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ORIGINAL RESEARCH

Changes in body weight and body composition in patients with active rheumatoid arthritis aged 65+ treated with 2-year low-dose add-on prednisolone in the randomised double-blind placebo-controlled GLORIA trial

Melek Güler-Yüksel ,[1] Martijn Kuijper,[1] Reinhard Bos,[2] Esmeralda Molenaar,[3] Jasper Emmering,[4] Sylvia Eshuis,[5] Adams Human,[6] Floor Reimann,[2] Maarten Boers ,[7] Marc R Kok [1]

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For numbered affiliations see end of article.

Correspondence to
Dr Marc R Kok;
kokmr@maasstadziekenhuis.nl

ABSTRACT

Objectives To investigate the effect of 2 years of add-on prednisolone 5 mg/day on body weight and composition in patients with active rheumatoid arthritis (RA) aged 65+ and the relation with disease activity.

Methods The Glucocorticoid Low-dose Outcome in Rheumatold Arthritis trial, a pragmatic, placebo-controlled, double-blind, randomised controlled trial investigated the balance of benefit and harm of 2 years of prednisolone 5 mg/day added to standard care in 451 patients with active RA aged 65+. In the current study, 449 patients were included, and body weight and Disease Activity Score of 28 Joints were measured at baseline and after 3, 6, 12, 18 and 24 months. In 57 patients, body composition was assessed at baseline and after 2 years with dual-energy X-ray absorptiometry. Data were analysed with longitudinal mixed models.

Results The mean (95% CI) change in body weight was 0.9 (0.3 to 1.6) kg in the prednisolone group and –0.4 (–1.1 to 0.2) kg in the placebo group (difference 1.3 (0.5–2.2), (p<0.01)). The treatment effect was independent of disease activity suppression and comprised mostly increase in (appendicular) lean mass after 2 years. There was no significant increase in total fat mass, nor redistribution of fat mass from peripheral to central tissues.

Conclusions Patients with active RA aged 65+ treated with prednisolone 5 mg/day for 2 years gained about 1 kg in weight, compared with minimal—non-significant—weight loss on placebo. Our data suggest that the small increase in weight is mostly lean mass, rather than increase or redistribution of fat mass traditionally associated with glucocorticoid treatment.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Randomised placebo-controlled trials on glucocorticoids in rheumatoid arthritis (RA) are rare and have only superficially examined changes in body weight during treatment, reporting 2-year gains between 1 and 5 kg in patients with early, active RA on prednisolone 5–10 mg/day.

WHAT THIS STUDY ADDS

⇒ We studied changes in body weight and body composition in the context of the Glucocorticoid Low-dose Outcome in Rheumatold Arthritis (GLORIA) trial, a large randomised placebo-controlled trial that studied the balance of benefit and harm of 2 years of prednisolone 5 mg/day added to standard care in patients with established, active RA aged 65+. Patients on prednisolone gained mean 0.9 kg, versus a loss of 0.4 kg in the placebo group, after 2 years. Changes in body weight were not significantly related to changes in disease activity. Body composition assessment suggests the gain was mostly lean body mass, rather than fat mass increase or redistribution.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ In the GLORIA study, there is only a small weight gain, compared with a non-significant weight loss, in patients with active, established RA aged 65+. This is in line with the main results of the GLORIA study showing a favourable balance of benefit and harm in this specific population of elderly patients with active, established RA. These findings are immediately applicable to clinical practice.

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterised by chronic inflammation of the joints leading to local cartilage and bone destruction, generalised bone loss and deterioration of the musculoskeletal system. Rheumatoid cachexia is a

Table 1 Baseline patient characteristics

	All patients included in the GLORIA study[22]		Patients with body composition analyses	
	Prednisolone (n=224)	Placebo (n=225)	Prednisolone (n=29)	Placebo (n=28)
Sociodemographic variables				
Female, n (%)	160 (71)	156 (69)	18 (62)	18 (64)
Age (years)	73 (5)	73 (5)	73 (5)*	75 (5)*
Weight (kg)	74.8 (13.3)	74.7 (13.8)	76.7 (12.2)	78.1 (12.3)
Height (cm)†	166 (9)	166 (10)	171 (9)*	168 (9)*
BMI (kg/m^2)	27.3 (4.5)	27.2 (4.4)	26.2 (3.3)*	27.7 (3.7)*
RA-related variables				
Disease duration (years)	11 (10)	10 (10)	16 (14)	9 (11)
IgM RF positive, n (%)†	148 (66)	151 (67)	18 (62)	14 (50)
ACPA positive, n (%)	119 (53)	134 (60)	16 (55)	13 (46)
IgM RF and ACPA positive, n (%)‡	106 (47)	115 (51)	14 (48)	10 (36)
DAS28†	4.4 (1.0)	4.6 (1.1)	4.0 (0.8)*	4.4 (0.9)*
HAQ‡	1.3 (0.7)	1.2 (0.7)	1.0 (0.6)	1.1 (0.6)
Previous glucocorticoid use, n (%)‡	105 (47)	105 (47)	12 (41)	11 (39)

Data are presented as mean (SD), unless otherwise specified.
*Trend (0.05<p<0.10) in difference between the prednisolone and placebo group within the group with body composition analyses.
†Statistically significant (p<0.05) in difference between the total group and the group with body composition analyses.
‡Trend (0.05<p<0.10) in difference between the total group and the group with body composition analyses.
ACPA, anticitrullinated protein antibodies; BMI, body mass index; DAS28, Disease Activity Score of 28 Joints; GLORIA, Glucocorticoid Low-dose Outcome in RheumatoId Arthritis; HAQ, Health Assessment Questionnaire; RA, rheumatoid arthritis; IgM RF, IgM rheumatoid factor.

condition characterised by loss of lean mass via energy hypermetabolism and decreased physical activity due to inflammatory activity and joint destruction, while fat mass is maintained.[1–4] Sarcopenic obesity, a syndrome characterised by progressive and generalised loss of skeletal muscle mass combined with increased fat mass, is also more prevalent in RA.[4–6] While loss of lean mass is resulting in less strength and physical disability,[5] more fat mass and in addition redistribution of fat mass from the peripheral to the centre (visceral) tissues contributes to the increased risk of metabolic syndrome and cardiovascular disease in RA.[7–11]

The last three decades have shown a significant improvement in treatment of RA due to earlier intensive use of disease-modifying antirheumatic drugs (DMARDs) combined with glucocorticoids as needed, coupled with implementation of the treat-to-target approach. Early and effective suppression of inflammation likely improves body composition directly, but also by improving physical activity. However, medication may also affect body composition: weight gain is one of the most common and feared patient-reported adverse event of glucocorticoids.[12] Clinical trials of prednisolone 5–10 mg daily in early, active RA reported gains between 1 and 5 kg in 2 years.[13–16] However, the effect of add-on low-dose prednisolone on body weight in elderly patients with established, active RA is unknown.

More importantly, the effect of low-dose prednisolone on body composition in RA still has to be unravelled. Whole-body dual-energy X-ray absorptiometry has made accurate assessment of body composition feasible at low cost and with low radiation doses; results correlate well with CT and MRI measurements.[17–19] Two small cross-sectional studies suggested an unfavourable effect of low-dose prednisolone on body composition in RA, but the changes in different components of body composition were inconsistent.[20 21] To date, no longitudinal data have been reported in this context, let alone trial data compared with placebo.

The current study is a secondary report and substudy of the placebo-controlled Glucocorticoid Low-dose Outcome in RheumatoId Arthritis (GLORIA) trial that assessed the balance of benefit and harm of 2 years of add-on prednisolone 5 mg daily in patients with active RA aged ≥65 years.[22] We report changes in body weight of the whole study population and relate these to changes in disease activity and changes in body composition in a subgroup of patients.

PATIENTS AND METHODS

Study design and study population

The GLORIA study is an investigator-initiated, double-blind, placebo-controlled, multicentre, randomised

Table 2 Changes in body weight and BMI after 2 years of prednisolone (5 mg/day) or placebo

	Prednisolone (n=224)	Placebo (n=225)	Difference between groups	P value
Body weight (kg)	0.9 (0.3–1.6)	–0.4 (–1.1 to 0.2)	1.3 (0.5–2.2)	<0.01
BMI (kg/m^2)	0.4 (0.1–0.6)	–0.1 (–0.4 to 0.1)	0.5 (0.2–0.8)	<0.01

Data are presented as mean (95% CI).
BMI, body mass index.

clinical trial performed in 28 clinical centres in 7 European Union countries, designed to assess the balance of benefit and harm of prednisolone 5 mg daily added to standard care during 2 years in patients with RA aged 65 years or older. Low-dose prednisolone use resulted in lower Disease Activity Score of 28 Joints (DAS28) and less progression of joint damage, with a trade-off of 24% increase in patients with—mostly non-severe—adverse events compared with placebo use.[22]

Body weight and body composition

In all patients, total body weight and height were measured in a standardised way: weight at 0, 3, 6, 12, 18, 24 months and height at 0 and 24 months. Body mass index (BMI) was calculated as total weight/baseline height^2 (kg/m^2). A total of 57 patients underwent body composition assessment at baseline—that is, before or shortly after the start of study treatment—and after 2 years in three clinical centres in the Netherlands (Maasstad Hospital, Medical Center Leeuwarden and Groene Hart Hospital) with Hologic Delphi (Hologic; Bedford, Massachusetts, USA). Body composition is expressed as fat mass, bone mass and lean (non-fat and non-bone) mass. Total fat mass is the sum of fat on trunk, arms, legs and head, also expressed as percentage of body mass (total fat mass/body weight), and as fat mass index (total body fat mass/height^2 (kg/m^2)). The distribution of fat is described by the ratio of trunk/appendicular (arm and leg) fat mass. Total bone mass is the sum of bone mass of trunk, arms, legs and head. Total lean mass is the sum of lean mass on trunk, arms, legs and head, also expressed as lean mass index (LMI; total body lean mass/height^2 (kg/m^2)); appendicular lean mass is also expressed in the corresponding index (ALMI; appendicular lean mass/height^2 (kg/m^2)).

Statistical analyses

Data are presented as mean (SD) or mean (95% CI) for normally distributed data, or as median (25th percentile–75th percentile) for skewed data. Baseline patient characteristics, as well as differences in these characteristics between groups (body composition vs total group), were analysed with simple descriptive statistics.

In the total group of patients, changes in body weight during 2 years of follow-up were analysed by a linear-mixed model. The model included weight measurements at all available time points up to 2 years (ie, 0, 3, 6, 12, 18 and 24 months). Weight measurements obtained after premature discontinuation of study medication were excluded from the analysis. The model included covariates for each time point and its interactions with treatment group as fixed effects. In addition, stratification factors that were used during the randomisation process, that is, previous use of glucocorticoids and start/switch of antirheumatic treatment at baseline, were included as fixed effects, whereas site was included as a random effect (random intercept). Correlation between residuals over time was modelled under the assumption of an unstructured covariance structure. The model was optimised with maximum likelihood. Hypotheses were tested by performing Wald tests on (linear combinations of) coefficients estimated by the model.

In the subgroup of patients with body composition analyses, between group differences in changes in body weight, BMI and body composition measures after 2 years were tested by the independent student's t-test.

The potentially confounding effect of cumulative disease activity on the relationship of weight change after 2 years (weight at 24 months minus baseline weight) with study treatment was analysed by a linear-mixed model. Baseline weight, treatment allocation, age, gender, cumulative disability (area under the curve (AUC)) of Health Assessment Questionnaire (HAQ) 0–2 years, cumulative disease activity (AUC of DAS28 0–2 years) and the interaction term treatment allocation–AUC DAS 0–2 years were included as fixed effects. In addition, the randomisation stratification factors were included as fixed effects or as random intercept (site). Because of missing data in both the outcome (weight change) and DAS28, multiple imputation using m=100 imputations was performed with available data on weight and DAS28 at intermediate time points as predictors, as well as all covariates in the model to ensure congeniality. Models were optimised with maximum likelihood, after which regression estimates were pooled by applying Rubin's rules.

To evaluate the mutual changes in body composition, given as the proportions total lean mass, total fat mass and total bone mass (adding up to 100%) of total body weight, log-ratio analyses were conducted to account for dependency of parts to the whole. For this, the logs of the ratios of two compartments (eg, total lean mass and total fat mass) compared with the reference compartment (eg, total bone mass) were calculated and modelled by a linear model for multivariable data. Similar log-ratio analyses were performed to evaluate changes in distribution of fat mass (eg, in the regions trunk, extremities and head). A more detailed description and rationale for

using log-ratio models for body composition data can be found elsewhere.[23]

The log ratios were modelled by a generalised least squares model, including the log-ratio as outcome and indicator variables for the two compartments, as well as its interactions with time (baseline and 24 months) and the three stratification factors as fixed effects. A Kronecker product correlation structure was used to allow a shared correlation parameter to be estimated for the correlation over time within compartments and a shared correlation parameter for the correlation between compartments within time points.[24] Heterogeneous variance was allowed for the two compartments. The model was optimised by maximum likelihood with the gls() function of the nlme package.[25] Hypotheses were tested by Wald χ^2 tests on linear combinations of the coefficients with the linearHypothesis() function of the car package.[26] The log-ratio analyses were conducted using R V.4.1.1.[27] Apart from the log-ratio analyses, all statistical analyses were performed with Stata V.14.2 (StataCorp, Texas, USA). For all analyses, a p value<0.05 was used to indicate statistical significance. No adjustments were made for multiple testing.

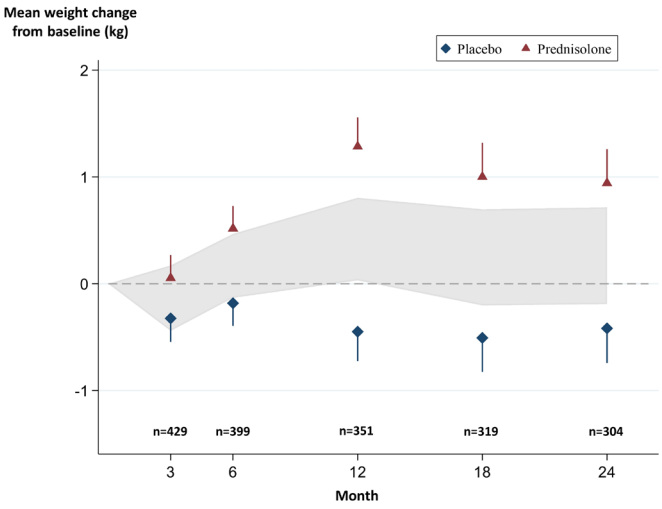

Figure 1 Changes in weight compared with baseline in the prednisolone (5 mg/day) and placebo group depicted in a 'null zone graph'. The null zone (grey area) is derived from the CI around the difference obtained from the t-test. There is a statistically significant difference in change in weight compared with baseline between the treatment groups when the mean of weight change of both groups falls outside the null zone; that is, from 6 months after starting treatment.[31]

RESULTS

Study population

In total, 451 patients were included and randomised to prednisolone or placebo. Two patients never started study medication and were excluded from the analyses, resulting in a total of 449 patients in the safety population (224 in the prednisolone group and 225 in the placebo group). Overall, 63% and 61% of the prednisolone and placebo group, respectively, completed the 2-year trial. Reasons for discontinuation were similar between the groups, mostly due to 'trial fatigue', COVID-related access issues and adverse events. Mean (SD) time on study medication for all patients was 19 (8) months. Good adherence was found in 89% of the prednisolone and 88% of the placebo patients.[22]

The treatment groups were well balanced at baseline. The majority of the patients were woman, mean age was 73 years, mean body weight 75 kg and mean BMI of 27 kg/m^2 (table 1). Patients had seropositive, established RA with a mean DAS28 of 4.5. Almost half of the patients had used glucocorticoids in the past. More details on demographics, previous and current DMARD use and on other concomitant medication and comorbidities have been described previously.[22]

A total of 57 patients included in 3 centres in the Netherlands received body composition analyses at baseline and after 2 years (29 in the prednisolone group and 28 in the placebo group). The body scans were performed at inclusion in the study —ie, before start study treatment— in 24 patients (42%) and in the other patients median 2 weeks after initiation (inner quartiles 1–4 weeks, maximum 62 days). The period between the two body scans was mean (SD) 23 (2) months.

Compared with the total GLORIA population, patients with body composition analyses were significantly taller and had a lower mean DAS28 (both p<0.05), with a trend (p<0.10) towards less rheumatoid factor and anti-cyclic citrulline peptidepositivity, lower HAQ and less previous glucocorticoid use (table 1). Within the group with body composition analyses, there were trends for lower age, higher height and lower BMI and DAS28 in the prednisolone group compared with the placebo group.

The pragmatic study protocol allowed adaptations in DMARD treatment and short-term use of open-label oral, intramuscular or local glucocorticoids for RA or other diseases when clinically necessary. The number of patients receiving short-term glucocorticoids for RA and the total number of administrations were slightly higher in the placebo group, and placebo patients received such short-term glucocorticoids on average more than 3 months earlier.[22]

Body weight changed by mean (95% CI) 0.9 (0.3 to 1.6) kg on prednisolone after 2 years, vs –0.4 (–1.1 to 0.2) kg on placebo, with a difference between treatment groups of 1.3 (0.5 to 2.2) kg (p<0.01; table 2). Likewise, BMI changed by 0.4 (0.1 to 0.6) kg/m^2 vs –0.1 (–0.4 to 0.1) kg/m^2 (difference 0.5 (0.2–0.8); p<0.01). The difference in weight change was significant starting at month 6 (figure 1). After 2 years, body weight increase>2 kg was observed in 40/136 (29%) patients in the prednisolone group compared with 23/126 patients (18%) in the placebo group (p=0.035). The increase in body weight after 2 years in the prednisolone group was not statistically different between patients with and without obesity (BMI ≥25 and BMI<25, respectively) at baseline (data not shown).

Table 3 Effect of variables on changes in body weight after 2 years: multivariable analysis

Variable	Changes in total weight after 2 years	
	Coefficient (95% CI)	P value
Prednisolone group	1.0 (0.1 to 2.0)	0.03
AUC DAS28 0–2 years	–0.8 (–1.6 to 0.1)	0.08
AUC DAS28 0–2 years–prednisolone group (interaction term)	0.5 (–0.5 to 1.5)	0.34
Combined test of AUC DAS28 0–2 years and interaction term (2df)		0.18
AUC HAQ 0–2 years	0.5 (–0.5 to 1.4)	0.34
Weight at baseline (kg)	–0.1 (–0.1 to –0.02)	<0.01
Female gender	–0.2 (–1.4 to 1.0)	0.76
Age (years)	–0.1 (–0.2 to –0.03)	<0.01

AUC, area under the curve; DAS28, Disease Activity Score of 28 Joints; HAQ, Health Assessment Questionnaire.

In multivariable regression analysis, higher age and weight at baseline were significantly associated with weight loss after 2 years, and prednisolone treatment remained significantly associated with weight gain with a coefficient (95% CI) of 1.0 (0.1 to 2.0) kg (table 3). However, the effect of AUC DAS28 0–2 years was not significantly associated with weight change (combined test of main effect and interaction p=0.18 (2df)).

Regarding body composition, 2 of 57 patients discontinued study medication prematurely and were excluded. The between-group difference in weight change resembled that seen in the total group (table 4). The change in body composition after 2 years was different in prednisolone compared with placebo patients (log-ratio analysis, p=0.02). Prednisolone patients showed small but favourable changes in body composition, that is, lean mass increases exceeding fat mass increases, with trends in differences for total lean mass and LMI, and even significant differences for appendicular lean mass (p=0.02), and its corresponding index (ALMI; p<0.01). No differences in change were seen in total fat mass; nor in fat distribution over the body, that is, trunk, extremities and head (log-ratio analysis, p=0.93).

DISCUSSION

In a controlled trial setting, we found that patients with established, active RA aged 65+ treated with prednisolone 5 mg daily for 2 years gained about 1 kg in weight, compared with minimal weight loss on placebo. Study of body composition in a subgroup suggested that the weight gain is in lean body mass, rather than increase or redistribution of fat mass traditionally associated with glucocorticoid treatment.

Weight gain is a notorious side effect of glucocorticoids in treatment of rheumatic diseases, feared by patients and doctors alike.[12 28] Previous trials in early RA with maintenance doses of 5–10 mg/day showed mean 1–5 kg increases in 2 years.[13–16] Our findings in the lower end of this spectrum might be explained by older age,

Table 4 Changes in body composition components after 2 years of prednisolone (5 mg/day) or placebo

	Prednisolone (n=28)		Placebo (n=27)			
	Baseline	2-year change	Baseline	2-year change	Difference in change	P value
Body weight (kg)	77.4 (13.3)	0.9 (–0.5 to 2.3)	79.0 (12.2)	–0.7 (–2.2 to 0.7)	1.6 (–0.4 to 3.6)	0.12
BMI (kg/m^2)	26.5 (3.7)	0.4 (–0.1 to 0.9)	28.3 (3.2)	–0.3 (–0.8 to 0.2)	0.7 (–0.1 to 1.3)	0.09
Body composition						0.02*
Total fat mass (kg)	28.8 (8.6)	0.3 (–0.7 to 1.2)	29.4 (7.0)	–0.4 (–1.4 to 0.6)	0.7 (–0.7 to 2.1)	
Total lean mass (kg)	46.4 (9.0)	0.7 (–0.1 to 1.4)	47.3 (10.3)	–0.3 (–1.1 to 0.5)	1.0 (–0.1 to 2.1)	
Total bone mass (kg)	2.2 (0.5)	–0.008 (–0.05 to 0.03)	2.3 (0.5)	0.03 (–0.008 to 0.07)	-0.04 (–0.02 to 0.1)	
Body composition in detail						
Fat mass						
% total body fat	37.0 (7.6)	–0.1 (–0.8 to 0.6)	37.4 (7.5)	–0.2 (–0.9 to 0.5)	0.1 (–0.9 to 1.1)	0.89
Ratio trunk/appendicular	1.06 (0.30)	–0.01 (–0.04 to 0.02)	1.09 (0.23)	–0.02 (–0.05 to 0.02)	0.00 (–0.04 to 0.05)	0.85
FMI (kg/m^2)	9.9 (3.1)	0.1 (–0.2 to 0.4)	10.6 (2.6)	–0.2 (–0.5 to 0.2)	0.3 (–0.2 to 0.7)	0.30
Lean mass						
Appendicular (kg)	18.5 (4.1)	0.4 (0.0 to 0.8)	19.4 (5.0)	–0.3 (–0.8 to 0.2)	0.7 (0.1 to 1.4)	0.02
LMI (kg/m^2)	15.8 (2.1)	0.3 (0.0 to 0.5)	16.8 (2.7)	–0.1 (–0.4 to 0.2)	0.4 (0.0 to 0.7)	0.05
ALMI (kg/m^2)	6.3 (1.0)	0.2 (0.0 to 0.3)	6.9 (1.4)	–0.1 (–0.3 to 0.0)	0.3 (0.1 to 0.5)	<0.01

Data are presented as mean (SD) or mean (95% CI), unless otherwise specified.
*Overall test for change in body composition (log-ratio analysis).
ALMI, appendicular lean mass index; BMI, body mass index; FMI, fat mass index; LMI, lean mass index.

established RA with moderate disease activity, more joint damage due to RA and osteoarthritis and other comorbidities.

High inflammatory disease activity is associated with significant more body weight loss, probably by hypermetabolism, and increases the likelihood of developing rheumatoid caxechia.[1–4] This suggests that prednisolone might have, besides a direct (increasing) effect, also an indirect (less decreasing) effect on weight due to effective suppression of inflammatory disease activity compared with placebo. In our study, such an indirect effect was not detectable, that is, the AUC of DAS28 was not a significant predictor when treatment and the interaction term were analysed in the model. This may be due to low power in the setting of a limited range of disease activity, but it could also be that such indirect effects of glucocorticoids are apparent only at higher levels of disease activity. Unfortunately, the number of body composition measurements was too small to study the effects of changes in inflammatory disease activity on body composition.

Very little is known about the effect of glucocorticoid use on changes in body composition in RA. Only one longitudinal clinical trial studied the effect of changes in body composition in patients with RA treated with different strategies including—higher dosages of— prednisolone.[23] Patients with recent-onset, active RA were randomised to either prednisolone 60 mg/day tapered to 7.5 mg/day in 6 weeks, methotrexate and sulfasalazin (COBRA) or prednisolone 30 mg/day tapered to 7.5 mg/week in 8 weeks and methotrexate (COBRA-light). After 26 weeks of treatment, patients in the COBRA group gained numerically more weight than those in the COBRA-light group (mean 2.1 vs 1.1 kg, p=ns). Remarkably, gains were caused by increases in fat mass. However, no redistribution of fat was seen.

In our study, add-on low-dose prednisolone caused small favourable changes in body composition, predominantly increased total and appendicular lean mass without significant changes in total fat mass, body fat percentage or redistribution of fat mass. Differences in dosing, population and time horizon are the most plausible explanations for the difference between our results and the COBRA-light study. The initially high, slowly tapered course of prednisolone in the COBRA and COBRA-light protocol might have biochemically different effects on body composition than low-dose prednisolone daily 5 mg in patients with active RA. Furthermore, differences in characteristics of the study populations might also explain the differences in body composition changes over time. The COBRA-light study studied recent-onset, more active, less damaged younger (mean age 51 years) patients with RA and reported changes in body composition after only 26 weeks of treatment.

In observational research, a recent review including 2240 middle-aged and older patients with RA showed that glucocorticoid use was associated with sarcopenia, whereas biological or targeted synthetic DMARD use was not, and conventional synthetic DMARD use might be even protective against sarcopenia.[29] In our placebo-controlled study, 2-year low-dose prednisolone was associated with predominantly lean mass, and not fat mass, increase. Apart from the study medication, most patients were on conventional DMARDs, mostly methotrexate, and only 15% used biological DMARDs, mostly tumor necrosis factor alpha inhibitors. Although more treatment switches were seen in the placebo group, no differences in DMARD treatment emerged between the treatment groups,[22] making it unlikely that treatment other than study treatment was of influence on weight and body composition. The problem with observational research, especially on the harms of glucocorticoids, is that these studies are irreparably confounded by indication.[30] Stated briefly, given the strong negative sentiments surrounding chronic glucocorticoid therapy, such treatment will only be instituted in patients with a poor prognosis (ie, severe and active RA). Such patients are at risk of a poor outcome regardless of treatment, but such outcomes are all attributed to glucocorticoids.

Strengths of this study include the prospective, randomised and placebo-controlled trial design and long follow-up in elderly patients with RA. A limitation is the relatively small proportion of the total GLORIA study population analysed for body composition, because only three centres in the Netherlands were able to participate. Because selection was not based on disease-related factors and randomisation was stratified by centre, the treatment contrasts are most likely generalisable to the whole study population. Further, a small majority of the patients underwent their initial body scan shortly after baseline, however, only median after 2 weeks. Finally, no data on diet and general physical activity was collected.

In conclusion, in established, active patients with RA aged 65+, 2 years of add-on prednisolone 5 mg daily caused a small weight gain, most likely a beneficial increase in (appendicular) lean mass. No unfavourable changes in body composition such as increase or redistribution of fat mass were found. Further research is needed to unravel the effects of different (cumulative) dosages of glucocorticoids on body composition.

Author affiliations
[1]Department of Rheumatology and Immunology, Maasstad Hospital, Rotterdam, The Netherlands
[2]Department of Rheumatology, Medical Centre Leeuwarden, Leeuwarden, The Netherlands
[3]Department of Rheumatology, Groene Hart Hospital, Gouda, The Netherlands
[4]Department of Radiology and Nuclear Medicine, Maasstad Hospital, Rotterdam, The Netherlands
[5]Department of Nuclear Medicine, Medical Centre Leeuwarden, Leeuwarden, The Netherlands
[6]Department of Nuclear Medicine, Groene Hart Hospital, Gouda, The Netherlands
[7]Department of Epidemiology & Data Science, Amsterdam UMC Locatie VUmc, Amsterdam, The Netherlands

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Contributors MG-Y: Concept, data curation, analysis, data collection, methodology, supervision, visualisation and writing draft. MK: Data curation, analysis, methodology, visualisation and writing draft. RB: Data collection. EM: Data collection. JE: Data collection. SE: Data collection. AH: Data collection. FR: Data collection. MB: Concept, data curation, analysis, funding, data collection, methodology, supervision, visualisation and writing draft. MRK: Concept, data collection, supervision and writing draft

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Competing interests MG-Y, MK, RB, EM, JE, SE, AH and FR: None. MB: Novartis. MRK: Galapagos, Lilly, Novartis.

Patient consent for publication Consent obtained directly from patient(s)

Ethics approval This study involves human participants and was approved by Ethics Committee (Medisch Ethische Toetsingscommissie) VU Medisch Centrum, Amsterdam, Netherlands. ID reference number: 2015.471NL55263.029.15. Participants gave informed consent to participate in the study before taking part.

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ORCID iDs
Melek Güler-Yüksel http://orcid.org/0000-0002-6071-0261
Maarten Boers http://orcid.org/0000-0002-6969-283X
Marc R Kok http://orcid.org/0000-0003-2394-6926

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