

## **Supplementary Material: Exploration of impact of a change in the cut off for ERI on the size of the cohorts**

### **ERI 1.5 U/Kg/wk/Hgb [g/L]**

Figures S1 and S2 show the distributions of ERI at index date for Epoetin Alfa and Darbepoetin for the hypo- and normoresponder cohorts.

**Figure S1.** Distributions of ERI at index date for Epoetin Alfa

**Figure S2.** Distributions of ERI at index date for Darbepoetin

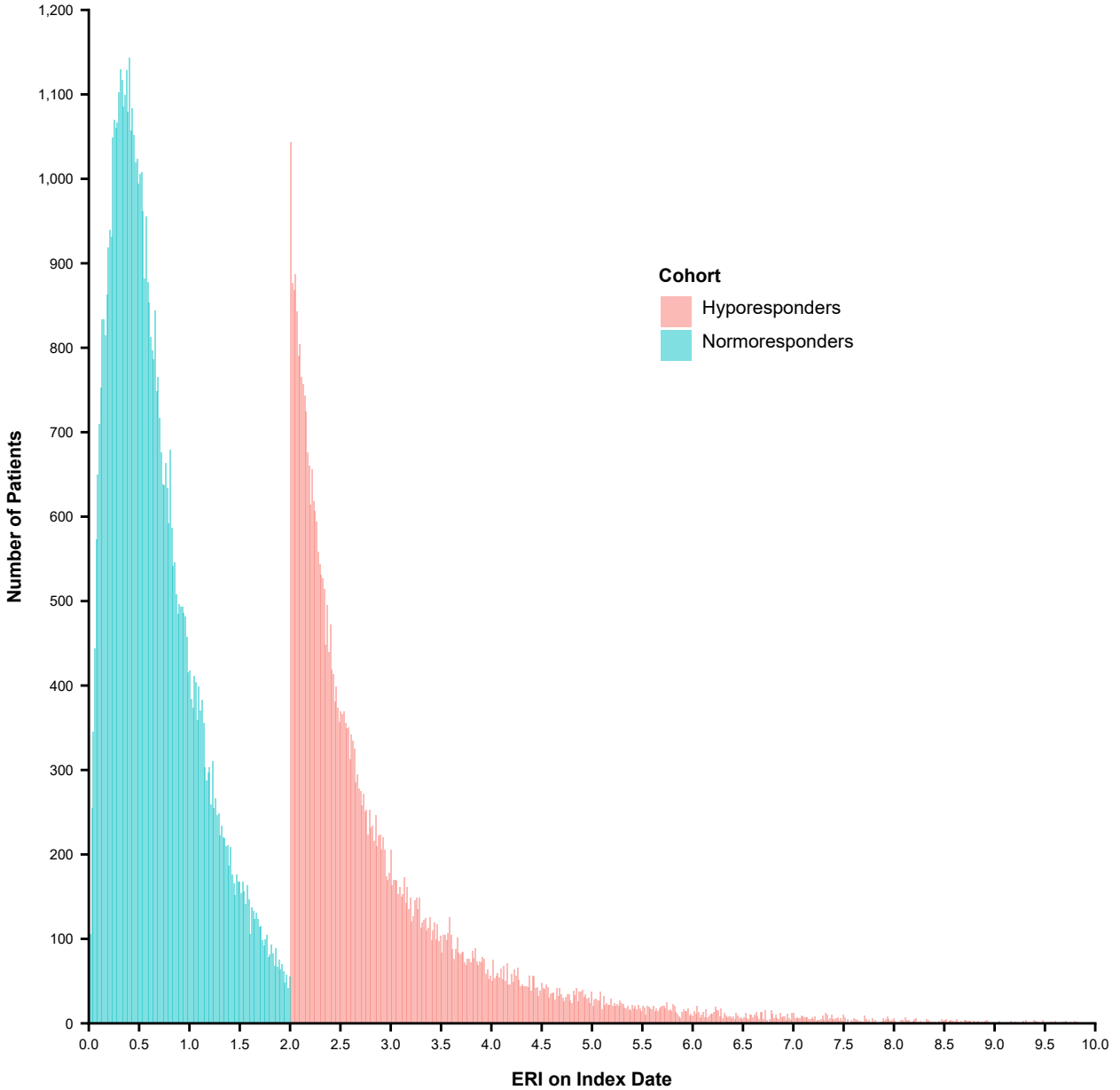
Notable in these figures S1 and S2 is the peak at ERI=2. There are two things we believe are driving this spike at the 2.0 ERI cutoff for Epoetin Alfa:

- 1) Bin width
  - a. The width of the bars in the histograms above is 0.015, meaning anyone from an ERI of 2.0 to 2.015 are included in this “spiked” bar.
- 2) Use of the first hyporesponsive month to classify hyporesponders
  - a. It is likely the case that many people that have an ERI very close to 2.0 in their first hyporesponsive month have subsequent months with higher ERIs of 2.1, 2.2, 2.3 etc. Because the index ERI corresponds to the first month, these subsequent months are not shown in the distribution, trending the histogram towards lower ERI values
- 3) The distributions for the normoresponder and hyporesponders
  - a. The distribution at index date for normoresponders indicates that not many would be reclassified as hyporesponders if a different ERI cut off were used however, if all the possible eligible index dates were reviewed (rather than the randomly selected index dates ones for this analysis) the distribution is different.
  - b. In figure S3 below we plotted the “highest ERI month” for the normoresponders to get a better sense of this potential shift should a lower ERI cutoff be used:

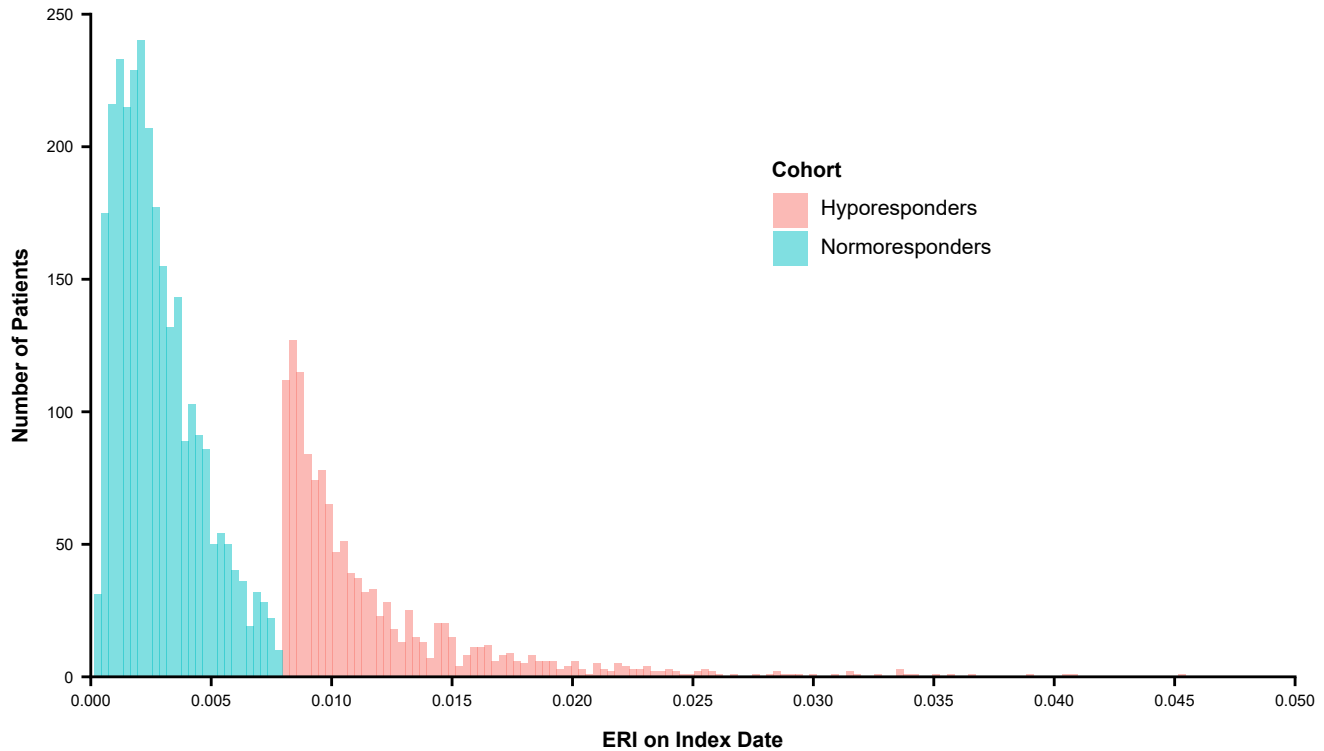
**Figure S3.** Distribution of Highest ERI Month among Normoresponders- Epoetin Alfa

- c. From this figure S3 we can see that among all normoresponders in our sample, roughly 20% have a month in which the ERI is between 1.5 and 2 and may be reclassified as hyporesponders were a cutoff of 1.5 be used.
- d. It should be noted that this is only an estimate of how many normoresponders would get reclassified; there are a few other eligibility criteria that are applied after the index month is chosen (e.g. these patients would have a different baseline/follow-up period, etc.). The same would be true for members of the hyporesponder cohort whose index month may change if they also had an ERI between 1.5 and 2 in a different month.

# Distribution of ERI on Index Date - Epoetin Alfa



## Distribution of ERI on Index Date - Darbeopetin



# Distribution of Highest ERI Month Among Normoresponders - Epoetin Alfa

