Modelling and prediction of recruitment in clinical trials by means of a biphasic hierarchical Weibull model

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Data on patient arrivals in a multicentre clinical trial

centre	phase	(inter-)arrival time in months
1	1	9.76
1	2	1.77
2	1	9.89
3	1	4.04
3	2	1.61
3	2	0.92
3	2	0.69
3	2	0.92
3	2	1.97
3	2	1.48
4	1	5.72
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follow-up of 24 months

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plan

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- The predictive distribution should cover 12 months.

Model construction (1/3) [two distinct phases]

A **Weibull(ρ_1, λ_1)** distribution is used to model the first phase.

A **Weibull(ρ_2, λ)** distribution is used to model the second phase.

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Model construction (2/3) [variation in recruitment speed between centres]

Let $\mathbf{U} \sim \mathbf{Gamma}$ denote a **centre-specific** frailty term $[\mathrm{E}(U) = 1, \mathrm{Var}(U) = \theta]$.

$$\boxed{\boldsymbol{\lambda} = \boldsymbol{\lambda_2} \times \boldsymbol{u}}$$

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Model construction (3/3)
[variation in recruitment speed over time]

- Consider the data at 6 months;
- Fit the phase 2 model and record the estimate of the overall recruitment speed λ_2;
- Repeat with the data at 7, 8, …, 24 months.

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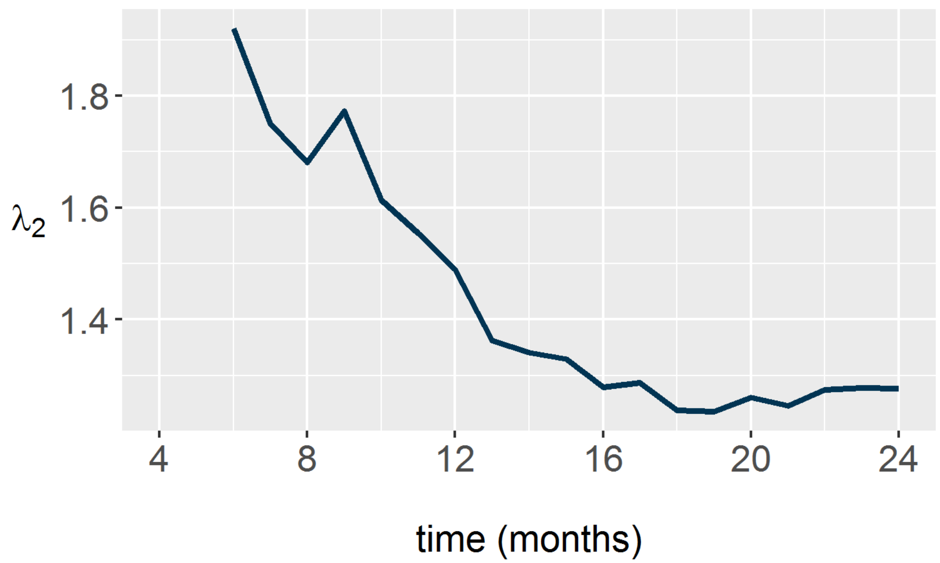

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Let $\boldsymbol{x}$ denote the time elapsed since the arrival of the first patient in the centre

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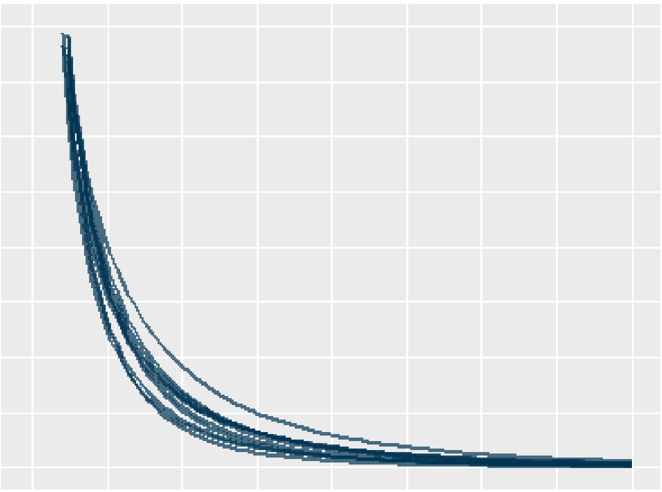
Prediction of the time needed to recruit the remaining patients...

- 30 centres entered the trial within the first 12 months.
- 141 patients were recruited during this time period.
- 20 new centres entered the trial over the following 12 months.
- A total of 514 patients were recruited over the 2 years period.
- Based on the data at 12 months, the predictive distribution of the time needed to recruit $514 - 121 = 393$ patients is derived...

… assuming that no new centres will enter the trial



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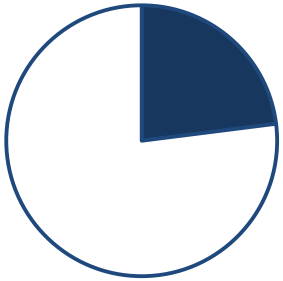

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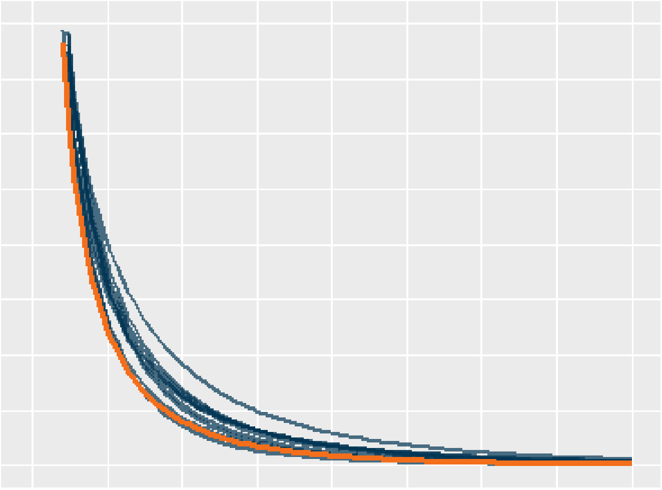

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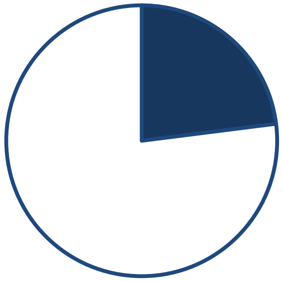

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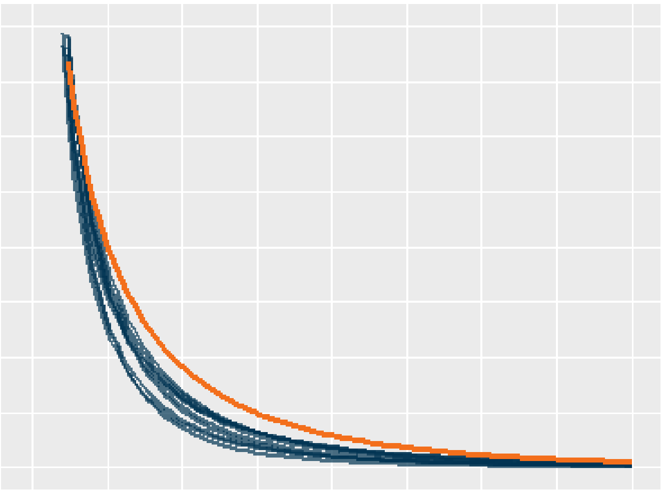

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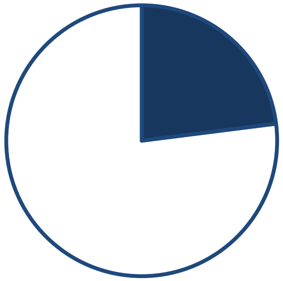

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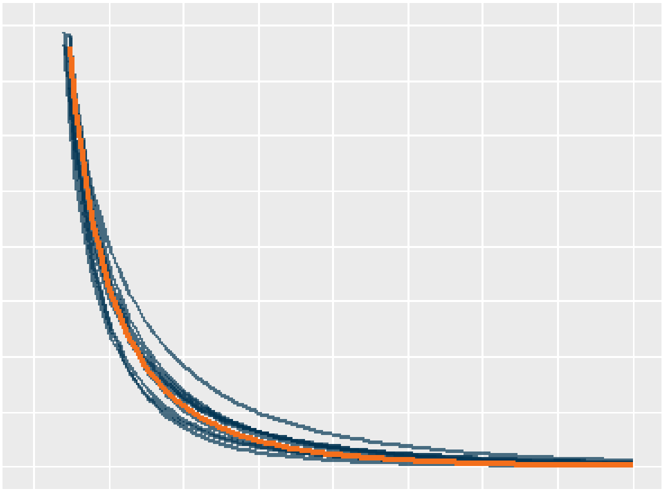

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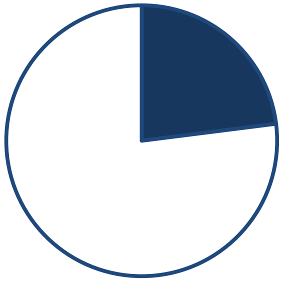

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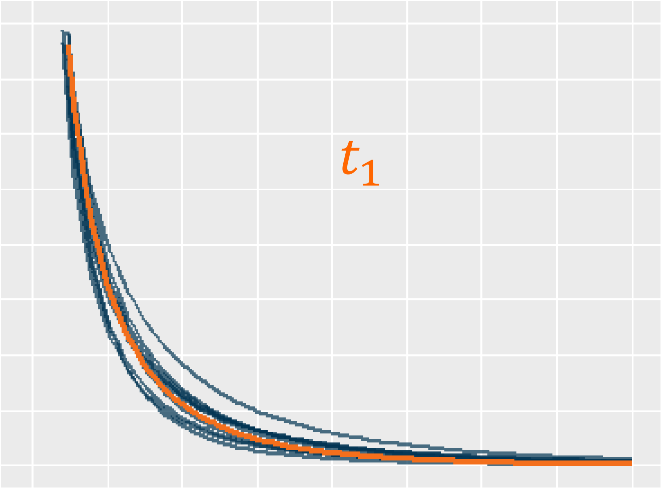

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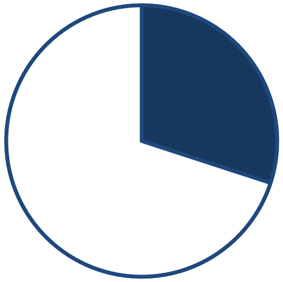

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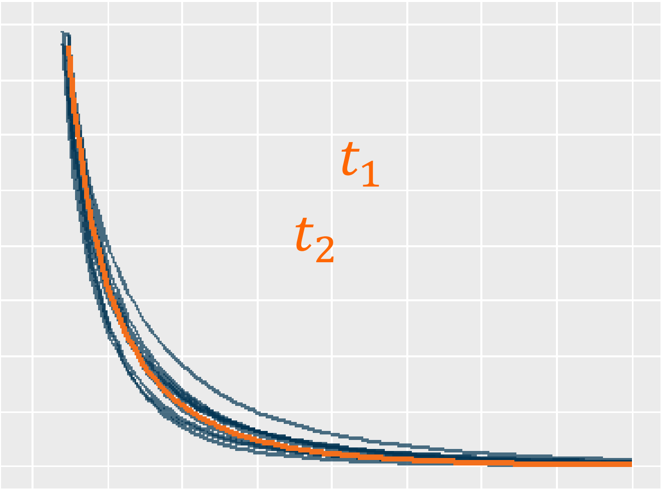

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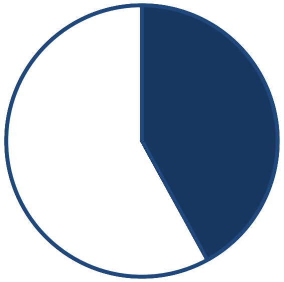

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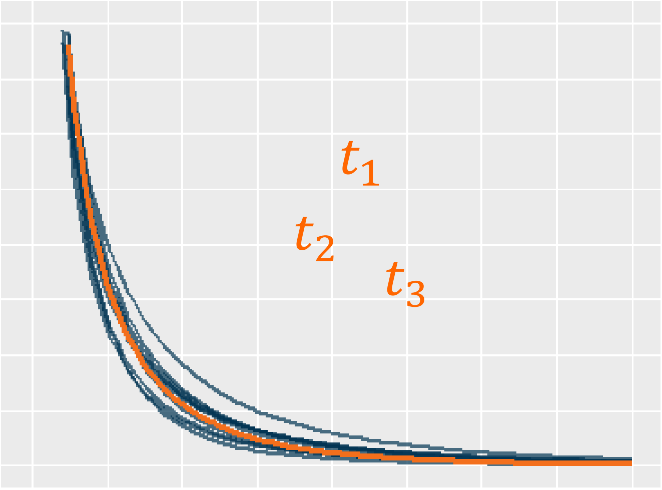

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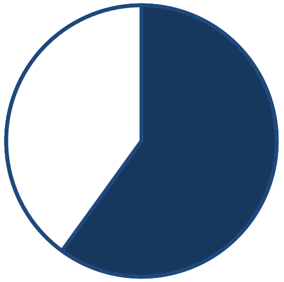

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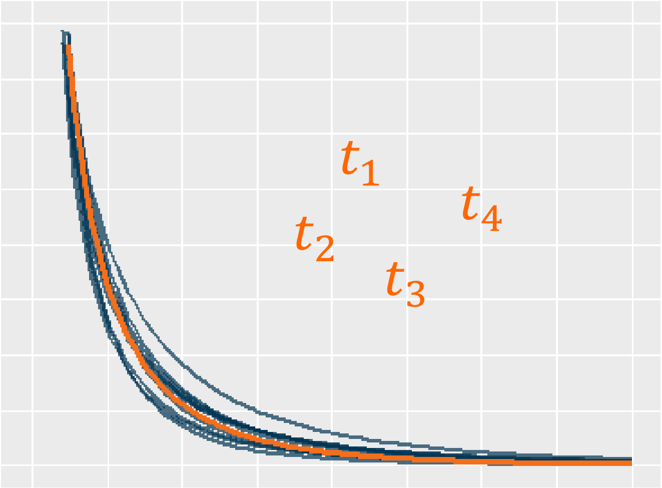

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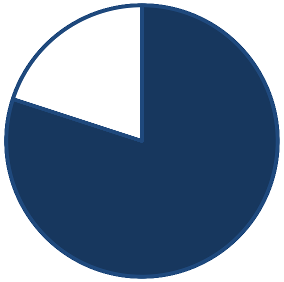

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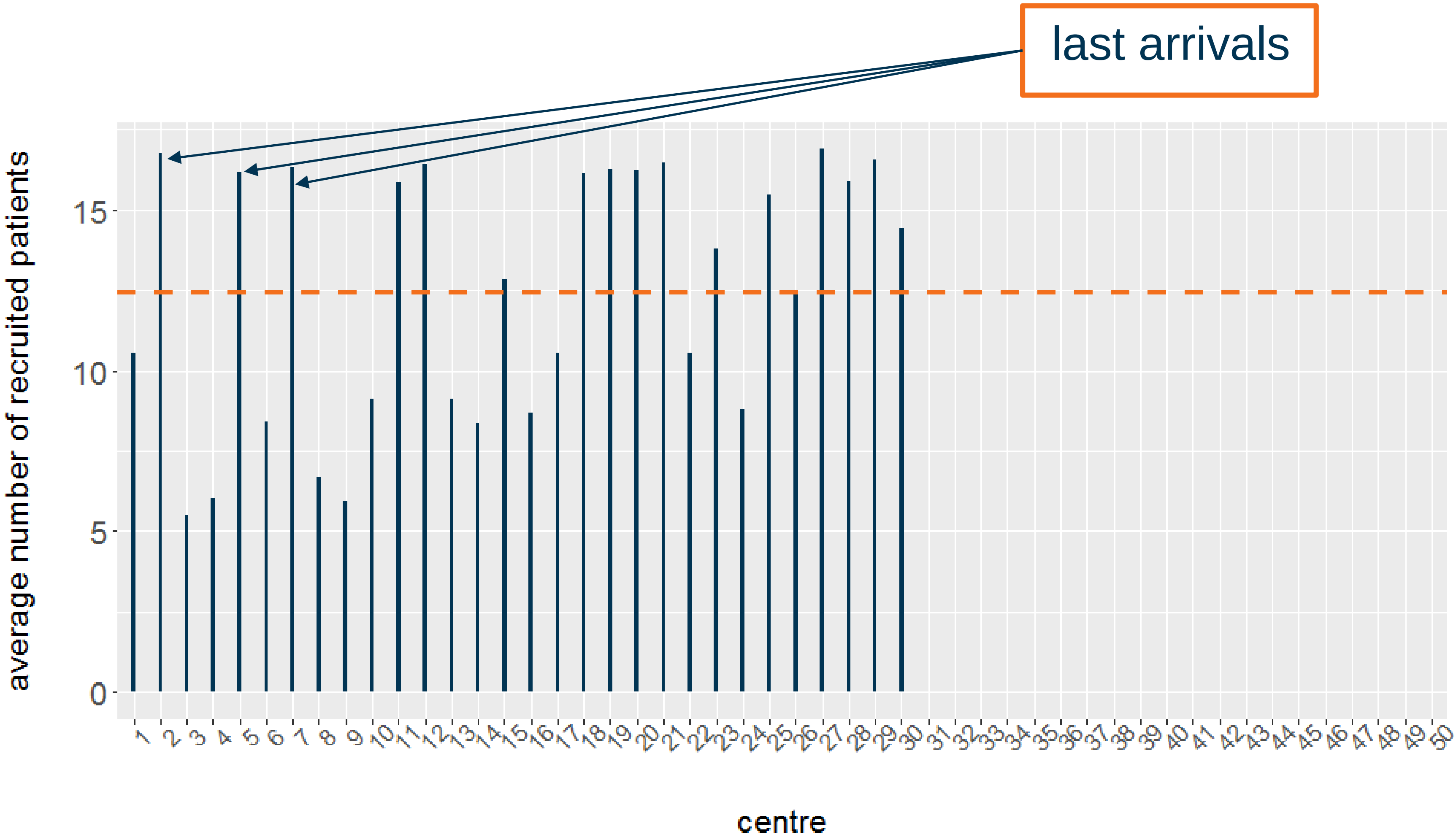

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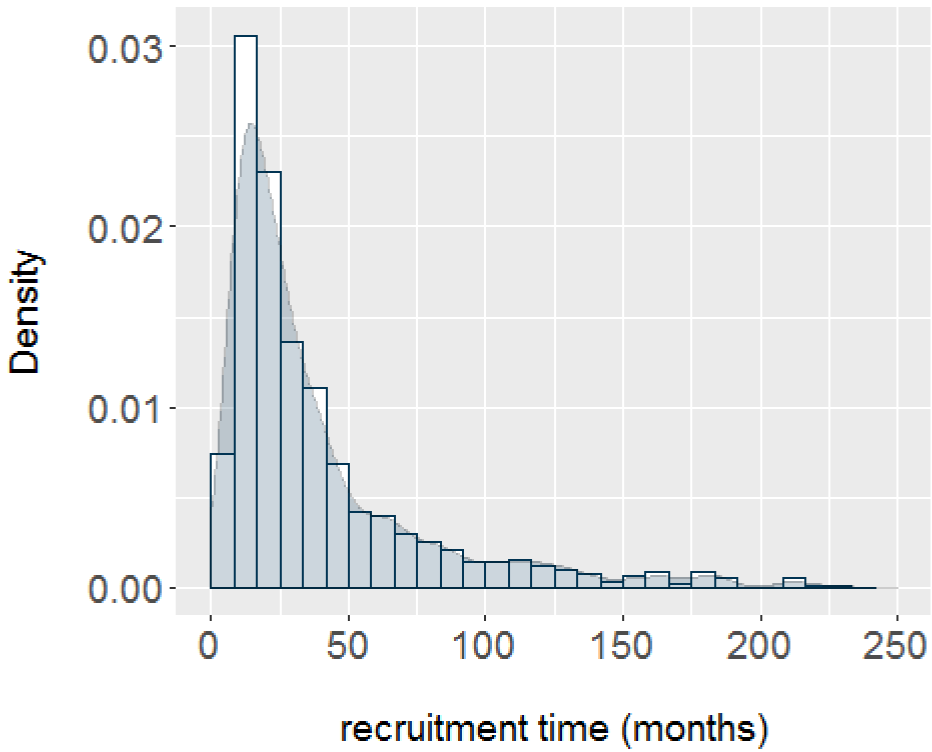

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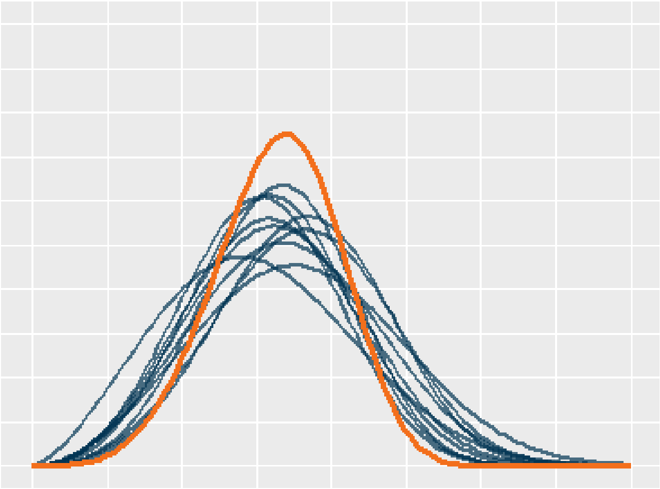

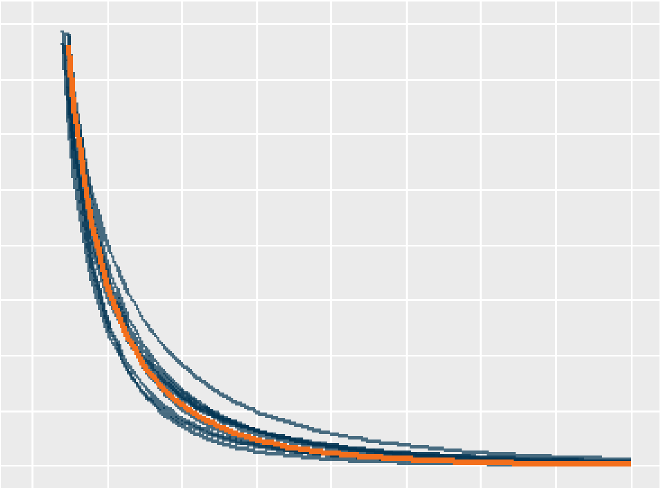

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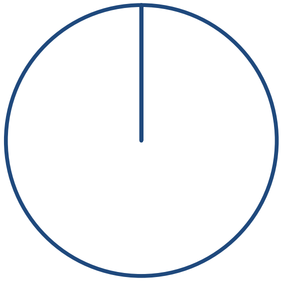

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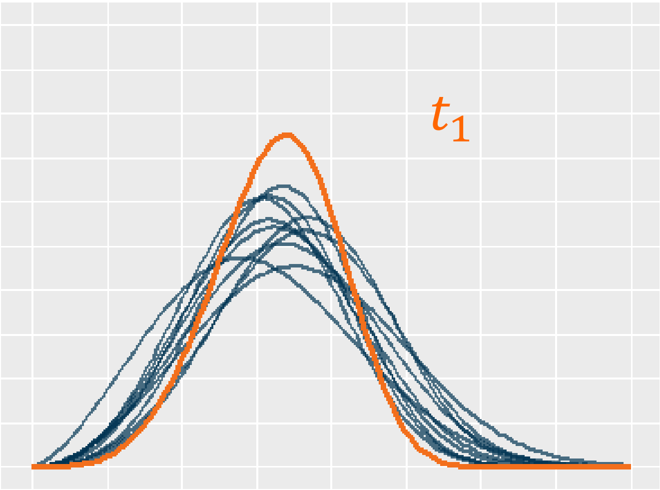

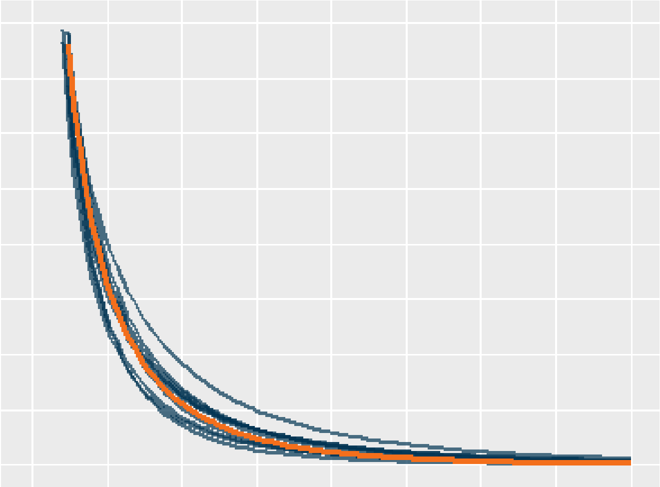

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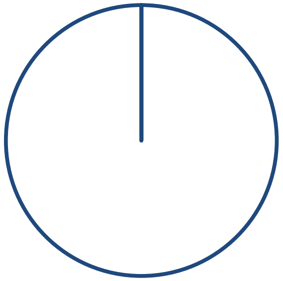

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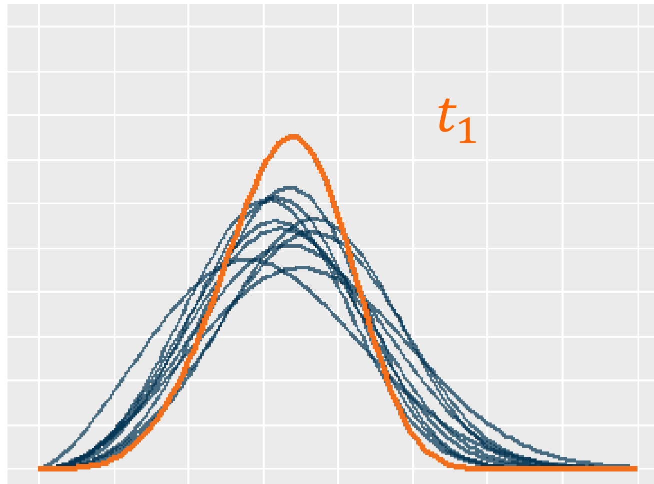

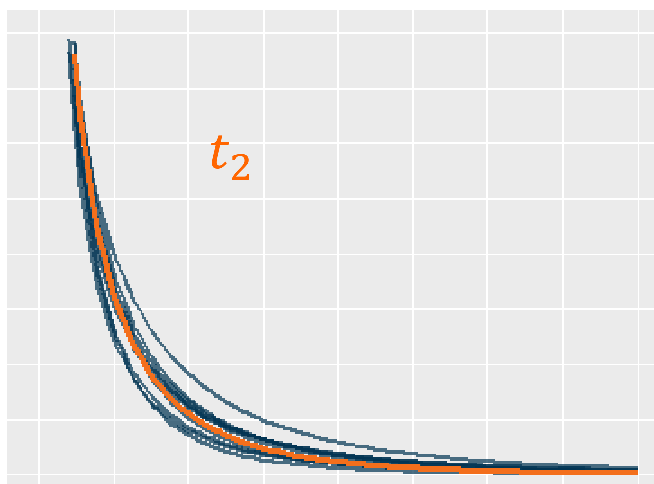

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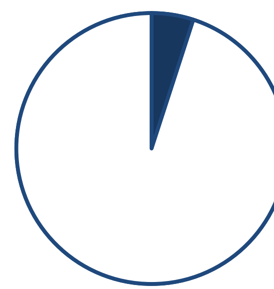

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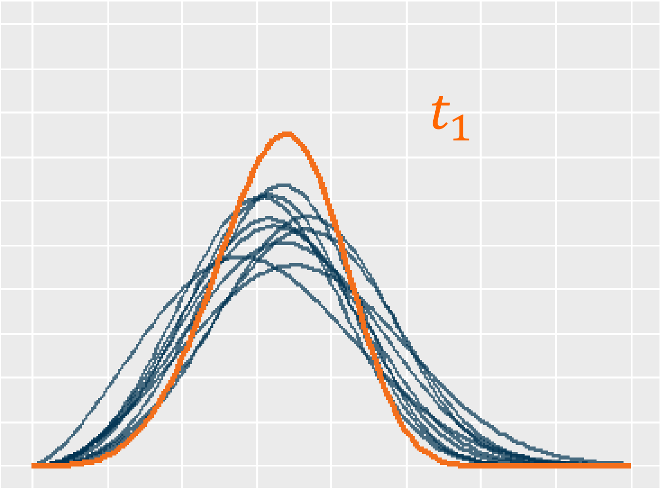

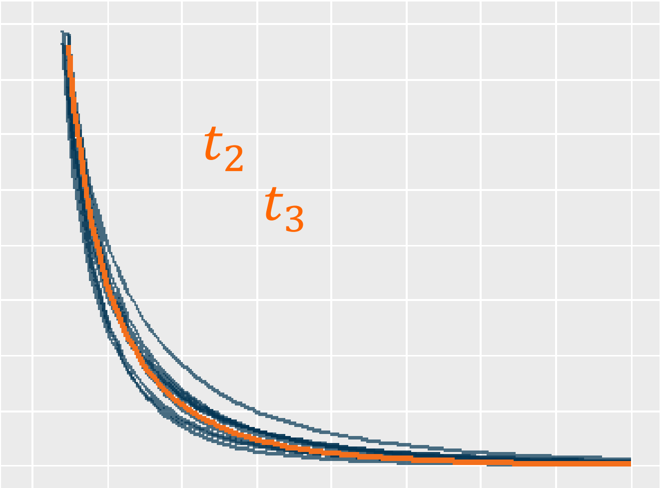

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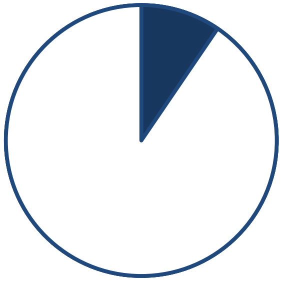

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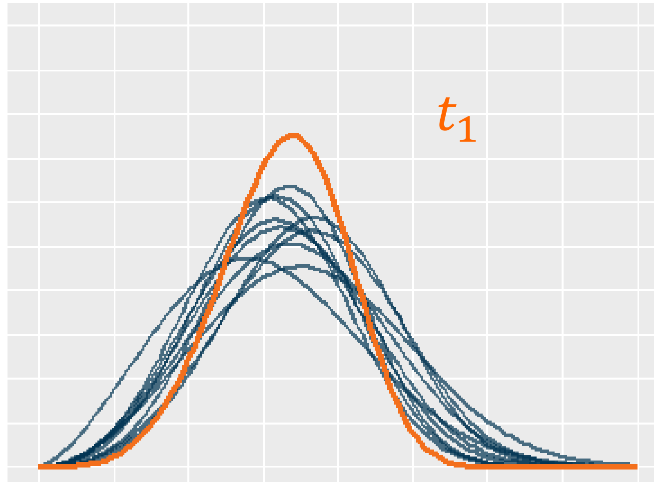

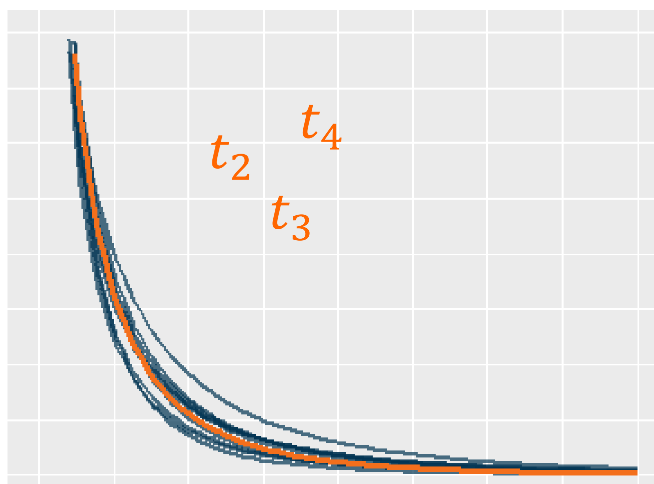

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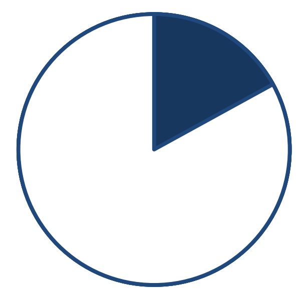

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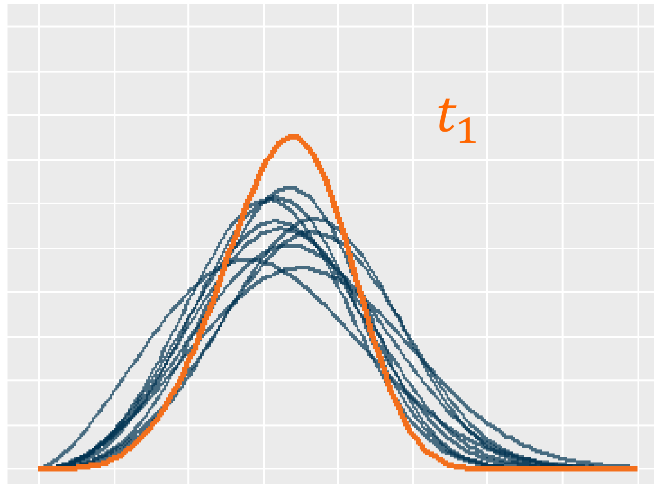

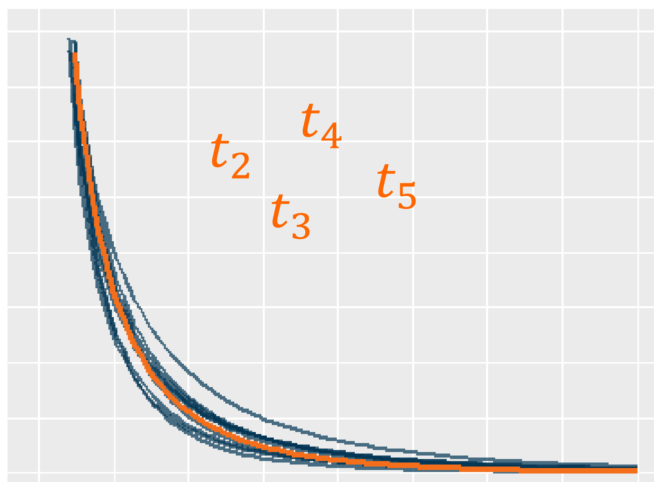

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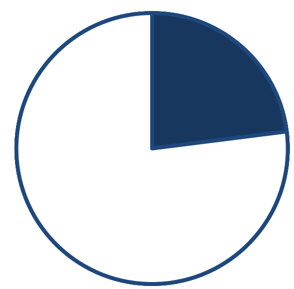

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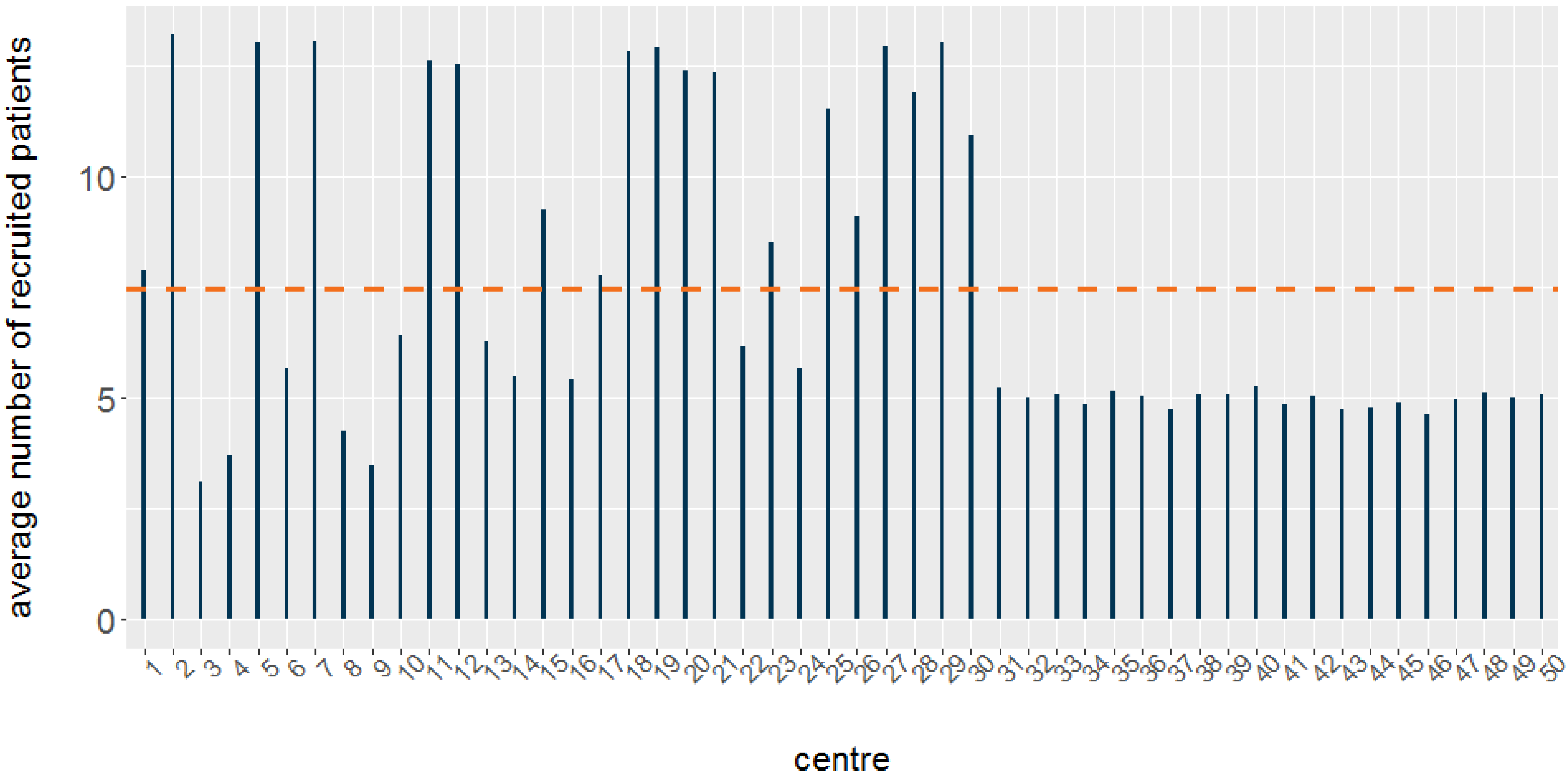

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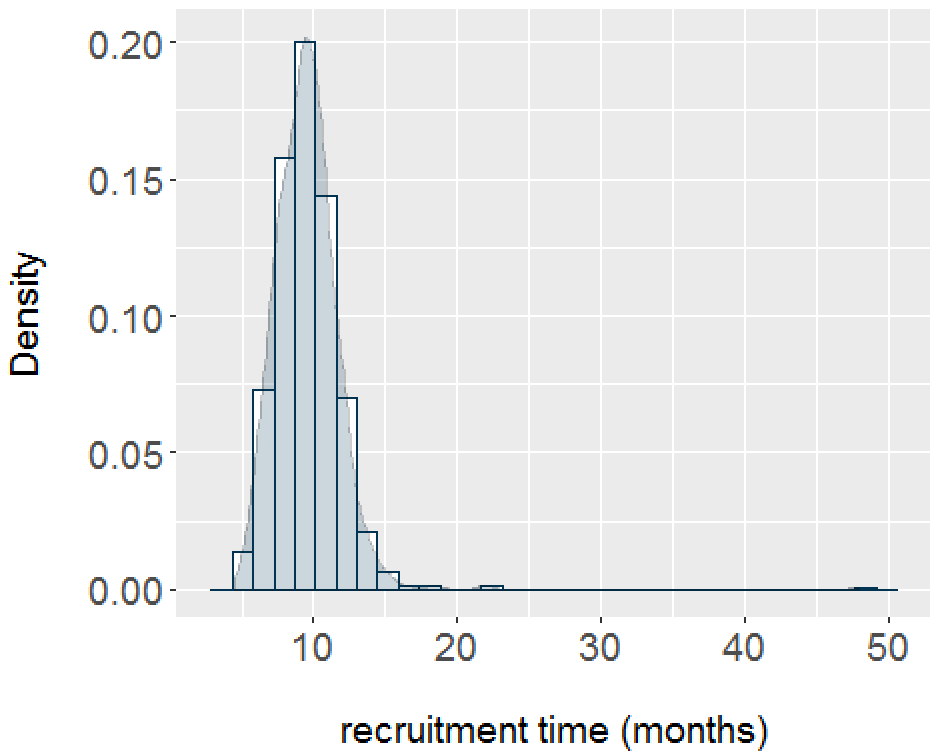

The same at 18 months
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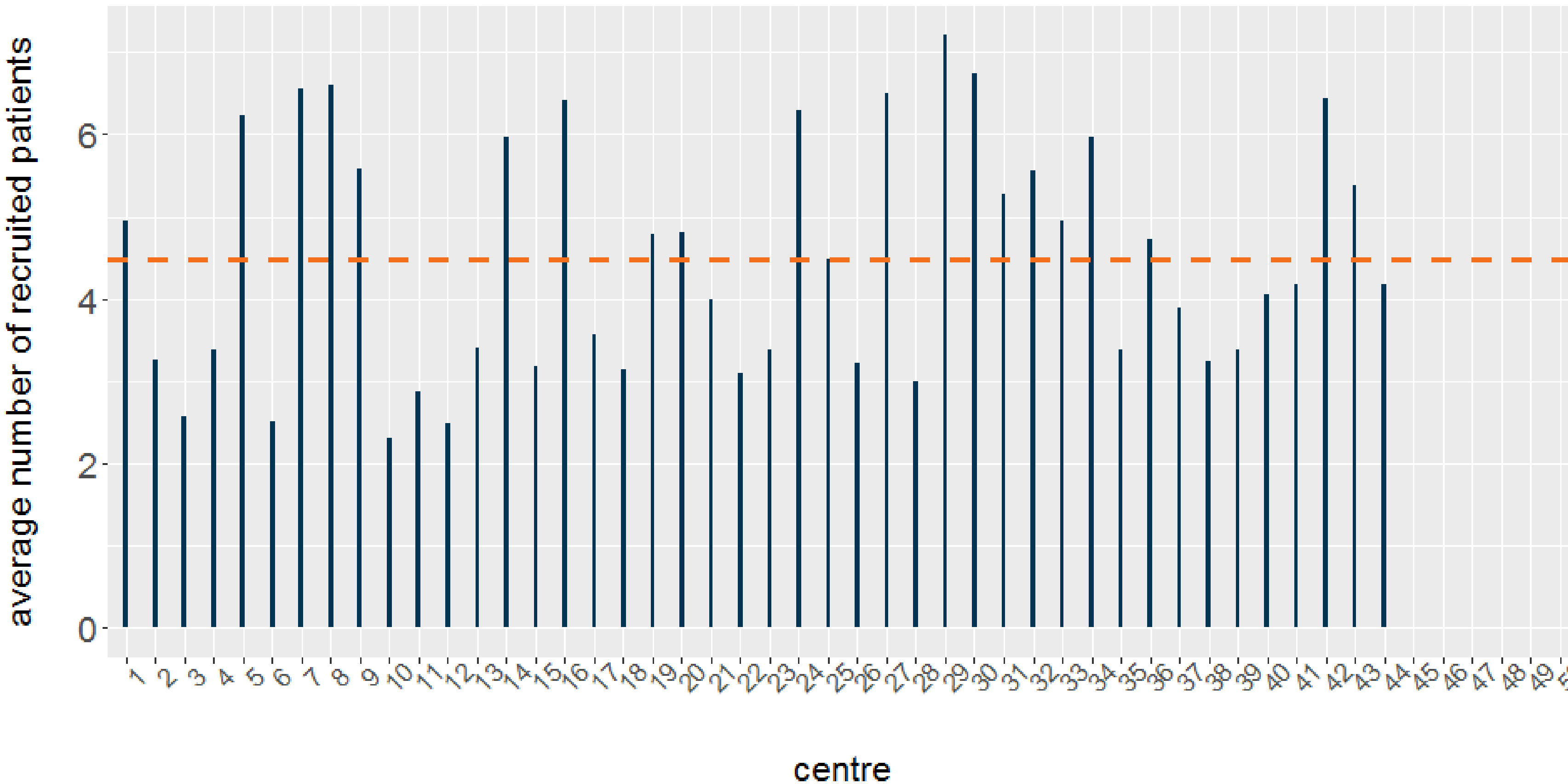

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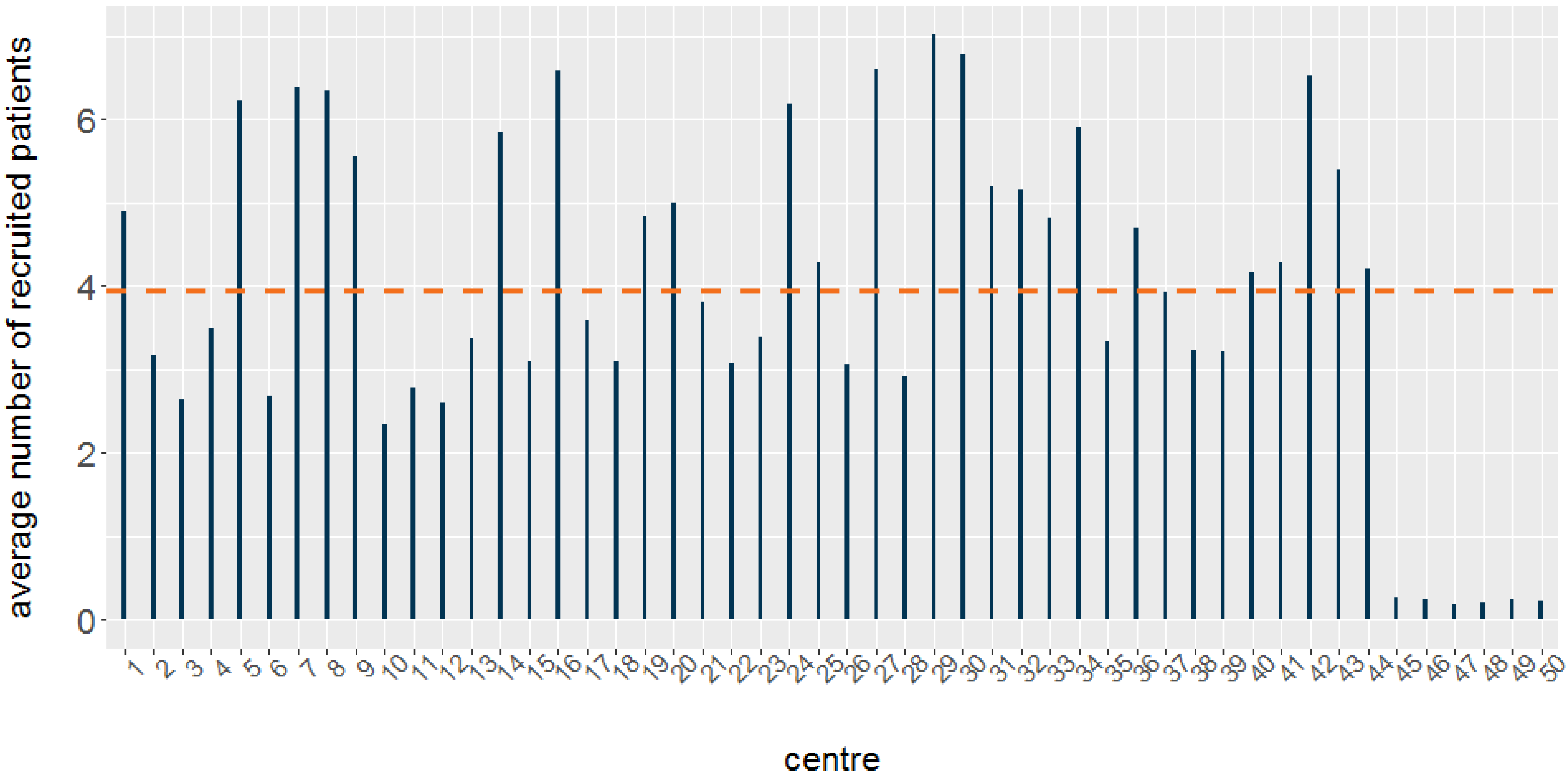

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