Oral Bisphosphonate Use And Latent Class Trajectories Of Kidney Function: A Cohort Study

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Disclosures

Funding

This research was funded by the NIHR HTA (project number 14/36/02) and was supported by the NIHR Biomedical Research Centre, Oxford.

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Conflicts of Interest

VS, DER, MSA, LM, FC and YB-S declare no relationships.

Consultancies: CC – Amgen, UCB, Radius and Nestle. AJ - Anthera Pharmaceuticals Inc. and Freshfields Bruckhaus Deringer. MKJ – UCB, Amgen and Lilly. DP-A – UCB.

Lecture fees: AD-P- Amgen, UCB, Roche, Gilead, EchoLight and Radius. DP-A - Amgen.

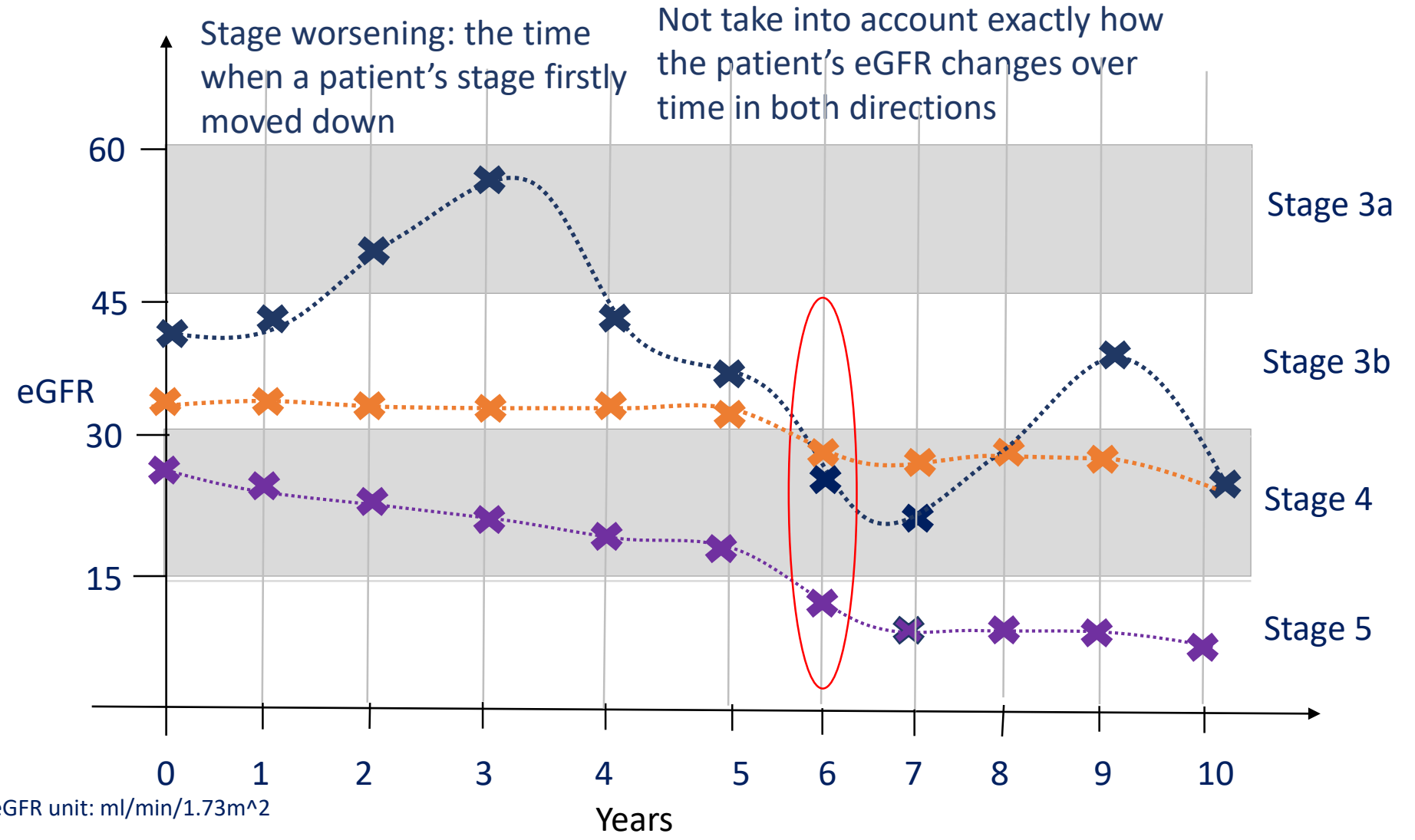
Industry sponsored grants: BA – Nycomed and UCB. DP-A – Amgen, UCB and Servier Laboratories.

Stock ownership: AD-P – shareholder of Active Life Sci.

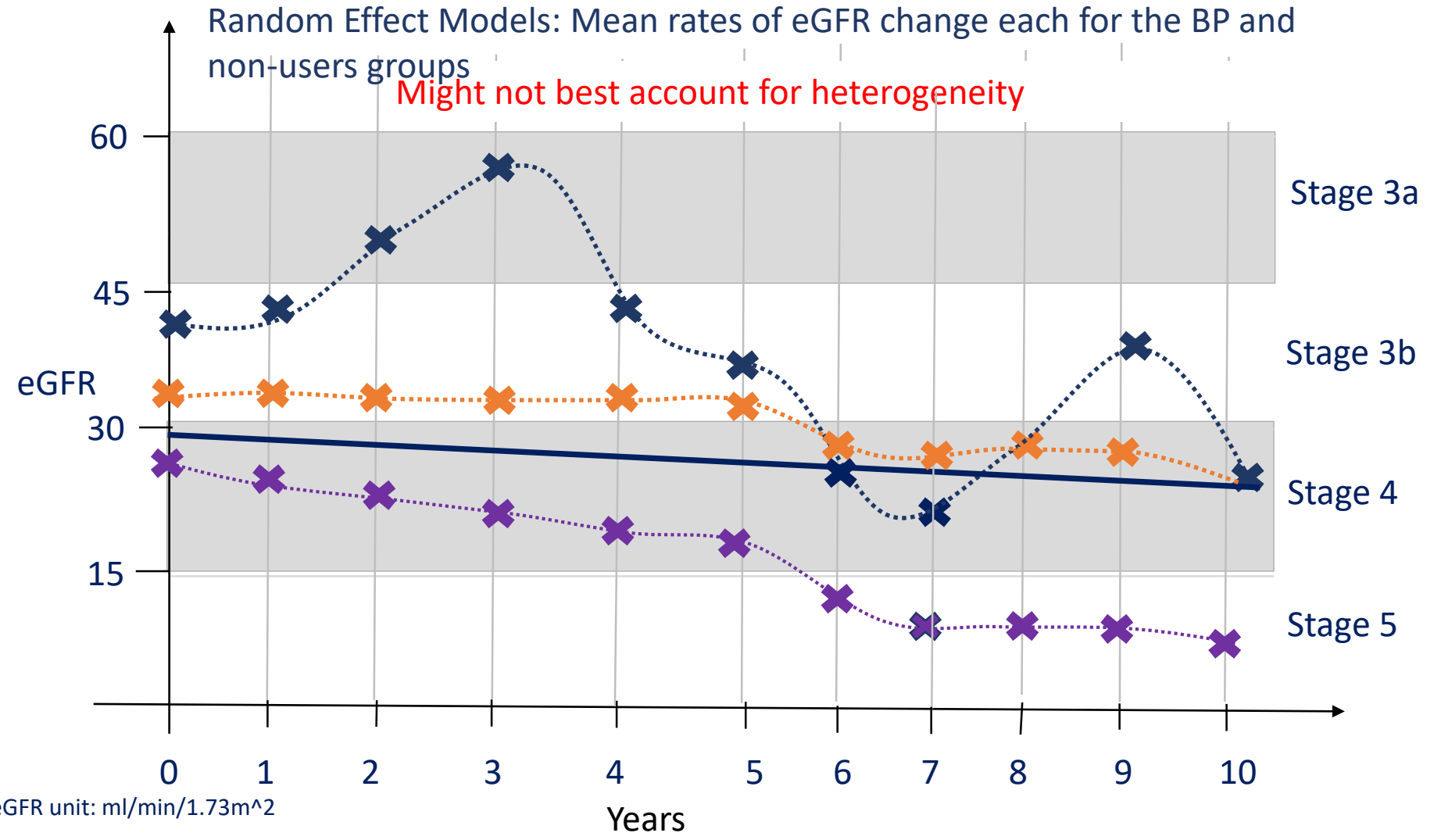
BisCK study

- A retrospective PS cohort identified in the CPRD to to explore the safety and effectiveness of the use of oral Bisphosphates (BP) in ≥stage 3B Chronic Kidney Disease (CKD) patients
- Inclusion/exclusion criteria:
  - Baseline eGFR measurement <45, (stage 3+ CKD)
  - eGFR measured after 1997
  - Aged at least 40
  - At least 1 year follow up & 1 eGFR
  - No BP use <1 year prior
  - No other anti-osteoporotic use
- Outcome Time Window
  - **BP users:** From 1st BP Rx & a recent eGFR<45 to the last Rx +210 days
  - **Non users:** From eGFR<45 to 10y/ end of enrolment/ 1st BP Rx & eGFR<45
  - Same patients could contribute both BP and non-user outcome time window

Problems of standard approaches



Problems of standard approaches



Objectives

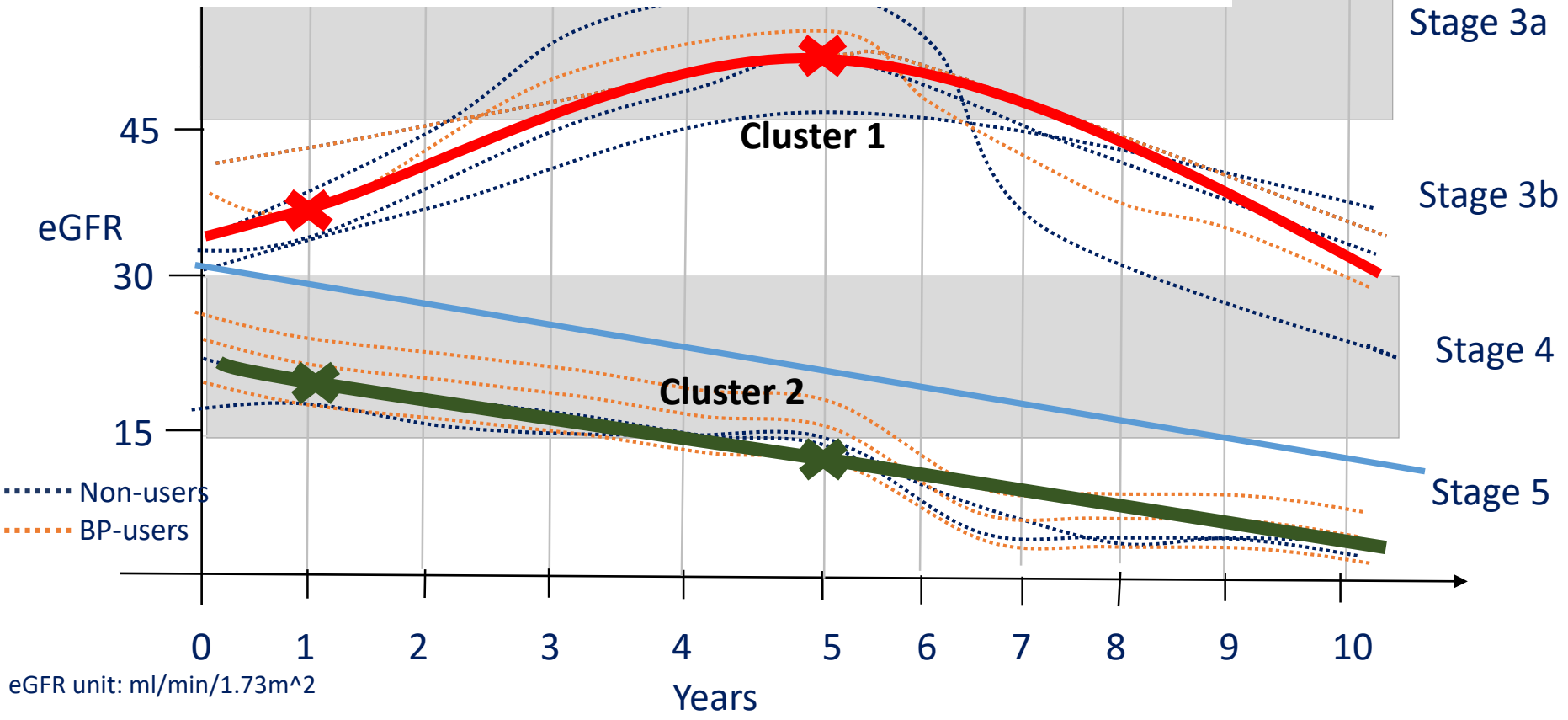
- To identify clusters of BisCK patients with different patterns of eGFRs over time
- To examine the association between the baseline Bisphosphonate use and the observed eGFR trajectories

Method-Growth Mixture Modelling[1]

Identify sub-populations based on similar intercepts and curves

Estimate size of variation per cluster

Linear curves with change points at 1 and 5 years



[1] Jung, T. and Wickrama, K. A. (2008), An Introduction to Latent Class Growth Analysis and Growth Mixture Modeling. Social and Personality Psychology Compass, 2: 302-317

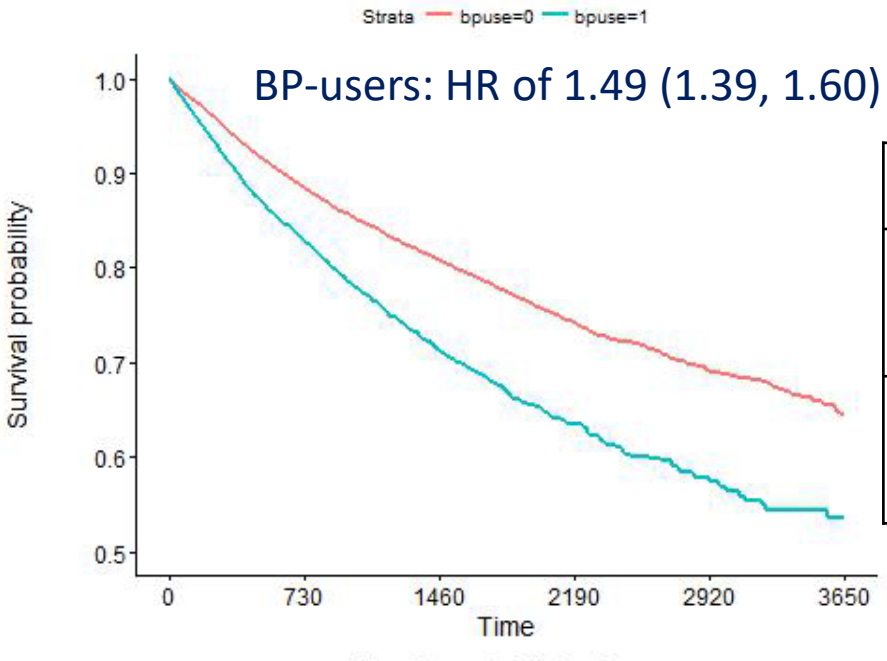
Method-Growth Mixture Model & Missing Data

- Missing at random (MAR) assumption
  - Intermittent missing
- Missing eGFRs due to truncation e.g. death or censored clearly violates the MAR assumption
- **Discrete time survival mixture models [1]**
  - to identify distinct clusters of intercepts/slopes & dropout probabilities

[1] Muthén & Masyn (2005) Discrete time survival mixture models *Journal of Educational and Behavioral Statistics* Vol 30, Issue 1, pp. 27 - 58

Results: stage down analysis

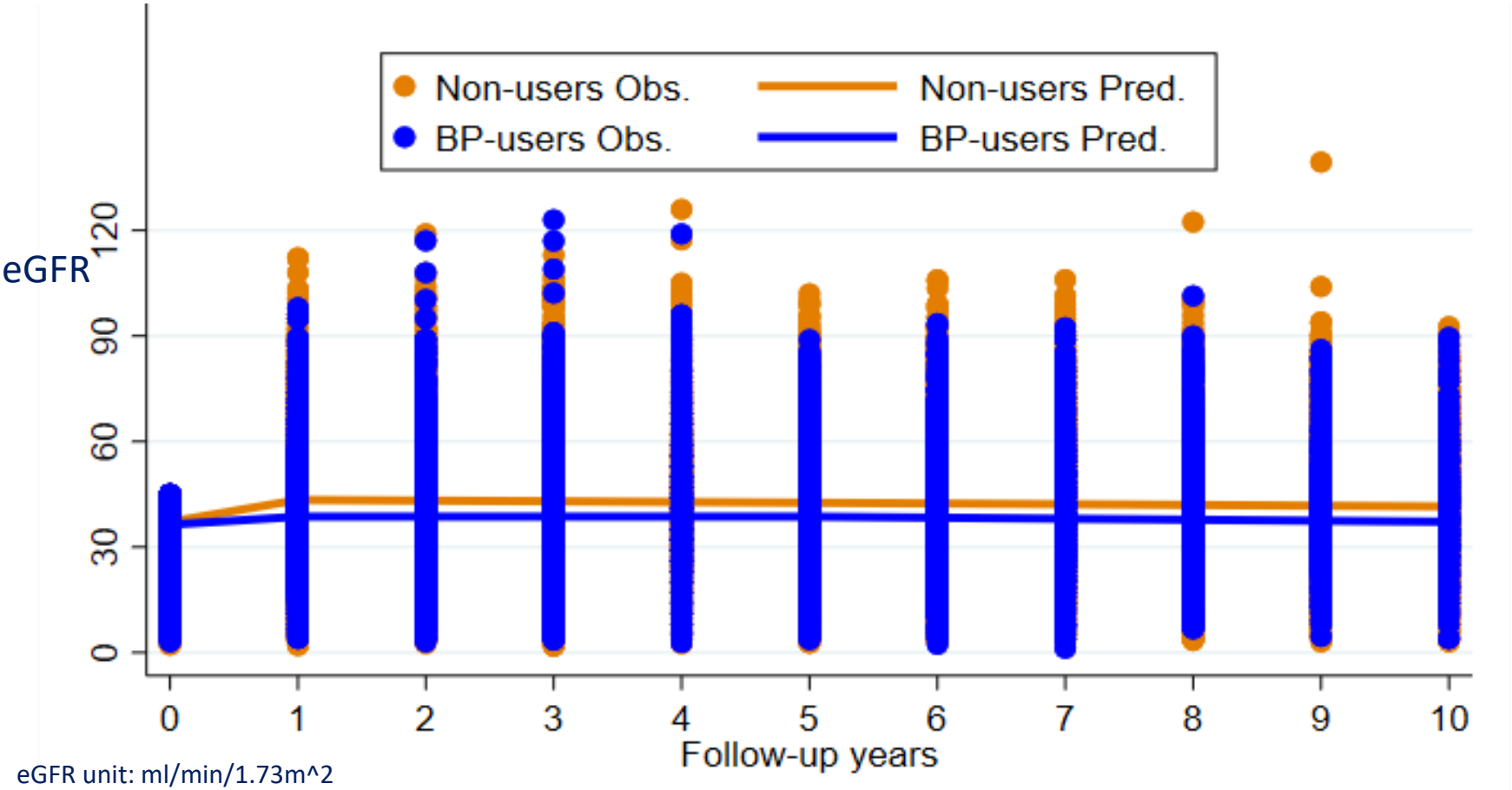
- 6,222 BP-users were PS matched to 24,610 non-users



	Down	Same	Up
BP-users	**1294 (21%)**	2168 (35%)	2843 (44%)
Non-users	**3343 (14%)**	5902 (24%)	15704 (62%)

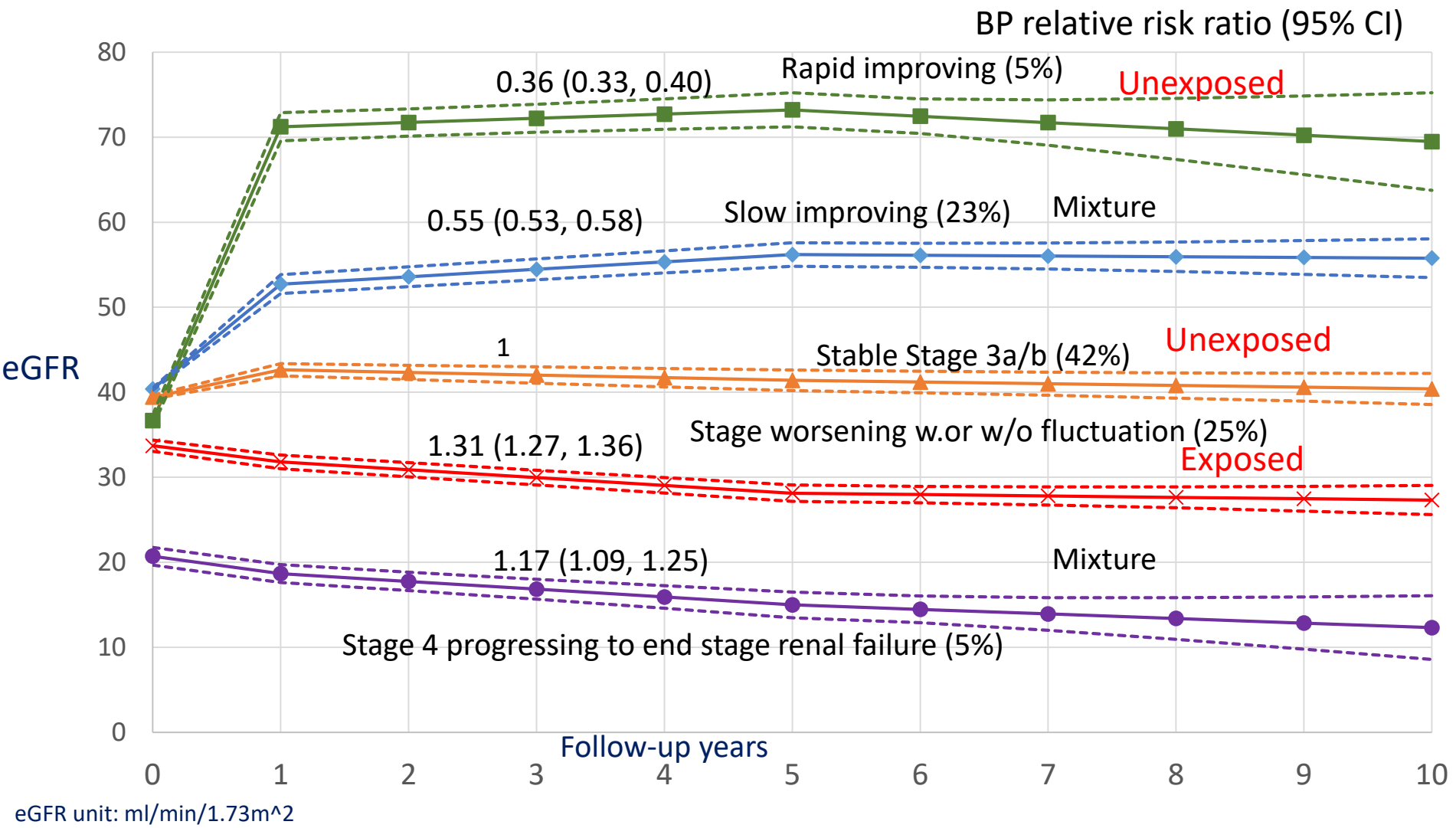
Results-random effect model

No significant difference in the mean change of eGFR per year between BP-users and non-users



eGFR unit: ml/min/1.73m^2

Results-Growth Mixture Modelling



eGFR unit: ml/min/1.73m^2

Conclusions

- The cost of dichotomising eGFRs
- Homogeneity assumption in the random effect model
- Growth Mixture Modelling better accounts for inter-individual differences in intra-individual changes of the repeatedly measured eGFRs

Limitations & Future work

Limitations

- A different study design could be used
- A different non-linear growth form, e.g. B-Splines, fraction polynomial or a different clustering approach, e.g. longitudinal k-mean

Future work

- Validation

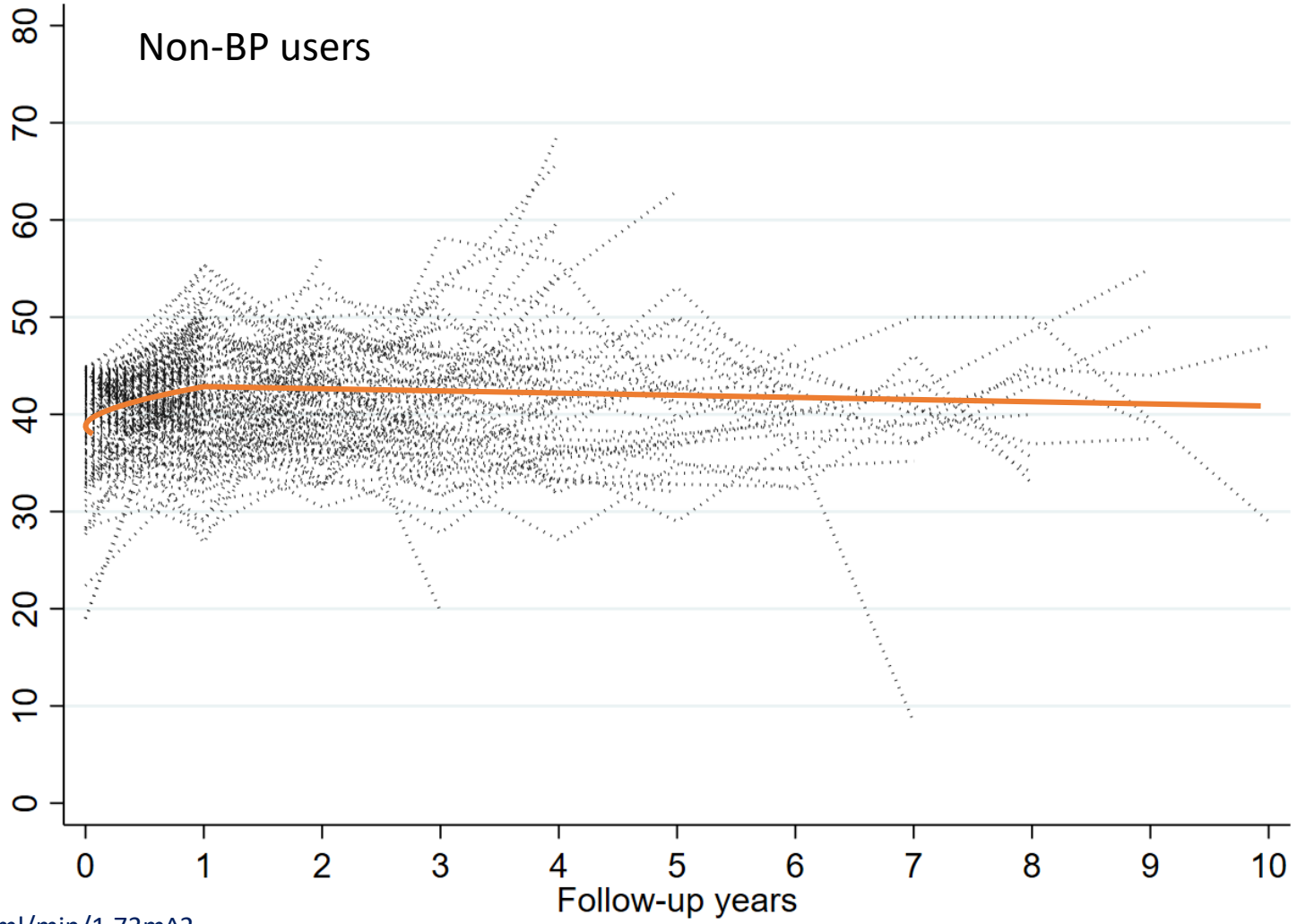
Thank you for listening

Acknowledgements:
This study is based in part on data from the Clinical Practice Research Datalink obtained under licence from the UK Medicines and Healthcare products Regulatory Agency. The data is provided by patients and collected by the NHS as part of their care and support. The interpretation and conclusions contained in this study are those of the author/s alone. Approval for the study was granted by the CPRD Independent Scientific Advisory Committee (protocol no. 15_153R2A).



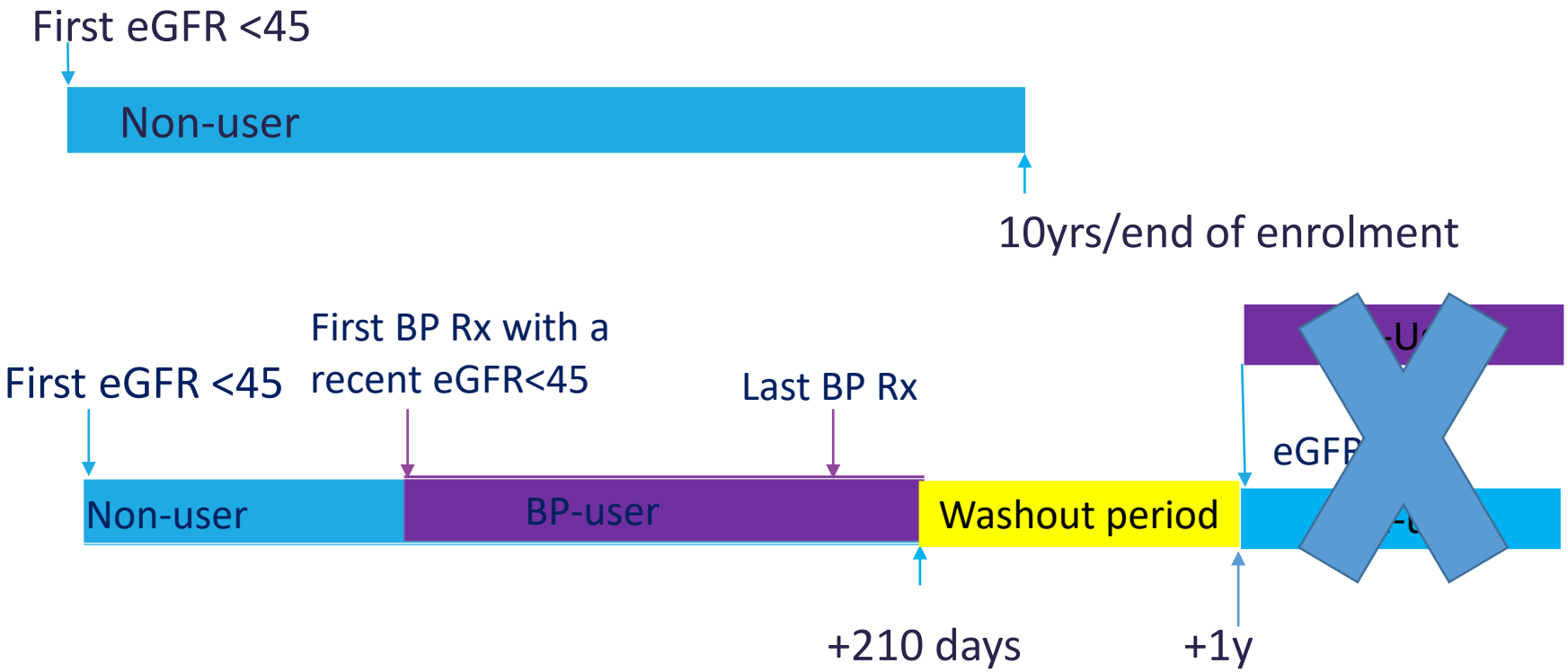
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Random sample of observed eGFR curves: G3 (Stable)

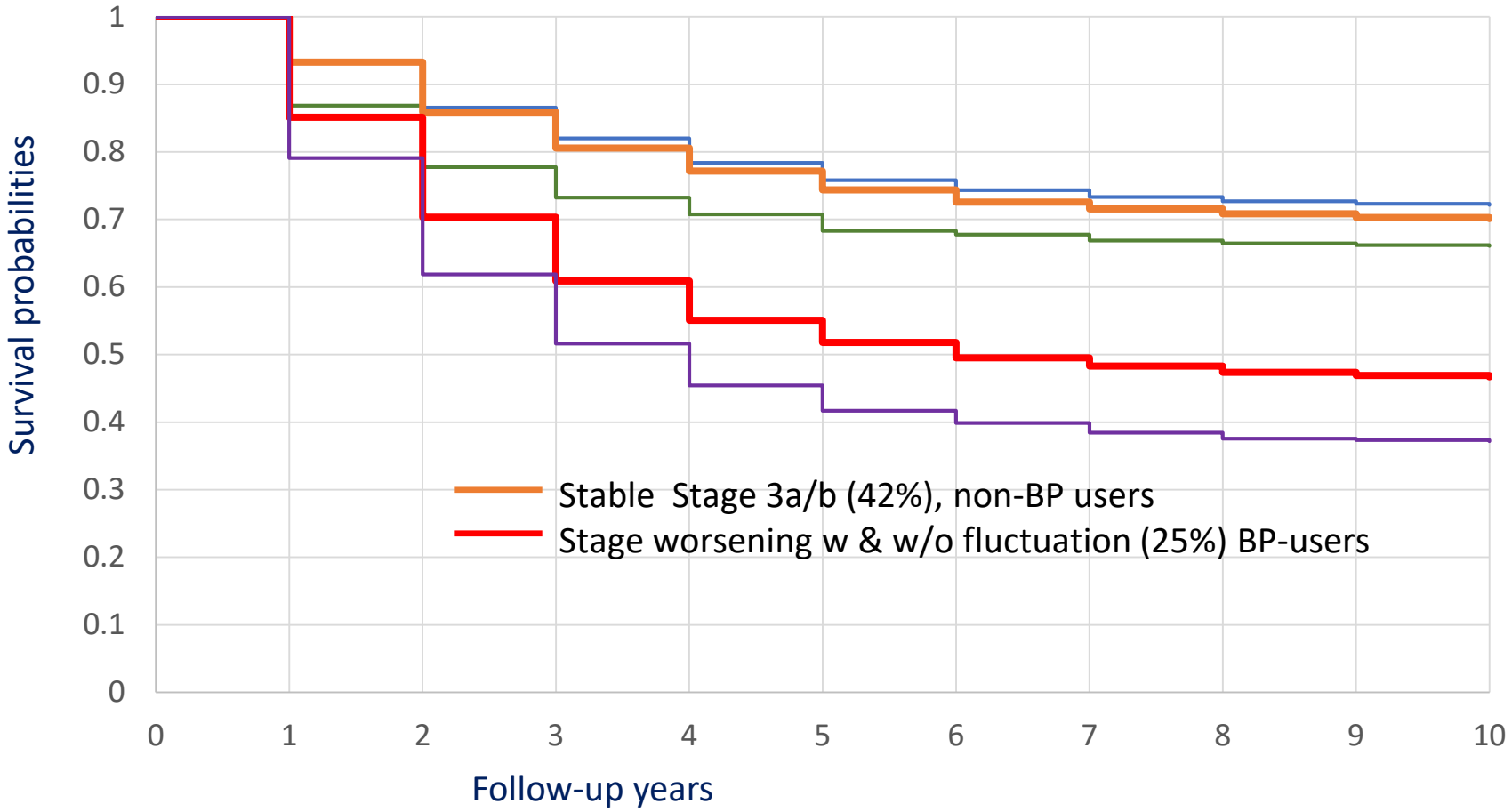


eGFR unit: ml/min/1.73m^2

Chronic Kidney Disease progression follow-up window



5-cluster survival probabilities



Random sample of observed eGFR curves: G4

