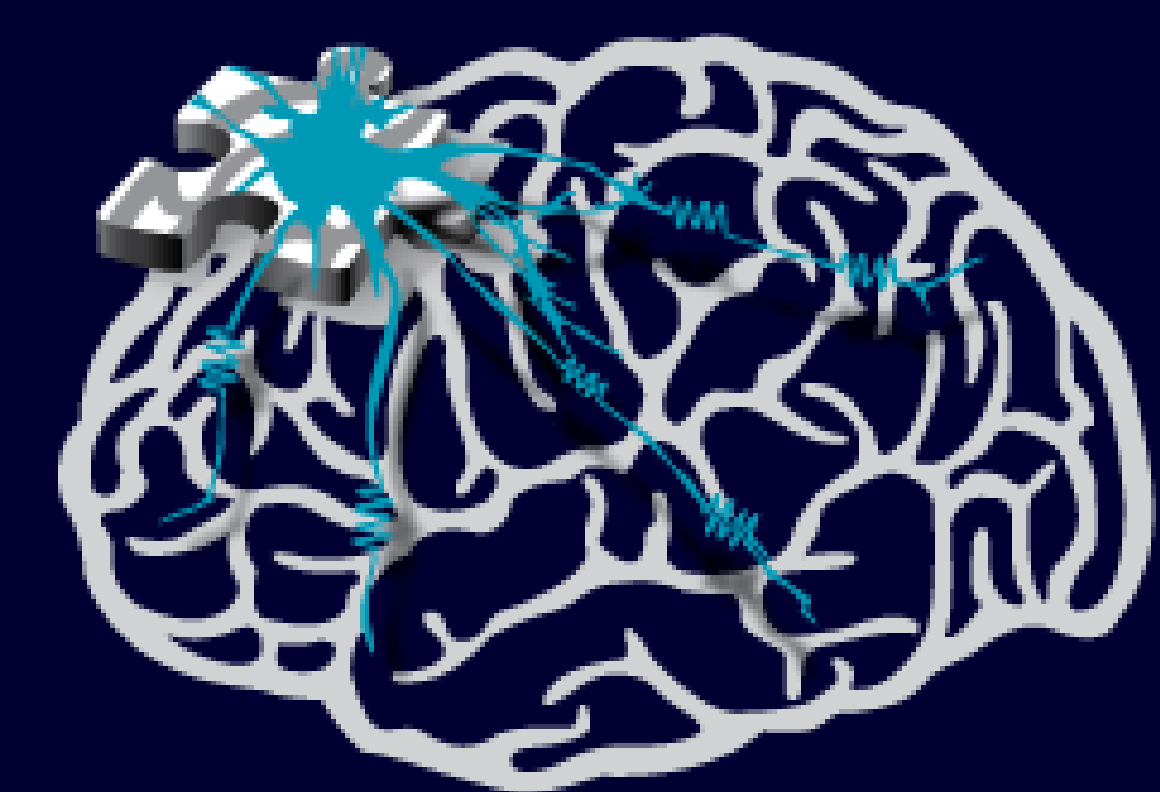




# Accelerated Brain Aging in Multimorbid Individuals



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## BACKGROUND

Brain age prediction algorithms estimate chronological age based on structural imaging information. Data from large cohorts of healthy controls are used to train these machine learning models, which output a predicted “brain age” when provided with various morphometric measurements derived from MR images. Differences between chronological age and this predicted “brain age”, known as Predicted Age Difference (PAD), can indicate a deviation from healthy brain aging, as has been demonstrated in clinical groups such as those with schizophrenia [1].

Accelerated aging has also been hypothesized to occur in marginally housed individuals, based on the high rates of multimorbidity and mortality [2]. This research aims to investigate the predicted brain age of a group of marginally housed individuals, and whether increases in PAD predict mortality.

## METHODS

The Hotel Study recruited and followed participants in precarious housing situations, over a period of 15 years. Demographic, neuroimaging, and clinical data were obtained, and the FreeSurfer package was utilized to calculate cortical and subcortical measurements from baseline T1w MRI scans. Participants with missing demographic data (n=2) or above the age of 60 at baseline (n=26) were excluded due to limitations of the ENIGMA-Brain Age algorithm used [3].

The predicted “brain age” estimation and PAD were calculated for the remaining 371 participants. A left truncated right censored Cox proportional hazard model was then used to determine the use of PAD as a risk factor for mortality.

	Male n=380 (75.5%)	Female n=91 (24.5%)
Age	40.7 (10.6)	39.4 (10.5)
CCI	2.7 (2.9)	3.5 (2.9)
PAD	6.0 (8.2)	2.5 (8.3)
Deceased	76 (27.1%)	25 (27.5%)

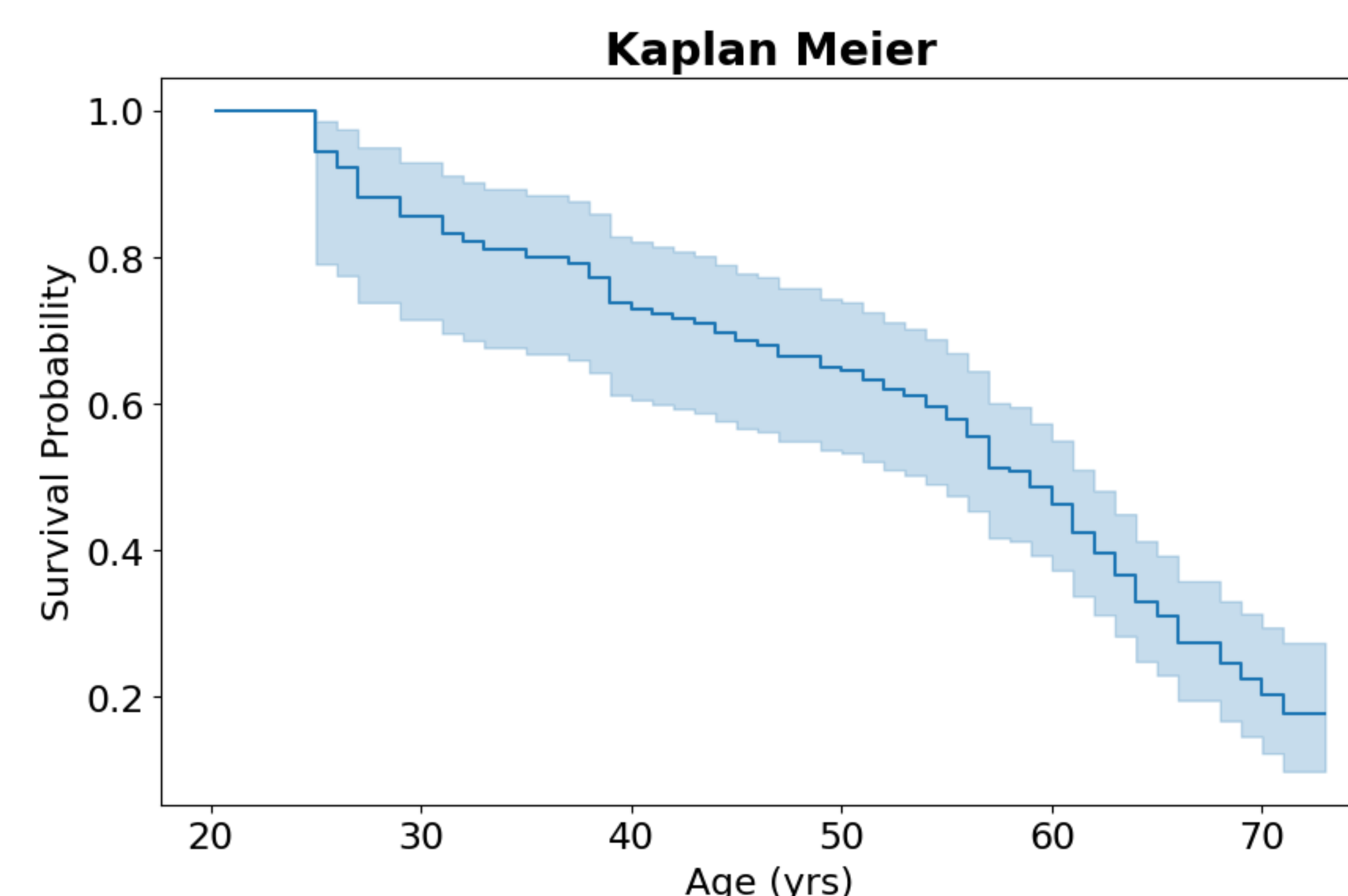
**Fig 1.** Mean (SD) of participant characteristics. CCI represents Charlson Comorbidity Index, and PAD represents Predicted Age Difference.

## RESULTS

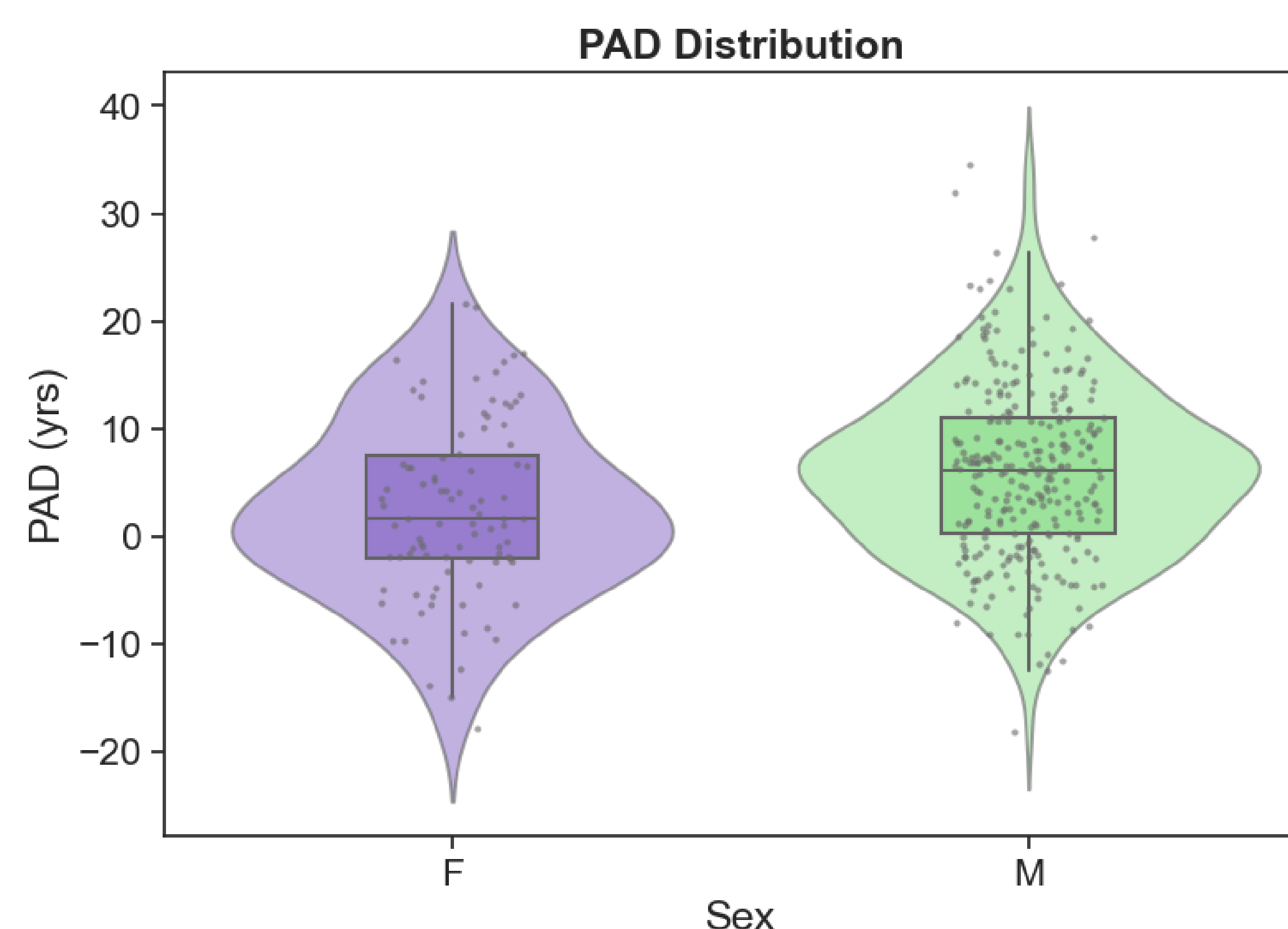
Crude mortality rate during the observation period was 28 deaths per 1000 person-years, with 101 / 371 (32%) of participants dying during the observed period.

The predicted “brain age” measurements were higher than chronological age in study participants, with a mean value of 5.2 (SD 8.3). The PAD values ranged from -18 to 35, and males had a higher mean PAD (6.0) than females (2.5).

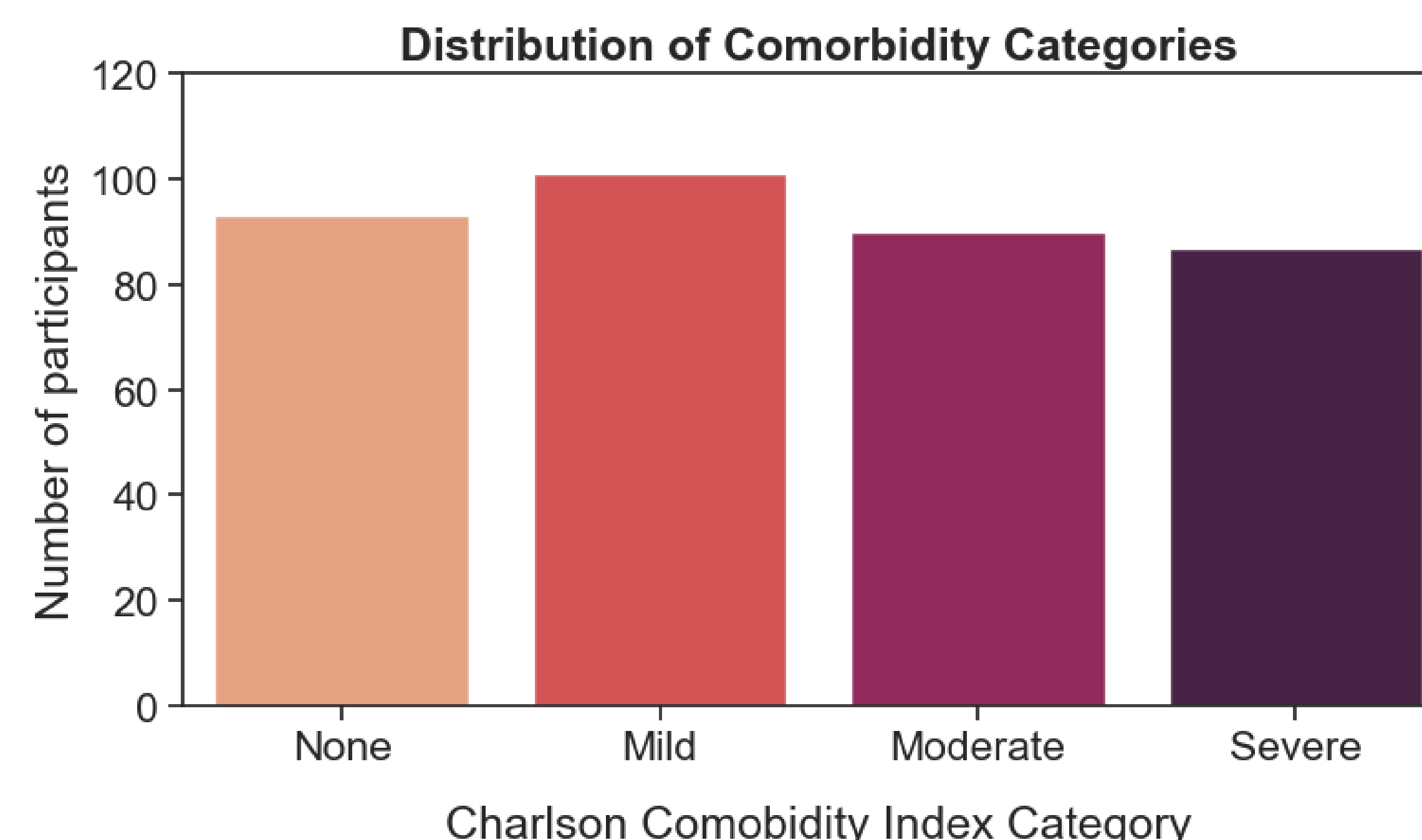
A left truncated right censored Cox proportional hazard model was calculated with covariates of sex, PAD, and Charlson Comorbidity Index (CCI). There was a significant association between both PAD and CCI and increased risk of mortality ( $p < 0.005$ ).



**Fig 2.** Kaplan Meier plot with survival probability by age.

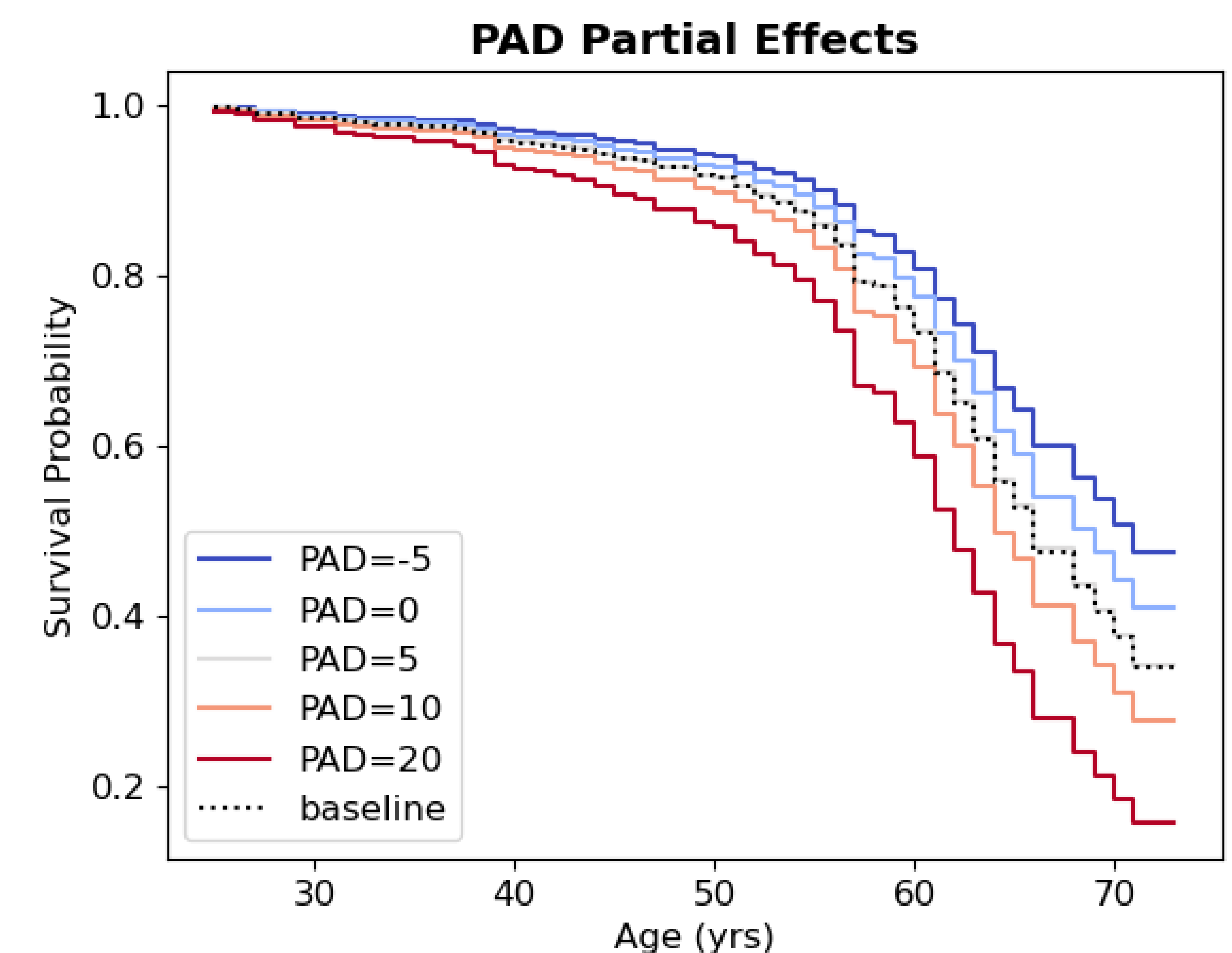


**Fig 3.** PAD values, separated by sex.



**Fig 4.** Charlson Comorbidity Index category frequency [4].

## CONCLUSIONS



**Fig 4.** Plot illustrating partial effects of PAD by modelling survival probability plots with various PAD values while holding all other covariates constant.

Our data show that PAD is higher in this population than in healthy controls, which could indicate an acceleration in brain aging. This measure may be helpful in predicting mortality, as it captured variance not otherwise explained by factors such as comorbidity.

Further research is needed to understand the specific factors that drive this increased PAD to develop interventions to mitigate accelerated aging in this population.

## REFERENCES

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- [3] Han et al. Mol Psychiatry, 26: 5124-5139, 2021.
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