 (1.6)	3.6 (2.4)	0.0001	<0.0001
Height, cm	167.4 (8.9)	159.5 (10.7)	<0.0001	<0.0001
Non conventional CV risk factors				
DAS28	2.3 (1.5)	2.9 (1.2)	0.006	0.01
CRP‡, mg/l	3.6 (3.7)	6.1 (3.1)	0.003	0.003
HAQ-DI	0.44 (0.55)	0.85 (0.59)	<0.0001	<0.0001
Number of deformed joints	6 (8)	10 (9)	0.005	0.003

Significant (p≤0.05) associations between public healthcare attendance and cardiovascular risk factors in logistic regression models are shown in bold italic.
*unadjusted, †adjusted for age and gender, as well as statin use and use of antihypertensives upon assessment of the associations between public care attendance and lipid variables and pulse pressure, respectively, ‡geometric mean and SD are given in view of non-normal distribution.
OR: odds ratio; CI: confidence interval; CV: cardiovascular; T: total; chol: cholesterol; BMI: body mass index; MDRD: Modification of Diet in Renal Disease; GFR: glomerular filtration rate; AIMS: Arthritis Impact Measurement Scale; DAS: Disease Activity Score; HAQ-DI: Health Assessment Questionnaire disability index.

The relation of public healthcare attendance to atherosclerotic cardiovascular risk in caucasian patients with RA

To further evaluate the potential effect of the type of healthcare attendance independent of ethnicity, we compared cardiovascular risk in private and public healthcare caucasian patients (columns 2, 3 and 4 in Table III). Public healthcare strongly associated with not only hypertension but also each of the other major conventional risk factor (odds ratios ranging from 1.86 to 3.46), thereby translating into a markedly enhanced likelihood of having one or more such risk factors (OR [95% CI]= 3.22 [1.52, 6.81]) and mean (SD) number of such risk factors (p=0.0003). Non-HDL cholesterol concentrations were higher (p=0.02) in public healthcare caucasian patients. With the exceptions of underweight and chronic kidney disease, public care consistently associated with substantially less favorable other conventional and non-conventional risk factor profiles. Adjustment for age, gender and statin therapy when appropriate (column 5 in Table III) did not materially alter the associations of public healthcare attendance with adverse cardiovascular risk factor profiles in caucasians with RA.

The relation of public healthcare attendance to NCEP ATPIII defined metabolic cardiovascular risk among patients with RA

The NCEP ATP III guidelines currently recommend that apart from addressing the major conventional risk factors of hypertension, dyslipidemia, smoking and diabetes, subjects with the metabolic syndrome should be identified in CVD risk assessment and management (15). The MetS and its individual com-

ponents were recently documented to also associate with atherosclerosis in patients with RA (6, 10). The previous analyses revealed associations of public healthcare attendance with the MetS prevalence. Fig. 1 shows the relation of public healthcare attendance to NCEP ATP III defined individual metabolic risk factors. In all patients (upper panel in Fig. 1), public healthcare attendance independently associated with elevated triglyceride (OR [95% CI]=4.23 [2.83, 8.34]) and glucose concentrations (OR [95% CI]=3.04 [1.62, 5.68]). The mean number (SD) of metabolic risk factors was 1.4 (1.1) and 2.0 (1.1) in public and private healthcare patients, respectively (p<0.0001 in univariate and p=0.0004 in age, gender and ethnicity adjusted analysis). In sensitivity analyses in caucasians (lower panel in Fig. 1), public healthcare attendance independently associated with increased waist circumference (OR [95% CI]=2.13 [1.15, 3.95]), reduced HDL cholesterol concentrations (OR [95% CI]=2.18 [0.99, 4.79]) and elevated triglyceride (OR [95% CI]=5.59 [2.69, 11.64]) and glucose concentrations (OR [95% CI]=5.40 [2.52, 11.54]). The mean (SD) number of metabolic risk factors was 1.3 (1.1) and 2.2 (1.2) in private and public healthcare caucasian patients, respectively (p<0.0001 in both univariate and age, gender and ethnicity adjusted analysis).

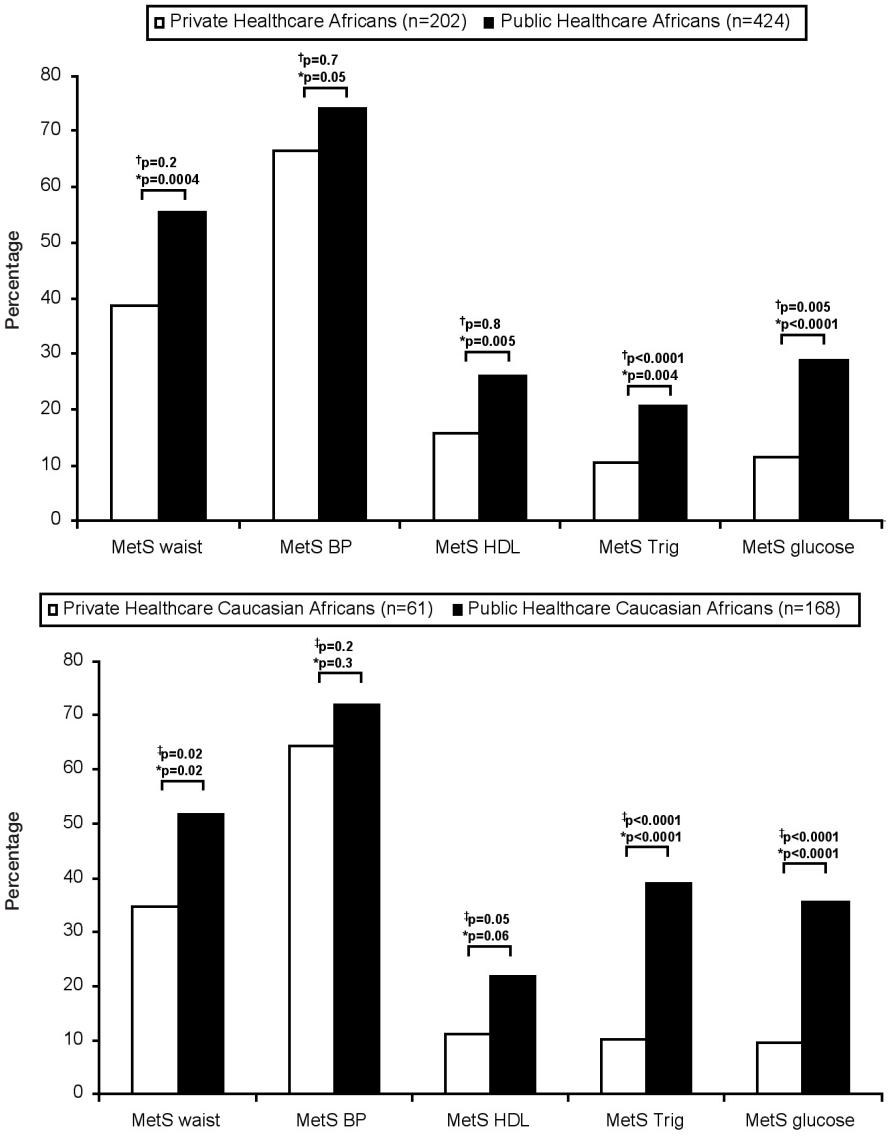

Fig. 1. Proportions of National Cholesterol Education Program Adult Treatment Panel III defined metabolic cardiovascular risk factors in all private and public healthcare Africans (upper panel) and in caucasian private and public healthcare Africans (lower panel) with rheumatoid arthritis.
*p-value in univariate analysis; †p-value in age, gender and black and caucasian ethnic origin adjusted analysis, ‡p-value in age and gender adjusted analysis.
MetS: metabolic syndrome; BP: blood pressure; HDL: high-density lipoprotein cholesterol; trig: triglycerides.

Discussion

Our main finding in the present study was that in patients with established RA, public healthcare attendance as an indicator of disadvantaged circumstances of life in our setting (30, 31, 33, 45) associated strongly with elevated conventional and non-conventional atherosclerotic CVD risk burdens. In adjusted analyses, patients seen in the public healthcare sector experienced a prevalence of hypertension that was increased by ~70% and that together with numerically increased frequencies of dyslipidemia, smoking and diabetes resulted in a higher mean number of major conventional CVD risk factors and an ~80% heightened likelihood of having one or more such risk factors. Moreover, public healthcare patients had higher metabolic cardiovascular risk and tension and depression scores, used alcohol less frequently, were 7 cm shorter and sustained increased non-conventional CVD risk that comprised heightened current and cumulative inflammatory burdens. Taking into account that atherosclerosis is prevalent in our private healthcare patients with RA as previously reported by us (5, 6, 8), our current findings indicate that patients with RA that attend the public healthcare sector are particularly in need of tight CVD risk management.

Most of our knowledge on CVD derives from studies performed in caucasian subjects living in developed countries (41). However, 80% of the CVD burden currently arises in middle and low income countries (41). Consequent to the ethnic grouping related differences in access to private medical schemes in our setting (30, 31, 33, 45), black and caucasian patients were most frequently seen in the public and private healthcare sector, respectively. The same phenomenon was recently reported in a study involving patients with RA in the

United States and documented to predict delayed disease modifying agent initiation (25). Nevertheless, we found that public healthcare attendance remained associated with enhanced conventional and non-conventional CVD risk burdens after adjustment for demographic characteristics that included ethnic origin. Moreover, in sensitivity analyses in caucasians, the association of public healthcare attendance with increased risk for atherosclerosis was even more consistent with odds ratios ranging from 2.06 to 3.69 for each of the modifiable major conventional risk factors including hypertension, dyslipidemia, smoking and diabetes.

Our findings that public healthcare caucasians experienced higher AIMS stress and depression, enhanced major and other conventional cardiovascular risk factor profiles as well as shorter stature than their private healthcare counterparts, suggest that the pathogenetic factors of the reportedly marked increase in incident coronary heart disease amongst socioeconomically deprived non-RA subjects in developed countries (17,18), are similarly important in patients with RA. We are currently testing this hypothesis.

Our study has strengths, limitations and implications for further investigations. We prospectively and comprehensively assessed CVD risk factor profiles in 626 patients with RA. Further, potentially important confounders were consistently taken into account upon investigating the relation of public healthcare attendance to CVD risk profiles and their global burdens. However, the cross-sectional design of our study precludes drawing inferences on the direction of causality. Due to the predominance of the black population and persistent major socioeconomic inequalities in South Africa (30, 31, 33, 45), despite enrolling 626 consecutive patients, only caucasians were seen in sufficient numbers in both the public and private healthcare sector to reliably assess the association of public healthcare attendance with cardiovascular risk in sensitivity analyses. Although we evaluated risk factors that included those that reportedly strongly predict CVD in not only the population at large but also patients with RA (1-12, 43, 44), we believe that our results set the stage for employing more direct measures of atherosclerosis in future studies that aim at investigating the impact of socioeconomic status on cardiovascular risk in this disease. Finally, whereas public healthcare attendance clearly reflects socioeconomic disadvantage in our context (30, 31, 33, 45), the use of measures including educational level, professional status, area of residence and income (19-28) would have the potential to allow for evaluating the effect of socioeconomic gradients on cardiovascular risk within different healthcare sectors. We are currently addressing these issues in our ongoing study.

In conclusion, we found that public healthcare attendance as an indicator of disadvantaged circumstances in life associated with markedly enhanced conventional and non-conventional risk burdens for atherosclerosis in RA independent of demographic characteristics. Since these relationships were even more consistent in sensitivity analyses in caucasians, our findings should also apply to patients with RA living in developed countries. Our results call for providing resources that are sufficient to permit rigorous CVD risk assessment and management in socioeconomically disadvantaged patients with RA.

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