



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

Participant Request

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**Center for Evidence-based Policy
Medicaid Evidence-based Decisions Project (MED)**

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Objectives

- To summarize the evidence for the effectiveness and cost effectiveness of different home-care services for patients with hemophilia
- To describe utilization management options for the appropriate use of factor replacement therapy in patients with hemophilia

Key Findings

- Home-based factor replacement is recommended as the standard of care for patients with hemophilia
- There is no comparative evidence on different home management strategies for patients with hemophilia
- Pharmacy and utilization management options are available to manage costs associated with factor replacement therapy, without decreasing quality of care

Background

Hemophilia is an inherited clotting disorder characterized by recurrent bleeding episodes. The most common types of hemophilia are hemophilia A, also known as factor VIII deficiency, and hemophilia B, or factor IX deficiency. Both are X-linked inherited disorders that manifest in male children of carrier females. Hemophilia A is the more common type, occurring in about 1 in 5,000 live male births, compared to hemophilia B, which occurs in about 1 in 30,000 live male births (Hoots & Shapiro, 2016a). Hemophilia is classified as mild, moderate, or severe based on factor activity level. Those with severe hemophilia are more likely to have spontaneous bleeding and be younger when they experience their first bleeding episode. Hemophilia A is more likely to be severe than is hemophilia B (Hoots & Shapiro, 2016a).

Factor Replacement Therapy

Factor VIII and IX products are used to treat hemophilia A and B, respectively. Factor products are derived from human plasma or produced from cell lines (recombinant products). Factor replacement is used to treat acute bleeding episodes, or as prophylaxis to prevent bleeding. Prophylactic factor replacement therapy is further classified as primary, secondary, tertiary, or intermittent (periodic) (Table 1) (Srivastava et al., 2013). The goal of prophylaxis is to prevent bleeding and to preserve normal musculoskeletal function. Clinical practice guidelines recommend tailoring prophylactic treatment as much as possible (Srivastava et al., 2013).

Table 1. Description of Factor Replacement Therapy Protocols

Protocol	When Initiated
Episodic treatment	At the time of clinically evident bleeding; to treat pain and serious bleeding
Primary prophylaxis	Before second joint bleed, in the absence of documented joint disease
Secondary prophylaxis	After second joint bleed and before onset of joint disease
Tertiary prophylaxis	After onset of joint disease
Intermittent prophylaxis	Given to prevent bleeding for periods not exceeding 45 weeks in a year

Source: Adapted from Srivastava et al., 2013

Factor replacement prophylaxis is the standard of care for children with severe hemophilia (Srivastava et al., 2013), and has been shown in randomized controlled trials to improve outcomes (Aronstam et al., 1976; Astermark et al., 1999; Feldman et al., 2006; Fischer et al., 2002; Gringeri et al., 2011; Manco-Johnson et al., 2007). However, prophylaxis requires more factor usage and is about three times more costly than episodic treatment (Medicaid Health Plans of America, 2013). In settings with significant resource constraints, lower doses of prophylaxis given more frequently may be an effective option (Srivastava et al., 2013). In very young children, one option is to start prophylaxis frequency at once a week and increase depending on bleeding and venous access.

About 30 percent of patients with hemophilia will develop inhibitors at some point (Hoots & Shapiro, 2016b). The cost of treatment for these patients may be up to four times higher than for those without inhibitors (Medicaid Health Plans of America, 2013).

Hemophilia Treatment Centers

In 1975, Congress authorized the creation of a network of comprehensive, multidisciplinary Hemophilia Treatment Centers (HTCs). These HTCs focus on preventive services, education, and family support, and include a team of providers including hematologists, pediatricians, nurses, social workers, physical therapists, orthopedists, and dentists. Today, about 70% of the approximately 20,000 individuals with hemophilia in the United States receive care at a HTC (National Hemophilia Foundation, 2015).

The Veterans Health Care Act of 1992 designated federally-funded HTCs as covered entities eligible to participate in the 340B Drug Pricing Program. About 100 of the 141 HTCs in the United States have elected to participate in the 340B Program. Under federal grant requirements, all revenues from the 340B program must be invested back into patient services, care coordination, research and other programs that directly benefit patients (National Hemophilia Foundation, 2015).

Home Infusion

Prior to establishment of HTC, most bleeding episodes were treated in hospitals or emergency departments. Between 1990 and 2010, the number of patients with hemophilia on a home therapy program increased 37%, from 4,442 to 6,166. In 2010, 77% of patients with severe hemophilia, 51% of those with moderate hemophilia, and 21% of those with mild hemophilia used home infusion therapy (Baker et al., 2013). Patients using home infusion receive education, monitoring, and support through a HTC (Teitel et al., 2004). Most HTCs include integrated pharmacy services and provide for or arrange infusion services (Medicaid Health Plans of America, 2013).

PICO and Key Questions

Populations

- Adults or children with hemophilia A or B

Interventions

- Continuous or episodic home nursing
- Multidisciplinary home care team visits

Comparator

- Usual care

Outcomes

- Joint bleeding
- Change in management
- Total factor use
- Hospital admission or readmission
- Physical function
- Quality of life

Key Questions

1. What is the effectiveness and cost-effectiveness of continuous or episodic home nursing care for patients with hemophilia?
2. What is the effectiveness and cost-effectiveness of episodic multidisciplinary home care team visits for patients with hemophilia?
3. What strategies or pathways have been described for utilization management of factor replacement for patients with hemophilia?

Methods

Center for Evidence-based Policy (Center) staff searched Medicaid Evidence-based Decision Project core sources for evidence and guidelines on home-based services for hemophilia (See Appendix A for search strategy). Center staff also conducted internet searches using terms for hemophilia, factor replacement, Medicaid, and utilization management to identify additional information on utilization management for factor replacement therapy.

Findings

Comparative Effectiveness and Cost Effectiveness of Home Nursing

Center staff identified no studies addressing the comparative effectiveness or cost effectiveness of different strategies for providing home health services for patients with hemophilia, and no studies evaluating the effectiveness or cost effectiveness of episodic multidisciplinary home care team visits versus usual care for patients with hemophilia.

Clinical Practice Guidelines on Home Factor Administration

The World Federation of Hemophilia (WFH) guidelines recommend home management for people with hemophilia “where appropriate and possible” (Srivastava et al., 2013). They specify that home factor replacement treatment must be supervised closely by the comprehensive care team and should only be initiated after adequate education and training. The recommendations do not address details of home nursing or team care such as frequency of episodic visits, however.

A frequently cited source for recommendations regarding home treatment is a narrative review published in 2004 (Teitel et al., 2004). This was not a systematic review; authors did not assess the methodological quality of included studies, report a literature search strategy, or specify study inclusion and exclusion criteria. The researchers summarized early studies demonstrating quality of life benefits for home treatment. These studies found that children on home treatment experienced decreased hospitalization and time lost from school, better integration with peer groups, and less pain (Ekert, Moorehead, & Williamson, 1981; Lazerson, 1972; Levine & Britten, 1973; Rabiner & Telfer, 1970). Studies of home treatment also reported positive effects on family life, including less tension and greater flexibility in arranging family activities (Ekert et al., 1981; Rizza & Spooner, 1977; Wincott, 1977). Adult men reported better quality of life as well, including greater feelings of self-sufficiency and self-confidence, and less negative emotions such as fear, anger, and depression (Ingram et al., 1979; Rabiner, Telfer, & Fajardo, 1972; Rizza & Spooner, 1977). Men also experienced less work absenteeism and more employment stability (Szucs et al., 1998).

Utilization Management of Factor Replacement for Patients with Hemophilia

The Medicaid Health Plans of America has published an [issue brief](#) on hemophilia treatment in Medicaid Managed Care (Medicaid Health Plans of America, 2013). This report provides an overview of issues related to Medicaid plan members with hemophilia, including considerations for cost management and pharmacy management. Recommendations related to cost management are excerpted below.

- Work with state policy leaders to develop an effective purchasing strategy for factor under Medicaid (either through a 340b or with sufficient rebates)
- Monitor factor costs to identify the most cost effective purchasing route
- Ensure that factor dosing is within recommended parameters and generates the appropriate clinical response for preventive and acute care (assay management)
- Ensure that pharmacy benefit managers or specialty pharmacy providers carry out the full scope of required factor management services, patient education, home care services and medical waste management
- Prevent wasted factor by ensuring appropriate pharmacy management and developing protocols for the number of doses kept in the patient homes
- Prevent acute or catastrophically expensive complications by coordinating with hospitals and other providers to plan for elective and emergency conditions
- Monitor and evaluate the total cost of care, including inpatient and emergency services, to evaluate use of avoidable acute care

Conclusions and Limitations

Center staff identified no evidence on the comparative effectiveness of different home care strategies (continuous vs episodic nursing care, team visits) for patients with hemophilia. Factor replacement in the home setting is considered the standard of care in patients with hemophilia based on reports of improved quality of life and community integration for both children and adults. Guidelines recommend home administration but are silent on the specific aspects and details of home nursing or multidisciplinary support strategies.

Appendix A: Search Strategy

Database: Ovid MEDLINE(R) <1946 to February Week 4 2016>

1 hemophilia.mp. or exp Hemophilia A/

2 hemophilia b.mp. or exp Hemophilia B/

3 exp Factor VIII/ or factor replacement.mp.

4 factor ix.mp. or exp Factor IX/

5 1 or 2 or 3 or 4

6 exp Home Nursing/

7 exp Home Care Services/ or home-based services.mp.

8 6 or 7

9 5 and 8

10 limit 9 to (english language and humans)

11 limit 10 to yr="2002 -Current"

References

- Aronstam, A., Arblaster, P. G., Rainsford, S. G., Turk, P., Slattery, M., Alderson, M. R., ... Kirk, P. J. (1976). Prophylaxis in haemophilia: a double-blind controlled trial. *British Journal of Haematology*, 33(1), 81-90.
- Astermark, J., Petrini, P., Tengborn, L., Schulman, S., Ljung, R., & Berntorp, E. (1999). Primary prophylaxis in severe haemophilia should be started at an early age but can be individualized. *British Journal of Haematology*, 105(4), 1109-1113.
- Baker, J. R., Riske, B., Drake, J. H., Forsberg, A. D., Atwood, R., Voutsis, M., & Shearer, R. (2013). US Hemophilia Treatment Center population trends 1990-2010: patient diagnoses, demographics, health services utilization. *Haemophilia*, 19(1), 21-26. DOI: <http://dx.doi.org/10.1111/j.1365-2516.2012.02915.x>
- Ekert, H., Moorehead, M., & Williamson, G. (1981). Home treatment of haemophilia. A follow-up study. *Medical Journal of Australia*, 2(1), 21-23.
- Feldman, B. M., Pai, M., Rivard, G. E., Israels, S., Poon, M. C., Demers, C., ... Association of Hemophilia Clinic Directors of Canada Prophylaxis Study, G. (2006). Tailored prophylaxis in severe hemophilia A: interim results from the first 5 years of the Canadian Hemophilia Primary Prophylaxis Study. *Journal of Thrombosis & Haemostasis*, 4(6), 1228-1236.
- Fischer, K., van der Bom, J. G., Mauser-Bunschoten, E. P., Roosendaal, G., Prejs, R., de Kleijn, P., ... van den Berg, M. (2002). The effects of postponing prophylactic treatment on long-term outcome in patients with severe hemophilia. *Blood*, 99(7), 2337-2341.
- Gringeri, A., Lundin, B., von Mackensen, S., Mantovani, L., Mannucci, P. M., & Group, E. S. (2011). A randomized clinical trial of prophylaxis in children with hemophilia A (the ESPRIT Study). *Journal of Thrombosis & Haemostasis*, 9(4), 700-710. DOI: <http://dx.doi.org/10.1111/j.1538-7836.2011.04214.x>
- Hoots, W. K., & Shapiro, A. D. (2016a). Clinical manifestations and diagnosis of hemophilia. *UpToDate*. Retrieved from <http://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-hemophilia>
- Hoots, W. K., & Shapiro, A. D. (2016b). Treatment of hemophilia. *UpToDate*. Retrieved from <http://www.uptodate.com/contents/treatment-of-hemophilia>
- Ingram, G. I., Dykes, S. R., Creese, A. L., Mellor, P., Swan, A. V., Kaufert, J. K., ... Biggs, R. (1979). Home treatment in haemophilia: clinical, social and economic advantages. *Clinical & Laboratory Haematology*, 1(1), 13-27.
- Lazerson, J. (1972). Hemophilia home transfusion program: effect on school attendance. *Journal of Pediatrics*, 81(2), 330-332.

- Levine, P. H., & Britten, A. F. (1973). Supervised patient-management of hemophilia. A study of 45 patients with hemophilia A and B. *Annals of Internal Medicine*, 78(2), 195-201.
- Manco-Johnson, M. J., Abshire, T. C., Shapiro, A. D., Riske, B., Hacker, M. R., Kilcoyne, R., ... Evatt, B. L. (2007). Prophylaxis versus episodic treatment to prevent joint disease in boys with severe hemophilia. *New England Journal of Medicine*, 357(6), 535-544.
- Medicaid Health Plans of America. (2013). Addressing the needs of members with hemophilia in Medicaid managed care: Issues and implications for health plans.
- National Hemophilia Foundation. (2015). Federal 340B drug pricing program in the news. Retrieved from <https://www.hemophilia.org/Newsroom/Advocacy-Legislative-News/Federal-340B-Drug-Pricing-Program-in-the-News>
- Rabiner, S. F., & Telfer, M. C. (1970). Home transfusion for patients with hemophilia A. *New England Journal of Medicine*, 283(19), 1011-1015.
- Rabiner, S. F., Telfer, M. C., & Fajardo, R. (1972). Home transfusions of hemophiliacs. *JAMA*, 221(8), 885-887.
- Rizza, C. R., & Spooner, R. J. (1977). Home treatment of haemophilia and Christmas disease: five years' experience. *British Journal of Haematology*, 37(1), 53-66.
- Srivastava, A., Brewer, A. K., Mauser-Bunschoten, E. P., Key, N. S., Kitchen, S., Llinas, A., ... Treatment Guidelines Working Group on Behalf of The World Federation of Hemophilia. (2013). Guidelines for the management of hemophilia. *Haemophilia*, 19(1), e1-47. DOI: <http://dx.doi.org/10.1111/j.1365-2516.2012.02909.x>
- Szucs, T. D., Offner, A., Kroner, B., Giangrande, P., Berntorp, E., & Schramm, W. (1998). Resource utilisation in haemophiliacs treated in Europe: results from the European Study on Socioeconomic Aspects of Haemophilia Care. The European Socioeconomic Study Group. *Haemophilia*, 4(4), 498-501.
- Teitel, J. M., Barnard, D., Israels, S., Lillicrap, D., Poon, M. C., & Sek, J. (2004). Home management of haemophilia. *Haemophilia*, 10(2), 118-133.
- Wincott, E. (1977). Psychosocial aspects of hemophilia: Problems, prevention, treatment modalities, research, and future directions. *Mount Sinai Journal of Medicine*, 44(3), 438-455.

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The Medicaid Evidence-based Decisions Project (MED) is housed at the Center. Its mission is to create an effective collaboration among Medicaid programs and their state partners for the purpose of making high-quality evidence analysis available to support benefit design and coverage decisions made by state programs. Further information about the MED Project and the Center is available at www.ohsu.edu/policycenter.

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