

# The natural evolution of haemophilia care: developing and sustaining comprehensive care globally

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**Summary.** Comprehensive care is vital for patients with haemophilia to prevent early death and free patients from the complications that inhibit living normal lives. Experience has shown that once introduced in a country, there is a progressive restoration of normal healthy lives to the haemophilia community. Accompanying this progress is a gradual decreased dependency on the haemophilia comprehensive centre – except during brief periods when expertise contained within the comprehensive centre is mandatory for life-saving clinical management or to prevent severe morbidity. During each stage of the

natural evolution of comprehensive haemophilia care in a country, challenges to the existence of the centre occur, which threaten the comprehensive treatment concept. The haemophilia community must understand this natural evolution and be prepared to work collaboratively with governments, physicians and other patients to ensure that centres retain the expertise to meet the emergent needs when they arise.

**Keywords:** haemophilia, cost of care, haemophilia treatments centres, physician shortage, health resource utilization, haemophilia care advocacy

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## Introduction

A significant proportion of the world's population is affected by hereditary defects in one or more of the clotting factors. These defects lead to abnormal and sometimes life-threatening bleeding episodes. Prior to the 1960s, when no comprehensive care was available, individuals with haemophilia suffered a similar fate worldwide. Severe joint disabilities appeared in early teens, and most patients died before the age of 20. Haemophilia was treated primarily with fresh blood transfusions, and as a result haemophilia associations were established for the purpose of recruiting the donors. Cryoprecipitate was discovered in 1964 and subsequent development of clotting factor concentrates dramatically increased clinical management options [1–3]. As concentrates could be easily stored, administered at home and carried with patients during travel, patients began to adopt a practise of home therapy. In developed countries, early treatment of bleeding episodes and home therapy quickly evolved as the primary management option. Training and education of patients about

disease management became necessary with the increasing popularity of home therapy. Specialized centres soon delivered services to meet these needs. These approaches on patient care produced significant effects on patient general health and survival, and as a result, the haemophilia community requested and received support for networks of haemophilia treatment centres (HTCs) from governments [4,5].

## The comprehensive care model

These centres provided comprehensive services based on an integrated public health approach [6,7]. This model, *the comprehensive care model*, has been one of the most successful public health programmes in many developed countries, resulting in significantly improved health for patients with haemophilia as well as producing a reduction in health-care utilization [8–10]. These programmes have been so successful at reducing the complications of haemophilia that the dynamics of haemophilia care has changed significantly. However, these changes are now producing other challenges for sustaining the current model.

Several factors set comprehensive care for haemophilia aside from routine patient care [11–14].

First, because haemophilia care is very specialized and affects many other areas of the patient's physical and mental health, it is best met through a

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multidisciplinary team approach. Thus, appropriately trained and experienced medical staff is needed to avoid poor therapeutic decisions that can lead to severe disability and mortality. The tasks of the comprehensive care team, which are critical to preventive care include diagnosis and assessment, education of the patient and his/her family, management of acute bleeding episodes, initiating and supervising home therapy, routine follow-up, preoperative assessment and postoperative management of the patient when surgery is necessary. In addition, the treatment centre provides support to the patient and family to prevent social or psychological distractions from interfering with health-care outcomes. A primary treatment team is organized in each centre to maximize the effect of the resources available. In most centres, this consists of a nurse coordinator, a medical director (usually a haematologist), a physiotherapist and a social worker. A referral team is organized to meet the specialized needs of individual patients on occasions. For example, this team may include specialists in dentistry, orthopaedic surgery, clinical genetics, rheumatology, infectious diseases or other areas of clinical medicine.

Secondly, maintaining such trained and experienced health-care providers can often be achieved only by concentrating patient care into specialized centres. The comprehensive care team works collaboratively with other centres, forming a treatment network to continually evaluate the treatment trends in the light of new discoveries and modify the standards of treatment to incorporate the new discoveries into the management of patients with haemophilia. To maximize the efficiency of the network, it is often divided into two to four layers or levels of treatment centres depending on the number of patients in a geographic area and the resources available [15]. For example, a country may form a basic clinic level, a HTC level and a comprehensive treatment centre level.

Thirdly, premium of care should be placed on preventive medicine, as medical complications resulting from haemophilia, such as infection with hepatitis viruses, HIV and progressive joint disease, are severe and extremely difficult and expensive to treat.

Successful modern haemophilia care depends on the principle of anticipating and preventing the complications of haemophilia rather than treating those complications following their occurrence. This principle of management of haemophilia has come to be termed comprehensive care and requires more resources and organization of care delivery than the standard physician–patient relationship used for the management of many diseases. However, its use

yields dramatic results by producing productive individuals living normal healthy lives without the crippling effects and early death produced by the complications of haemophilia [8].

Fourthly, maintaining a coordinated network of speciality centres enables patient access to clinical research and evaluation needed to make well-informed decisions. Good prevention requires that patients and their families make well-informed decisions regarding their physical, psychological and social health, which is consistent with the most up-to-date medical knowledge. Under the comprehensive care model, the responsibility for assisting patients and their families with these decisions fall into the ‘comprehensive care team’. This team comprises expertise from a number of medical specialties that are coordinated for each patient’s medical requirement and health status.

And finally, careful structure of the speciality centres enables optimal delivery of care based on the allocation of limited resources.

### **Economics of haemophilia care – the ‘Nine Hundred Pound Gorilla’**

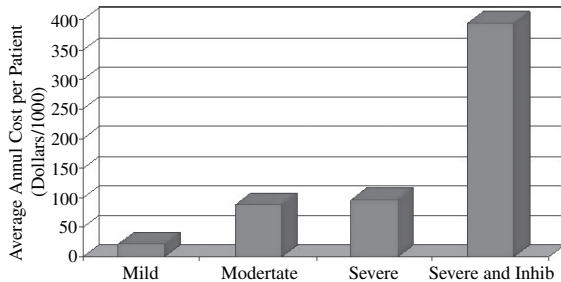
Before addressing the trends in haemophilia care, it is important to understand how economics influences health care for haemophilia. This issue greatly affects the manner in which countries of different economic development approach comprehensive care with their governments.

During the past two decades, the cost of this care rose exponentially because improved safety of treatment products produced a 5–10 times increase in cost. Today the cost of optimum care for haemophilia is beyond the reach of individuals with haemophilia so that others, whether from government or private insurance, must bear the expense. As a result, the haemophilia community must continually convince others to accept this financing responsibility. By nature, the payers’ focus is on the bottom-line economics, i.e. ‘the most served with the least cost’. This attitude complicates the efforts of the haemophilia community. In countries with emerging economies, economic issues will be the primary force determining how far patients and physicians can push their goals. In the developed countries, only constant pressure from patient groups prevents reductions in services for haemophilia patients, when these countries attempt to reduce rising health-care costs [16–20].

To illustrate the magnitude of the economic effect, we can examine the United States, where the cost of haemophilia care is close to the median of the most

**Table 1.** Relative cost of medical services in a selected cohort of 70 boys receiving episodic infusions for bleeding events and 27 boys receiving infusions prophylactically in haemophilia treatment centres during a 2-year period [21].

Type of services	Total cost (\$)	Medical services	Concentrate cost
Episodic care	23 435	1525 (6%)	22 112 (94%)
Prophylactic care	75 944	3075 (4%)	72 944 (96%)
Medical provider	1.5% of costs		
Hospitalizations	1.7% of costs		

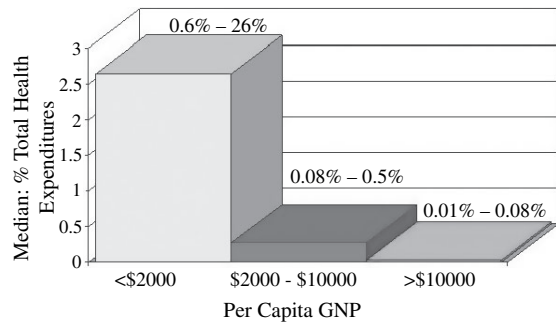


**Fig. 1.** Average annual cost of clotting factor per patient depending on severity and presence of circulating inhibitor [22].

developed countries. In 1996, the annual financial support of episodic care for an average haemophilia patient was about \$23 000 (Table 1) [21] and for prophylaxis treatment, \$76 000. (Note that the medical provider cost was only 1.5% and hospital costs were only 1.7% of these costs, both very modest.) Another study in 2001 reported that the annual cost could be staggering for patients with combined severe haemophilia and inhibitors to clotting factor (Fig. 1) [22,23].

In fact, if cost alone were the deciding factor in haemophilia care, it might be very difficult to convince governments of the developed countries to fully finance haemophilia care. For countries with emerging economies, the prospect is even worse. Cogent arguments against considering the cost factor as the decisive one must include a consideration of the government's view of the cost factor on the nation's total health expenditures.

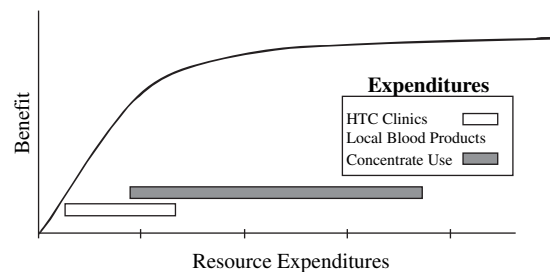
To illustrate this point, suppose the average patient requires (for the minimum level of health care) 20 000 U Factor VIII per year costing \$0.35. Multiplying the haemophilia population times the annual expected average cost per patient approximates the financial need of the country's haemophilia population. The percentage of total health expenditures of each country needed to provide that care could then be calculated using total health expenditures supplied by the World Bank (Fig. 2). It becomes very



**Fig. 2.** Percentage of countries' total health expenditures needed to provide minimal standardized care. Modified from Evatt and Robillard, 2000 [27].

clear from these crude estimates that countries with the lowest gross national product would expend significant (and often unrealistic) amounts of their total health-care budgets to provide adequate care for their relatively few patients with haemophilia. Seeing these numbers would make any Ministry of Health of these countries assume that haemophilia care is not affordable by their government [24]. This attitude is reflected by the recent (unsuccessful) proposal by individuals at the World Health Organization to remove clotting factor concentrates from the essential medicine list because haemophilia care was deemed unaffordable for governments in developing countries [25,26].

To counter this attitude by government officials, proposed programmes must be presented, which are compatible with each country's economy. For example, it must be argued that the comprehensive care model can produce significant improvement in health status and quality of life without the expenditures used in the developed countries [27]. The relationship between the developed expenditures and haemophilia outcomes is a continuum and exhibited by a typical cost-benefit type curve (Fig. 3). During the early portion of the curve, relative small expenditures used



**Fig. 3.** Theoretical effect of resource expenditures on benefit. The curve represents a theoretical relative effect of resource expenditures on the proportion of benefit to patients. From O'Mahony, 2004 [25].

for the organization of the care delivery, education of medical personnel and patients and modification of blood bank practises yield large benefits to patients. Addition of modest amounts of concentrates greatly amplifies this trend. As more resources become available, additional services such as orthopaedic surgery, prophylaxis and immune tolerance can be added, but these will increase the cost and benefit for fewer patients.

Presented in terms of real data, each year 23% of the patients in the United States use no clotting factor products and another 50% use about 30% of the total clotting factor products consumed (CDC Unpublished HSS Data 1996–1998). That means the remaining 25% of the patient population, i.e. those receiving intermittent prophylaxis, continued prophylaxis and immune tolerance use 70% of the factor (Fig. 4). If these uses were arranged in terms of a priority typical of the most developing countries, a cost–benefit curve appears to show the relationship of these benefits to expenditures (Fig. 5).

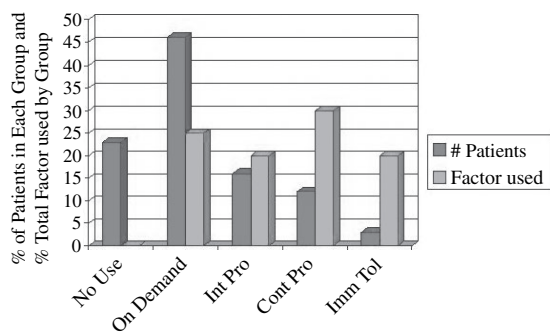


Fig. 4. Distribution of clotting factor needs based on factor usage 1995–1998. Int Pro, intermittent prophylaxis; Cont Pro, continuous prophylaxis; Imm Tol, immune tolerance (CDC unpublished HSS data 1996–1998).

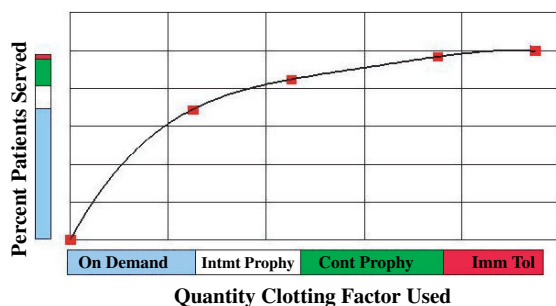


Fig. 5. Relationship of clotting factor used (shown on abscissa) to percentage of patients served (shown on ordinate) when the quantity of clotting factor used is prioritized by On Demand, Intermittent Prophylaxis (Intmt Prophy), Continuous Prophylaxis (Cont Prophy) and Immune Tolerance (Imm Tol) (CDC Unpublished HSS Data 1996–1998).

Rather than being discouraged by such economic realities, the haemophilia community must use this information to clearly argue for the benefits of comprehensive care, based on scientific data, advocating for a health-care plan in line with their country's economic capacity. Stepwise improvements in the delivery system should subsequently be requested, as the economy improves and resources become available [28]. In the developed countries, where cost cutting is a constant threat, the haemophilia community (patients and physicians) must understand the changes that these benefits have produced in health-care utilization, speak with one voice of the benefits of maintaining high-quality care and advocate for changes in the HTC, which will ensure its continued existence.

### The argument for the comprehensive care model

In the developed countries, substantial socioeconomic benefits, including increased employment, decreased health-care resource utilization and lower cost of care result from using the comprehensive care approach [2–5,29,30]. Healthy, happy patients who now have access to sufficient treatment products and live without the crippling complications of haemophilia (as well as third-party payers) may wonder why they still need comprehensive care. In other words, why not obtain a source of clotting factor and receive care from less specialized sources. In fact, some patients do turn to other sources for care because of this opinion. It is important to understand, however, that leaving the comprehensive care environment significantly increases risks even in the healthiest patients [30]. For example, nearly 3000 patients (comprising approximately 18% of the US haemophilia population) were studied from 1993 to 1995 to determine whether comprehensive care was necessary to maintain the health outcomes achieved by the HTCs. In the United States, about two thirds received comprehensive care from the HTCs and one third from outside the HTC network. In this study, the mortality risk was 70% higher for those patients (despite their having milder clinical symptoms) receiving non-comprehensive care from sources other than the HTCs compared with those who received comprehensive care within an HTC [30]. Especially, at risk were patients who had residual complications resulting from earlier forms of treatment. For example, persons with severe liver disease had 2.4 times the risk of death; persons with HIV infection (but no AIDS) had five times the mortality risk and those with AIDS 33 times the mortality risk in the non-comprehensive environment.

Several factors were responsible for these effects. Although all patients had access to good health care and clotting factor concentrates in both groups, the clinical management in comprehensive care was conducted by an integrated team (the integral concept of the HTC). This team included a number of specialists, e.g. infectious and hepatic disease specialists, allowing easy access of each patient to expert input for his/her individual treatment. In addition, HTCs also produced lower mortality by the use of home factor-infusion programmes [29]. These programmes are beneficial in two ways. First, such programmes require intensive patient training and close monitoring by the management team. In addition, because of the extensive patient and family education and expert consultation received during the periods of haemostatic stress, the patient becomes a knowledgeable and motivated partner in the management of his/her own health care. He/She is more capable of making well-informed decisions. Finally, treatment of bleeds occurs at the earliest possible moment, usually preventing the complications of life-threatening bleeds that result in death or severe morbidity.

In countries with emerging economies, the effect of comprehensive care is just dramatic [24,25,27]. Frequently, because of the limitation of resources, access to clotting factor concentrates is more restricted. In these situations, however, even the modest expenditures used to modify the structure and organization of the care delivery (with emphasis on prevention), to educate medical personnel and patients and to modify blood bank practises to improve the safety and supply of therapeutic products yield huge economic and quality of life benefits. These benefits can be directly measured in terms of reduction in the number of early deaths, increased life expectancy, decreased joint deformities and increased levels of education and employment [28].

### **Impact of the success on clinic utilization in the developed countries**

In spite of (and perhaps because of) the impressive success of comprehensive care, HTCs in many developed countries are now facing two major threats to their ability to deliver this form of health care to the haemophilia population: (i) the success of the prevention programmes has reduced the need for frequent or day-to-day management of patients; and (ii) an imminent shortage of providers trained in managing bleeding and clotting disorders.

By design, successful preventive care used by the comprehensive care programmes has, over time,

produced a significant reduction in the utilization of health-care resources. When national networks of treatment centres for haemophilia care were initiated, the burden from residual complications was considerable [31,32]. Patients, who were still living, were afflicted with multiple target joints, infected with hepatitis viruses and not uncommonly had residual neurological damage. HTCs were very busy managing these complications and attempting to prevent new ones. The AIDS epidemic of the early 1980s placed additional burdens on the staffs of the HTCs [33]. Safe products from the mid-1980s eliminated for younger patients the threats of infectious complications, and the preventive management of the patient produced dramatic effects on the lives of patients. Now patients who are 16 or younger receiving care in HTCs are not infected with HIV, HCV or HBV [34]. Joint disease has essentially disappeared, and these patients look forward to a normal energetic life with excellent employment opportunities [9]. Home care programmes and well-educated patients have reduced the dependency on the HTCs for day-to-day care. As a result, there has been a marked reduction in the number of clinic visits, hospitalizations, life-threatening bleeds and management needs for complications such as joint destruction. For example, in 2000, the National Hemophilia Foundation (NHF) in the United States surveyed 130 HTCs concerning the utilization of clinic facilities [35]. Responses indicated that the average number of visits to a treatment centre in the United States numbered only 5.2 per week. (The average census of the patient registries during this period was approximately 130 patients.) Staff utilization was also much lower than expected. Sixty-nine per cent of the non-physician staff was involved in haemophilia care, but only 20% of the physician staff time was so used. At the same time, CDC examined clinic records in 16 centres in six states covering the years 1996–1998 and found that the average number of visits to the clinics was only 5.4, similar to the NHF data (CDC Unpublished HSS Data 1996–1998) [28]. As hospitals and universities observe the decreased utilization of haemophilia clinics, there often has been pressure to cut medical care costs at the expense of the HTCs. To ensure that the quality of care for patients with haemophilia is available for the future, the haemophilia community must address these pressures.

### **Impact on trained physician availability**

Accompanying the decreased utilization of HTCs, a second problem appeared in countries with

successful haemophilia programmes – an imminent shortage of physicians trained to manage bleeding disorders. Several major factors contribute to this shortage. Foremost is the effect of decreased dependency on the HTC for health services. Because of the decreased dependency, a rising number of physicians, faced with falling demands for services, have been forced to treat patients other than bleeding patients, i.e. oncology or haematological malignancies, in order to maintain a living. Under these conditions, haemophilia and blood coagulation becomes secondary for salary support and career advancement. Because of the low time commitment of these haematologists, department chairmen too often consider haemophilia practise a ‘hobby’. As hospitals and university medical schools are under increasing pressure to close clinics that are deemed inefficient, they often decide that haemophilia clinics are too expensive to maintain for the number of patients they serve. Oncology services have come to dominate in haematology departments in many countries. Department chairmen see these as the imminent need for department resources. Those serving haemophilia have seen a decline in their status in favour of physicians whom departmental chairmen view as more in line with the new trends.

This process does not go unnoticed among young physicians seeking a career path. Seeing the effects on earnings, status and the trends in patients’ needs, it is understandable that they would be attracted to oncology rather than bleeding disorders. Each year, American Medical Association publishes data in the United States on persons completing speciality training [36]. For several years, these data indicate that although the total number of specialists trained in haematology has been increasing, those from programmes that traditionally had an emphasis on bleeding and clotting disorders have declined precipitously but those with emphasis on oncology have risen more rapidly. Similar information was obtained from discussions with the Committee on Training Programs, American Society of Hematology. This trend is not just a US problem but is widespread throughout the developed countries, although particular features of the health-care system in each country may modify its immediate impact. As the present generation of haematologists trained in haemophilia care retire, the HTCs must work hard to identify and recruit replacements or modify the method of haemophilia care delivery to meet these challenges.

How critical is this issue? Currently, in a number of developed countries, the pending shortage of physicians trained in managing bleeding and clotting

disorders threatens the existence of many centres, as the attrition of highly trained staff becomes a significant issue for patients and staff [28,37]. For example, in the United States, about 10 centres have closed because of the loss of physicians. A search on the Internet for ‘haematologist shortages and haemophilia’ quickly identifies the depth of the problem in several countries. Some centres, after failing to recruit haemostasis specialists, have assigned the service to physicians trained in other specialties such as oncology. If these trends continue, the shortages of physicians could significantly reduce the capacity of the system to deliver care to individuals with haemophilia.

Unfortunately, political forces quickly step in to provide inappropriate answers – especially, if there is an appearance of dollar savings to the general public. Already in the United States, The National Conference of State Legislators issued a report on 31 December, 2005, entitled *Strategy 8: Managing Health Care Better* [38]. Particularly disturbing was the following proposal excerpted from that report:

In Mississippi, pharmacists play a role in disease management by monitoring patient compliance and medication interactions. Pharmacists complete coursework and pass an examination on diabetes, asthma, hyperlipidemia, and coagulation disorders [emphasis supplied]. Patients have 15- to 30-minute (or longer) sessions with their pharmacists up to 12 times per year. Using pharmacists rather than physicians in disease management may be particularly useful in states with a shortage of health care professionals.

Can you imagine the health disaster produced by replacing comprehensive care by pharmacists!

### Options for maintaining care

Immediate action is needed to reverse this trend. The time necessary to train specialists in coagulation requires several years. The haemophilia community cannot wait until the shortage becomes more critical before taking action. The practise environment must be made more attractive for young physicians by providing training opportunities, stimulating the research environment for the research of blood coagulation disorders and restructuring the HTCs to provide full-time activities in the field of coagulation.

The first step is encouraging the interest of young trainees. Although such interest is often a result of having a mentor who generates an interest in coagulation, it needs to be fostered by providing

opportunities for education and career advancement. National haemophilia societies and professional haematology organizations need to provide training grants for young fellows and young university faculty to train, teach or conduct investigations in the field of haemostasis including haemophilia. Governments and industry should also be encouraged by the haemophilia community to provide grants for clinical and bench research in the field of haemostasis.

These steps have been initiated in several developed countries but more is needed. The young physician training in haemostasis must feel that he/she will practise his/her speciality more than 20–25% of the time. The HTC's need to be restructured to ensure a full-time practise in blood clotting disorders [28,39,40]. Clinics must be expanded to include other persons with bleeding disorders and those with clotting defects that produce thrombosis. Although patients with haemophilia may think that sharing resources with other coagulation disorders will decrease their access to health care, on the contrary, experience has shown that centres that taken these steps have gained resources, renewed energy and status that has greatly benefited the haemophilia patient and made available additional services to all patients with clotting disorders. An example is in Ireland, where the switch of services to haemostasis and thrombosis centres amplified the resources, services and staff severalfold [25, B. O'Mahony, personal communication].

### Role of patient advocacy

The role of patient advocacy in the development of modern patient care cannot be overstressed. The influence of haemophilia societies began following WWII, when a period scientific and medical progress occurred with increasing use of blood transfusions to treat many patient problems [41]. The major activity during these years of the national societies was conducting blood drives for haemophilia and advocating governments for improved care. These groups became powerful influences on governments to finance research, improve blood services and experiment with and subsequently introduce health-care delivery systems for patients with haemophilia.

In the mid-1960s, the discovery of cryoprecipitate and following, the manufacture of clotting factor concentrates, changed the dynamics of haemophilia care. Comprehensive HTC's were introduced during the mid-1970s. The lives of patients improved so much that the members of patient organizations soon lost much of the dynamic energy they had exhibited during the prior two decades. As a result, little

pressure existed to quickly improve the safety of clotting factor preparations, which still routinely transmitted hepatitis – then considered an acceptable risk [42].

In the 1980s, the AIDS epidemic ushered a tragic decade for haemophilia, yielding death, economic ruin, broken families and lives. As a result, patient organizations again became dynamic, often militant and very political. Their goal was to ensure that blood products were safe and that as a patient group; they would never again be at risk for such an epidemic. Their impact on worldwide product safety, the organization of care and the governments accepting responsibility for haemophilia care has been legendary and they deserve credit for a major portion of the progress that has been made in these areas.

The imminent danger is that as 'life becomes good' again, the patient organization will lose much of their energy and threats to their health-care systems, which are developing, will overcome many of the gains they have made.

### Future role of patient organizations

The patient organizations must recognize and adapt to these forces that threaten haemophilia care in the developed countries. Political process and care delivery systems are dynamic entities that change depending on the issues beyond the control of the haemophilia community. Haemophilia organizations cannot plan or think in a static environment because of the threats and changes that are occurring presently [43–46]. They need to understand that as national care plans for haemophilia achieve their goal, they must restructure them to ensure that the system will still supply them expertise to meet their needs. National societies must define new purpose for their organizations. Most importantly, they must understand the political processes in their country. When they work hand in hand with the physicians as a single voice, their credibility and power increase in an exponential fashion. It is the nature of politicians and government officials to exploit divisions within a community requesting services, for there are always many more requests than resources, and disagreement on the need of services is a reason for delaying action. Therefore, the haemophilia community must understand the needs of its population and voice clear realistic goals. Objectives must be set to meet these needs and national plans must be based on sustainable goals. The community must stay focused – direct their energies at things that advance its plan. It must understand the economics of the country and

establish working relations with governments. It must anticipate that most government officials will look only at the bottom line economically and will have to be convinced that the resources invested in haemophilia benefits the country's society as a whole.

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