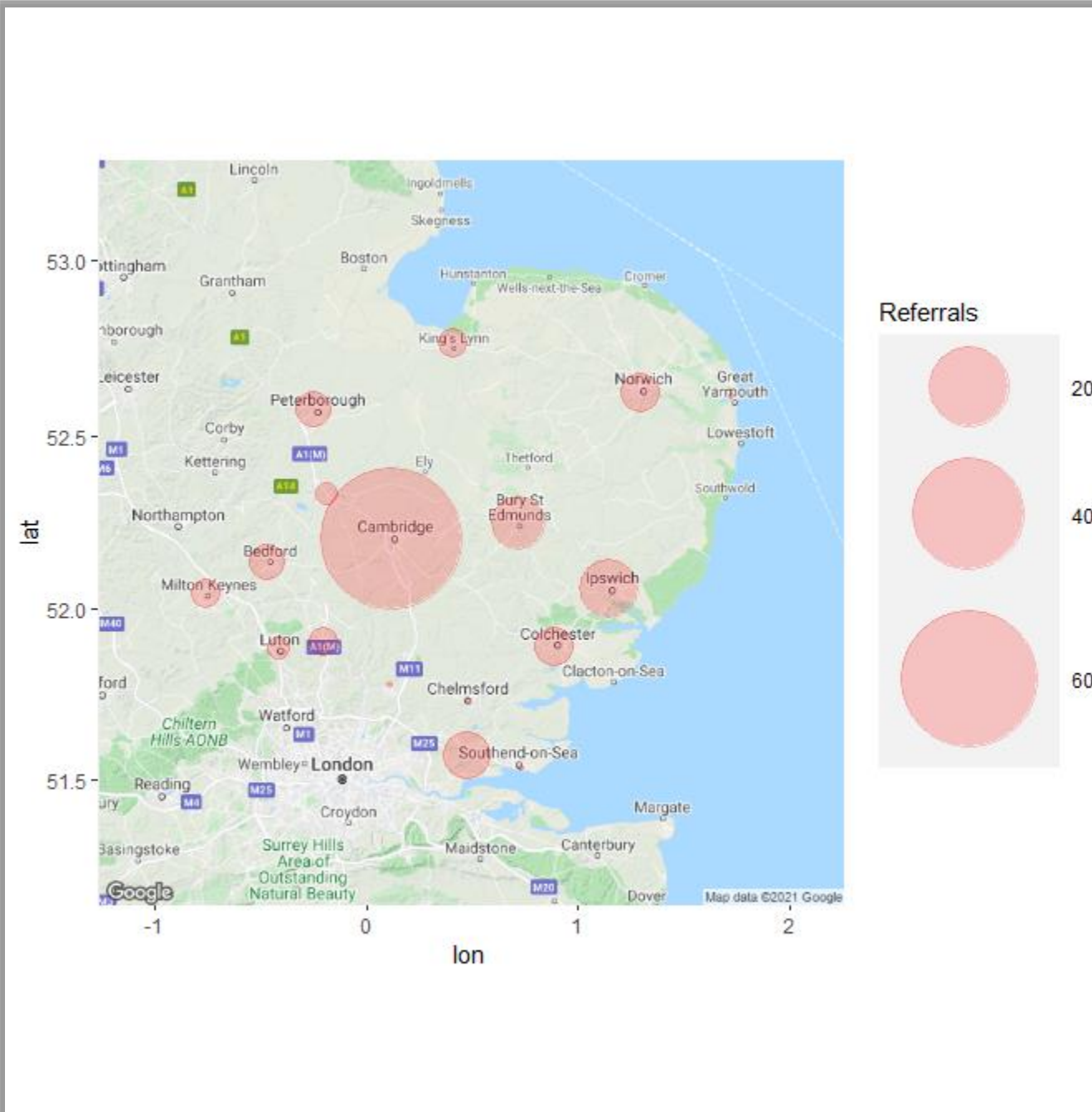
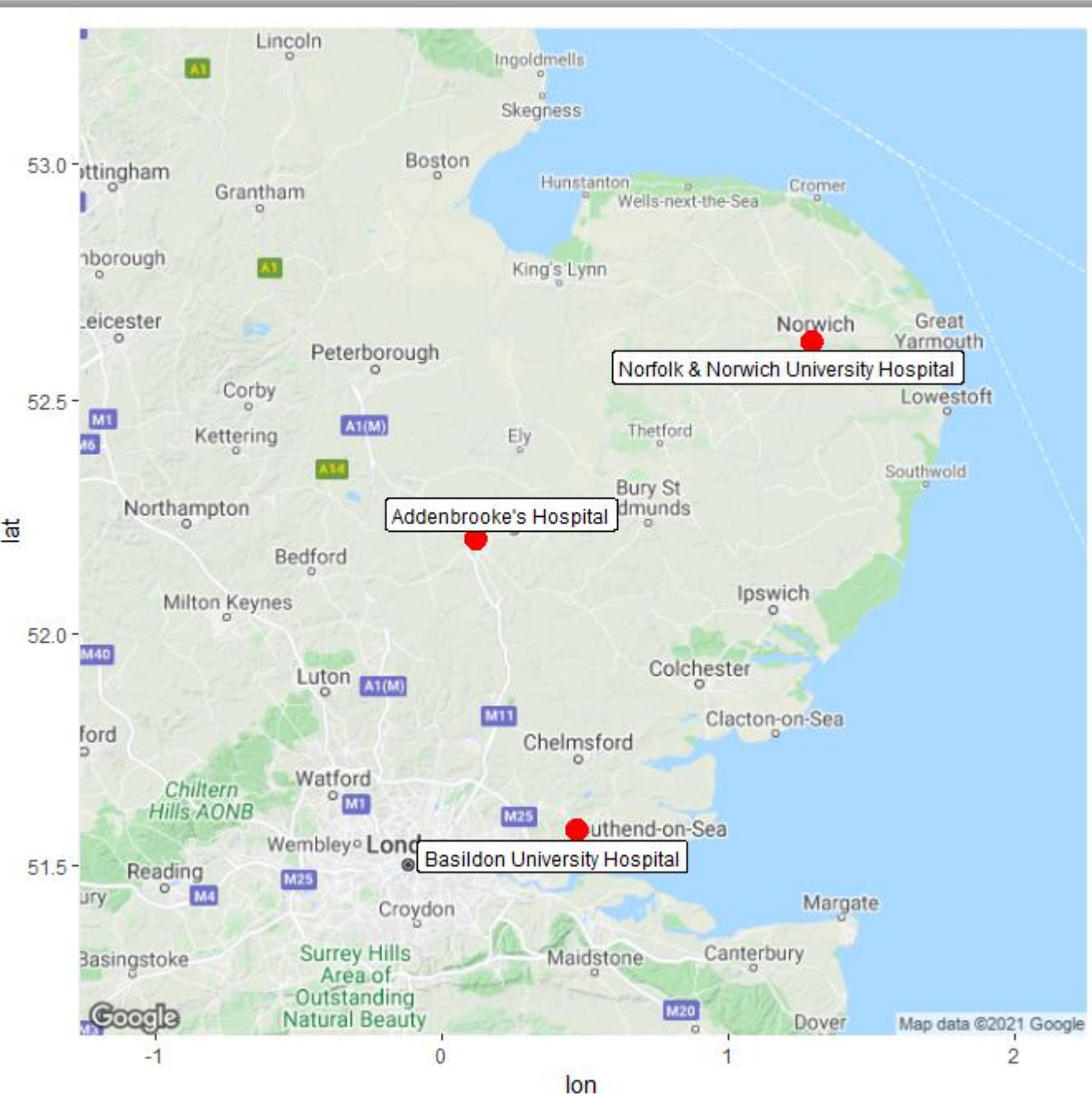


Introduction

Primary biliary cholangitis (PBC) remains a leading indication for liver transplantation (LT) in the UK. PBC patients with inadequate biochemical response to ≥ 12 months of treatment with ursodeoxycholic acid (UDCA) 13 – 15 mg/kg/day have increased risk of disease progression and future need for LT. These high-risk patients are eligible for second-line treatment of PBC with obeticholic acid (OCA). In the UK, second-line treatment with bezafibrate (BZF) or fenofibrate may also be considered. The East of England (EoE) PBC multi-disciplinary team (MDT) was established in 2017 to deliver second-line treatment with OCA to patients across the region.

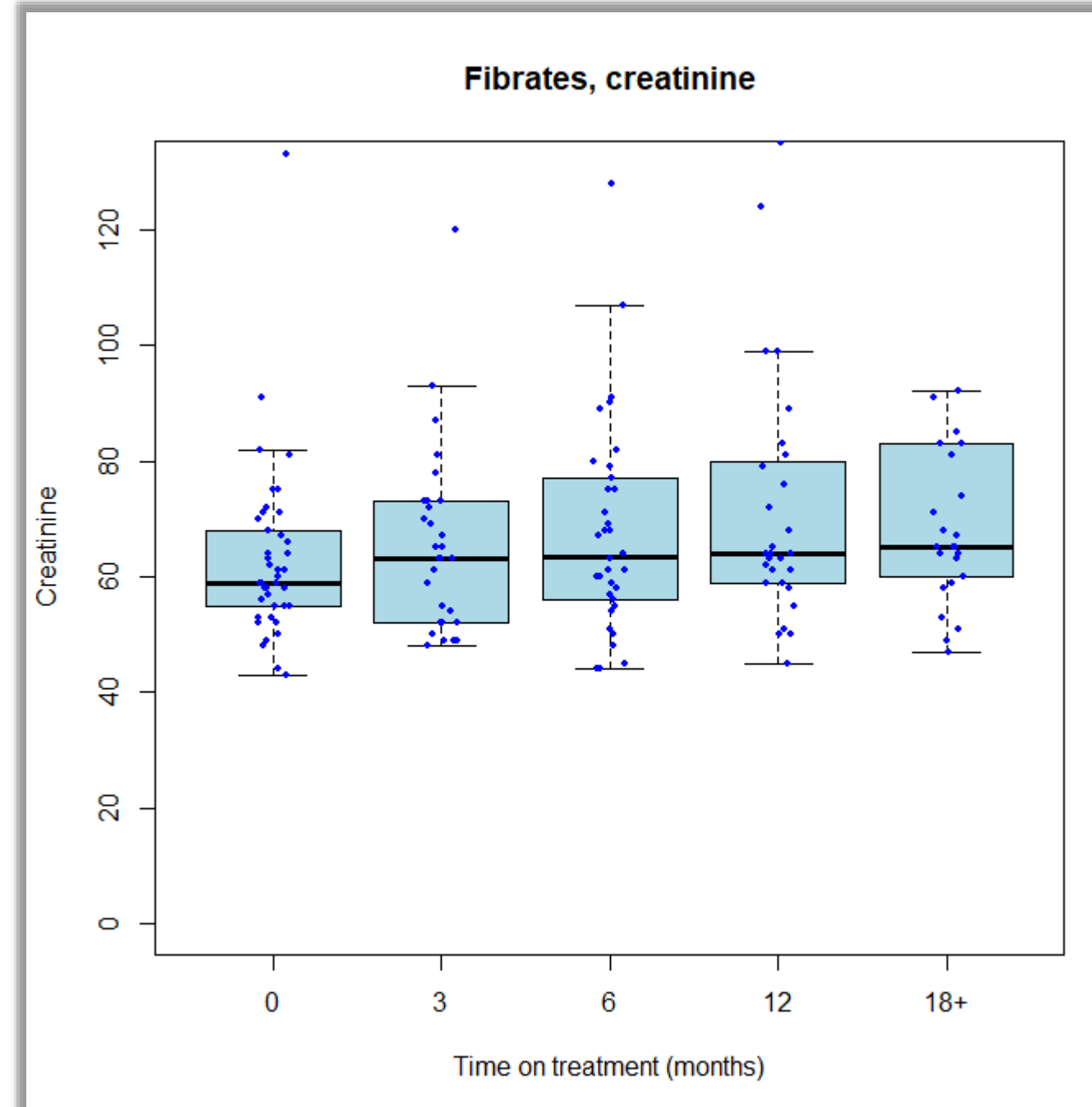
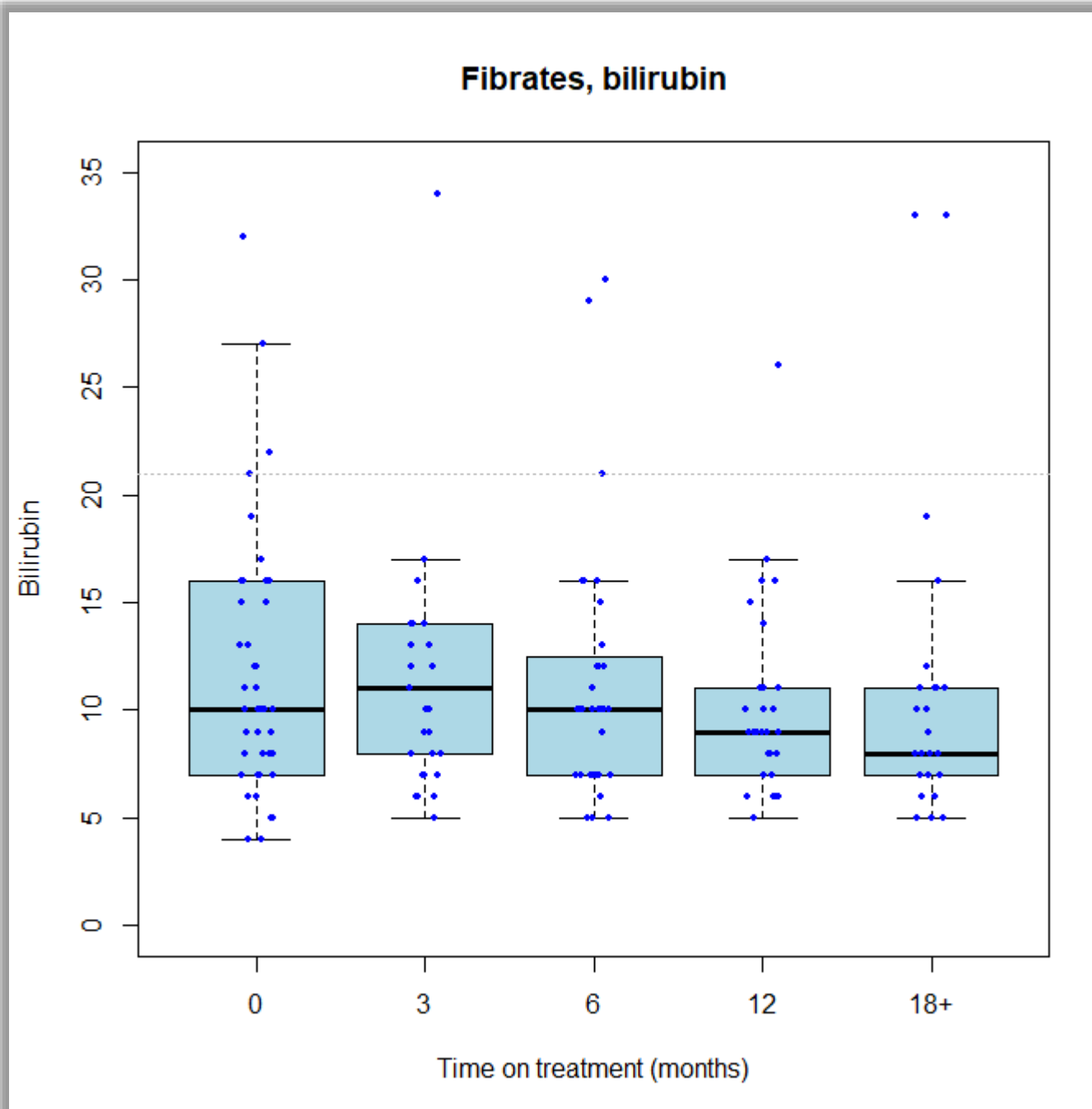
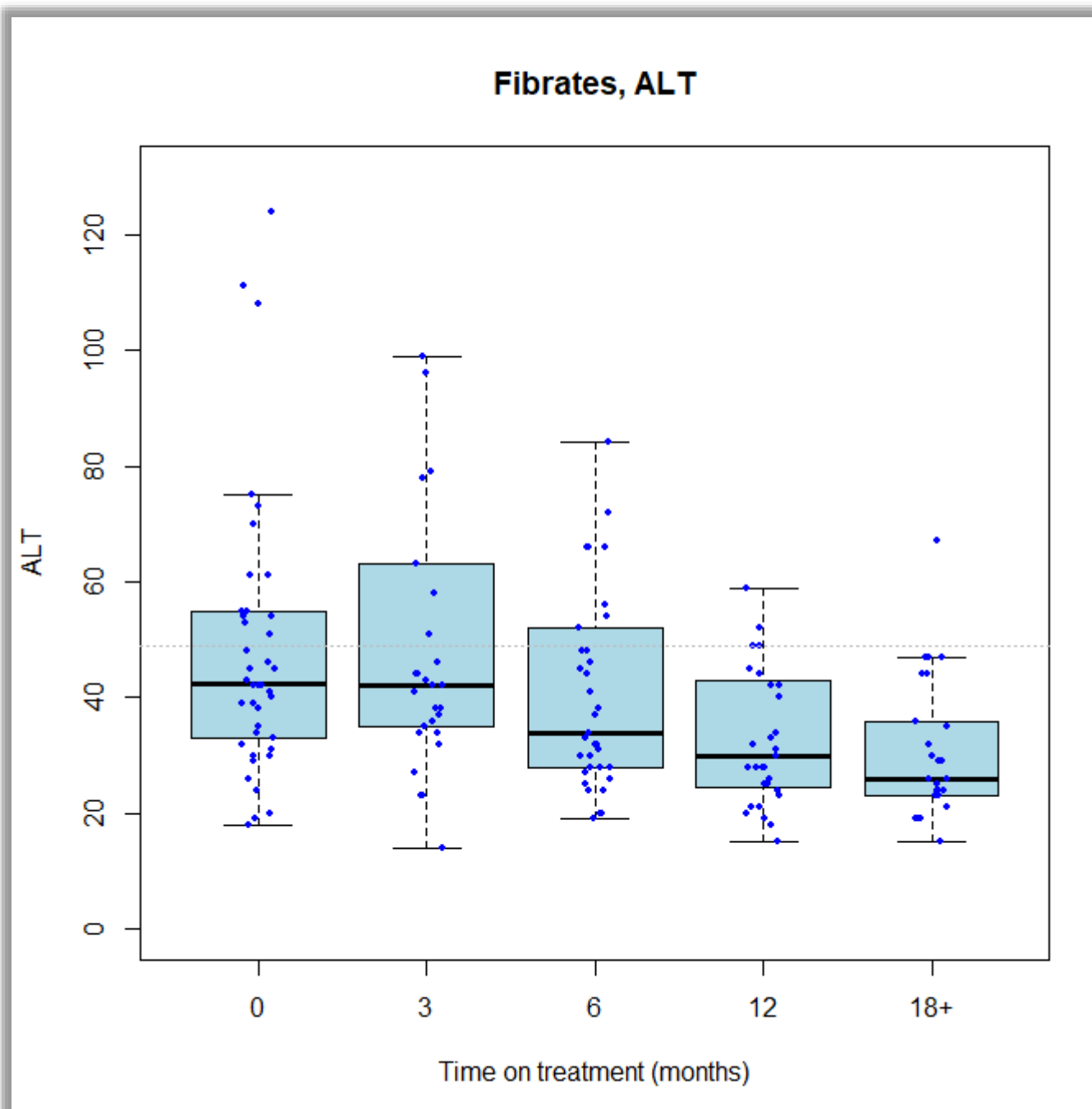
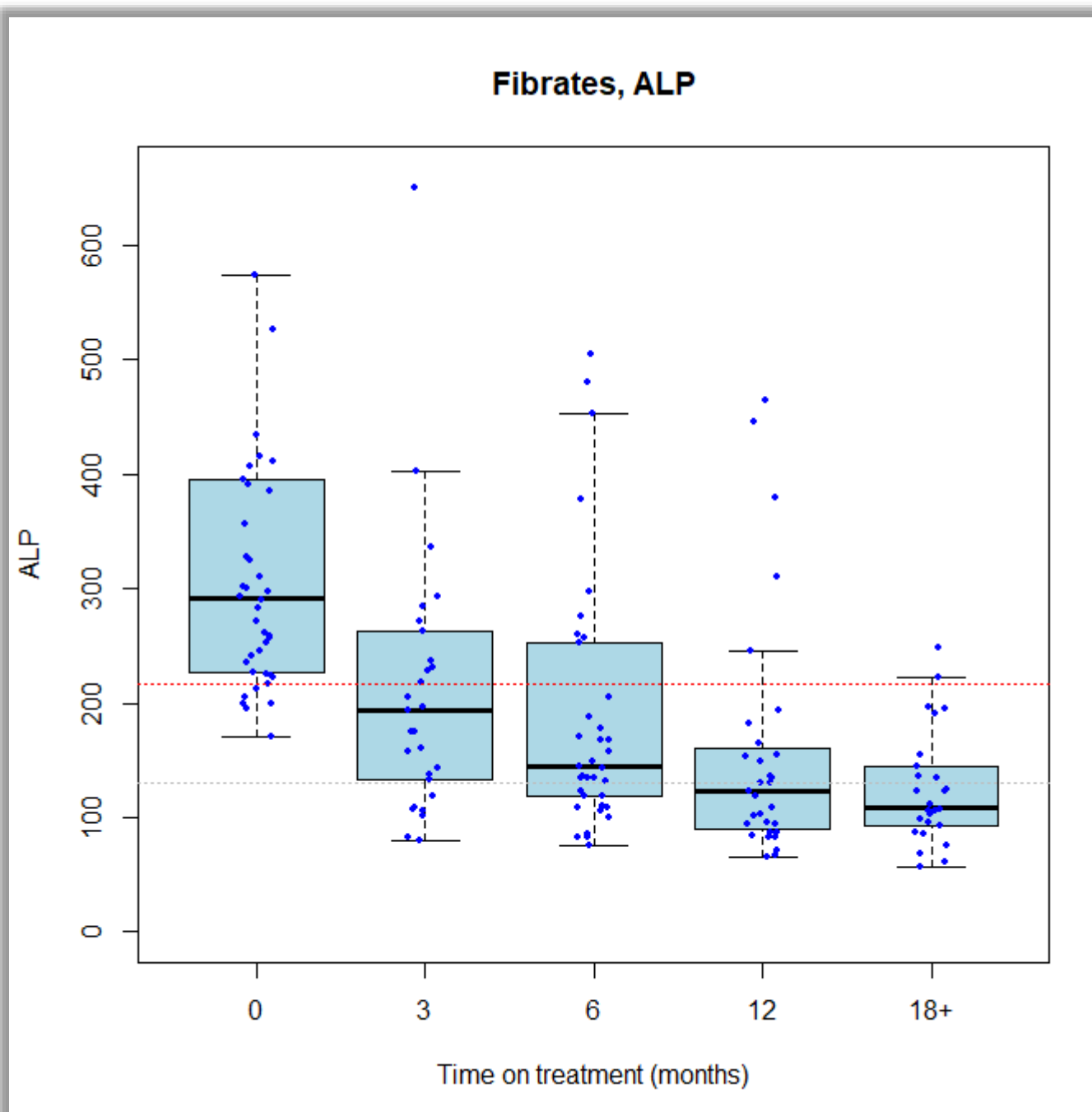
Protocol: High-risk PBC patients are referred to one of three hubs: Addenbrooke's Hospital (Cambridge University Hospitals NHS Foundation Trust); Basildon Hospital (Mid and South Essex NHS Foundation Trust); or Norfolk and Norwich University Hospital. They attend at least one outpatient appointment at their nearest hub, and treatment of their PBC is discussed the next meeting of the EoE PBC MDT. Broadly, patients who are eligible for second-line treatment are considered for BZF if (1) their PBC is early in stage and only moderately active; (2) they have normal renal function; and (3) they do not require treatment with a statin. Otherwise, they are prioritized for OCA. All patients are offered enrollment in a clinical trial if they fulfill the eligibility criteria. Treatment with BZF is monitored remotely by a specialist nurse at one or other hub site for at least six months. Treatment with OCA is monitored remotely for at least 12 months. Patients with inadequate response to BZF may be switched to OCA; conversely, BZF may be added to the treatment of patients with inadequate response to OCA.

Referrals and MDT activity

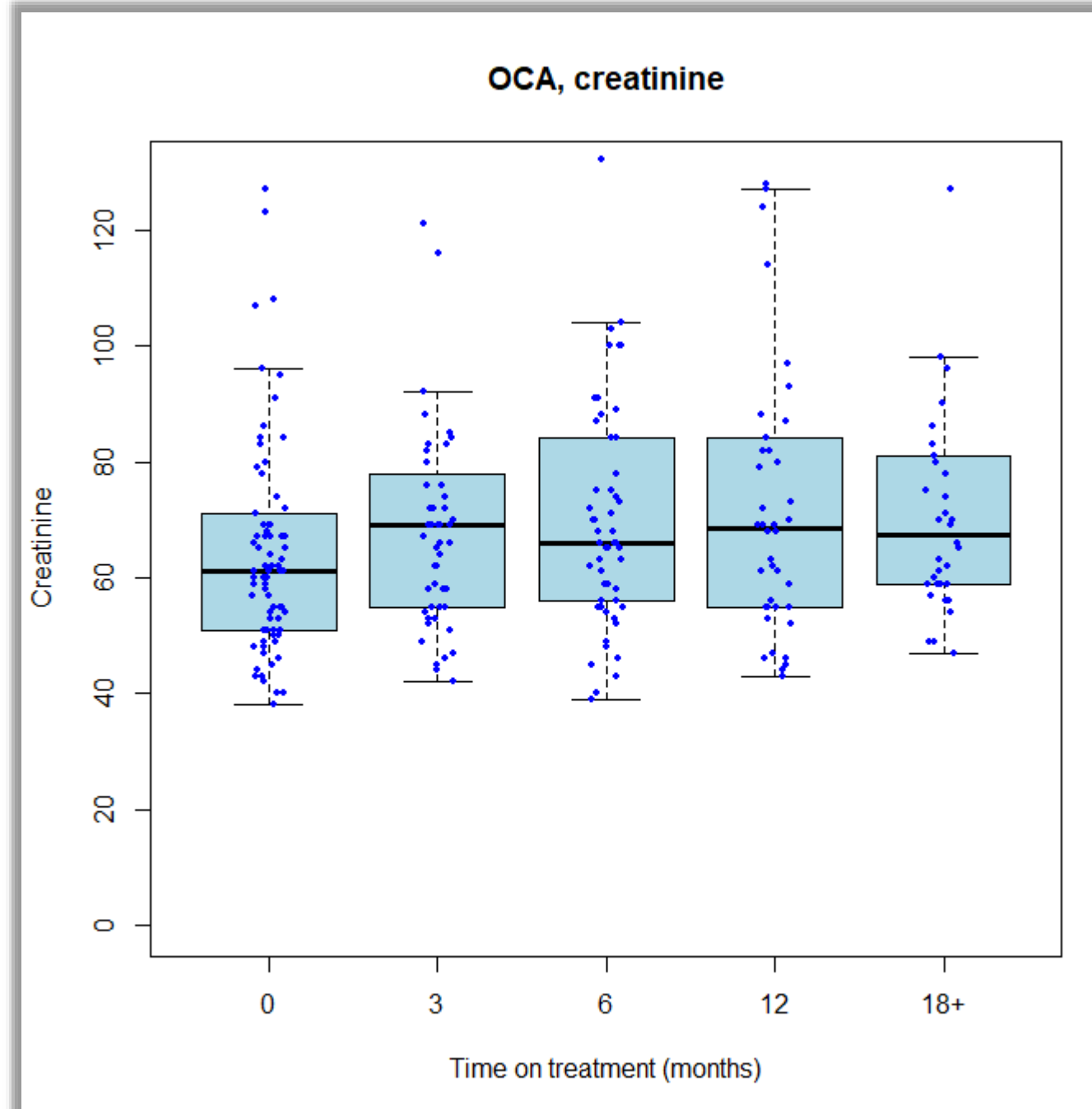
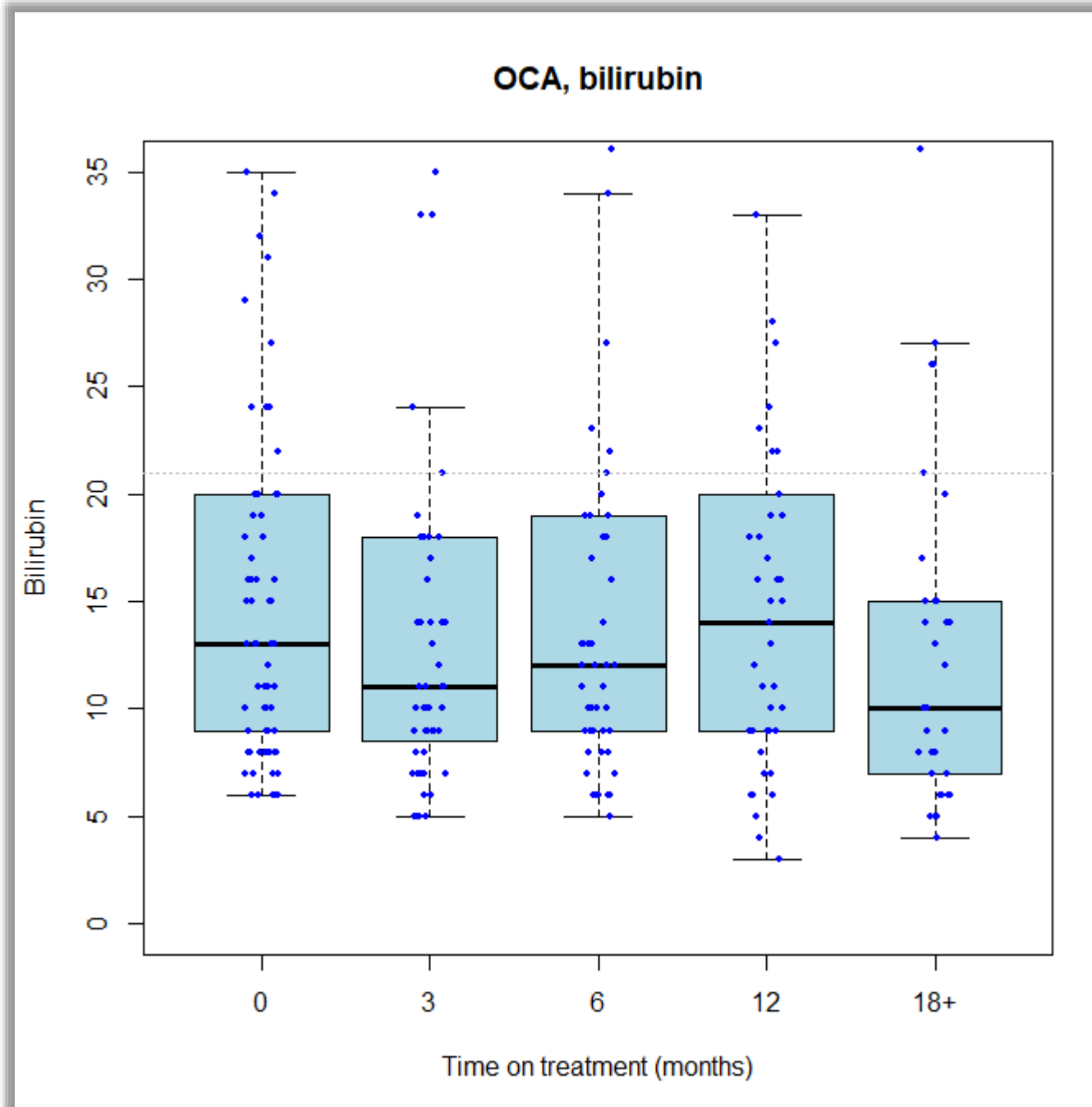
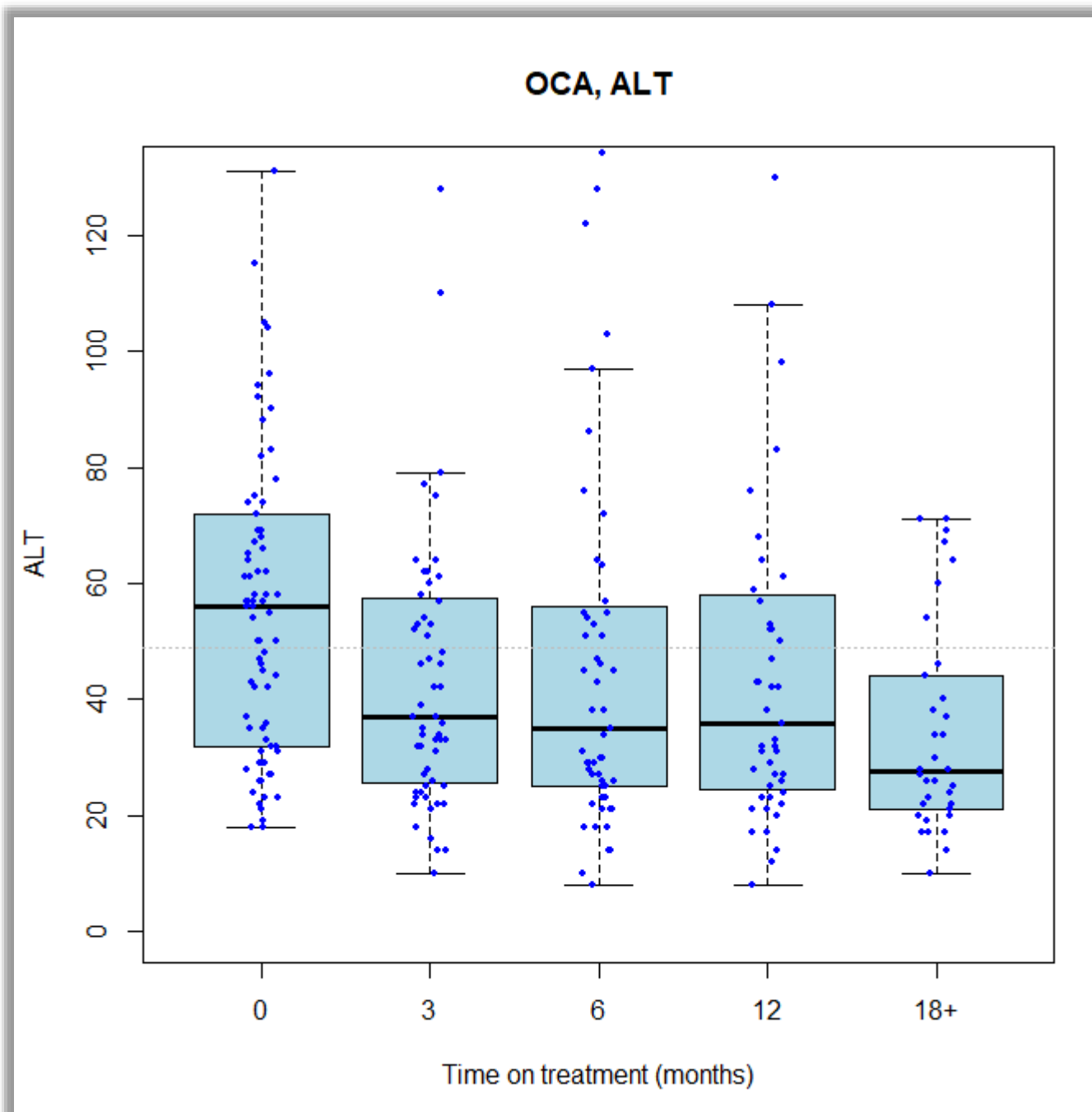
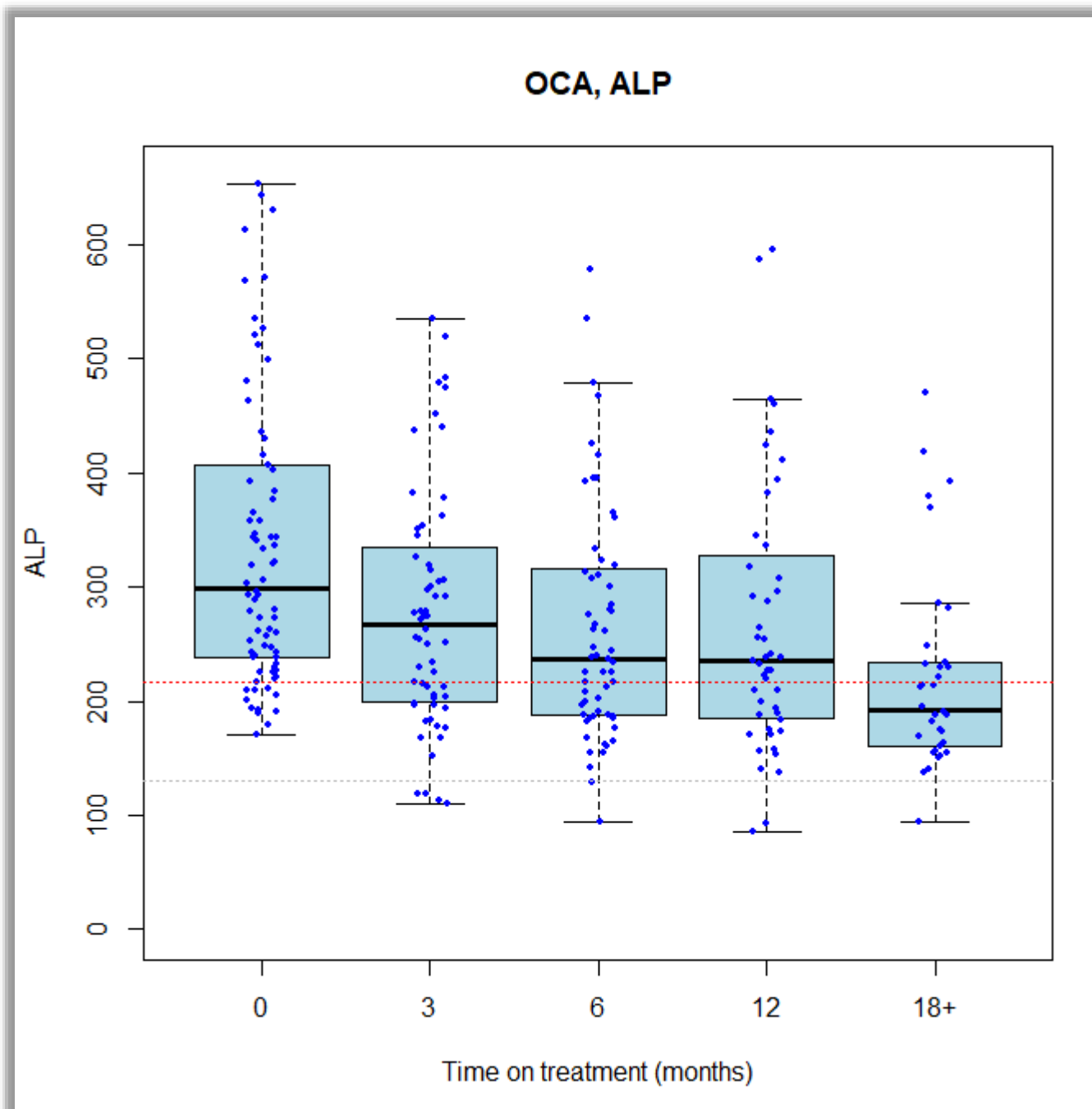


To date, 130 PBC patients have been reviewed by the EoE PBC MDT. This is the fewer than the number of patients anticipated to need second-line treatment in this region (N=300). The panel above right highlights variation in the number of referrals from Trusts across the EoE, which might reflect differences in catchment populations.

Fibrates



Obeticholic acid



Outcomes

| | Started | Continued | To OCA | To BZF | BZF added | SLT stopped |
|--------------|---------|-----------|--------|--------|-----------|-------------|
| Fibrate | 43 | 36 | 5 | - | - | 2 |
| OCA | 71 | 53 | - | 6 | 3 | 12 |
| Too mild | 14 | - | - | - | - | - |
| Too advanced | 2 | - | - | - | - | - |

The table above shows the outcomes for patients reviewed by the EoE PBC MDT.

A total of 43 patients started second-line treatment with fibrates. Of these, 36 continue to take a fibrate. In 5 cases, the fibrate was switched to OCA owing to inadequate response to the fibrate. Two patients stopped fibrates owing to renal impairment and have not yet resumed second-line treatment. Treatment with fibrates is generally well-tolerated but some patients report mild gastrointestinal disturbance. Minor increase in the serum creatinine is seen in most patients. Acute kidney injury occurred in two (as above).

The boxplots above ("Fibrates") show improvement in the liver tests and stable renal function in those who continue treatment with fibrates.

A total of 71 patients started second-line treatment with OCA. Of these, 53 continue to take OCA. In 6 cases, OCA was switched to bezafibrate (BZF) owing to pruritus. In 3 cases, BZF was added to OCA owing to inadequate response to second-line treatment with OCA alone. Five patients initially treated with OCA have undergone liver transplantation. Seven patients have died; none of these deaths are attributable to second-line treatment of PBC. The boxplots above ("Obeticholic acid") show steady improvement in the liver tests in those who continue treatment with OCA. Note that in the EoE, patients prioritized for treatment with OCA generally have more advanced or more active PBC; therefore, slower response to second-line treatment might be anticipated.

Overall, second-line treatment of PBC in the EoE has proven effective and well-tolerated. Hepatologists across the region should be encouraged to refer high-risk patients to the EoE PBC MDT.

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