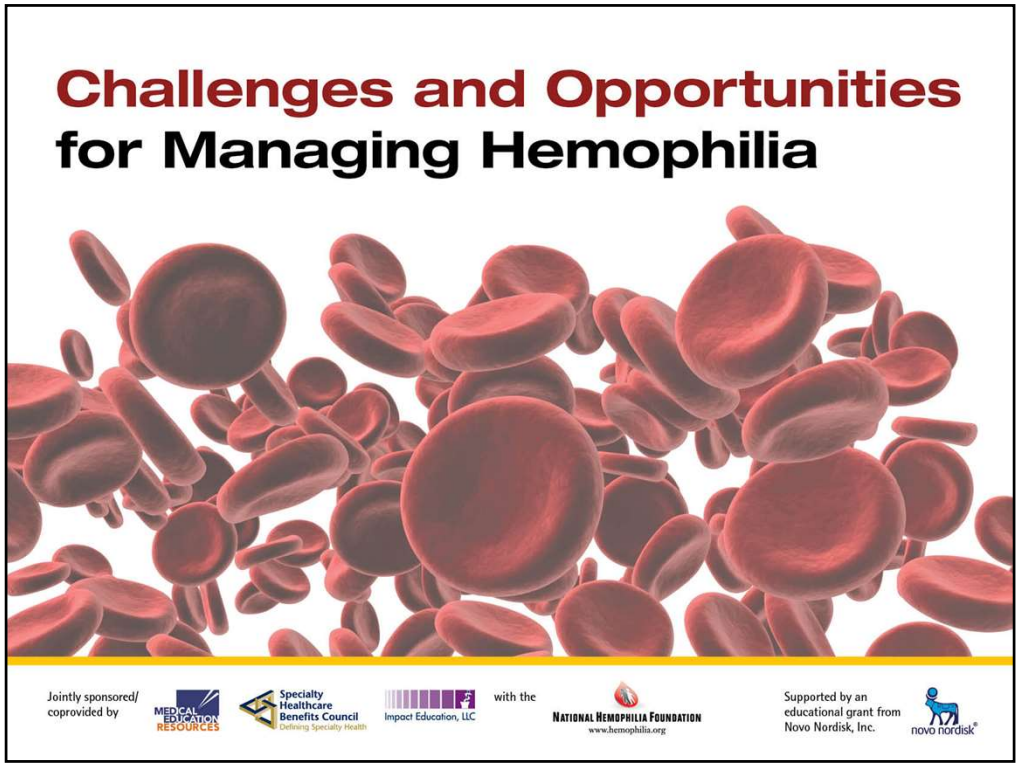
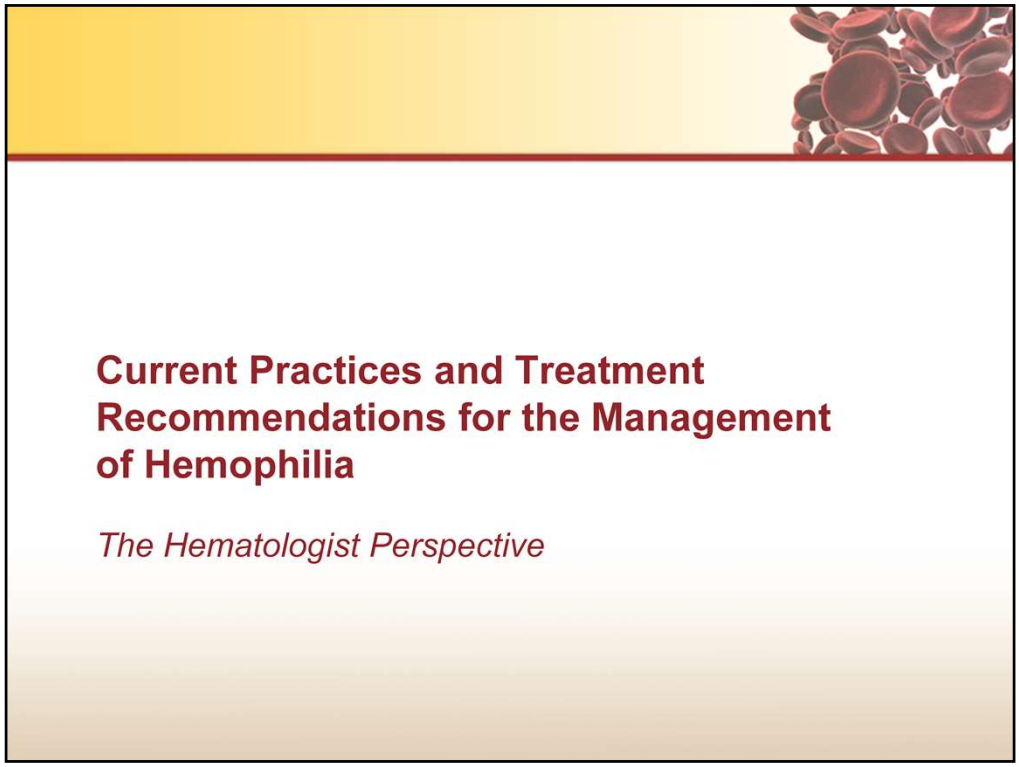
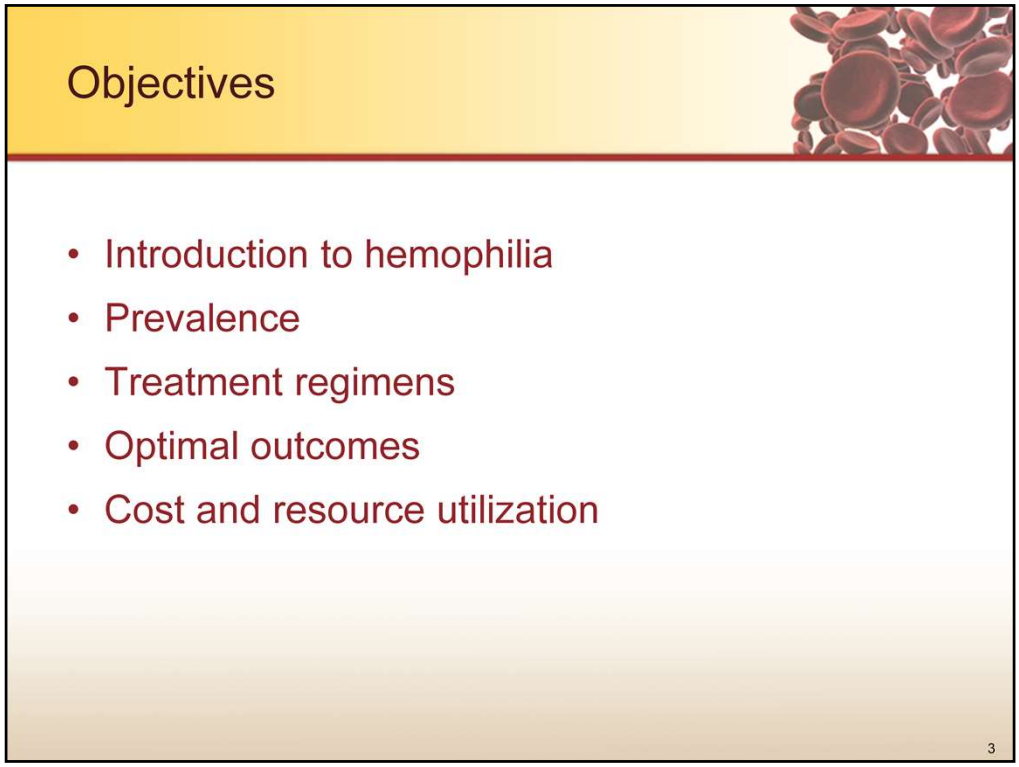


Welcome to the continuing education activity entitled “Challenges and Opportunities for Managing Hemophilia”. We are pleased to provide you with what we hope will be an informative and meaningful program.

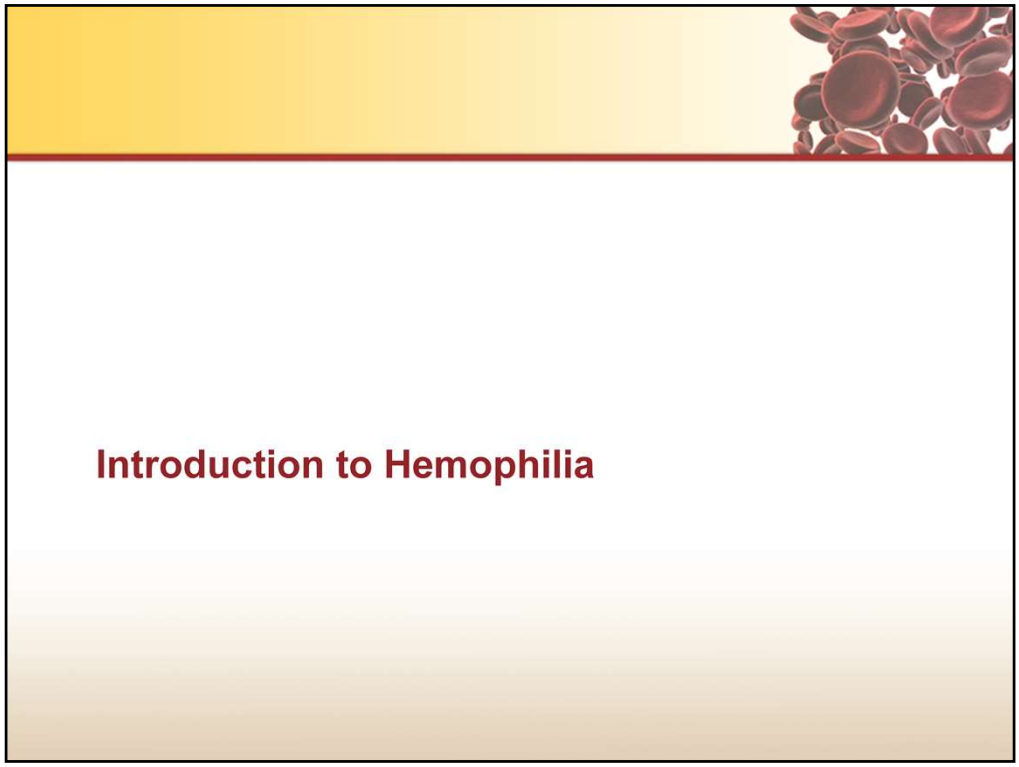
We would like to acknowledge that this activity is supported by an educational grant from Novo Nordisk and we would like to thank them for their support.



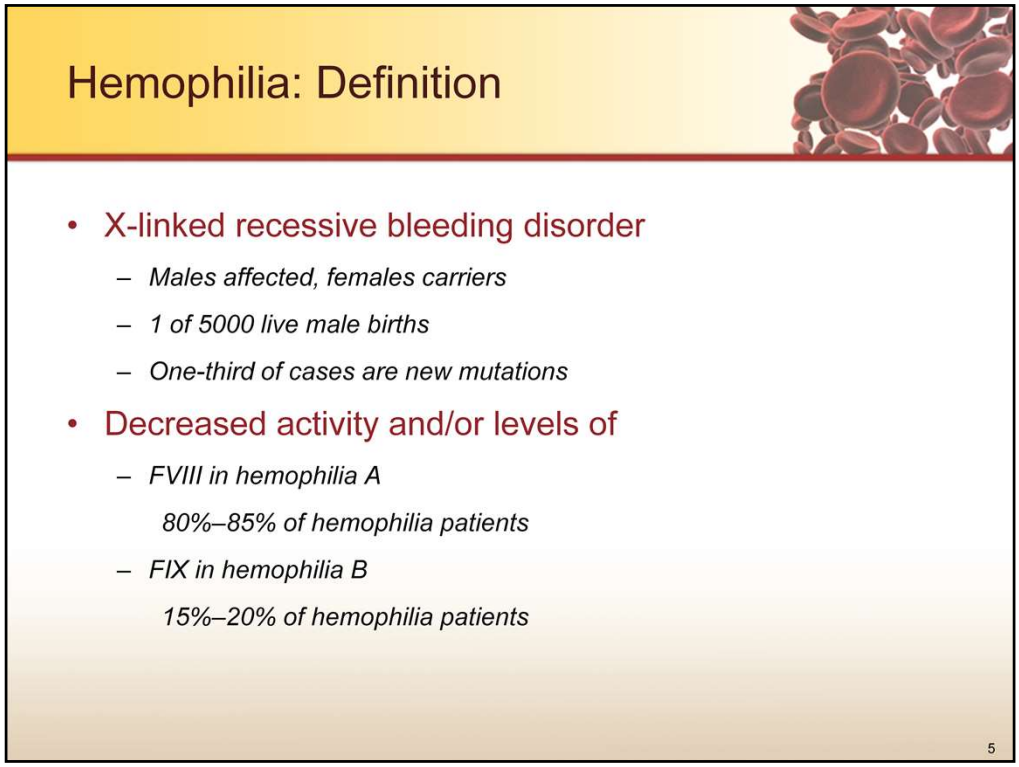
This presentation, entitled “Current Practices and Treatment Recommendations for the Management of Hemophilia,” will provide information from the Hematologist Perspective.



The objectives of this presentation are to provide an introduction to hemophilia, prevalence of sequelae, treatment regimens, optimal outcomes, and cost and resource utilization.



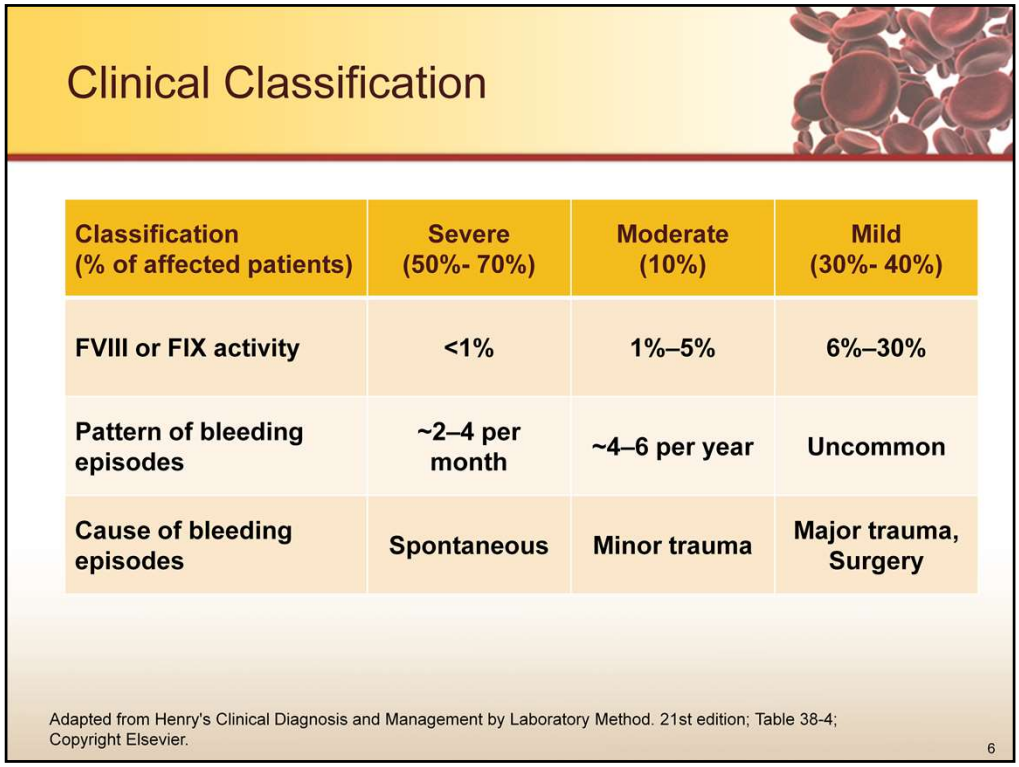
Let us start with an introduction to hemophilia.



Hemophilia is an X-linked disorder. It primarily affects males because of its X-linked nature. Females can be carriers, including some who have low enough levels of factor deficiency that they are actually symptomatic.

Hemophilia affects approximately one in five thousand live male births, and about a third of the cases are new mutations and do not have a family history.

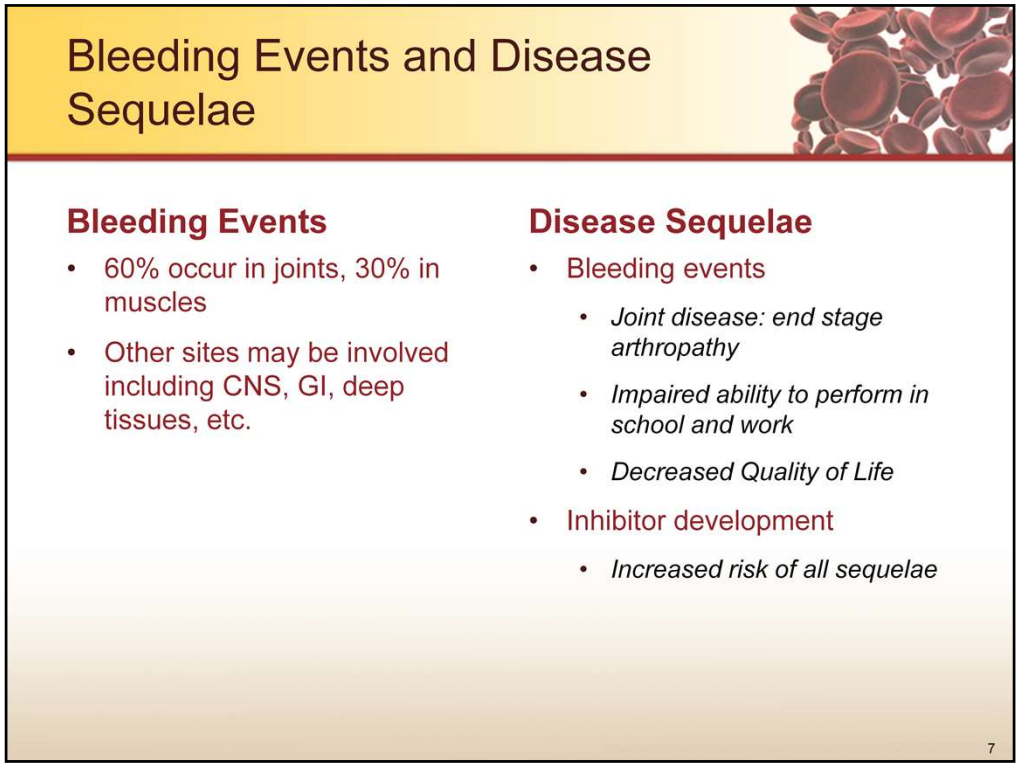
There are two types of hemophilia. They are clinically indistinguishable. The more common type is hemophilia A, which is a deficiency of factor 8, one of the key clotting factors in blood. Hemophilia A affects approximately 80% to 85% of patients with hemophilia. The other type is Hemophilia B, which results from a deficiency of clotting factor 9 and affects about 15% to 20% of hemophilia patients.



Hemophilia is divided into three severity categories based upon the level of the coagulation factor that is detectable in the patient's blood. We classify patients as severe, with a clotting factor level of less than 1%; moderate, with a clotting factor level of 1% to 5%; and mild, with a clotting factor level between 5% and approximately 30 or 40%.

Of the total affected population, approximately 50 to 70% of patients have severe deficiency; approximately 10% have moderate deficiency; and 30 to 40% have mild deficiency. Patients with severe hemophilia bleed approximately two to four times monthly and their bleeding episodes are often characterized as spontaneous in nature. Spontaneous bleeding is due to the normal stress of everyday activity that precipitates microbleeding that progresses in patients with hemophilia to clinically evident hemorrhagic episodes.

In moderate deficiency states, patients experience approximately four to six bleeding episodes yearly, often in association with minor injury. Patients with mild deficiency bleed infrequently and usually only in association with injury, trauma, intervention, or surgery.



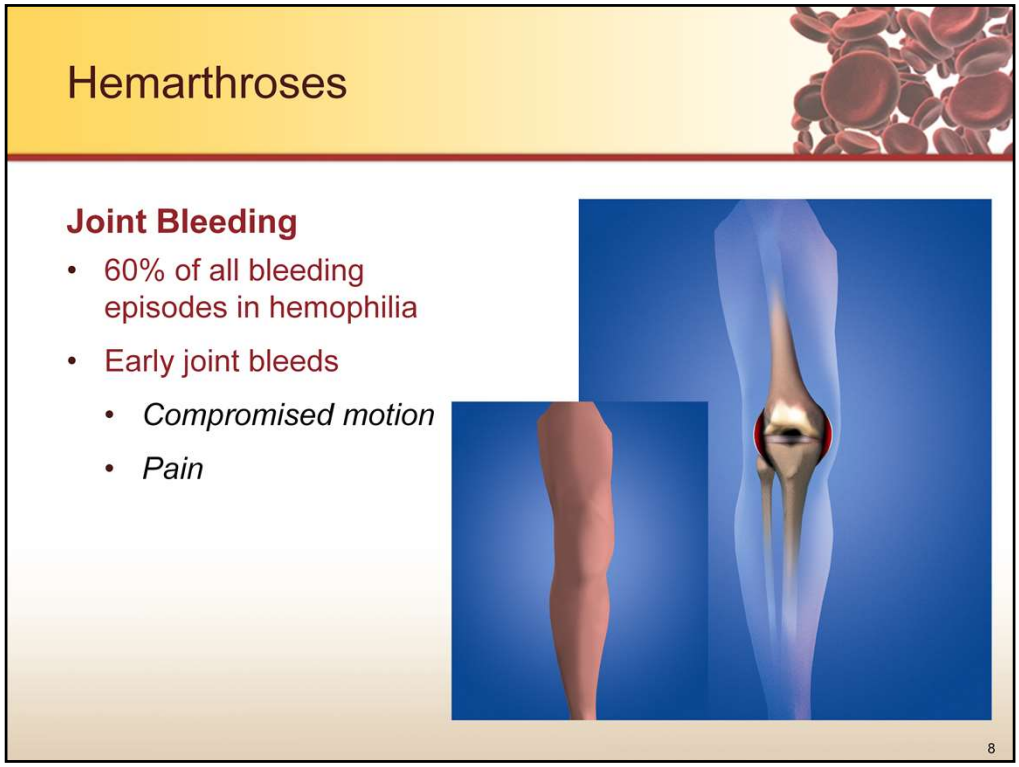
Characteristic bleeding events that occur in patients with hemophilia are joint and deep tissue or muscle bleeds. Approximately 60% of bleeding events associated with severe hemophilia occur in the joints and 30% in the muscles. Other sites can be involved, including the central nervous system, gastrointestinal tract and other deep tissues. Bleeding events that occur into joints are termed hemarthroses. Repetitive bleeding into joints leads to joint disease that may progress to end stage arthropathy, which is often associated with interference with function and disability.

This level of joint disease often leads to chronic pain and ambulatory challenges and negatively impacts an individual's quality of life by interfering with everyday activities and ability to work and/or perform in school. For example, a patient with severe joint disease in their near ankle may find it difficult to stand for long periods of time or maneuver up and down stairs. This in turn leads to restrictions in the types of work and activities that an individual can perform.

The potential for acute and long-term consequences of bleeding events depends on the location and severity of the bleed. Certain locations are considered critical with the potential for a bleeding episode to become life or limb threatening. For example, a small amount of bleeding into the central nervous system can result in significant sequelae. Due to this, pregnant females who are known carriers will have delivery plans established to protect the potentially affected infant from birth injury and central nervous system

hemorrhage.

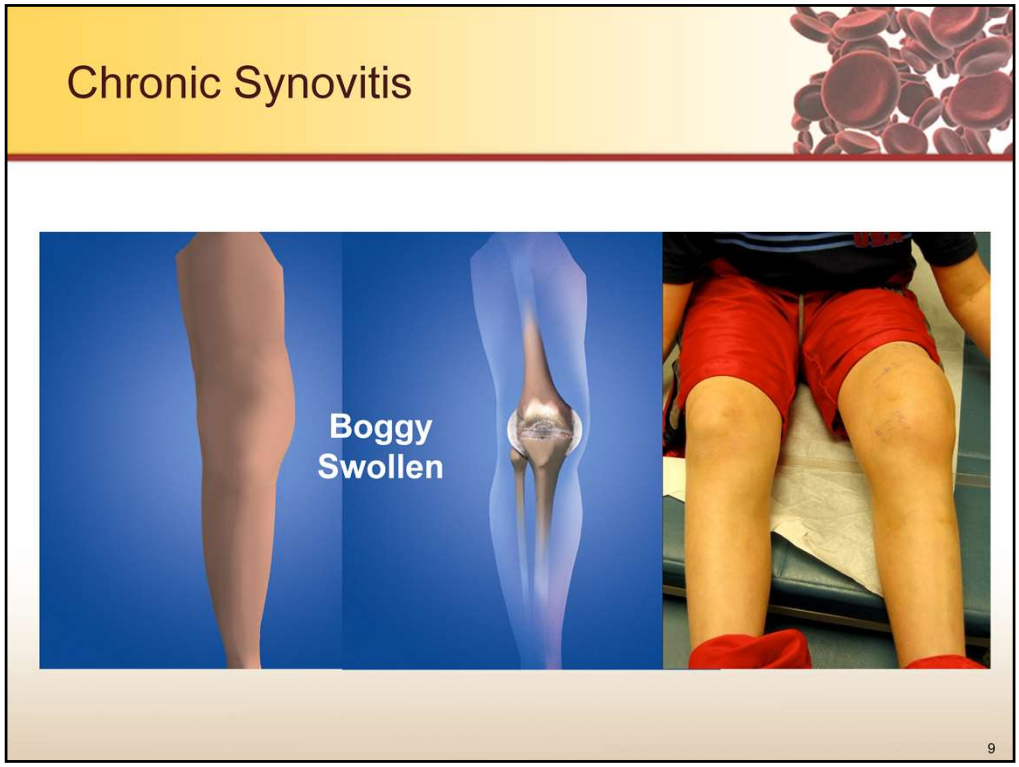
A continued important consequence of hemophilia is the development of an inhibitory antibody, termed an inhibitor. This specific sequela is discussed later in more depth.



Using a knee as an example, we are going to walk through some of the stages of hemarthroses, or joint bleeds, and look at the pathology that ensues with repeated bleeding into joints. As mentioned, about 60% of all bleeding episodes in hemophilia are in the joints.

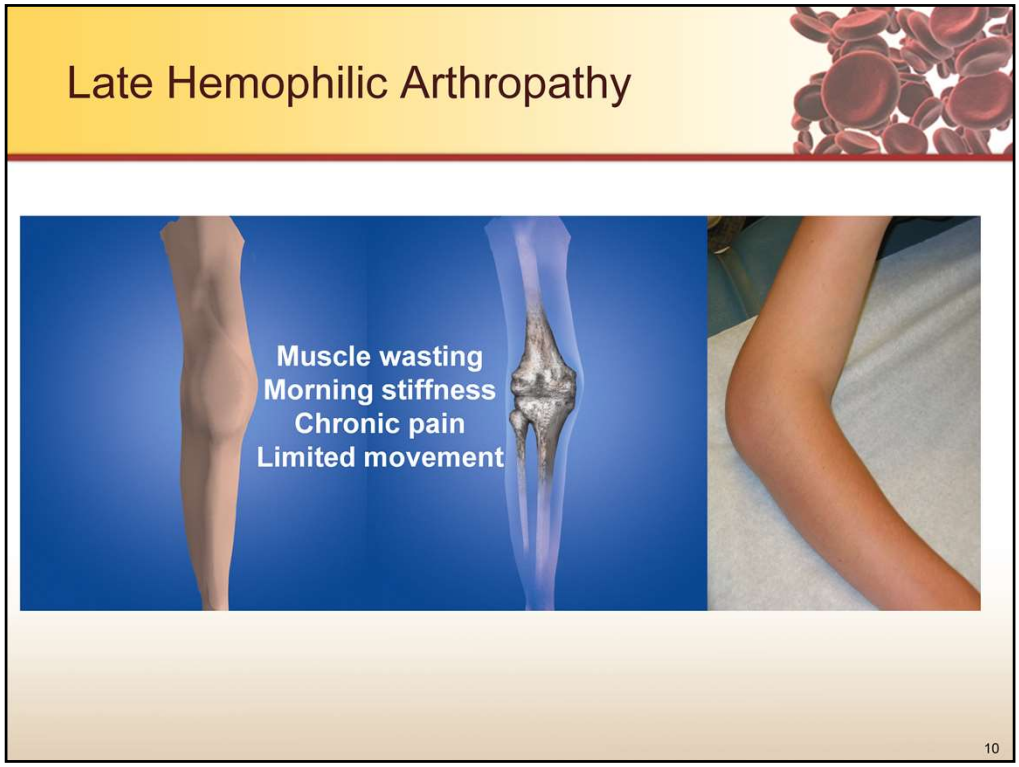
On the right is a picture of a normal knee joint. The femur, tibia and fibula come together to form the knee. The cartilage buffers the interface of these bones, and the joint is surrounded by ligaments and muscles. When blood leaks into the joint it has a small confined space in which it accumulates. Accumulated blood stretches the capsule, which is highly innervated and results in significant pain and reduced range of motion, or R-O-M.

In addition, blood contains substances that cause inflammation. An inflammatory reaction in the joint contributes to acute and chronic pain and development of joint disease. Early signs of hemarthrosis may include compromised motion of the joint and pain or a bubbling sensation. Warmth is inconsistently present and is dependent upon the extent of the hemarthrosis.



In contrast, repeat bleeding within the joints can lead to a condition known as synovitis. This slide depicts a patient with synovitis and the inner structures of the knee joint that represent this condition. Following an intra-articular bleed, the breakdown of erythrocytes results in the deposition of cytoplasmic iron into the synovium, the membrane that lines the joint, and chondrocytes of the articular cartilage.

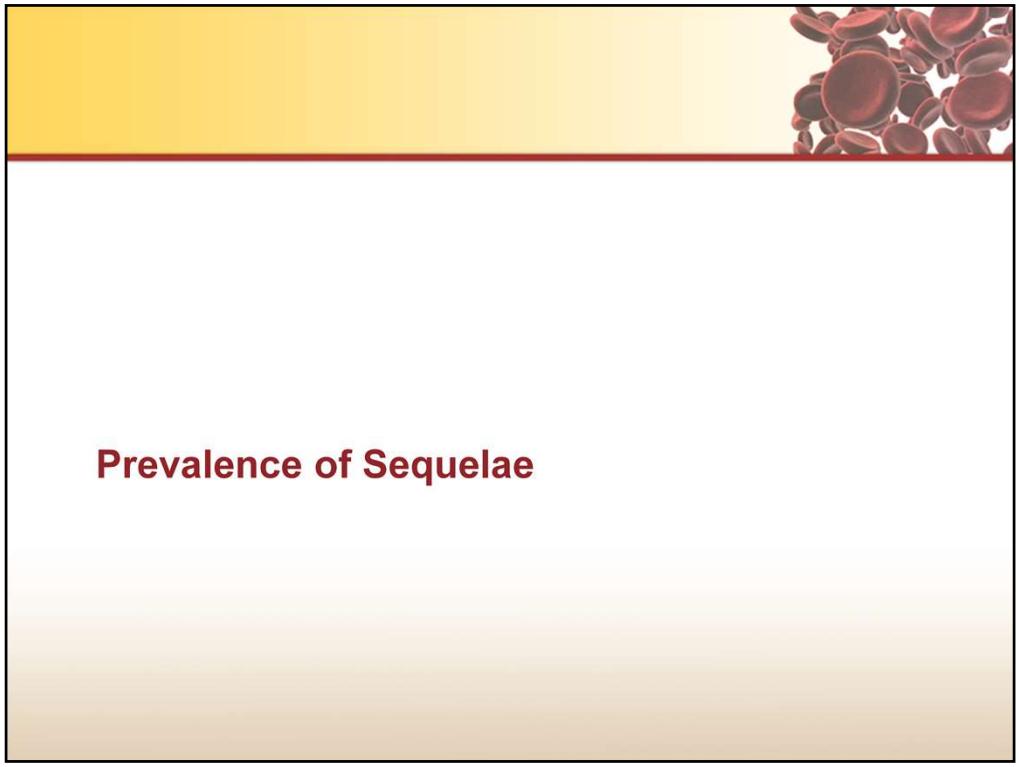
Recurrent intra-articular bleeding triggers inflammation of the synovium, leading to synovial hypertrophy . A hypertrophied synovium is more easily injured and more likely to bleed. This initiates a vicious cycle of bleeding, chronic synovitis and rebleeding. As synovitis develops, the synovium becomes clinically palpable and the joint may remain permanently swollen even in the absence of pain. Inflammation of the synovium ultimately destroys cartilage in bone as it is associated with elevated concentrations of hydrolytic enzymes in the synovial fluid. Pain and arthritis develop.



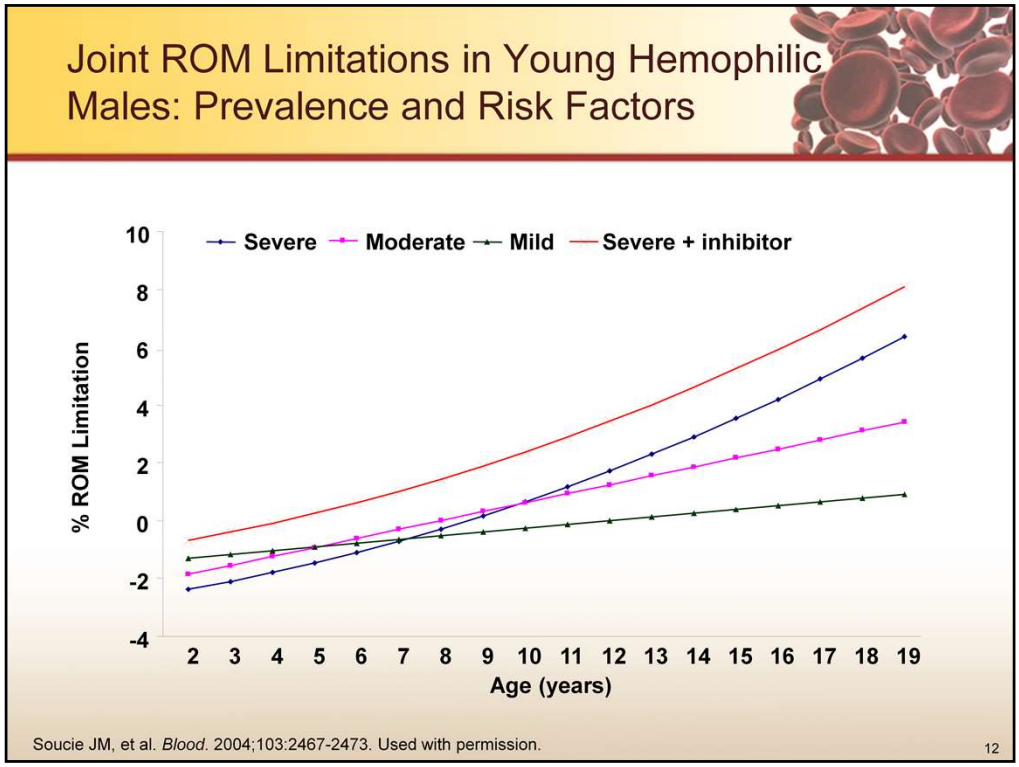
This slide demonstrates a visual representation of late hemophilic arthropathy. The synovitis has resulted in cartilage degeneration, bone erosion, and advanced arthropathy with stiffness, chronic pain, and limited R-O-M. In the most severe cases, bones may fuse, resulting in a completely nonfunctional joint. In addition, muscle wasting occurs. Other associated conditions may include osteopenia, decreased ability to perform activities of daily living, participation in gainful employment, and a decreased quality of life.

Late stage hemophilic arthropathy may require orthopedic surgery to alleviate pain and/or restore function. A variety of orthopedic procedures may be utilized and are dependent upon the desired goal, age of the patient, presence of osteopenia, specific affected joint, and stage of joint disease.

The ability to achieve normal function depends upon a variety of factors, including muscle wasting and contracture, compliance with the prescribed postoperative physical therapy program, and the current capabilities of prosthetic devices. The picture on the right depicts a flexion contracture with limited extension of the elbow.



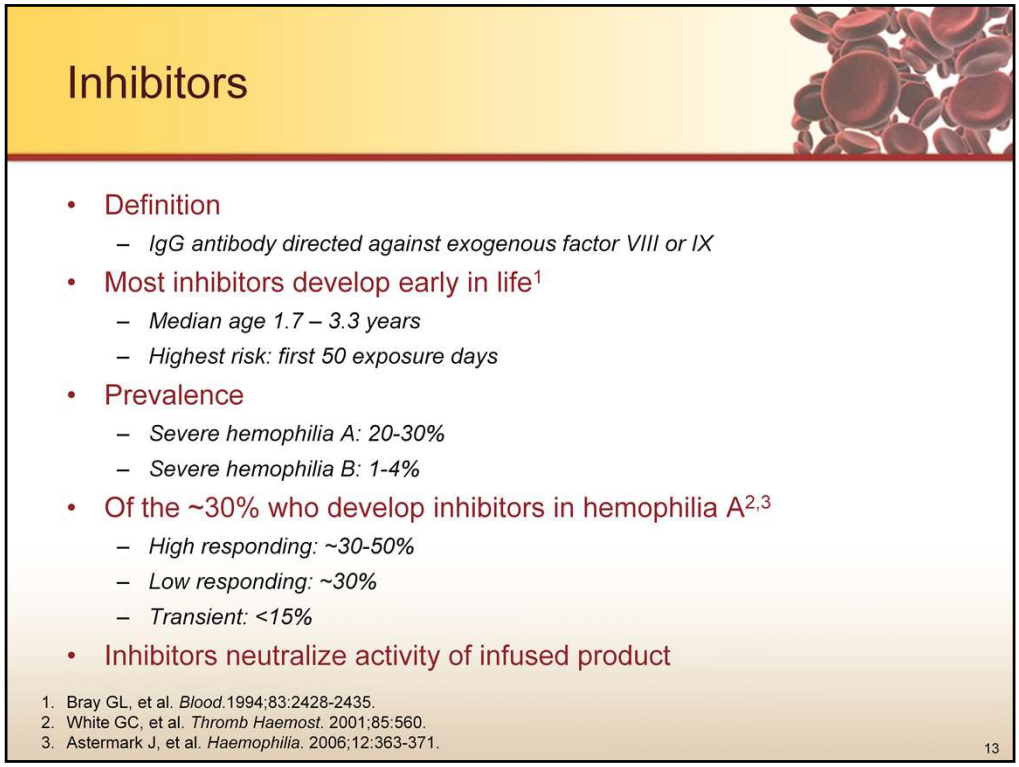
Let us now discuss prevalence of complications, morbidity and mortality associated with hemophilia.



This graph demonstrates R-O-M limitation associated with different levels of severity of hemophilia. The data was obtained from the Centers for Disease Control and Prevention, or C-D-C, through their Universal Data Collection, or UDC, study, and was published in *Blood* by Dr. Soucie and colleagues in 2004. The UDC was conducted through the federally recognized Hemophilia Treatment Center, or H-T-C, Network and collected data on diagnosis, R-O-M, infectious disease screening, and quality of life in individuals affected with bleeding disorders.

The bottom black-colored curve depicts mild hemophilia. Although these patients have infrequent bleeding episodes, as they age they experience some limitation in R-O-M. This limitation becomes more pronounced in patients with moderate deficiency, the fuchsia curve, and even more pronounced in those with severe deficiency, the navy blue curve.

This decreased R-O-M is clearly related to the frequency of bleeding episodes experienced with each level of deficiency. The most limited R-O-M observed in the affected population is that experienced by patients who have inhibitors, the top red line.



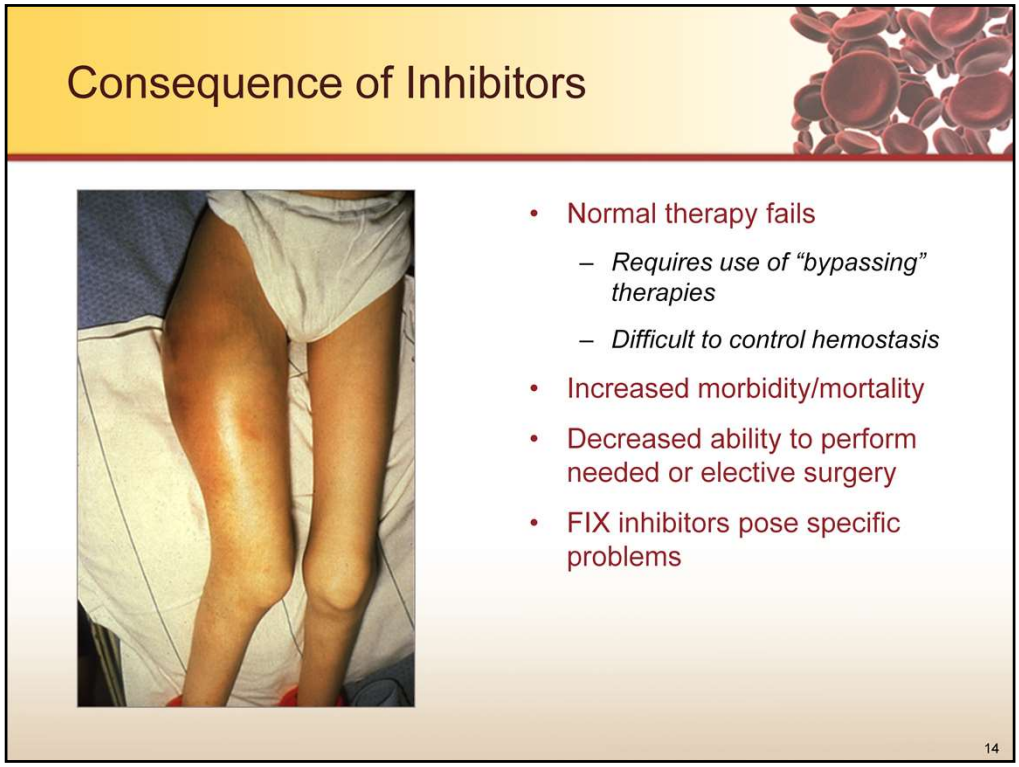
Inhibitors are antibodies that develop after normal exogenous replacement factor exposure, either factor 8 or factor 9. The majority of inhibitory antibodies are I-g-G. Most inhibitors develop early in life with a median patient age of 1.7 to 3 $^{1}/_{3}$ years of age. The highest risk for inhibitor development is within the first 50 exposure days. The median number of exposure days for inhibitor development documented in clinical trials of recombinant products is approximately nine. At 100 days, the risk of inhibitor development is very low, although not nonexistent.

The prevalence of inhibitor development is more common in factor 8 deficiency, or hemophilia A, where it occurs in approximately 20 to 30% of the severely affected population. Inhibitors are uncommon in hemophilia B, even in severe disease, with a prevalence rate of 1 to 4%.

Inhibitors are categorized into three main groups: high responding, low responding, and transient. The level of inhibitors is measured in Bethesda units. Patients with high responding inhibitors, those with greater than or equal to 5 Bethesda units at any time, represent 30 to 50% of those with inhibitors, while low responding inhibitors, less than 5 Bethesda units despite repeated exposure comprise approximately 30%, and transient inhibitors less than 15% of the population.

Regardless of type, an inhibitor can affect therapy and negatively impact outcome. Patients

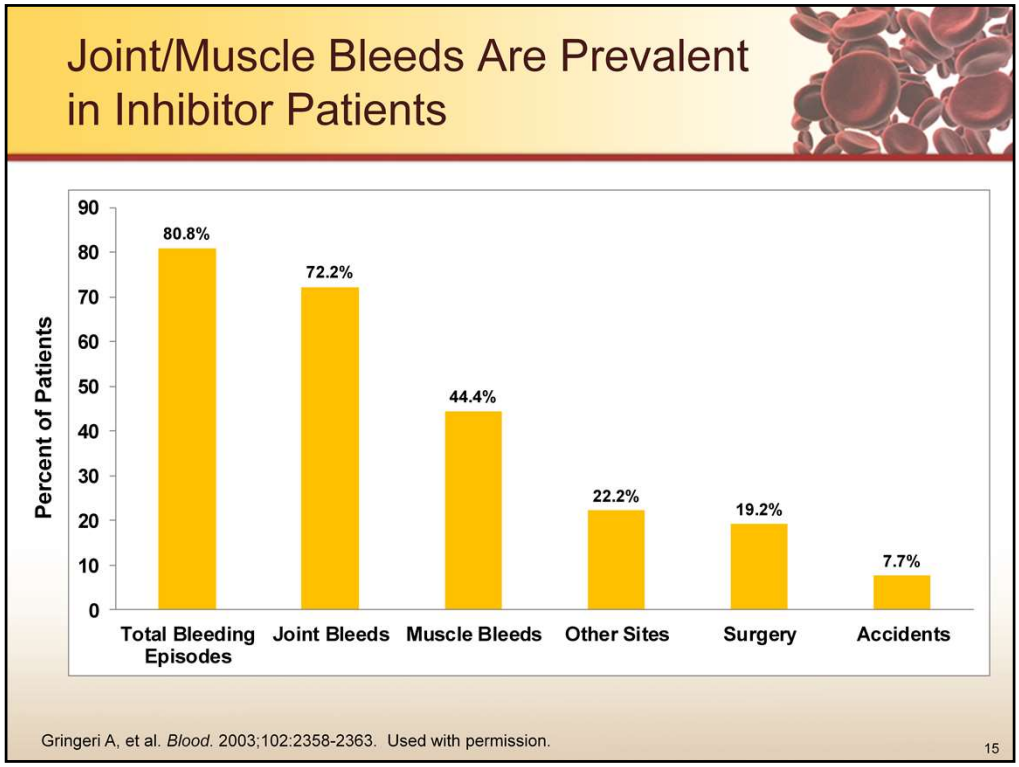
with high responding inhibitors are the most vulnerable population. Inhibitors neutralize the activity of the infused product, making standard replacement therapy often ineffective, and result in difficulty achieving hemostasis. Therefore bleeding episodes in patients with inhibitors are prolonged, and as a result, the morbidity they experience is increased. Alternate hemostatic therapies are often required.



The consequence of inhibitor development is the failure of normal replacement therapy and need for use of alternative hemostatic agents. These alternative agents, called bypassing therapies, often achieve cessation of bleeding. Patients with inhibitors have the highest rate of morbidity and mortality within the hemophilia population. There is a decreased ability to perform needed or elective surgery in these patients because of the difficulty achieving consistent reliable hemostasis.

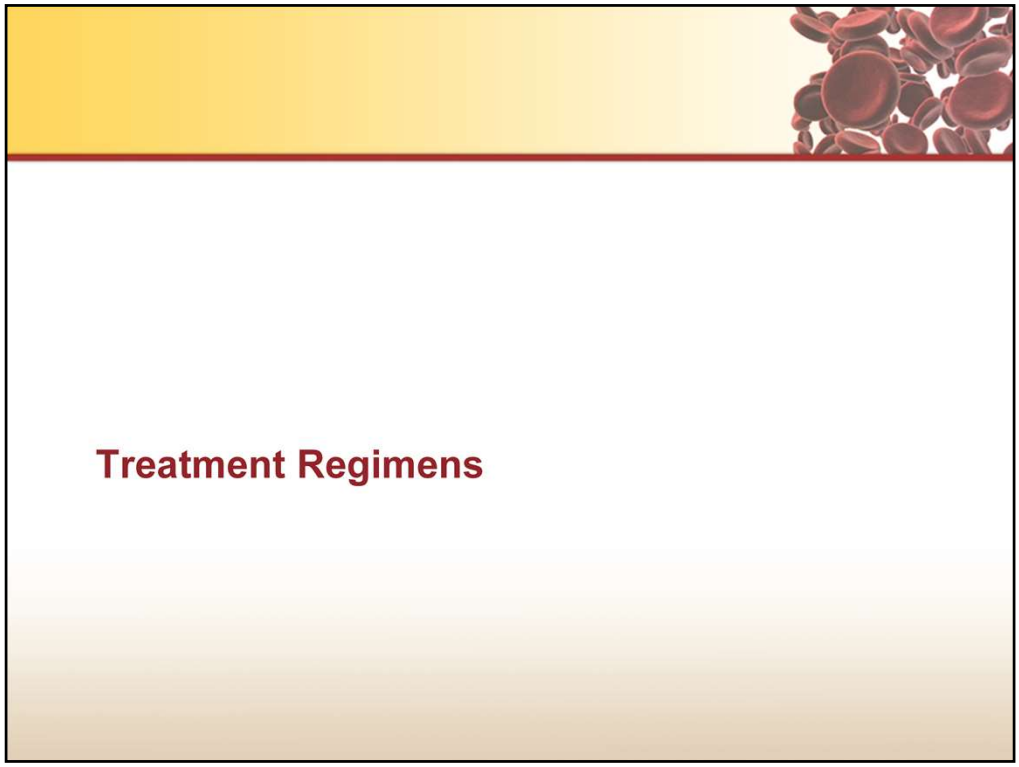
The cost of care for patients with inhibitors is far greater than for hemophilia patients without inhibitors. Patients with inhibitors may require very frequent therapy for months or years, depending upon the regimen utilized. Therapy administered to eradicate the inhibitor is called immune tolerance induction.

Interestingly, although inhibitors in the factor 9 deficient population are far less common as compared to the factor 8 deficient population, they do present specific problems that pose an even greater risk of morbidity. These problems include the development of anaphylactic reactions associated with exposure to factor 9 protein and development of nephrosis with immune tolerance programs utilized to eradicate the inhibitor.

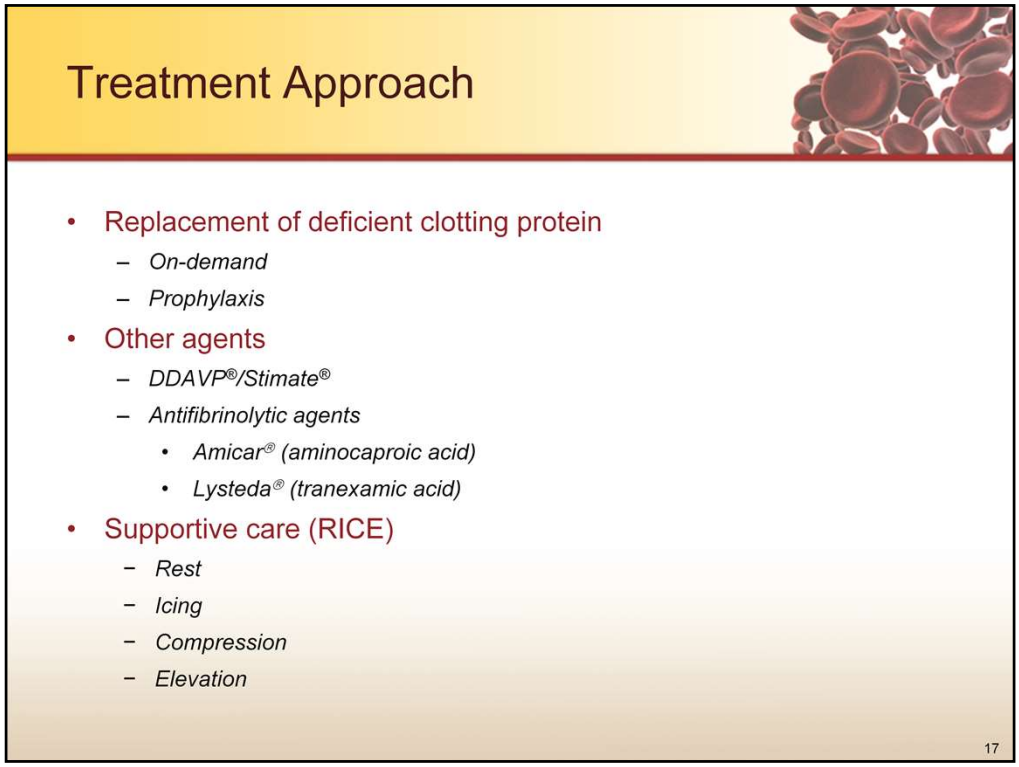


A report from Italy published by Dr. Gringeri et al demonstrated that in patients with inhibitors, the increased frequency of bleeding episodes resulted in increased limitation in joint R-O-M. This was also previously demonstrated in the report from Soucie et al on slide number 12. Dr. Gringeri et al reported that hemarthroses occurred in approximately 75% of inhibitor patients with muscle bleeds, comprising approximately 45% of bleeding episodes.

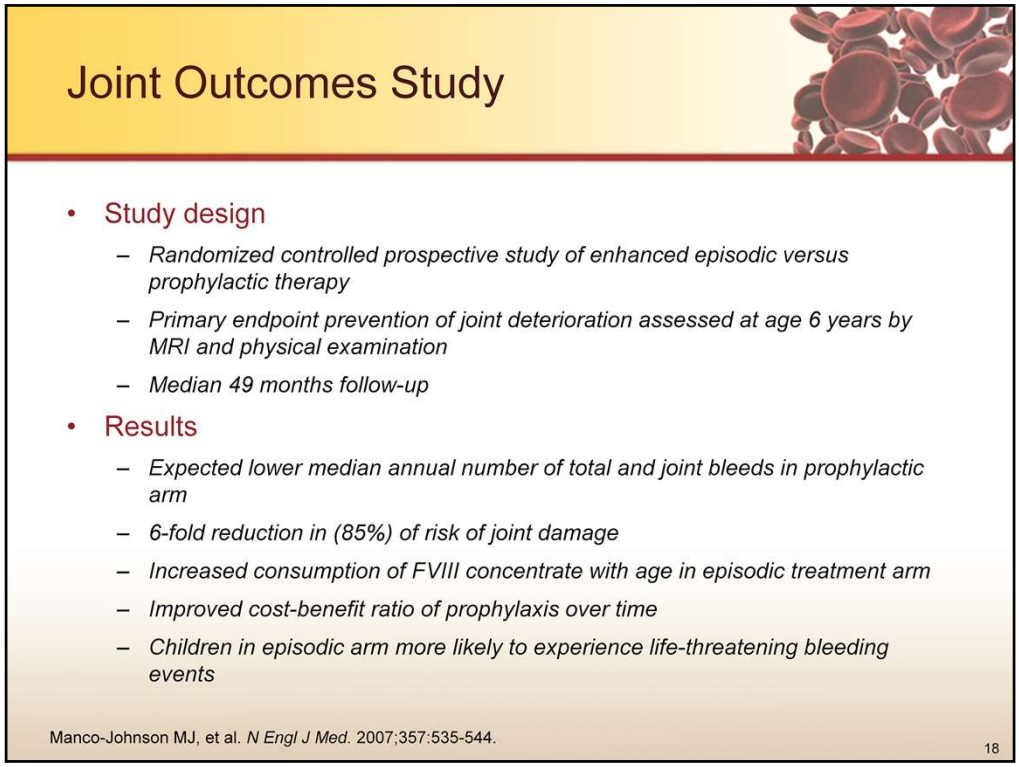
If we look at the distribution of bleeding among patients with inhibitors, the graph shows that 80.8% of patients are going to have bleeding episodes associated with their inhibitor. The vast majority of these are going to be joint bleeds, but there is also significant bleeding into muscles as well as other sites, bleeding associated with surgery, even when trying to optimize their replacement regimen with bypassing agents, and of course bleeding related to accidental trauma.



We are now going to shift our discussion to treatment regimens utilized in patients with hemophilia.



The mainstay of therapy for patients with hemophilia without inhibitors is replacement of the deficient clotting factor protein to a level that will achieve and maintain hemostasis required to either treat or prevent bleeding episodes. The treatment of bleeding episodes once experienced is defined as “on-demand” or “episodic care,” while treatment of patients with infusions to prevent bleeding episodes is defined as prophylaxis. In addition, other agents and supportive care measures are utilized for treatment of hemophilia, including DDAVP® and/or Stimate®. These are utilized in mild factor 8 deficiency and for some forms of von Willebrand disease. Antifibrinolytic agents are useful adjunctive therapies, especially for procedures or bleeding events involving mucus membranes. These agents prevent clot lysis and allow adequate healing to occur. Other supportive measures include the use of RICE, or rest, ice, compression, and elevation, which are commonly utilized for bleeding episodes.

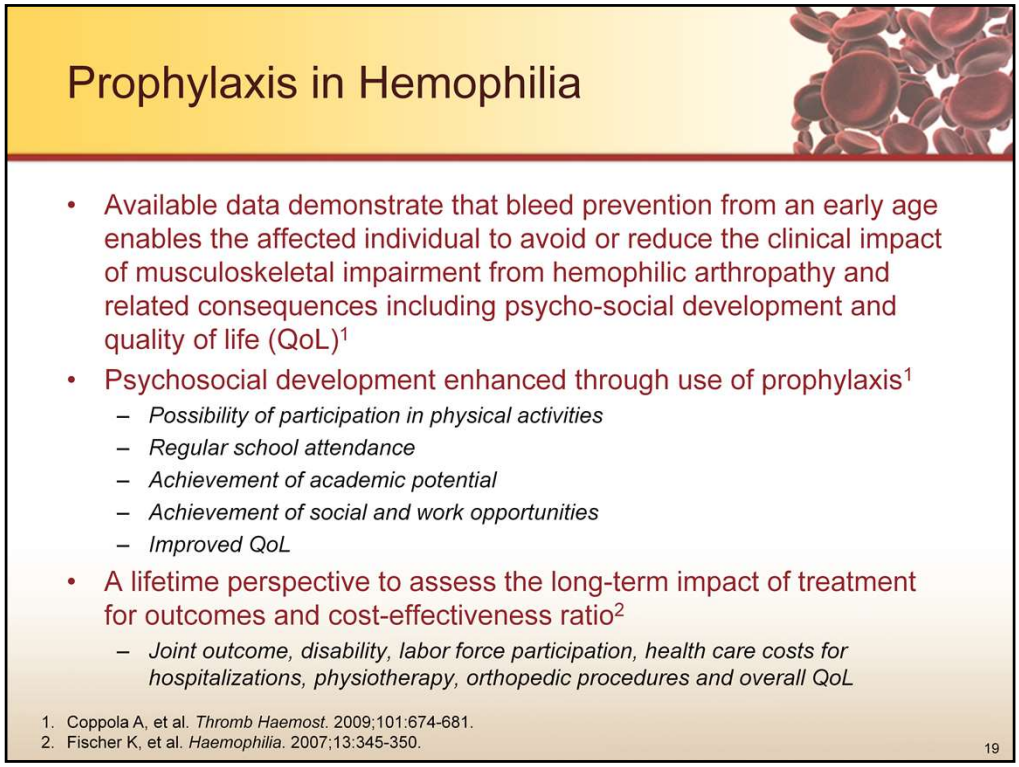


A landmark study published in the *New England Journal of Medicine* in 2007 by Dr. Manco-Johnson et al, called the Joint Outcomes Study, documented the superiority of prophylactic treatment regimens in the prevention of joint disease.

This randomized, controlled, prospective study compared an enhanced on-demand therapeutic regimen to prophylactic infusion therapy. The primary endpoint was prevention of joint disease assessed at age 6 years by MRI and physical examination. The median follow-up was 49 months. Interestingly, the on-demand therapy utilized in this study was more aggressive than that used in common practice, offering patients best care in a randomized protocol with evaluation against prophylaxis.

The results of this study revealed an expected lowered median annual number of total bleeds and hemarthroses in the prophylaxis arm, showing success of prophylaxis therapy in suppression or prevention of bleeding episodes. There was a six-fold reduction, 85%, of risk of joint damage in the prophylaxis arm. Also of interest was the increased consumption of factor 8 concentrate with age observed in the episodic treatment arm. There was an improved cost-benefit ratio of prophylaxis over time.

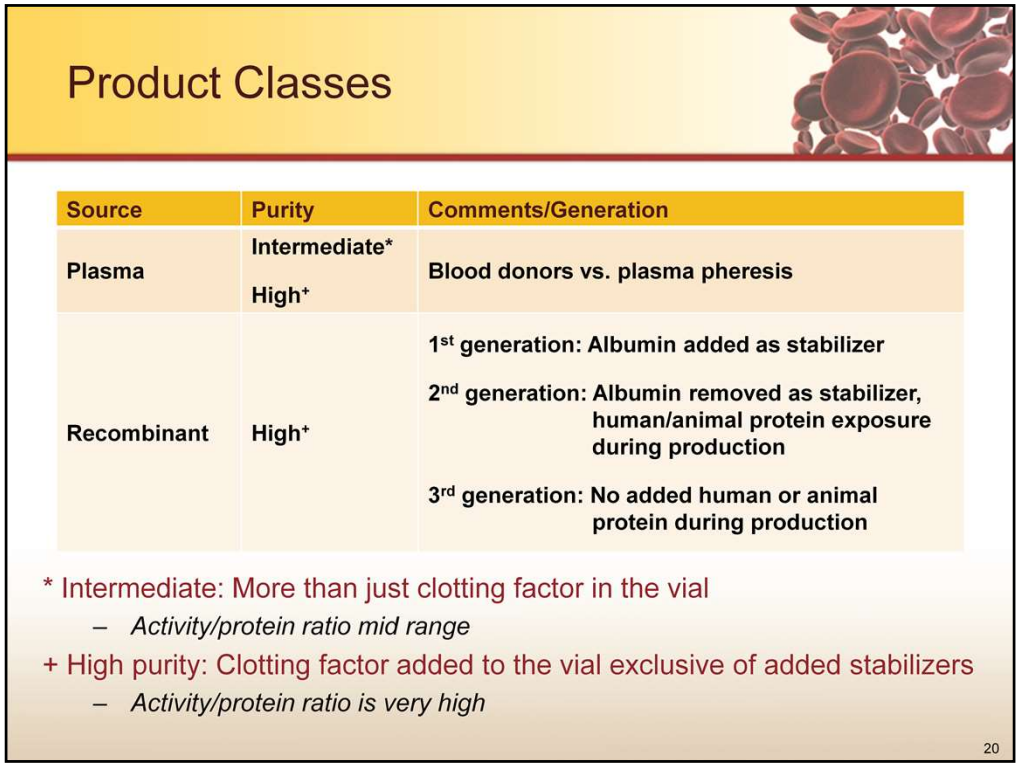
In addition, children in the episodic arm were more likely to experience life-threatening bleeding events, including intracranial hemorrhage, a severe sequelae of hemophilia that was not observed in the prophylaxis arm.



Presently available data demonstrate that bleed prevention from an early age enables the affected individual to avoid or reduce the clinical impact of musculoskeletal impairment from hemophilic arthropathy. In addition, there are associated improvements in related nonphysical bleeding consequences, including improved psychosocial development and quality of life. Psychosocial development is enhanced through the use of prophylaxis by allowing patients to participate in physical activities, improving their general health, their sense of well-being, and their interaction with peers.

Additionally, prophylaxis improves school attendance and decreases absenteeism, allowing patients the opportunity to achieve their academic potential. Patients treated with prophylaxis are more able to actively participate in society and have better employment opportunities throughout their life span. This improves their overall quality of life.

When evaluating prophylaxis, a lifetime perspective is required to assess treatment-related long-term outcomes and cost effectiveness. Joint outcome, disability, labor force participation, health care costs for hospitalization, rehabilitation, physiotherapy, orthopedic interventions and overall quality of life must be considered when assessing the outcomes of hemophilia.



Presently a variety of clotting factor replacement options exist for hemophilia. These replacement options may be divided into two major product categories: plasma-derived, meaning manufactured from blood donors; and recombinant, or manufactured through genetic engineering. It is important to note that these products are not licensed as generic, nor should they be treated as such.

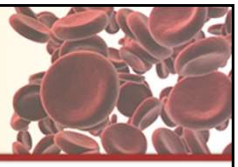
Further product subcategorization for plasma-derived products is based upon purity, including intermediate or high purity, which is dependent upon the number of other plasma proteins present in the concentrate.

Genetically engineered products are further subdivided into three categories: specifically first, second, and third generation, based upon the presence of albumin as a stabilizer in first generation, or exposure to a human or animal protein in the manufacturing process in second generation products. Third generation recombinant products are those where there is no added human or animal protein, either in the manufacturing process or in the final product.

It is important to note that product choice for each patient is a crucial decision for both care providers and patients. The hemophilia population was affected during the late 1970s through the 1980s with a variety of viral blood-borne infections, including hepatitis B and C, and HIV. Therefore the risks and benefits for each product should be carefully discussed and

weighed before a product is chosen.

Treating Hemophilia is Complex and Requires Expertise and Judgment



Site of Bleeding	Typical Target FVIII Range	Typical Duration of Replacement Therapy (days)
Joint: 60% of bleeding episodes	30-50%	1-2
Muscle: 30% of bleeding episodes	30-50%	1-2
Gastrointestinal tract	40-60%	7-10
Oral mucosa	30-50%	Until bleed cessation
Epistaxis	30-50%	Until bleed cessation
Hematuria	30-100%	Until bleed cessation
CNS	60-100%	7-10
Retroperitoneal	50-100%	7-10
Trauma or Surgery	50-100%	Until healed

CNS=central nervous system.
From World Health Organization. Delivery of Treatment for Haemophilia. 2002. Used with permission.

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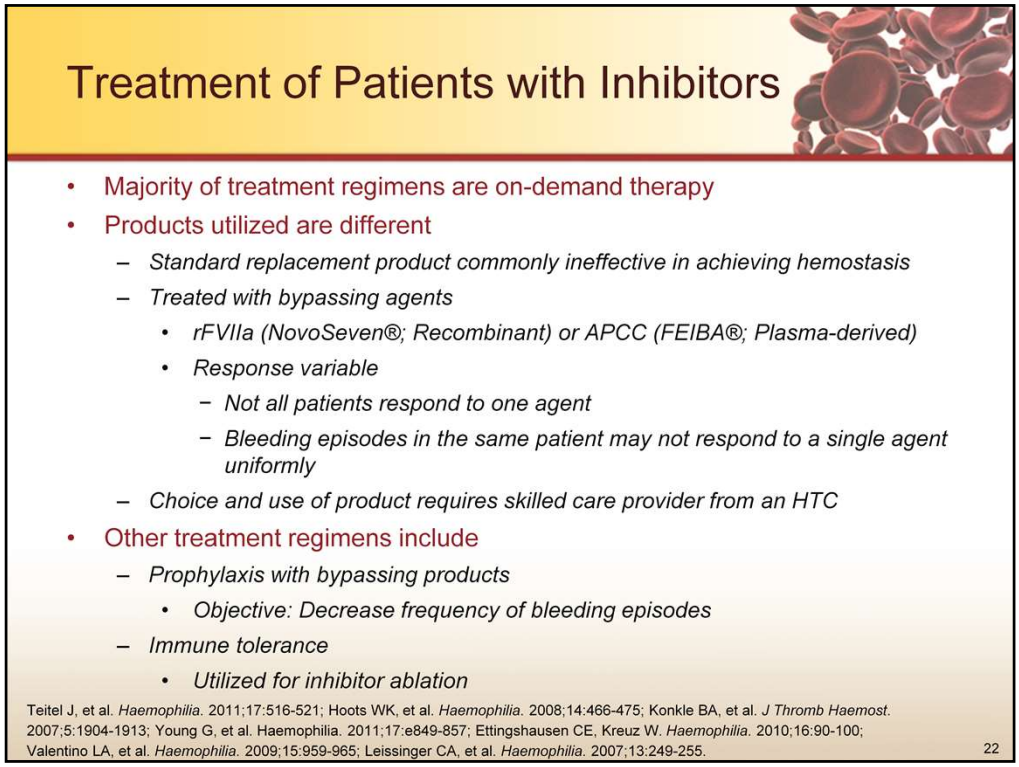
The treatment of hemophilia is complex and requires an expert with experience in these disorders. This slide demonstrates general guidelines published from the World Health Organization, or WHO, for the treatment of hemophilia.

Although these represent good initial general guidelines, the treatment of a specific bleeding episode requires knowledge of the patient's therapeutic response, their individual pharmacokinetics, their inhibitor status, and the severity of the bleed to determine the appropriate target hemostatic level and duration of therapy.



Bleeding episodes in patients with inhibitors are difficult to treat and treatment products and regimens are different, as compared to those patients without inhibitors. The primary mode of treatment utilized in patients with inhibitors is on-demand therapy. The products utilized are termed bypassing agents, with the two presently available products including recombinant activated factor 7-a, or NovoSeven®, and activated prothrombin complex concentrate, A-P-C-C or FEIBA®, which is a plasma-derived product.

Bypassing therapies achieve hemostasis through an alternate route. Although largely effective, the predictability of response is not equal to standard replacement therapy utilized in patients without inhibitors. Not all patients respond reliably to either of the bypassing agents, and therefore it is important to recognize that individual patient response is variable for each product and each bleeding episode.

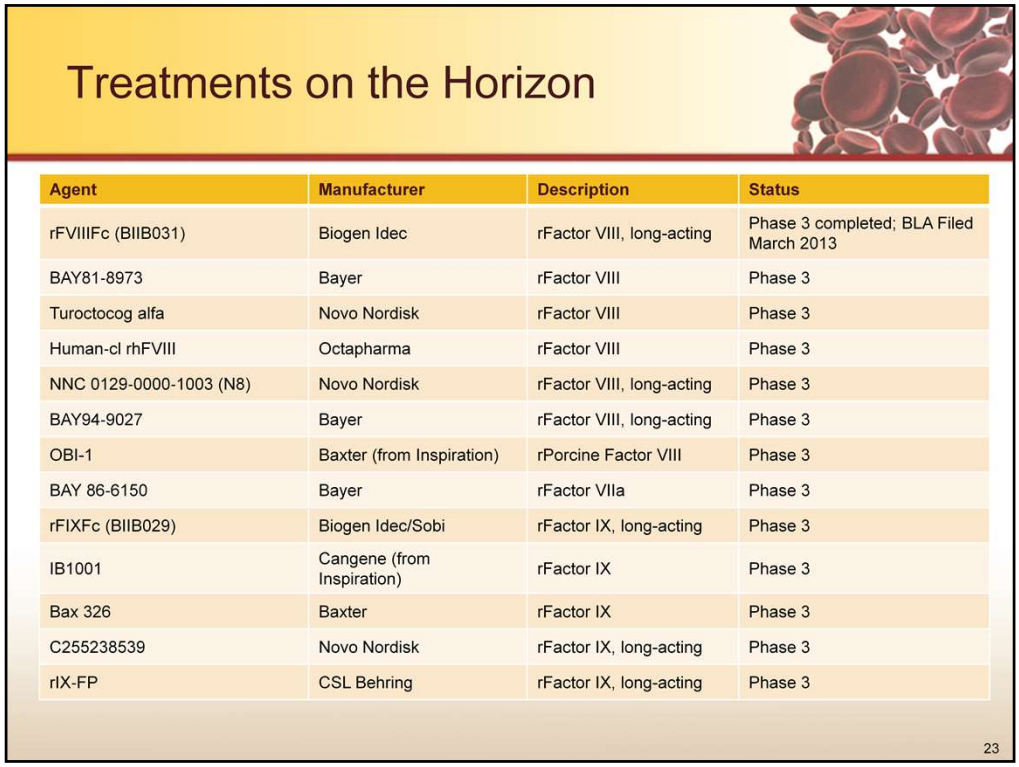
Bleeding episodes in the same patient may not respond to one specific agent uniformly. Choice in the use of bypassing products is required and treatment of bleeding events in inhibitor patients necessitates the expertise of skilled H-T-C care providers.

Prophylaxis in inhibitor patients has been performed with bypassing products and has some demonstrated success in suppression of bleeding events. There have been some recently published reports for both recombinant FVIIa and FEIBA® with prophylaxis, and recombinant FVIIa has been shown in a prospective, randomized study to decrease the

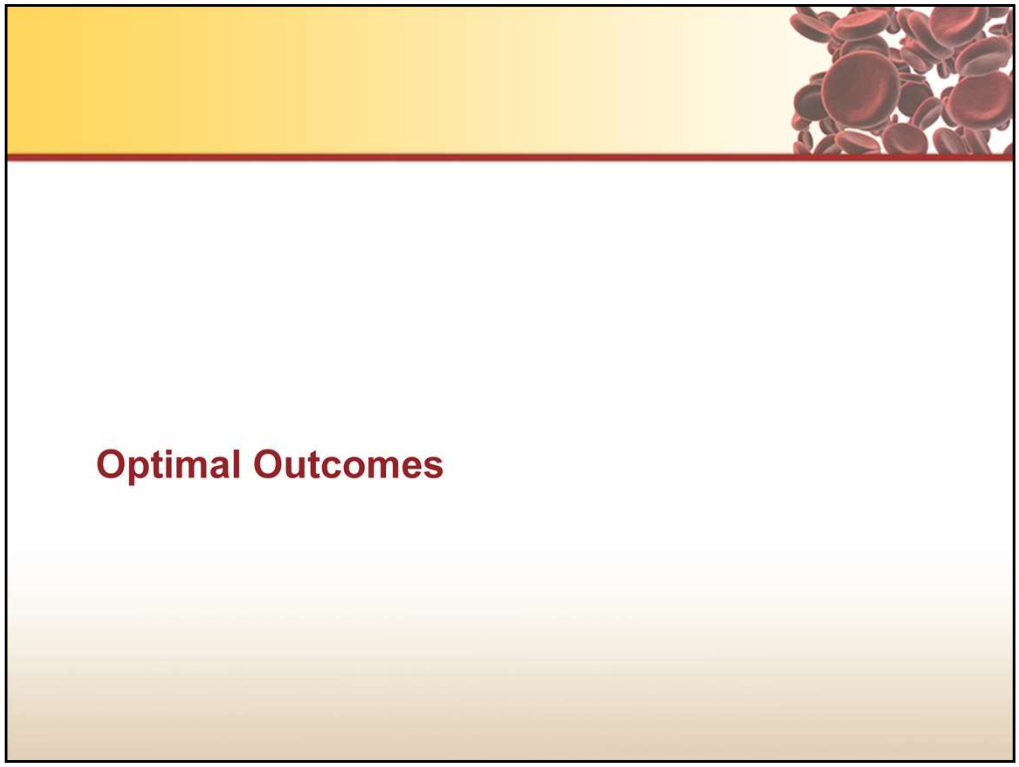
frequency of bleeding episodes experienced by inhibitor patients. It can decrease the frequency of bleeding episodes; improve quality of life measures, so there's an increasing application of prophylactic strategies.

In addition, other inhibitor treatment modalities include methods to attempt to eradicate the inhibitor, termed immune tolerance induction regimens, where patients are given high doses of factor 8 or factor 9 over long periods of time, ultimately to have the inhibitor ablated. This can take anywhere from several months to years to achieve and is reasonably successful in about two-thirds to three-quarters of patients. Immune tolerance protocols may be difficult to manage and require significant consumption of expensive medical resources.

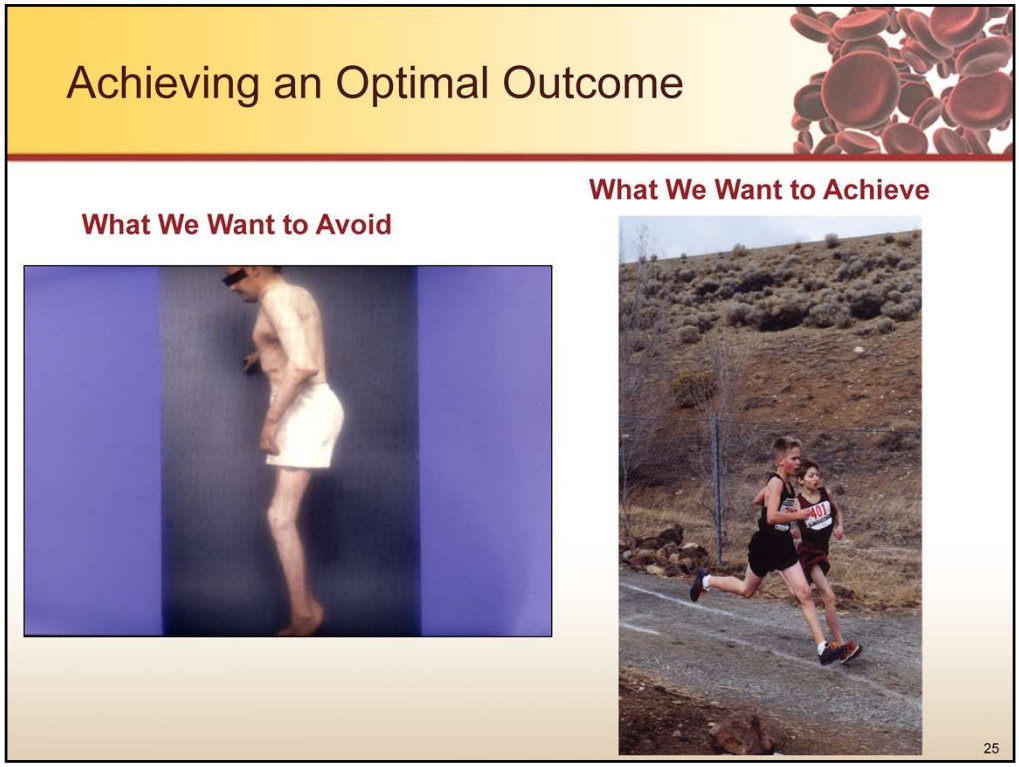
Importantly, if the inhibitor is eradicated, the patient may then be able to utilize standard replacement therapy. These standard replacement therapies are easier to administer and achieve more reliable hemostasis as compared to bypassing products, making immune tolerance induction an important therapeutic option.



The past few years have witnessed the development of many new factor replacement products for the treatment of hemophilia, including bypassing products for inhibitor patients. Some of these new products currently in clinical trials also include modified proteins that result in a more prolonged half-life and will allow decreased infusion frequency to administer prophylaxis. It is hoped that these initial products in this new category will be licensed in 2013. This slide depicts a listing of many of these new products in clinical trials. Many of these products have already gone through Phase 3 and some have been submitted for biological license application. It will require some skill and oversight in how to apply these in the proper settings within our patient population.

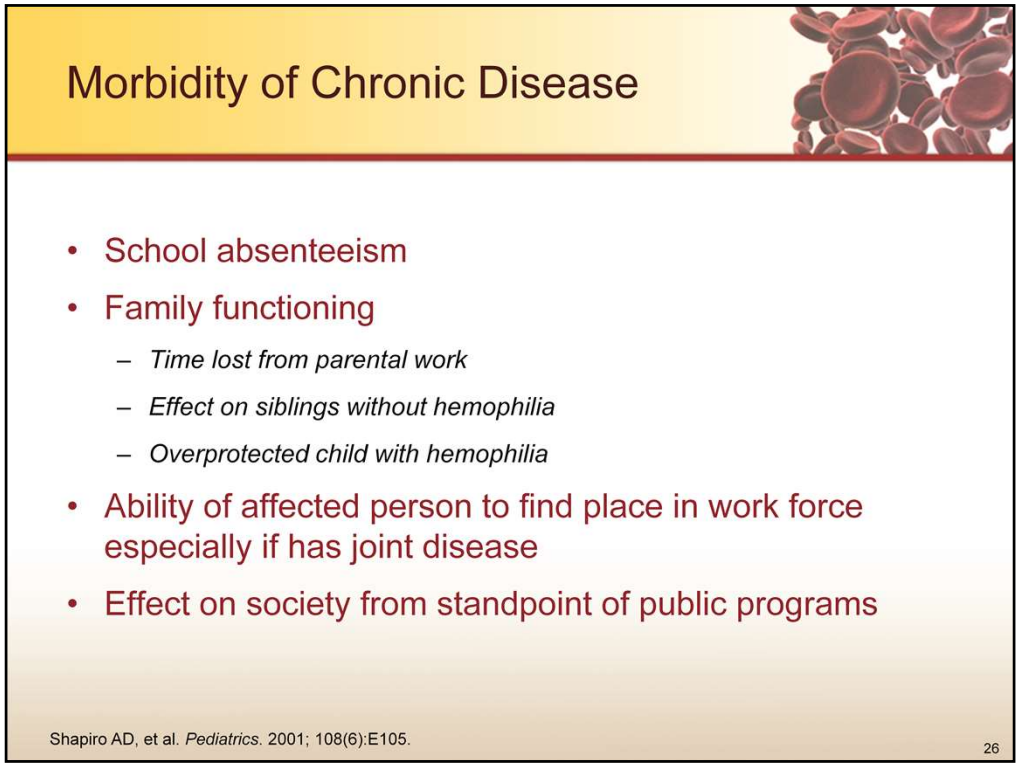


We are now going to briefly review optimal outcomes and how to achieve these in hemophilia.



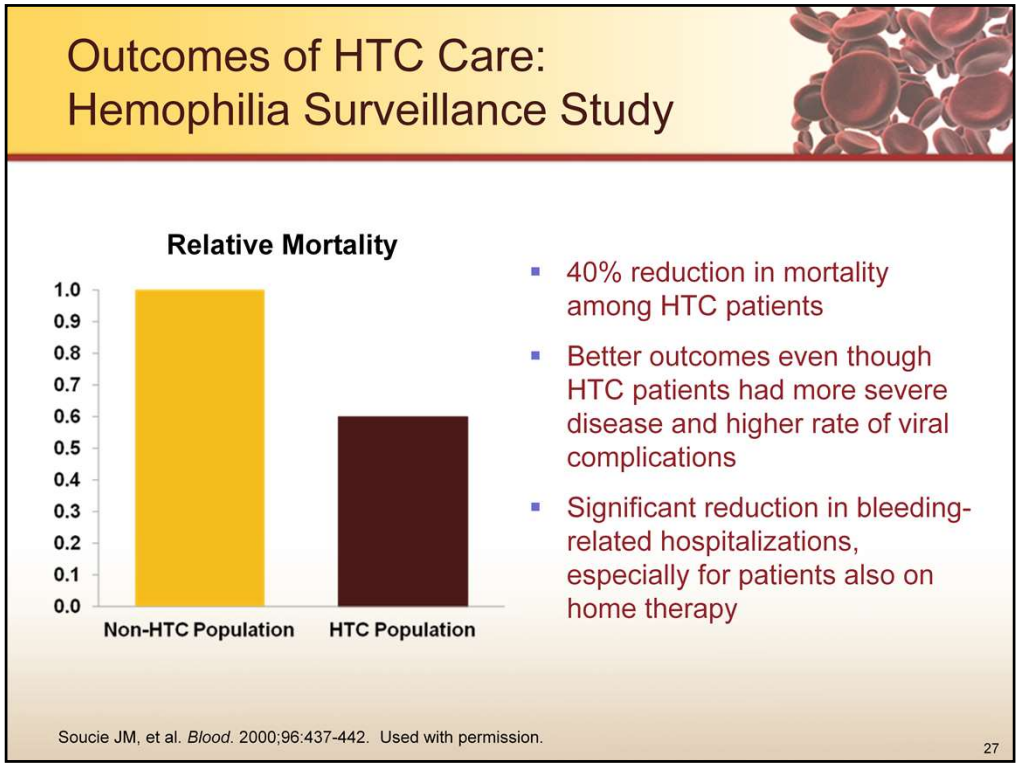
This slide depicts two individuals affected with severe hemophilia A. The gentleman on the left is older and was treated with on-demand therapy. The result of repeated bleeding episodes is advanced arthropathy of the shoulders, elbows, wrists, hips, knees and ankles. This greatly interferes with normal daily activities and likely employment and overall quality of life. This outcome is what we now strive to avoid.

On the right you see a patient with severe hemophilia running next to an unaffected individual. This child was treated with prophylaxis since an early age, and has a normal musculoskeletal examination. This young man participates in sports and represents what we want to now strive to achieve.



Beyond the musculoskeletal complications of hemophilia, there exist other important morbidities of chronic disease that must be considered to achieve an optimal outcome. School absenteeism can be a significant problem in chronic diseases and impacts an individual's ability to achieve their scholastic potential. Family functioning can also be affected. Parents of children with chronic disease are at increased risk of loss of time from work. In addition, unaffected siblings may have their psychosocial functioning impacted. Children with hemophilia are at risk of being over-protected with resultant impact on independence and psychosocial functioning.

Ultimately the ability of a person with hemophilia with significant joint disease to find their place in the work force is diminished. Therefore the societal total effect must be considered and include individual productivity, the use of public programs, and the ability to become an active, functioning member of the work force. It is in the best interest of the individual and society to have patients who are most able to achieve optimal individual outcomes.



As of May 2013, H-T-Cs represented a network of 144 comprehensive care centers in the United States. They are federally funded through the Department of Health and Human Services and/or Centers for Disease Control. The majority of patients affected by hemophilia in the United States receive their care through an H-T-C. This graph depicts important data published by Dr. Soucie and colleagues in *Blood* in 2000, and clearly demonstrates the impact of the H-T-C Network on outcomes.

These data are from a study conducted by a C-D-C project entitled the Hemophilia Surveillance Study that included six states and involved the C-D-C, state health departments, and the H-T-C in each respective state. Detailed case findings were performed throughout each state to identify all affected patients with hemophilia, including those treated outside of the H-T-C Network.

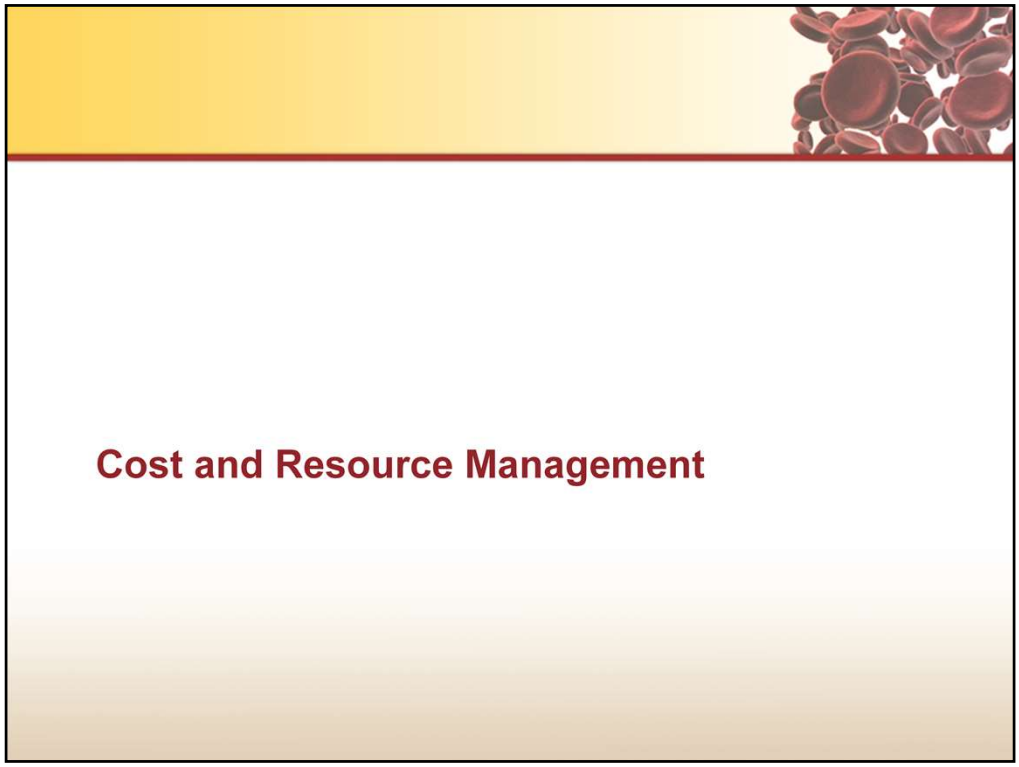
The study identified and followed 2,950 people affected with hemophilia for an average period of 2.6 years. Of those in the study, 79% had hemophilia A and 42% had severe disease. Included in the group were individuals with inhibitors and comorbidities that included HIV, hepatitis C, and severe liver disease.

Outcomes over time were documented, including the use of product, hospitalization, morbidity and mortality. Importantly, the patient population treated within an H-T-C represented a more severe population with a higher percentage of severely deficient patients, those with inhibitors, H-I-V, AIDS and liver disease. Despite having a more severely affected population as compared to patients treated outside of the H-T-C Network, there was a documented 40% reduction in mortality among H-T-C patients. There was also a significant reduction in bleeding-related hospitalizations, and an increased number of

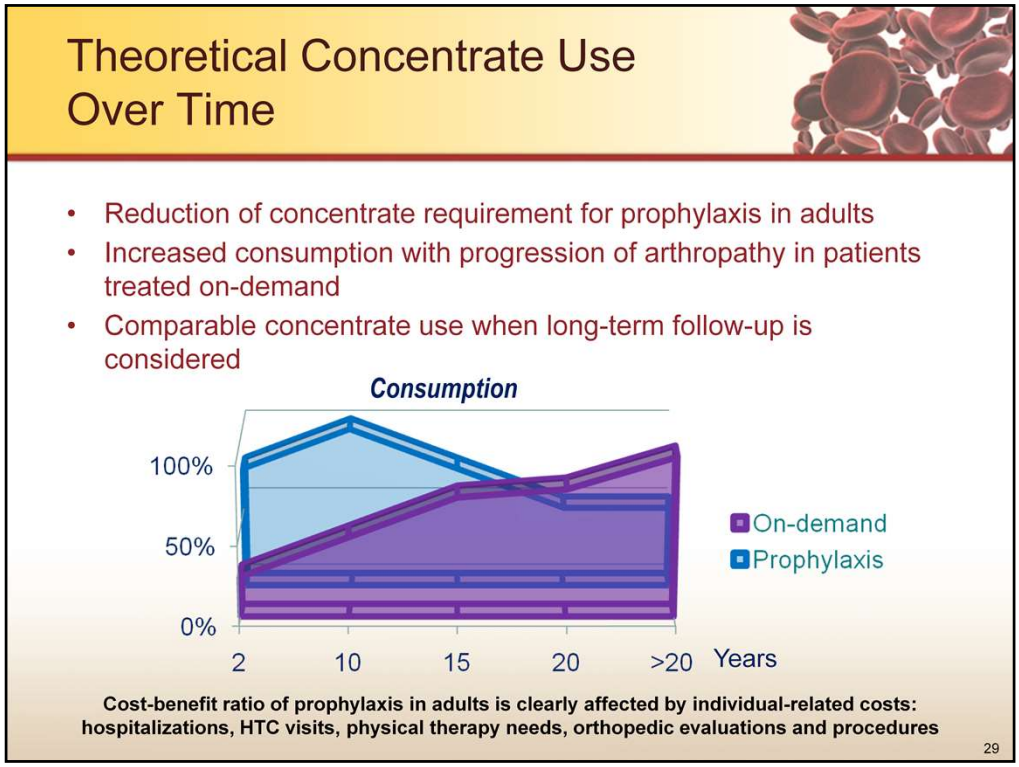
patients on home therapies in those patients cared for within the H-T-C Network.

These findings are quite significant and clearly demonstrate the important impact of comprehensive care provided by H-T-Cs. There are several documented explanations for why care provided through the H-T-C Network is more comprehensive and cost effective. One is the expertise of the hematologists within the H-T-C Network.

Another is the broad range of services available through the H-T-C, including but not limited to clinical management, orthopedic and dental care, and patient education, training and counseling. H-T-Cs also have the capability to measure clotting factor activities in real time through on-site coagulation laboratory facilities. In addition, H-T-Cs are associated with blood banks and/or pharmacies to provide the full range of factor concentrates required by the population served. Other sites of care typically do not provide this range of services.



Cost and resource utilization are important in all medical conditions. Hemophilia is a costly disorder and is one of the most expensive chronic conditions affecting the US population on a per patient basis. We now turn our discussion towards issues of cost and resource utilization.



Shown here is a theoretical factor concentrate use curve over time for both on-demand and prophylactic treatment regimens. The data depicted is not based on a particular patient or group of patients and is theoretical in nature. A variety of important points are illustrated by this graph.

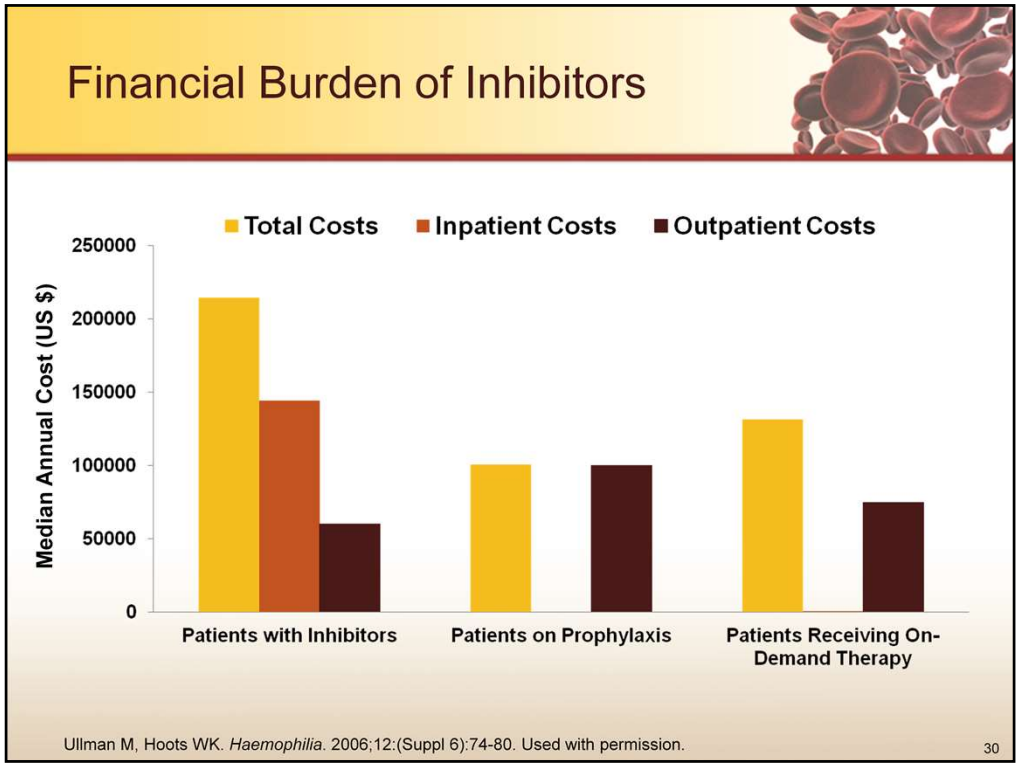
Patients treated with an on-demand regimen are likely to utilize less factor concentrate in the early stages of treatment as compared to those treated with prophylaxis. This is due to the infrequency of bleeding events experienced and the patient's age and weight.

As on-demand patients develop increased frequency of bleeding events, their joint pathology progresses, and their use of replacement therapy accelerates. By the time patients treated with on-demand regimens reach adulthood, their factor consumption peaks, and they have the clinical sequelae of repeated bleeding events.

Prophylactic regimens clearly utilize more medical resource and result in increased cost early on. With prophylaxis there is a significant investment up front to prevent bleeding episodes and achieve optimal musculoskeletal and other associated outcomes. Patients who reach the adult years with healthy joints and musculature often experience a decreased rate of bleeding and need for replacement therapy even when they change from a prophylactic to an on-demand regimen. Therefore in the long run, prophylactic regimens may be more cost effective compared to on-demand regimens by virtue of decreased joint

disease, increased productivity, and decreased consumption of clotting factor concentrate for recurrent bleeding events and orthopedic interventions.

Comparing these two treatment methods, it can be shown that over the patient's lifetime, the best therapy is prophylaxis, the more intensive therapy utilized early on to achieve optimal outcome. On-demand therapy, although more cost effective in the early years, results in increased musculoskeletal damage and increased use of medical economic resources over time.

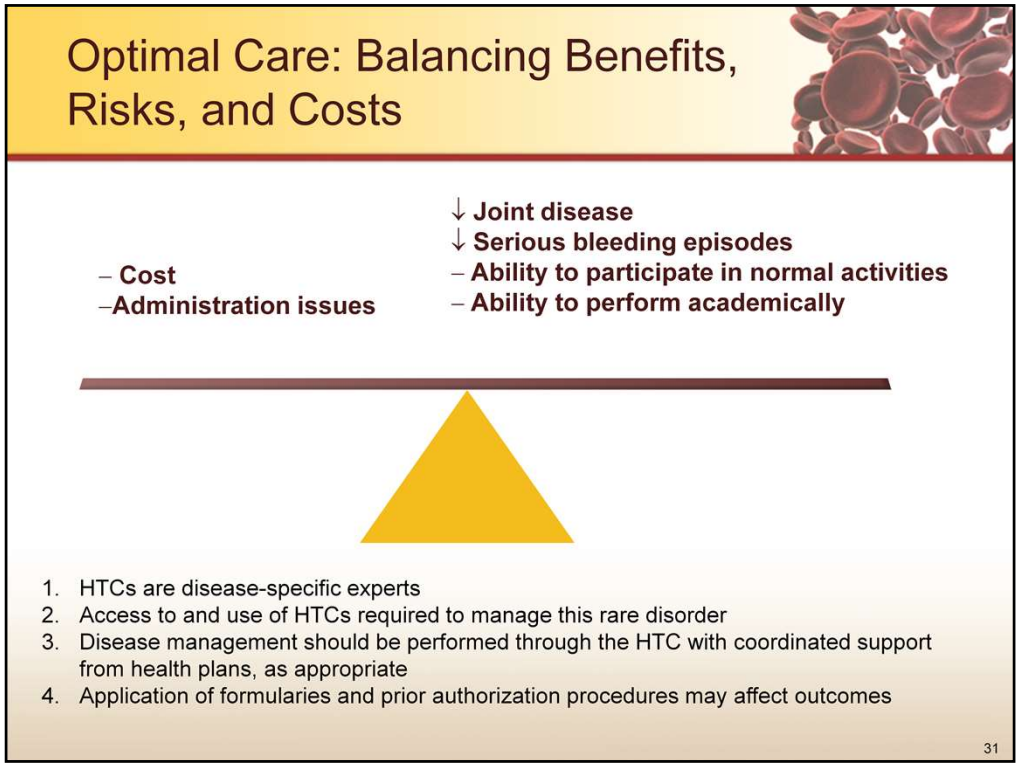


It is important to emphasize the financial burden associated with the development of inhibitors in hemophilia. Patients with inhibitors commonly represent cost outliers for both H-T-Cs and patients' insurers.

This graph shows an estimate of median annual cost. On the right side of the graph are patients treated on-demand and the yellow bar shows the overall total cost of caring for that patient. A significant proportion of it is the outpatient cost, shown in brown, which is really the cost of clotting factor. However, there is still some incremental cost because patients treated on-demand are going to accumulate joint disease and other pathologies that are going to tax the overall cost of care.

In the middle are patients who have utilized prophylaxis from early in childhood into adulthood. We can see that their total costs of care are really equal to their outpatient cost, so that the total cost to manage them is simply providing the factor and enabling prophylaxis.

Finally, if we look at the impact of inhibitors, we can see that inhibitors do incur more overall cost and tend to have to have more inpatient cost as well. Since the majority of patients often are not on prophylaxis, their outpatient management may actually be proportionally less.



In summary, achieving optimal care in outcomes for the hemophilia patient population requires a balance with careful weighing of benefits, risks, and costs. The cost of care for hemophilia is significant. H-T-Cs can and do decrease the cost of care and help achieve individual optimal outcomes. Prophylaxis decreases joint disease and serious bleeding episodes and yields an increased ability to participate in normal activities and to perform academically. Therefore prophylaxis may reduce the long-term cost of care while improve quality of life.

H-T-Cs have been proven to be the disease-specific expert in the management of this uncommon condition. Access to and use of an H-T-C is required to manage this rare disorder. Disease management should only be performed through the H-T-C with the coordinated support from health plans, as needed. The use of restricted formularies and pharmacy benefit managers, prior authorizations for every dispensation affect outcome and negatively impact care.