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Hemophilia is a hereditary clotting disorder which is caused by a deficiency of factor VIII (hemophilia A) or IX (hemophilia B). Due to the X-chromosomal inheritance pattern patients are primarily male, while women can be carriers of the disease.

This thesis aimed to describe changes in both the medical situation and social functioning of hemophilia patients. The first part focuses on medical and social functioning of hemophilia patients taking into account changes in treatment and the effect of viral infections. In the second part the hemorrhagic risk of carriers of hemophilia is evaluated.

In the Netherlands a series of five postal surveys have been performed from 1972 onwards. In chapter 2.1 we studied mortality, causes of death and life expectancy of hemophilia patients between 1992 and 2001. We performed a prospective cohort study among 967 patients with hemophilia. The findings were compared with those of previous cohorts, together spanning 30-years of observation from 1972 onwards, which shows the period before, during and after the use of potentially contaminated clotting products. We observed an excess mortality of hemophilia during the last decade. Although currently clotting factor products are safe from the Human Immunodeficiency Virus (HIV) and hepatitis C virus (HCV), viral infections had a large influence on mortality. AIDS was responsible for the largest number of deaths (24% of deaths) and 15% of deaths were due to hepatocellular carcinoma or chronic liver disease. Without the effects of HIV and HCV the rate of death among patients with severe hemophilia was 1.4-fold higher than expected. The remaining excess risk in all likelihood resulted from hemorrhages. Life expectancy of patients with severe hemophilia decreased compared to earlier studies, mostly due to AIDS. Patients with
severe hemophilia not affected by hepatitis C or HIV had a life expectancy of 71 years, which was still slightly lower than the life expectancy of the Dutch male population of 76 years.

In chapter 2.2 we investigated the most important medical and social developments over the last three decades of hemophilia treatment. In April 2001, we sent questionnaires to all known Dutch hemophilia patients, with a response of 70%. We compared different age categories, and children were defined as patients younger than 16, adolescents as patients between 16 and 25 and adults as patients aged above 25 years. Changes in treatment were reflected by an increase in the use of prophylaxis; especially in children. The occurrence of hemorrhages has gradually decreased. Hospital admissions decreased from 47% of all patients in 1972 to 18% in 2001. Despite intensified treatment limited improvement was observed in self-reported impairment of joint function in patients older than 16 years.

In chapter 2.3 we compared social functioning and health-related quality of life between hemophilia patients and the general male population. We assessed data on full-time or part-time participation in work, disability and health related quality of life in hemophilia patients between 15 and 64 years old. In the analysis we compared our findings with the general population, separately for patients born before the introduction of prophylaxis (30-64 years of age) and patients born after the introduction of prophylaxis (15-30 years old). Our study showed that although important physical improvements had been achieved, hemophilia patients were less involved in full time labour and were more often occupationally disabled. The involvement in labour seems to be important for quality of life as employed patients had a higher quality of life than patients without employment.

Chapter 2.4 reports on the prevalence of hepatitis C and the use of antiviral therapies during the last decade among patients with hemophilia. Hepatitis C is a major co-morbidity among patients with hemophilia who received inadequately or non-virus inactivated clotting factor concentrates before 1992. Analyses were performed in the HiN-5 population. The study
population for the present study consisted of 771 patients who had received clotting factor products before 1992 of whom 638 reported their hepatitis C status. A total of 441 of the 638 (68%) patients ever had a positive test for hepatitis C virus (HCV); 344 patients (54%) had a current infection, and 97 (15%) had cleared the virus. Among 344 patients currently HCV infected, 111 (32%) had received treatment for hepatitis C, while 34% (33/97) of patients with an infection in the past had been treated for hepatitis C.

In 2002 the prevalence of hepatitis C among patients with hemophilia who had received clotting factor products before 1992 was 54%. The majority of patients with a current HCV infection had not been treated with antiviral therapy.

In chapter 2.5 the uptake of recombinant factor VIII in the Netherlands was assessed. In comparison with other biotech substitutions, the adoption of recombinant Factor VIII (rFVIII) has been relatively slow. We sent a postal questionnaire to all Dutch haemophilia patients and haemophilia treating physicians, to determine which factors predicted whether a patient used plasma derived FVIII (pdFVIII) or rFVIII and to investigate patients’ and doctors’ opinions on both products. The use of recombinant FVIII varied widely between centers. Younger patients, those not infected with HIV or hepatitis C virus, and those who did not have family members who used pdFVIII, switched more often from pdFVIII to rFVIII. Patients who rated themselves as innovative, who had family members who used rFVIII, and those who were treated in a large hemophilia treatment center, also more often had switched. For physicians and patients alike, the respondents generally did not see large differences between rFVIII and pdFVIII, except for the risk of infections and the knowledge on long-term effects (both larger for pdFVIII). Although hemophilia patients represent one of the most empowered patient groups, physicians appear to have been influential in choosing between pdFVIII and rFVIII.

In chapter 3.1 bleeding in carriers of hemophilia were investigated. A wide range of factor VIII and IX levels was observed both in carriers and non-carriers. In carriers extreme
lyonisation may lead to low clotting factor levels. A postal survey was performed in all women tested for carriership of hemophilia between 1985 and 2001. We compared bleeding after trauma and medical interventions in carriers and non-carriers. Clotting factor levels lower than 0.60 IU/ml were increasingly associated with prolonged bleeding from small wounds, prolonged bleeding after tooth extraction, tonsillectomy and operations. We showed that carriers of hemophilia have a higher risk of bleeding compared to non-carriers especially after medical interventions.