

# The Evolving Hemophilia Managed Care and Specialty Pharmacy Environment:

## Recommendations for a New Health Care Ecosystem



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# Agenda



- 2:05 PM – 2:30 PM      The Evolving Managed Care and Specialty Pharmacy Landscape  
*Vanita K. Pindolia, PharmD, BCPS*
- 2:30 PM – 3:00 PM      An Advanced Review of Inhibitors and Prophylaxis Treatment  
*Michael Tarantino, MD*
- 3:00 PM – 3:15 PM      Moderated Faculty Panel Discussion
- 3:15 PM – 3:50 PM      Measuring Success: Tools and Resources to Document Outcomes  
of Payer and Specialty Pharmacy Hemophilia Management  
*Edmund Pezalla, MD*  
*Michael Zeglinski, RPh*
- 3:50 PM – 4:30 PM      HTC, Managed Care, and Specialty Pharmacy Collaboration  
(Case-Based Presentations)
- 4:30 PM – 4:55 PM      Moderated Faculty Panel Discussion and Audience Q&A
- 4:55 PM – 5:00 PM      Key Takeaways and Closing Comments

# Educational Objectives



*After completing this activity, the participant should be better able to:*

- Describe current and evolving strategies used by managed care organizations (MCOs) and specialty pharmacy providers to facilitate high quality care for members with hemophilia
- Summarize the most recent clinical recommendations for the treatment of patients with hemophilia, including prophylactic factor replacement
- Explain the severe complication of hemophilia treatment known as inhibitor development and its significant clinical and economic consequences
- Identify processes for MCOs and specialty pharmacy providers to improve communications with HTC
- Apply collaborative methods that enable the benefits of the comprehensive care model provided by HTCs to be realized by multiple hemophilia stakeholders including MCOs and specialty pharmacy providers
- Provide accurate and appropriate counsel as part of the managed care treatment team

# The Evolving Hemophilia Managed Care and Specialty Pharmacy Environment:

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# The Evolving Managed Care and Specialty Pharmacy Landscape

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Henry Ford Health System/Health Alliance Plan of Michigan

# Faculty Disclosure



- The ***faculty*** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

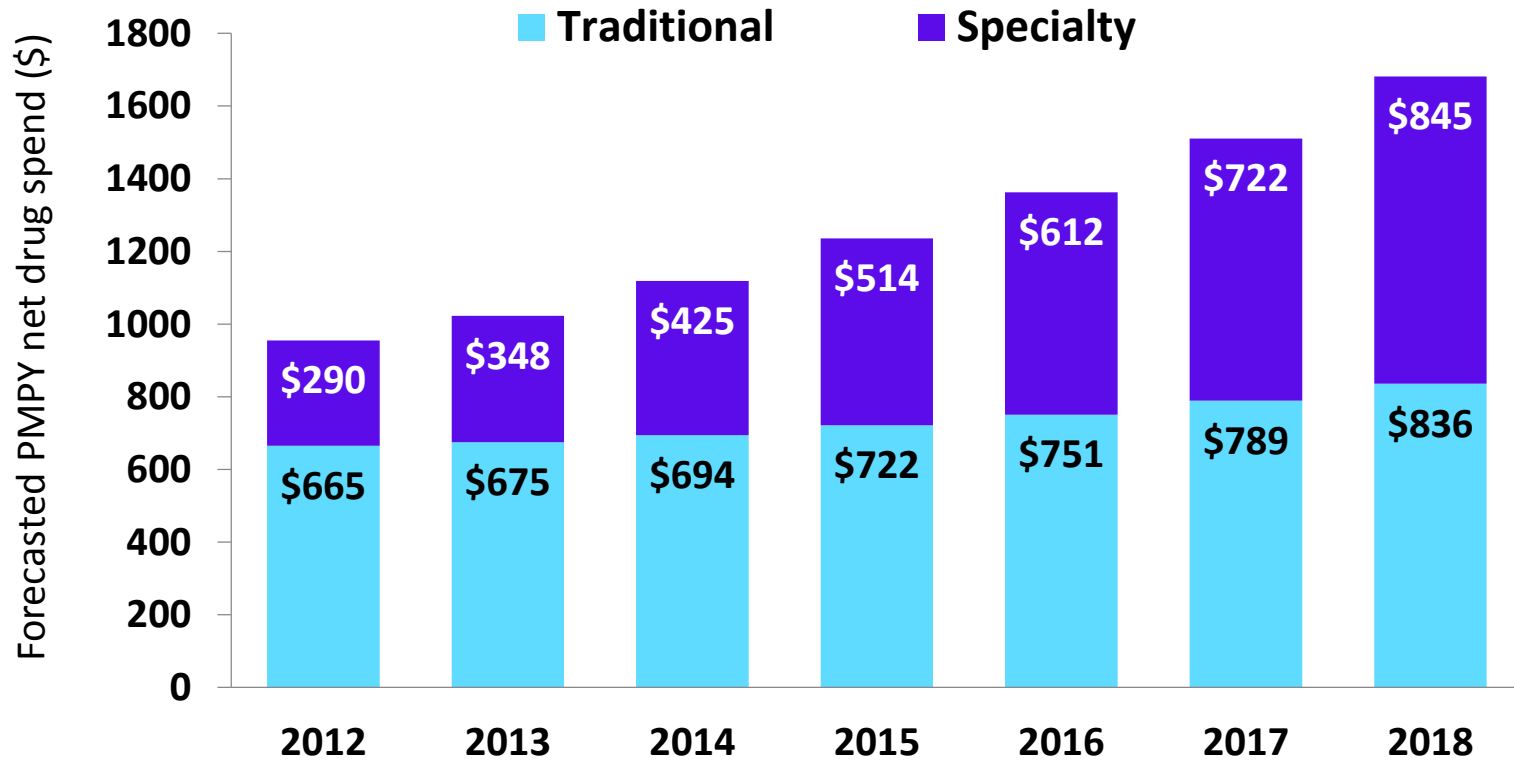
## **Vanita K. Pindolia, PharmD, BCPS**

- No financial interests/relationships relating to the topic of this activity

# Pharmacy Spending on Specialty Drugs Expected to Grow



## Spending on Specialty Drugs Projected to Surpass Sales of Traditional Agents by 2018



PMPY=per member per year

# Key Drivers of Specialty Trend



## High Cost Per Patient

Accounts for 25% of pharmaceutical spending in the US

Annual growth at 15-20%

Annual drug cost ranges from \$15,000-\$250,000+ per patient

Manufacturer price increases for existing drugs

Limited generics available as products mature:

- First wave of non-biologic specialty drugs losing patent protection
- Biosimilars for biologic specialty drugs

## Increasing Utilization

Flourishing pipeline

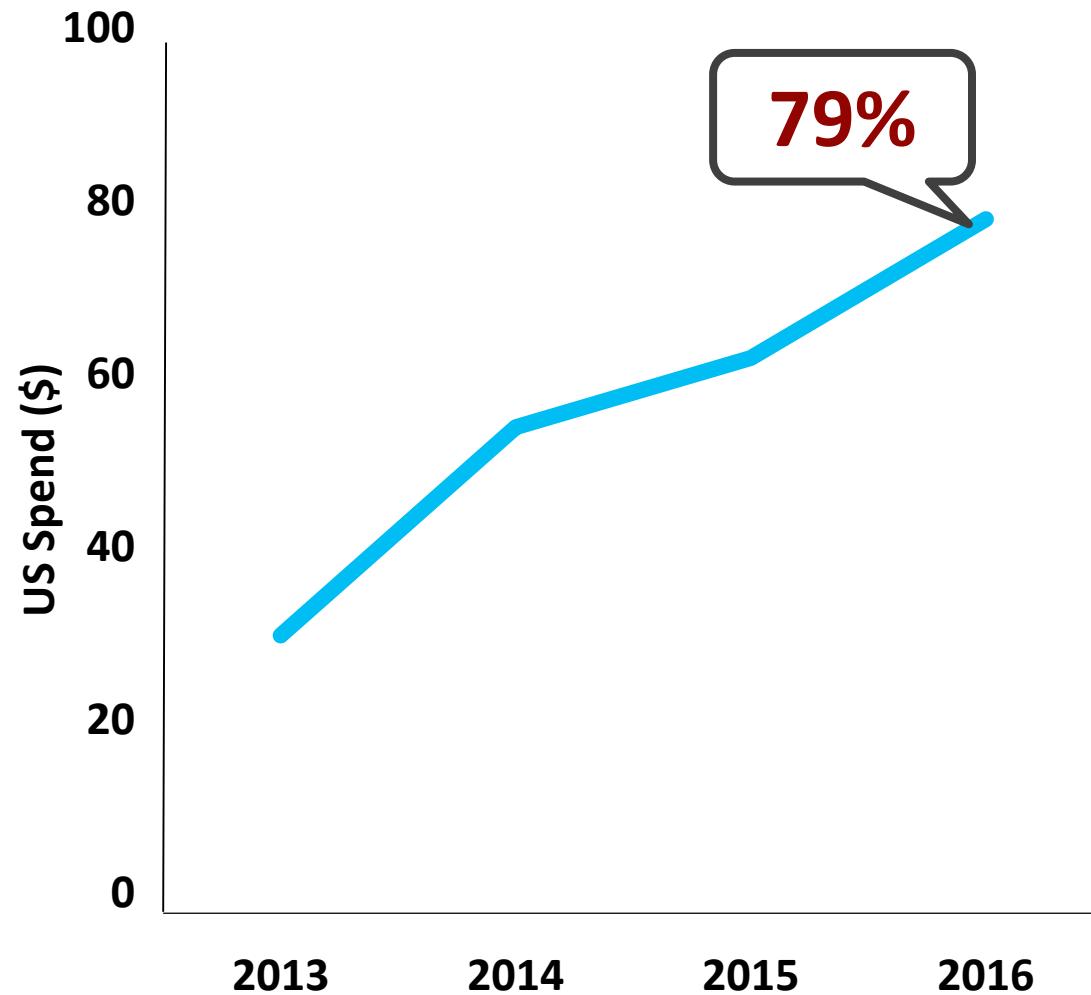
New indications for existing drugs

Earlier use of biologics in treatment regimen for diseases where nonbiologic options are available

Episodic vs. chronic treatment



# Hemophilia Drug Spending is Projected to Increase



Drivers of spending trend include:

- Rising drug acquisition costs and more sophisticated agents entering the market
- Increased utilization of prophylactic regimens

# The Hemophilia Trend is Driven Largely By Unit Cost



## TOP SPECIALTY THERAPY CLASSES RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
1	Inflammatory Conditions	\$80.03	8.5%	15.7%	24.3 %
2	Multiple Sclerosis	\$52.36	3.2%	9.7%	12 .9%
3	Oncology	\$41.64	8.9%	11.7%	20.7 %
4	Hepatitis C	\$37.95	76.1 %	666.6%	742.6 %
5	HIV	\$27.24	4.5%	10.3%	14.8 %
6	Miscellaneous Specialty Conditions	\$11.10	27.3%	8.2%	35.6 %
7	Growth Deficiency	\$9.98	-0.9%	7.5%	6.6 %
8	Hemophilia	\$5.49	-0.8%	17.6%	16.9 %
9	Pulmonary Arterial Hypertension	\$5.41	7.6%	6.2%	13.8 %
10	Transplant	\$5.13	0.8%	-3.1%	-2.3 %
	<b>TOTAL SPECIALTY</b>	<b>\$311.11</b>	<b>5.8%</b>	<b>25.2%</b>	<b>30.9%</b>

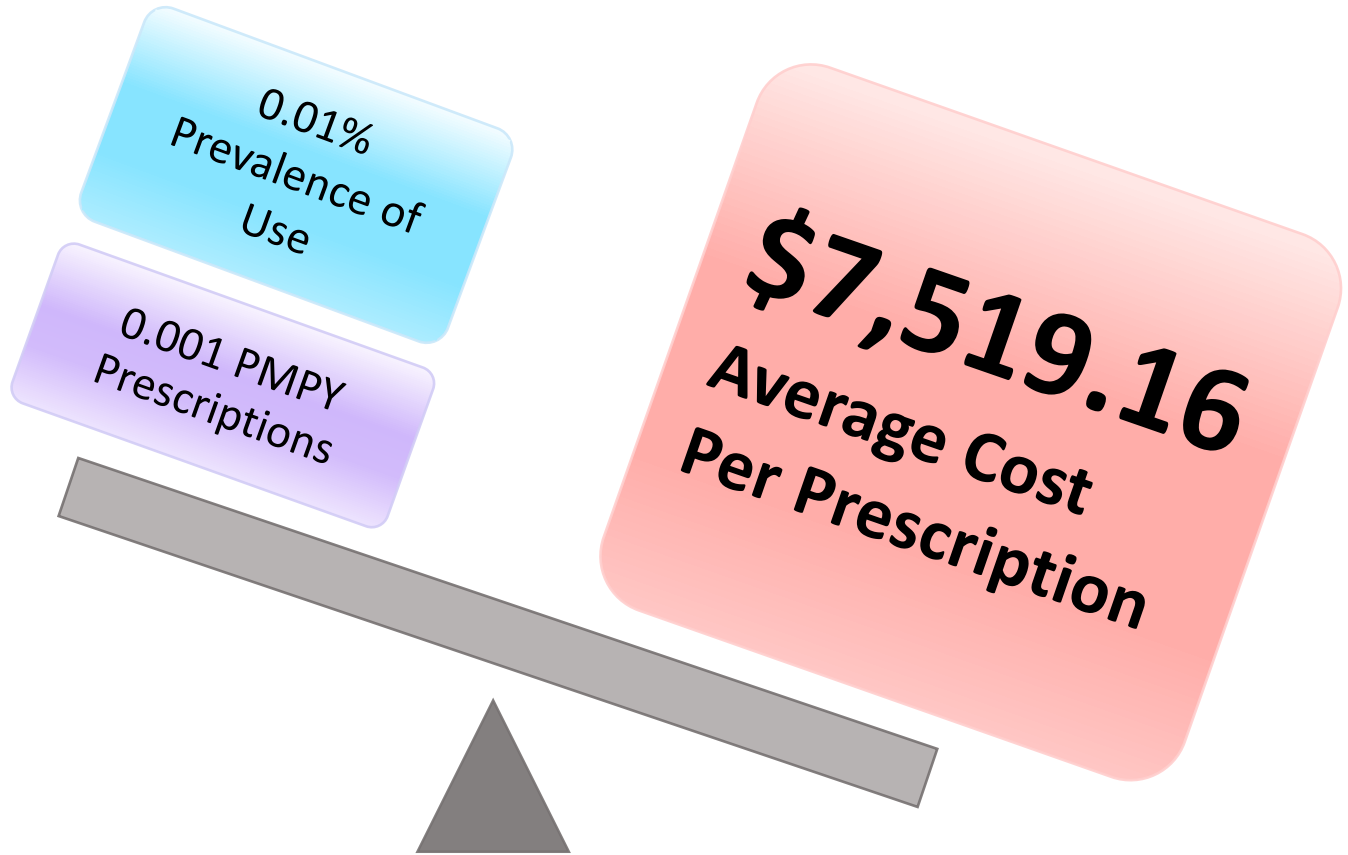
# Hemophilia: A Low Prevalence, But High Cost Disease



Condition	Estimated Prevalence	Estimated Per Patient Cost of Care (\$)
Diabetes <sup>1</sup>	25,800,000	7,900 – 14,000
COPD <sup>2</sup>	15,000,000	2,000 – 43,000
Multiple Sclerosis <sup>3,4</sup>	300,000	28,000 – 58,000
Hemophilia <sup>5</sup>	20,000	180,000 – 300,000

1. American Diabetes Association. *Diabetes Care*. 2013;36:1033-46.
2. Dalal AA, et al. *Int J Chron Obstruct Pulmon Dis*. 2010;5:341-9.
3. Gleason PP, et al. *J Manag Care Pharm*. 2013;19:542-8.
4. Rocky Mountain MS Center. <https://www.mscenter.org/education/ms-the-basics>. Accessed March 31, 2015.
5. Fischer K, et al. *Blood*. 2013;122:1129-36.

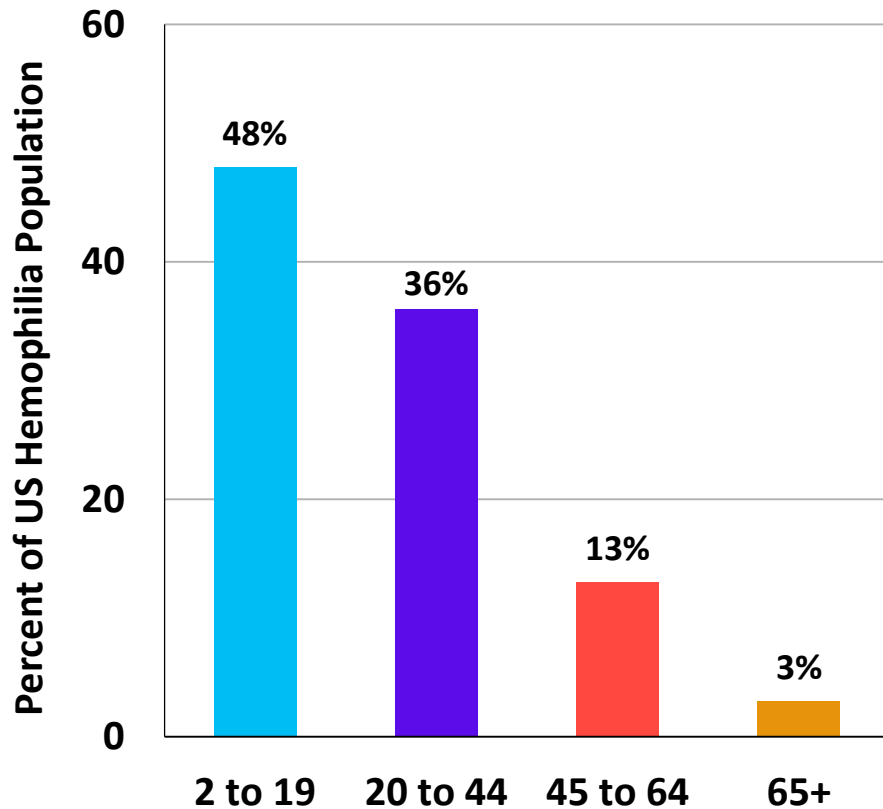
# Hemophilia: A Low Prevalence, But High Cost Disease



# Hemophilia Patients Require Healthcare Across the Lifespan



**Age Distribution of the US Hemophilia Population<sup>1</sup>**



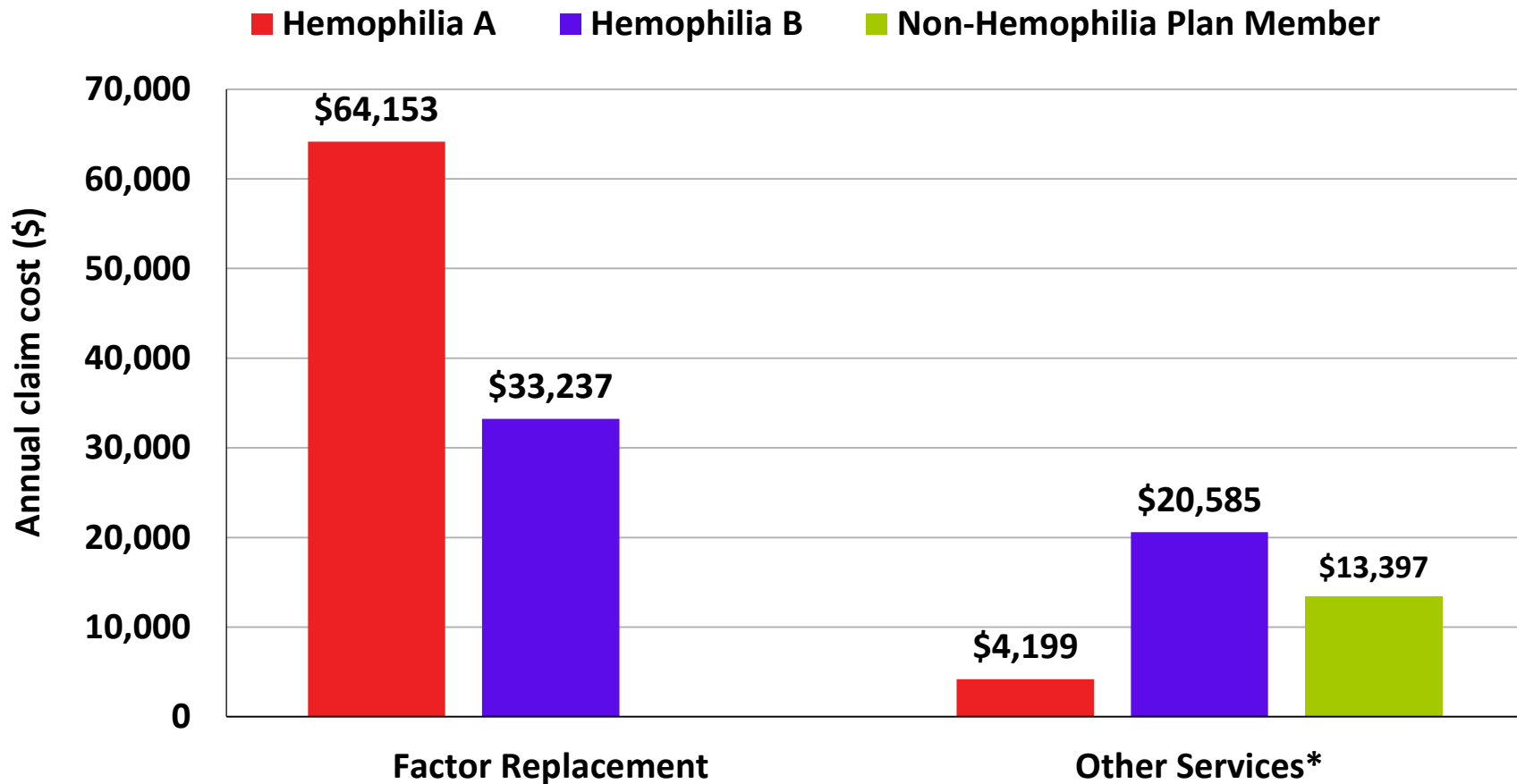
- Age of diagnosis is <2 years of age<sup>2</sup>
- Life expectancy exceeds 70 years<sup>2</sup>
- Older patients tend to have comorbidities (eg, CVD, HCV, and HIV)<sup>2</sup>
- ~50% of hemophilia patients are insured under commercial plans<sup>3</sup>

1. Centers for Disease Control and Prevention. Report on the Universal Data Collection Program, 2005-2009, January 2014:1-26.

2. Centers for Disease Control and Prevention. Hemophilia. <http://www.cdc.gov/ncbddd/hemophilia/data.html>. Accessed March 12, 2015.

3. Express Scripts. 2014 Drug Trend Report. <http://lab.express-scripts.com/drug-trend-report/>. Accessed March 12, 2015.

# Average Annual Claim Costs for Hemophilia in a Commercial Population

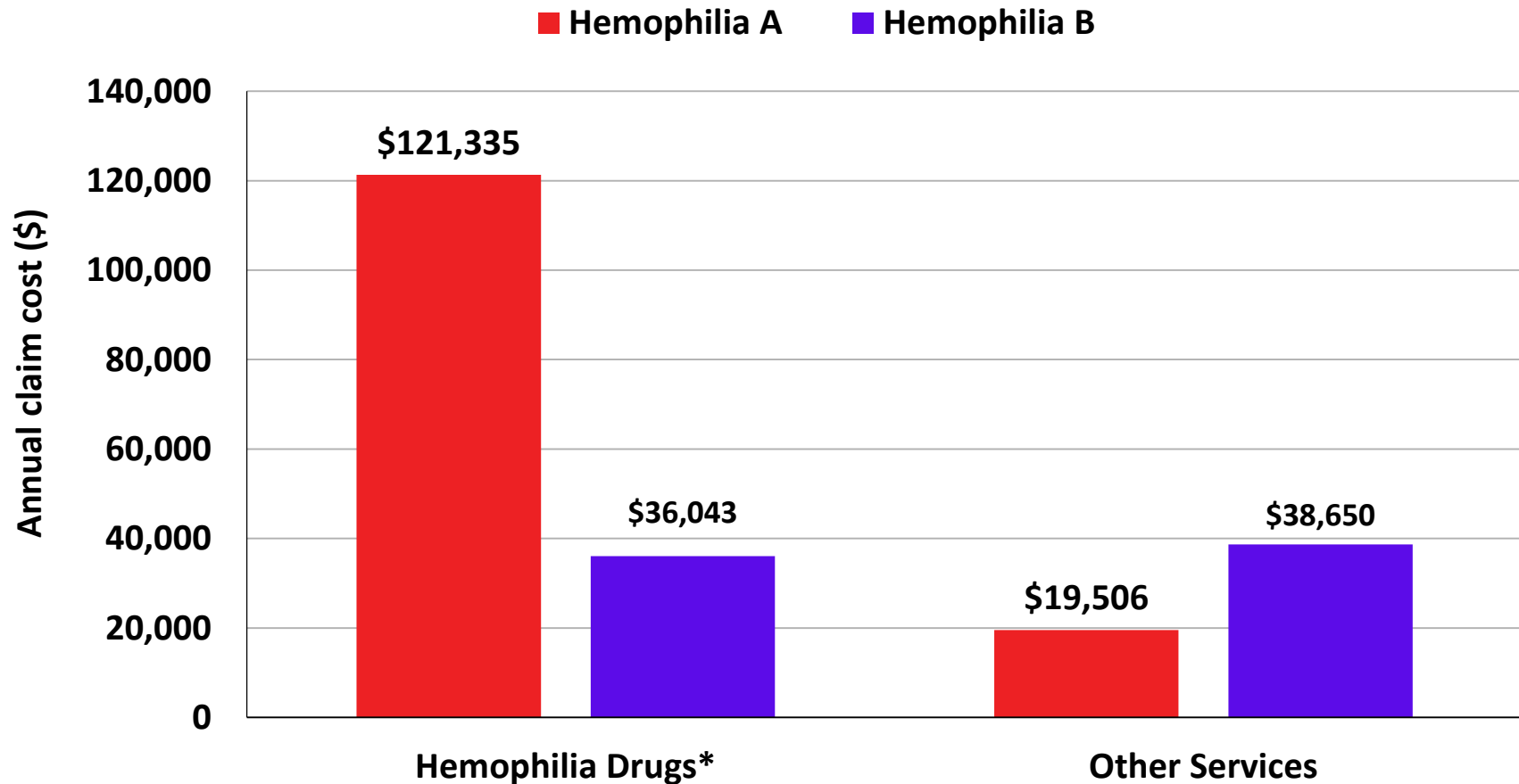


\*In- and outpatient facility fees, professional costs, and other non-pharmacologic direct healthcare costs.

Milliman Report. An actuarial study of hemophilia. October 24, 2013.

<http://www.milliman.com/uploadedFiles/insight/2014/hemophilia-actuarial-study.pdf>. Accessed March 10, 2015.

# Average Annual Claim Costs for Hemophilia in a Medicaid Population



• Medicaid claim costs reflect the increased severity of hemophilia in this population as well as the greater number of comorbidities

\*Includes factor, anti-inhibitor drugs, and other treatment drugs.

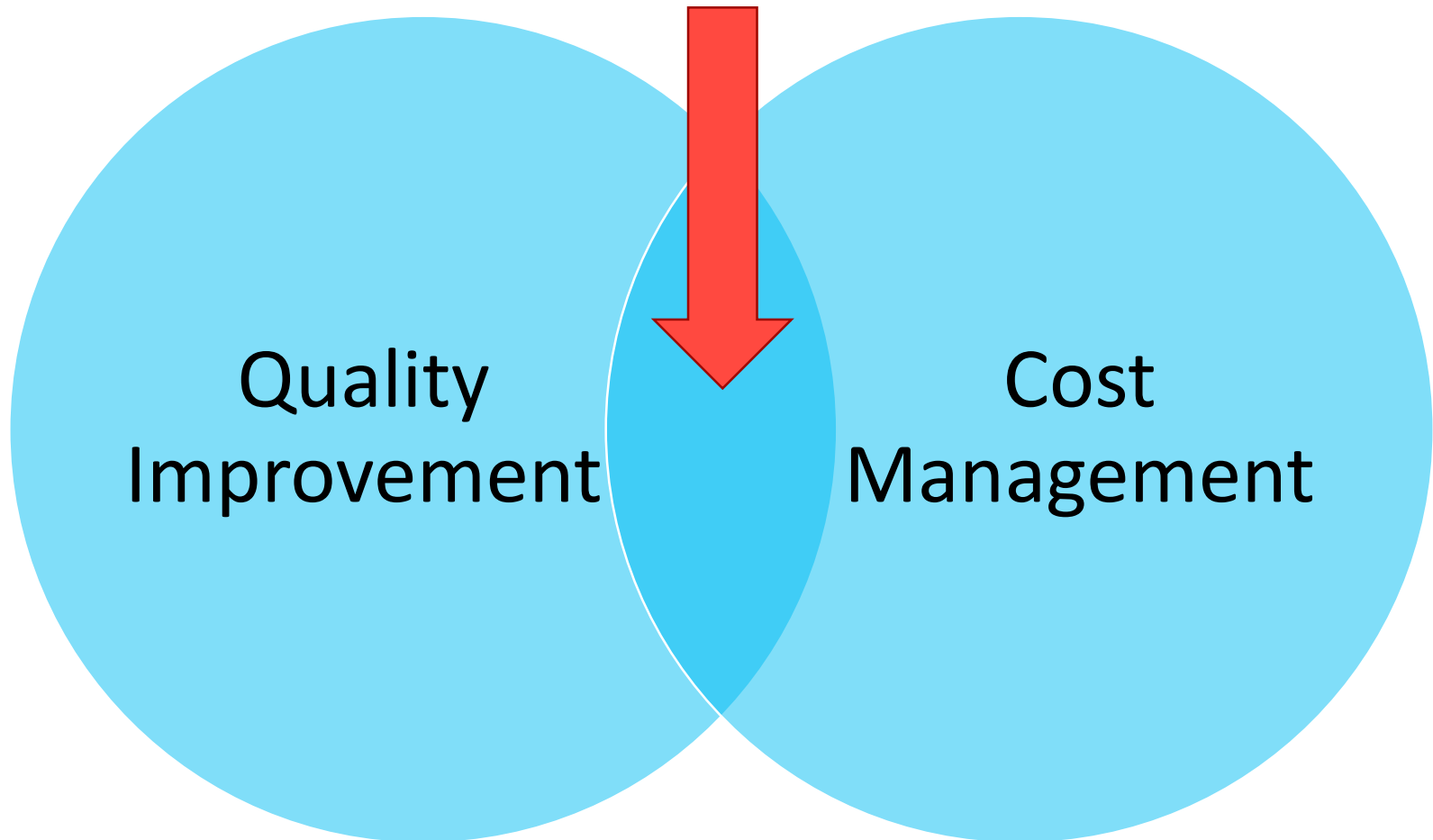
Milliman Report. An actuarial study of hemophilia. October 24, 2013.

<http://www.milliman.com/uploadedFiles/insight/2014/hemophilia-actuarial-study.pdf>. Accessed March 10, 2015.

# Payer Management Interventions Seek to Improve Care Quality and Manage Disease Costs

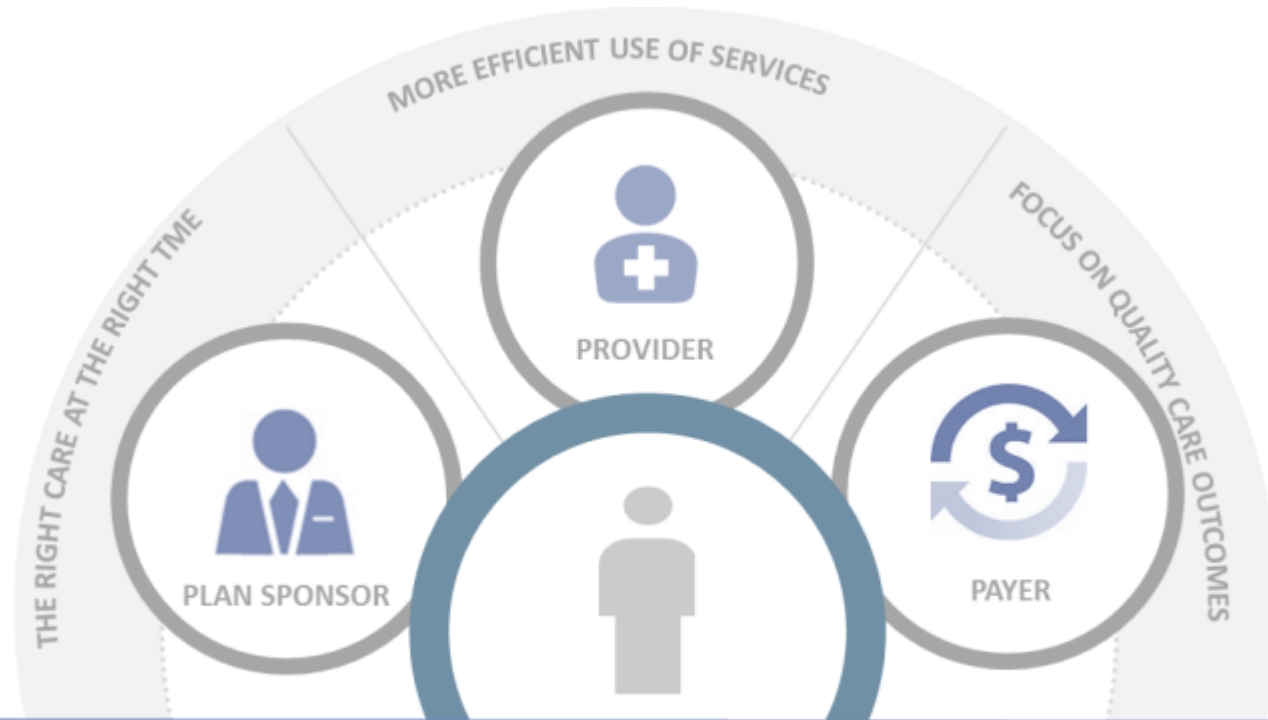


Goal of Payer Intervention





# The Right Alignment of Stakeholders Drives the Best Possible Patient Outcomes



**PLAN SPONSOR – PROVIDER**  
Incentives based on quality  
decision support technology

**HEMOPHILIA TREATMENT  
CENTER ACCESS**

**PROVIDER - PAYER**  
Plan design steering to quality  
and efficiency

# Improving the Quality of Hemophilia Care: Payer Perspective



Quality Initiative	Strategy to Achieve
Treatment access and quality	<ul style="list-style-type: none"><li>• Integrate hemophilia care in network management and medical management strategies</li><li>• Establish relationships with HTC's, specialty pharmacy, and specialized medical providers</li></ul>
Care management	<ul style="list-style-type: none"><li>• Coordinate multidisciplinary outpatient and home-based services</li></ul>
Cost management	<ul style="list-style-type: none"><li>• Utilize cost-effective approaches for administration of factor replacement while keeping in mind the individualized treatment needs of each patient</li></ul>
Pharmacy management	<ul style="list-style-type: none"><li>• Evaluate all services required to manage hemophilia</li><li>• Secure cost-effective and timely factor replacement services for routine and emergency needs</li></ul>
Risk management	<ul style="list-style-type: none"><li>• Identify financing solutions (eg, risk adjustment or carve outs) to ensure member access to care</li></ul>
Patient involvement	<ul style="list-style-type: none"><li>• Involve patients in all decisions impacting their care</li><li>• Include support partners and caregivers to increase adherence to recommended care</li></ul>

# Balancing Cost and Quality: Payer Cost Management Strategies



## Goal: Ensure Lowest Total Costs

- Benefit design
  - Factor drugs covered under Medical or Pharmacy benefit
  - Drug Tier
    - Coinsurance
    - Fixed copayment fee
- Channel management
  - Preferred specialty pharmacy provider(s)
    - Single Source/Multisource
  - Narrow networks
    - Mandatory specialty pharmacy use for purchase/administration of specialty drugs
  - 340B programs

Johnson K. *Formulary Watch*. 2013. <http://formularyjournal.modernmedicine.com/formulary-journal/content/tags/specialty-drugs/current-trends-specialty-drug-utilization-and-managem?page=full>. Accessed March 12, 2015.

Burns J. *Manag Care*. February 2012. [http://www.managedcaremag.com/archives/1202/1202.narrow\\_networks.html](http://www.managedcaremag.com/archives/1202/1202.narrow_networks.html). Accessed March 12, 2015.

# Hemophilia Cost Management Best Practices



- Ensure factor dosing is within recommended parameters and generates appropriate clinical response (assay management)
- Ensure that pharmacy benefits managers (PBMs) or specialty pharmacy providers (SPPs) deliver required services including patient education, home care services, and factor management
- Minimize waste by developing protocols for the number of doses kept in patient homes
- Prevent expensive complications by coordinating with hospitals and other providers to plan for elective surgery and preparing for emergencies
- Monitor and evaluate total cost of care, including inpatient and emergency services, to assess use of avoidable acute care

# Balancing Cost and Quality: Utilization Management Strategies



## Goal: Ensure Appropriate Use

- Formulary management
- Clinical management including personalized regimens
- Prior authorization, quantity limits
- Maximize operational efficiency by reducing waste, mitigating billing errors, minimizing inappropriate use
- Managed care often contracts with specialty pharmacy providers for utilization management services including prior authorization, formulary management, clinical management, reporting, access, etc.

# Hemophilia Utilization Management Best Practices



- Contract with an experienced hemophilia pharmacy provider
- Ensure pharmacy providers meet patient needs for consistent, timely services, products, and infusion supplies
- Ensure any vendor manages factor cost through appropriate assay testing and product inventory management
- Develop policies to ensure correct dosing and stock for at-home use
- Monitor quality and accountability of pharmacy providers

# Specialty Pharmacy Interventions May Improve Quality and Manage Total Costs



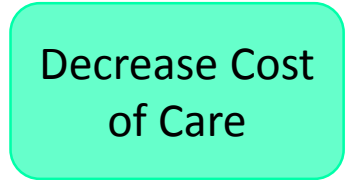
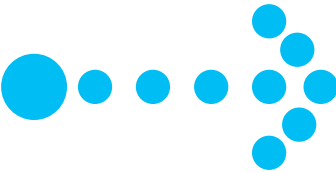
Dose Optimization and Management



Patient Assessment before Refill (assay)



Patient Education



# Balancing Cost and Quality: Care Model Delivery Strategies



**Goal: Ensure the Delivery of Quality Care  
at the Best Price**

- Utilize health care delivery strategies that may provide lower costs without sacrificing quality including:
  - Centers of Excellence
  - Accountable Care Organizations (ACOs)
  - Patient-centered medical homes (PCMH)
- Utilize networks of pharmacy providers that can reduce drug costs through appropriate utilization



# Hemophilia Care Delivery Best Practices



- Comprehensive Hemophilia Treatment Centers (HTCs) emphasize prevention services to reduce or eliminate complications
- Includes the use of preventive medicine, education, and psychosocial support
- Provides access to multidisciplinary health care professionals:
  - Hematologists
  - Orthopedists
  - Physical therapists
  - Nurses
  - Social workers
  - Other specialists (e.g., pharmacist, dentist, nutritionist, genetic counselor)

# Summary



- While the traditional pharmaceutical trend has remained relatively flat, specialty drug spending has increased consistently over the past several years
  - Unit cost increases among specialty agents have contributed significantly to this trend
- Hemophilia is a low prevalence, but high cost disease and patients require treatment across their lifespan with specialty therapeutics such as clotting factor concentrate and bypassing agents
- Access to care is necessary to optimize treatment outcomes; however, there is a need to strike a balance between cost and quality of care
- Several strategies have been devised to effectively manage cost and utilization while delivering high quality care from the payer and specialty pharmacy perspective

# The Evolving Hemophilia Managed Care and Specialty Pharmacy Environment:

## Recommendations for a New Health Care Ecosystem



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**NATIONAL HEMOPHILIA FOUNDATION**  
*for all bleeding disorders*





# An Advanced Review of Inhibitors and Prophylaxis Treatment

**Michael Tarantino, MD**

Professor of Pediatrics, Division of Pediatric Hematology/Oncology

University of Illinois College of Medicine

Medical Director

Bleeding & Clotting Disorders Institute



- The **faculty** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:
- **Michael Tarantino, MD**
  - *Consulting Fees:* Amgen, Baxalta Inc., Biogen Inc., Bio Products Laboratory U.S.A., Inc., Cangene Corporation, Grifols, Pfizer, Inc.
  - *Speaker:* Biogen Inc., Bio Products Laboratory U.S.A., Inc., Grifols, Novo Nordisk, Inc., Pfizer, Inc.
  - *Honoraria:* Baxalta Inc., Biogen Inc., Bio Products Laboratory U.S.A., Inc., Grifols, Novo Nordisk, Inc., Pfizer, Inc.
  - *Research:* Amgen, Baxalta Inc., Cangene Corporation, Novo Nordisk, Inc.
  - *Royalty:* Up-to-Date

# Hemophilia Etiology and Epidemiology



- X-linked recessive bleeding disorder caused by a functional or quantitative deficiency of one of the coagulation proteins
  - Factor VIII: hemophilia A
  - Factor IX: hemophilia B
- Inability to form a clot leads to spontaneous bleeding or bleeding following trauma or surgery
- Current prevalence in the United States: ~20,000 males across all ethnic and racial groups
  - Hemophilia A: 1 in 5,000 live (male) births
  - Hemophilia B: 1 in 30,000 live (male) births

# Clinical Classification



<b><u>Classification</u></b> <b>(% of patients)</b>	<b><u>Severe</u></b> <b>(50% - 70%)</b>	<b><u>Moderate</u></b> <b>(10%)</b>	<b><u>Mild</u></b> <b>(30% - 40%)</b>
FVIII or FIX activity	<1%	1% - 5%	6% - 40%
Pattern of bleeding episode	2-4 per month	4-6 per year	uncommon
Cause of bleeding	Spontaneous	Following minor trauma	Following major trauma or surgery

# Hemophilia Care Management: Treatment Priorities



- Treatment priorities for persons with hemophilia
  - Prevention of bleeding
  - Immediate infusion of clotting factors if excessive bleeding does occur
  - Prevention of disability
- Advances in hemophilia care allow for a near normal life expectancy
  - Use of prophylactic (preventive) factor infusion protocols
    - Advent of longer-acting factor may lead to decreased number of infusions/week for many



# Treatment Goals, Approach, and Strategies



Goals	Approach	Strategies
<ul style="list-style-type: none"><li>• Rapid and effective replacement of missing coagulation factor in order to:<ul style="list-style-type: none"><li>• Raise factor levels</li><li>• Decrease frequency and severity of bleeding</li><li>• Prevent the complications of bleeding</li></ul></li></ul>	<ul style="list-style-type: none"><li>• Comprehensive hemophilia treatment center (HTC) staffed by a multidisciplinary team of experts who care for patients with bleeding disorders</li></ul>	<ul style="list-style-type: none"><li>• Episodic or “on demand” factor replacement</li><li>• Prophylaxis</li></ul>

# Treatment Options



- Replacement of missing clotting protein
  - Hemophilia A: concentrated FVIII product
  - Hemophilia B: concentrated FIX product
- Desmopressin acetate (DDAVP)/Stimate
  - Synthetic vasopressin analog used in many patients with **mild** hemophilia A for joint, muscle, and oro-nasal bleeding and before and after surgery
- Adjunctive therapies
  - Antifibrinolytic agents
  - Supportive measures including immobilization and rest

# Control and Prevention of Bleeding with Factor Replacement



Bleeding Episode	Factor Level Required (% of normal)	Frequency of Administration*
<b>Minor</b> <ul style="list-style-type: none"> <li>• Early hemarthrosis</li> <li>• Minor muscle or oral bleed</li> </ul>	30-50	Every 12-24 hours ± antifibrinolytic
<b>Moderate</b> <ul style="list-style-type: none"> <li>• Bleeding into muscles or oral cavity</li> <li>• Definite hemarthrosis</li> </ul>	50-80	Every 12-24 hours until resolved
<b>Major</b> <ul style="list-style-type: none"> <li>• GI, intracranial, intra-abdominal, intrathoracic, CNS, or retroperitoneal bleeding</li> </ul>	80-100	Every 12-24 hours until resolved
<b>Special Case Scenarios</b> <ul style="list-style-type: none"> <li>• Patients already on prophylaxis, patients using long-acting factor products, etc.</li> </ul>	Variable	Variable

\*Recommended FVIII dosing:

Dosage in FVIII units = (Weight in kilograms) x (Factor percentage desired) x 0.5 (per product indications)

# Factors VIII and IX



	<b>FVIII</b>	<b>FIX</b>
Intravenous infusion (either IV push or continuous)	√	√
Dose	20 - 50+ units / kg body weight	40 - 100+ units / kg body weight
Half-life	8 - 12 hours	18 - 24 hours
Average change in plasma factor activity with each unit/kg infused	+2%	+1%

Depending on level of purity

# Hemophilia Management Challenges



- Prophylaxis<sup>1-6</sup>
  - Identification of optimal trough level
  - Cost-benefit of targeting higher trough levels
  - Use of prophylaxis beyond pediatric patients
  - Perisurgical considerations
  - Impact of prophylaxis on CVD risk
- Formation of inhibitory antibodies<sup>7,8</sup>
  - Genetic predisposition
  - Factor exposure during heightened immune response
    - Infections, immunizations, surgery
    - More frequent (or continuous) factor infusions in mild or moderate cases
  - Eradication of the inhibitor in severe cases

1. Fischer K, et al. *Blood*. 2013;122:1129-1136. 2. Manco-Johnson MJ, et al. *Haemophilia*. 2013;19:727-735. 3. Gringeri A, et al. *Haemophilia*. 2012;18:722-728. 4. Simpson ML, Valentino LA. *Expert Rev Hematol*. 2012;5:459-468. 5. Sørensen B, et al. *Haemophilia*. 2012;18:598-606. 6. Konkle BA. *Am J Hematol*. 2012;87 Suppl 1:S27-32. 7. National Institutes of Health. <http://www.nhlbi.nih.gov/health/health-topics/topics/hemophilia/signs>. Accessed July 15, 2015. 8. Shapiro A. *Hematology Am Soc Hematol Educ Program*. 2013;2013:37-43.

# Prophylaxis



- Prophylactic use of clotting factor concentrates forms the basis of modern treatment of severe hemophilia A and B
- The use of prophylaxis in patients with hemophilia without inhibitors, even in the setting of preexisting joint disease, has become more routine
  - In children, the early start of prophylaxis as primary or secondary prophylaxis has become the “gold standard” of care
  - In adults, prophylaxis is reasonably continued when started as primary or secondary prophylaxis in childhood to maintain healthy joint function

# Prophylaxis Protocols



Protocol	Definition
Primary prophylaxis	Regular, continuous* treatment initiated in the absence of documented joint disease, determined by physical examination and/or imaging studies, and started before the second clinically evident large joint bleed and age 3 years†
Secondary prophylaxis	Regular, continuous* treatment started after $\geq 2$ bleeds into large joints† and before the onset of joint disease documented by physical examination and imaging studies
Tertiary prophylaxis	Regular, continuous* treatment started after the onset of joint disease documented by physical examination and plain radiographs of the affected joints
Intermittent (“periodic”) prophylaxis	Treatment given to prevent bleeding for periods not exceeding 45 weeks in a year

\*Continuous is defined as the intent of treating for 52 weeks/year and receiving a minimum of an a priori defined frequency of infusions for at least 45 weeks (85%) of the year under consideration.

†Large joints = ankles, knees, hips, elbows, and shoulders

# Perisurgical Prophylaxis Considerations



- Postsurgery complications are not uncommon and should be managed on the basis of underlying etiology, with duration and dose varying according to the individual case
- Patients should have a multi-disciplinary team involved, including HTC staff, before, during, and after surgery
- Anesthesiologist should have experience treating patients with bleeding disorders
- Institutional laboratory able to perform clotting factor activity and inhibitor testing with STAT service is imperative
- Dosage and duration of clotting factor concentrates (CFCs) depend on the type of surgery being performed
- Target trough levels of 80% to 100% immediately after surgery are recommended; factor clearance changes during post-op period



# Suggested Perisurgical Plasma Factor Peak Level and Duration of Administration



	HEMOPHILIA A		HEMOPHILIA B	
	DESIRED LEVEL (IU/DL)	DURATION (DAYS)	DESIRED LEVEL (IU/DL)	DURATION (DAYS)
<b>Surgery (major)</b>				
• Pre-op	80-100		60-80	
• Post-op	60-80	1-3	40-60	1-3
	40-60	4-6	30-50	4-6
	30-50	7-14	20-40	7-14
<b>Surgery (minor)</b>				
• Pre-op	50-80		50-80	
• Post-op	30-80	1-5, depending on type of procedure	30-80	1-5, depending on type of procedure

# New Therapeutics Have the Potential to Revolutionize Prophylaxis



- Extended half-life (EHL) or long-acting factor products
  - FVIII and FIX
  - EHL agents have been recently approved with several more expected in the next few years

What the Data Says...	What We Hope...	The Unknowns...
<ul style="list-style-type: none"><li>• Longer half-life</li><li>• Less frequent dosing</li></ul>	<ul style="list-style-type: none"><li>• More effective prophylaxis</li><li>• Improved adherence</li><li>• Greater individualization of treatment</li></ul>	<ul style="list-style-type: none"><li>• Will long-acting factors work as well as expected?</li><li>• What impact will they have on cost, adherence, and quality-of-life?</li></ul>

# EHL Hemophilia Replacement Factor Research and Development



- Extending the half-life of FVIII and FIX has been a major focus of current efforts to improve therapy
- Current therapies must be administered multiple times per week to maintain circulating FVIII and FIX >1% of normal
- Strategies have been applied to extend the plasma half-life of these coagulation factors and two long-acting products have been FDA-approved
  - March 2014: Alprolix™ approved as the first long-acting recombinant Factor IX concentrate<sup>1</sup>
  - June 2014: Eloctate™ approved as the first long-acting recombinant Factor VIII concentrate<sup>2</sup>

1. Alprolix™ [Coagulation Factor IX (Recombinant), Fc Fusion Protein] prescribing information. Cambridge, MA: Biogen Idec, Inc.; March 2014.

2. Eloctate™ [Antihemophilic Factor (Recombinant), Fc Fusion Protein] prescribing information. Cambridge, MA: Biogen Idec, Inc.; June 2014.

# Recently Approved and Emerging Treatments



FVIII Agent	Description	Status
NOVOEIGHT (turoctocog alfa)	rFactor VIII	Approved October 2013
ELOCTATE (rFVIII-Fc)	rFactor VIII, long-acting	Approved June 2014
Nuwiq	rFactor VIII	Pending regulatory review
Bax855 (Advocate)	rFactor VIII, long-acting	Pending regulatory review
Simoctocog alfa	rFactor VIII	Phase 3
N8-GP	rFactor VIII, long-acting	Phase 3
BAY94-9027	rFactor VIII, long-acting	Phase 3
FIX Agent	Description	Status
RIXUBIS	rFactor IX	Approved June 2013
ALPROLIX (rFIX-Fc)	rFactor IX, long-acting	Approved March 2014
IXinity	rFactor IX	Approved June 2015
C255238539	rFactor IX	Phase 3
rIX-FP	rFactor IX, long-acting	Phase 3
Inhibitor Agent	Description	Status
OBIZUR	rFactor VIII (porcine seq)	Approved October 2014
BAY 86-6150	rFactor VIIa	Phase 3
LR769	rFactor VIIa	Phase 2/3

# Inhibitors



- Inhibitors (antibodies to the infused replacement factor) may develop in ~15-20% of patients<sup>1</sup>
  - Prevalence is higher in hemophilia A (~30%) vs. hemophilia B (2-5%)
- Inhibitors neutralize the procoagulant effect of the infused factor as well as naturally produced factor protein<sup>1</sup>
- Typically develop early in life (median age 1.7 – 3.3 years)<sup>1</sup>
- Greatest risk for inhibitor development occurs within the first 50 exposures to infused product<sup>1,2</sup>

1. DiMichele D. World Hemophilia Federation. Inhibitors in Hemophilia: A Primer. Available at: <http://www1.wfh.org/publication/files/pdf-1122.pdf>. Accessed July 15, 2015.  
2. Bray GL, et al. *Blood*.1994;83:2428-2435.

# What Are Inhibitors?



- Polyclonal allo-antibodies of the IgG isotype, predominantly of the IgG4 subclass that is directed to clotting factor
- Highly heterogeneous among patients
- Display changes in epitope specificity over time
- Neutralize the procoagulant activity of clotting factor, increase factor clearance, and render infusion of clotting factor concentrate ineffective

# How Do Inhibitors Develop?

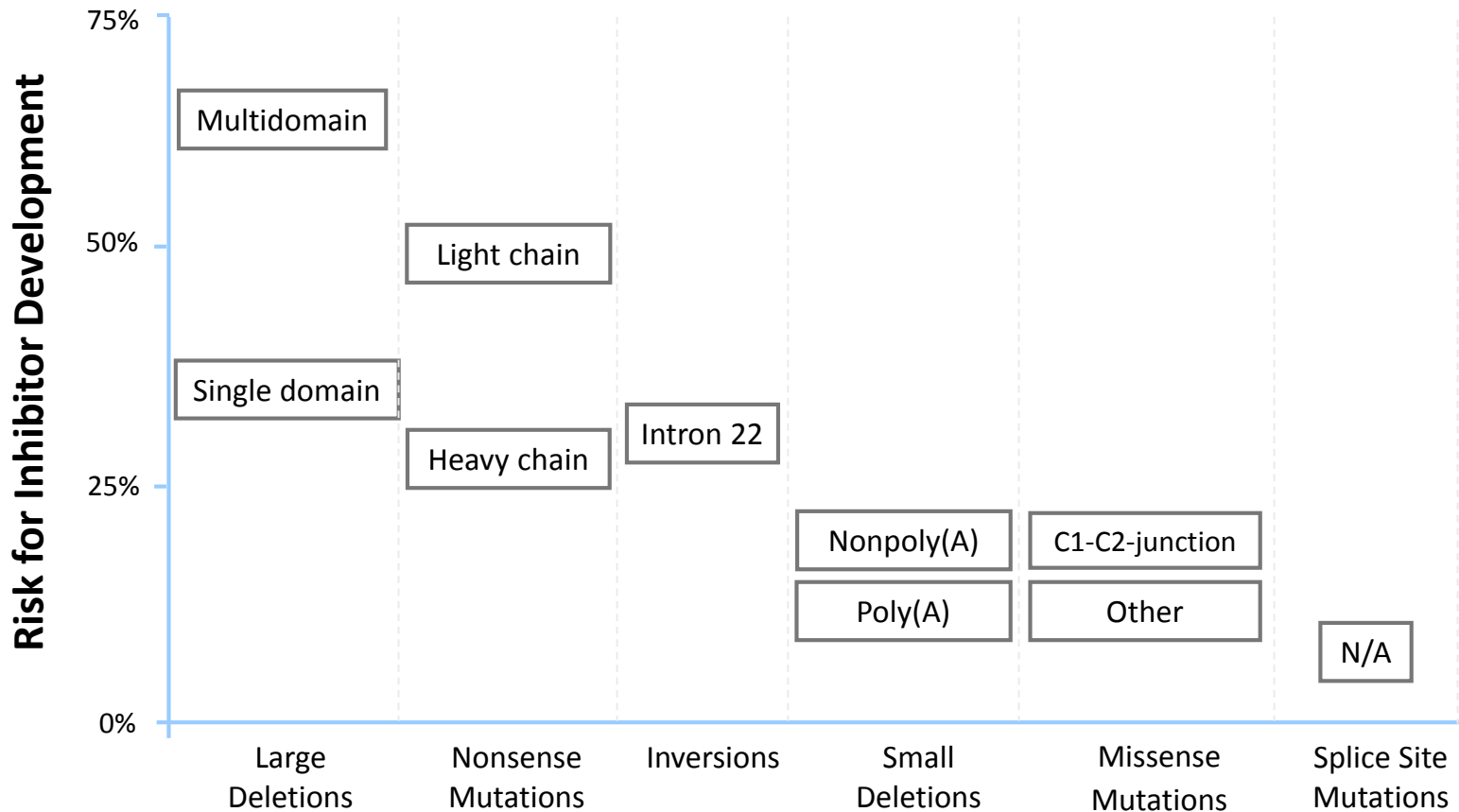


- Clotting factor is a soluble glycoprotein; administration to an immune competent individual may result in immune response
- Genotype of deficient clotting factor protein may influence for the development of inhibitors

# Inhibitor Development



## Risk for Inhibitor Development, by Mutation Type



N/A = not applicable (ie, risk unknown).



# Who Will Develop An Inhibitor?



## Risk Factors

- **Ethnicity**
  - People of African or Hispanic ancestry have a 2x greater risk
- **Family history of antibodies to factor**
- **Inherited predisposition**
  - Siblings with hemophilia >> Extended relatives with hemophilia
- **Severe hemophilia**

# When Will An Inhibitor Develop?



- Development occurs most often between the age of 1 and 2 years, after an average of 9 to 12 treatments with rFVIII
- Risk is greatest during the first 50 exposures to rFVIII

# What Prevents Inhibitors from Developing More Frequently?



There are several possible mechanisms:

1. Anti-factor antibodies are neutralized in the periphery
2. B cells (and T cells) can be rendered anergic by an intrinsic mechanism (also referred to as “tolerance”)
3. Any antibodies produced are primarily directed towards sites of the factor molecule that are not involved in its function (also referred to as “non neutralizing antibodies”)

# Managing Inhibitors



- Treating bleeds: Use of high-dose factor or bypassing agents
  - FVIII impractical and ineffective if BU > 5
  - Activated prothrombin complex concentrates (aPCC)
  - Recombinant FVIIa
    - Factor VIII Inhibitor-Bypassing Activity
    - Coagulation Factor VIIa (Recombinant)
  - Limitations include their unpredictable efficacy and lack of lab monitoring
- Eradicating the Inhibitor: Immune Tolerance Therapy (ITT)
  - Regular infusions of factor VIII or IX administered for a period of weeks to years in an effort to increase the tolerance of the immune system
  - Limitations include variable efficacy (70%-85% for FVIII and ~30% for FIX)
  - Time consuming and expensive

# Preventing Bleeding in Persons with Hemophilia and an Inhibitor



- Goals for prevention of bleeding should be the same for persons with or without inhibitors
- Lifestyle change
  - Limit activity to less risky sports and other activities
  - Target a healthy BMI
  - Avoid foods or medications that increase bleeding
- Consider prophylactic dosing of aPCC or rFVIIa

# Rationale for Prophylaxis



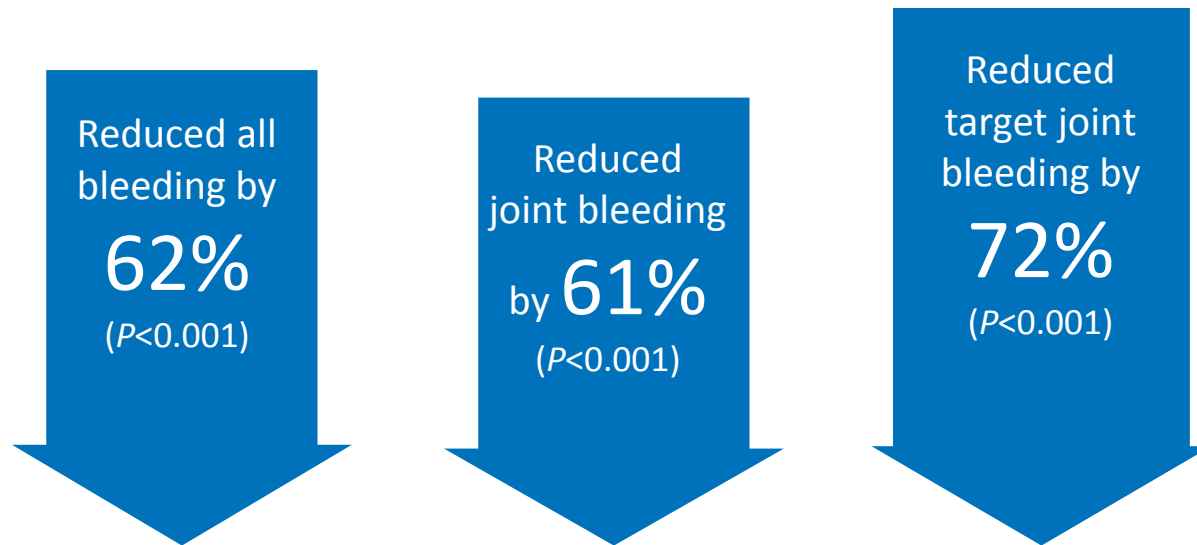
- FVIII prophylaxis can prevent joint hemorrhage and subsequent arthropathy, target joints, and disability<sup>1-3</sup>
  - Recommended by MASAC, WFH, and WHO as optimal therapy for persons with severe hemophilia without inhibitors<sup>4-6</sup>
- Patients with inhibitors are at increased risk for difficult-to-control bleeding and complications; therefore, bleed prevention or reduction is of critical importance<sup>7,8</sup>
  - Prophylactic treatment may also improve Health-Related Quality-of-Life (HRQoL)<sup>9-11</sup>

1. Manco-Johnson MJ, et al. *N Engl J Med*. 2007;357(6):535-544. 2. Gringeri A, et al. *J Thromb Haemost*. 2011;9(4):700-710. 3. Manco-Johnson MJ, et al. *J Thromb Haemost*. 2013;109(4):625-632. 4. US National Haemophilia Foundation. MASAC [Medical and Scientific Advisory Council] Recommendation 179. Available at: <http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=57&contentid=1007>; Accessed July 31, 2013. 5. Srivastava A, et al. *Haemophilia*. 2013;19(1):e1-47. 6. Berntorp E, et al. *Bull World Health Organ*. 1995;73:691-701. 7. Kasper CK. World Federation of Hemophilia: 2004, No. 34. 8. Leissinger CA. *Haemophilia*. 1999;5(suppl 3):25-32. 9. Leissinger C, et al. *N Engl J Med*. 2011;365:1684-1692. 10. Gringeri A, et al. *Haemophilia*. Published online April 14, 2013; DOI:10.1111/hae.12178. 11. Antunes S, et al. *Haemophilia*. Published online August 1, 2013; DOI:10.1111/hae.12246.

# Pro-AICC–Study Results



When compared with Anti-Inhibitor Coagulant Complex (AICC; FEIBA®) on-demand treatment, AICC prophylaxis 85 U/kg  $\pm$  15% given on 3 nonconsecutive days weekly:



# PROOF—Study Results



When compared with AICC on-demand treatment, AICC prophylaxis  $85 \pm 15$  U/kg given every other day:

Reduced median ABR for all bleeds by **72.5%**  
( $P=0.0003$ )

Reduced median ABR for joint bleeds by **73.8%**  
( $P=0.0006$ )

Reduced median ABR in new target joints\* by **100%**  
( $P=0.0271$ )

ABR = Annualised bleeding rate; AICC = Anti-Inhibitor Coagulant Complex (FEIBA®)

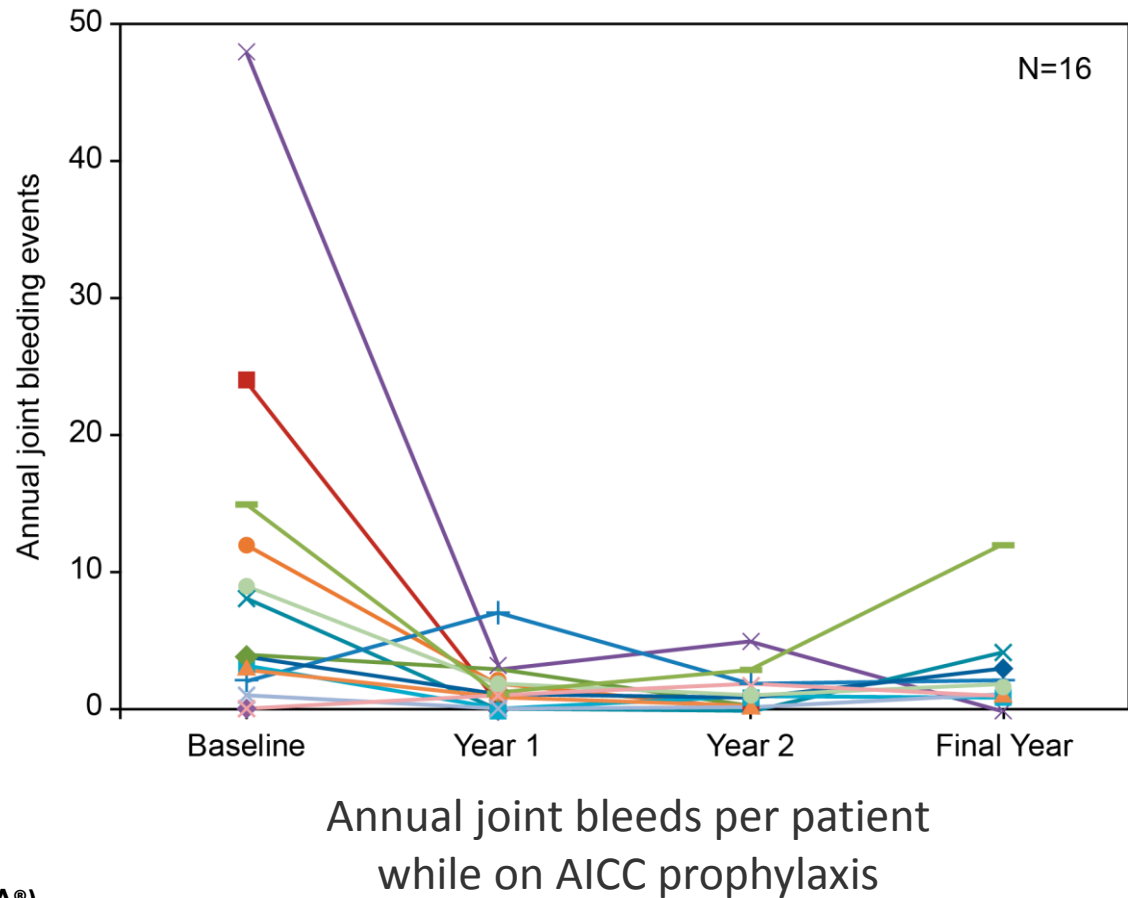
\*Not significant



# Prophylaxis with AICC in Paediatric Patients with Haemophilia A and Inhibitors

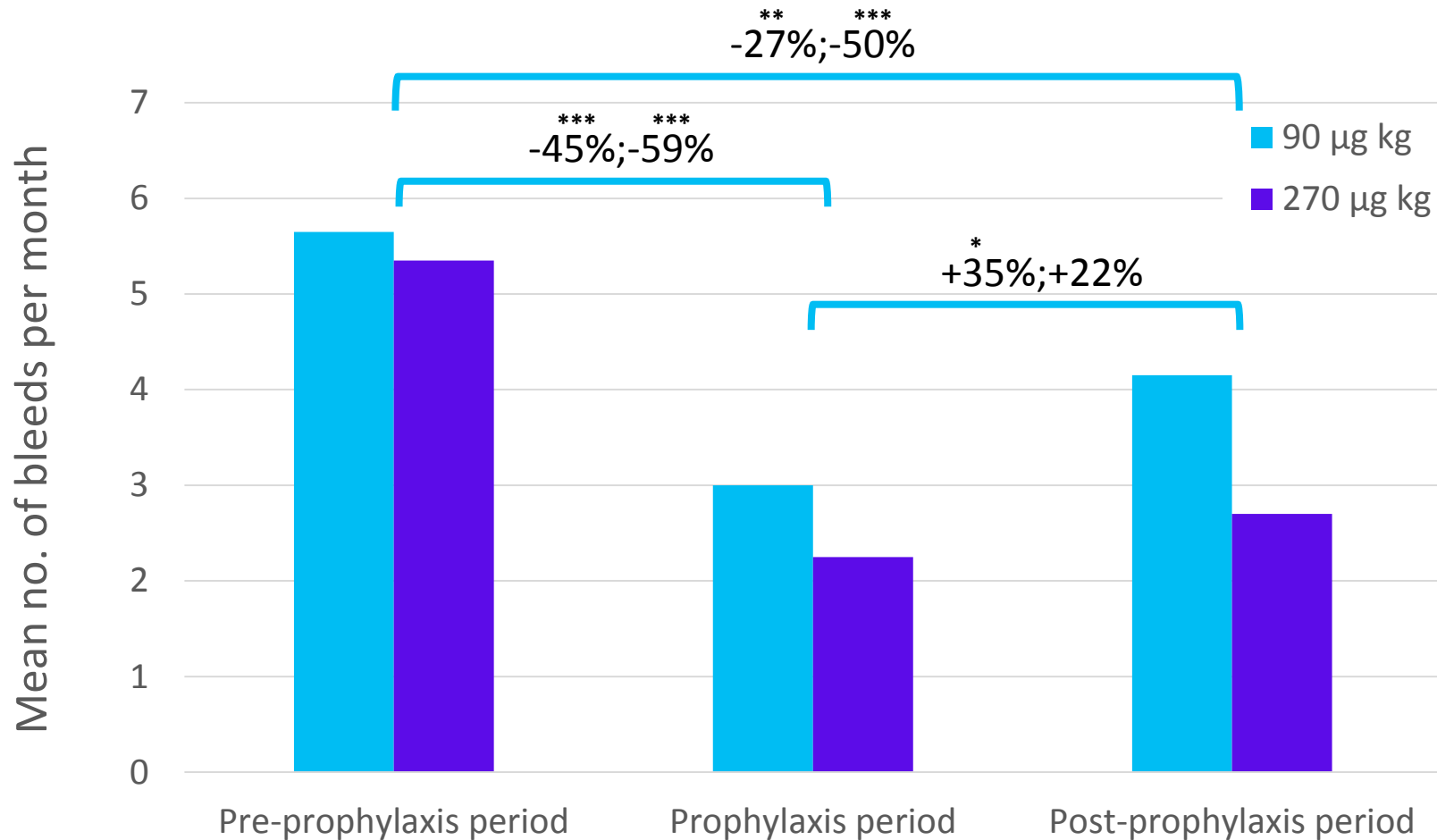


- AICC prophylaxis in paediatric patients decreased the annual number of joint bleeds by a mean of 85.4% the first year ( $P=0.0179$ ) and improved joint status



AICC = Anti-Inhibitor Coagulant Complex (FEIBA®)

# Randomized, Prospective Clinical Trial of Recombinant Factor VIIa for Secondary Prophylaxis in Haemophilia with Inhibitors



\* $P \leq 0.05$ ; \*\* $P \leq 0.01$ ; \*\*\* $P \leq 0.001$

Konkle et al. *J Thromb Haemost.* 2007;5:1904-13.

# Bypassing Factor VIII or Factor IX



- Attributes of aPCCs and rFVIIa
  - Hemostasis for the grand majority of bleeds
  - Experience in surgery for persons with inhibitors
  - Prophylaxis reduces joint, target joint, overall bleeds

# Dilemmas in Treating Hemophilia with Inhibitors Present

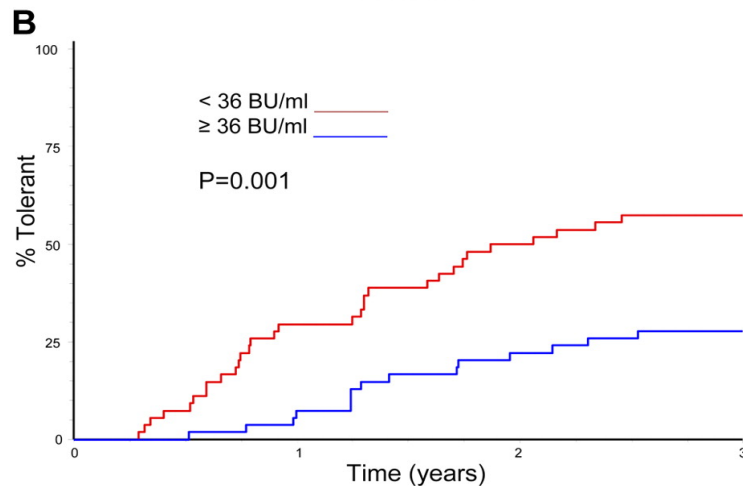
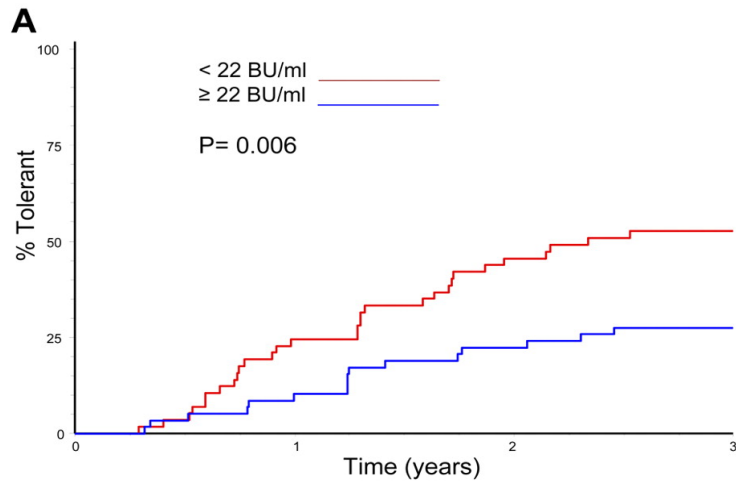


- Treating and preventing bleeds
  - No universally effective agent
    - aPCC work in some, for some, not all
    - rFVIIa works in some, for some, not all
  - No laboratory test that accurately predicts or confirms hemostasis
  - rFVIIa has short half-life, needs frequent infusions
- Inducing Immune Tolerance
  - Not effective in 1/4 to 1/3 of patients
  - The role of or need for von Willebrand factor in preventing and clearing inhibitors is uncertain
  - Immune suppression/modulation (i.e., anti-CD20 agents) variably effective that may be temporary

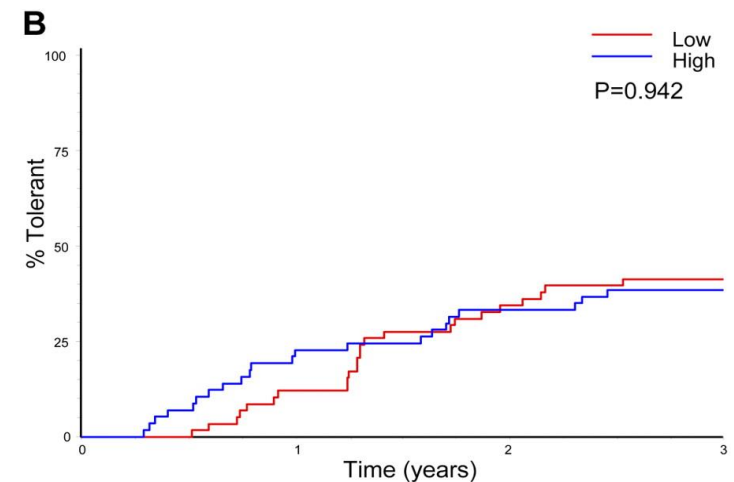
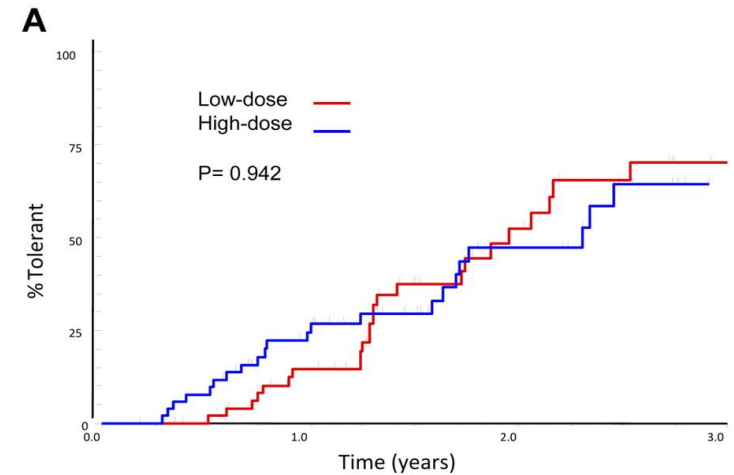
# The Principal Results of the International Immune Tolerance Study



## Time to tolerance by median peak inhibitor titres



## Time to success by treatment arm



# von Willebrand Factor-containing pdFVIII in Haemophilia A Immune Tolerance Induction



## OBJECTIVES:

- To report retrospective collection of data on the use of a single vWF/pd-FVIII concentrate in primary and rescue ITI.

## METHODS:

- Retrospective chart review of hemophilia A inhibitor patients at 11 US institutions who received vWF/pd-FVIII concentrate in primary or rescue ITI.

## RESULTS:

- Primary ITI complete or partial success in 75% (6 of 8)
- Secondary ITI complete or partial success in 52% (13 of 25)

# Primary and Rescue Immune Tolerance Induction in Children and Adults: a Multicentre International Study with a vWF-containing Plasma-derived FVIII



Immune tolerance induction (ITI) outcome in primary and rescue ITI patients (children: <18 years old; adults: ≥18 years old). Results are shown as number of patients and percentage.

	Outcome	ITI regimen		
		Primary	Rescue	All regiments
Children	Complete success	21 (65.6)	6 (35.3)	27 (55.1)
	Partial success	7 (21.9)	6 (35.3)	13 (26.5)
	Failure	4 (12.5)	5 (29.4)	9 (18.4)
	Total	32	17	49
Adults	Complete success	5 (55.6)	1 (50)	6 (54.5)
	Partial success	3 (33.3)	1 (50)	4 (36.4)
	Failure	1 (11.1)	0 (0)	1 (9.1)
	Total	9	2	11
All patients	Complete success	26 (63.4)	7 (36.8)	33 (55)
	Partial success	10 (24.4)	7 (36.8)	17 (28.3)
	Failure	5 (12.2)	5 (26.3)	10 (16.7)
	Total	41	19	60

Values within parenthesis are expressed in percentage.

# Factors Associated With ITI Success



- Initiating ITI in patients whose inhibitor levels are below 10 BU/mL and ideally below 5 BU/mL
- Initiating ITI in patients whose inhibitor levels have never gone higher than 200 BU/mL and have ideally stayed below 50 BU/mL
- Initiating ITI within 5 years of inhibitor diagnosis



# Prompt IT Induction at Inhibitor Diagnosis Regardless of Titre May Increase Overall Success in Haemophilia A: Data From Two US HTC's



- DEFINITIONS

- **SUCCESS:** negative inhibitor titre and ability to use FVIII concentrate for treatment/bleed prevention;
  - **PARTIAL SUCCESS:** inhibitor titre 1 to <5 BU with ability to use FVIII concentrate for treatment of bleeding;
  - **FAILURE:** ITI ongoing >3 years without achieving success/partial success, or ITI discontinuation.
- **58 SUBJECTS:** 32 of 39 (82%) with high-responding inhibitor (HRI) achieved success, 7 failed.
  - HRI subjects were subdivided based on ITI start time:
    - 23/39 subjects started within 1 month of detection and 22/23 (**96%**) achieved success.
    - Of these 23, 13 started ITI with an inhibitor titre  $\geq 10$  BU; 13/13 (**100%**) achieved success.
    - 11 of 39 HRI subjects had an interval >6 months until ITI start; 7 (**64%**) achieved success.
  - A titre  $\geq 10$  BU at ITI start did not influence outcome in subjects when ITI was initiated within 1 month of detection.

# Summary



- Inhibitors and prophylaxis considerations represent two of the greatest clinical challenges in the treatment of hemophilia
  - Aggressive and vigilant therapeutic intervention is crucial to success and the minimization of morbidity/mortality
  - Emerging therapeutics in the form of recombinant and EHL agents present promising options for the elimination of inhibitors and the advancement of prophylaxis, respectively

# The Evolving Hemophilia Managed Care and Specialty Pharmacy Environment:

## Recommendations for a New Health Care Ecosystem



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## *Video*

# Hemophilia Treatment Centers: The Value of the Integrated Care Model in Creating Positive Outcomes

**Produced by Believe Limited, in partnership with the  
National Hemophilia Foundation and Impact Education, LLC**



**CCSC***Hemo.com*

**Supported by a charitable donation by Baxalta US, Inc.**

# The Evolving Hemophilia Managed Care and Specialty Pharmacy Environment:

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# Measuring Success: Tools and Resources to Document Outcomes of Payer and Specialty Pharmacy Hemophilia Management

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National Medical Director for Pharmacy Policy and Strategy

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# Faculty Disclosure



- The ***faculty*** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

## **Edmund Pezalla, MD, MPH**

- *No financial interest/relationships relating to the topic of this activity*

# Key Components of Data Collection and Analysis for Hemophilia Quality Improvement



## Collaboration Between Payers and Providers is Imperative



Growing but still underutilized

- Will be a key feature of future payer/provider interactions



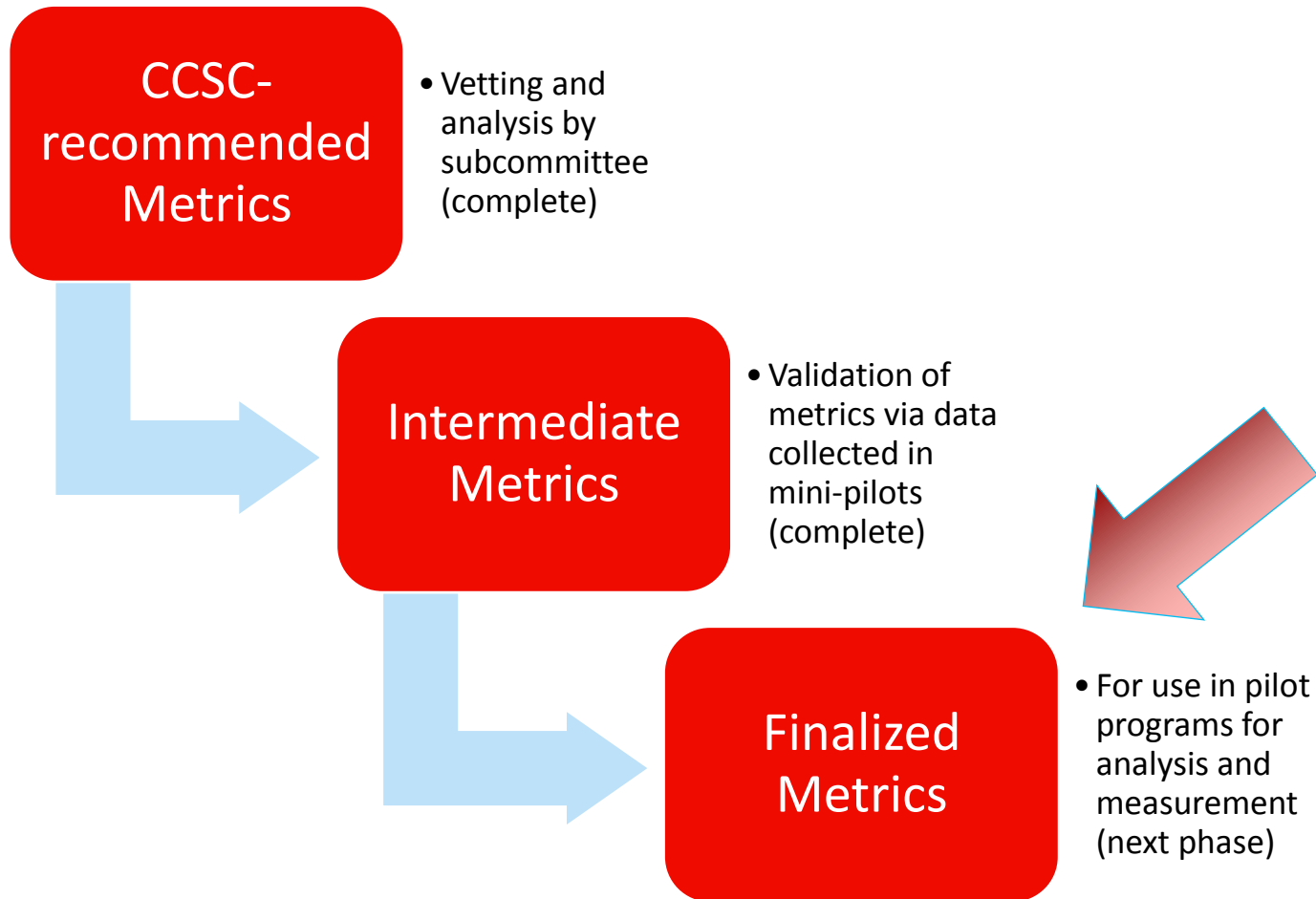
# The CCSC Initiative Strives to Facilitate Payer-Provider Collaboration



- Ongoing quality improvement (QI) and cost management initiative
- Driven by the insights of a prominent group of stakeholders:
  - Hemophilia treatment center (HTC) directors, clinicians, and administrators
  - Payer/managed care medical and pharmacy directors from a mix of large national and regional health plans
- Developing a framework for metric-driven pilot programs incorporating data reporting between payers and HTCs to be replicated across the United States

**Goal: facilitate cost-effective hemophilia management integrating the HTC comprehensive care model**

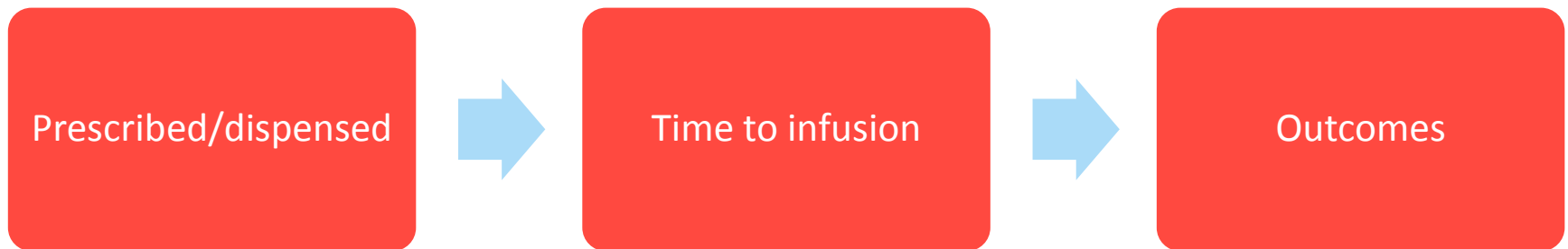
# CCSC Metric Development Process



# CCSC Development of Metrics



- Based on the data collection and reporting experiences presented by HTC and payer advisors participating in mini-pilot initiatives, a consensus was reached on the metrics to capture data that accurately reflects true outcomes and costs
- Discussion of the metrics commenced with a model used in previous CCSC meetings, followed by eventual agreement on finalized metrics



# CCSC Finalized Metrics



- Advisors designated 5 distinct metrics each considered desirable for the purposes of meaningful data sharing and collaboration
- Metrics were subsequently discussed in detail to refine specific components to be included in data collection and reporting

## Payer Metrics

Prescribed dose/dispensed dose/weight ( $\pm$ range)

Number of bleeds/time to treatment

ED visits/hospitalizations

Unit cost of factor

Total cost per patient

## HTC Metrics

Prescribed dose/dispensed dose/weight ( $\pm$ range)

Number of bleeds/time to treatment

ED visits/hospitalizations

Home infusion (%)

Points of contact

# Finalized Metrics

## *Patient Classification*



To be reported by the HTC, as payer claims data does not provide all of the pertinent detail:

- Diagnosis (A or B)
  - Severity (mild, moderate, or severe)
  - Inhibitor status (Y or N)

# Finalized Metrics

*Prescribed dose/dispensed dose/weight ( $\pm$ range)*



To be reported by the HTC's using an integrated pharmacy model or payers if an SPP is used for factor dispensation:

- Product
- Total units
- U/kg
- Units dispensed
- **Prescribed dose/dispensed dose**
  - $\pm$ 10% according to MASAC guidelines; payers desire  $\pm$ 5%

*Crucial for payers*



# Finalized Metrics

## *Number of bleeds/time to treatment*



To be reported by the HTC:

- Total number of bleeds
- Type of bleed (joint or non-joint)
- Type of treatment (prophylaxis or on-demand)

# Finalized Metrics

## *ED visits/hospitalizations*



To be reported by both the HTC and the payer:

- ED visit with hemophilia listed as 1° or 2° diagnosis code (ie, in the first two lines of the claim)
  - While payers have ED data, they do not always have the details to understand the specifics for a given patient scenario



# Finalized Metrics

## *Cost of factor*



To be reported by the payer:

- Total factor cost
- Total factor cost/patient
- Site of care
  - Facility (hospital/ED)
  - Ambulatory (infusion center, physician's office, HTC)
  - Home/self

# Finalized Metrics

## *Home infusion (%)*



As an indicator of cost-saving, to be reported by the HTC:

- Percent of patients/families independently infusing at home
- Percent of patients/families infusing at home with nursing assistance

# Finalized Metrics

## *Total cost per patient*



To be reported by the payer:

- Total cost of pharmacy claims
- All other medical claims costs
- Total cost per patient

# Finalized Metrics

## *Patient contacts*



As an indicator of quality care, to be reported by the HTC:

- Comprehensive care visits
- Other visits
  - Follow-ups
    - Medical provider
    - Social work
    - Nurse
    - PT
  - Patient/family education
  - Infusions
  - Offsite visits (home and school)
- Collaboration with other providers
- Telemedicine
- Case management contacts
  - Telephone
  - E-mail
  - Text

# Summary



- Data collection and reporting on the part of both payers and HTC's can be used to identify best practices and areas for care process improvements
- HTC's and individual providers routing factor dispensation through SPPs also play an important role in data reporting
- Transparency and communication are key to this collaborative process which may be facilitated by quality metrics and pilot programs recently developed as part of the CCSC initiative

# The Evolving Hemophilia Managed Care and Specialty Pharmacy Environment:

## Recommendations for a New Health Care Ecosystem



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# Measuring Success: Tools and Resources to Document Outcomes of Payer and Specialty Pharmacy Hemophilia Management

**Michael Zeglinski, RPh**

Senior Vice President, Specialty Pharmacy

OptumRx<sup>®</sup>/BriovaRx<sup>®</sup>

# Faculty Disclosure



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## **Michael Zeglinski, RPh**

- *Consulting Fees: Sanofi*



# The Evolving Role of Specialty Pharmacy



## Manage Patient

- Access to service
- Holistic care model

## Manage Outcomes

- High quality care focus
- Adherence & persistency

## Manage Payer

- Control spend
- Demonstrate quality care services
- Network requirements

# Managing the Complexities of Specialty Pharmacy is Multi-Faceted



Improving Member  
Well-Being



Providing Proactive  
Service



Balancing Cost  
& Care

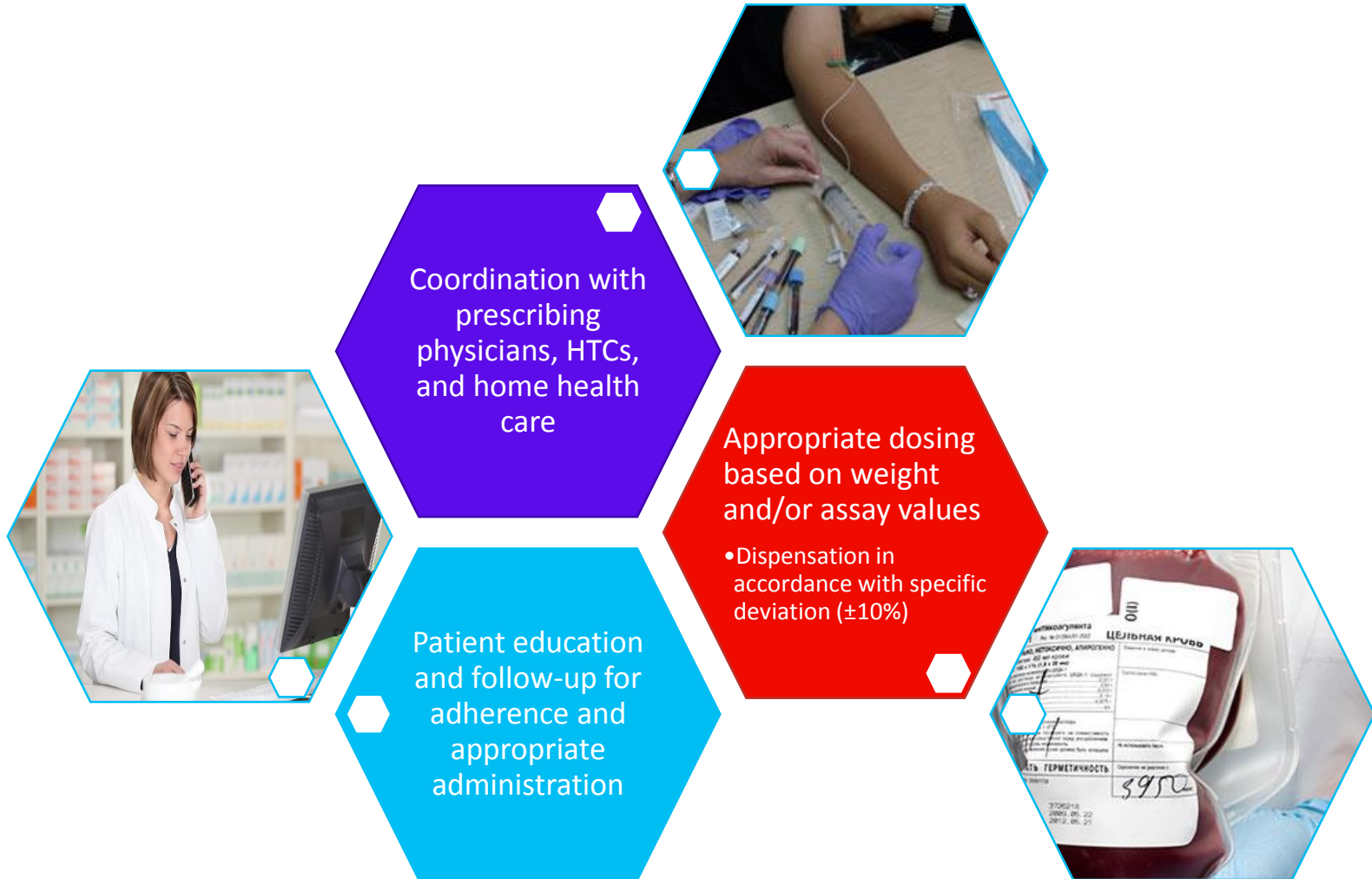


Connecting  
Communities

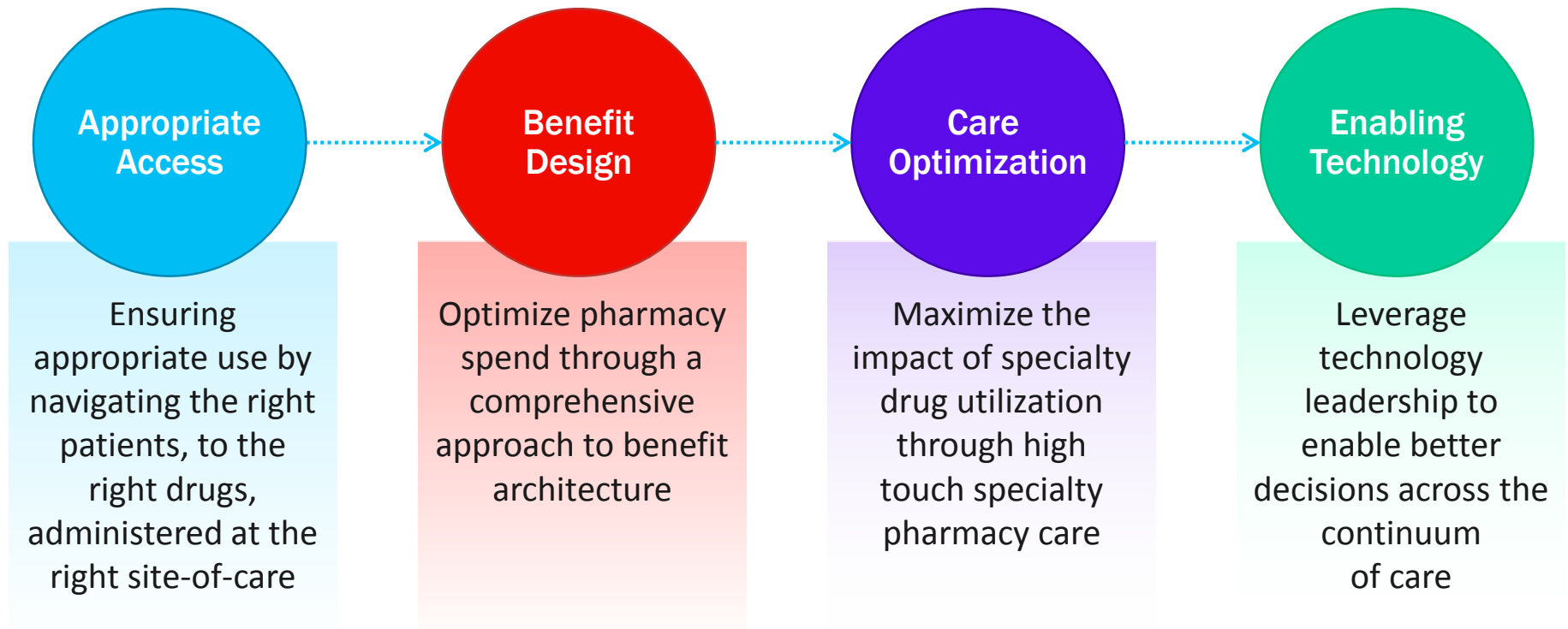


Driving Outcomes  
through Clinical  
Excellence

# Key Components of Specialty Pharmacy Care in the Management of Hemophilia



# Strategies for Improving Outcomes While Managing Spend



# Patient Engagement Improves Outcomes While Managing Cost



## Innovative Tools & Resources

- Video consultation
- Educational videos
- Mobile app
- Individualized plan of treatment

## Promoting Quality Outcomes

- Dedicated clinical management team
- Intervention based monthly assessment and monitoring

## Managing Payer Cost

- Manage appropriateness of treatment
- Monitoring of in-home inventory
- Minimal assay variance

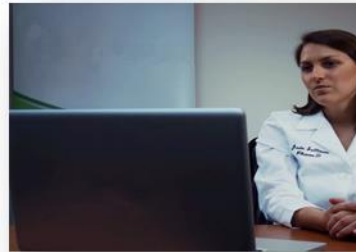
# Innovative Tools and Resources

## Promote Engagement and Adherence



### Live Multimedia

Live video education and counseling sessions with pharmacist



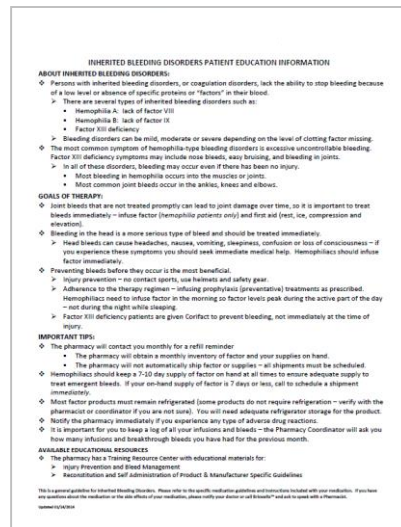
### Web-based Tools & Mobile App

Easily accessible information to connect patients with education tools and community resources



### Written Patient Information Guide

Written resources to promote understanding of condition and treatment



### Community Resources

Educational and instructional videos designed to engage patients in disease management & treatment



# Important Components of Hemophilia Patient Education Messaging



Highlighting the importance of adherence

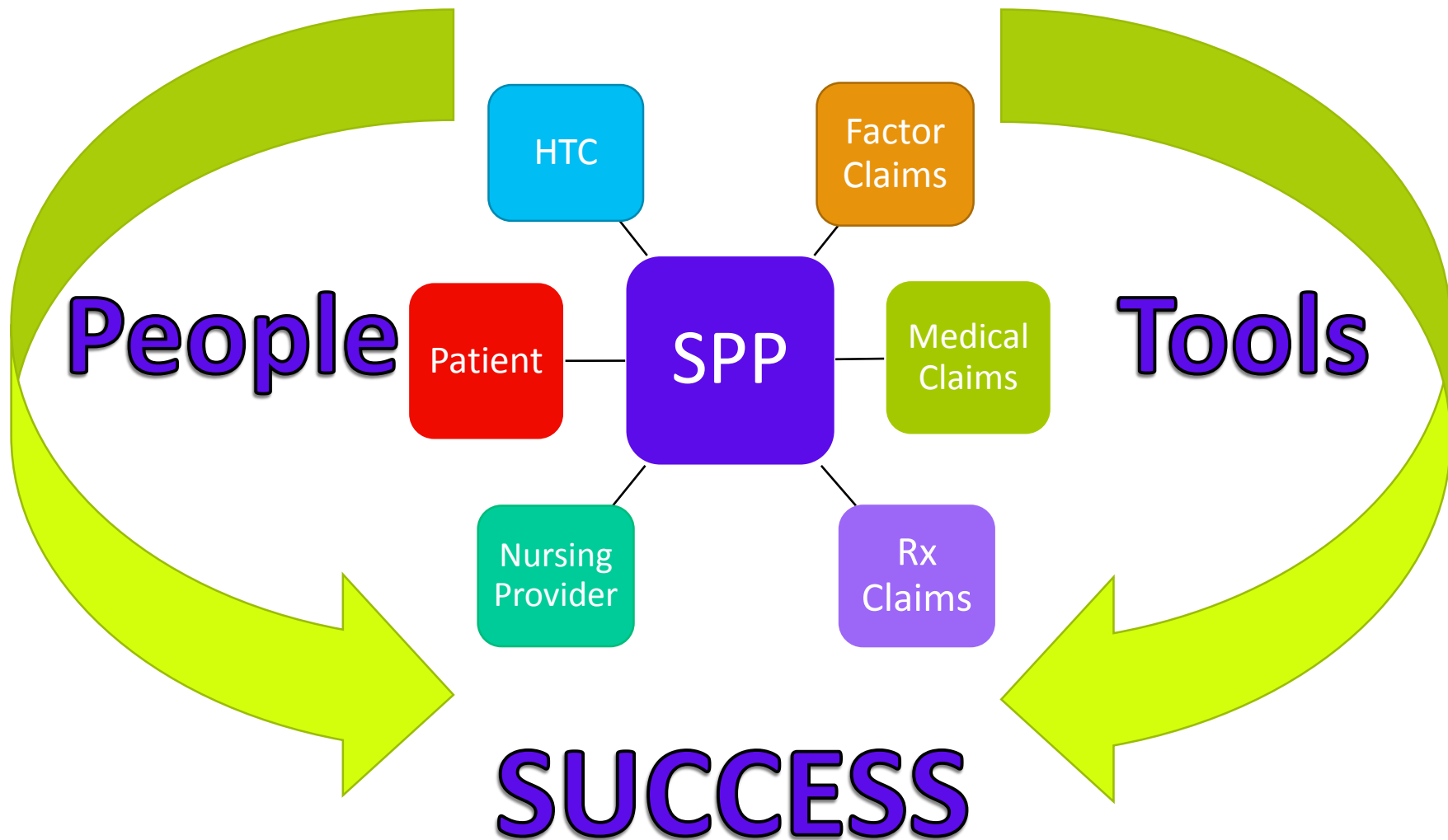
Self-administration technique and training

Preparing for and coping with adverse events

Clotting factor concentrate storage

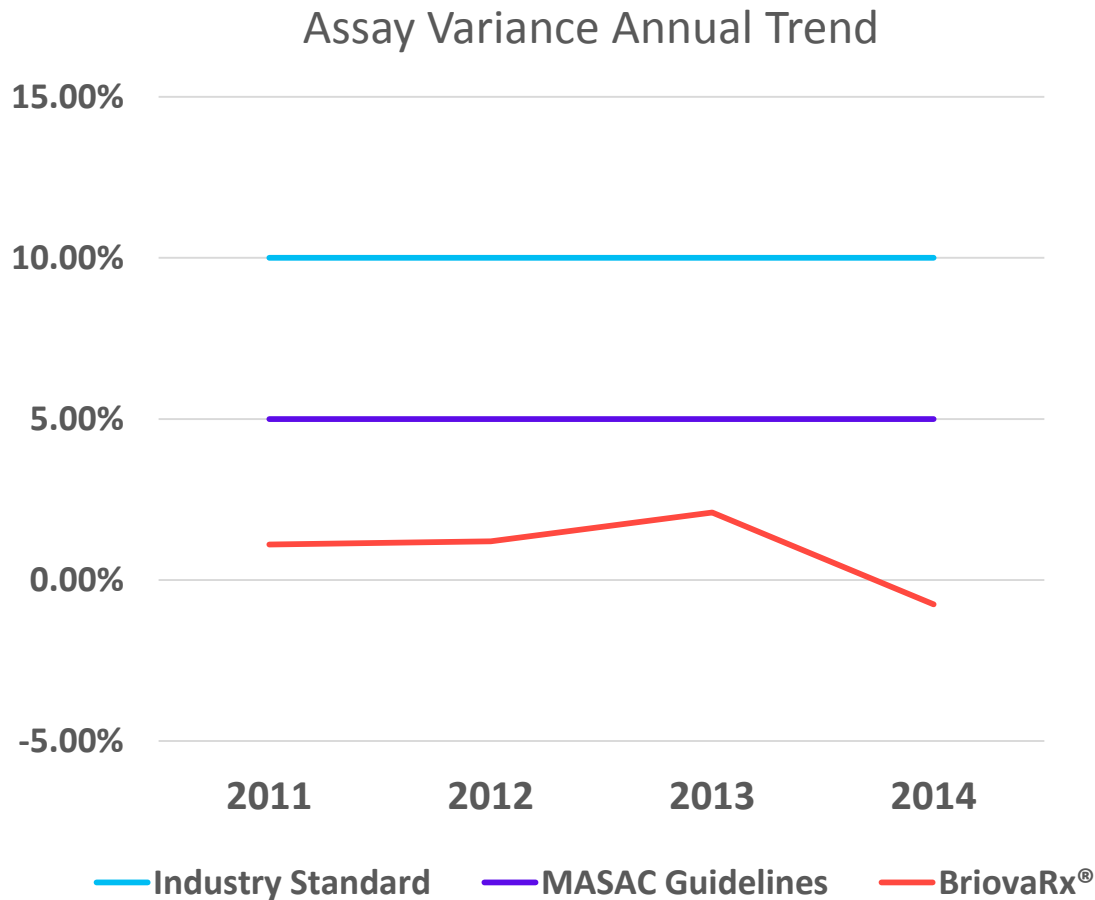
Immediate treatment for breakthrough bleeding

# The Formula for Successful Hemophilia Management and Quality Care





# Assay Prescription Management Results: Annual Trend



MASAC recommendations regarding standards of service for pharmacy providers of clotting factor concentrates for home use to patients with bleeding disorders. <http://www.hemophilia.org/sites/default/files/document/files/masac188.pdf>. Accessed July 30, 2015.

# Assay Prescription Management Results: Payer Savings



## Sample Savings Model\*

Variance	Dose (IU)	Cost PMPM**	Cost PMPY
10%	1650	\$19,800	\$237,600
5%	1575	\$18,900	\$226,800
2%	1530	\$18,390	\$220,680

**Lower variance drives  
cost down for payers**

- \$16,920 annual savings at 2% variance compared to 10%

\*Based on 40% desired factor rise for 75kg FVIII severe deficiency patient

\*\*Calculated at cost of \$1.00 per IU for 12 doses per month

PMPM=per member per month; PMPY=per member per year

# Summary



- Specialty pharmacies are increasingly called upon to provide quality care in the management of patients with costly chronic diseases such as hemophilia
- In certain scenarios, SPPs may be called to coordinate care and data management for these patients
  - Coordination with prescribing physicians, HTC's, and home health care
  - Appropriate dosing based on weight and/or assay values
  - Patient education and follow-up for adherence and appropriate administration
- Quality improvement initiatives must likewise be driven through the specialty pharmacy, which is relied upon for data collection and reporting

# The Evolving Hemophilia Managed Care and Specialty Pharmacy Environment:

## Recommendations for a New Health Care Ecosystem



Jointly provided by





# HTC, Managed Care, and Specialty Pharmacy Collaboration

**Case-based Presentations**



## Brian, a 37-year-old Male with Severe Hemophilia A

Managed by an HTC Using  
an Integrated Pharmacy Model

# Brian, 37-year-old Male with Severe Hemophilia A



- Severe hemophilia A, intron 22 inversion, and a history of intermittent on-demand FVIII replacement
- Presented for the first time at an HTC with severe arthropathy after a recent change in employment/insurance coverage
- Reports history of an inhibitor in childhood that resolved without specific treatment
- HIV positive and is well managed on his current antiretroviral regimen
- Arthropathy of both knees and the right ankle

# Social/Family History



- Single with variable employment history; recently obtained a new position in restaurant equipment sales
- No dependants, lives alone
- Commercial health coverage through his new employer
- Despite severe disease, reports bleeding 1 to 2 times per month, mostly in knees



# Initial HTC Assessment



Brian underwent an initial comprehensive care visit and assessment by HTC staff:

- Nurse
  - Disease overview, number and sites of bleeds
  - Patient education regarding potential need for prophylaxis in the future based on the hematologist's assessment
- Hematologist
  - Discussion of previous bleeding events and general health history
  - Discussion of arthropathy and surgical intervention based on cumulative damage that has accrued in knee
  - Review of HIV management
- Physical Therapist
  - Performs assessment on musculoskeletal and functional status
  - Discusses an individually tailored exercise program based on Brian's knee deterioration, including a focus on strengthening other joints
  - Discusses expectation of outcomes if surgery is ordered
- Social Worker
  - Discusses Brian's concerns related to employment and the adverse effect that surgery may have on work obligations

# Surgical Procedure



- Bilateral total knee arthroplasty (TKA) was recommended by the orthopedist after consultation with the hematologist and physical therapist due to intense pain and difficulty walking
- Started on a preoperative FVIII regimen to achieve plasma factor levels of  $\geq 80$  IU/dL
- Underwent bilateral TKA and developed a 20 BU inhibitor during the immediate postoperative period

# Postsurgical Intervention



- Because of continuing oozing at the surgical wound, Brian was switched to rFVIIa 90  $\mu\text{g}/\text{kg}$  administered every 2 h and then modified based on clinical response
- rFVIIa was discontinued, and aPCC 50 IU/kg every 8 h was used to achieve hemostasis in preparation for discharge

# Inhibitor Management



- Immune tolerance induction (ITI) was started with daily rFVIII 100 IU/kg; aPCC was used to control intercurrent bleeding
- Inhibitor initially peaked at 30 BU
- Over the next 12 months with daily infusion, inhibitor was eradicated and his functional status improved
- Due to the demands of his job, Brian remained on self-administered rFVIII prophylaxis at a dose of 50 IU/kg QOD

# Long-Acting rFVIII for Prophylaxis



- Upon follow-up visit with the HTC, Brian voiced concern regarding the inconvenience of prophylactic regimen in light of daily responsibilities of his job
- In particular, he mentioned missing at least 1 dose per week due to travel and other occupational demands
- Brian also complained of persistent pain in the right ankle, and is showing early signs of worsening arthropathy after further assessment
- Taking these concerns into consideration, the hematologist prescribed a recently approved long-acting rFVIII concentrate

# Payer Review/Claims Approval



- After submitting the claim for newly approved long-acting rFVIII concentrate, the HTC pharmacy awaited approval before filling prescription
- Payment of the claim was held pending further review; request for submission of supporting information from the hematologist
- Hematologist called the payer and made note of Brian's adherence concerns and occupational demands in claim submission, citing the bilateral TKA and signs of damage in the right ankle
- Claim for long-acting rFVIII was paid after receiving additional information from hematologist

# Conclusion



- Brian has been adherent to his new long-acting rFVIII concentrate prophylactic regimen
  - Accredited change in adherence to the new regimen being less of an inconvenience to his work schedule
- Damage in Brian's right ankle has been limited
  - With regularly scheduled physical therapy provided through the HTC and a home exercise regimen, no further surgery has been required

# Faculty Discussion



## Clinical

- What patient characteristics do you take into account when considering a long-acting factor product?
- Can you comment on the impact of these products thus far from a patient experience/adherence perspective?

## Payer/SPP Management

- What are your current processes for the review and addition of long-acting factor products to your formulary?
- Do you have specific criteria in place for the approval of a claim for one of these agents?
- Can you comment on the clinical and financial impact that long-acting factor products and newer recombinant products have had on the payer and SPP operations?





## Kevin, 5-year-old Male with Severe Hemophilia A

Managed an HTC with Factor Dispensation Via Specialty Pharmacy Provider

# Kevin, 5-Year-Old Male with Severe Hemophilia A



- Diagnosed at birth with severe hemophilia A
- Lives in rural community and is transported to an HTC as necessary, with at-home factor delivery provided through a specialty pharmacy provider (SPP)
- At age 2, following 10 exposures to rFVIII concentrate for soft tissue and joint bleeding, patient developed an inhibitor (peak titer, 250 BU)

# Family Background



- Youngest of 3 children, with one brother who has hemophilia and history of inhibitors that resolved with ITI
- Kevin and his older brother travel to the nearest HTC for comprehensive care visits, which is 4 hours away by car
- Assays and other lab work are routed through a local laboratory that reports results to the HTC
- Family has been financially burdened by the out-of-pocket costs of caring for two children with hemophilia with inhibitors

# Inhibitor Management: ITI



- ITI was recommended to eradicate the inhibitor but was delayed to allow the inhibitor titer to drop to 10 BU
- Before ITI started, bleeding episodes were treated on-demand with rFVIIa delivered via the SPP
- The HTC received ongoing results from the local laboratory to monitor titer monthly and subsequently sent an order to SPP when the requisite level was reached (9 BU)
- A home health agency, contracted through the SPP, made an initial visit to educate the family on administration of ITI with rFVIII at a dose of 200 IU/kg per day
- The inhibitor titer peaked at 450 BU and then gradually decreased, but never fell below 30 BU, and ITI was discontinued after 24 months of therapy

# Inhibitor Management: Bypassing Agent Prophylaxis



- After discontinuing high-intensity ITI, Kevin began to experience repeated left ankle bleeds that were treated on-demand with rFVIIa provided through the SPP
- Upon notification of increased factor delivery to the patient's home from the SPP, the HTC followed-up with the family and hematologist suggested prophylaxis with a bypassing agent
- To avoid the potential complications associated with an in-dwelling line, the family was again trained by the SPP-contracted home health agency on peripheral infusion techniques
- Prophylaxis began with aPCC at 85 IU/kg 3x weekly in lieu of daily rFVIIa

# 3-Month HTC Follow-Up



- The family visited the HTC 3 months after initiation of aPCC prophylaxis for further evaluation
- While bleeding frequency had decreased, Kevin had suffered 3 hemarthroses during 3 months of prophylaxis, indicating that the prophylactic regimen needed to be revisited
- Based on a discussion the family had with the HTC social worker regarding financial troubles, the hematologist queried the SPP regarding delivery of aPCC
  - Although the family claimed to be adherent to the regimen, it was discovered that several shipments were not received
- Rather than modifying the aPCC regimen to be administered every other day, the HTC case manager made arrangements for the family's enrollment in a copay assistance program to facilitate adherence to the current regimen

# Subsequent Follow-Up Visit



- After another 3 months of 3x weekly aPCC, Kevin was determined to be well managed upon the family's next visit to the HTC
- HTC follow-up calls with the family in the interim, as well as follow-up with the SPP to determine that aPCC shipments were being received at the home, confirmed adherence

# Conclusion



- Kevin has experienced no additional breakthrough bleeding on 3x weekly aPCC at 85 IU/kg
- The HTC continues to monitor adherence via follow-up calls to the parents and product delivery reports from the SPP
- Current prophylactic regimen will be continued for an additional 3 months before reevaluation



# Faculty Discussion



## Clinical

- What clinical criteria play a role in determining the best course of management when encountering a patient with an inhibitor?
- Can you describe the advantages and disadvantages of both ITI and the use of bypassing agents in the management of inhibitors?

## Payer/SPP Management

- Can you describe the different ways in which SPPs support HTCs and community hematologists in the management of patients with hemophilia?
- What tools and interventions do SPPs have at their disposal for addressing hemophilia-specific challenges such as in-home infusion and therapeutic adherence?
- How would you characterize the interaction of SPPs with HTCs and payers in terms of means and frequency of contact and data/information sharing?

# The Evolving Hemophilia Managed Care and Specialty Pharmacy Environment:

## Recommendations for a New Health Care Ecosystem



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