How Do Glucocorticoids Used in Rheumatic Disease Affect Body Weight? A Narrative Review of the Evidence

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Glucocorticoids (GCs) are widely used to effectively treat inflammatory disease, but GCs have a number of recognized side effects. Patients and clinicians view these side effects differently, with clinicians most concerned with serious side effects such as osteoporosis and diabetes mellitus. Consequently, these side effects are well researched with clinical guidelines and recommendations. A side effect of particular concern to patients is weight gain, but this topic has not been well researched, and consequently clinicians find it difficult to provide patients with accurate information about the potential of weight gain. The aim of this review is to provide an overview of GC use specifically in rheumatic disease, patient views on GC therapy, and GC-induced weight gain. We will discuss the evidence, including the extent and the impact of weight gain on the patient, and highlight areas that warrant further investigation.

Introduction

Since their introduction in 1948 (1), glucocorticoids (GCs), or steroids, have been widely used to treat inflammatory disease. Despite their clinical effectiveness, there are many recognized adverse effects of concern to both patients and clinicians. Informed treatment decisions by patients and clinicians are based on the balance of GC benefits and harms (2,3). These decisions require information on the probability and nature of the benefits and harms (e.g., the onset, duration, and reversibility of the adverse effect) and are subject to a value judgement, a construct of how important the outcome is to the individual (4). While clinicians may view certain adverse events as nonserious and thus of less importance, patients may judge these differently. Patient attitudes toward GC-associated adverse effects have previously been shown to differ from those of clinicians (5). One side effect of particular concern to patients is weight gain (6,7). In clinical practice, patients commonly decline GCs because of concerns about weight gain, even when potential benefits are high and clinicians believe the benefit/harm balance is favorable.

The impact of GCs on body composition can be profound. In humans, this impact results in central deposition of adipose tissue, with a marked catabolic effect on bone and muscle. A number of mechanisms are proposed, with the final impact being determined by the combination of these (Figure 1). The actions of GCs include an increase in appetite, insulin resistance at the liver, which impairs effective management of excess calorie intake and promotes a liver lipogenic program, and catabolic actions on bone and muscle, which mobilize amino acids for gluconeogenesis in the liver. Additionally, relevant actions include suppression of the reproductive axis, resulting in sex steroid deficiency, which further impacts muscle mass and function. The GC dose relationship to these effects is complex, reflecting the large variation in GC sensitivity seen in individuals. In a systematic review, a dose-response relationship of oral GCs was not found on energy intake, appetite, and body weight or body composition. The authors suggested that duration was important, with short-term therapy having small increases in energy intake but not in weight gain, and longer-term GC therapy resulting in clinically significant weight gain (8). Adverse effects are thought to be more significant at daily dose-equivalent exposures of >5 mg prednisolone (9), with adverse effect risk appearing to rise as an exponential to the daily GC dose (10,11).

In this review, we provide an overview of GC use specifically in rheumatic disease, patient views on GC therapy, and GC-induced weight gain. We discuss the evidence found during our literature search (for search strategy, see Supplementary Appendix A, available on the Arthritis Care & Research web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.23879/abstract), including the extent and the impact of weight gain on the patient. We highlight...
areas that warrant further investigation to aid informed treatment decisions, for both the clinician and patient, regarding weight gain.

**GC utilization in rheumatic disease**

GCs are an effective treatment for various inflammatory and autoimmune disorders. An estimated 0.85% of the adult general population have received oral GCs at some time and 0.75% are prescribed GCs for at least 3 months (12). Respiratory disease and rheumatic diseases were the most frequently recorded indications for both long-term and overall GC therapy (12,13). GC therapy prescribed for rheumatic conditions for <30 days is uncommon (14). Specifically for inflammatory musculoskeletal conditions, there are reports of up to 2 in every 3 patients with rheumatoid arthritis (RA) ever using GCs (15-17). Current guidelines from the European League Against Rheumatism (EULAR) still advocate their use in early RA because of their powerful and rapid efficacy (18). Uptake in systemic lupus erythematosus exceeds 70% (19), with near universal use in conditions such as vasculitis and polymyalgia rheumatica (20). This widespread use of GC therapy reflects their efficacy. However, GCs are also well known for a range of adverse effects associated with dose, duration, and timing, including osteoporosis and fracture, infection, diabetes mellitus, cataracts, glaucoma, weight gain, adrenal insufficiency, skin changes, and cardiovascular disease. These effects have been reviewed widely elsewhere (21). The safety of certain GC-associated adverse events is far more widely studied and understood than for others. For example, there is much research investigating GC-induced osteoporosis and fractures, supporting numerous clinical guidelines and recommendations (American College of Rheumatology recommendations [22]; National Institute for Health and Clinical Excellence guidelines). Yet for other events such as weight gain and insomnia, 2 of the side effects that patients are most concerned about (6,7), much less is known. So how do patients currently view GC treatment and this potential side effect in the absence of good evidence?

**Patient beliefs about GC treatment**

Evidence about patient beliefs toward medication shows patients express a high level of perceived need for GC treatment but also a high level of concern for treatment consequences (23-26). A survey of GC users in France found 86% considered GCs to be efficient and 68% considered GCs unsafe (24). Of 98 systemic sclerosis patients, 73% showed concern for adverse consequences, with 82% worried about the long-term effects of GCs (26).

Larger clinical trials show low withdrawal rates due to reasons other than adverse medication effects but rarely include further details (27-30). Both in the Circadian Administration of Prednisolone in Rheumatoid Arthritis trial (26), and in the more recent Giant-Cell Arteritis Actema trial (30), patient withdrawals did not include detailed reasons. Bakker et al (29) reported that of 108 of the 347 patients starting the Computer Assisted Management of Rheumatoid Arthritis (CAMERA) trial, 80% withdrew because of potential GC use and 20% due to time constraints. In the West of Scotland Early Rheumatoid Arthritis Corticosteroid Trial...
(WOSERACT), a randomized clinical trial (RCT) of low-dose prednisolone compared to placebo, of 247 RA patients eligible, 19% (46 of 247) chose not to take part in the trial due to concerns over the prospect of taking GCs (28). A cross-sectional survey conducted in 2 WOSERACT outpatient clinics in Glasgow investigated attitudes toward GC treatment. Researchers found that 68% of patients (100 of 148) with RA were unwilling to be treated with oral GCs, and when asked to list known side effects, weight gain was the side effect listed most often by respondents (31).

**Patient beliefs about weight gain**

Patients’ concerns about GC treatment have been shown to be different from those of clinicians. In a study from 2010, the risk of osteoporosis, cardiovascular disease, and diabetes mellitus were ranked in the top 5 most worrisome adverse effects by both patients and clinicians. Weight gain was ranked the fourth most worrisome adverse effect by patients but only the sixth most worrisome for clinicians (5). As shown in a cross-sectional study investigating attitude toward GC use, GC-naive patients considered weight gain as a major side effect, more so than osteoporosis (78% [116 of 148] versus 10% [15 of 148]) (31). A recent survey of online health community users in the UK who reported GC use found that weight gain was the side effect most important to users (7). Similarly, in a survey of patients with antineutrophil cytoplasmic antibody–associated vasculitides from the UK, Canada, and the US who used GCs also found that weight gain and change in appearance were widely described as salient side effects across all countries (33).

Further evidence from social media indicates concerns from GC-treated patients about weight gain that may otherwise be unreported. PatientsLikeMe is a patient-powered network where patients contribute health and well-being information in real time to inform other patients and aid research. At the time of writing (March 2018), of all prednisone-treated patients, irrespective of indication (n = 4,950), the most commonly reported side effects were weight gain (n = 435) and increased appetite (n = 108). In patients with RA only (n = 271), weight gain (n = 85) and increased appetite (n = 21) were again the most commonly reported adverse effects (https://www.patientslikeme.com/treatments/show/139-prednisone-side-effects-and-efficacy?brand=f). Analysis of public discussions on social media platforms such as Facebook and Twitter can also be informative and has proven a useful tool to support pharmacovigilance by highlighting patterns not seen in spontaneous reporting from clinicians (34). In a recent study of Twitter posts mentioning prednisolone or prednisone, insomnia and weight gain were the most commonly discussed adverse events (6).

This evidence supports the idea that weight gain is a common side effect of importance to patients and influences patient decision-making. Accurately describing to patients when this weight gain may occur would be valuable, as well as discussing for how long and whether weight gain returns to baseline following GC cessation and at what rate. The following sections describe the current evidence.

**Probability and extent of weight gain**

When reviewing the literature on the extent of weight gain in GC-treated RA populations and indeed for other nonrheumatic disease populations (8), the extraction of this outcome and comparability is difficult between studies, with some reporting mean weight gain (28,29,35–38) or others reporting the proportion of individuals experiencing weight gain (35,39) or weight gain in terms of total fat mass (40). In the group of RCTs investigating the efficacy of GCs, reporting weight gain as an adverse event over a similar time period, weight gain findings were inconsistent. A mean weight change ranging between no change to a weight gain of 5 kg was reported in GC-treated groups, compared to no change to a 3 kg weight gain in the untreated groups over 1–2 years (28,29,35–38) (Table 1). Two further RCTs reported the proportion of patients with weight gain. In the active treatment group, 4 of 80 gained weight, and none had weight gain in the placebo group (35). In another, 8 of 98 patients in the treatment arm gained weight (39), with both studies omitting to report the extent of weight gain. One study as part of the larger multicenter Combinatietherapie Bij Reumatoïde Artritis (COBRA) light trial (40) reported that in the GC-treated group of 38 prednisolone-naïve early RA patients total body mass increased by 1.6 kg and total fat mass by 1.3 kg. At 26 weeks, the prevalence of overweight and obesity increased to 50% and 13%, respectively.

The comparison of studies on weight gain and GC use is further complicated by the complex nature of the dose and duration of GC use and how this usage is measured and reported. Most of the RCT examples above used GC doses ranging from 5 mg to 10 mg, where weight gain in the treated group (prednisolone exposure of 7.5 mg, considered a low dose), ranged from no weight gain (36) to 4 kg (26) and 5 kg (35). The RCTs using a dose of prednisolone higher than 10 mg indicated weight gain of mean ± SD 2.9 ± 4.2 kg (29) and change of weight from mean ± SD 77 ± 19 kg to 80 ± 20 kg (37). These studies tapering from 60 mg to 7.5 mg, considered a high dose of prednisolone, showed weight increases of 2.5 kg (95% confidence interval [95% CI] 1.8, 3.2) (38) and mean ± SD body mass index change from 25.7 ± 4.0 kg/m² to 26.3 ± 4.2 kg/m² (40) (Table 1). There was no clear dose-response evidence from RCTs, although across all doses there were significant weight increases. The greatest difference between groups was 4.7 kg in the study of 5 mg prednisolone versus placebo over a 2-year period (35) (Table 1).

Cohort studies include patients on a wide range of dosages and, in theory, thus allow comparison between different real-world dosages and their impact on weight gain. There is some evidence from observational research to suggest a dose-response relationship. A study of patients with RA found increased frequency...
| Study type | Author, year (ref.) | Population | Aim | No. | Prednisolone exposure | Length of follow-up | Mean weight change at end of follow-up | How weight was measured |
|------------|---------------------|------------|-----|-----|-----------------------|---------------------|--------------------------------------|------------------------|
| RCT        | Kirwan, 1995 (36)   | RA, duration <2 years | Efficacy of GCs | Prednisolone (n = 61), placebo (n = 67) | 7.5 mg; low dose | 2 years | No significant increase in weight | Measured at each study visit |
| RCT        | Hickling, 1998 (45) | RA, duration <2 years | To report response to prednisolone discontinuation | Prednisolone (n = 36), placebo (n = 39) | 7.5 mg; low dose | 3 years | By 3 years prednisolone group lost 3.1 kg (95% CI 1.9, 4.3) vs. placebo 1.5 kg (95% CI 0.3, 2.7) | Measured at each study visit |
| RCT        | Boers, 1997 (38)    | RA, duration <2 years | Efficacy of GCs | Prednisolone (n = 77), placebo (n = 79) | 60 mg tapered to 7.5 mg at week 6 until week 28 when prednisolone was stopped; high dose | 56 weeks | Weight increase at 28 weeks: significant difference between groups: 2.5 kg (95% CI 1.8, 3.2) in GC group and 0.7 kg (95% CI −0.2, 2.2) in placebo group; weight gain at 56 weeks: no significant difference | Measured at each study visit |
| RCT        | Wassenberg, 2005 (35) | RA, duration <2 years | Efficacy of GCs | Prednisolone (n = 80), placebo (n = 86) | 5 mg; low dose | 2 years | Prednisolone +5 kg; placebo +0.3 kg | Measured at each study visit |
| RCT        | Van Everdingen, 2002 (37) | RA, duration <1 year | Efficacy of GCs | Prednisolone (n = 40), placebo (n = 41) | 10 mg; low dose | 2 years | Prednisolone significant increase from 77 ± 19 kg to 80 ± 20 kg; placebo no significant change | Measured at each study visit |
| RCT        | Capell, 2004 (28)   | RA, duration <3 years | Efficacy of GCs | Prednisolone (n = 84), placebo (n = 83) | 7 mg; low dose | 2 years | Prednisolone 4 kg; placebo 3 kg | Measured at each study visit |
| RCT        | Bakker, 2012 (29)   | RA, duration <1 year | Efficacy of GCs | Prednisolone (n = 117), placebo (n = 119) | 10 mg; low dose | 2 years | Prednisolone 2.9 ± 4.2 kg; placebo 1.3 ± 5.3 kg | Measured at each study visit |
| RCT        | Wung, 2008 (42)     | Severe GPA | To assess the quantity, duration, and progression of weight change in patients who received GCs for active GPA under WGET protocol | n = 157, all used prednisone | 1 mg/kg/day tapered to nothing over 12 weeks, restarted if disease flares; low dose | 1 year | 3.9 ± 6.9 kg (4.4% increase), 38 patients (24%) gained ≥10 kg | Measured at each study visit |

(Continued)
| Study type | Author, year (ref.) | Population | Aim | No. | Prednisolone exposure | Length of follow-up | Mean weight change at end of follow-up | How weight was measured |
|------------|---------------------|------------|-----|-----|-----------------------|--------------------|----------------------------------------|----------------------|
| RCT substudy | Konijn, 2016 (40) | Early RA | To investigate effect of high-down and step-down prednisolone regimens on body composition | n = 108; n = 38 with DXA scan at start of treatment | Prednisolone 60 mg/day, tapered to 7.5 mg/day in 6 weeks; MTX and SSZ; prednisolone 30 mg/day, tapered to 7.5 mg/day in 8 weeks and MTX high dose | 26 weeks | Total body mass increase 1.6 kg; total fat mass increase 1.3 kg; BMI increased from 25.6 to 26.2 in glucocorticoid-treated patients; prevalence of overweight increase and obesity relative to baseline | Measured at baseline (before or soon after treatment) and after 26 weeks |
| RCT | Verschueren, 2017 (39) | Early RA | To compare the effectiveness of different initial csDMARD combinations, with or without GC remission 52 weeks after treatment initiation | High risk n = 289: COBRA classic: MTX, SSZ + weekly step down prednisolone n = 98; COBRA slim: MTX + weekly step down prednisolone n = 98; COBRA avant-garde: MTX, LEF + weekly step down prednisolone (30–5.5 mg) n = 93; low risk n = 90, COBRA slim n = 43, MTX no GC n = 47 | COBRA classic: 60–7.5 mg. COBRA slim and COBRA avant-garde: 30–5.5 mg; high dose | 2 years | Not given, only number with weight gain | Asked about AEs at each visit, including weight gain |
| Cohort | Pincus, 2013 (44) | RA | Analysis of prednisolone treatment over 25 years | n = 290 | Various | 25 years | 2.7 kg in those monitored 1 year or less; no change if monitored for >1 year | Measured at clinic visits |
| Cohort | Curtis, 2006 (11) | GC users | Assessing prevalence of adverse events, dose, and duration dependence | n = 2,167 | Various | 18 months | 60–80% reported weight gain; weight gain increased with increased cumulative dose | Self-reported |
| Register | Huscher, 2009 (41) | RA | Patterns relating frequency of adverse effects to dosage and duration | GC use for >6 months (n = 472); no GC use in past 12 months (n = 307) | Various | 12 months | No GC use: 9.5% reported weight gain; GC users: <5 mg/day, 8.7%; 5–7.5 mg/day, 22.4%; and >7.5 mg/day, 21.3% reported weight gain | Self-reported |

* RCT = randomized clinical trial; RA = rheumatoid arthritis; GC = glucocorticoid; 95% CI = 95% confidence interval; GPA = granulomatosis with polyangiitis; WGET = Wegner’s Granulomatosis Etanercept Trial; DXA = dual x-ray absorptiometry; MTX = methotrexate; SSZ = sulfasalazine; BMI = body mass index; csDMARD = conventional synthetic disease-modifying antirheumatic drug; COBRA = Combinatietherapie Bij Reumaatode Artritis trial; LEF = leflunomide.
of reported weight gain at higher doses, with ~20% of patients reporting weight gain at prednisolone doses of 5 mg/day or more versus <10% reporting weight gain at <5 mg/day or no prednisolone in the past 12 months (41). Curtis et al (11) reported that in long-term users of GCs with a variety of conditions, there were significantly increased odds of reporting weight gain, at cumulative doses >1.7 grams compared to cumulative doses <1.7 grams, with odds ratios (ORs) increasing with higher cumulative doses compared to <1.7 grams, from OR 1.42 (95% CI 1.08, 1.85) at 1.7–2.8 grams to OR 2.20 (95% CI 1.65, 2.95) at >4.7 grams. One significant challenge in observational analyses is that GC treatment is often dynamic, with dosages changing through time, and weight is measured at infrequent and sporadic intervals. Few statistical models are yet able to consider the impact of time-varying exposure on a continuous outcome through time. While RCTs commonly study a fixed dose and collect outcome data at fixed intervals, thereby potentially allowing the examination of trajectories of weight gain, they often only report weight gain from baseline to the end of the study.

### Time scale of weight gain and loss

The timescale and pattern of weight gain following GC exposure is not well defined in the literature. In clinical trials, those patients reporting a 5-kg gain over 2 years could, for example, represent a gain in the first month then plateau, or they could be indicative of a steady increase over the 2-year period. In a cohort study, Curtis et al (11) found that a high percentage of long-term GC users reported very bothersome weight change at all quartiles of cumulative prednisone-equivalent GC dosage, which may indicate weight change occurring early in a GC course. Data from 3 trials showed that weight gain occurred, all showing that weight gain occurred early after GC initiation. Data from the Wegner’s Granulomatosis Etanercept Trial (WGET) showed that weight gain occurred in the first 9 months and plateaued up to the end of follow-up at 1 year (42). In COBRA, weight gain was significantly higher in the prednisone group at 26 weeks but not at 56 weeks, perhaps indicating a plateau of weight gain, although prednisolone was tapered in most patients after 28 weeks (38,42). In the CAMERA-II study, body mass index (BMI) was found to increase over time, but the amount by which BMI increased diminished over time. However, the change in weight was explained by disease activity rather than treatment with GCs (43). A cohort study followed 290 prednisolone-treated RA patients at a single clinic and showed that those treated for ≤1 year had an increase in mean weight of 2.7 kg at the last visit. Those treated for >1 year, however, had a lower mean weight at the last visit compared to baseline (44). Not all evidence supports early weight gain; an online survey found that the prevalence of weight gain increased with increasing duration of exposure to GCs; of those patients exposed <15 days, 11% reported weight gain compared to 60% of those exposed for >6 months (24).

### Weight loss following discontinuation of steroids

Only a few studies have described weight loss following discontinuation of GCs. One study followed patients in a clinical trial for a year after finishing study treatment. During the trial, patients were randomized to either 7.5 mg prednisolone or placebo and were treated for 2 years, during which time there was no significant difference between the groups in terms of weight gain. A year after finishing the study treatment, the prednisolone group had lost on average 3.1 kg, and the placebo group’s weight had increased by 1.5 kg (45). Data from WGET followed a proportion of patients to 2 years or further. In those who achieved remission, weight gained during the first year was maintained. In those who had disease flares and were treated with GCs and cyclophosphamide, the mean weight gain was 1.03 kg (42).

The evidence around weight gain after GC initiation and weight loss after GC discontinuation gives some indication of effects. Some evidence exists, for example, that weight gain may occur early after GC initiation and may be linked to dose and disease activity, but clearly there is a need for more longitudinal studies to understand weight gain over time, both during and after GC treatment.

### Impact of weight gain

As mentioned above, understanding drug safety and decision-making require consideration not just of the likelihood and extent of side effects, but also the impact that such adverse events might have on individuals. This impact in turn will affect patients’ value judgements and decision-making. The impact of GC-induced weight gain has received relatively little attention, despite studies reporting its importance to patients (11,46). For example, over 40% of patients with RA considered weight gain as “most bothersome in everyday life and ascribed to glucocorticoids” compared to other listed adverse effects (46).

Weight gain can have both physical and psychological impact. Obesity is linked to an increased risk of comorbidities such as type 2 diabetes mellitus, cancer, and cardiovascular disease (47). It also has negative consequences for psychological concepts such as body image and self-esteem. In a meta-analysis, overweight individuals were shown to have low self-esteem, with a stronger relationship in those perceiving themselves as heavy rather than individuals who actually are overweight (48). Body image may be regarded as a multifaceted construct composed of an individual’s misconception of their own body size and an attitudinal construct concerning body dissatisfaction, body shape, and weight concerns. The increased appetite and calorie intake associated with GCs may have a negative influence on body image, as described in a study investigating food calorie intake and influence on body image in healthy volunteers (49). To our knowledge, however, there are no reported studies investigating the relationship between body image or self-esteem specifically with drug-induced weight gain.
Indirect impact of weight gain

Patients experiencing undesirable side effects, such as weight gain and associated worries, may potentially alter their GC adherence. Lower adherence has the consequence of inadequate treatment efficacy to control disease, potential escalation to more intensive treatment, and waste of medication. In a cross-sectional study of patients on long-term (> 3 months) GC treatment, 125 of 255 patients gained > 3 kg of weight over 2 years. Respondents were grouped into level of adherence (good versus poor). In all, 65% of poor adherers gained 3 kg or more, compared to 45% of good adherers (50). In the behavioral literature, the Necessity-Concerns Framework has been consistently shown to underpin medication adherence, where those patients more skeptical of their medication, with low perceived need for their medication and high concern, are more at risk of nonadherence (51). In a cross-sectional study of GC users, 46% (83 of 181) reported a high concern and lower perceived need for medication necessity, and of these, a third were classified as low adherers, and the remaining were classified as optimal adherers (23). Similarly, in a systemic sclerosis population, the higher the level of necessity to level of concern, the higher the medication adherence (26). However, in a population of patients experiencing adrenal inefficiency, nonadherence was associated with more GC concerns but not with necessity (32).

The concern with weight gain may well impact adherence to GCs and thereby result in poorer outcomes for patients. Future research into GCs and weight gain may allow doctors to provide patients with more detailed information about the potential extent of weight gain and potential loss after finishing GC treatment. This information may help reduce patients’ concerns and thereby increase adherence.

Summary

Recommendations from EULAR guidelines outline the need to consider and discuss adverse effects with patients before GC treatment commences (2,3). However, for weight gain, the extent, timing, reversibility of weight gain, and its impact are largely unknown or, at best, imprecise and thus cannot be communicated. Consequently, the clinician and therefore the patient will not be making an informed treatment decision. This review shows that weight gain is one of the GC side effects most important to patients. However, weight gain is not well measured or reported in studies, with studies often not designed to evaluate weight gain primarily, with some relying on patient self-reporting of weight changes. A systematic review of GCs and energy intake, appetite, and weight gain across all diseases came to a similar conclusion, recommending further RCTs that are well designed and adequately powered to determine the effects of GCs on body weight (6). Evidence suggests that the psychological well-being of patients, expressed through concerns toward GC treatment itself, the worries about weight gain, and the psychological implication of the resulting weight gain, are important issues needing attention.

Certain similarities may be drawn out and learned from extensive work carried out on antipsychotic drugs, known for causing substantial weight gain. After weight gain was identified as a side effect of antipsychotic drugs, studies have been routinely recording weight. This improved data collection has allowed greater understanding of the extent of weight gain with these drugs, and a clinically significant level of weight change has been established (52). Replication of all aspects of antipsychotic drug weight gain recording may not be possible for GCs because future large-scale clinical trials of GCs in rheumatology are unlikely. Collection of high-quality data regarding GC exposure, including dose and timing, in addition to longitudinal weight measurements in rheumatology cohorts, is needed. This information will provide potential important insight to examine both the rate of onset with dosage change and the speed of weight loss following discontinuation.

For the patient, having the clinician acknowledge and discuss potential weight gain before initiation of GC treatment is important. Weight monitoring during GC treatment and addressing patient concerns together with better information about the likelihood and extent of weight gain and potential loss after a period of GC treatment cessation may well improve the psychological well-being of patients. These improvements may, in turn, lower uncertainty and increase confidence in GC use by patients and maintain persistence over the GC course to ultimately improve the control of disease progression.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Dixon had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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REFERENCES

1. Hench PS, Kendall EC. The effect of a hormone of the adrenal cortex (17-hydroxy-11-dehydrocorticosterone; compound E) and of pituitary adrenocorticotropic hormone on rheumatoid arthritis. Proc Staff Meet Mayo Clin 1949;24:181–97.
2. Duru N, van der Goes MC, Jacobs JW, Andrews T, Boers M, Buttgereit F, et al. EULAR evidence-based and consensus-based recommendations on the management of medium to high-dose glucocorticoid therapy in rheumatic diseases. Ann Rheum Dis 2013;72:1905–13.
3. Hoes JN, Jacobs JW, Boers M, Bumpass D, Buttgereit F, Caeyers N, et al. EULAR evidence-based recommendations on the management of systemic glucocorticoid therapy in rheumatic diseases. Ann Rheum Dis 2007;66:1560–7.
4. Henxheimer A. Communicating with patients about harms and risks. PLoS Med 2005;2:e42.
5. Van der Goes MC, Jacobs JW, Boers M, Andrews T, Blom-Baikers MA, Buttgereit F, et al. Patient and rheumatologist perspectives on...
glucocorticoids: an exercise to improve the implementation of the European League Against Rheumatism (EULAR) recommendations on the management of systemic glucocorticoid therapy in rheumatic diseases. Ann Rheum Dis 2010;69:1015–21.

6. Patel R, Belousov M, Jami M, Dasgupta N, Winakor C, Nenadic G, et al. Frequent discussion of insomnia and weight gain with glucocorticoid therapy: an analysis of Twitter posts. NPJ Digit Med 2018;1.

7. Costello R, Patel R, Humphreys J, McBeth J, Dixon WG. Patient perceptions of glucocorticoid side effects: a cross-sectional survey of users in an online health community. BMJ Open 2017;7:e014603.

8. Berthon BS, Donald-Wicks LK, Wood LG. A systematic review of the effect of oral glucocorticoids on energy intake, appetite, and body weight in humans. Nutr Res 2014;34:179–90.

9. Strehl C, Bijlsma JW, de Wit M, Boers M, Caeyers N, Cutolo M, et al. Defining conditions where long-term glucocorticoid treatment has an acceptably low level of harm to facilitate implementation of existing recommendations: viewpoints from an EULAR task force. Ann Rheum Dis 2016;75:952–7.

10. Peckett AJ, Wright DC, Riddell MC. The effects of glucocorticoids on adipose tissue lipid metabolism. Metabolism 2011;60:1500–10.

11. Curtis JR, Westfall AO, Allison J, Bijlsma JW, Freeman A, George V, et al. Population-based assessment of adverse events associated with long-term glucocorticoid use. Arthritis Care Res (Hoboken) 2006;55:420–6.

12. Fardet L, Petersen I, Nazareth I. Prevalence of long-term oral glucocorticoid use with long-term glucocorticoid use. Arthritis Care Res (Hoboken) 2017;35:7.

13. Van Staa TP, Leufkens HG, Abenhaim L, Begaud B, Zhang B, Zhang Y, et al. American College of Rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Care Res (Hoboken) 2010;62:1515–26.

14. Sokka T, Toloza S, Cutolo M, Kautiainen H, Makinen H, Gogus F, et al. Systemic glucocorticoid therapy: risk factors for reported adverse events and beliefs about the drug: a cross-sectional online survey of 820 patients. Clin Rheumatol 2015;34:2119–26.

15. Zerah L, Arena C, Morin AS, Blanchon T, Cabane J, Fardet L. Patients’ beliefs about long-term glucocorticoid therapy and their association to treatment adherence. Rev Med Interne 2012;33:300–4. In French.

16. Morin C, Fardet L. Systemic glucocorticoid therapy: risk factors for reported adverse events and beliefs about the drug: a cross-sectional online survey of 820 patients. Clin Rheumatol 2015;34:2119–26.

17. Home R, Parham R, Driscoll R, Robinson A. Patients’ attitudes to medicines and adherence to maintenance treatment in inflammatory bowel disease. Inflamm Bowel Dis 2009;15:837–44.

18. Strehl C, Bijlsma JW, de Wit M, Boers M, Caeyers N, Cutolo M, et al. Defining conditions where long-term glucocorticoid treatment has an acceptably low level of harm to facilitate implementation of existing recommendations: viewpoints from an EULAR task force. Ann Rheum Dis 2016;75:952–7.

19. Cooper C. Use of oral corticosteroids in the United Kingdom. QJM 2000;93:105–11.

20. Smolen JS, Landewe R, Bijlsma JW, Thein NS, Dougados M, et al. Low-dose prednisone chronotherapy for rheumatoid arthritis: a randomised clinical trial (CAPRA-2). Ann Rheum Dis 2013;72:204–10.

21. Buttgereit F, Mehta D, Kirwan J, Szechinski J, Boers M, Alten RE, et al. Low-dose prednisone chronotherapy for rheumatoid arthritis: a randomised controlled trial. Ann Rheum Dis 2003;63:797–803.

22. Bakker MF, Jacobs JW, Welsing PM, Versappen SM, Tekstra J, Ton E, et al. Low-dose prednisolone inclusion in a methotrexate-based, tight control strategy for early rheumatoid arthritis. Ann Intern Med 2012;156:329–39.

23. Stone JH, Tuckwell K, Dimonaco S, Klearman M, Aringer M, Blockmans D, et al. Trial of tocilizumab in giant-cell arthritis. N Engl J Med 2017;377:317–28.

24. Bobson JC, Dawson J, Cronholm PF, Ashdown S, Easley E, Kellom KS, et al. Patient perceptions of glucocorticoids in anti-neutrophil cytoplasmic antibody-associated vasculitis. Rheumatol Int 2018;38:675–82.

25. Chapman SC, Liahana S, Carroll P, Horne R. Glucocorticoid therapy for adrenalin insufficiency: nonadherence, concerns and dissatisfaction with information. Clin Endocrinol (Oxf) 2016;84:684–71.

26. Verschueren P, De CD, Corluy L, Joos R, Langenaken C, Taelman V, et al. Low-dose prednisone inclusion in a methotrexate-based, tight control strategy for early rheumatoid arthritis. Ann Intern Med 2012;156:329–39.

27. Gogus F, et al. Frequent discussion of insomnia and weight gain with glucocorticoid therapy: an analysis of Twitter posts. NPJ Digit Med 2017;4:1–9.

28. Blockmans D, et al. Digital drug safety surveillance: monitoring pharmaceutical products in twitter. Drug Saf 2014;37:343–50.

29. Kass-Hout T, et al. Digital drug safety surveillance: monitoring pharmaceutical products in twitter. Drug Saf 2014;37:343–50.

30. Vandenbroeck E, Jacobs JW, Siewertsz van Reesema DR, for the Low-Dose Prednisolone Study Group. Very low-dose prednisolone in early rheumatoid arthritis retards radiographic progression over two years: a multicenter, double-blind, placebo-controlled trial. Arthritis Rheum 2005;52:3371–80.

31. Van Everdingen AA, Jacobs JW, Siewertsz van Reesema DR, for the Low-Dose Prednisolone Study Group. Very low-dose prednisolone in early rheumatoid arthritis retards radiographic progression over two years: a multicenter, double-blind, placebo-controlled trial. Arthritis Rheum 2005;52:3371–80.

32. Half of U.K. patients with rheumatoid arthritis are prescribed oral glucocorticoid therapy in primary care: a retrospective drug utilisation study. Arthritis Res Ther 2015;17:375.

33. Smolen JS, Landewe R, Breedveld FC, Buch M, Burmester G, Dougados M, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis 2014;73:492–509.

34. Smolen JS, Landewe R, Breedveld FC, Buch M, Burmester G, Dougados M, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis 2014;73:492–509.

35. Van Staa TP, Leufkens HG, Abenhaim L, Begaud B, Zhang B, Zhang Y, et al. American College of Rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Care Res (Hoboken) 2010;62:1515–26.

36. Kirwan JR. The effect of glucocorticoids on joint destruction in rheumatoid arthritis. N Engl J Med 1995;333:142–7.

37. Van Everdingen AA, Jacobs JW, Siewertsz van Reesema DR, for the Low-Dose Prednisolone Study Group. Very low-dose prednisolone in early rheumatoid arthritis retards radiographic progression over two years: a multicenter, double-blind, placebo-controlled trial. Arthritis Rheum 2005;52:3371–80.

38. Van Everdingen AA, Jacobs JW, Siewertsz van Reesema DR, for the Low-Dose Prednisolone Study Group. Very low-dose prednisolone in early rheumatoid arthritis retards radiographic progression over two years: a multicenter, double-blind, placebo-controlled trial. Arthritis Rheum 2005;52:3371–80.
1-year results of CareRA, a randomised pragmatic open-label superiority trial. Ann Rheum Dis 2017;76:511–20.

40. Konijn NP, van Tuyl LH, Boers M, van de Ven PM, den UD, Ter Wee MM, et al. The short-term effects of two high-dose, step-down prednisolone regimens on body composition in early rheumatoid arthritis. Rheumatology (Oxford) 2016;55:1615–22.

41. Huscher D, Thiele K, Gromnica-Ihle E, Hein G, Demary W, Dreher R, et al. Dose-related patterns of glucocorticoid-induced side effects. Ann Rheum Dis 2009;68:1119–24.

42. Wung PK, Anderson T, Fontaine KR, Hoffman GS, Specks U, Merkel PA, et al. Effects of glucocorticoids on weight change during the treatment of Wegener’s granulomatosis. Arthritis Care Res (Hoboken) 2008;59:746–53.

43. Jurgens MS, Jacobs JW, Geenen R, Bossema ER, Bakker MF, Bijlsma JW, et al. Increase of body mass index in a tight controlled methotrexate-based strategy with prednisone in early rheumatoid arthritis: side effect of the prednisone or better control of disease activity? Arthritis Care Res (Hoboken) 2013;65:88–93.

44. Pincus T, Sokka T, Castrejón I, Cutolo M. Decline of mean initial prednisone dosage from 10.3 to 3.6 mg/day to treat rheumatoid arthritis between 1980 and 2004 in one clinical setting, with long-term effectiveness of dosages less than 5 mg/day. Arthritis Care Res (Hoboken) 2013;65:729–36.

45. Hickling P, Jacoby RK, Kirwan JR. Joint destruction after glucocorticoids are withdrawn in early rheumatoid arthritis. Arthritis and Rheumatism Council Low Dose Glucocorticoid Study Group. Br J Rheumatol 1998;37:930–6.

46. Nassar K, Janani S, Roux C, Rachidi W, Etaouil N, Mkinsi O. Long-term systemic glucocorticoid therapy: patients representations, prescribers perceptions, and treatment adherence. Joint Bone Spine 2014;81:64–8.

47. Guh D, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis A. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. BMC Public Health 2009;9:1–20.

48. Miller CT, Downey KT. A meta-analysis of overweight and self esteem. Personality Soc Psychol Rev 1999;3:68–84.

49. Vocks S, Legenbauer T, Heil A. Food intake affects state body image: impact of restrained eating patterns and concerns about eating, weight and shape. Appetite 2007;49:467–75.

50. Arena C, Morin AS, Blanchon T, Hanslik T, Cabane J, Dupuy A, et al. Impact of glucocorticoid-induced adverse events on adherence in patients receiving long-term systemic glucocorticoid therapy. Br J Dermatol 2010;163:832–7.

51. Horne R, Chapman SC, Parham R, Freemantle N, Forbes A, Cooper V. Understanding patients’ adherence-related beliefs about medicines prescribed for long-term conditions: a meta-analytic review of the necessity-concerns framework. PLoS One 2013;8:e80633.

52. Bak M, Fransen A, Janssen J, van Os J, Drukker M. Almost all antipsychotics result in weight gain: a meta-analysis. PLoS One 2014;9:e94112.