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Estimating hemophilia prevalence and life expectancy

Hemophilia is a genetic disorder that prevents blood from clotting normally, leading to prolonged bleeding. The two major types of hemophilia are caused by a mutation in either the F8 (hemophilia A) or F9 (hemophilia B) gene, which causes a deficiency in clotting factors VIII and IX, respectively. The severity of the disease (ranging from mild to severe) depends on the mutation or deletion observed in the F8 and F9 genes. The main treatment for hemophilia is replacement therapy, which involves injecting a patient with the missing clotting factor. This treatment can be expensive or, in lower-income countries, not available. When replacement therapy is available, serious problems associated with hemophilia A or B can be prevented and the life expectancy of the individual should approximate that of the general population.

To better understand the global burden of hemophilia, it is essential to have accurate data on the number of males with hemophilia across countries. Men are almost exclusively affected as the genes for these proteins are located on the X chromosome of which men have only one copy. The aim of this study was to accurately estimate prevalence at birth of hemophilia and life expectancy by type (A or B) and severity. Global comparisons of expected and observed numbers of patients with hemophilia can provide insights into the efficiency of healthcare systems.

IN BRIEF: Hemophilia is more prevalent in men than previously thought and is still associated with a lower life expectancy.

What did the researchers do?

A team of researchers with the Data and Demographics Committee of the World Federation of Hemophilia applied new analytical approaches to national patient registries in six high-income countries (Australia, Canada, France, Italy, New Zealand and the United Kingdom), including the Canadian Bleeding Disorders Registry at McMaster University. They estimated prevalence of hemophilia in men by type and severity. Prevalence at birth was estimated using data from the three most established registries (Canada, France and the United Kingdom). A life expectancy disadvantage (i.e. increased risk of early death) was calculated for patients in high-income countries.

In addition, the observed global number of patients with hemophilia, as reported by the World Federation of Hemophilia, was compared to the expected global number of patients, calculated using data from national statistical databases and estimates of prevalence at birth.

What did the researchers find?

Hemophilia in high-income countries is more common than previously thought. Prevalence at birth (per 100,000 males) is:

- 24.6 cases for all severities of hemophilia A
- 9.5 cases for severe hemophilia A
- 5.0 cases for all severities of hemophilia B
- 1.5 cases for severe hemophilia B

Despite factor replacement therapy, this study observed that patients with hemophilia still have a shorter life expectancy. The life expectancy disadvantage in high-income countries is 30% reduction for hemophilia A, 37% for severe hemophilia A, 24% for hemophilia B, and 27% for severe hemophilia B.

The estimated number of male patients with hemophilia worldwide, assuming the same survival as the general population, was calculated to be 1,125,000. In comparison, the observed number of male patients with hemophilia worldwide is 196,706. The striking difference between expected and observed numbers of patients with hemophilia suggests underdiagnosis and under-reporting.

How can you use this research?

This study demonstrates the value of long-term studies in rare diseases. Establishing accurate estimates of hemophilia prevalence is critical to informing policy, allocating resources, and anticipating the demand for plasma protein products such as factor VIII and factor IX.

These findings also provide insights into the adequacy of healthcare systems in supporting hemophilia patients worldwide. They suggest many patients are never diagnosed or reported to a registry. There are large gaps to fill in the care of these patients, including use of more efficient diagnostic approaches to ensure patients can access current treatment options.

About the research team: The research group includes members of the McMaster Centre for Transfusion (MCTR), which receives funding support from Canadian Blood Services: **Dr. Alfonso Iorio,** lead researcher and professor in the department of health research methods, evidence and impact at McMaster University, and **Dr. Federico Germini**, PhD student in the health research methodology program at McMaster University. The Canadian Bleeding Disorders Registry, established at McMaster University as a clinical database for patients in Canada, helps clinicians manage patients with bleeding disorders and has quickly become a top-class resource for the hemophilia community worldwide.

This Research Unit is derived from the following publication:

Iorio A, Stonebraker JS, Chambost H, Makris M, Coffin D, Herr C, Germini F; Data and Demographics Committee of the World Federation of Hemophilia. Establishing the Prevalence and Prevalence at Birth of Hemophilia in Males: A Meta-analytic Approach Using National Registries. *Ann Intern Med.* 2019 Sep 10. doi: 10.7326/M19-1208.

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