HHS Public Access

Author manuscript

Haemophilia. Author manuscript; available in PMC 2023 November 01.

Published in final edited form as:

Haemophilia. 2022 November ; 28(6): 986–995. doi:10.1111/hae.14647.

Prevalence of comorbid conditions among older males with haemophilia receiving care in haemophilia treatment centers in the United States

J. Michael Soucie[1,2], **Binh Le**[1], **Brandi Dupervil**[1], **Jacqueline N. Poston**[3]

[1]Division of Blood Disorders, Centers for Disease Control and Prevention,Atlanta, Georgia, USA

[2]Synergy America, Inc., Duluth, Georgia, USA

[3]Division of Hematology and Oncology, Department of Medicine and Division of Clinical Pathology, Department of Pathology, Larner College of Medicine at the University of Vermont, Burlington, Vermont, USA

Abstract

Introduction: Increased survival among men with haemophilia has brought with it an increased risk of age-related comorbidities that may be challenging to treat in the presence of a bleeding disorder.

Aim: Estimate the prevalence of several age-related comorbidities among older males with haemophilia receiving care in the U.S. haemophilia treatment center (HTC) network compared to that among the general population.

Methods: People with bleeding disorders who receive care in network HTCs can volunteer to participate in a surveillance registry that collects detailed clinical information including the presence of comorbid conditions at annual visits. We used registry data collected on males with haemophilia age 45 years and older to calculate lifetime prevalence of obesity, diabetes, hypertension, cardiovascular disease, renal disease, cancer, anxiety and depression. Comparable data on the U.S. general male population was obtained from the National Health Interview Survey.

Results: During the surveillance period, 1592 middle-aged (45–64 years) and 645 older (≥65 years) patients with haemophilia had comorbidity data collected during 6435 HTC visits. Most haemophilia patients in both age groups had a higher prevalence of anxiety, depression and diabetes, but a lower prevalence of hypertension, coronary heart disease, stroke and myocardial infarction compared to the general U.S. male population. In addition, middle-aged patients had lower rates of leukemia, whereas older patients had higher rates of obesity than the general population.

Conclusion: These findings highlight the mental stress associated with this chronic condition and support continued public health obesity prevention efforts in the haemophilia community.

Correspondence: J. Michael Soucie, MS-S106-3, Centers for Disease Control and Prevention, 4770 Buford Highway, Atlanta, GA 30341-3717, USA. Msoucie@cdc.gov.

Keywords

comorbidity; haemophilia; surveillance

1 | INTRODUCTION

Therapeutic advances in haemophilia treatment have led to increased survival among men with haemophilia and along with it, the risk for the development of age-related comorbidities.[1] In addition to those directly related to the bleeding disorder, including joint disease and complications of exposure to HIV and hepatitis, age-related increases in hypertension and obesity may increase the risk for cardiovascular disease and chronic renal disease.[2] Additionally, many patients with haemophilia have chronic pain, musculoskeletal impairments, and carry the psychological burden of blood-borne infections, which may contribute to increased rates of depression or anxiety.[3,4] While the prevalence of these comorbidities may not be higher than that of the general male population, in many cases, these conditions pose a greater therapeutic challenge in the presence of a bleeding disorder and hematologists may need to assist in the care of these complicating conditions.

In the United States, most people with haemophilia and other hereditary bleeding disorders receive care in a network of specialized haemophilia treatment centres (HTCs). About 140 of these HTCs located across the country receive federal funding and comprise the U.S. HTC Network (USHTCN). To monitor the care and outcomes of patients, the Centers for Disease Control and Prevention (CDC) has partnered with the USHTCN and the American Thrombosis and Hemostasis Network (ATHN) to collect data through a public health surveillance system called Community Counts (CC).

The purpose of this study is to use data collected in CC over a 7-year period on a variety of comorbid conditions to estimate the burden of these conditions among men 45 years and older receiving care for haemophilia in the USHTCN. Additionally, the prevalence of these conditions among men in this haemophilia cohort is compared to that among similar aged men in the U.S. general population.

2 | METHODS

The CC public health surveillance system for bleeding disorders has been previously described.[5] Briefly, HTC staff collect demographic and clinical information from patients and/or medical records during annual comprehensive clinic visits using standardized data collection forms. Data are entered into ATHN study manager software using a unique patient identification key that is linked to the patient only at the HTC to assure patient confidentiality. In the U.S., most HTCs operate within educational institutions that provide ethical oversight for patient participation in surveillance and research. Most institutions with HTCs regard CC as a surveillance project and require only patient authorization for participation. In a few HTCs,CC is considered research and, therefore, participants provide informed consent under Institutional Review Board guidance.

Data collection tools included in the software consist of a population profile tool that was used to collect demographic and baseline clinical information on all patients who receive care in the HTC during the year and a registry tool which was used to record more detailed clinical data on a subset of patients who volunteered to participate during their annual clinic visit each year. For this study, we used population profile data on date of birth, sex, race and Hispanic ethnicity, current zip code of residence, haemophilia type, baseline factor activity level and history of infection with either human immunodeficiency (HIV) or hepatitis C (HCV) viruses. From the registry, data collected on a history of any of the following comorbid conditions according to clinic records or patient recall were used: hypertension, coronary artery disease, stroke (either acute ischemic stroke or transient ischemic attack), myocardial infarction, chronic kidney disease, diabetes, leukemia, liver cancer, any type of cancer, anxiety or depression. When information on a comorbid condition was not present in the clinic record, HTC staff could consult the patient to determine whether they ever had or been told by a physician that they had the condition. In addition, height and weight without shoes were measured and used to calculate body mass index (BMI) with a value 30 or greater indicative of obesity.

Haemophilia severity was defined based on values of baseline factor activity as severe (< 1%), moderate (1–5%) or mild (> 5% – < 40%). Current residential zip code information was used to determine state of residence, which was then used to define four regions of the country as follows: Northeast (CT, DE, MA, ME, NH, NJ, NY, PA, RI, VT), Southeast (AL, AR, DC, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA, WV), Midwest (IA, IL, IN, KS, MI, MN, MO, ND, NE, OH, SD, WI) and West (AK, AZ, CA, CO, HI, ID, MT, NM, NV, OR, UT, WA, WY).

For comparison with comorbidity in the general male population, we used similar data collected in CDC's National Health Interview Survey (NHIS).[6] The NHIS is a cross-sectional household interview survey of the non-institutionalized U.S. population. Data from 2019 were used for all comorbidities except for chronic renal disease which used data from 2018 since these data were not available for 2019. Households are selected using geographically clustered sampling techniques and all members of a selected household were interviewed prior to 2019. In 2019, one 'sample adult' and one 'sample child' from each household were randomly selected for interview. Both methods are designed to yield nationally representative data on health conditions. We used the responses from males in the adult sample to the following questions during the interview: 'Have you ever been told that you had hypertension, coronary heart disease, a heart attack, stroke, cancer (including any cancer, leukemia, liver), weak or failing kidneys', or 'Have you ever had diabetes, anxiety disorder, depression'. Self-reported height and weight were used to calculate BMI.

The prevalence was the proportion of study subjects with the condition at any time before or during the surveillance period. Because we are estimating lifetime prevalence of the conditions, the patient's age at the last surveillance visit was used. Since the prevalence of most of the conditions that we studied are known to increase substantially with age, we assigned a two-level age group variable based on census data classifications as follows: middle-aged (age 45–64 years) and older (age ≥65 years). Confidence intervals for all prevalence estimates were calculated using the Wald method. Differences in the prevalence

between groups of patients defined by demographic and clinical characteristics were considered statistically significant at the 5% level when the 95% confidence intervals did not overlap. Data from similarly aged male participants of the NHIS were analyzed using methods that accounted for the stratified, cluster sample design to determine the weighted prevalence of each health condition among U.S. males aged 45 and above. Since there were no regional differences in the prevalence of any of the conditions among the males with haemophilia, no regional matching with NHIS participants was performed. Confidence intervals for the prevalence of comorbid conditions among the U.S. general male population were calculated as above and were used to evaluate comorbidity prevalence differences between patients and the general population for statistical significance. All data management and analysis procedures were performed using SAS 9.4 software (SAS Institute, Cary, NC, USA).

3 | RESULTS

During the period December 2013 through March 2021, 4776 males aged 45 years or older with haemophilia had at least one visit to a network HTC among whom 2237 (47%) agreed to participate in the registry and had a total of 6564 (mean = 2.9) surveillance visits and formed the study population. Patients resided throughout the U.S. and there were no differences in age distributions across the regions. About 70% of the cohort had haemophilia A and the distribution of type was similar across the middle-aged and older patient groups (Table 1). The distribution of severity by haemophilia type was 39%, 20%, 41% for haemophilia A and 28%, 39%, 33% for haemophilia B (severe, moderate, mild, respectively). The proportion of patients with severe disease was much lower among the older age group compared to the middle-aged group (Table 1). The majority of patients were non-Hispanic and white. There were fewer non-white patients among the older patient group compared to the middle-aged group. Nearly three-fourths of all patients had a history of HCV infection, whereas about one-fourth of the cohort had a history of HIV infection. The older age group had a lower proportion of chronic infections than the middle-aged group, especially HIV (Table 1).

Table 2 shows the overall prevalence of the comorbid conditions comparing males with haemophilia to the general US male population, as well as the prevalence of the conditions among those with haemophilia according to demographic and clinical characteristics. Overall, males with haemophilia had a lower prevalence of hypertension, coronary artery disease, stroke, myocardial infarction and leukemia compared to the general population. Notably, the prevalence of diabetes, anxiety, depression and obesity was higher among males with haemophilia.

There were also variations in prevalence of the conditions among males with haemophilia according to patient characteristics. Depression was more common among patients with haemophilia A than B. Patients with severe haemophilia had a higher prevalence of obesity, diabetes, liver cancer, anxiety and depression than those with mild or moderate disease (Table 2). Patients in the older age group had a much higher prevalence of hypertension, coronary heart disease, stroke, diabetes and cancer than those in the middle-aged group. Black patients had a higher prevalence of hypertension, chronic kidney disease and diabetes

than whites, while Hispanic patients had a significantly lower prevalence of hypertension and cancer than non-Hispanic patients. There were no regional differences seen in the prevalence of any of the comorbid conditions among the patients. Patients with a history of either HIV or HCV infection had a higher prevalence of chronic kidney disease, diabetes, liver cancer, anxiety and depression than those without these infections. Those with HIV had a lower prevalence of obesity than those uninfected.

Given the strong influence of age on most of these comorbidities, age group specific prevalence comparisons were made between males with haemophilia and the general male population (Table 3). In addition, because racial and ethnic differences in prevalence were seen among the patients for hypertension, and racial differences for diabetes, and chronic kidney disease, we also provide the stratum-specific prevalence for these comorbidities. In both age groups, the haemophilia population had a lower prevalence of coronary heart disease, stroke and myocardial infarction compared to the general US male population. In most cases, the prevalence of these conditions was less than half that of US males (Figure 1). On the other hand, males with haemophilia had a much higher prevalence of anxiety and depression in both age groups compared to the general population. The prevalence of these conditions was more than double among middle-aged and about onethird higher among older males with haemophilia (Figure 1). There was no difference in the prevalence of liver cancer or of any type of cancer among the haemophilia cohort compared to the general male population regardless of age group. Additionally, the middle-aged group with haemophilia had a lower prevalence of leukemia, whereas the older haemophilia age group had a higher prevalence of obesity than males in the general population.

Overall, the prevalence of hypertension was lower in middle-aged and older haemophilia patients, however, this decrease was seen among only white and non-Hispanic patients (Table 3). The overall higher prevalence of diabetes among patients was present for both age groups among whites but among middle-aged blacks only. The apparent higher prevalence of chronic kidney disease among middle-aged patients was no longer present when stratified by race.

4 | DISCUSSION

This study estimates the burden of chronic conditions among a cohort of men with haemophilia aged 45 years and older who received care in the USHTCN and compares the prevalence to that of similarly aged men in the U.S. general population. The chronic conditions present in our haemophilia cohort mirror those in the general population, although the rates differ somewhat between the populations.

Men in the haemophilia cohort had lower rates of hypertension (among whites and non-Hispanics), coronary artery disease, stroke and myocardial infarction. Cardiovascular disease prevalence was lower in patients with severe haemophilia compared to those with mild haemophilia. This is particularly striking given patients with severe haemophilia in our cohort had higher rates of known cardiac disease risk factors, including diabetes, hypertension and HIV[7–9]. While the haemophilia cohort had lower levels of cardiovascular disease irrespective of age compared to the US general male population, the prevalence

of cardiovascular disease was much higher in the older compared to the middle-aged haemophilia group. This may be due to age-related risks of cardiovascular disease, but it is also possible that our prevalence estimate may have been impacted by the lower proportion of patients with severe haemophilia in the older age group. Previous studies have reported conflicting findings about cardiovascular disease among patients with haemophilia. Some suggest haemophilia may be protective against cardiovascular disease,[10] while others have reported higher rates of cardiovascular disease and cardiovascular disease risk factors among patients with haemophilia.[11] Patients with haemophilia may have similar atherosclerotic clot burden as the general population but experience fewer symptomatic cardiovascular events due to lower thrombin generation.[12] If hypocoagulability is indeed protective, cardiovascular events may rise in the aging haemophilia population as hemostasis improves with novel therapeutics and with rising clotting factor activity with age.[13] Further study is needed to understand the impact of haemophilia on cardiovascular outcomes especially given the unique challenges of managing cardiovascular disease in the haemophilia population, particularly when procedures and/or antiplatelet or anticoagulation therapies are required.

The impact of hypertension on cardiovascular disease in patients with haemophilia remains unclear. This study found lower rates of hypertension than previously reported in two smaller studies of haemophilia patients,[14,15] however, it is important to note that our findings were based on medical records and self-report rather than blood pressure measurements. Although our cohort had a lower overall prevalence of hypertension among whites and non-Hispanics than the general US population, the prevalence of hypertension increased with haemophilia severity. Prior studies have suggested that vascular remodeling from small renal bleeds can lead to renal injury, which may increase the risk of hypertension in the hemophilia population.,[16,17] However, other studies[18] have not found an increased risk of renal injury from hematuria in patients with hemophilia suggesting that other factors may be contributing to hypertension in patients with hemophilia. The impact of severe haemophilia on hypertension may shift and warrants continued monitoring as patients with severe haemophilia live longer with improved bleeding prophylaxis.

The prevalence of diabetes was significantly higher among the white and middle-aged black haemophilia cohort than among general US male population. We are not aware of previous reports linking diabetes to hereditary haemophilia. However, a recent study suggests that diabetes may be linked to HCV infection in patients with haemophilia.[19] The prevalence of diabetes was significantly higher among patients in our cohort who had a history of HCV infection (Table 2). In addition, the prevalence of obesity was also high among patients with haemophilia in both age groups, especially among the oldest patients and possibly contributed to the higher rate of diabetes that we found.,[20,21] A higher proportion of patients with haemophilia had obesity and diabetes compared to males in the general U.S. population in both age groups; 10.2% vs. 6.8% in the middle-aged and 14.2% vs. 8.6% in the older age group, respectively, ($P < .05$ for both). Other studies have also found higher rates of obesity in haemophilia patients including in younger cohorts. Given the increased risk of disability[22] and all-cause mortality,[23,24] from obesity in the general population, continued public health efforts to prevent obesity in the haemophilia population are warranted. Additionally, obesity adversely impacts joint outcomes and may lead to increased rates of disability in the haemophilia population.[25] Disability from joint bleeding prior to the availability of effective

treatment products may have contributed to the markedly higher obesity rate among the older age group.

The rates of anxiety and depression in the haemophilia cohort were higher than that of the general population with the highest prevalence among those with severe haemophilia. This finding highlights the underlying psychological burdens associated with chronic disease, long-term pain and musculoskeletal handicaps.[3] Furthermore, a high prevalence of HCV and HIV may impact psychological well-being and should be considered in this cohort of haemophilia patients who were disproportionately impacted by HCV and HIV infection from contaminated blood products.[3] It is unclear whether the high levels of anxiety and depression are associated with higher rates of joint bleeding and whether these comorbidities will be impacted by improved bleeding prophylaxis. This study highlights the need to understand and address the high rates of anxiety and depression in patients with hemophilia.

There are several limitations of this study that should be considered when interpreting our findings. First, since HTCs are not necessarily the providers of primary care, some patients may have comorbid conditions (e.g. hypertension) that are not known to HTC staff. However, for the CC surveillance, HTC staff relied on the clinic record and patient recall to determine whether a patient had ever been diagnosed with any of the studied conditions. Also, the presence of obesity among patients in CC surveillance was based on measured height and weight whereas NHIS relied on self-report which tends to underestimate weight. Therefore, although the methods of ascertainment are similar, methodologic differences may have affected the accuracy of prevalence assessment for some conditions more than others and contributed to some of the differences in prevalence that we observed.

Second, it is important to recognize that we assessed the prevalence of these conditions in a survival cohort of patients. The relatively low prevalence of severe haemophilia and history of HIV and HCV infections reflects the increased mortality experienced by this generation of males with haemophilia and is likely to have also influenced the prevalence of some of the studied comorbidities. For example, high mortality rates among patients with liver cancer may explain why we did not see the expected higher prevalence of this complication of HCV infection in our cohort. The burden of comorbidities in the ageing haemophilia population will likely shift as more patients with haemophilia live normal lifespans without chronic infectious diseases like HIV and HCV.

Third, the excess mortality among patients with severe haemophilia may have resulted from differences between patients and the general US adult population in the distribution of age within the two age groups, which may have influenced the comorbidity comparisons. However, the distribution of ages within the two age groups were nearly identical between patients and US adults.

Finally, the patients included were those who received care at an HTC and chose to participate in the CC surveillance. It is possible that patients with certain comorbidities may have been too ill to participate which may have influenced our estimates. In addition, this study does not reflect the entire haemophilia population age ≥ 45 years who received care in the HTCs; the proportion of patients in this age group who participated was 47%

of the total number of similarly aged patients with haemophilia who visited an HTC during the surveillance period. By comparison, the overall non-response rate for the adult sample in NHIS was somewhat higher at 59.1%.

5 | CONCLUSION

The presence of comorbidities presents unique challenges for the ageing haemophilia population. Even in the absence of haemophilia, comorbidities are linked to poor health outcomes. Notably, this study highlights the higher burden of depression, anxiety and obesity in the ageing haemophilia population; comorbidities which are all associated with higher all-cause mortality. Additional investigation is needed to understand why the haemophilia population has a higher rate of these comorbidities and how they affect overall health and wellbeing. The impact of haemophilia severity on age-related conditions may become more apparent as more patients with severe haemophilia live a normal lifespan. Additionally, comorbidities in the ageing haemophilia population may shift with declines in iatrogenic HCV and HIV infections and improvements in bleeding prophylaxis. The findings from this study can be used to inform providers as they utilize evidence-based management decisions and supports the need for ongoing surveillance of comorbidities in patients with haemophilia.

ACKNOWLEDGEMENTS

The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of the American Thrombosis and Hemostasis Network (ATHN), or the Hemophilia Treatment Center Network (HTCN). The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. JNP is a consultant for TeraImmune. None of the other authors have relations that might be perceived as a conflict of interest. JMS, BL designed the study, conducted the research, analysed the data and wrote the paper. BD, JNP designed the study, conducted the research and wrote the paper.

The Community Counts surveillance data are available via a data visualization tool that displays de-identified data on patients with bleeding disorders who are enrolled in Community Counts in an interactive, visual format (https://www.cdc.gov/ncbddd/hemophilia/communitycounts/data-viz.html). However, due to ethical restrictions related to protecting patient confidentiality, additional individual-level data generated from the Community Counts surveillance system cannot be made publicly available.

FUNDING INFORMATION

The author(s) received no specific funding for this work

DATA AVAILABILITY STATEMENT

The Community Counts surveillance data are available via a data visualization tool that displays de-identified data on patients with bleeding disorders who are enrolled in Community Counts in an interactive, visual format (https://www.cdc.gov/ncbddd/hemophilia/communitycounts/data-viz.html). However, due to ethical restrictions related to protecting patient confidentiality, additional individual-level data generated from the Community Counts surveillance system cannot be made publicly available.

REFERENCES

1. Sarah CD, Sau WK, Rosemary JS. Mortality rates, life expectancy, and causes of death in people with hemophilia A or B in the United Kingdom who were not infected with HIV. Blood. 2007;110:815–825. [PubMed: 17446349]
2. Angelini D, Konkle BA, Sood SL. Aging among persons with hemophilia: contemporary concerns. Semin Hematol. 2016;53:35–39. [PubMed: 26805905]
3. Tuienburg A, Mauser-Bunschoten EP, Verhaar MC, Biesma DH, Schutgens REG. Cardiovascular disease in patients with hemophilia. J Thromb Haemost. 2009;7:247–254. [PubMed: 18983484]
4. Siboini SM, Mannucci PM, Gringeri A. Health status and quality of life of elderly persons with severe hemophilia born before the advent of modern replacement therapy. J Thromb Haemost. 2009;7:780–786. [PubMed: 19220727]
5. Manco-Johnson MJ, Byams VR, Recht M, et al. Community counts: evolution of a national surveillance system for bleeding disorders. Am J Hematol. 2018;93:E137–E140. [PubMed: 29473207]
6. National Center for Health Statistics. National Health Interview Survey, 2018, 2019. Public-use data file and documentation. ftp://ftp.cdc.gov/pub/Health_Statistics/nchs/. Accessed 2021.
7. Almdal T, Scharling H, Jensen JS, Vestergaard H. The independent effect of type 2 diabetes mellitus on ischemic heart disease, stroke, and death: a population-based study of 13,000 men and women with 20 years of follow-up. Arch Intern Med. 2004;164:1422–1426. [PubMed: 15249351]
8. Rapsomaniki E, Timmis A, George J. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. Lancet. 2014;383:1899–1911. [PubMed: 24881994]
9. Hsue PY, Deeks SG, Hunt PW. Immunologic basis of cardiovascular disease in HIV-infected adults. J Infect Dis. 2012;205(3):S375–82. [PubMed: 22577211]
10. Darby SC, Kan SW, Spooner RJ, et al. Mortality rates, life expectancy, and causes of death in people with hemophilia A or B in the United Kingdom who were not infected with HIV. Blood. 2007;110:815–825. [PubMed: 17446349]
11. Sharathkumar AA, Soucie JM, Trawinski B, Greist A, Shapiro AD. Prevalence and risk factors of cardiovascular disease (CVD) events among patients with haemophilia: experience of a single haemophilia treatment centre in the United States (US). Haemophilia. 2011;17:597–604. [PubMed: 21323799]
12. Kamphuisen PW, ten Cate H. Cardiovascular risk in patients with hemophilia. Blood. 2014;123:1297–1301. [PubMed: 24385539]
13. Mari D, Mannucci PM, Coppola R, Bottasso B, Bauer KA, Rosenberg RD. Hypercoagulability in centenarians: the paradox of successful aging. Blood. 1995;85:3144–3149. [PubMed: 7756646]
14. von Drygalski A, Kolaitis NA, Bettencourt R. Prevalence and risk factors for hypertension in hemophilia. Hypertension. 2013;62:209–215. [PubMed: 23630949]
15. Fransen van de Putte DE, Fischer K, Makris M, et al. Increased prevalence of hypertension in haemophilia patients. Thromb Haemost. 2012;108:750–755. [PubMed: 22955860]
16. Barnes RFW, Cramer TJ, Hughes TH, von Drygalski A. The hypertension of hemophilia is associated with vascular remodeling in the joint. Microcirculation. 2017;24(7). doi:10.1111/micc.12387
17. Barnes RF, Cramer TJ, Sait AS, Kruse-Jarres R, Quon DV,von Drygalski A. The hypertension of hemophilia is not explained by the usual cardiovascular risk factors: results of a cohort study. Int J Hypertens. 2016:2016:2014201. doi:10.1155/2016/2014201 [PubMed: 27965893]
18. Benedik-Dolnicar M, Benedik M. Haematuria in patients with haemophilia and its influence on renal function and proteinuria. Haemophilia. 2007;13:489–492. [PubMed: 17880434]
19. Pandey B, Barnes RFW, Sun HL. Risk of diabetes in haemophilia patients compared to clinic and non-clinic control cohorts. Haemophilia. 2022;28:445–452. [PubMed: 35238443]
20. Sainaghi PP, Castello L, Bergamasco L, Carnevale Schianca GP, Bartoli E. Metabolic characteristics of glucose intolerance: the critical role of obesity. Exp Clin Endocrinol Diabetes. 2008;116:86–93. [PubMed: 17972239]

21. Knowler WC, Barrett-Connor E, Fowler SE. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393–403. [PubMed: 11832527]
22. Alley DE, Chang VW. The changing relationship of obesity and disability, 1988–2004. JAMA. 2007;298:2020–2027. [PubMed: 17986695]
23. Berrington de Gonzalez A, Hartge P, Cerhan JR. Body-mass index and mortality among 1.46 million white adults. N Engl J Med. 2010;363:2211–2219. [PubMed: 21121834]
24. Aune D, Sen A, Prasad M. BMI and all-cause mortality: systematic review and non-linear dose-response meta-analysis of 230 cohort studies with 3.74 million deaths among 30.3 million participants. BMJ. 2016;353:i2156. doi:10.1136/bmj.i2156 [PubMed: 27146380]
25. Soucie JM, Wang C, Siddiqi A, Kulkarni R, Recht M, Konkle BA, the Hemophilia Treatment Center Network. The longitudinal effect of body adiposity on joint mobility in young males with haemophilia A. Haemophilia. 2011;17:196–203. [PubMed: 21332880]

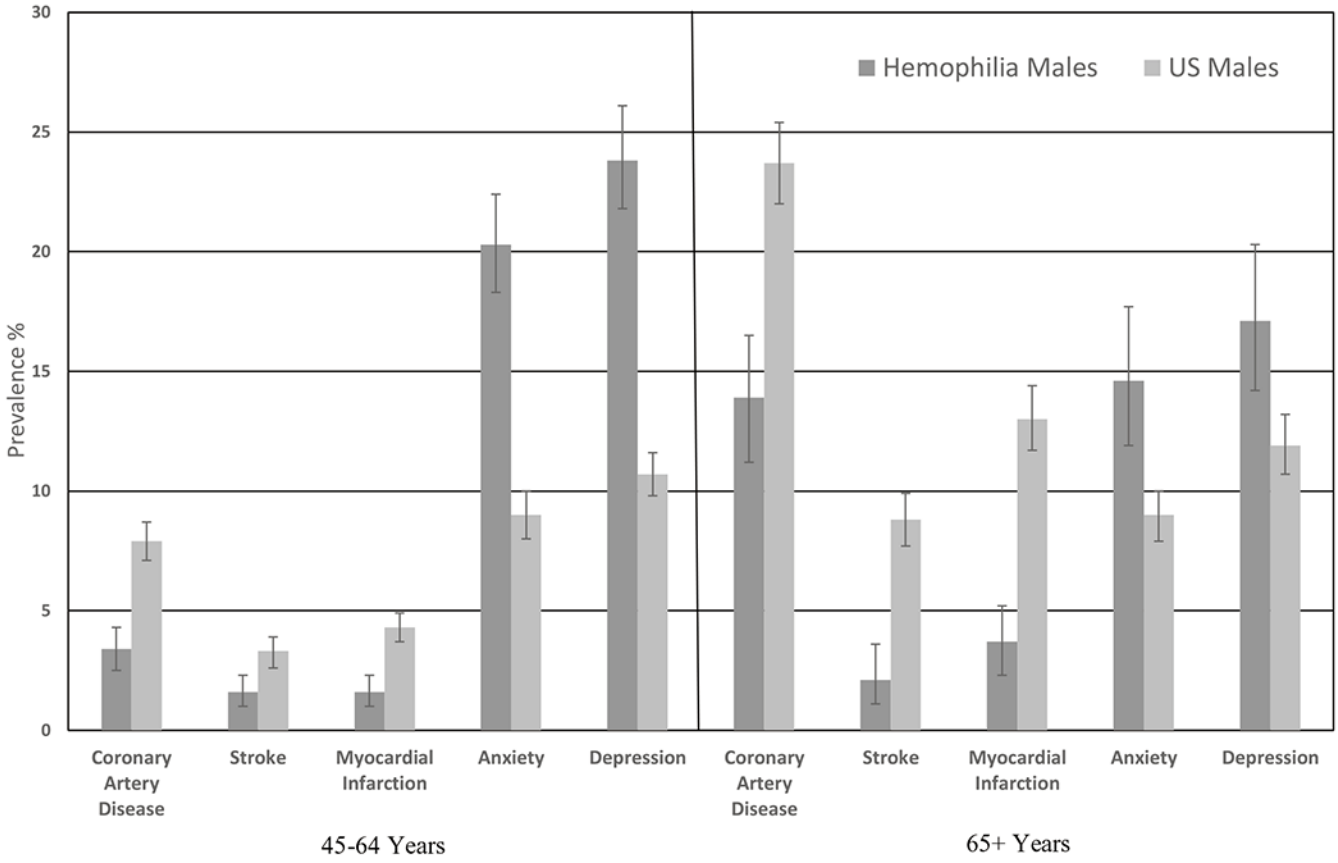

FIGURE 1.
Prevalence of selected comorbidities with 95% confidence intervals

TABLE 1

Characteristics of 2237 males 45+ years old with hemophilia receiving care in USHTCN, 2013–2021

	All		Age 45–64 years		Age ≥65 years	
Characteristic	**N**	**%**	**N**	**%**	**N**	**%**
Hemophilia Type						
A	1609	72.0	1160	72.9	449	69.6
B	628	28.0	432	27.1	196	30.4
Severity						
Mild	859	38.4	533	33.5	326	50.5
Moderate	579	25.9	416	26.1	163	25.3
Severe	799	35.7	643	40.4	156	24.2
Race						
White	1935	86.5	1333	83.7	602	93.3
Black	199	8.9	175	11.0	24	3.7
Other	83	3.7	66	4.2	17	2.7
Unknown	20	.9	18	1.1	2	.3
Ethnicity						
non-Hispanic	2092	93.5	1472	92.5	620	96.1
Hispanic	125	5.6	107	6.7	18	2.8
Unknown	20	.9	13	.8	7	1.1
Region						
Northeast	535	23.9	370	23.2	165	25.6

Characteristic	All		Age 45–64 years		Age ≥65 years	
	N	%	N	%	N	%
Southeast	630	28.2	461	29.0	169	26.2
Midwest	698	31.2	470	29.5	228	35.3
West	374	16.7	291	18.3	83	12.9
History of HIV						
Yes	543	24.3	487	30.6	56	8.7
No	1621	72.5	1061	66.6	560	86.8
Unknown	73	3.2	44	2.8	29	4.5
History of HCV						
Yes	1570	70.2	1204	75.6	366	56.7
No	618	27.6	258	22.5	260	40.3
Unknown	49	2.2	30	1.9	19	3.0

TABLE 2

Prevalence of comorbid conditions by clinical and demographic characteristics among 2237 males 45+ years old with hemophilia receiving care in USHTCN, 2013–2020

Condition	Hypertension		Coronary Artery Disease		Stroke		Myocardial Infarction		Chronic Kidney Disease	
	Percent	95% CI	Percent	95% CI	Percent	95% CI	Percent	95% CI	Percent	95% CI
U.S. males	49.5*	48.1–50.8	13.8*	12.9–14.7	5.3*	4.7–5.9	7.6*	6.9–8.2	4.3	3.7–4.8
Males with Hemophilia	38.6	36.6–40.7	6.4	5.4–7.4	2.4	1.8–3.0	2.2	1.6–2.9	4.9	4.0–5.8
Hemophilia Type										
A	37.8	35.4–40.2	6.1	4.9–7.3	2.6	1.8–3.4	2.1	1.4–2.8	5.3	4.2–6.4
B	40.8	37.0–44.7	7.2	5.2–9.2	1.8	.7–2.8	2.6	1.3–3.8	4.0	2.5–5.5
Severity										
Mild	36.5	33.2–39.7	7.8	6.0–9.6	2.2	1.2–3.2	2.2	1.2–3.2	4.0	2.7–5.3
Moderate	38.3	34.4–42.3	7.4	5.3–9.6	2.4	1.2–3.7	2.4	1.2–3.7	4.8	3.1–6.6
Severe	41.2	37.8–44.6	4.2	2.8–5.5	2.5	1.4–3.6	2.1	1.1–3.1	6.0	4.4–7.7
Age (years)										
45–64	33.7	31.4–36.0	3.4	2.5–4.3	1.6	1.0–2.3	1.6	1.0–2.3	4.2	3.2–5.2
65+	50.9*	47.1–54.8	13.9*	11.2–16.5	4.2*	2.6–5.8	3.7	2.3–5.2	6.7	4.8–8.6
Race										
White	37.7	35.5–39.8	6.8	5.6–7.9	2.3	1.6–3.0	2.5	1.8–3.2	4.1	3.2–5.0
Black	50.8*	43.8–57.7	4.0	1.3–6.8	4.5	1.6–7.4	1	.0–2.4	10.6*	6.3–14.8
Ethnicity										
non-Hispanic	39.3*	37.2–41.4	6.7	5.6–7.7	2.5	1.8–3.2	2.4	1.7–3.0	5.0	4.1–6.0

Condition	Hypertension		Coronary Artery Disease		Stroke		Myocardial Infarction		Chronic Kidney Disease	
	Percent	95% CI	Percent	95% CI	Percent	95% CI	Percent	95% CI	Percent	95% CI
Hispanic	28.0	20.1–35.9	3.2	.1–6.3	.8	.0–2.4	0	–	4.0	.6–7.4
History of HIV										
Yes	37.4	33.4–41.5	4.2	2.6–6.0	2.6	1.2–3.9	1.8	.7–3.0	8.5*	6.1–10.8
No	39.3	36.9–41.6	7.1	5.9–8.5	2.4	1.7–3.2	2.4	1.7–3.0	4	3.0–4.9
History of HCV										
Yes	40.1	37.7–42.5	5.3	4.2–6.4	2.4	1.7–3.2	2.2	1.4–2.9	6.2*	5.0–7.4
No	35.0	31.2–38.8	8.8	6.6–11.0	2.4	1.2–3.7	2.3	1.1–3.5	2.1	1.0–3.3
Region										
Northeast	41.4	37.2–45.5	6.4	4.3–8.5	2.6	1.3–4.0	2.4	1.1–3.8	4.3	2.6–6.0
Southeast	36.5	32.8–40.3	5.7	3.9–7.5	2.7	1.4–4.0	2.2	1.1–3.4	4.6	3.0–6.2
Midwest	40.1	36.5–43.8	7.6	5.7–9.6	2.3	1.2–3.4	2.2	1.1–3.2	5.2	3.5–6.8
West	35.7	30.8–40.5	5.4	3.1–7.6	1.6	.3–2.9	2.1	.7–3.6	5.9	3.5–8.3

Condition	Diabetes		Any Cancer		Leukemia		Liver Cancer	
	Percent	95% CI	Percent	95% CI	Percent	95% CI	Percent	95% CI
U.S. males	15.8	14.9–16.7	15.2	14.3–16.1	2*	1.3–2.8	.8	.3–1.4
Males with Hemophilia	24.0*	22.2–25.8	13.4	12.0–14.8	.7	.3–1.0	1.8	1.2–2.3
Hemophilia Type								
A	24.3	22.2–26.4	12.9	11.3–14.6	.5	.2–.8	1.8	1.1–2.4
B	23.3	20.0–26.6	14.5	11.8–17.3	1.1	.3–1.9	1.9	.8–3.0
Severity								

	Diabetes		Any Cancer		Leukemia		Liver Cancer	
Condition	**Percent**	**95% CI**	**Percent**	**95% CI**	**Percent**	**95% CI**	**Percent**	**95% CI**
Mild	21.3	18.5–24.0	14.8	12.4–17.1	.7	.1–1.3	.5	.1–.9
Moderate	23.1	19.7–26.6	11.4	8.8–14.0	.5	.0–1.1	2.1	.9–3.2
Severe	27.6*	24.5–30.7	13.3	10.9–15.6	.8	.2–1.4	3.0*	1.8–4.2
Age (years)								
45–64	21.5	19.5–23.5	9.3	7.8–10.7	.6	.2–.9	1.5	.9–2.1
65+	30.2*	26.6–33.7	23.5*	20.2–26.8	.9	.2–1.7	2.5	1.3–3.7
Race								
White	22.8	21.0–24.7	14.2	12.6–15.8	.7	.3–1.0	2.0	1.4–2.6
Black	35.7*	29.0–42.3	8.5	4.7–12.3	0	–	.5	.0–1.5
Ethnicity								
non-Hispanic	24.0	22.2–25.9	13.8*	12.3–15.2	.6	.3–1.0	1.9	1.3–2.4
Hispanic	21.6	14.7–29.8	6.4	2.1–10.7	1.6	.0–3.8	.8	.0–2.4
History of HIV								
Yes	26.4	22.7–30.1	14.8	11.8–17.8	.4	.0–1.3	3.7*	2.1–5.3
No	23.4	21.3–25.4	13	11.4–14.6	.7	.3–1.1	1.2	.6–1.7
History of HCV								
Yes	26.1*	24.0–28.3	13.3	11.6–15.0	.7	.3–1.1	2.6	1.8–3.3
No	19.1	16.0–22.2	13.9	11.1–16.6	.3	.0–.8	0	–
Region								
Northeast	24.4	20.8–28.1	12.6	9.8–15.4	.4	.0–.9	1.3	.4–2.3

	Diabetes		Any Cancer		Leukemia		Liver Cancer	
Condition	**Percent**	**95% CI**	**Percent**	**95% CI**	**Percent**	**95% CI**	**Percent**	**95% CI**
Southeast	24.4	21.1–27.8	11.3	8.8–13.7	.6	.0–1.3	1.3	.4–2.1
Midwest	21.1	18.1–24.2	15.1	12.4–17.8	.9	.2–1.6	2.7	1.5–4.0
West	28.1	23.5–32.6	14.8	11.1–18.3	.8	.0–1.7	1.6	.3–2.9

	Anxiety		Depression		Obesity	
Condition	**Percent**	**95% CI**	**Percent**	**95% CI**	**Percent**	**95% CI**
U.S. males	9	8.2–9.7	11.2	10.4–11.9	33.6	32.3–34.9
Males with Hemophilia	18.5*	16.9–20.1	21.9*	20.2–23.6	37.3*	35.2–39.4
Hemophilia Type						
A	19.0	17.1–20.9	23.4*	21.4–25.5	36.4	33.9–38.9
B	17.3	14.3–20.2	18.1	15.1–21.1	39.8	35.7–43.8
Severity						
Mild	15.1	12.7–17.5	17.0	14.5–19.5	42.5	39.0–46.0
Moderate	16.2	13.1–19.2	19.3	16.0–22.5	40.0	35.8–44.3
Severe	23.9*	20.9–26.8	29.2*	26.0–32.3	29.8*	26.4–33.2
Age (years)						
45–64	20.2*	18.2–22.1	23.9*	21.8–26.0	38.0	35.5–40.5
65+	14.5	11.7–17.2	17.0	14.0–19.8	35.7	31.7–39.6
Race						
White	18.7	17.0–20.4	22.1	20.2–23.9	37.2	34.9–39.5
Black	16.2	11.0–21.3	21.7	16.0–27.5	41.0	33.8–48.2
Ethnicity						

Condition	Anxiety		Depression		Obesity	
	Percent	95% CI	Percent	95% CI	Percent	95% CI
non-Hispanic	18.7	17.0–20.4	21.6	19.8–23.3	36.8	34.6–39.0
Hispanic	16.8	10.2–23.4	27.2	19.4–35.0	47.3	38.1–56.6
History of HIV						
Yes	23.8*	20.2–27.4	30.9*	27.0–34.8	24.6	20.7–28.4
No	17.1	15.3–19.0	19.6	17.7–21.5	41.7*	39.1–44.2
History of HCV						
Yes	21.5*	19.5–23.6	26.3*	24.1–28.4	33.8	31.3–36.3
No	11.6	9.1–14.1	11.8	9.3–14.6	45.1	41.0–49.3
Region						
Northeast	20.6	17.1–24.0	20.0	16.6–23.4	32.0	27.8–36.2
Southeast	15.2	12.4–18.0	19.5	16.4–22.6	38.6	34.6–42.7
Midwest	18.3	15.4–21.2	21.7	18.7–24.8	41.3	37.4–45.1
West	21.6	17.4–25.8	29.1	24.5–33.7	35.2	30.0–40.4

* Indicates prevalence value that is significantly greater ($P < .05$) than comparison group(s).

TABLE 3

Prevalence of comorbid conditions among males with hemophilia and U.S. males by age group

Medical Condition	Age 45–64 years		Age 65+ years	
	Males with Haemophilia %(95% CI)	U.S. Males %(95% CI)	Males with Haemophilia %(95% CI)	U.S. Males %(95% CI)
Hypertension	33.7 (31.4–36.0)	41.2 (39.5–43.0) *	50.9 (47.1–54.8)	63.3 (61.4–65.1) *
White race	32.1 (29.6–34.6)	41.1 (39.2–43.0) *	49.9 (45.9–53.9)	62.5 (60.5–64.5) *
Black race	48.6 (41.2–56.0)	51 (46.3–55.7)	66.7 (47.8–85.5)	74.2 (68.5–79.8)
non–Hispanic ethnicity	34.1 (31.7–36.6)	42.5 (40.7–44.4) *	51.5 (47.6–55.5)	63.3 (61.5–65.1) *
Hispanic ethnicity	26.2 (17.8–34.5)	33.7 (29.1–38.3)	38.9 (16.4–61.4)	63 (54.8–71.3)
Coronary artery disease	3.4 (2.5–4.3)	7.9 (7.1–8.7) *	13.9 (11.2–16.5)	23.7 (22.0–25.4) *
Stroke	1.6 (1.0–2.3)	3.3 (2.6–3.9) *	2.1 (1.1–3.6)	8.8 (7.7–9.9) *
Myocardial infarction	1.6 (1.0–2.3)	4.3 (3.7–4.9) *	3.7 (2.3–5.2)	13.0 (11.7–14.4) *
Chronic kidney disease	4.2 (3.2–5.2) **	2.3 (1.7–2.9)	6.7 (4.8–8.6)	7.1 (6.0–8.2)
White race	3.1 (2.2–4.0)	1.8 (1.2–2.4)	6.3 (4.4–8.3)	6.9 (5.7–8)
Black race	10.9 (6.2–15.5)	5.1 (2.8–7.4)	8.3 (0–19.4)	9.6 (5.6–13.7)
Diabetes	21.5 (19.5–23.5) **	12.2 (11.2–13.3)	30.2 (26.6–33.7) **	21.8 (20.3–23.3)
White race	20.1 (17.9–22.2) **	11.3 (10.1–12.4)	29.0 (25.4–32.6) **	20.3 (18.7–22.0)
Black race	34.3 (27.2–41.3) **	16.5 (12.9–20.1)	45.8 (25.9–65.8)	32.7 (26.9–38.4)
Any cancer	9.3 (7.8–10.7)	8.3 (7.3–9.2)	23.5 (20.2–26.8)	26.9 (25.3–28.5)
Leukemia	.6 (.2–.9)	2.5 (1.1–3.9) *	.9 (.2–1.7)	1.8 (.9–2.6)
Liver cancer	1.5 (.9–2.2)	.8 (0–2.0)	2.3 (1.2–3.8)	.9 (.4–1.4)

Medical Condition	Age 45–64 years		Age 65+ years	
	Males with Haemophilia %(95% CI)	U.S. Males %(95% CI)	Males with Haemophilia %(95% CI)	U.S. Males %(95% CI)
Anxiety	20.3 (18.3–22.4) **	9.0 (8.0–10.0)	14.6 (11.9–17.7) **	9.0 (7.9–10.0)
Depression	23.8 (21.8–26.1) **	10.7 (9.8–11.6)	17.1 (14.2–20.3) **	11.9 (10.7–13.2)
Obesity	38.0 (35.4–40.6)	37.6 (35.8–39.3)	35.7 (31.7–39.7) **	26.8 (25.1–28.6)

* Age-group specific prevalence of condition significantly ($P < .05$) higher among U.S. males.

** Age-group specific prevalence of condition significantly ($P < .05$) higher among males with hemophilia.