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## Background

Cystic fibrosis related diabetes (CFRD) is one of the main complications of cystic fibrosis (CF), occurring in the 40-50% of CF patients, following inflammatory-degenerative damage of the pancreas. The secretion of altered pancreatic juice, more acid and rich in protein, leading to the obstruction of the pancreatic ducts, determines an increase of intraductal pressure, inflammation, amyloid deposition, fatty infiltration, pancreatic damage, and parenchymal atrophy. These alterations cause damages ranging from pancreatic insufficiency to insulin and glucagon deficiency. The onset of diabetes in CF patients worsens the patient's overall clinical condition, affecting nutritional/weight status, pulmonary function, infectious exacerbations and short- and long-term microvascular complications. Moreover, CFRD causes neuropathy, gastropathy, retinopathy and diabetic nephropathy, similarly to other forms of diabetes.

## Patients and methods

We selected a sample of 17 insulin treated patients (Group T) and a sample of 17 controls with CF but normal glucose metabolism (Group C). Group T was in turn subdivided into overt diabetics patients and pre-diabetics patients (impaired glucose tolerance -IGT or indetermined glucose tolerance-INDET) on the basis of glycated hemoglobin and OGTT. For each patients in Group T an observation period was established starting with the first insulin administration and ending after 12 months. For Group C patients, a compatible year of observation was chosen to compare with the year of study of the first sample. Data regarding Body Mass Index (BMI), Forced Vital Capacity (FVC), Forced Expiratory Volume (FEV1) and Peak Expiratory Flow (PEF) were collected at time 0, and at time 12. The number of respiratory infectious episodes during the year of observation and during the preceding year were recorded for Group T; the same parameters were studied in the two sub-groups in the early stages of glucose alteration (IGT, INDET).

## Results

### Group T vs Group C

Group T BMI significantly increased after one year of insulin treatment ( $P < 0.001$ ); Group C BMI after one year of observation was not significantly changed

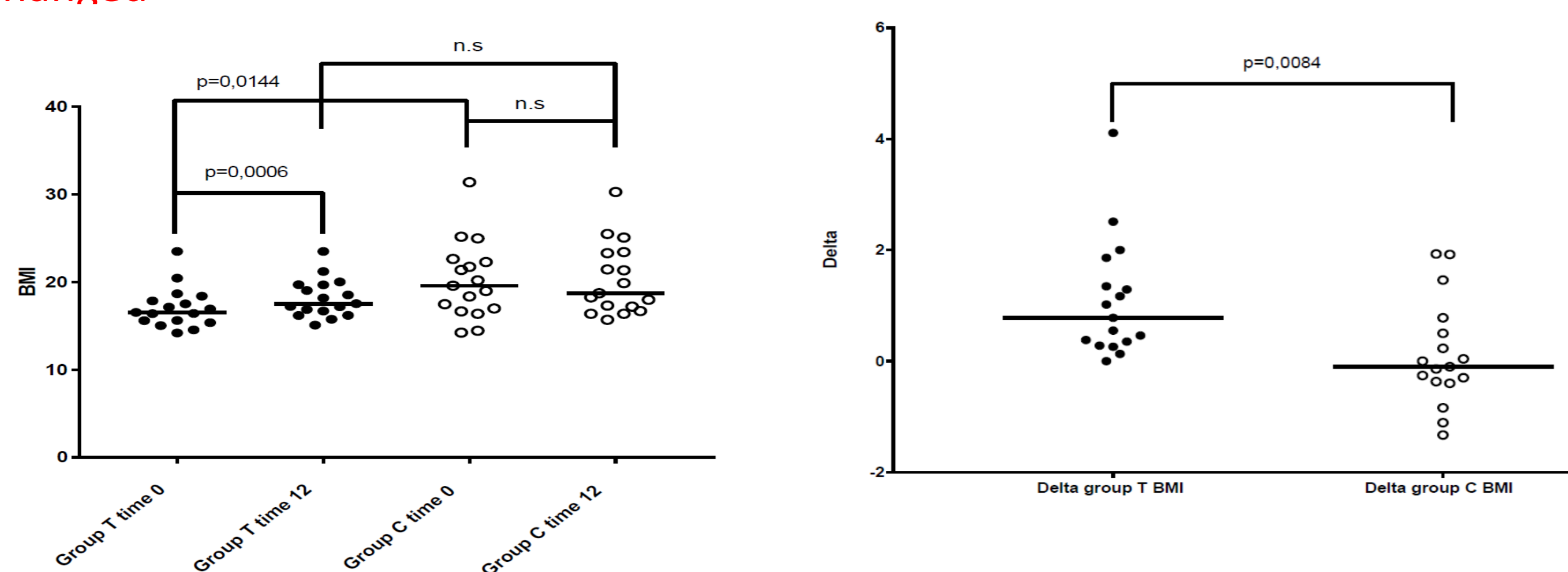


Figure 1-2: group T and group C BMI and delta BMI comparison

In Group T FVC, FEV1 and PEF increase after one year of insulin treatment, but only PEF had a statistically significant increase. No changes were observed for respiratory indexes in Group C

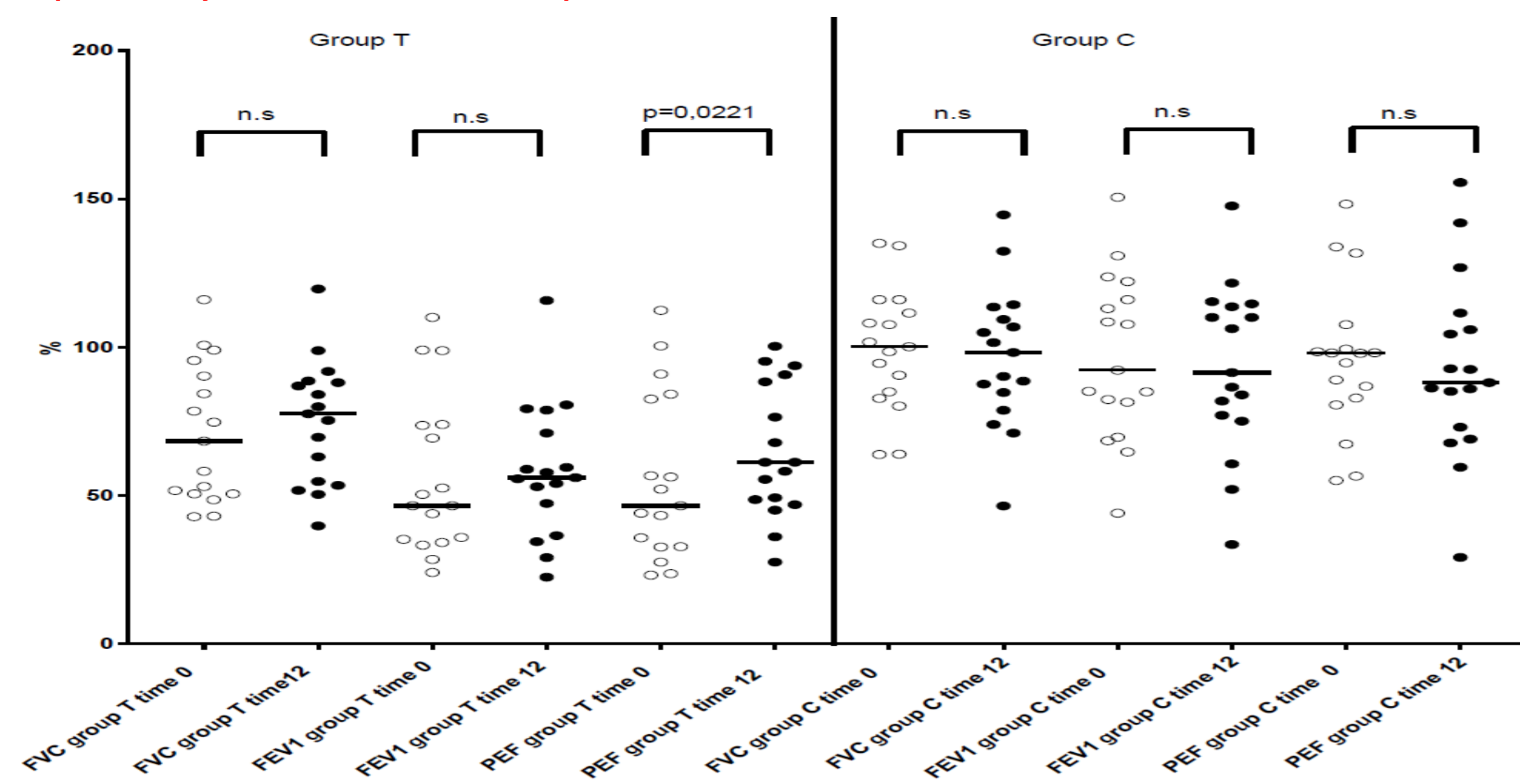


Figure 3: time 0-time 12 respiratory indexes comparison

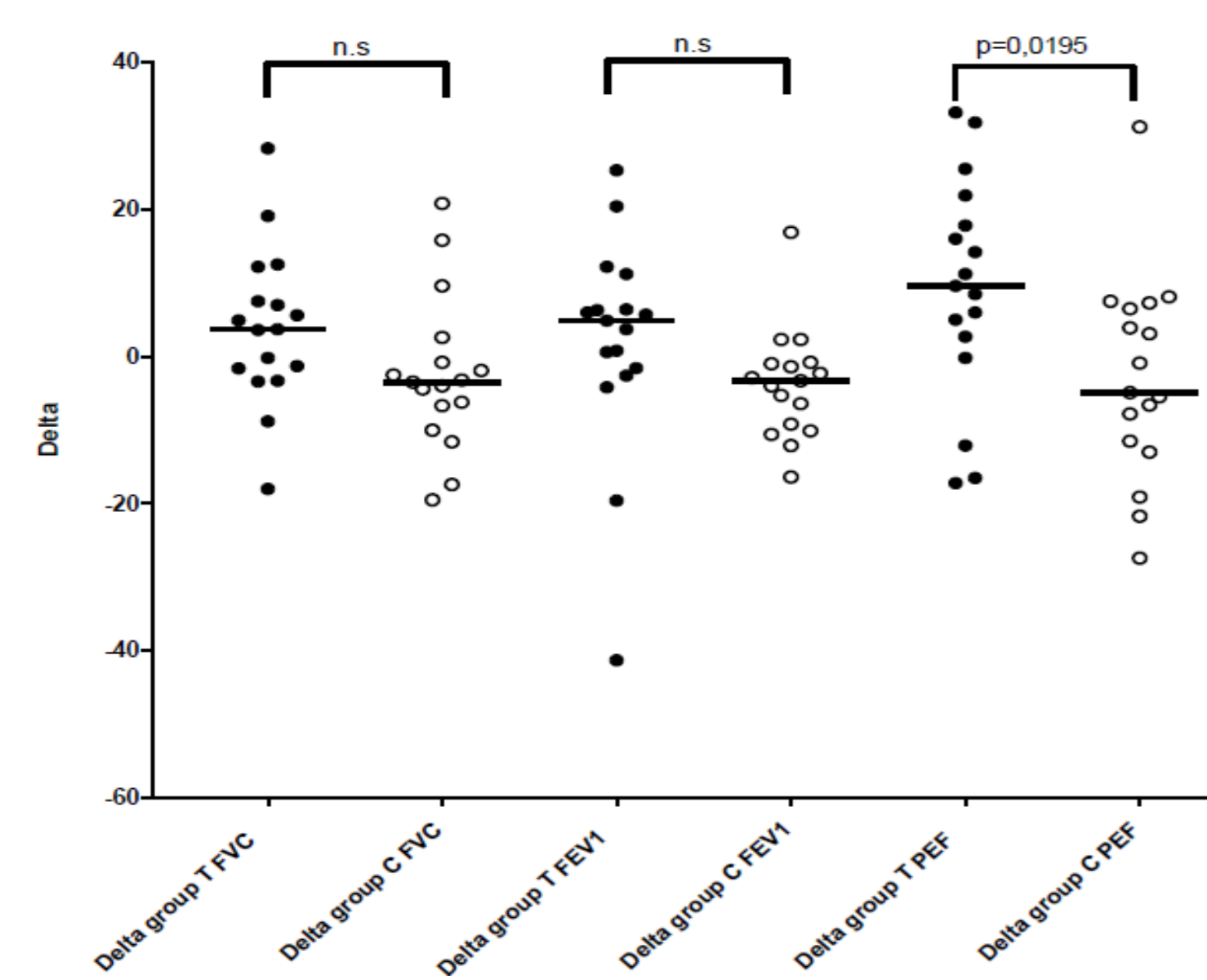
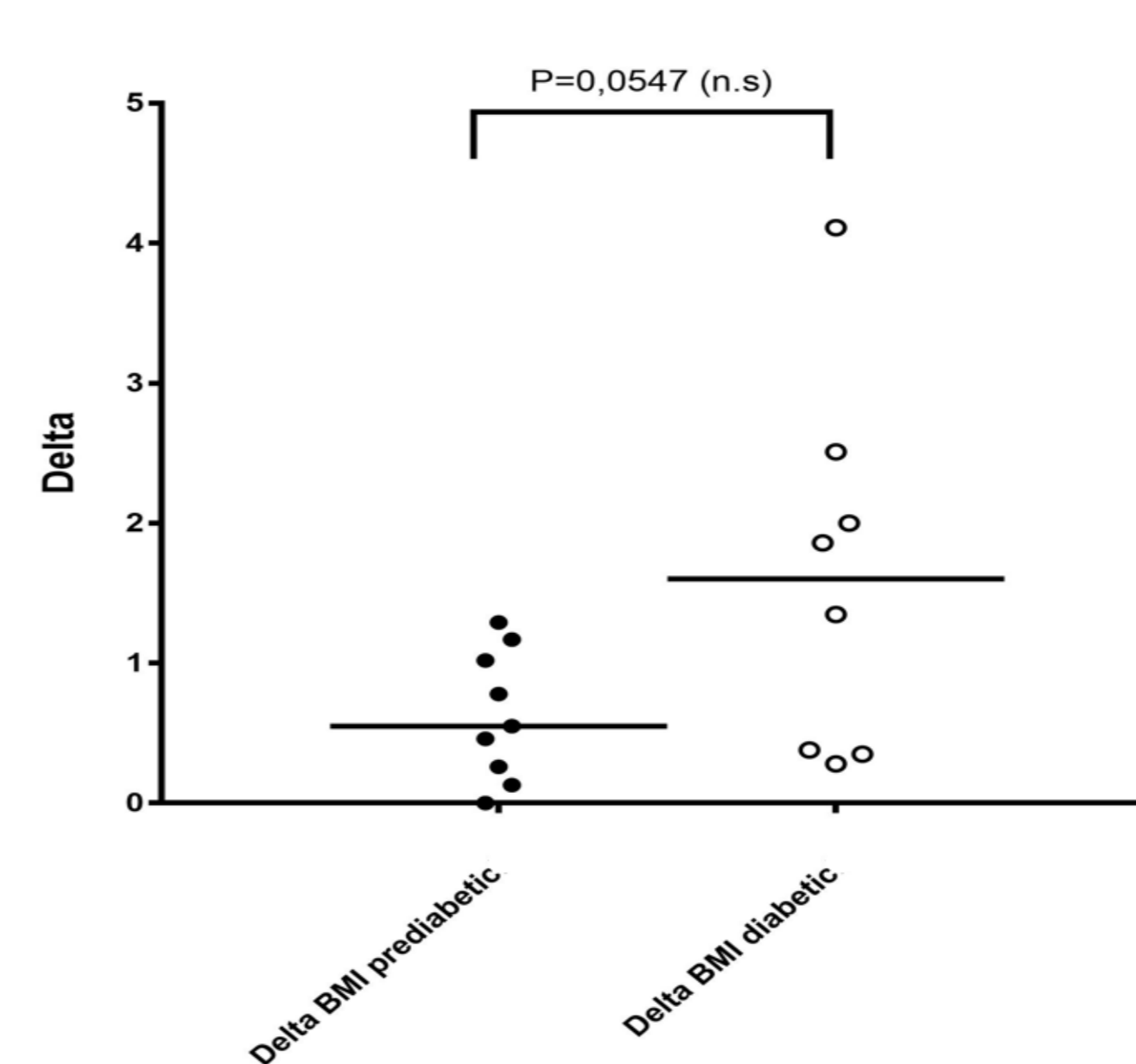


Figure 4: group T- group C delta respiratory indexes comparison

Comparing the Delta values observed between 0 time vs 12 months time for the respiratory indexes, we confirmed the positive change in Group T vs Group C, significantly different only for PEF, the main effort-dependent respiratory index.

### Pre-diabetics vs Diabetics



BMI showed a greater increase in diabetic vs prediabetic patients, with a p value close to significance ( $P=0,0547$ ).

There were no statistically significant differences in respiratory indexes between the two subgroups after 12 months insulin treatment

Figure 5: pre diabetics-diabetics delta BMI comparison

Evaluation of infectious episodes revealed a reduction of the number of episodes in treated patients more evident in those with pre-diabetes.

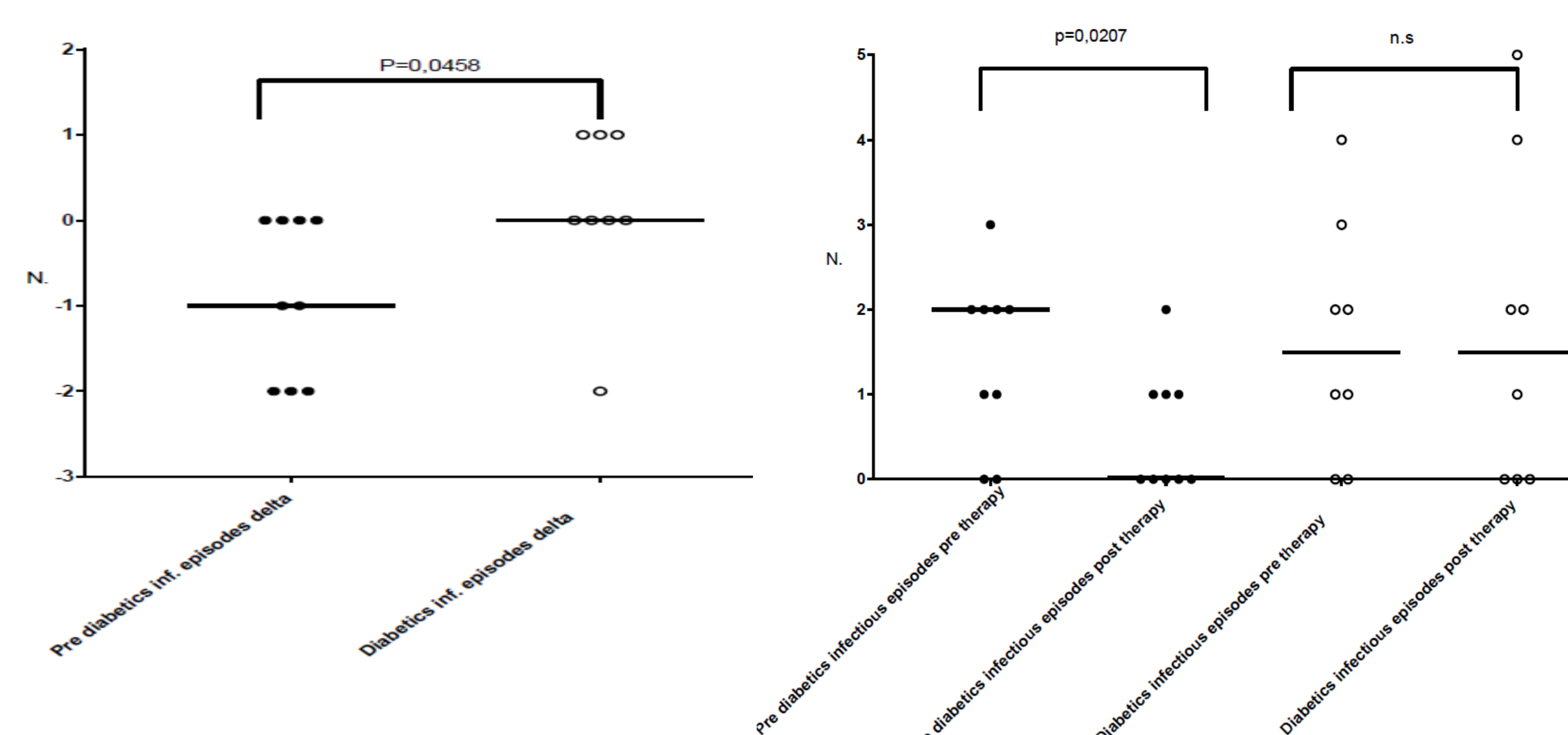


Figure 6-7: pre diabetics-diabetics infectious episodes comparison

## TAKE

- BMI is lower in diabetic and prediabetics CF patients compare to CF patients with normal glucose metabolism and can improve after insulin treatment

## HOME

- Insulin deficiency could contribute to aggravate the restrictive component of CF, through the inadequate development of the thoracic muscles necessary to perform a maximal forced expiration
- Insulin treatment of prediabetes could reduce the number of infectious episodes in CF patients

## MESSAGE

- Early insulin treatment of CF patients with diabetes or prediabetes, could improve patients' quality of life, reducing the number of admissions and comorbidity