



Adherence and Cost Effectivity of Home-Based Prophylaxis Over Institutionalized Prophylaxis in Patients with Hemophilia

Anupam Dutta¹ Dipjyoti Boruah¹ Angshuman Boruah¹ Arijit Das¹

¹Department of Medicine, Assam Medical College and Hospital, Dibrugarh, Assam, India

Address for correspondence Dipjyoti Boruah, MSc, Research Associate, Department of Medicine, Assam Medical College and Hospital, Dibrugarh, Assam, 786002, India (e-mail: boruahdipjyoti265@gmail.com).

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Abstract

Purpose: Home-based prophylaxis in hemophilia facilitates the treatment of patients with hemophilia (PwH) at home resulting in an improved quality of life, experiencing less pain and greater flexibility in daily activities. This literature studies the cost effectivity and adherence to prophylaxis treatment after the implementation of home-based prophylaxis therapy in PwH registered under the Hemophilia Treatment Centre (HTC) of Assam Medical College and Hospital.

Materials and Methods: PwH and their parents were advised for self/home infusion after being trained by a medical professional for 6 months. Data were collected on the skip in prophylaxis treatment by PwH and their traveling cost to access the prophylaxis treatment before and after the implementation of home infusion, through questionnaire and telephonic interview.

Results: The mean number of days of skip in prophylaxis was significantly reduced from 25 (± 11) to 4 (± 2) days after implementation of home infusion. The mean transportation cost was also found to be significantly decreased from Rs. 3297 (± 2251) to 440 (± 279). Before home/self-infusion, 77% of the registered PwH were found to skip prophylaxis doses more than 12 times a year but after home infusion, no PwH were found to skip more than 12 doses a year.

Conclusion: Home therapy facilitates the PwH to strictly adhere to the prophylaxis regime significantly reducing the skipping of doses to be administered to the PwH. The risks of regular traveling and the burden of transportation expenditure to avail the prophylaxis treatment was also found to be reduced significantly.

Keywords

- ▶ home care
- ▶ self-infusion
- ▶ prophylaxis treatment
- ▶ economic and traveling burden

Introduction

Hemophilia, a sex-linked inherited disorder characterized by recurrent bleedings due to the deficiency of clotting factor VIII (hemophilia A) and IX (hemophilia B) in blood, manifests

mostly in males though it is occasionally seen in females too. In one-third of the cases, spontaneous mutation has been reported. Frequent bleeding into the joints, muscles, or soft tissues may cause severe problems which may later cause serious disabilities in the joints. Excessive bleeding following

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trauma and surgery can be life threatening. Hemophilia is treated with factor concentrate according to the deficient factor in the blood. Treatment may be on demand but prophylaxis therapy minimizes the chances of emergency bleeding, pain and disability. Hemophilia treatment needs lifelong clotting factor replacement.¹ Prophylaxis therapy is the gold standard and home therapy particularly empowers patients with hemophilia (PwH) with effective management.² The World Federation of Hemophilia (WFH) guidelines recommend home management for PwH where appropriate and possible.¹ Home treatment refers to the prevention, evaluation, and treatment of bleeding at home by the PwH or their family members. It facilitates immediate and early treatment, reducing pain and the risk of deformity and hospitalizations associated with complications.^{3,4} Intravenous infusion of factor concentrate is one of the most important home therapies. Early treatment of bleeds due to home infusion can reduce the long-term effect of joint haemorrhages.⁵ Another problem of treating hemophilia is the burden of huge expenses the patients and their family members has to bear to avail the treatment. Of all expenses, the cost of factor concentrate is the keystone of management shares 90% of the economic load.⁶ However, now a days factor concentrate are being served free for treatment by the government of various states. Thus, this issue no further seems to be a burden in the management of hemophilia. However, some other new challenges in affording the treatment comes into view that includes expenditures for medical care, transportation charges in repeated clinical visits, and non-medical home services. In our study, some of the PwH are from remote areas of Arunachal Pradesh, Nagaland, and Dimapur and they experiences financial problem in affording the transportation cost for regular prophylaxis in the Hemophilia Treatment Centre (HTC) of Assam Medical College and Hospital. Traveling long distances to avail the treatment may risk their health for which there may be negligence in the treatment. Thus, we conceptualized the idea of home therapy and later during the lockdown of 2020 due to the novel coronavirus, home therapy was aggressively up taken by almost all the PwH and their parents as it became a necessary for the continuation of regular prophylaxis at their home. This study provides an insight of implementation of self/home infusion and its impact in the adherence to the prophylaxis regime by PwH/CwH. It also focuses on the transportation cost that a PwH and their parents has to bear to avail the treatment to continue prophylaxis. Studies found that children on home treatment experienced decreased hospitalization and better adherence to the prophylaxis regime, less days of absence from school, better integration with peer groups, and less pain.^{5,7,8} Adult men reported better quality of life as well, including greater feelings of self-sufficiency and self-confidence, less work absenteeism, more employment stability, and less negative emotions such as fear, anger, and depression.⁹⁻¹² In this study, we wanted to evaluate the adherence to prophylaxis treatment in PwH after implementation of home infusion therapy. We also wanted to evaluate the cost effectivity of home infusion therapy.

Materials and Methods

This is a retrospective study conducted over a period of 5 years with 94 PwH registered under HTC of Assam Medical College and Hospital. The HTC of Assam Medical College includes a team of hematologists, pediatricians, trained nurses, social workers, physiotherapists, orthopedists, and dentists to provide necessary care to the PwH. OPDs are conducted bimonthly, where necessary treatments were provided to the PwH/CwH. Factor concentrate doses are provided to them for the treatment of bleed and continuation of prophylaxis regime.

The study included 94 subjects registered under Hemophilia Treatment Center (HTC) of Assam Medical College and Hospital, undergoing prophylaxis treatment, aged between 8 and 35 years. All subjects and their parents were trained for self or home infusion by trained medical professionals at HTC for 6 months. PwH were trained for self-infusion, and the parents of CwH were trained to infuse their child as per the calculated dose prescribed by doctors of HTC. In case of any emergency bleeding, the PwH and their parents were advised to infuse factor at the very first suspected sign of clinical bleeding. Along with factor infusion, the PwH and their parents were also trained for appropriate documentation of the treatment records of factor dosage used, correct storage, and handling of the products, careful preparation of factor concentrate and disposal of infusion equipment. During the training period, positive home therapy experiences were shared among the PwH and their family members to increase their self confidence in executing home therapy and function effectively in the face of any emergency. The PwH and the parents were first allowed for infusion under the supervision of medical professionals and after four or five successful infusion at HTC, they were supplied with the required amount of factors for home infusion. Data were collected based on a questionnaire and telephonic interview for doses of factor used by them for prophylaxis in HTC or local medical centers before they were being trained for home infusion. Proper consent was obtained from each PwH after providing the detailed information about the study. A questionnaire was prepared that included personal history, family history, socioeconomic status, travel details, details of financial expenditure incurred during hospital visits, joint bleeding (ABR-annual bleeding rate), HJHS (hemophilia joint health score), functional assessment that were obtained from each PwH enrolled for the study. Records of self/home infusion were obtained from the record book maintained by the PwH and their parents when they perform factor infusion at home according to the provided prophylaxis regime by the physician. Bleeding rates and cost of transportation per prophylaxis treatment in HTC were also recorded by the PwH. Transportation cost was calculated by taking into account the cost of transport per unit distance travelled in rupees per month. Records of the skip in prophylaxis treatment were collected from the maintained records books of the PwH/CwH. Although PwH executes home therapy after proper training, all the PwH were called at least once every month to the treatment center for clinical

examination by doctors, physiotherapists, dental surgeons to minimize any possible internal bleeds or to improve the joint health. Orthopedic expert opinion was taken on individual case-based issues as and when needed.

Statistical Analysis

Statistical analysis was done using SPSS 16 (available at the institution where the study was carried on). Data have been summarized as mean and standard deviation for numerical variables and numbers (percentage) for categorical variables. Chi square test and paired - sample t-test were used for the test of significance between two groups. Probability (p) value <0.001 was considered statistically significant.

Results

Distribution of studied population across Assam and nearby states (Arunachal Pradesh and Nagaland) was shown in the map by Google My Maps (► Fig. 1). During the study period, 77% of the PwH were found to involve actively in home infusion by 2020 (► Table 1), out of which 43% were involved in self infusion of factor, i.e., the PwHs of this category could inject factor concentrates by themselves. They usually included school going children and teenagers. Also, 34% depends on their family members (parents, guardians, etc.) for factor infusion at home, and they were categorized as the PwH with home infusion. They included mostly the small children. Rest 23% had to depend on health professionals to avail the treatment (► Fig. 2). After the implementation of home therapy, a significant reduction in transportation cost was seen. Before the practice of home infusion, the mean cost of transportation to avail the treatment was Rs. 3297 (2251), which got significantly reduced to Rs. 440 (279) (► Table 2).

Table 1 Table showing the implementation of home Infusion in the above years

Year	% of implementation of Home/self-infusion
2016	2
2017	4
2018	5
2019	9
2020	77

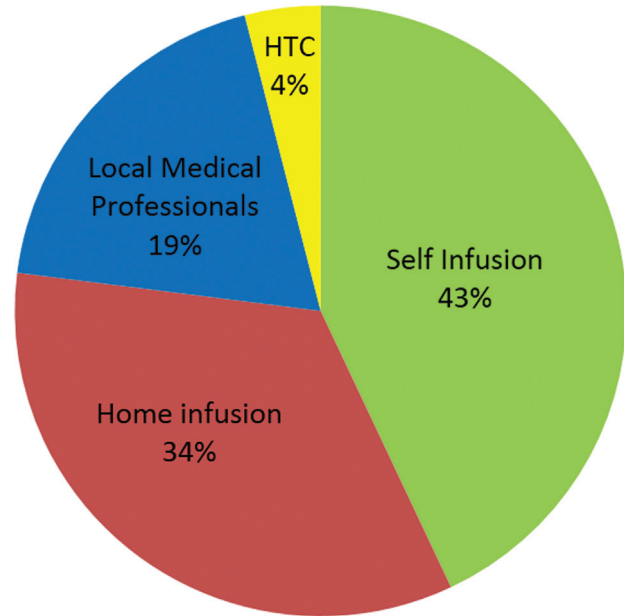


Fig. 2 Proportion of PwH undergoing prophylaxis treatment based on factor infusion.

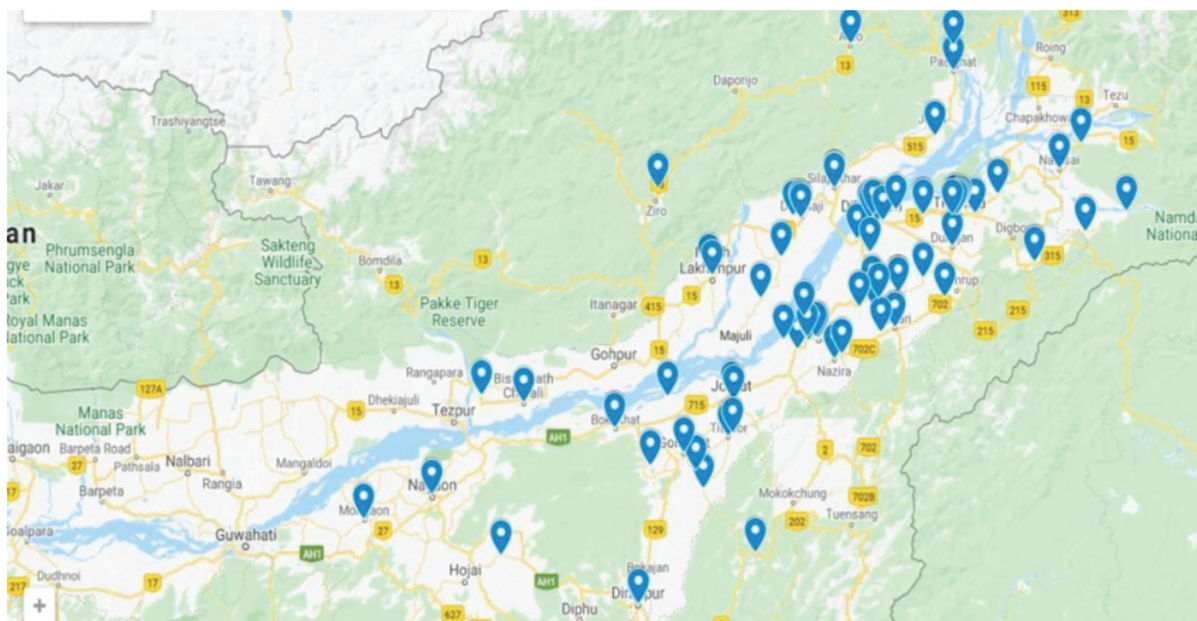


Fig. 1 Geographical distribution of patients across upper Assam and neighboring states (Arunachal Pradesh and Nagaland). Google My Maps: Google LLC, Amphitheatre Parkway, Mountain view, CA 94043, USA.

Table 2 Mean and standard deviation of transportation cost and skip in prophylaxis treatment before and after implementation of home infusion

Parameters	Before home infusion Mean (\pm SD)	After home infusion Mean (\pm SD)	P-value
Skip in day of prophylaxis treatment	25 (\pm 11)	4(\pm 2)	<0.001
Transportation cost in Rupees	3297(\pm 2251)	440(\pm 279)	<0.001

Note: Values are presented as mean (\pm standard deviation).
p-Value calculated by paired simple t-test.

Also, 48 (51%) of the registered PwH has an expenditure of more than 2400 rupees per month in receiving prophylaxis treatment while after home infusion, no PwH were found to expend more than Rs 2400 in a month in transportation to continue prophylaxis and 83 (88%) were found to expend below Rs 800, which was the minimum transportation cost per distance that a PwH has to bear (**Table 3**). It is because regular visit to the HTC for prophylaxis factor infusion was not required after the implementation of home infusion. Earlier PwH/CwH solely depend on medical professionals, and they visit HTC twice a week along with their parent or relative for factor infusion for which the cost of transportation was very high but after implementation of home infusion their visit to HTC got reduced to once a month, which significantly reduced the cost.

Table 3 Transportation fare in PwH before and after implementation of home infusion

Transportation cost (Rs)	No. of PwH, before implementation of home infusion, n (%)	No. of PwH, after implementation of home infusion n (%)	p-Value
₹0-₹800	11 (12)	83 (88)	<0.001
₹801-₹1600	13 (14)	9 (10)	
₹1601-₹2400	22 (23)	2 (2)	
more than ₹2400	48 (51)	0 (0)	
Total	94 (100)	94 (100)	

Note: Values are presented as number and percentage.
p-Value calculated by chi-square test.

Table 4 Skip in prophylaxis doses before and after implementation of home infusion

(Number of Skip/year)	No. of patient undergoing prophylaxis at HTC n (%)	No. of patient undergoing prophylaxis at home n (%)	p-Value
No skip	0 (0)	56 (60)	<0.001
1-3 skip	1 (1)	21 (22)	
4-6 skip	4 (4)	6 (6)	
7-9 skip	3 (3)	5 (5)	
9- 12 skip	14 (15)	6 (6)	
More than 12 times skip	72 (77)	0 (0)	

Note: Values are presented as number and percentage.
p-Value chi square test.

Home infusion also reduced the number of days of skip in prophylaxis treatment, significantly from 25 (11) days to 4 (2) days (**Table 2**). Also, 56 (60%) of the subjects did not skip any prophylaxis doses after the implementation of home infusion, strictly adhering to the prescribed treatment regime (**Table 4**). Then, 72 subjects were found to skip prophylaxis treatment prescribed by the physician more than 12 times a year before the practice of home infusion whereas after implementing it, no subjects were found to skip more than 12 prophylaxis treatment in a year. This indicates that home-infusion facilitated the PwH/CwH to stick to the prophylaxis regime more strictly, skipping less doses. However, it can be seen from the table that 38 (40%) studied subjects were still found to skip doses of prophylaxis treatment, with a maximum of one to three skip per year by 21 (22%) PwH/CwH.

Discussion

The benefits of prophylaxis treatment in decreasing the bleeding rates, joint damage, and improving the quality of life are dependent on adherence to the prescribed treatment regime.¹³⁻¹⁵ Patients with low adherence rates are found to experience more bleeds.¹⁶ Although home infusion has improved the quality of life of these PwH to a large extent but still it could be seen that 19% of PwH are still dependent on medical personnel and 4% still visits HTC for factor infusion. This may be due to the lack of confidence due to failed venipunctures and insufficient knowledge in using the venous access device. Some PwH also stated that they were

afraid of self-infusion without proper guidance. However, literature shows nonadherence to prophylaxis treatment regime may be intentional where patients makes a deliberate decision of not taking factors or it may be unintentional usually due to forgetting.¹⁶ PwH with mild bleeding phenotypes suffer from less bleeds and therefore they are more relaxed and less concern about the treatment and the possible severe outcome of illness.¹⁷

Another critical challenge of skipping prophylaxis is the cost of treatment, which also proved to be one of the significant barrier.¹⁸ PwH intentionally skip prophylaxis treatment to reduce the economic burden. Socioeconomic factors including family size, family structure, social support, income, literacy, and culture norms also affects the family's ability to understand the disease and its consequences and patient willingness to accept treatment recommendations.¹⁹

These challenges can be overcome by repeated education about the need of prophylaxis treatment for improving the disease consequences. Self-care and home infusion must be promoted for better adherence to the prophylaxis treatment and management of bleeding episodes. Continuous practice of self-infusion under the supervision of medical professionals, adequate education, training, and support from HTC can encourage them to take responsibility for their own health and risk behaviors. Patient awareness camp should be done to advocate the PwH and their family members about hemophilia to access the safe and effective treatments and benefits of the prophylaxis treatment and how the strict adherence to it can help the PwH to lead a normal and healthy life.

The families of PwH in the study were seen to approve the benefits of training for home therapy. They believed home infusion facilitated early treatment minimizing the emergency problems and their life are better controlled than before. During the ongoing pandemic and prevailing lockdown, the PwH and their parents were bound to self-infuse the factor concentrates and thus could minimize their bleeding episodes to a great extent. Studies also showed that the number of hospitalization due to emergency bleeds decreases after implementing the home infusion of factors.⁴ Previous study on regular prophylaxis showed less absenteeism from work and school, more active social participation, and more employment stability in PwH.^{20,21} Home infusion was also found to be cost beneficial to the PwH and their families. It substantially reduced the transportation cost that PwH has to bear for prophylaxis treatment at HTC. PwH from remote and distant areas found difficulties in travelling mainly during active bleeds, which compelled them for home infusion. Earlier PwH were found to travel twice a week to receive their prophylaxis doses, which substantially reduced to once a month after full implementation of home infusion.

A 2-year crossover study of home versus hospital-based treatment in 36 children with hemophilia A and B found that more products were used during home care and that it was given with significantly shorter delay from the onset of bleeding.²² Children missed only 2.5 days of school for each bleeding episode treated at home, compared with 6.2

days for hospital-based care.³ Studies demonstrated the success of home therapy in reducing the bleeding episodes that have created a boon to the life of PwH.^{5,7,8,21}

For effective implementation of home infusion for a better quality of life, hemophilia nurses could set the example of those patients and families as peer educators who had carried out better home therapy and conduct peer education focused on experience-sharing. Peer-based home therapy education may compensate for the lack of confidence and doubts and therefore may be an appropriate approach to promote the self/home infusion in these PwH.

Home infusion facilitated a cost beneficial treatment. Repeated visit to HTC for prophylaxis is a burden to PwH and their families. Distance and cost are the barriers for most of the PwH belonging to the remote areas during emergency bleed and they found home infusion has helped them to reduce the time of treatment and cost of transportation they have to bear for continuing prophylaxis treatment.

The burden of routine traveling for prophylactic infusion of factor concentrates during the pandemic of COVID 19 was reduced due to home infusion. Most PwH could perform home/self-infusion with ease. Home infusion training increased the confidence level of the patient and their parents as they became a part of the treatment. Although home infusion/self-infusion was mainly adopted as the only way of treatment during the pandemic but this strategy was continued to be encouraged by our treatment center for their obvious benefits in number of ways. A routine monthly checkup of each PwH by the health experts of HTC also helped them to reduce the emergency bleeding episodes and improved the joint bleeds. Moreover, by adopting home infusion of factor concentrates, these PwH became proactive and also encourage new PwH and their family members to execute home therapy, which can benefit them to a great extent at the time of emergency and lead a normal healthy life.

Conclusion

Home management care in hemophilia improves the quality of life in PwH as it helped in better adherence to the treatment regime that resulted in less pain and greater flexibility in daily activities, less financial burden, less absenteeism from school and work, and can engage more actively on their daily activities without the fear of being bleeding unconsciously.^{5,7,8,21} The success of home infusions shifted the dependency of PwH on health professionals to their family members and also reduced the expenditure cost, time, and potential risk of health of PwH belonging to distant area. Although similar studies were carried out in different parts of the world but the results of this study will reinforce such treatment options in difficult areas such as hilly and remote areas of North Eastern part of India.

Author's Contribution

All authors have substantive intellectual contributions to this study.

Anupam Dutta contributed to the planning and conducting the study.

Dipjyoti Boruah contributed to the collection of data and preparation of the manuscript.

Angshuman Boruah contributed to statistical analysis.

Arijit Das contributed to the collection of data.

Statement of Institutional Review Board Approval

Research of the following manuscript has been approved and recommended by Institutional Ethics Committee (H), Assam Medical College, Dibrugarh. (Reg. No. ECR/636/Inst/AS/2014) on September 22, 2021. For authentication, the document of recommendation by institutional ethics committee has been attached in the PDF format.

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Conflict of Interest

None declared.

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References

- 1 Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al; Treatment Guidelines Working Group on Behalf of The World Federation Of Hemophilia. Guidelines for the management of hemophilia. *Haemophilia* 2013;19(01):e1–e47
- 2 Ergün S, Sülü E, Başbakkal Z. Supporting the need for home care by mothers of children with hemophilia. *Home Healthc Nurse* 2011;29(09):530–538
- 3 Teitel JM, Barnard D, Israels S, Lillicrap D, Poon MC, Sek J. Home management of haemophilia. *Haemophilia* 2004;10(02):118–133
- 4 Soucie JM, Symons J IV, Evatt B, Brettler D, Huszti H, Linden J. Hemophilia Surveillance System Project Investigators. Home-based factor infusion therapy and hospitalization for bleeding complications among males with haemophilia. *Haemophilia* 2001;7(02):198–206
- 5 Rabiner SF, Telfer MC. Home transfusion for patients with hemophilia A. *N Engl J Med* 1970;283(19):1011–1015
- 6 Rodriguez-Merchan EC. The cost of hemophilia treatment: the importance of minimizing it without detriment to its quality. *Expert Rev Hematol* 2020;13(03):269–274
- 7 Ekert H, Moorehead M, Williamson G. Home treatment of haemophilia. A follow-up study. *Med J Aust* 1981;2(01):21–23
- 8 Levine PH, Britten AF. Supervised patient-management of hemophilia. A study of 45 patients with hemophilia A and B. *Ann Intern Med* 1973;78(02):195–201
- 9 Rabiner SF, Telfer MC, Fajardo R. Home transfusions of hemophiliacs. *JAMA* 1972;221(08):885–887
- 10 Ingram GI, Dykes SR, Creese AL, et al. Home treatment in haemophilia: clinical, social and economic advantages. *Clin Lab Haematol* 1979;1(01):13–27
- 11 Rizza CR, Spooner RJ. Home treatment of haemophilia and Christmas disease: five years' experience. *Br J Haematol* 1977;37(01):53–66
- 12 Szucs TD, Offner A, Kroner B, Giangrande P, Berntorp E, Schramm W. The European Socioeconomic Study Group. Resource utilisation in haemophiliacs treated in Europe: results from the European Study on Socioeconomic Aspects of Haemophilia Care. *Haemophilia* 1998;4(04):498–501
- 13 du Treil S, Rice J, Leissing CA. Quantifying adherence to treatment and its relationship to quality of life in a well-characterized haemophilia population. *Haemophilia* 2007;13(05):493–501
- 14 Collins PW, Blanchette VS, Fischer K, et al; rAHF-PFM Study Group. Break-through bleeding in relation to predicted factor VIII levels in patients receiving prophylactic treatment for severe hemophilia A. *J Thromb Haemost* 2009;7(03):413–420
- 15 Fischer K, Van Der Bom JG, Prejs R, et al. Discontinuation of prophylactic therapy in severe haemophilia: incidence and effects on outcome. *Haemophilia* 2001;7(06):544–550
- 16 van Os SB, Troop NA, Sullivan KR, Hart DP. Adherence to prophylaxis in adolescents and young adults with severe haemophilia: a quantitative study with patients. *PLoS One* 2017;12(01):e0169880
- 17 Santagostino E, Mancuso ME, Tripodi A, et al. Severe hemophilia with mild bleeding phenotype: molecular characterization and global coagulation profile. *J Thromb Haemost* 2010;8(04):737–743
- 18 Khair K, Lawrence K, Butler R, O'Shea E, Christie BA. Assessment of treatment practice patterns for severe hemophilia A: a global nurse perspective. *Acta Haematol* 2008;119(02):115–123
- 19 Thornburg CD, Duncan NA. Treatment adherence in hemophilia. *Patient Prefer Adherence* 2017;11:1677–1686
- 20 Dutta A, Boruah D, Dutta TS, et al. Improvement in school absence after factor replacement in students with haemophilia in Upper Assam, India. *The Journal of Haemophilia Practice* 2020;7(01):136–142
- 21 Lazerson J. Hemophilia home transfusion program: effect on school attendance. *J Pediatr* 1972;81(02):330–332
- 22 Strawczynski H, Stachewitsch A, Morgenstern G, Shaw ME. Delivery of care to hemophilic children: home care versus hospitalization. *Pediatrics* 1973;51(06):986–991