Leveraging Data Science to Uncover Hemophilia Care in Jordan from Hakeem Database

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His Majesty King Abdullah II

His Royal Highness Crown Prince Al-Hussein Bin Abdullah II

Revolutionizing Hemophilia Care in Jordan,

*"The Ministry of Health (MOH) proudly unveils this groundbreaking report, a **monumental step forward** in our unwavering commitment to revolutionizing healthcare for Jordanians with hemophilia. This first-of-its-kind collaboration with the Royal Medical Services (RMS) unites data from both institutions, painting a **comprehensive picture** of hemophilia patients and demonstrating our dedication to the health and well-being of individuals living with hemophilia in Jordan.*

*Hemophilia, a debilitating genetic disorder, significantly impacts patients, their families, and the healthcare system. This **landmark report** tackles this challenge head-on, providing unparalleled insights into prevalence, demographics, and specific needs. It offers critical analyses of treatment strategies, hospital burden, and the symptomatic dimensions of hemophilia, offering an insightful perspective within the unique Jordanian context.*

*The report's impact is **multifaceted**. It empowers healthcare professionals by informing **evidence-based practices** and personalized medicine, while guiding future research and training. For patients and families, it serves as a **beacon of hope**, confirming the government's recognition of their struggles and commitment to improvement. Policymakers and stakeholders gain a **data-driven roadmap** to formulate targeted policies that address the hemophilia community's specific needs.*

***Beyond the data**, the MOH advocates for **unified therapies and care models** across all healthcare sectors. Collaboration is key to improving the quality of life for hemophiliacs.*

*As we share these insights, we acknowledge the need for continued action. We invite physicians, researchers, caregivers, and stakeholders to develop **innovative projects** based on the report's findings. This will fuel **sustained advocacy** and action. The MOH remains steadfast in leveraging these findings to **strengthen healthcare services**, **ensure equitable access to care**, and **champion ongoing research**.*

*Our deepest gratitude goes to all who contributed to this initiative, along with those who tirelessly support Jordanians living with hemophilia. **Together, we are unwavering in our pursuit of a healthier Jordan, where everyone has the chance to thrive.***

Minister of Health

Dr. Feras Hawari

Standing Together for Jordanian Hemophilia Care,

The Royal Medical Services (RMS), unwavering in our commitment to the well-being of hemophilia patients, proudly join the Ministry of Health (MOH) in unveiling this ***groundbreaking*** *first-ever hemophilia report for Jordan. This collaborative effort marks a* ***paradigm shift*** *in understanding and addressing the challenges faced by our hemophilia community.*

The report bridges a critical knowledge gap. By combining comprehensive data from both RMS and MOH, the key players in hemophilia care, we shed light on regional distribution, treatment strategies, facility utilization, and the lived experiences of Jordanian hemophilia patients. United, we've created a comprehensive view of hemophilia, specific to our nation's context.

This report isn't just about data. It's a catalyst for ***innovation****. By championing new therapies and collaborative care models, we equip healthcare professionals with the knowledge they need to* ***transform*** *their practices. This empowers them to adopt* ***personalized medicine approaches****, ultimately leading to* ***better care*** *for hemophilia patients.*

This report's significance goes beyond healthcare. It serves as a public recognition of the struggles faced by hemophilia patients and their families. By making this information public, we demonstrate our ***firm commitment*** *to* ***improving their quality of life*** *and the well-being of the entire Jordanian community.*

This is just the beginning. A springboard for ***long-term actions****. The RMS remains resolute in utilizing the report's findings to* ***transform*** *healthcare services as we are committed to collaboration across healthcare sectors to ensure everyone receives the care they deserve, while relentlessly pursuing new research breakthroughs.*

Moving forward, together with all stakeholders, the RMS remains dedicated to ***revolutionize*** *Jordan's healthcare system.*

We extend our deepest gratitude to all contributors and ***welcome future partnerships*** *to serve our nation.*

General Manager of Royal Medical Services

Dr. Yousef AL Zureiqat

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1. Acknowledgements

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2- **Dr. Ruba Hazaymeh**, Hematologist at Hematology and Oncology Department, Queen Rania for Children Hospital, Royal Medical Services
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Another thanks to **HDA team** at **Electronic Health Solutions** for their back end support and commitment to establish the national hemophilia electronic registry that enabled the production of this study.

2. Table of Content

3. Executive Summary

Patient Demographics: The analysis of electronic records from the Ministry of Health and the Royal Medical Services revealed **460** patients with congenital hemophilia (types A, B, or C). The analysis revealed **377/**460 patients with congenital hemophilia (A), **97%** of which were male, **212**/377 (**56.23%**) resided in Amman, and **199**/377 (**52.79%**) severe cases. As of **2023**, there were **373** patients with hemophilia (A) still alive, with **152**/373 (**40.75%**) being under 15 years of age.

Healthcare Utilization: For the period of 2017 to 2023, hemophilia (A) patients spent **9,715** bed days hospitalized, with **13,126** outpatient visits, **92** surgeries, and **3,874** emergency visits. Various treating specialties required for hemophilia management, often available only in limited tertiary hospitals, resulted in patients traveling long distances for care.

Treatment Challenges: Approximately **11%** of severe hemophilia cases developed "inhibitors" to FVIII, which led providers to change the treatment plan to other regimens such as bypassing or biological agents.

Current Status and Calls for Actions:

Jordan has demonstrated a strong commitment and significant strides in addressing thalassemia and hemophilia. Key actions taken include:

- ✓ **Establishment of Dedicated Centers**: Jordan has established 3 specialized centers to provide comprehensive care for thalassemia and hemophilia patients.
- ✓ **Regulatory Framework**: The country has implemented regulations to ensure consistent access to essential medications, including extended coverage periods for supply tenders and diversified supply chains.
- ✓ **Treatment Protocol Advancement**: Jordan has adopted innovative treatment protocols, emphasizing preventive medicine and home therapy. Bioagents have been introduced for high-risk patients.
- ✓ **Patient Engagement**: The Ministry of Health has prioritized patient engagement, fostering open communication and education initiatives.
- ✓ **Leveraging Health Information Systems**: Jordan has implemented Hakeem, the national electronic medical record in ministry of health and royal medical services which enabled extended analysis of disease management and burden

To build upon these achievements and further improve patient outcomes, we urge the global community to:

1- Support the expansion of treatment centers to meet the growing patient needs.
2- Encourage research collaborations to advance in understanding the disease.
3- Provide training and technical assistance to healthcare professionals to enhance their skills and knowledge.
4- Promote patient education and support programs to empower individuals with thalassemia and hemophilia.
5- Facilitate data sharing and encourage the best practices for data exchange cross sectors to optimize care and resource allocation.

By working together, a future where effectively managing hemophilia is possible and patients can live **fulfilling** lives.

3.1 Purpose

Hemophilia, a congenital bleeding disorder, necessitates lifelong monitoring and treatment. It results in spontaneous or injury-induced bleeding, leading to complications such as joint problems, arthropathy, and reduced mobility. As a result, patients may face challenges in fully participating in society, and, in some instances, experience premature mortality. This report leverages data from Hakeem database, Jordan's National Electronic Health Record system utilized in Ministry of Health (MOH) and Royal Medical Services (RMS) Hospitals, to gain comprehensive insights into the challenges of managing hemophilia and its enduring impact on the quality of life of individuals with hemophilia in Jordan.

3.2 Conclusions

From the electronic records of the MOH and RMS in Jordan, the following data was obtained:

In total **494** patients were found with different coagulation factors defects, among these patients:

- **377** (**76.13%** ± 3.6%, CI 95%) had congenital factor VIII deficiency (Hemophilia (A)).
- **80** (**16.19%** ± 3.5%, CI 95%) had congenital factor IX deficiency (Hemophilia (B)).
- **3** (**0.61%** ± 1%, CI 95%) had congenital factor XI deficiency (Hemophilia (C)).

Among the **377** **congenital hemophilia (A)** patients, the following was found:

- **365**/377 (**96.82%** ± 1.24%, CI 95%) were **males**.
- **212**/377 (**56.23%** ± 4.96%, CI 95%) from **Amman**.
- **154**/377 (**40.85%** ± 5%, CI 95%) under **15** years.
- **373**/377 (**98.94%** ± 0.8%, CI 95%) **alive** by 2023.
- **45**/377 (1**1.94%** ± 3.6%, CI 95%) were **non-Jordanian**.
  - **29**/45 (**64.44%** ± 11.36%, CI 95%) **Syrians**.
  - **13**/45 (**28.89%** ± 14.01%, CI 95%) **Palestinians**.
  - **3**/45 (**6.67%** ± 11.23%, CI 95%) **Iraqis**.
- **199**/377 (**52.79%** ± 4.9%, CI 95%) **severe**.
- **64**/377 (**16.98%** ± 4.05%, CI 95%) **moderate.**
- **111**/377 (**29.44%** ± 4.78%, CI 95%) **mild**.

Typically, severe hemophilia (A) patients are regularly prescribed factor VIII replacements as prophylaxis and home therapies. In some cases, patients' antibodies develop inhibitors against the administered factor VIII, When this occurs, the factor is unable to stop the bleeding, physicians typically switch to factor VII as an alternative bypassing agent [15,16]. Additionally, a few patients with inhibitors in Hakeem database began new technology treatments, such as biological agents that replace the function of factor VIII without being affected by inhibitors. Among our severe hemophilia (A) patients, **21**/199 (**10.5%** ± 4.55%, CI 95%) developed "inhibitors".

In Hakeem databases, the total units of factor VIII dispensed for hemophilia (A) patients in **2023** was **9,604,000 IU**, with an average of **46,850 IU** per patient. However, there was a notable variance of average units between these patients (Standard Deviation = **67,750 IU**), potentially due to various factors such as age, weight, severity, and complications affecting the targeted level of factor VIII. Additionally, medication availability may have limited physicians, forcing them to reduce the planned

amounts. Patients with Hemophilia (A) who developed "inhibitors" consumed **360 mg** of factor VII in **2023**, with an average of **60.03 mg** per patient (Standard Deviation = **47.66 mg**).

In **2023**, **111** hemophilia (A) patients spent approximately **1,074** days hospitalized in **20** tertiary and peripheral hospitals within the Ministry of Health and Royal Medical Services. Furthermore, there were nearly **2,522** outpatient visits, **449** emergency visits, and **16** surgeries. In **2022**, approximately **178** patients with hemophilia (A) experienced **1,466** bleeding events, including **484** swellings, **460** pains, **393** bleeds, **106** bruises, and **23** other events, primarily affecting the knees, elbows, and ankles.

The top treating specialties involved in hemophilia management included hematology, emergency, internal medicine, pediatrics, dentistry, physiotherapy, orthopedics, surgery, and gastroenterology. However, these specialties are often only available in limited tertiary hospitals, leading patients to travel long distances, sometimes **exceeding 300 kilometers**, from southern or northern regions to the middle region where most treating specialties are available in Jordan.

One of the recommended solutions for cross-functional healthcare services is the establishment of centers of excellence in each region of Jordan (northern, middle, and southern), offering at least orthopedics and physiotherapy services. This is especially crucial for better hemophilia management, given the young age of the population and the potential long-term impact on their quality of life due to early childhood onset of complications. The average age of hemophilia (A) patients in our database was **20.71** years.

4. Introduction

4.1 Overview

Hemophilia is an X-linked genetic disorder transmitted from either a carrier mother or an affected father to their offspring. It arises from a mutation in one of the genes responsible for producing the clotting factor proteins essential for blood clot formation, and since these genes are situated on the X chromosomes, males can only inherit the condition from their mothers. In the rare case where a female inherits affected X chromosomes from both parents, she would also have hemophilia [1]. Within Hakeem database, **12**/377 (**3.18%** ± 2.36%, CI 95%) individuals were females.

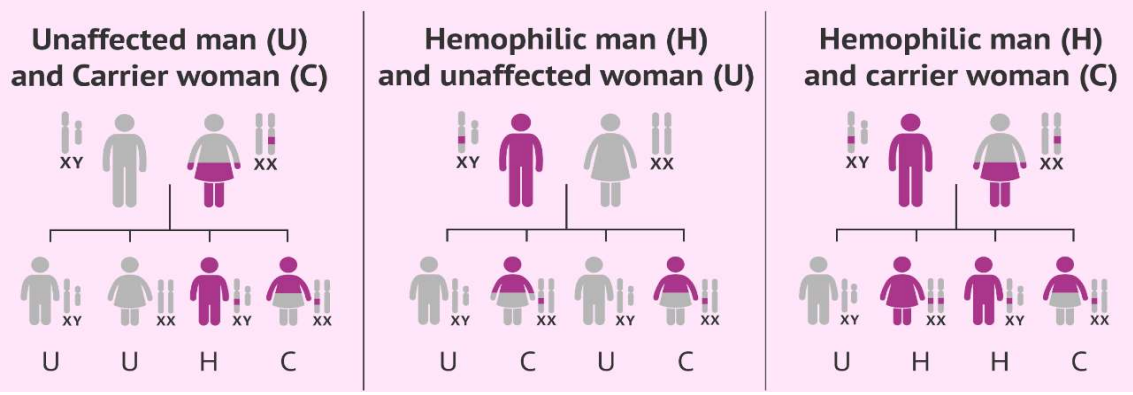


Figure 1: Possible Hemophilia Inheritance Patterns [18]

Various types of hemophilia exist, with the most prevalent being hemophilia (A), characterized by a deficiency of clotting factor VIII, as evidenced by **377** patients recorded in Hakeem database. Another common type is hemophilia (B), which results from a deficiency of clotting factor IX, with **80** patients identified, indicating a ratio of **4.7** (A) patients to **1** (B) patient. Table 1 provides an overview of general statistics pertaining to individuals with hemophilia in Hakeem database.

Category	Patients	% of Patients	Avg. Age	% of Males
Coagulation Defects	**494**	**100.00%**	**20.55**	**95%**
Hemophilia A - Factor VIII	**377**	**76.32%**	**20.71**	**97%**
Hemophilia B - Factor IX	**80**	**16.19%**	**23.21**	**99%**
Hemophilia C - Factor XI	**3**	**0.61%**	**18.33**	**67%**
Other Coagulation Factors Deficiencies	**34**	**6.88%**	**12.65**	**62%**
1	2	0.40%	11.00	100%
10	5	1.01%	17.80	60%
13	3	0.61%	20.00	100%
7	24	4.86%	10.79	54%
Total	**494**	**100.00%**	**20.55**	**95%**

Table 1: Hemophilia Patients in Hakeem Database as of 2023

The conventional approach for managing hemophilia (A & B) involves the artificial replacement of the deficient clotting factor through infusion into the veins using a prepared factor concentrate. When administered regularly (known as prophylaxis), this method can help prevent numerous bleeding episodes and arthropathy, which is the primary cause of morbidity and reduced quality of life for individuals with hemophilia. However, some patients may develop inhibitors (antibodies) that impede the clotting factors from functioning as anticipated, necessitating the transition to alternative bypassing agents or novel technologies such as biological agents. In these instances, the disease becomes severe, making treatment exceptionally challenging and leading to increased cost of care, ultimately resulting in a significantly diminished quality of life.

Figure 2: Hemophilia Management Approaches

The complications associated with hemophilia bleeds contribute to a wide-ranging treatment burden experienced by both the patient and the healthcare provider. These complications may include severe internal bleeding (potentially life-threatening), infections, and joint damage. Individuals with hemophilia experience a lower health-related quality of life compared to the general population, likely due to the physical limitations and psychosocial challenges associated with the disease [2 - 6].

Subsequent sections will delve into the impact and long-term progression of hemophilia (A) and endeavor to quantify the direct impact it could have on an individual's quality of life. Nevertheless, it is challenging to comprehensively measure all aspects of impact since this analysis focuses retrospectively on extracting information about healthcare utilization from the patients' electronic health records. The indirect impact, such as absence from work, limited physical activities, increased

risk of obesity, restricted social engagements, severe pain leading to stress and depression, and transportation costs, remain beyond the scope of this report.

4.2 Background

As of **2023**, Hakeem was implemented in **39** out of 45 Ministry of Health and Royal Medical Services hospitals, with approximately 9 million registered medical records.

Within the Ministry of Health, hemophilia is primarily managed in three specialized centers for Thalassemia and Hemophilia, which are operated by the main tertiary hospitals. The largest of these centers is in "Al-Bashir Women's & Children's Hospital" in **Amman**, utilizing Hakeem since **2017**. This referral center treats patients from across Jordan, particularly from the central and southern regions. The second largest center, located in "Princess Rahmah Hospital" in **Irbid**, has been using Hakeem since **2014** and primarily serves the northern region of Jordan. The third center is situated in "Zarqa Governmental Hospital" in **Zarqa**, utilizing Hakeem since **2015**.

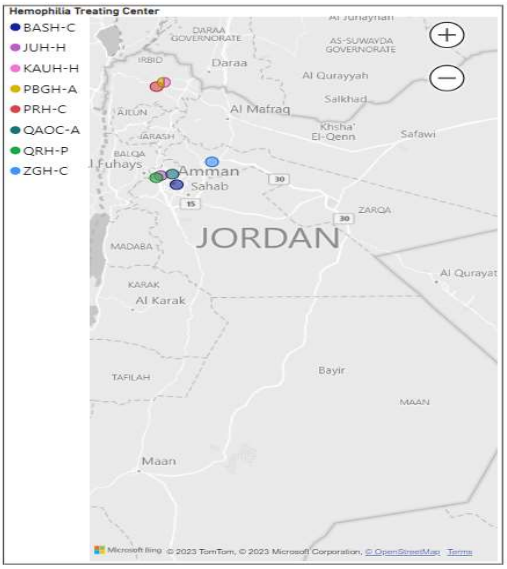


Figure 3: Hemophilia Treating Locations in Jordan

While other hospitals may provide treatment for hemophilia patients in their hematology, internal medicine, or emergency departments, patients requiring specialized treatment plans are referred to designated specialized centers, typically the nearest one. In the Royal Medical Services, pediatric military patients from across the kingdom are primarily treated in the hematology department at "Queen Rania for Children Hospital" in **Amman**, using Hakeem since **2016**. However, adult patients in the Royal Medical Services are mainly treated in the hematology department at "Queen Alia Oncology Hospital" in **Amman**, with Hakeem implementation since **2020**.

The two main university hospitals in Jordan also provide treatment for hemophilia patients, however, they do not utilize Hakeem. Unfortunately, no such centers are known to exist within the private

healthcare sector of Jordan. Table 2 presents the distribution of known hemophilia treatment centers in Jordan, along with the number of hemophilia (A) patients registered in Hakeem database.

Hemophilia Treating Centers in Jordan

Domain	Governorate	Code	Patients	Type	Full Name
JUH	Amman	JUH-H	1	Department	Pediatrics and Adults Hematology and Oncology Department at Jordan University Hospital
MOH	Amman	BASH-C	187	Center	Pediatrics and Adults Thalassemia and Hemophilia Center at Bashir Hospital
RMS	Amman	QAOC-A	38	Department	Adults Hematology and Oncology Department at Queen Alia for Oncology Military Hospital
RMS	Amman	QRH-P	44	Department	Pediatrics Hematology and Oncology Department at Queen Rania Military Hospital
KAUH	Irbid	KAUH-H	3	Department	Pediatrics and Adults Hematology and Oncology Department at King Abdulla University Hospital
MOH	Irbid	PBGH-A	21	Department	Adults Hematology and Oncology Department at Princess Basma Hospital
MOH	Irbid	PRH-C	41	Center	Pediatrics Thalassemia and Hemophilia Center at Princess Rahmeh Hospital
MOH	Zarqa	ZGH-C	42	Center	Pediatrics and Adults Thalassemia and Hemophilia Center at Zarqa Hospital
Total			**377**		

Table 2: Thalassemia and Hemophilia Treating Centers in Jordan with Patients Registered in Hakeem Database as of 2023

Table 3 displays the distribution of male patients with hemophilia (A) across Jordan's male population. The population statistics are sourced from the latest estimations provided by the National Department of Statistics in Jordan [8,9]. The table illustrates the correlation between the distribution of hemophilia (A) male patients and the male population in each governorate, as evidenced by an equal variance two-sample t-test with a one-tailed distribution of % population vs. % patients, resulting in a p-value of **0.94**.

Notably, the national health strategy of 2016 – 2020 indicated that **2.5%** of the population is covered by the university hospitals [10]. Consequently, it is expected that some additional patients with hemophilia are being treated at these hospitals. However, information about these patients is unavailable as these hospitals do not utilize Hakeem.

Male Patients by Governorate

Governorate	Male Population	% Male Population	Male Patients	100K Rate	% Patients	95% CI	Expected Patients (20.1 WHF)	% Identified
Amman	2,510,634	42.00%	205	8.2	56.16%	(49 - 59)	504.64	41%
Irbid	1,105,874	18.50%	58	5.2	15.89%	(12 - 19)	222.28	26%
Zarqa	854,811	14.30%	43	5.0	11.78%	(9 - 15)	171.82	25%
Mafraq	340,729	5.70%	12	3.5	3.29%	(2 - 5)	68.49	18%
Balqa	310,840	5.20%	8	2.6	2.19%	(1 - 4)	62.48	13%
Karak	197,264	3.30%	11	5.6	3.01%	(2 - 5)	39.65	28%
Jarash	149,442	2.50%	4	2.7	1.10%	(0 - 3)	30.04	13%
Aqaba	119,554	2.00%	3	2.5	0.82%	(0 - 2)	24.03	12%
Madaba	119,554	2.00%	2	1.7	0.55%	(0 - 2)	24.03	8%
Ajloun	107,599	1.80%	2	1.9	0.55%	(0 - 2)	21.63	9%
Ma'an	101,621	1.70%	8	7.9	2.19%	(1 - 4)	20.43	39%
Tafila	59,777	1.00%	2	3.3	0.55%	(0 - 2)	12.02	17%
			7	Infinity	1.92%	(1 - 4)		0%
Total	**5,977,700**	**100.00%**	**365**	**6.1**	**100.00%**	**(95 - 98)**	**1,201.52**	**30%**

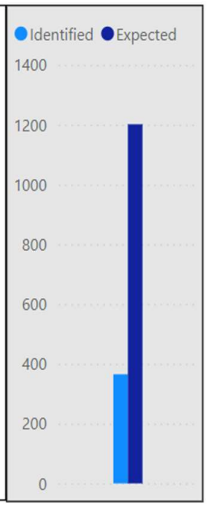


Table 3: Distribution of Male Hemophiliacs (A) by Governorates as of 2023

*[*blank governorates indicate patients with missing address information]*

The overall rate per 100,000 males from this database is estimated to be approximately **6.1**, with the range varying from **1.7** in Madaba to **8.2** in Amman. The highest rates are observed in the primary governorates in Jordan, such as Amman (**8.2**), Irbid (**5.2**), Zarqa (**5.0**), Karak (**5.6**), and Maan (**7.9**), where the largest tertiary hospitals are situated. According to the World Hemophilia Federation, the expected range is between 17.1 – 20.1 hemophilia (A) patients per 100,000 males, equating to 1 in 5,000 males [13,14]. Globally, most patients are misidentified based on the expectation of **20.1** per 100,000 males, resulting in our identified vs. expected percentage being **30%.**

Patients need to travel across Jordan to a funded Thalassemia and Hemophilia center to receive their specialized treatments as illustrated in table 4.

Patients by Owner and Governorate

Region		1					2					3					Total
Owner	Total	Ajloun	Irbid	Jarash	Mafraq	Total	Amman	Balqa	Madaba	Zarqa	Total	Aqaba	Karak	Ma'an	Tafila	Total	
BASH-C	7	7						151	8	2	1	162	2	10	3	1	16	185
QRH-P			1	6			7	30			2	32		1	3	1	5	44
ZGH-C											42	42						42
PRH-C			1	29	2	8	40	1				1						41
QAOC-A				5	1	1	7	27			1	28	1		2		3	38
PBGH-A				17	1	3	21											21
KAUH-H				2		1	3											3
BASH-A								1				1						1
JUH-H								1				1						1
Others								1				1						1
Total	**7**	**7**	**2**	**59**	**4**	**13**	**78**	**212**	**8**	**2**	**46**	**268**	**3**	**11**	**8**	**2**	**24**	**377**

Table 4: Hemophilia (A) Patients by Thalassemia and Hemophilia Center and Patient's Governorate (Address) as of 2023

*[*blank governorates indicate patients with missing address information]*

Despite having received significant support in the past for the treatment of hemophilia patients from the World Federation of Hemophilia and the Jordanian Society for Thalassemia and Hemophilia, the influx of refugees from neighboring and regional countries like Syria has led to an increased percentage of non-Jordanian hemophilia patients, with **45**/377 identified as non-Jordanians. This has presented additional challenges for the government concerning the accessibility and availability of treatments, potentially influencing the approach toward preventive medicine for all patients.

Nationality		Middle	Northern	Southern	Total
⊞ **Jordanian**		**247**	**61**	**24**	**332**
⊟ **Refugee**	**7**	**21**	**17**		**45**
Iraq	2	1			**3**
Palestinian	2	11			**13**
Syrian	3	9	17		**29**
Total	**7**	**268**	**78**	**24**	**377**

Table 5: Hemophilia (A) Patients by Nationality as of 2023

*[*blank governorates indicate patients with missing address information]*

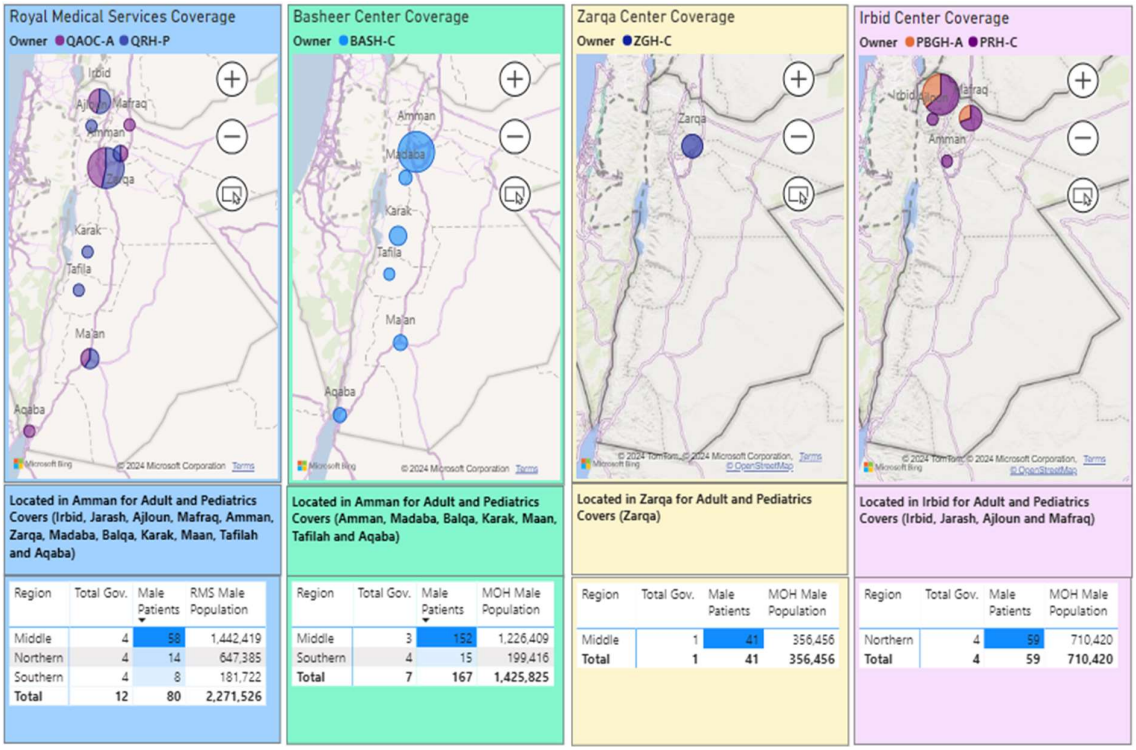


Figure 4: Male Population and Patients Coverage per Thalassemia and Hemophilia Centers in MOH and RMS as of 2023

Ideally, Ministry of Health covers around **42%** of Jordan's population while Royal Medical Services covers around **38%**, this is based on the latest estimations announced in the National Health Strategy 2016 – 2020 [10]. Based on that, figure 4 shows the 4 main Thalassemia and Hemophilia centers along with the number of governorates and projected population they are expected to serve. The projected population is calculated by multiplying the coverage proportion by the estimated male population of the governorates within the scope of that center.

5. Epidemiological Summary of Hemophilia (A) – Hakeem Database

In the United States, approximately 1 in every 5,000 male births are living with hemophilia (A) and are under the care of federally funded hemophilia treatment centers [13]. Hemophilia (A) holds the highest prevalence among hemophilia cases in the UK, with a prevalence ranging between 1 in every 5,000 to 10,000 males, as reported by the NHS [12]. Within Hakeem database, Hemophilia (A) emerged as the most prevalent type, occurring in approximately **1** in every **10,000** male births. The distribution of the total **377** hemophilia (A) patients in the Hakeem database, categorized by severity and owner, is depicted in Figure 5.

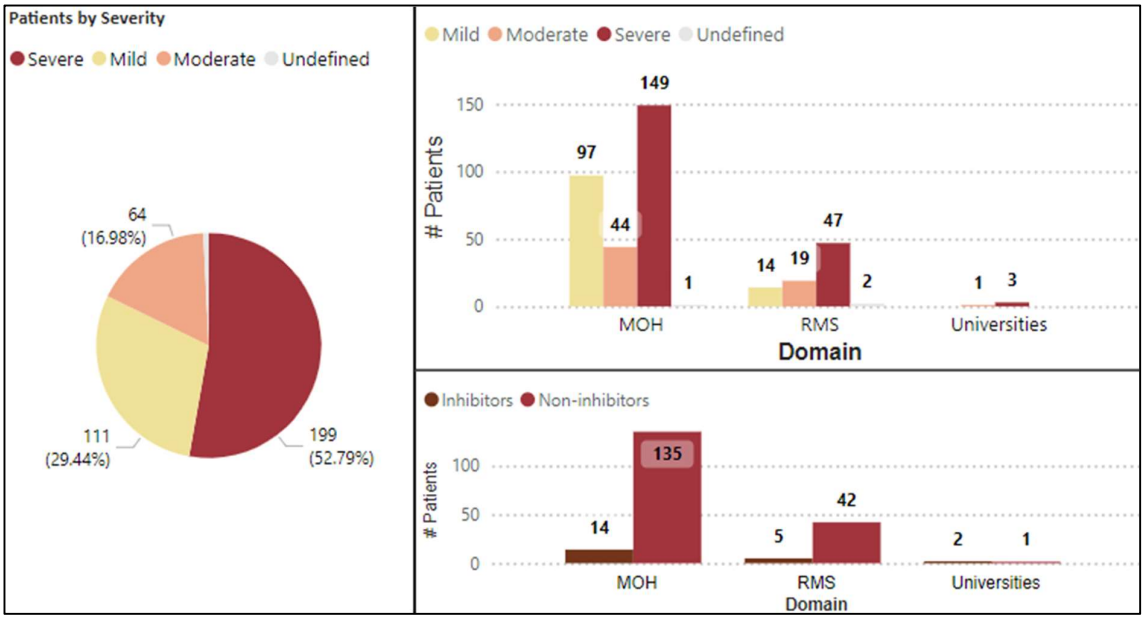


Figure 5: Hemophilia (A) Patients by Severity in Ministry of Health and Royal Medical Services as of 2023

By **2023**, **373** hemophilia (A) patients were alive. Figure 6 shows their distribution by age group (bins of 5 Years). The figure shows the right skew.

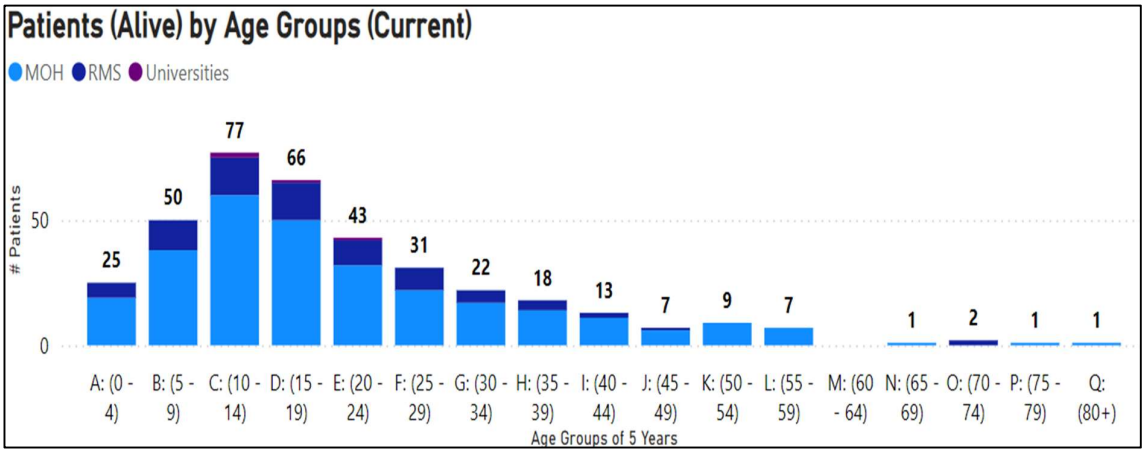


Figure 6: Alive Hemophilia (A) by Age Groups (Bins of 5 Years) by Domain as of 2023

Historically, individuals with hemophilia had significantly reduced life expectancies due to complications arising from the condition. Nevertheless, as per the World Federation of Hemophilia, the projected life expectancy for individuals with hemophilia (A) should now be akin to that of the general population, provided proper treatment is administered. Within Hakeem database, only **5**/373 (**1.34%** ± 1.87%, CI 95%) alive patients with hemophilia (A) were recorded as being above 60 years old, and **41**/373 (**11%** ± 3.6%, CI 95%) were above 40 years old. Moreover, **261**/373 (69.97% ± 4.43%, CI 95%) hemophilia (A) patients were below 25 years old. This is notably lower in comparison to the typical life expectancy of 73 years in Jordan [7].

Table 6 exhibits the estimated male population and their age group distribution, contrasting it with the distribution of identified male patients with hemophilia (A) in Hakeem database.

The table indicates that the identified male patients have lower percentages compared to the total male population percentages across all age groups above 40 years (**3.56%** vs. 6%, **1.92%** vs. 5%, **2.47%** vs. 4%, **1.92**% vs. 3%, **0.27%** vs. 3%, **0.55%** vs 0%, and **0.27%** vs. 0%).

Expected Patients by Age Groups

Age Groups	Male Population	Identified Male Patients	% Population	% Identified Patients	Expected Male Patients
A: (0 - 4)	687,435	27	12%	7.40%	138.17
B: (5 - 9)	735,257	49	12%	13.42%	147.79
C: (10 - 14)	633,636	73	11%	20.00%	127.36
D: (15 - 19)	591,792	63	10%	17.26%	118.95
E: (20 - 24)	591,792	43	10%	11.78%	118.95
F: (25 - 29)	520,060	31	9%	8.49%	104.53
G: (30 - 34)	460,283	22	8%	6.03%	92.52
H: (35 - 39)	406,484	17	7%	4.66%	81.70
I: (40 - 44)	352,684	13	6%	3.56%	70.89
J: (45 - 49)	298,885	7	5%	1.92%	60.08
K: (50 - 54)	221,175	9	4%	2.47%	44.46
L: (55 - 59)	155,420	7	3%	1.92%	31.24
N: (65 - 69)	185,309	1	3%	0.27%	37.25
O: (70 - 74)	17,933	2	0%	0.55%	3.60
Q: (80+)	5,978	1	0%	0.27%	1.20
Total	**5,977,700**	**365**		**100.00%**	**1,201.52**

Table 6: Estimated Jordanian Male Population vs. Identified Male Patients in Hakeem Database as of 2023

According to the US National Hemophilia Foundation, the initial recombinant factor VIII product, known as Koate DV and produced by Baxter Healthcare, was approved by the US Food and Drug Administration (FDA) in 1992 [17]. Experts in Jordan specializing in this field recollect that plasma-derived factor VIII concentrates began to be widely used as the standard treatment for hemophilia (A) in the early **1980s**. Subsequently, once the Jordanian FDA approved the recombinant product in the late 1990s, it gradually became the preferred medication. However, during that period, the high cost and limited availability restricted access to this treatment.

As of **2023**, both plasma-derived and recombinant factor VIII concentrates are used interchangeably and are commonly prescribed by most physicians at renowned hemophilia treatment centers. This

development provides optimism for an improved life expectancy among the younger generations in Jordan.

Figure 7 displays the distribution of hemophilia (A) patients, and their planned therapies categorized by severity.

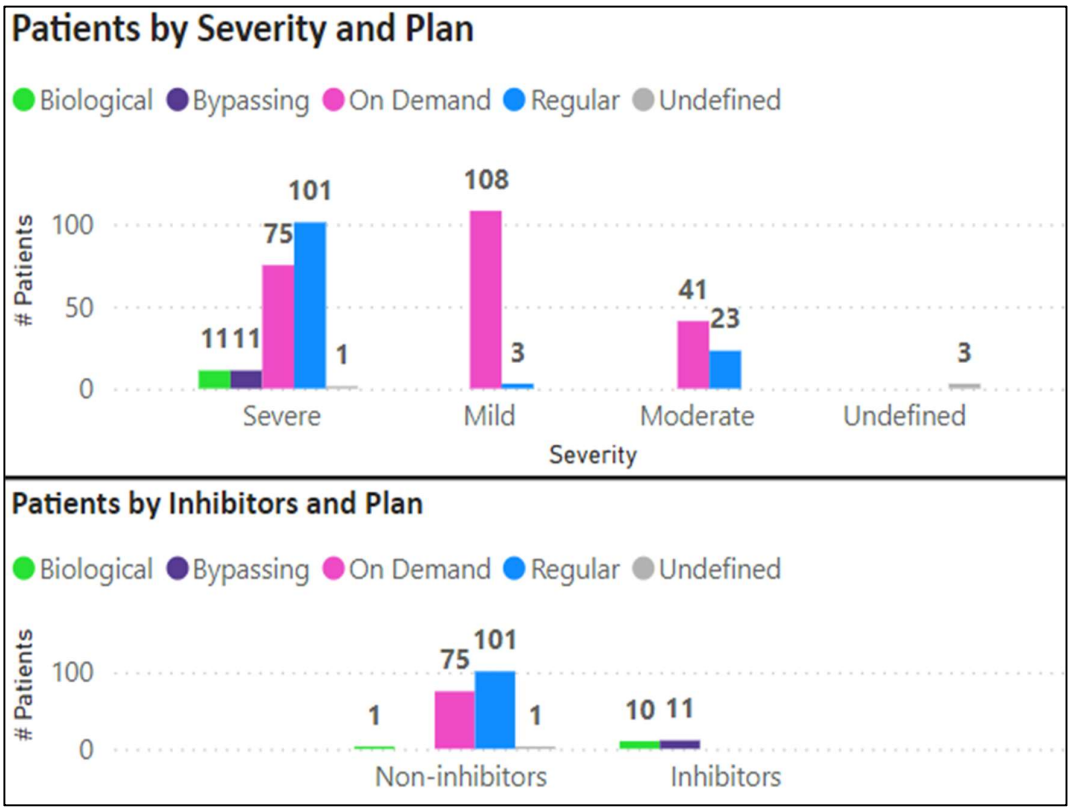


Figure 7: Hemophilia (A) Cases by Severity and Therapy Plans as of 2023

As noted from the Figure:

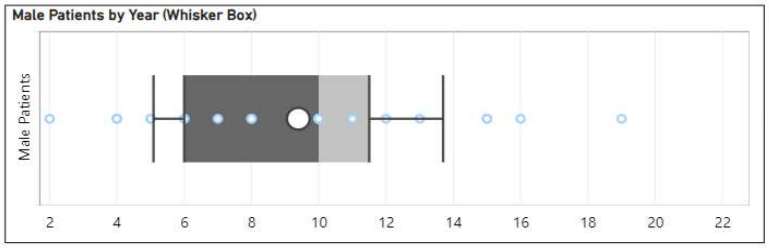
- **75**/199 (**31%** ± 6.34%, CI 95%) severe cases of hemophilia (A) are on demand plans.
- **(10** + **11)**/21 (**100%**) severe with inhibitors hemophilia (A) patients are on either bypassing or biological agents.

The incidents of Jordanian hemophilia (A) male patients with respect to the total Jordanian male births for the last **22** years (**2000** – **2022**) is shown in table 7. Jordanian Male birth statistics are taken from Jordan Department of Statistics online data bank [8,9].

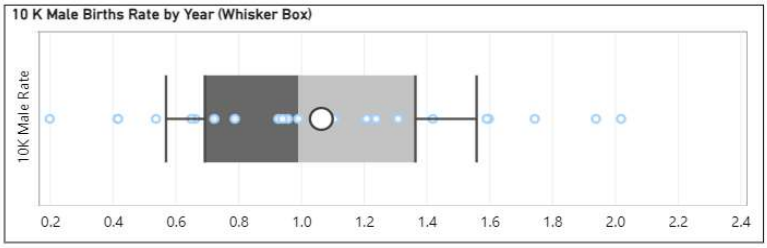
Despite the average rate of approximately 1.0 per 10,000 Jordanian Male Births depicted in table 7 for the period 2000-2022, the pattern exhibits inconsistency over these years, as indicated by the whisker box and control charts displayed in figures 8 and 9 (ranging from 0.7 for Q1 to 1.4 for Q3, with an IQR=0.7).

This could be attributed to various factors, including the absence of a birth screening program in Jordan to assess factor levels. Consequently, many patients are diagnosed incidentally when the first bleeding occurs due to events like trauma, spontaneous incidents, or when the patient undergoes

early medical interventions such as circumcision, dental work, or surgery. Unfortunately, there is limited available data regarding the diagnostic process, particularly due to the restricted availability of factor VIII assay kits, which are only accessible in specific labs within the Ministry of Health and Royal Medical Services. In numerous instances, patients are diagnosed in other facilities, primarily in university hospital labs.



Median Type	Inclusive
Whisker Type	One Standard Deviation
Mean	9
Quartile 1	6
Median	10
Quartile 3	12
Maximum	19
Minimum	2
IQR	6
Upper Whisker	14
Lower Whisker	5



Median Type	Inclusive
Whisker Type	One Standard Deviation
Mean	1.1
Quartile 1	0.7
Median	1.0
Quartile 3	1.4
Maximum	2.0
Minimum	0.2
IQR	0.7
Upper Whisker	1.6
Lower Whisker	0.6

Figure 8: Incidents of Male Patient with Hemophilia (A) Whisker Box Analysis for the Period 2000 – 2022

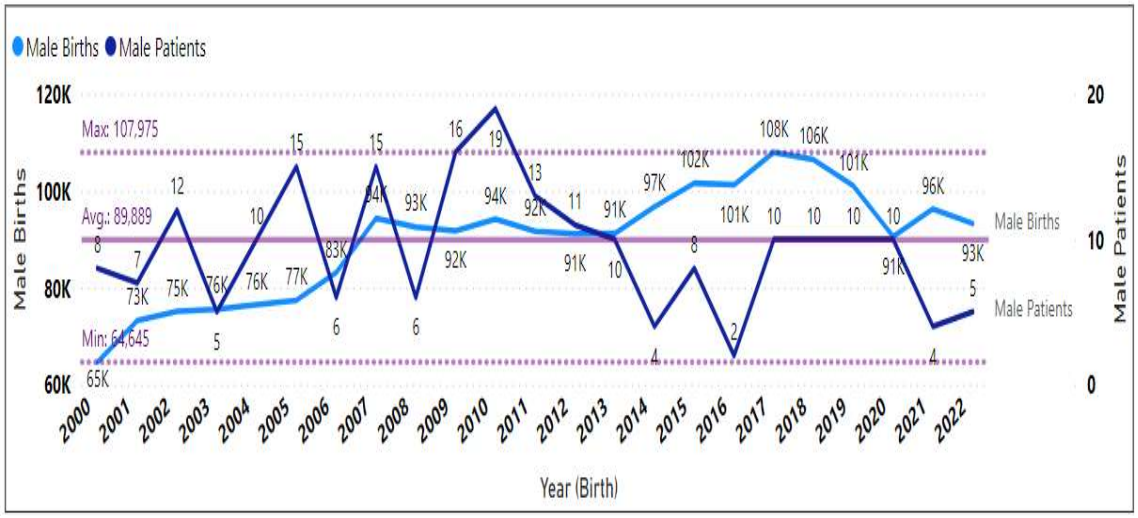


Figure 9: Annual Incidents of Jordanian Male Patient with Hemophilia (A) for the Period 2000 - 2022

Year (Birth)	Male Births (Total)	Male Births (Hemophilia A)	per 10K Male Births
2000	64,645	8	1.2
2001	73,200	7	1.0
2002	75,146	12	1.6
2003	75,553	5	0.7
2004	76,478	10	1.3
2005	77,384	15	1.9
2006	83,099	6	0.7
2007	94,333	15	1.6
2008	92,536	6	0.6
2009	91,788	16	1.7
2010	94,141	19	2.0
2011	91,655	13	1.4
2012	91,124	11	1.2
2013	91,218	10	1.1
2014	96,708	4	0.4
2015	101,588	8	0.8
2016	101,268	2	0.2
2017	107,975	10	0.9
2018	106,438	10	0.9
2019	101,036	10	1.0
2020	90,584	10	1.1
2021	96,279	4	0.4
2022	93,275	5	0.5
Total	**2,067,451**	**216**	**1.0**

Table 7: Jordanian Male Births vs. Jordanian Male Patients with Hemophilia (A) for the Period 2000 - 2022

6. Methodology and Data Collection

To better understand the burden of hemophilia (A) in Jordan and the disease effect on the patient's quality of life, (HDA) electronic registries were utilized. HDA stands for Health Data Analytics, a platform for big data warehousing, statistical, BI, and AI tools that is built on top of Hakeem database to aggregate and analyze data found in Hakeem database with other sources.

In HDA, a unique case file is created for each patient with a coagulation factor deficiency. This is done through the following data lineage activities as illustrated in figure 10:

1- A suspect list was extracted from Hakeem database if the patient:
   a. Was diagnosed with one of the coagulation factor deficiencies (using the provider narrative text, ICD9 or ICD10),
   b. Received factor medications,
   c. Has low levels of factor assay in his/her laboratory tests,
   d. Found in external resources that are imported from the clinic's logs,
   e. Or, registered at the Jordanian Hemophilia Society.
2- The files were then reviewed to merge the duplicates and to confirm with the hematology departments at Ministry of Health and Royal Medical Services for clinical indications and evidence of the coagulation factor deficiency. Some patients are simply **automatically confirmed** if strong evidence of the coagulation factor deficiency was available in their files such as bleeding events, confirmation notes by multiple hematologists, regular plans for factor concentrates, multiple confirmed factor level tests, etc.
3- A link to the medical records from all facilities within the Ministry of Health and Royal Medical Services is created.
4- Finally, facility related information is extracted, and summarization models are created to be used for burden analysis.

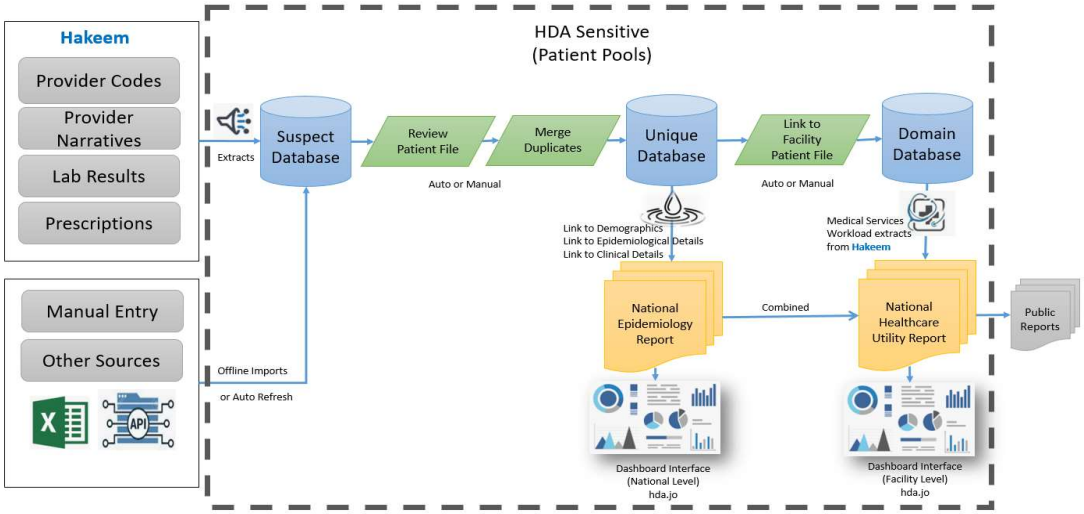


Figure 10: HDA Data Collection Process for Hemophilia Patients

The creation of the suspect list is essential such that in the likelihood of miscoding the disease other clinical indications are used to increase the sensitivity of capturing all hemophilia patients. Fortunately, hemophilia has specific clinical indications that are easy to track from the pharmacy or lab if available, accordingly a status of review was automatically assigned to each file such that:

A- **Confirmed**: patients had indications collected from the suspect list and confirmed by one of the known hemophilia centers in Ministry of Health or Royal Medical Services.
B- **HDA**: confirmed automatically when patients had multiple indications collected from the suspect list but unknown to any of the known hemophilia centers in Ministry of Health or Royal Medical Services, the patient may be treated in peripheral hospitals.
C- **New**: patients collected from the suspect list but not reviewed yet, examples: suspected or diagnosed by a surgeon, emergency physicians or dentists without being referred to a hematologist, only one low factor level test that is not repeated or confirmed. Nothing can be done to these patients except to wait for them to visit back the healthcare facility for re-evaluation.

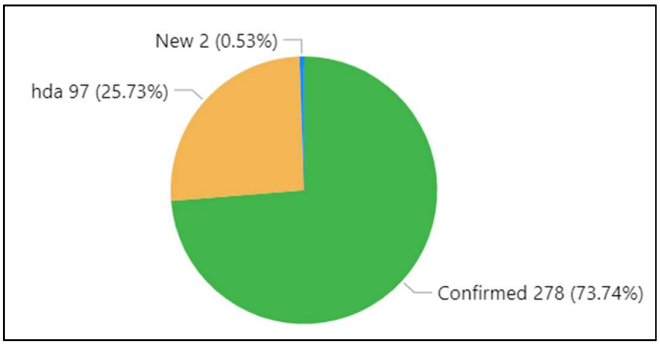


Figure 11: Unique Hemophilia (A) Patients by Status of Review as of 2023

For this report, our goal is to describe the burden of hemophilia (A) disease in terms of healthcare utilization in contrast to the benefits gained for managing and controlling complications, as well as the long-term impact on patients' lives. This exercise aims to establish a baseline for justifying the burden in terms of equity, justice, and fairness to the patients. Therefore, the burden and impact will primarily be reflected in healthcare utilization metrics, such as bed days occupied, outpatient visits, emergency visits, surgeries, and medications. Additionally, the impact will be evident in events directly related to inadequate disease management, including swelling, redness, bruising, bleeding, hemarthrosis, hematomas, and pain.

Throughout this report:

A. 95% confidence levels for proportions intervals were calculated based on the Wilson score interval without continuity.
B. Chi-Square-Tests or T-Tests were used to compare any two samples of observations.
C. One standard deviation for Whisker Box calculations.
D. Due to lack of costing data in Jordan public sector, costing calculations were done as follows:
    a. Interventions and procedures: it was based on the price paid by the patient (10%), based on insurance pricing lists, added to the percentage of support paid by the government (90%).

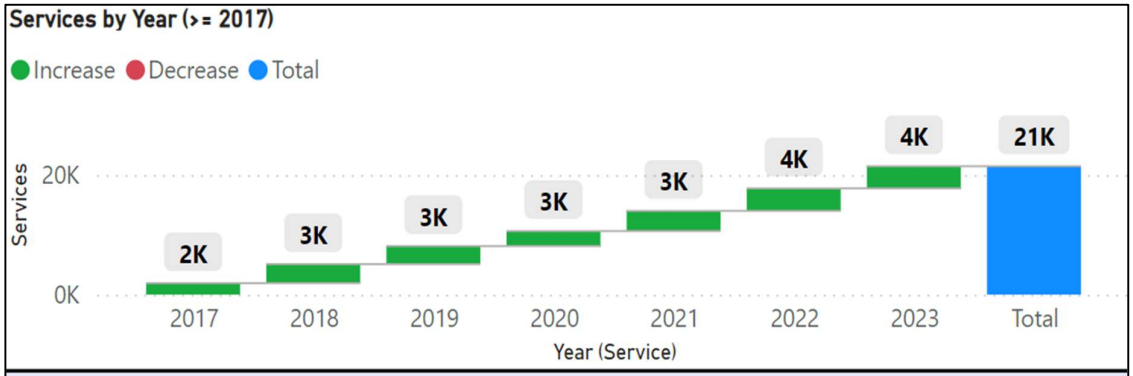
b. Medications: it was based on the average price of medication times the quantity dispensed.
c. Bed Days: it was based on an average cost of bed day estimated by the subject matter experts (around 200 JODs per bed day).
d. Out visit consultation: it was based on an average cost of consultation + administrative cost estimated by the subject matter experts (around 50 JODs per visit).
e. Emergency consultation: it was based on an average cost of consultation + administrative cost estimated by the subject matter experts (around 75 JODs per visit).

E. Severity of hemophilia (if not defined by the specialists) was considered severe if the factor deficiency was less than 1%, regular factor VIII replacement plans were in high dosages, or more than 3 bleeds per 3 months in the patient's history was reported. Moderate if the factor level was less than 5% but more than 1% and mild if the factor was more than 5 but less than 50.
F. Regardless of the Bethesda unit (BU), any patient with inhibitors was labeled as an "inhibitor". If no information indicated the development of inhibitors or if the Bethesda units (BU) were zero, the patient was labeled as a "non-inhibitor".
G. Plans were based on the regimen of medication therapy (if not explicitly reported by the physicians):
    a. **On-demand** if the patient didn't have regular prescriptions for either prophylaxis or home therapies and rather was only treated when needed for a certain bleeding event or medical procedures. This is the default plan to be set for any patient initially.
    b. **Regular** was set for patients with regular prescriptions (prophylaxis or home therapy).
    c. **Bypassing** was used for patients with inhibitors on factor VII as a bypassing agent.
    d. **Biological** was used for patients on new technologies such as biological agents.

7. Discussion (Burden in Jordan)

7.1 Healthcare Services

Healthcare services were extracted from the inpatient, outpatient, emergency, and surgery settings in all hospitals implementing Hakeem for the specific hemophilia (A) records listed in the registry for the period 2017 – 2023. A summary of these services can be seen in figure 12.



Service	Facilities	Patients	Services	Bed Days	Avg. Services per Patient	Total Cost	Avg. Cost per Patient
⊞ Admission	34	283	4,368	9,715	15	1,942,900	6,865
⊞ Emergency	28	262	3,874		15	290,550	1,109
⊞ Out Visit	23	283	13,126		46	656,300	2,319
⊞ Surgery	11	50	92		2	158,175	3,228
Total	**36**	**341**	**21,459**	**9,715**	**63**	**3,047,925**	**8,938**

Figure 12: Hemophilia (A) Patients Healthcare Services for the Period 2017 - 2023

Further more, the following observations were noted for each service:

Hospital Admissions:

- **283** patients with hemophilia (A) were admitted between 2017 – 2023 for a total of **4,368** admissions, during which they spent **9,715** bed days hospitalized.
- **93.15%** of these admissions occurred in Ministry of Health hospitals.
- **31.89%** of the patients were pediatrics (under 15 years old).
- The annual average per patient ranged from **4 – 7** admissions, with approximately **84%** of these admissions being for **severe** cases.

Outpatient Department Visits:

- **283** patients with hemophilia (A) visited the outpatient departments between 2017 – 2023 for a total of **13,126** visits.
- **99.69%** of these visits occurred in Ministry of Health hospitals.
- **39.53%** of the patients were pediatrics (under 15 years old).
- The annual average per patient ranged from **7 – 16** visits, with around **83.93**% of these visits being for **severe** hemophilia (A) cases.

Emergency Department Visits:

- **262** hemophilia (A) patients visited the emergency departments between 2017 – 2023 for a total of **3,874** visits.
- **97.91%** of these visits occurred in Ministry of Health hospitals.
- **39.78** of the patients were pediatric (under 15 years old).
- The annual average per patient ranged from **4 – 8** emergency visits, with approximately **78.27%** of these visits being for **severe** hemophilia (A) cases.

Surgeries:

- **50** patients with hemophilia (A) underwent **92** surgeries between 2017 – 2023.
- **39.13%** of these surgeries took place in Ministry of Health hospitals.
- **54.35%** of the patients undergoing surgeries were pediatric (under 15 years old)
- The annual average per patient ranged from **1 – 3** surgeries, with around **66.67%** of these surgeries being for **severe** hemophilia (A) cases.4

Ministry of Health hospitals experienced higher occupancy in admissions (**93.15%**), outpatient visits (**99.69%**), and emergency visits (**97.91%**), whereas Royal Medical Services hospitals had a slightly higher occupancy in surgeries (**60.87%**).

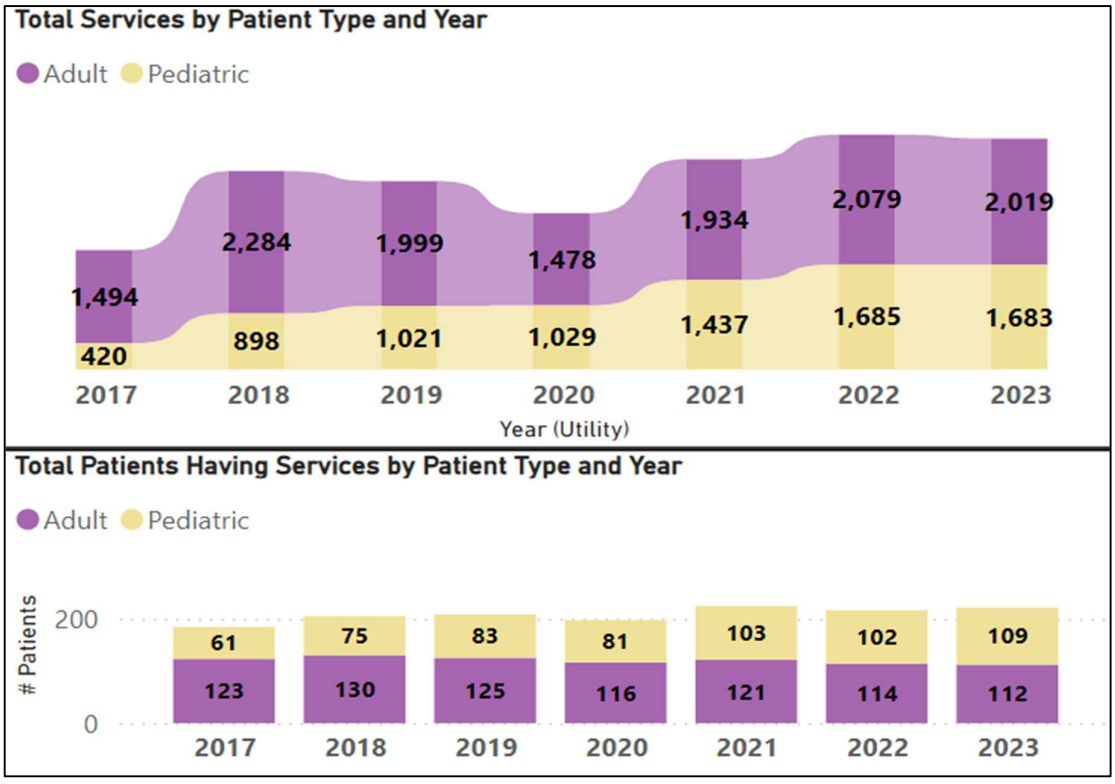


Figure 13: Hemophilia (A) Patients Healthcare Services for the Period 2017 - 2023

Figure 13 illustrates the utilization of services by adults compared to pediatric patients. Over the years, adult patients have utilized services significantly more than pediatric patients, as indicated by a p-value of **0.0043** from a two-tailed t-test comparing service utilization counts between adults and

pediatrics. In **2023**, the average number of services per adult patient was **18.02**, compared to **15.44** services per pediatric patient. This highlights the importance of early detection and management for pediatric patients to prevent future complications.

Table 8 shows all services utilizations (admissions, out visits, emergencies, and surgeries) per year and severity:

Admission by Year and Severity

Severity	2017	2018	2019	2020	2021	2022	2023	Total
⊟ Severe	506	607	386	318	618	608	623	3,666
Non-inhibitors	438	521	311	263	550	543	582	3,208
Inhibitors	68	86	75	55	68	65	41	458
⊞ Mild	65	84	55	24	46	63	46	383
⊞ Moderate	29	44	40	27	45	84	40	309
⊞ Undefined	2		1		1		6	10
Total	602	735	482	369	710	755	715	4,368

Emergency by Year and Severity

Severity	2017	2018	2019	2020	2021	2022	2023	Total
⊟ Severe	316	395	375	405	688	515	339	3,033
Non-inhibitors	275	361	346	372	643	477	319	2,793
Inhibitors	41	34	29	33	45	38	20	240
⊞ Mild	68	90	66	56	57	72	76	485
⊞ Moderate	62	38	43	40	68	67	33	351
⊞ Undefined		2	2				1	5
Total	446	525	486	501	813	654	449	3,874

Out Visit by Year and Severity

Severity	2017	2018	2019	2020	2021	2022	2023	Total
⊟ Severe	682	1,575	1,765	1,391	1,483	1,985	2,159	11,040
Non-inhibitors	624	1,473	1,653	1,331	1,373	1,833	1,997	10,284
Inhibitors	58	102	112	60	110	152	162	756
⊞ Mild	93	241	157	118	183	144	143	1,079
⊞ Moderate	81	90	124	121	169	201	208	994
⊞ Undefined		1					12	13
Total	856	1,907	2,046	1,630	1,835	2,330	2,522	13,126

Surgery by Year and Severity

Severity	2017	2018	2019	2020	2021	2022	2023	Total
⊟ Severe	2	11	3	4	9	21	12	62
Non-inhibitors	2	5	3	4	8	20	12	54
Inhibitors		6			1	1		8
⊞ Mild	8	3	2		3	2	2	20
⊞ Moderate		1		3		2		6
⊞ Undefined			1		1		2	4
Total	10	15	6	7	13	25	16	92

Table 8: Services Provided for Hemophilia (A) Patients by Year and Severity for the Period 2017 - 2023

Key points to be noted in the data from table 8 are as follows:

- There was a decrease in utilization during the COVID-19 pandemic in 2020.
- The utilization of healthcare services for hemophilia (A) patients with inhibitors was not as high as anticipated in Ministry of Health and Royal Medical Services hospitals. This could be attributed to two factors:
    a. The number of patients with inhibitors is relatively low, being:
        i. **21**/377 (**5.57%** ±2.86%, CI 95%) with respect to **all** hemophilia (A) patients.
        ii. **21**/199 (**10.55%** ±4.63%, CI 95%) with respect to **severe** hemophilia (A) patients.
    b. Factor VII supplies, which are used as a bypassing agent for patients with inhibitors, were limited in both Ministry of Health and Royal Medical Services hospitals.
    c. Many patients were referred to university hospitals for follow-up and interventions once they developed inhibitors.

Figure 14 shows the average services vs. standard deviation of services per patient by severity. The graph illustrates that, as anticipated, there is a low average of services and standard deviation for mild and moderate patients. Conversely, the severe hemophilia (A) patients exhibited the highest average utilization, but with a high standard deviation, indicating a significant variance in the services provided

to patients in this severity group. It is important to note that patients with inhibitors, especially those with high titers, are predominantly referred to university hospitals.

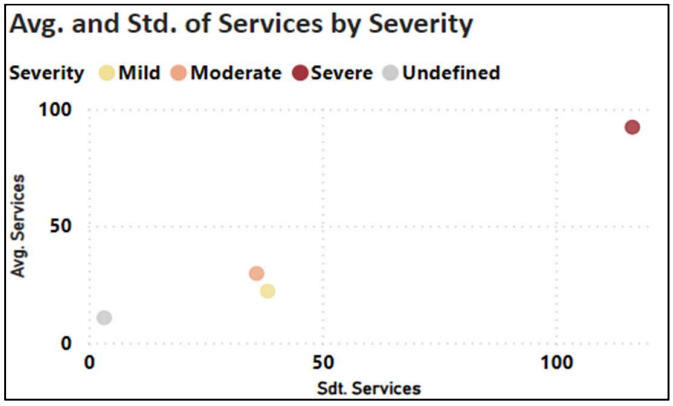


Figure 14: Average and Standard Deviation of Services per Hemophiliac (A) by Severity for the Period 2017 - 2023

Table 9 shows the top 10 treating specialties by service:

Top 10 Treating Specialties

Sections	Admission	Emergency	Out Visit	Surgery	**Total**
Hematology and Oncology	254		10,056		**10,310**
Emergency Medicine	32	3,874	1,348		**5,254**
Internal Medicine	2,450		207		**2,657**
General Pediatrics	1,186		397		**1,583**
Dentistry	9		218	1	**228**
Rehabilitation and Physiotherapy	3		225		**228**
Orthopedics	16		164	46	**226**
General Surgery	124		80	7	**211**
Gastroenterology and Hepatology	37		59		**96**
Pediatric Hematology and Oncology	61		10		**71**

Table 9: Top 10 Treating Specialties for Hemophilia (A) Patients for the Period 2017 - 2023

The relevant medical specialties, apart from the internal medicine sub-sections, include dentistry, orthopedics, rehabilitation, and general surgery. Despite their prominence, these specialties contribute to a relatively low percentage of the overall treatment. Early management of arthropathy and consistent follow-ups with healthcare providers, particularly in rehabilitation and physiotherapy, would enhance the durability of joint functions and help delay potential movement limitations or other complications. However, accessibility to such specialized services is essential. Unfortunately, these services are only available in limited tertiary hospitals located far from patients' residences. In Amman, where most treating specialties are available, there are **212**/377 (**56.23%** ±4.94%, CI 95%) hemophilia (A) patients, leaving the remaining patients required to travel to access the specialized treatment needed for their disease management plans.

This revision clarifies that there are other patients who need to travel for treatment and improves the flow of the sentence.

7.2 Surgical Intervention

The type of surgeries done in Royal Medical Services vs. the ones done in Ministry of Health for hemophilia (A) patients during the years **2017** – **2023** are shown in table 10:

Ministry of Health by Year and Procedure

Surgery	2017	2018	2019	2020	2021	2022	2023	Total
Drainage	5							5
Botox Treatment			1		1	1		3
Circumcision			1			2		3
Hematoma Debridement	2					1		3
Appendectomy		1			1			2
Hemostasis			1			1		2
Herniotomy		1		1				2
ORIF LCP Plate		1		1				2
Tonsillectomy	1	1						2
Compartment Release					1			1
Craniotomy			1					1
Cystoscopy							1	1
Fasciotomy					1			1
Laparotomy						1		1
Minor Undefined OR							1	1
Nail Excision		1						1
Pilonidal Cyst Removal		1						1
Scrotal Exploration						1		1
Total Thyroidectomy			1					1
Undefined Excision	1							1
Wound Revision				1				1
Total	9	6	5	3	4	7	2	36

Royal Medical Services by Year and Procedure

Surgery	2017	2018	2019	2020	2021	2022	2023	Total
Adenoid and Tonsil Surgery (ASTS)						1		1
Arthroscopic Synovectomy				1				1
Catheterization of Iliac Artery							1	1
Central Line Insertion					2			2
Cesarean Section			1		1		1	3
Circumcision	1						2	3
Craniotomy				1				1
Dental Under GA							1	1
Hematoma Debridement					1	1		2
Hip Aspiration						1		1
Laser Cordotomy					1			1
Manipulation Under Anesthesia (MUA)						1		1
Minor Undefined OR							2	2
Necrotic polydactyly Removal						1		1
Pars Plana Vitrectomy (PPV)							1	1
Perianal Abscess				1				1
Portacath Insertion or Removal		1			2	1		4
Rifampicin Injection		7			2	12	5	26
Sebaceous Cyst Removal		1						1
Total Knee Arthroplasty (TKA)				1			1	2
Total	1	9	1	4	9	18	14	56

Table 10: Ministry of Health Surgeries (Left) vs Royal Medical Services Surgeries (Right) for the Period 2017 – 2023

As indicated by figure 15, the estimated cost of **62** surgeries for severe hemophilia (A) patients was approximately **102,525** JODs. Since Hakeem did not include financial data in this report, the cost estimates were derived from insurance price estimations. These amounts do not cover other services and interventions provided to the patient during their hospitalization period while undergoing surgery. For example, the "Total Knee Arthropathy (TKA)" operation done for one of the patients in 2020, as extracted from Hakeem database, involved approximately 36 days of hospitalization, with around 2 weeks of preparations before the surgery to regulate factor VIII level, during which the patient received approximately 114,000 IUs. Subsequently, the patient spent the remaining period recovering. Additionally, the patient underwent 5 x-rays, 1 CT scan, and 1 ultrasound for the knee, along with nearly daily chemistry and hematology lab tests, as well as the regular use of painkillers and prophylactic antibiotics. These additional services must be considered when estimating the complete cost of the surgery package.

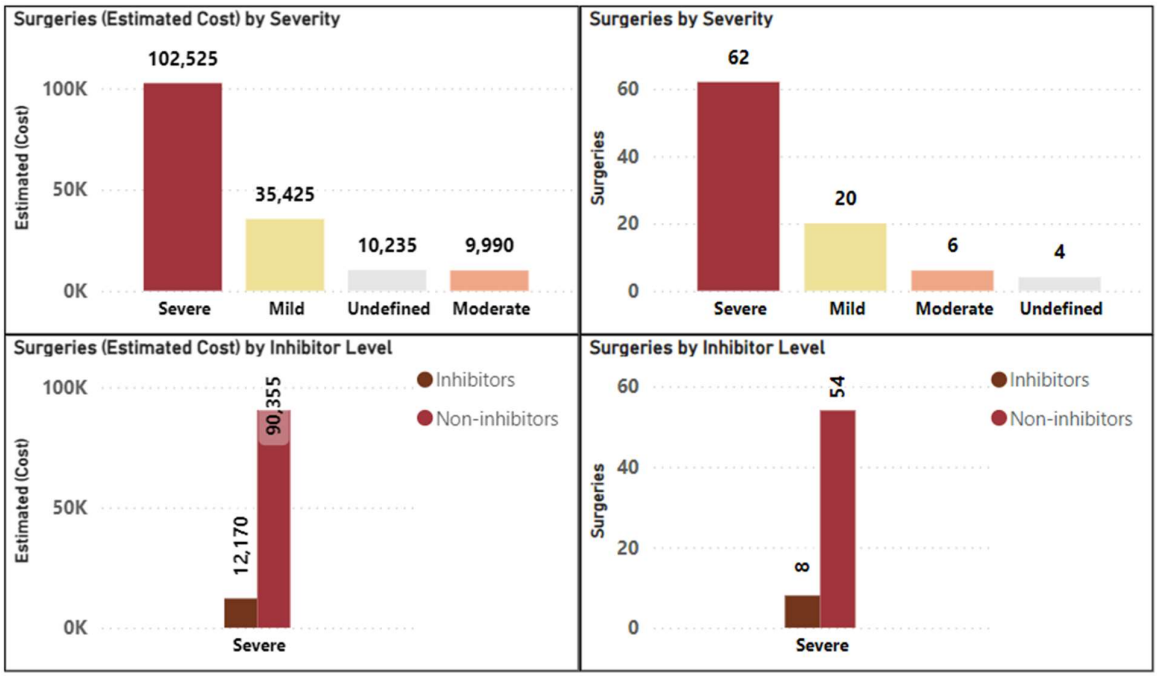


Figure 15: Surgeries and Estimated Cost of Surgeries by Severity for Hemophilia (A) Patients for the Period 2017 – 2023

7.3 Medication

A summary of the medications consumption for hemophilia (A) management between 2017 – 2023:

General Medication Consumption:

- Approximately **300,602** "units per dose" of various medications were prescribed for **346** patients with hemophilia (A) through **26,181** electronic prescriptions in both outpatient and inpatient settings.
- **75.26%** of these prescriptions were in Ministry of Health hospitals
- **6.24%** of the patients being under 15 years old.
- The annual average per patient ranged from **132 – 203** "units per dose", and around **39.1%** of these medications were for severe hemophilia (A) cases.

Factor VIII Medication Consumption in Both Outpatient and Inpatient Settings:

- Approximately **114,339** "units per dose" and **52,298,000** IU of Factor VIII were prescribed for **296** hemophilia (A) patients through **16,452** electronic prescriptions in both outpatient and inpatient settings.
- **52.4%** of these prescriptions were in Ministry of Health hospitals.
- **27.86%** of the patients being under 15 years old.
- The annual average "unit per does" per patient ranged from **19,720 IU – 53,330 IU**, and around **86.31%** of these medications were for severe hemophilia (A) cases.

Factor VIII Medication Consumption in Outpatient Settings:

- Approximately **83,783** "units per dose" and **37,637,000 IU** of Factor VIII were prescribed for **243** hemophilia (A) patients through **12,198** outpatient electronic prescriptions.
- **35.22%** of these prescriptions were in Ministry of Health hospitals.
- **32.03%** of the patients being under 15 years old.
- The annual average per patient ranged from **17.15 IU – 44.61 IU**, and around **85.6%** of these medications were for severe hemophilia (A) cases.

Factor VIII Medication Consumption in Inpatient Settings:

- Approximately **30,556** "units per dose" and **14,661,000 IU** of Factor VIII were prescribed for **187** hemophilia (A) patients through **4,254** inpatient electronic prescriptions.
- **96.5%** of these prescriptions were in Ministry of Health hospitals.
- **17.15%** of the patients being under 15 years old.
- The annual average per patient ranged from **16,900 IU – 44,340 IU**, and around **88.13%** of these medications were for severe hemophilia (A) cases.

Factor VII Medication Consumption:

- Approximately **841** "units per dose" and **1,677 mg** of Factor VII were prescribed for **21** hemophilia (A) patients through **222** electronic prescriptions in both outpatient and inpatient settings.
- **88.25%** of these prescriptions were in Ministry of Health hospitals.
- **26.67%** of the patients being under 15 years old.

- The annual average per patient ranged from **16 mg – 61.30 mg**, and around **99%** of these medications were for severe hemophilia (A) patients of which 88.94% with inhihibitors .

Here are some noteworthy findings from the above summary:

- Despite Royal Medical Services having approximately **82** patients with hemophilia (A) and Ministry of Health having **291** hemophilia (A) patients, **64.78%** of the total units of factor VIII prescribed as outpatient were in Royal Medical Services hospitals.
- Approximately **37,637,000 IU** were consumed as outpatient prescriptions, while only **14,661,000 IU** were consumed in inpatient prescriptions, indicating a shift towards prophylaxis and home therapy, as detailed in figure 16.

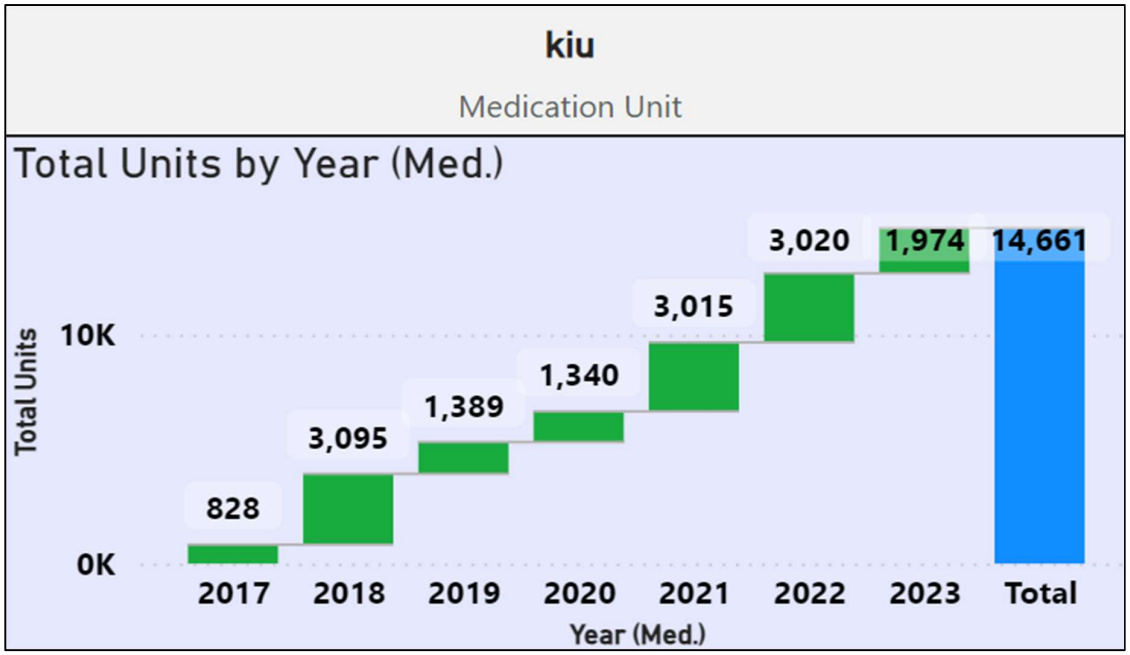


Figure 16: Total Units Consumed of Factor VIII as Outpatient Prescriptions for the Period 2017 – 2023

The cost of factor VIII vs. factor VII prescribed during the period 2017 – 2023, categorized by severity, is depicted in Figure 16. The figure highlights a significant increase in cost per patient for factor VII compared to factor VIII. For instance, in **2023**, **154** patients with severe hemophilia (A) on factor VIII incurred approximately **848 thousand JODs** in costs, whereas only **6** severe cases of Hemophilia (A) on factor VII incurred around **221** thousand JODs. This represents a ratio of **5.5:36.8**, indicating an increase of **nearly 6.7 times**.

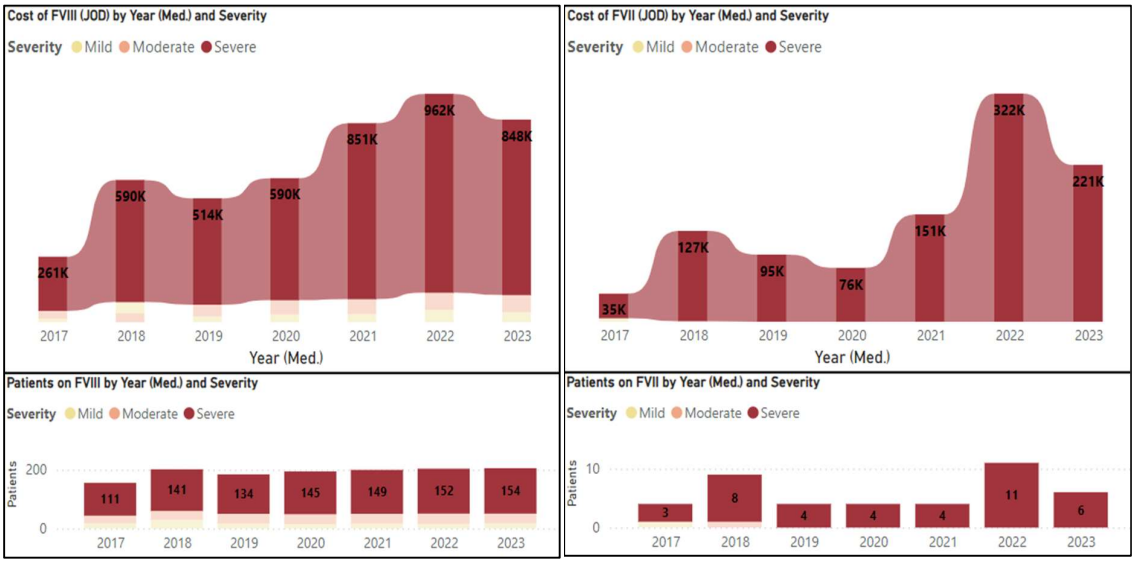


Figure 17: Cost of Coagulation Factors Prescribed for Hemophilia (A) Patients by Severity and Year for the Period 2017 – 2023

Other than the coagulation factors, the most frequently prescribed medications included those for arrhythmia and hypertension, pain control, seizures, gastric issues, infections, COPD, nutritional supplements, diabetes, and anti-inflammatory medications, as depicted in Figure 18.

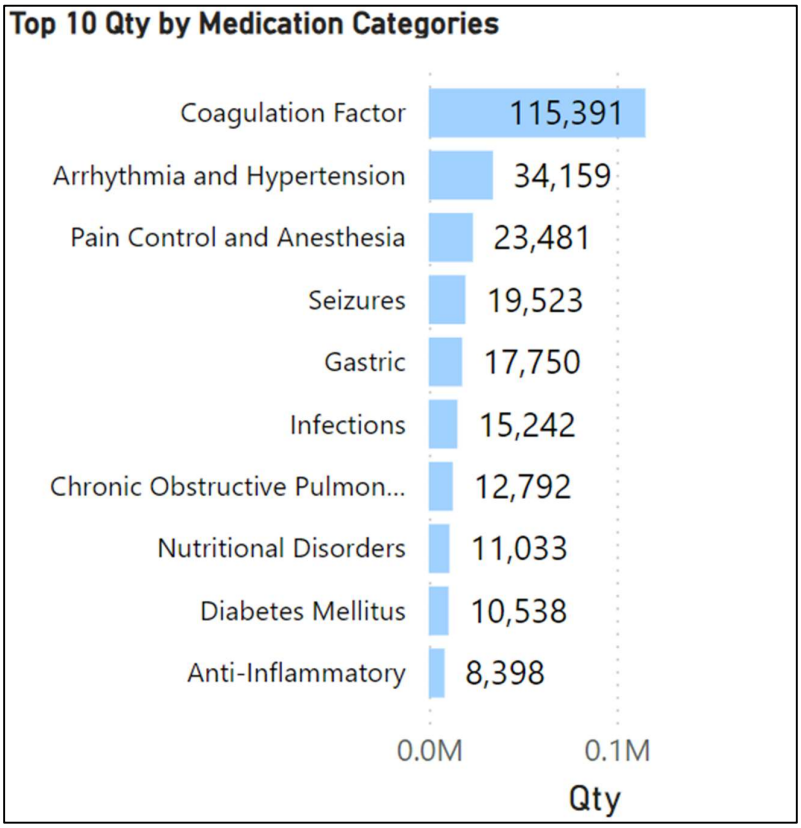


Figure 18: Prescribed Medications for Hemophilia (A) Patients by Indication for the Period 2017 – 2023

7.4 Bleeds

Within Hakeem systems, a general-purpose hematology eForm is utilized to document clinical findings for all hematology and oncology patients. Consequently, extracting detailed information specifically related to complications of hemophilia (A) posed challenges. As a result, we opted to focus on the year **2022** as a smaller study sample to comprehend various complaints that could arise in hemophilia (A) patients. These were categorized as events such as bleeds, hematoma, hemarthrosis, as well as other occurrences including swellings, pain, bruises, tenderness, etc.

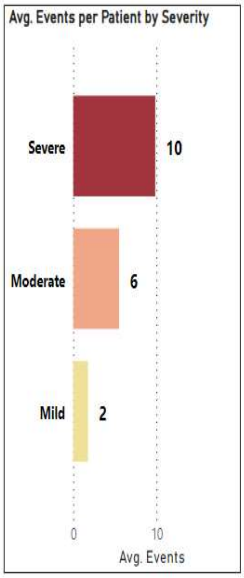
We identified approximately **1,466** events encountered by **178** patients with hemophilia (A), with an average age of **12** years old, and an average of **10** events per severe case of hemophilia (A). These events affected around **57** different body parts, with the knees, elbows, and ankles being the top three affected areas:

- **426**/1,466 (**29%** ±2.3%, CI 95%) events affected the knees
- **250**/1,466 (**17%** ±1.9%, CI 95%) events affected the elbows
- **226**/1,466 (**16%** ±1.8%, CI 95%) events affected the ankles

Unfortunately, insufficient information was available to summarize these events by their causes. However, a few physicians reported occurrences of spontaneous bleeds, trauma, injuries, medical procedures, medication administration, and circumcision. A summary of these events is presented in Figure 19.

Total Events by Affected Body Section

Event	Arms	Core and Internal	Head and Neck	Legs	Unknown	Total
All Bleeds	97	41	74	156	25	393
Bleed	21	31	58	15	13	138
Hemarthrosis	67	1	1	122	9	200
Hematoma	9	9	15	19	3	55
Other Events	264	86	43	639	41	1,073
Blurring				1		1
Bruise	12	5	15	46	28	106
Osteoarthritis	2			1		3
Pain	114	56	13	269	8	460
Pallor		3				3
Redness				1		1
Swelling	132	13	13	321	5	484
Tenderness	4			2		6
Weakness		9				9
Total	361	127	117	795	66	1,466



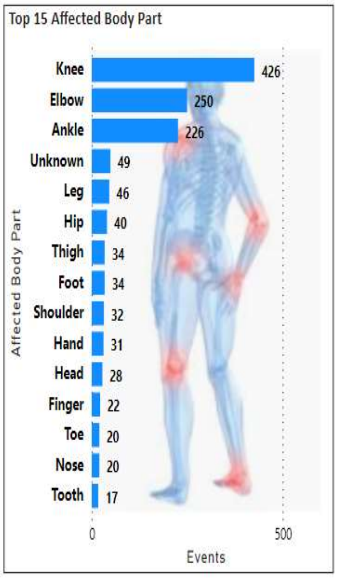


Figure 19: Total Events Encountered by Hemophilia (A) Patients by Affected Body Part and Severity in 2022

7.5 Insights

In 2022, we compiled comprehensive data for **362** hemophilia (A) patients born before 2022. The resulting summary by severity is presented in Table 11. On average, severe patients encountered approximately **3** events and **1** bleed. The average cost of their coagulation factors was around **7,058 JOD** with an average overall healthcare utilization of approximately **1,705 JOD**.

Severity	Patients	Tot. Cost (Hemo Med.)	Tot. Cost (Services)	Grand Cost	Tot. Bleeds	Tot. Events	Avg. Cost (Hemo Med)	Avg. Cost (Services)	Avg. Events	Avg. Bleeds
⊟ Severe	192	1,354,926	327,335	1,682,261	333	1235	7,056.91	1,705	6.43	1.73
Non-inhibitors	172	942,286	287,960	1,230,246	299	1134	5,478.41	1,674	6.59	1.74
Inhibitors	20	412,640	39,375	452,015	34	101	20,632.00	1,969	5.05	1.70
⊞ Moderate	61	83,486	64,030	147,516	37	173	1,368.62	1,050	2.84	0.61
⊞ Mild	109	59,406	31,930	91,336	13	33	545.01	293	0.30	0.12
Total	362	1,497,818	423,295	1,921,113	383	1441	4,137.62	1,169	3.98	1.06

Table 11: Summary of Healthcare Services for Hemophilia (A) Patients by Severity in 2022

Figure 20 shows number of hemophilia (A) patients categorized by number of events and severity.

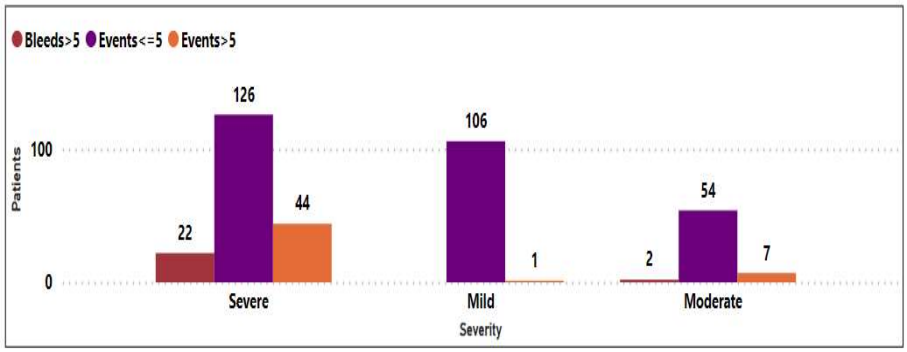


Figure 20: Events and Bleeds per Hemophilia (A) Patients by Severity in 2022

The figure illustrates that out of **192** patients born before 2022, with severe hemophilia (A), **66** individuals (**35%** ±6.7%, CI 95%) experienced more than 5 events or bleeds in 2022, as follows:

- **22** severe hemophilia (A) patients experienced more than 5 bleeds in 2022
- **44** severe hemophilia (A) patients experienced more than 5 events in 2022
- **126** severe hemophilia (A) patients experienced less than 5 events in 2022

Using the summary data we generated, we computed the Hospital Free Days Yearly percentage (HFRY%); the underlying concept of this percentage is straightforward: A healthy patient does not require healthcare services (inpatient, outpatient, or emergency). Therefore, the annual hospital free days for a perfectly healthy individual are 365. Any day a patient was either admitted to the hospital or visited the outpatient or emergency departments in any healthcare facility for treatment will be subtracted from these annual healthy days. This is calculated by the following formula:

(365 – [Bed Days + Outpatient visits + Emergency Visits] / 365) * 100%

The underlying concept we seek to elucidate is that effective disease management protocols typically aim to reduce the necessity for reactive care. Therefore, the greater the investment in preventive measures, the more favorable the outcomes on the patient's health status, which is expected to manifest in reduced healthcare utilization. To this end, our objective was to limit a patient's time spent in a hospital to less than 10% of their life, equating to a maximum of 36 days spent on healthcare services. **35**/362 (**10%** ±3.1%, CI 95%) patients spent more than 36 days in healthcare settings during the year 2022.

As we wrap up this report, the primary objective remains evident: to advance disease management. The key focus continues to be improving the quality of life and reducing hospitalization days.

8. List of Tables

9. List of Figures

10. References

[1] Centers for Disease Control and Prevention. National Center on Birth Defects and Developmental Disabilities. Hemophilia Facts. October 12, 2023. Accessed October 26, 2023. https://www.cdc.gov/ncbddd/hemophilia/facts.html.

[2] Café, A., Carvalho, M., Crato, M. et al. Haemophilia A: health and economic burden of a rare disease in Portugal. Orphanet J Rare Dis 14, 211 (2019), https://doi.org/10.1186/s13023-019-1175-5.

[3] von Mackensen S, Gringeri A, Siboni SM, Mannucci PM; Italian Association Of Haemophilia Centres (AICE). Health-related quality of life and psychological well-being in elderly patients with haemophilia. Haemophilia. 2012 May;18(3):345-52. doi: 10.1111/j.1365-2516.2011.02643.x. Epub 2011 Sep 12. PMID: 21910788.

[4] Carvalhosa, A. M. B. e., Henrard, S., Lambert, C., & Hermans, C. (2013). Physical and mental quality of life in adult patients with haemophilia in belgium: the impact of financial issues. Haemophilia, 20(4), 479-485, https://doi.org/10.1111/hae.12341.

[5] Forsyth, Angela & Blamey, Greig & Lobet, Sebastien & McLaughlin, Paul. (2020). Practical Guidance for Non-Specialist Physical Therapists Managing People with Hemophilia and Musculoskeletal Complications. Health. 12. 158-179. 10.4236/health.2020.122014.

[6] Oliveira, L. G., Ferreira, R. S., Silva, A. P., Silva, F. A. S., & Silva, A. O. (2013). Health-related quality of life (HRQoL) in hemophilia: results of the Hemophilia-Specific Quality of Life Index (Haem-A-QoL) at a Brazilian blood center. Revista Brasileira de Hematologia e Hemoterapia, 35(4), 273-277.

[7] Department of Statistics (DOS) of Jordan. (2015). Mortality in Jordan: Maternal and Adult Mortality. Retrieved from http://www.dos.gov.jo/dos_home_e/main/population/census2015/Mortality.pdf.

[8] Population Estimates for The End of 2022, Jordan, https://dosweb.dos.gov.jo/DataBank/Population/Population_Estimares/PopulationEstimatesbyLocality.pdf.

[9] Population Estimates for The End of 2022, Jordan, https://dosweb.dos.gov.jo/DataBank/Population/Population_Estimares/PopulationEstimates.pdf.

[10] The National Strategy for Health Sector in Jordan, 2016- 2020, The Hashemite Kingdom of Jordan The High Health Council, http://www.hhc.gov.jo/uploadedimages/8f70aace-ce1e-4762-9e86-4f3d75219beb.pdf.

[11] World Health Organization. (2023). Jordan. Retrieved from https://data.who.int/countries/400.

[12] NHS England. (2013). B05/S/a 2013/14 NHS STANDARD CONTRACT FOR HAEMOPHILIA (ALL AGES) SECTION B PART 1 - SERVICE SPECIFICATIONS. Retrieved from https://www.england.nhs.uk/wp-content/uploads/2013/06/b05-haemophilia.pdf.

[13] World Federation of Hemophilia. "WBDR 2022 Data Report published – WFH - World Federation of Hemophilia." June 29, 2023. https://wfh.org/article/wbdr-2022-data-report-published/.

[14] World Federation of Hemophilia. (2022). Global State of Hemophilia Care 2022. Retrieved from https://wfh.org/article/wfh-2022-annual-report-released/.

[15] Centers for Disease Control and Prevention. (2023, October 24). Hemophilia Inhibitors. Retrieved from https://www.cdc.gov/ncbddd/hemophilia/inhibitors.html.

[16] Centers for Disease Control and Prevention. (2023, October 24). Hemophilia Treatment. Retrieved from https://www.cdc.gov/ncbddd/hemophilia/treatment.html.

[17] National Hemophilia Foundation. (2023). Bleeding disorders A-Z: Overview: History. Retrieved from https://www.hemophilia.org/bleeding-disorders-a-z/overview/history.

[18] Invitra. "Hemophilia and Pregnancy: Scheme Hemophilia." Invitra, October 12, 2023. Web. October 26, 2023. https://www.invitra.com/en/hemophilia-and-pregnancy/scheme-hemophilia/