Interventions for Hemophilia A & B: Clinical Practice Guidelines & Cost-effectiveness

Prepared for the Washington State Bleeding Disorder Collaborative for Care

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Dr. Ray has no conflicts of interests to disclose

Presentation Overview

- Background
- Prior MED Work
- PICO and Objectives
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- Findings
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  - Economic Evaluations
- Summary and Limitations

Background

- Hemophilia is a rare, X-linked, inherited bleeding disorder
  - Insufficient or dysfunctional factor VIII (A) or IX (B)
- Half of patients experience severe disease
  - Characterized by spontaneous bleeding episodes
- Morbidity and mortality arise from bleeding episodes
  - Into brain, joints, head/neck tissues, or deep muscles
- Treatment evolved from whole blood infusions, to isolated factors, now includes recombinant factor products
- Center for Evidence-based Policy (Center) report includes a full list of treatment interventions

Prior MED Work on Hemophilia

Home Care Services and Utilization Management for Appropriate Use of Factor Replacement Therapy in Patients with Hemophilia

Participant Request

March 2016

Use of Ultrasound to Diagnose Hemarthrosis and Monitor Joint Health in Hemophilia

Participant Request

March 2016

Weight-based Dosing Strategies for Factor Replacement Therapy in Hemophilia A and B

Participant Request

March 2016

All reports available at the MED clearinghouse

PICO and Objectives

- **PICO**
  - **Population:** Adult or pediatric patients with hemophilia A or B
  - **Intervention:** Full list included in Table 2 of the Center report
  - **Comparison:** Usual care, other active interventions
  - **Outcomes:** Direct and indirect economic costs; cost-effectiveness
- **Objectives**
  - Summarize clinical practice guidelines for interventions
  - Summarize evidence on estimated direct and indirect medical costs, non-medical costs, and cost-effectiveness for interventions

Interventions

Factor VIII Agents	
Human	Hemofil M, Koate-DVI, Monoclate-P
Recombinant	Eloctate, Helixate FS, Kogenate FS, Novoeight, Nuwiq, Recombinate, Refacto
Recombinant Porcine	Obizur
Recombinant/ Albumin Free Method	Advate
Recombinant Factor /Platelet Activating Factor	Xyntha
Human/Won-Willebrand Factor Complex	Alphanate, Humate-P, Wilate
Factor IX Agents	
Human	AlphaNine SD, Mononine
Recombinant	Alprolix, BeneFIX, Ixinity, Rixubis
Prothrombin Complex Concentrates (PCC)	
Human/ 3-factor	Bebulin, Bebulin Vapor Heated (VH), Profilnine, Profilnine Solvent/Detergent treated (SD)
Human/ 4-factor	Kcentra
Bypass Agents	
Human Activated PCC	FEIBA
Recombinant Factor VIIa	NovoSeven RT

Methods

- **Search strategy**
  - Medicaid Evidence-based Decisions Project (MED) core evidence and guidelines sources
  - Ovid MEDLINE® search
    - Systematic reviews, meta-analyses, technology assessments
    - Published after 1/1/2006
    - English
- **Quality assessment**
  - Methodologic quality assessed using standardized MED tools
  - Rated as good, fair, or poor methodologic quality

Overview of Findings

- **Guidelines**
  - National Blood Authority of Australia (***DRAFT***)
  - Nordic Hemophilia Council (Nordic)
  - United Kingdom Haemophilia Centre Doctors Organization (U.K.)
  - World Federation of Hemophilia (WFH)
- **Evidence on Costs**
  - No estimates of costs or outcomes comparing specific clotting factors identified
  - One systematic review analyzed estimates of costs for the use of bypass agents in patients with inhibitors

Findings: Guidelines

- **Identified 4 clinical practice guidelines**
  - Methodologic quality
    - Poor: Nordic, UK, WFH
    - Fair: Australia
  - Quality downgraded for absence of clearly defined evidence process, method of translating evidence to recommendations, editorial independence

Findings: Guidelines

- Australia, Nordic and UK guidelines all recommend recombinant factors over plasma-derived
- WFH recommends both viral eradicated plasma-derived and recombinant factors
- All support prophylaxis beginning by age three and second clinical bleeding episode
- No single prophylaxis regimen was recommended
- rFVIIa or aPCC recommended for individuals with inhibitors

Findings: Cost-effectiveness

- **Systematic review on estimates of costs for use of bypass agents in patients with inhibitors**
  - Fair methodologic quality
  - Total direct medical costs to treat single episode in home (*in 2010 U.S. dollars)*
    - aPCC: $11,485-$49,010
    - rFVIIa: $9,078-$49,507
  - Efficacy estimates frequently based on industry funded single arm trials (9 of the 11 included studies)
  - With higher efficacy and lower doses for their product
  - Authors note, head-to-head trials do not demonstrate superior efficacy for either product

Hay, J. & Zhou, Z. *J Med Econ;* 14(4)

Findings: Narrative Reviews

- **Estimates of costs and outcomes for prophylaxis vs. on-demand therapy**
  - Estimates range from cost-saving and clinically beneficial (i.e. “dominant”) to over €1 million per QALY
  - Author recommends adherence to established published guidelines for economic evaluations to allow accurate comparisons
- **Estimates of costs and outcomes for bypass agents**
  - Depending on efficacy estimates rFVIIa or aPCC may be best value
    - rFVIIa better value when efficacy is >90% vs. 60% for aPCC
    - aPCC better value when efficacy equal (85% both)

Miners, A. *Hemophilia.* 2013;19(2); Baghaipur, M. & Steen Carlsson, K. *Eur J Haem.* 2015;94(s77)

Findings: Multinational Estimates for Prophylaxis

- **Sweden and Netherlands implemented prophylaxis in 1960s with different protocols**
  - As of 2013, a citizen with Hemophilia A:
    - In the Netherlands, uses 3 x 1000 IU of FVIII/week
    - In Sweden, uses 3 x 1500 to 2000 IU every other day
  - At a median age of 24 years, more of the Swedish cohort remained free of significant arthropathy (98% vs. 54%, $p<0.01$)
  - Mean annual costs in US dollars: $179,600 (Dutch) vs. $297,900 (Swedish), difference largely driven by factor costs
  - Notably, Dutch children initiated prophylaxis nearly a year later than the Swedes (1.8 years vs. 0.6 years, $p<0.01$)

Fischer, K., et al. *Blood;* 122(7)

Summary and Limitations

- Limited literature on costs related to treatment for hemophilia
  - Available evidence often biased by industry-funded estimates of efficacy and dosing
- All clinical practice guidelines support prophylaxis
- Majority of guidelines support recombinant factors over plasma-derived
- Future treatments, including potential for gene therapy, are likely to increase intervention costs, but may have long-term safety profiles which decrease medical costs and improve quality of life

Questions?


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