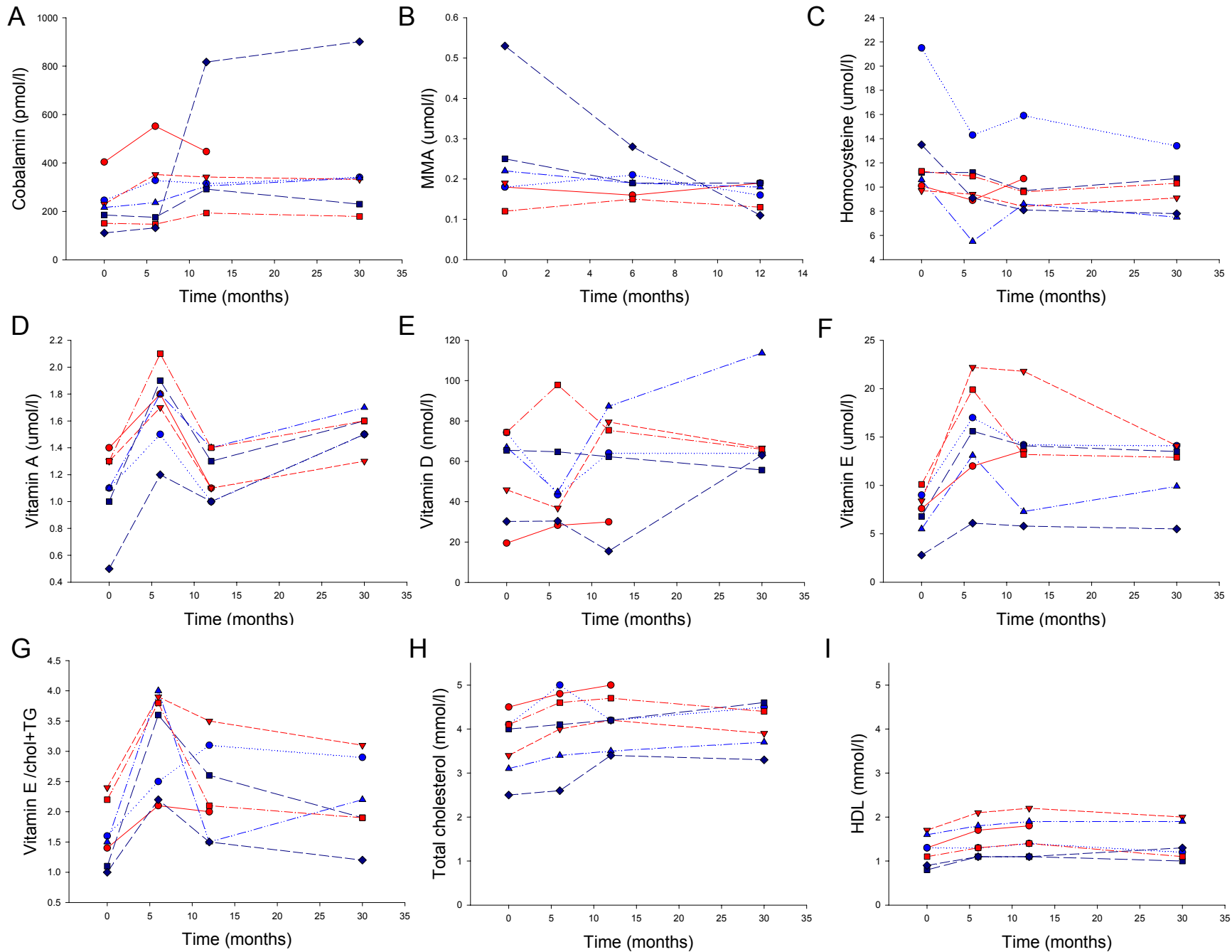
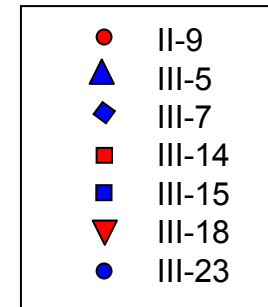
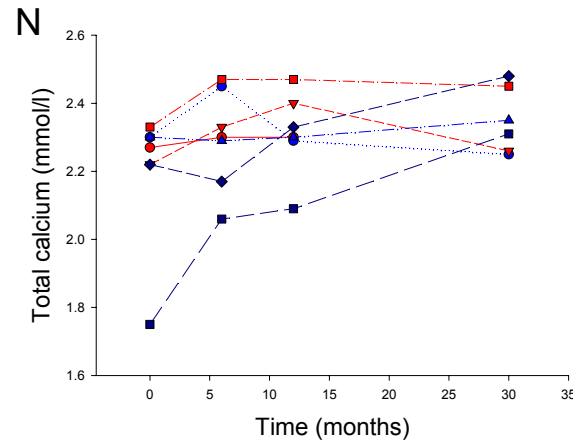
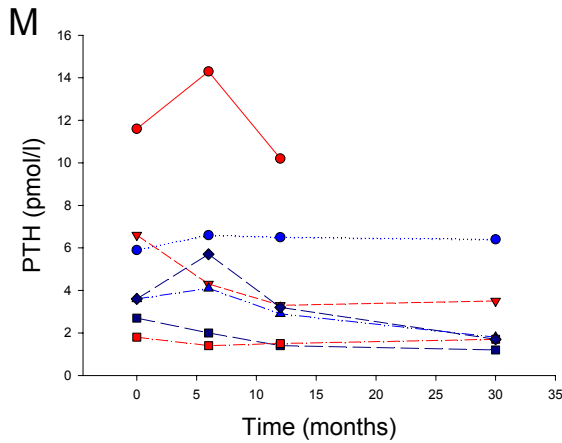
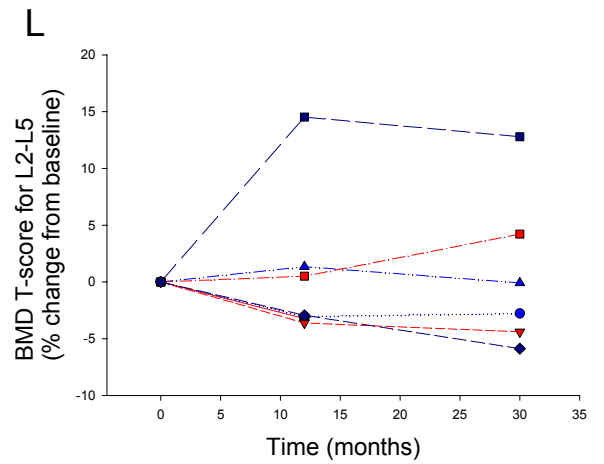
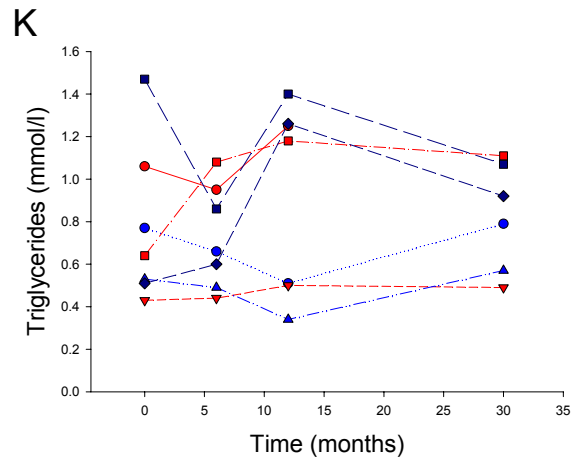
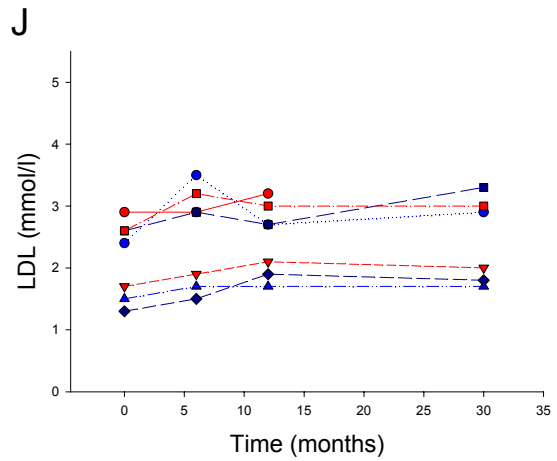


# Online Appendix Figure 1: Development of selected clinical variables in individual subjects.





**Online Appendix Figure 1: Development of selected clinical variables in individual subjects.** The individuals are represented by the same symbols in each panel.

**A)** Two subjects (III-7 and III-14) had cobalamin levels below the reference range [175-700 pmol/l] at baseline. Subject III-7 was subsequently treated with vitamin B12 supplementation, and as a result cobalamin levels increased substantially at 12 and 30 months.

**B)** Methylmalonic acid levels (MMA) were raised above the reference range [0.05-0.26  $\mu$ mol/l] in one subject (III-7), but normalized with vitamin B12 supplementation treatment.

**C)** All patients had homocysteine levels within the reference range [ $<15$   $\mu$ mol/l].

**D)** Vitamin A levels were low in subject III-7 at baseline, but within the reference range [ $>0.70$   $\mu$ mol/l] at six, 12 and 30 months.

**E)** Subject II-9 had vitamin D levels below the reference range [30-150 nmol/l] at all time points, although with a slight improvement. Subject III-7 had borderline low vitamin D levels at baseline and six months that decreased at 12 months, but normalized at 30 months. Some of the fluctuations seen in the vitamin D levels may be due to seasonal variations, as the baseline and 12 months controls were performed in November, while the six and 30 months controls were performed in late April/ early May.

**F)** All the patients had vitamin E levels below the reference range [ $>11.6$   $\mu$ mol/l] at baseline, but vitamin E was normalized in six subjects after six months of PEST. Subject III-5 later relapsed, and subject III-7 consistently showed low values.

**G)** Vitamin E levels corrected for cholesterol and triglyceride levels [2.1-7.0] were below the reference range in 5/7 subjects at baseline, but were normalized in all but one subject at six months, whereafter it declined somewhat in some subjects.

**H)** Total cholesterol values were below the normal range [3.3-7.7 mmol/l] in two subjects (III-5 and III-7) at baseline, and increased slightly in all subjects with PEST treatment. Subject III-7 maintained values below the reference range. All the subjects had values in the lower end of the reference range for

**I)** HDL [0.8-2.1 mmol/l], **J)** LDL [1.8-5.7 mmol/l] and **K)** triglycerides [0.45-2.45 mmol/l].

**L)** Bone mineral density (BMD) measured at the level of L2-L5 increased in two patients (III-14 and III-15), remained stable in one, and decreased approximately as expected per year in three patients.

**M)** Parathyroid hormone levels (PTH) were increased above the reference range [0.7-5.6 pmol/l] in three subjects at baseline, and stayed high in subjects II-9 and III-23 throughout the study. However, they both had normal levels of total calcium [2.20-2.55 mmol/l] (**N**), while one subject (III-15) had low total calcium levels that were normalized at 30 months.