

Metformin Treatment of PCOS: St. Georges Hospital Endocrine Unit Clinical Experience.

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Introduction

- PCOS is the most common endocrine condition affecting women. Patients with the condition suffer from a wide range of symptoms including endocrine, gynaecological, diabetic and dermatological as well as eating disorder psychiatry.
- Obesity is present in at least 30% of cases of PCOS (1). Weight loss has been shown to improve the symptoms of the condition significantly. Even a modest weight loss of 5% improved ovulatory function (2,3) and so weight loss is a primary treatment goal
- Patients with PCOS are often treated with metformin as a first line drug as it has been shown to regulate menstrual cycles improve insulin resistance and reduce long term sequelae.
- There is a strong link between obesity and insulin resistance and therefore insulin sensitising drugs such as metformin could have a role in weight loss in PCOS. For this reason many clinicians also use metformin to aid weight loss, although the evidence regarding its efficacy as a weight loss treatment is conflicting (1,4). Although these results are largely from carefully supervised controlled trials these do not necessarily reflect the reality of daily clinical practice.

Aim

- We aim to evaluate the long term effects of prescribing metformin on one aspect of PCOS, namely weight loss, in a busy University Hospital endocrine unit.
- Given the apparently low compliance, a secondary aim was to quantify the common side effects experienced by patients receiving metformin.

Methods

- 43 patients classified as having PCOS and prescribed metformin were identified. Information was gathered from the hospital notes including presenting weight, dates of taking metformin and changes in weight that occurred whilst on treatment. Side effects of the medication were also recorded.
- Time on metformin was calculated, as well as the weight change whilst on the drug for each patient. The change in weight whilst on or off the drug over time was analysed using a linear regression model.
- 35 patients had been monitored whilst on and off the drug. For these patients weight change was calculated during treatment or no treatment. As the time periods were variable an average per day was calculated in order to compare results using a paired T test.

Patient population

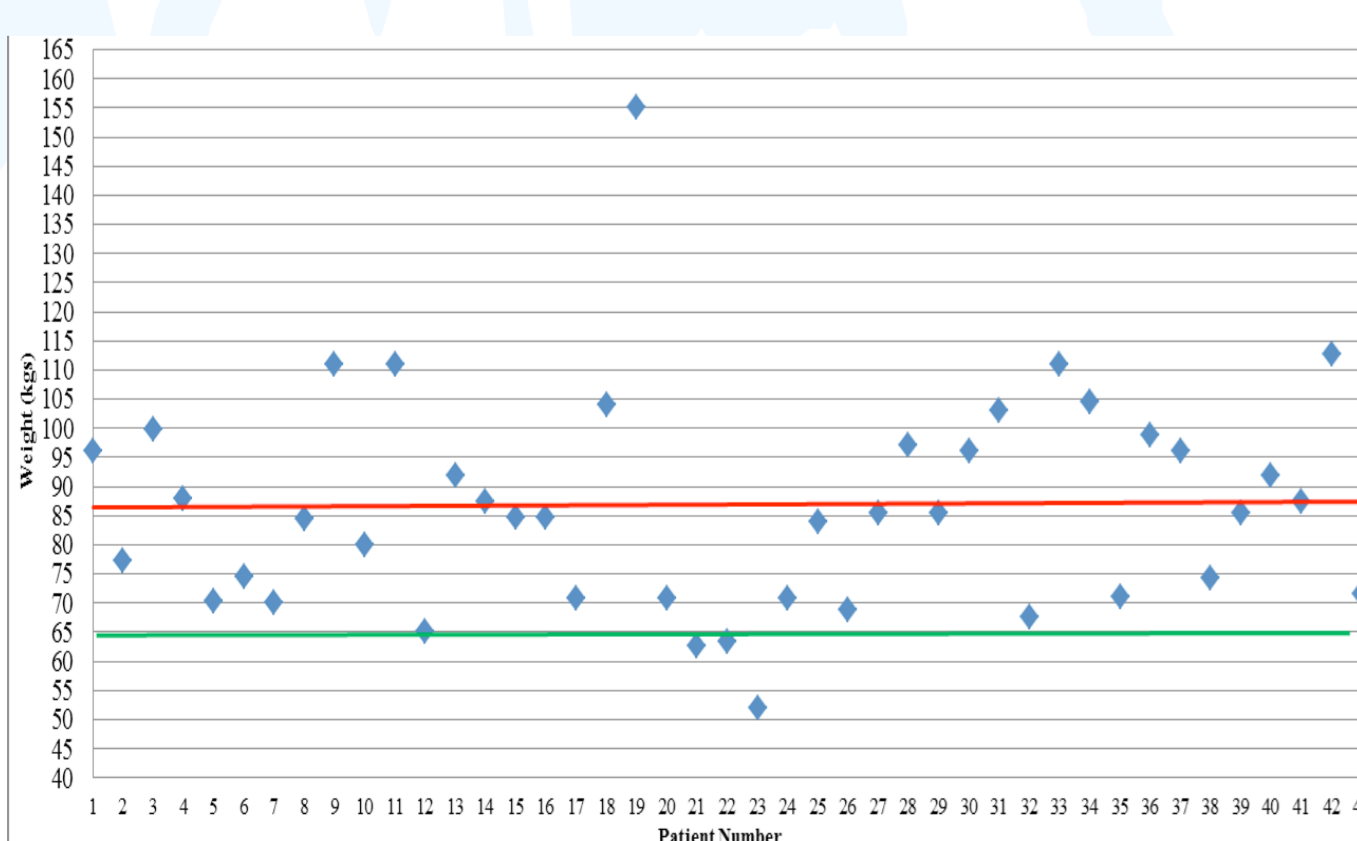


Figure 1: The blue dots represent patients' weight at presentation to clinic. The average weight of patients when they first attended clinic is 86.5kgs, demonstrated by the red line. The green line represents the weight equivalent to the lowest BMI in the overweight category. There was a large range from the lowest weight at 52.1kgs to the maximum weight at 155kgs.

Results

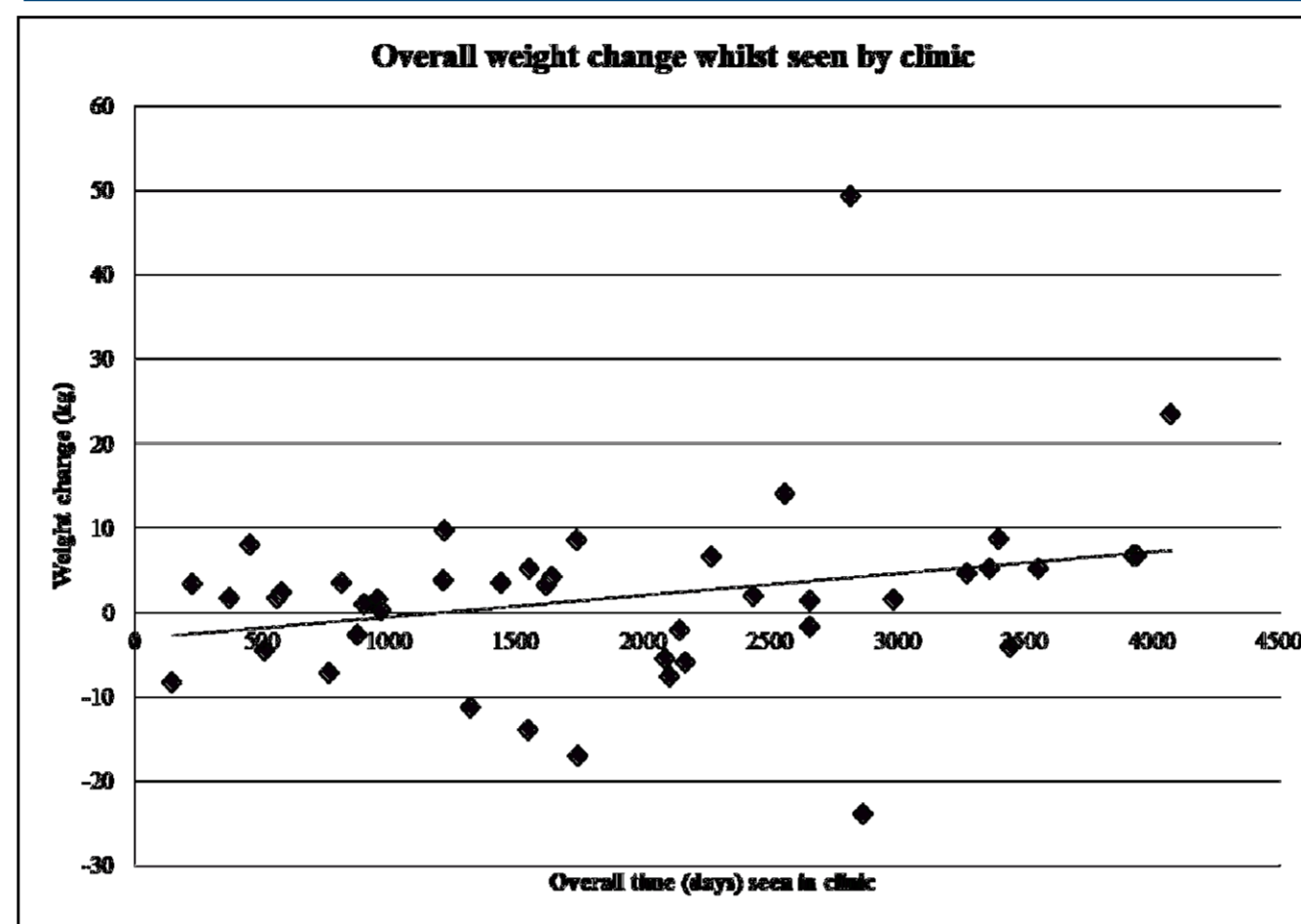


Figure 2: The blue diamonds represent individual patients and their total weight change whilst seen by the clinic. The average weight change was a gain of 1.85kgs. There was a wide range of weight change from a weight loss of 24kgs to a gain of 49.3kgs.

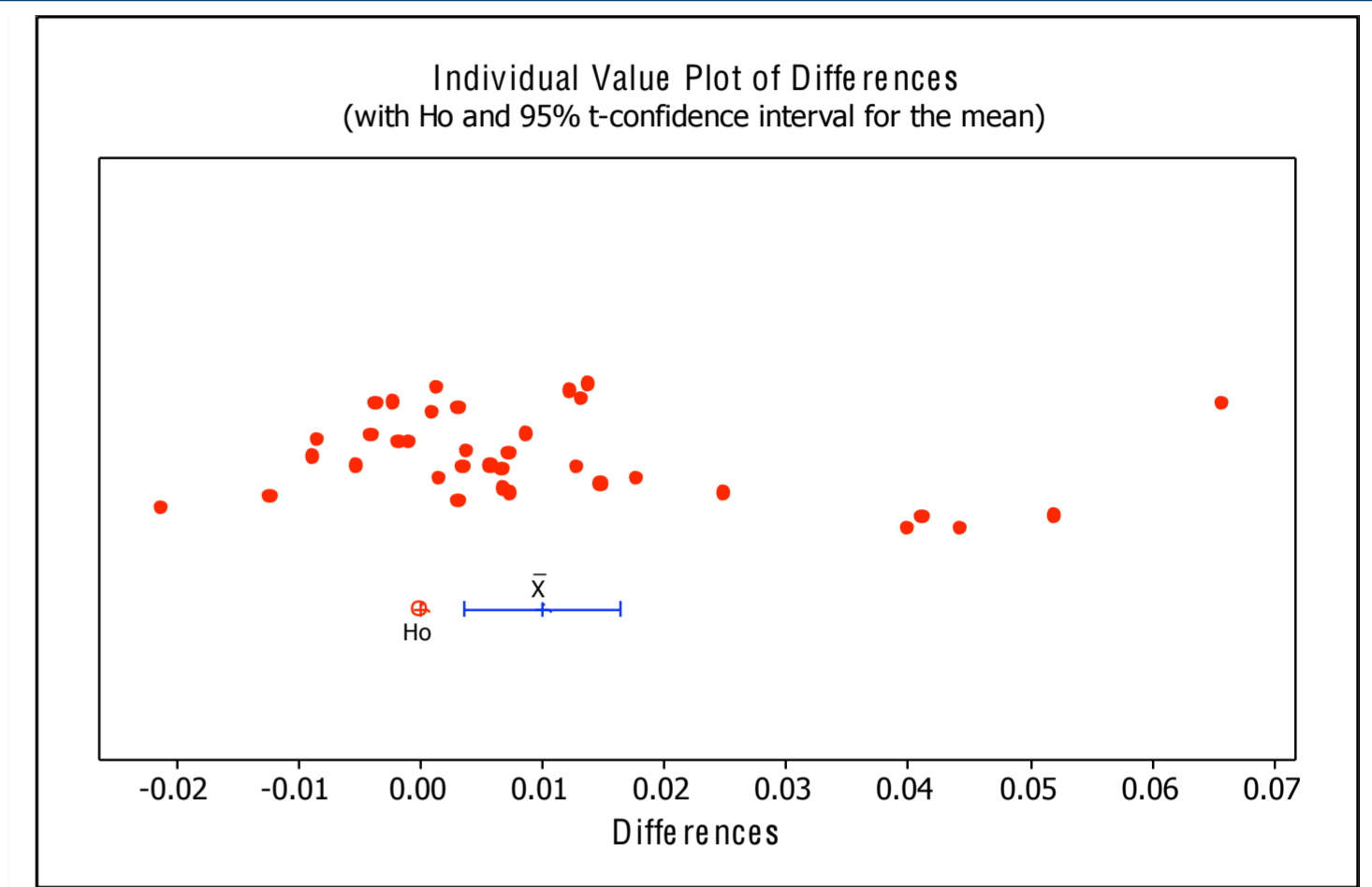


Figure 3: The red dots represent the differences in weight change per day from the weight gain not on metformin to the weight loss on the drug for each patient. The Ho sign represents the null hypothesis, and all the data points to the right of this are significant. The x sign represents the average change in weight, as well as the confidence interval.

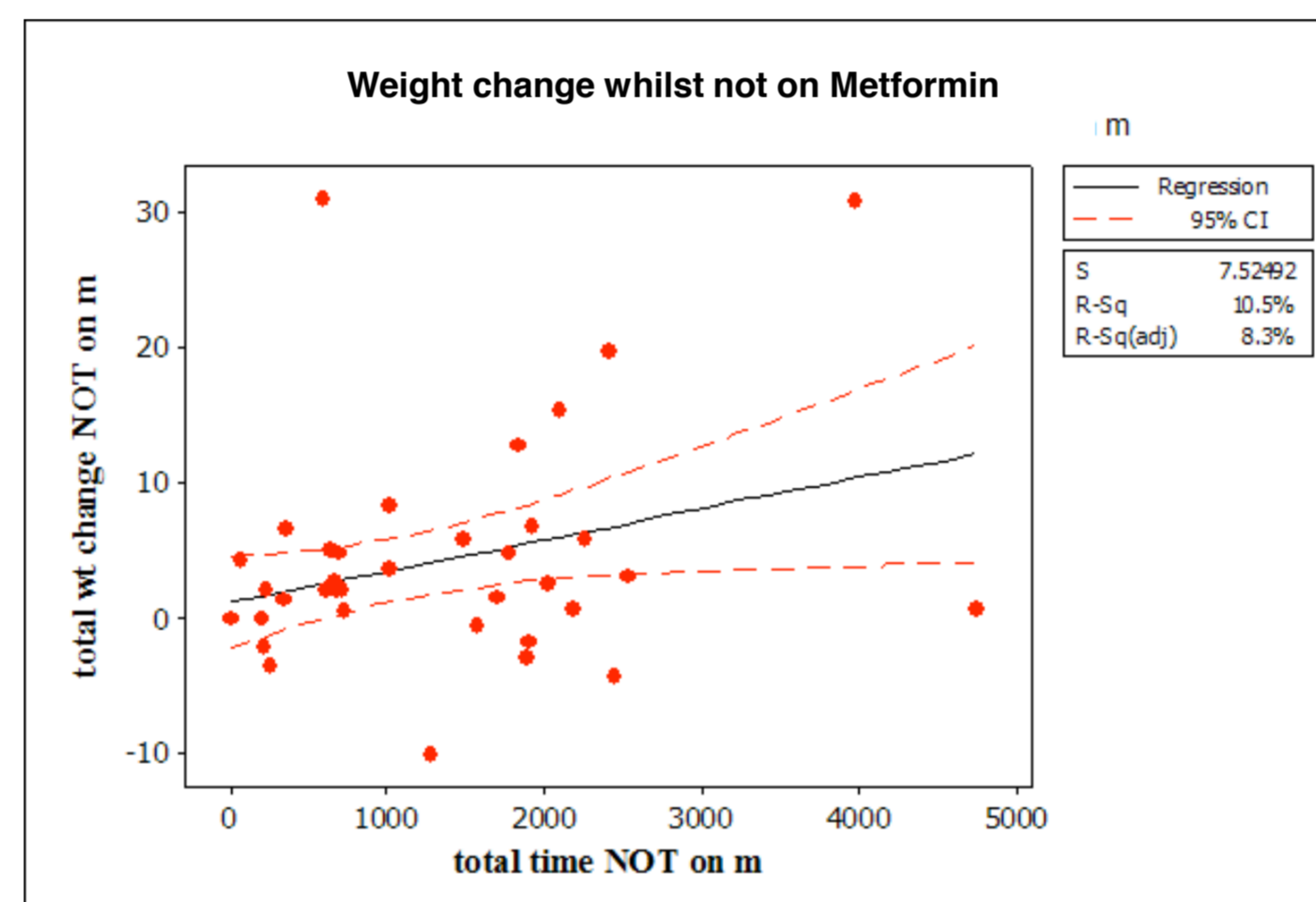


Figure 4: Individual patients change in weight whilst not on metformin. The linear relationship between the total time not on metformin and the total weight change whilst not on the drug is demonstrated by the black line. The slope of the line is 0.0023 which is the change in weight, for every day not taking metformin.

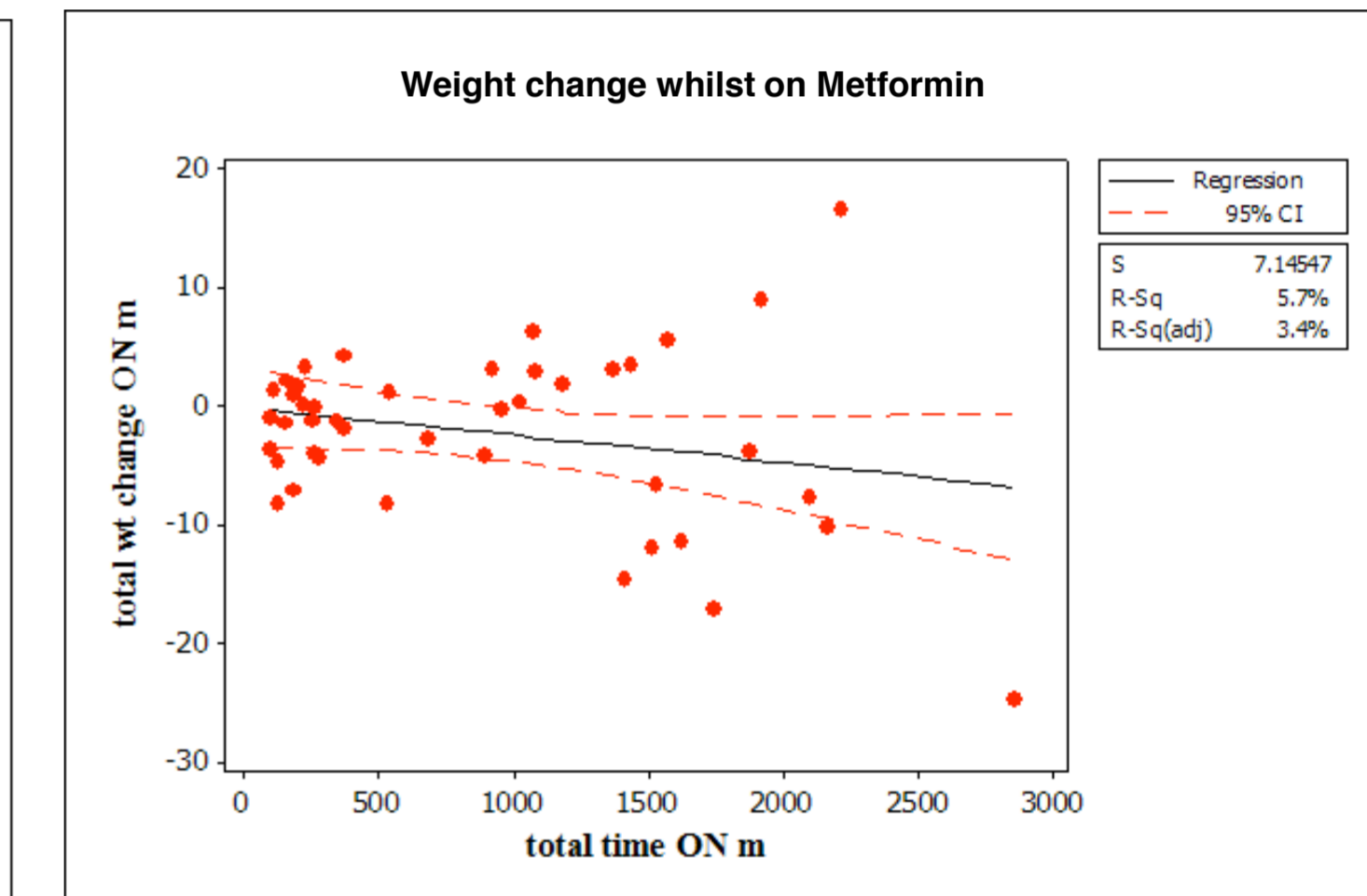


Figure 5: Individual patients change in weight whilst on metformin. The linear relationship between the total time on metformin and the total weight change is demonstrated by the black line. The slope of the line is -0.0023 and it is the change in weight for every unit increase in X, or day on metformin.

	N	Mean wt change (g)
Not on M	35	5.7
On M	35	-4.2
Difference	35	9.9

Table 1: The average weight change whilst not on metformin per day was 5.7grams. The average weight change whilst on metformin was a loss of 4.2grams per day. The different between these values is approximately 10 grams.

	wt change/ week (kgs)	wt change per year (kgs)
Not on M	0.04	2.09
On M	-0.03	-1.55
Difference	0.07	3.64

Table 2: The hypothesised weight gain and loss in patients not taking metformin or taking metformin per week, month and year.

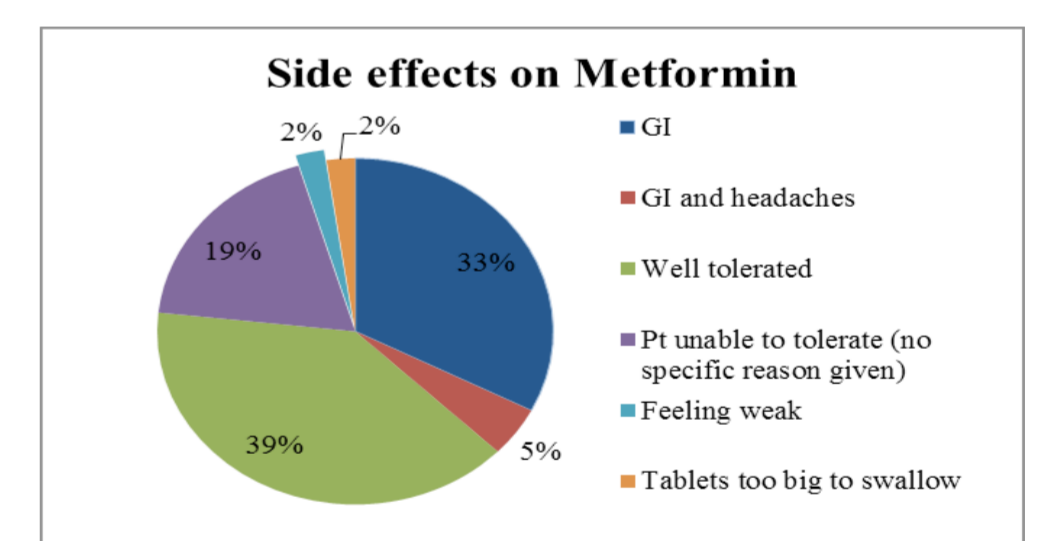


Figure 6: 61% of patients experienced side effects on metformin, with the most common side effect being GI upset.

Discussion

- Metformin is frequently used to treat PCOS and one of the desired outcomes is weight loss. In St. George's, patients on metformin lost 1.55kgs per year, which is equivalent to 11,960kcal. The change in weight on metformin when compared to not being on metformin was found to be significant. Thus, this study concludes that metformin does help women with PCOS lose weight.
- The average weight gain whilst not on metformin was 2.09kgs per year, which is equivalent to 16,127kcal. Interestingly this is very similar to the calorie saving determined by Robinson et al in patients with PCOS (5). They measured patients' metabolic rate using continuous indirect calorimetry and found that patients with PCOS have a reduced post prandial thermogenesis resulting in a reduced energy expenditure roughly equivalent to 17,000kcal a year.
- Metformin compliance is poor as most patients suffer adverse side effects. Metformin was most frequently taken for a course of <6 months and most patients stopped taking the drug due to unpleasant GI side effects. Published data show that the extended release preparation of metformin is better tolerated, and there were fewer side effects. Indeed in this study 60% of the patients who were still taking metformin at the end of their treatment had been switched to the slow release formula. The slow release preparation of metformin is three times more expensive than the immediate release preparation however, which might explain why it is not prescribed initially
- This was a retrospective observational study and there were numerous variables and confounding factors in each patient which could not be controlled for. Despite the limitations, this study gives an interesting insight into the effectiveness of metformin as a weight loss treatment in patients with PCOS in this particular clinic. It demonstrates that although metformin is a difficult drug to comply with due to side effects, patients can succeed in losing weight on the drug.

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