

# Blood pressure trends in relation to clotting factor utilization in patients with severe hemophilia

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## Problem & Objectives

- There is a high prevalence of hypertension among patients with hemophilia (PWH).
- PWH are at risk of intra-cranial hemorrhage.
- Most PWH are on prophylactic clotting factor replacement.
- It is unknown if clotting factor replacement increases blood pressures.

## Methods

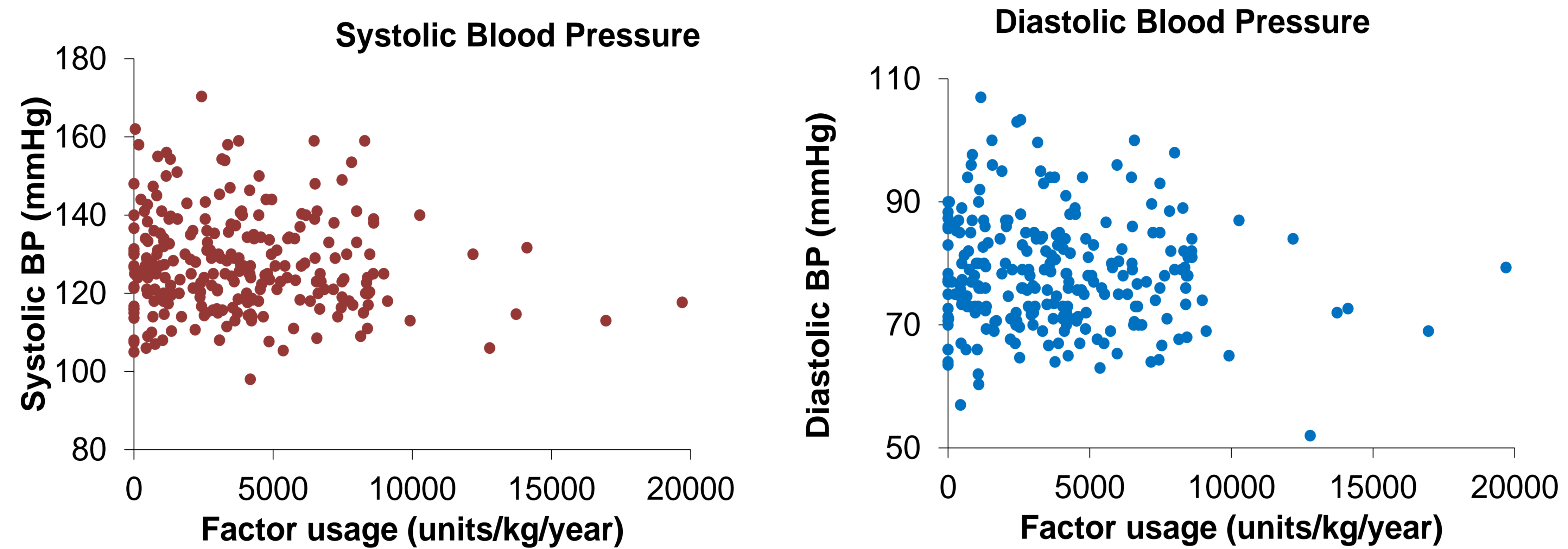
- Patients with severe hemophilia from:
  - University of California San Diego
  - Los Angeles Orthopaedic Hospital
  - St Paul's Hospital, Vancouver
- N = 251.
- We fitted generalized additive models (GAMs) with a spline function.
- The outcome was either log(systolic blood pressure) or diastolic blood pressure.
- Each model was adjusted for age.
- Clotting factor usage was expressed in units/kg/year.
- Models were also adjusted for site, hemophilia type (A or B), smoking status, diabetes, viral infections (HepC, HIV), anti-hypertensive medications, body mass index (BMI), renal function (logCreatinine and eGFR), logBMI or logTotalCholesterol.

## Acknowledgments

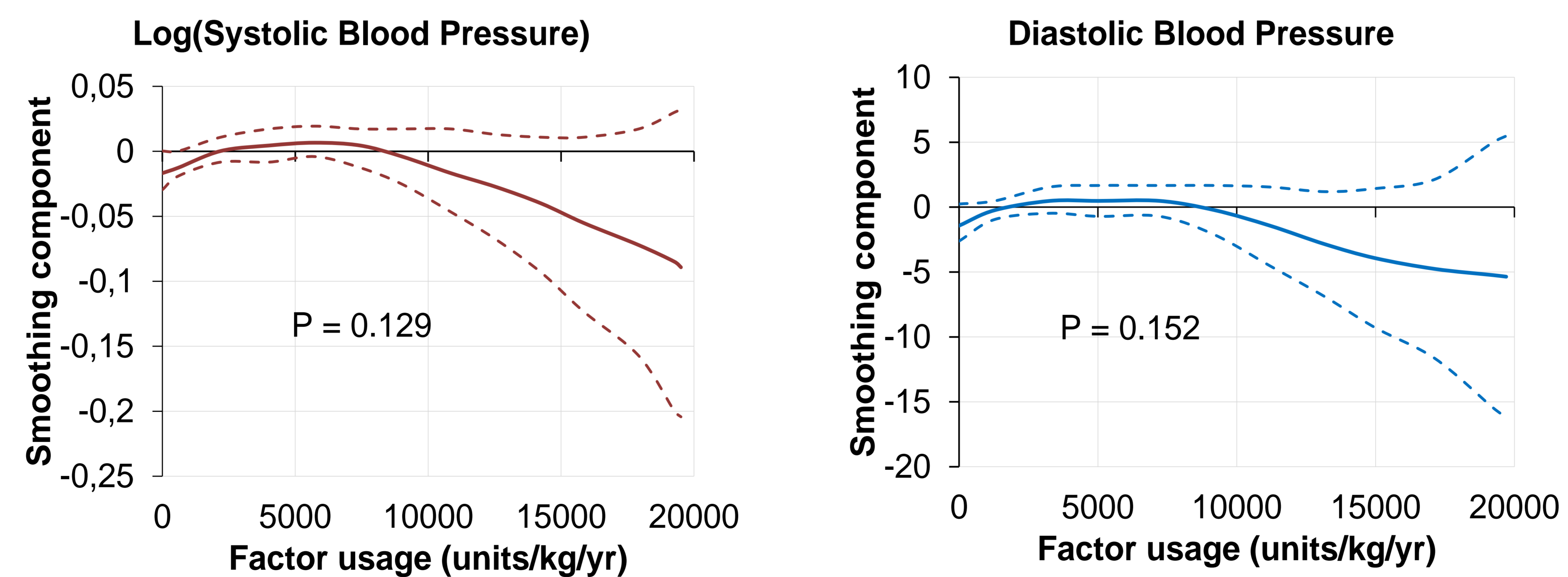
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## Systolic and Diastolic Blood Pressure

**Result 1:** Scatter plots demonstrate that systolic and diastolic BP do not increase with increased annual clotting factor usage.



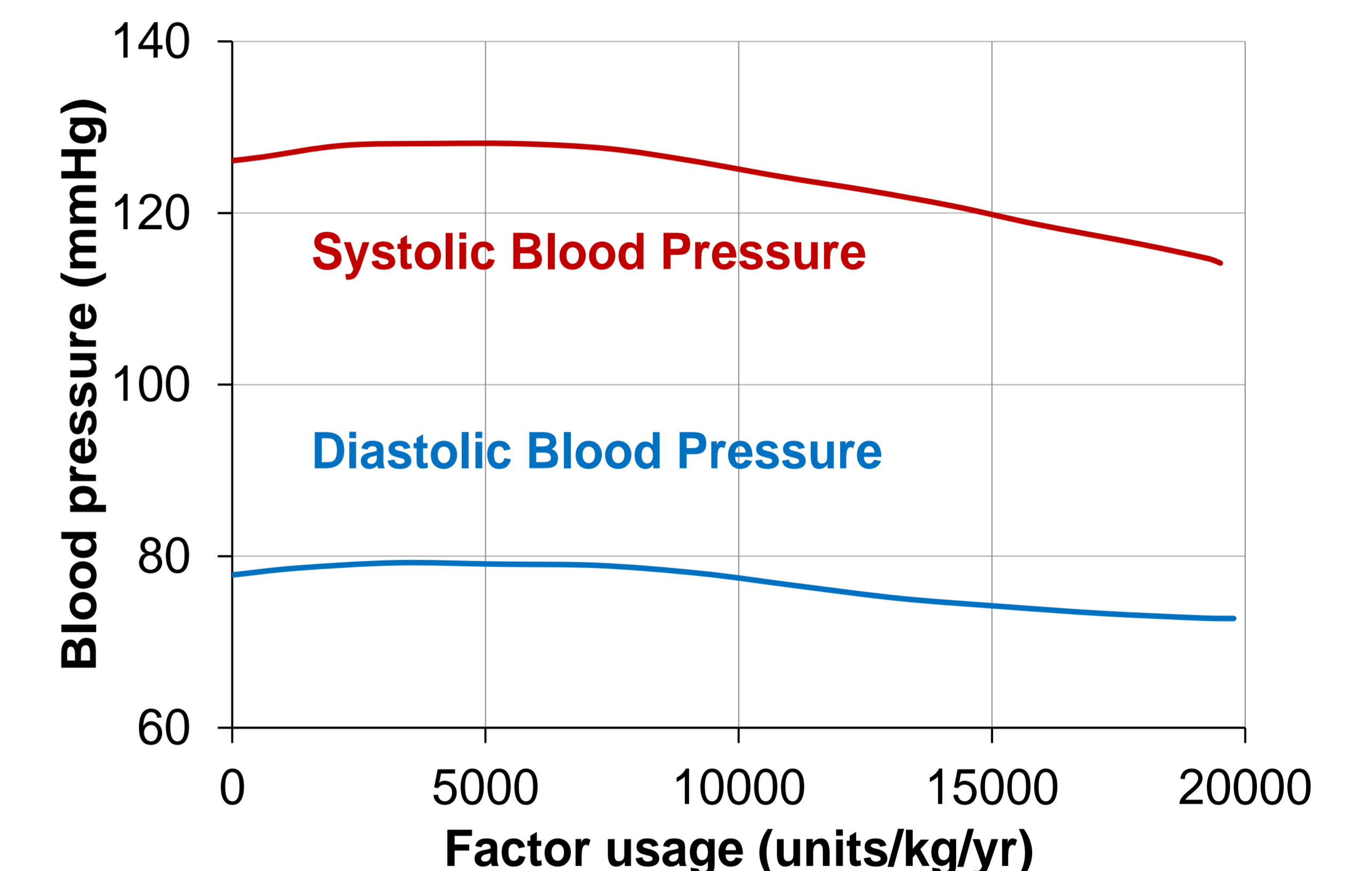
**Result 2:** The non-linear function fitted by each GAM model indicates slightly improved blood pressures with increased annual clotting factor usage. The curves are not significantly different from a straight line.



- Note the wide confidence intervals (the broken lines) towards the right hand side of each graph.
- The p-values are from a test of the null hypothesis that the curves differ from a straight line.
- The models shown above were adjusted for age. Adjustment with other covariates produced curves of similar shape.

**Result 3:** We can use the models to calculate the blood pressure of an average male at different levels of annual factor usage.

- Modeled systolic and diastolic blood pressures in relation to clotting factor usage are shown for 40-year old males.
- The downward trend in blood pressure at high levels of factor usage is illustrated.



## Conclusions

- There is no evidence for an increase in blood pressure with more intense clotting factor replacement.
- Therefore higher clotting factor usage does not appear harmful with respect to blood pressure.
- Rather, blood pressure values may be lower when factor consumption exceeds 10,000 units/kg/year.
- However, there are too few data points at these high levels to provide enough statistical power to confirm these results.
- Further investigations to determine the relationship of clotting factor usage and blood pressure in PWH may be warranted.

