

Factors Associated with Prophylaxis Use in Persons with Hemophilia in the United States

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INTRODUCTION

- Long-term (continuous) prophylaxis, the regularly scheduled infusion of factor concentrate to prevent bleeding, is recommended as preventive therapy for all young males with severe hemophilia in countries where safe factor is readily available.¹
- Prophylaxis has been shown to be useful even when factor levels are not maintained above 1% at all times; benefits include decreased joint bleeding, preservation of joint function and improved quality of life.^{2,3}
- Although prophylaxis is recommended as the treatment of choice for persons with severe hemophilia of all ages, prevalence of use in the United States varies geographically and is used by only a portion of the population for whom it is recommended.

OBJECTIVES

- Describe the prevalence of continuous prophylaxis use in the US among a large, nationally representative sample of males with moderate and severe hemophilia A and B, building on a previous study of prophylaxis in the US by Baker *et al* (2011).⁴
- Examine the association of nine clinical and demographic characteristics with the prevalence of prophylaxis use and identify those having the greatest statistical significance;
- Increase knowledge regarding interaction of clinical and demographic characteristics that may encourage or impede use of prophylaxis in the US. Are there identifiable characteristics that act as barriers or promoters of prophylaxis use?

METHODS

- The study sample included 9,725 males with moderate or severe hemophilia A or B aged 2-79 who participated in the Universal Data Collection (UDC) surveillance project between 1998-2011. UDC data represents 85% of persons with hemophilia who received care at 135 HTC's.
- Data from each individuals' most recent UDC visit was used.
- Exclusion criteria included intermittent prophylaxis use, a diagnosis of HIV or symptomatic liver disease, inhibitor titer ≥ 5 Bethesda units, immune tolerance therapy at the time of visit and incomplete height or weight data at the time of the most recent visit.
- Prevalence of prophylaxis use was calculated for the following demographic and clinical characteristics: age, ethnicity, health insurance status and type; body mass index (BMI); geographic region; hemophilia type (A or B); severity and self-infusion status.
- Pearson's Chi-square test or Fisher's exact test assessed associations in bivariate analyses; logistic regressions assessed independent association in multivariate analyses. Adjusted odds ratios and 95% confidence intervals were computed. All statistical tests were based on two-sided tests with a significance level of 0.05.
- Quartic polynomial logistic regression models were constructed; figures based on these models were developed to illustrate the mean predicted probability of using prophylaxis with advancing age among a subset of the sample population.

RESULTS

- The study sample was representative of the overall UDC population and included 5,573 youths 2-19 years (57%) and 4,152 adults >19 years (43%).
- 65% were non-Hispanic white; 14% Hispanic, 13% African-American and 8% other or mixed race.
- 63% had severe hemophilia, of whom 60% used prophylaxis, compared to 16% of those with moderate disease.
- 75% of the sample had hemophilia A, of whom 50% used prophylaxis, compared to 25% of those with hemophilia B.
- 26% of all adults (20 years and older) used prophylaxis. Use decreased with advancing age: 32% of 20-39 year-olds; 11% of 40-59 year-olds and 8% of those 60 and older.
- 57% of youths 2-19 years used prophylaxis. Use was highest among those 6-11 years (64%) and lowest among teens 12-19 years (53%).
- Characteristics significantly associated with prophylaxis use (after logistic regression) included age, ethnicity, insurance status and type, hemophilia type (A or B), hemophilic severity, self-infusion status and geographic region. Although BMI was negatively associated with prophylaxis use among adults in the bivariate analysis, this association disappeared after logistic regression.
- Health care coverage is vital: 98% of those using prophylaxis had health insurance. Prophylaxis was used by 53% of those with commercial insurance and by 45% of those with public coverage (such as Medicaid or Medicare), compared to 13% of those without coverage.
- 34% of adults who self-infused used prophylaxis, compared to 12% of those who did not.
- Hispanics were more likely to use prophylaxis ($P=0.03$) than Non-Hispanic Whites or African-Americans in all age groups except 6 to 11 year-olds (Fig. 1).
- Prevalence of use varied significantly ($P<0.0001$) among four US Census Bureau regions (Midwest, Northeast, South and West). Overall, 52% of 1,107 individuals in the West used prophylaxis, compared to 39% of 1,065 individuals in the Midwest. Geographic variation increased with increasing age (Fig. 2). Among those 20 and older, 18% of individuals living in the South treated prophylactically, compared to 37% in the West. Among youths 2-19, prophylaxis use ranged from 53% in the Midwest to 62% in the West.

RESULTS

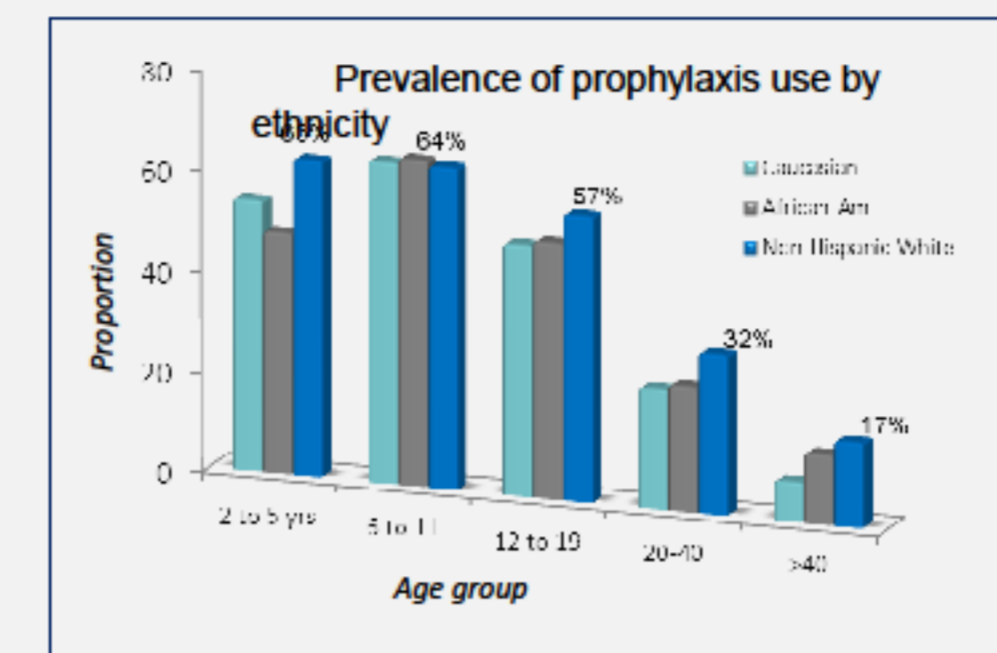


Fig. 1

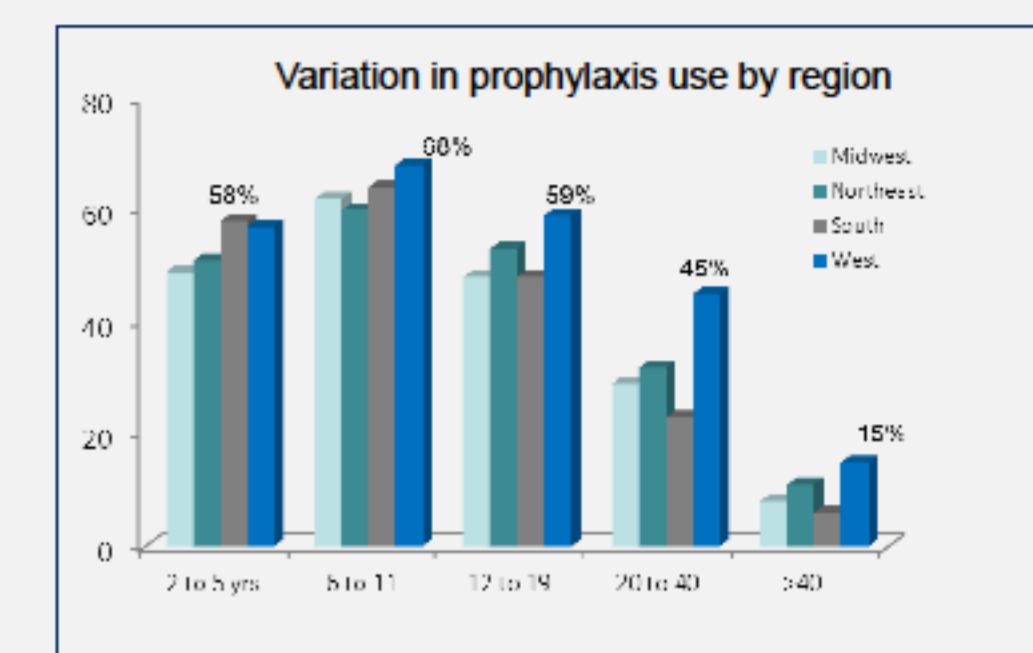


Fig. 2

The maps below (Figures 3-5) illustrate geographic variation in prophylaxis use among persons with severe hemophilia A and B seen at HTC's, a phenomenon noted previously by Soucie *et al*.⁵ Among the 12 hemophilia regions, the proportion with severe hemophilia A using prophylaxis ranged from 57% to 77%; among those with severe hemophilia B, use ranged from 33% to 57%. Why do we find significant variation in the adoption of a treatment that is universally recommended?

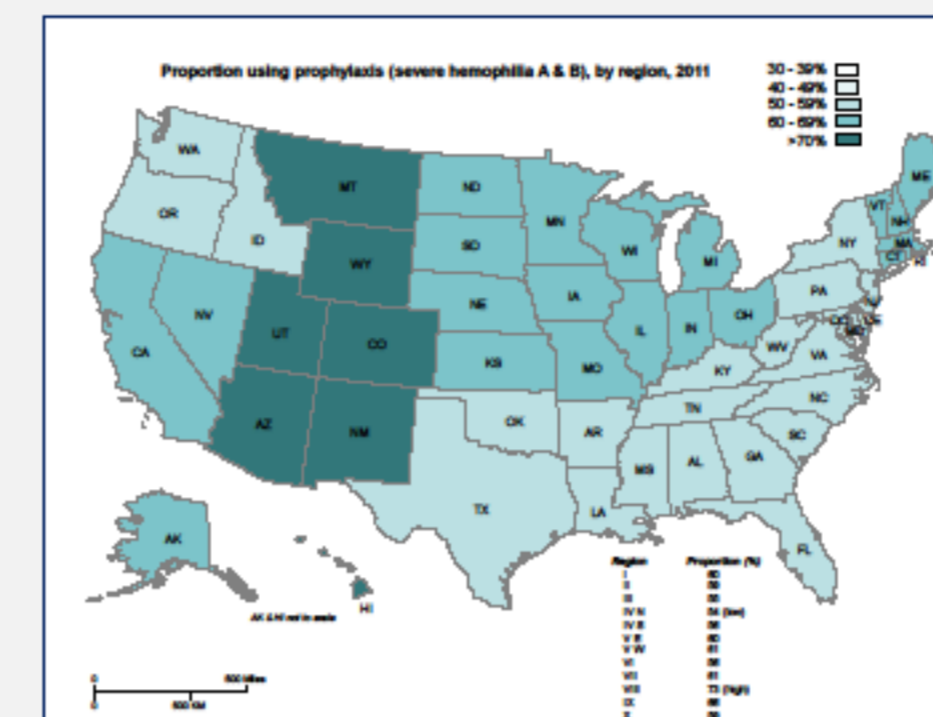


Fig. 3

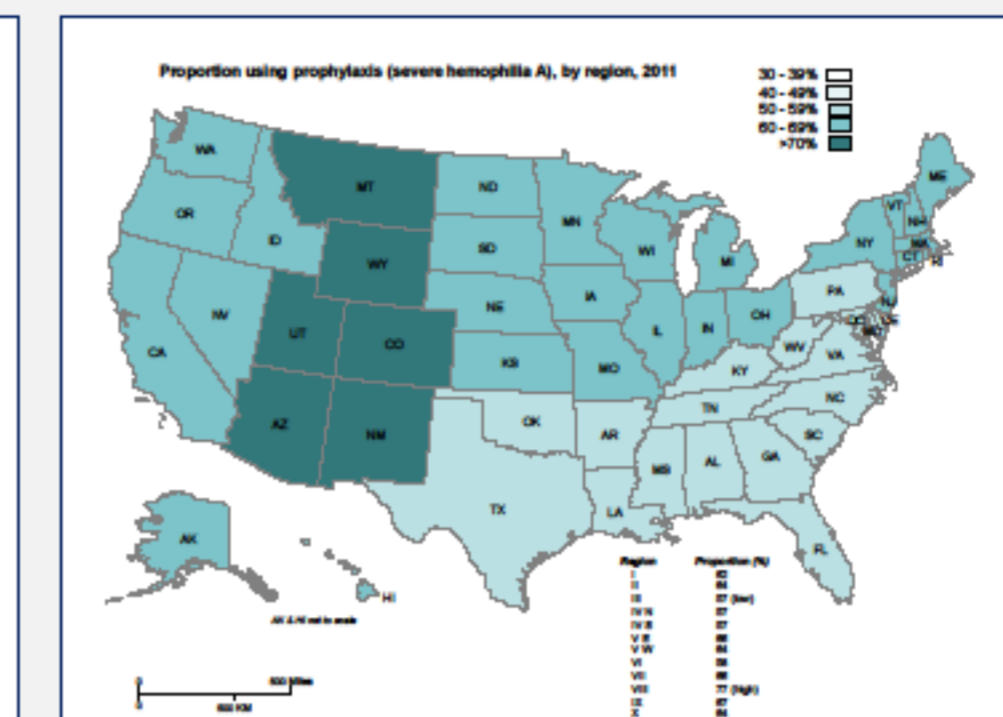


Fig. 4

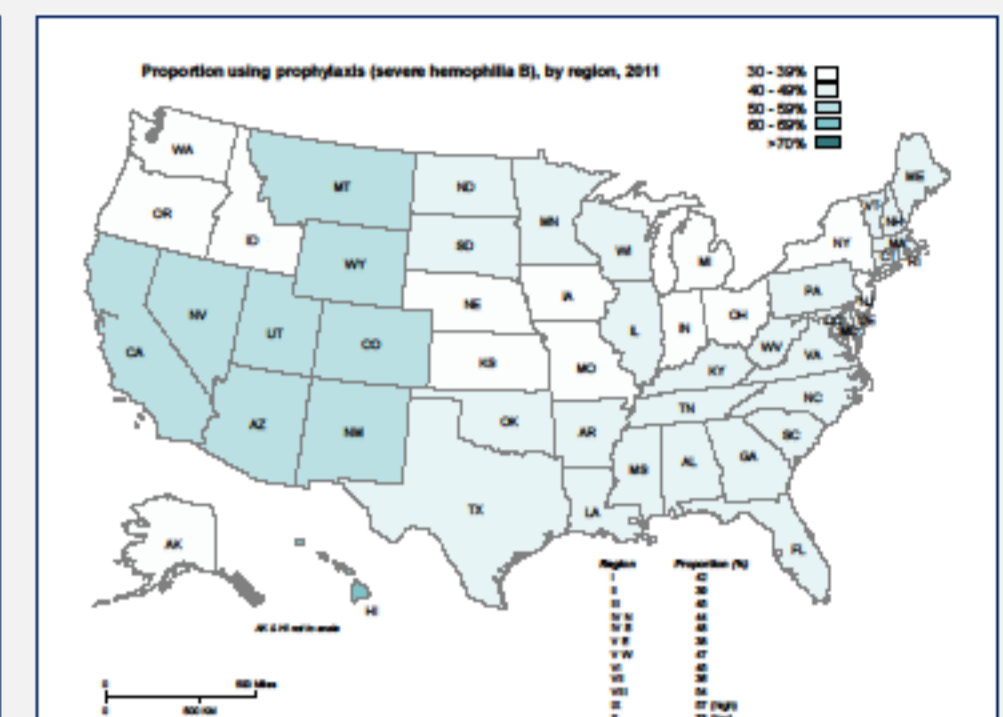


Fig. 5

Predictive probability graphs (Figs. 6-8) based on logistic regression models, may help us visualize the way in which several variables are likely to interact, given a specific set of characteristics, such as age, diagnosis, insurance status and residence in a geographic region.

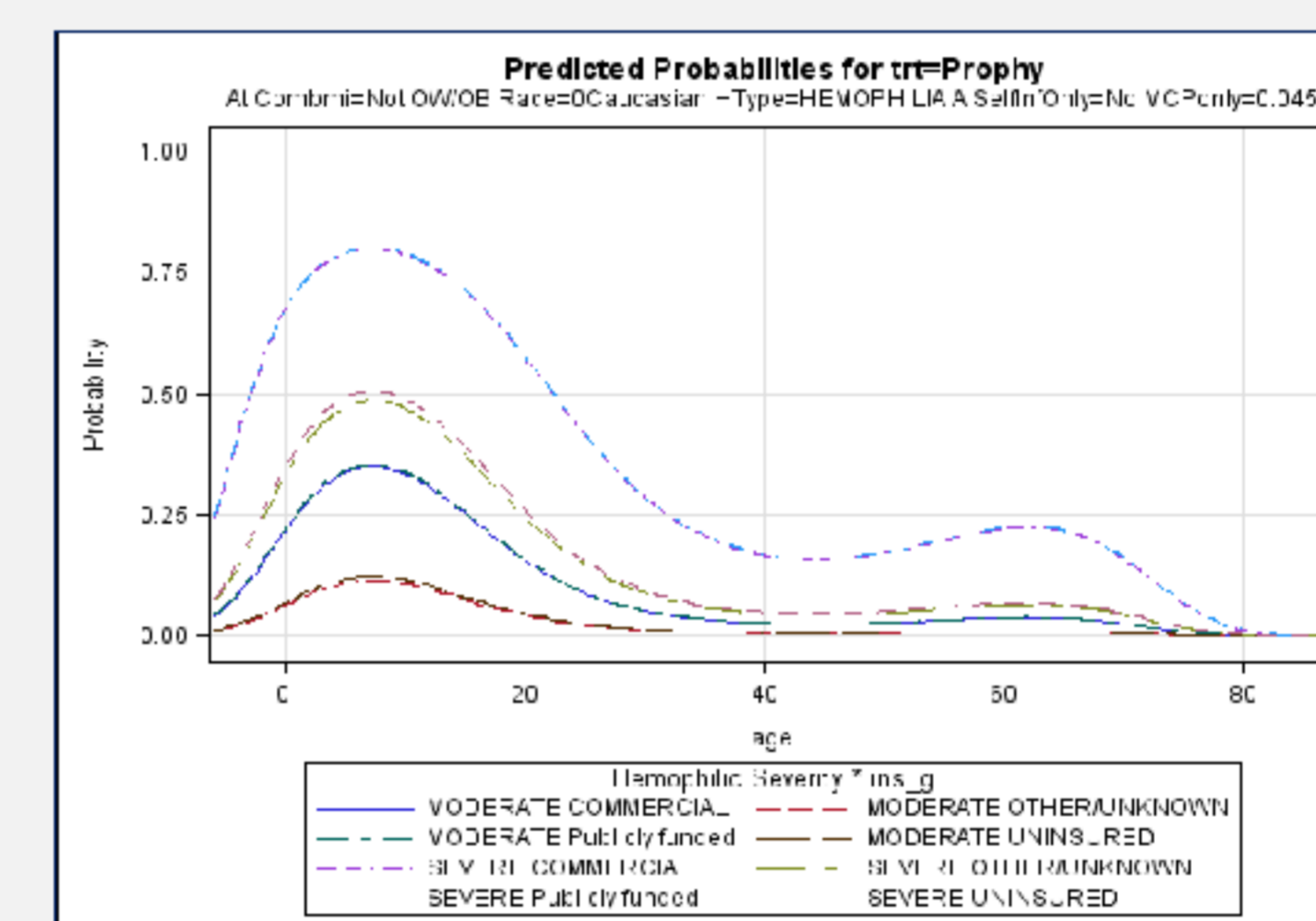


Fig. 6

Fig. 6 illustrates the interaction of insurance coverage, age and prophylaxis use. Both public and commercial insurance appear to provide similar levels of access, while lack of coverage lowers the probability of prophylaxis use.

Fig. 7 (below left) illustrates a higher prevalence of prophylaxis in all ages among residents of western states.

Fig. 8 (below right) examines ethnicity, age and prophylaxis. Hispanic individuals are most likely to use prophylaxis, while African-Americans are the least likely; the difference in prevalence between the two groups increases after age 30.

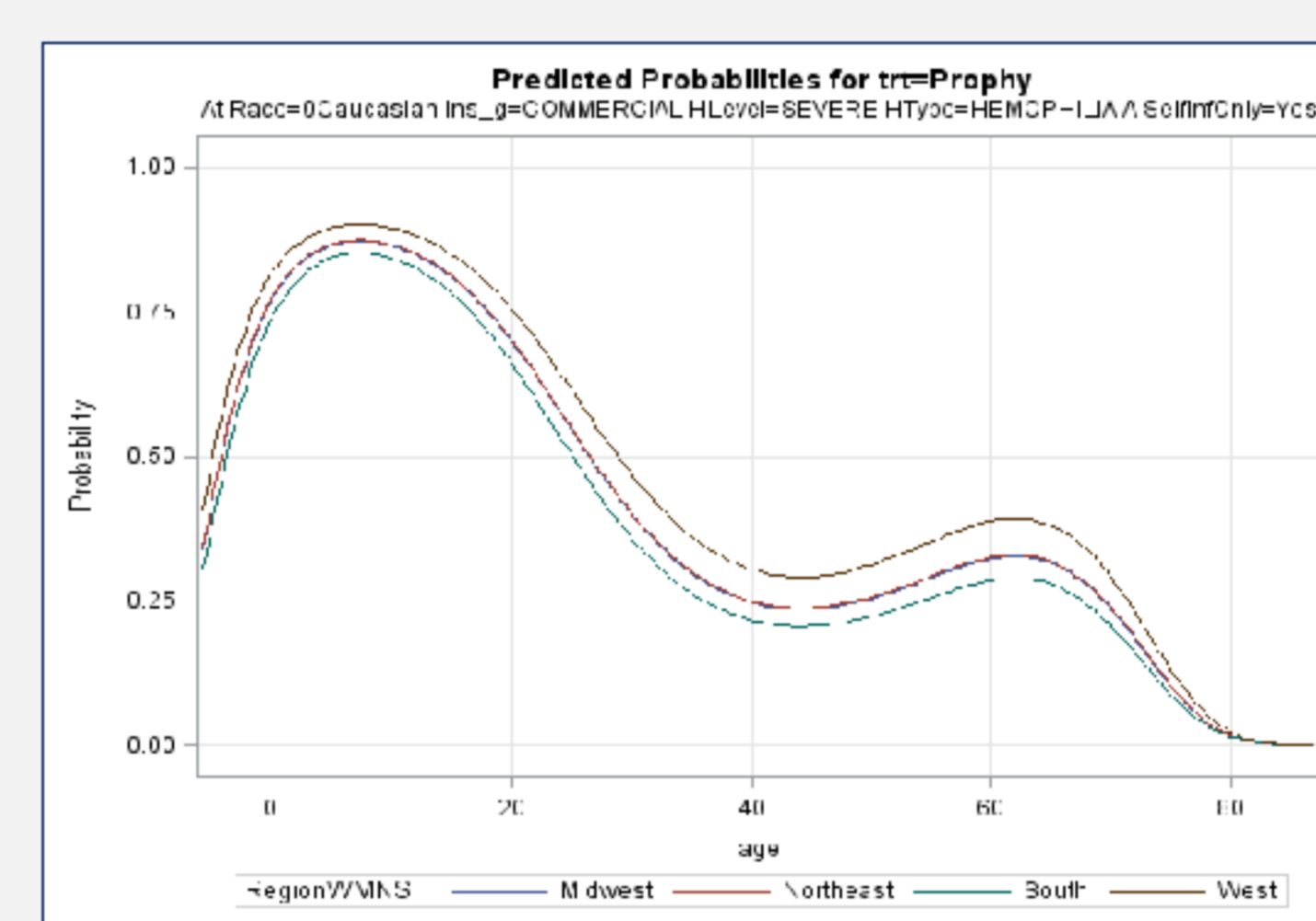


Fig. 7

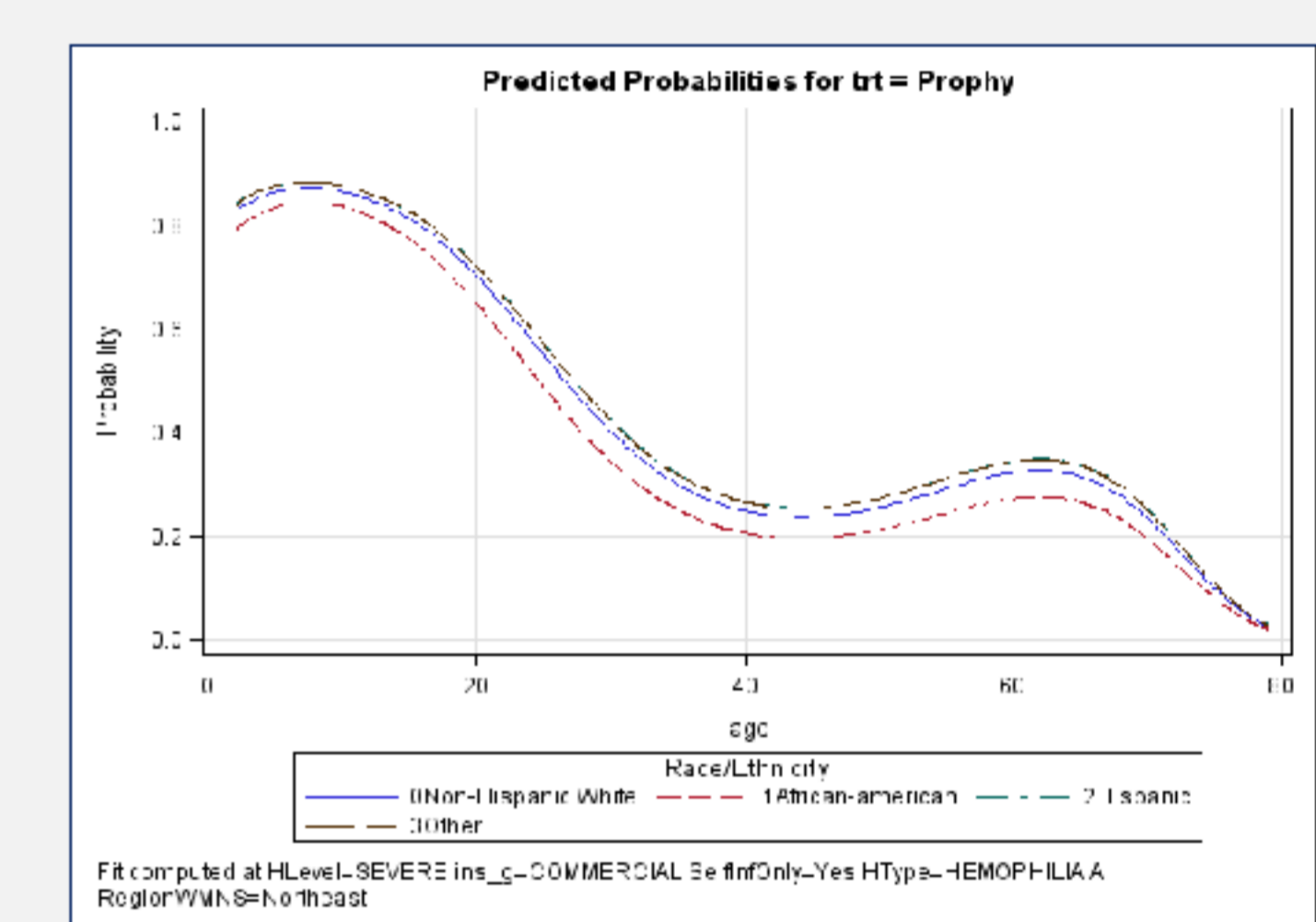


Fig. 8

DISCUSSION & CONCLUSIONS

- Prophylaxis has been accepted as the state-of-the-art treatment for persons of all ages with severe hemophilia, but is used by only a portion of the US children, youths and teens for whom it is recommended (71%, 83% and 68%, respectively).
- Many issues regarding prophylaxis are still debated by clinicians, such as when to begin, when (or even if) to stop, and the optimal dosing regimen.^{1,6} In short, management of a prophylactic regimen is both an art and a science. The geographic variation in prophylaxis use described here may be a reflection of regional differences in provider preference and practice (or even uncertainty), as well as the interplay of various clinical and demographic factors.
- The practice of prophylaxis continues to evolve. While prophylaxis for children and teens is widely accepted, prophylaxis for adults is not. Although use into adulthood is increasing (32% of those 20-39 years), there are no clear-cut guidelines regarding the optimal adult regimen, and few evidence-based recommendations.⁶ This lack of consensus may contribute to the greater geographic variation in prophylaxis use among adults (range of 18-37%), compared to the variation among youths 2-19 years (range of 53-62%).
- Current demographic trends in the hemophilia community emphasize the need to identify, understand and prevent modifiable barriers to prophylaxis in patients of all ages. These trends include a growing population of senior persons who are at increased risk of bleeding because of co-morbidities and aging, an increasing prevalence of young persons with above-normal body mass index who face increased joint morbidity, and the advent of novel long-acting factor concentrates.^{6,7}

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