The Global Burden, Incidence, and Prevalence of Chronic Hepatitis C

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BACKGROUND

- Chronic infection with the hepatitis C virus (HCV) is a major cause of chronic liver disease, which may lead to cirrhosis and predispose patients to the development of liver cancer.[1]
- The long-term impact of chronic HCV infection on the liver is highly variable, ranging from minimal liver damage to extensive fibrosis, and decompensated cirrhosis with or without hepatocellular carcinoma (HCC).
- HCV is spread primarily through direct contact with human blood, including via blood transfusions in settings in which the blood supply is not suitably screened, reuse of needles and syringes that have been inadequately sterilised, and sexual contact with infected persons.[1]
- Due to slow disease progression, symptoms of HCV often appear late after exposure/infection, and many individuals have no knowledge of their infection or of the hepatic diseases that may follow. Consequently, the virus is unknowingly spread further, and it is estimated that the number of chronically infected persons worldwide may exceed 200 million.
- Six HCV genotypes, numbered 1 to 6, and many subtypes have been described.[2]
  - The diverse genotype and subtypes originated from different areas in Africa and Asia, and some have spread throughout the world.
  - Genotype 1 (G1) (subtypes 1a and 1b) is the most prevalent genotype worldwide, with a higher prevalence of 1a in the United States (US) and 1b in Europe.
  - G1 is associated with more aggressive disease, with increased insulin resistance, worse response to therapy, and higher risk of developing cirrhosis and HCC.[3]
  - G3 is associated with increased steatosis (up to 73% of patients vs. 51% of patients with other genotypes) and fibrosis.[3]
- The primary goal of HCV therapy is to cure the infection by eliminating detectable circulating HCV. The combination of pegylated interferon (PEG-IFN) alfa and ribavirin is the approved and well-accepted standard of care for chronic HCV.
- Many drugs for HCV are at various stages of preclinical and clinical development. New therapeutic strategies aim toward treating specific genotypes, increasing efficacy, shortening treatment, simplifying administration, and improving tolerability and patient adherence.

OBJECTIVE

- To identify and understand HCV prevalence and mortality rates, disease course, and the availability of data on patient and viral characteristics that may affect treatment and outcomes.

METHODS

- A targeted review was undertaken in Medline, using a predefined search strategy, to update a review conducted in 2009 and to identify studies describing HCV burden.
- Additional searches were performed on the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) conference and key epidemiological websites.
- The focus for this research was studies conducted in Australia, Brazil, Canada, China, France, Germany, Italy Japan, Mexico, the Netherlands, South Korea, Spain, Sweden, the United Kingdom (UK), and the US.

RESULTS

- The targeted review identified 1,773 references.

Prevalence

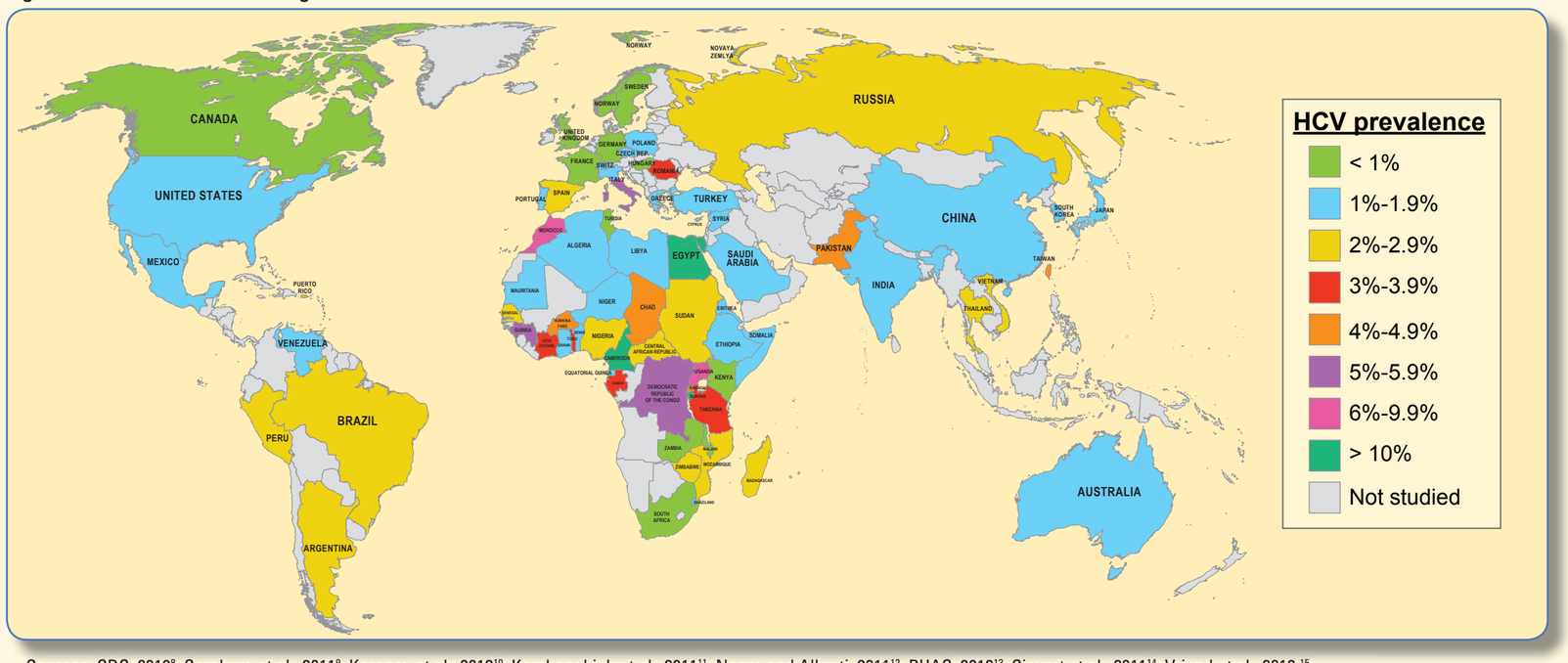
- Results indicated that between 1990 and 2005 globally, the number of people with HCV increased from more than 122 million to more than 185 million, and HCV prevalence increased from 2.3% to 2.8%.[6]
  - Asia Pacific, Tropical Latin America, and North America were estimated to have low prevalence (< 1.5%).
  - Australasia, Western Europe, and Central Latin America were estimated to have moderate prevalence (1.5%-3.5%).
  - East Asia was estimated to have the highest prevalence (> 3.5%).
  - Data for most regions showed an increase in prevalence as a function of age, followed by a gradual decrease after peak prevalence was reached in the group aged 55 to 64 years.
- A more recent estimate suggested a total global prevalence of 2.35%, with 159 million HCV-infected individuals in 2010 (Table 1).[7]
  - Differences between the two estimates may be explained by the methodology used to calculate the estimate, differing boundaries and definitions of regions, and the year for which the prevalence estimates are given.
- Figure 1 presents the identified HCV prevalence results by country.
- HCV screening programmes and mandatory reporting are present in only a few countries, so actual prevalence is likely to be even greater.

Table 1. Regional Prevalence of HCV in 2010

Region	HCV Prevalence (%)	No. of HCV-Infected Individuals
Africa	3.2	28.1 million
Americas	1.5	14 million
Asia	2.1	83 million
Australia and Oceania	1.2	0.4 million
Europe	2.3	17.5 million
Middle East	4.7	16 million
Total	2.35	159 million

Source: Lavanchy, 2011.[7]

Figure 1. HCV Prevalence Among Adults

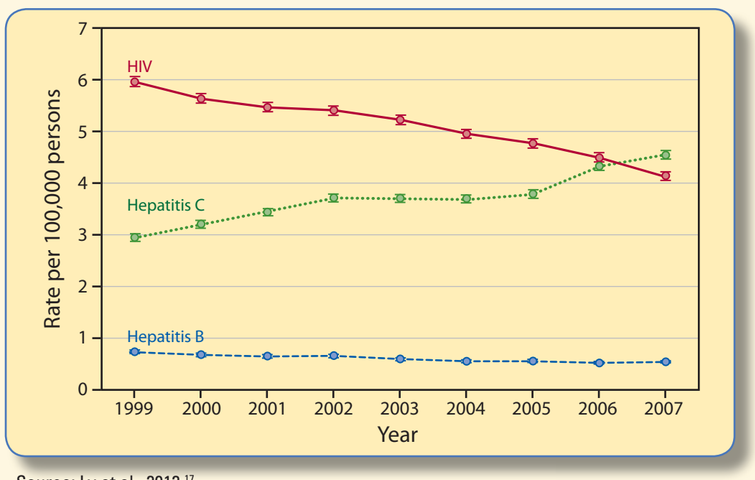


Sources: CDC, 2010[8]; Cornberg et al., 2011[9]; Karoney et al., 2013[10]; Kershenobich et al., 2011[11]; Negro and Alberti, 2011[12]; PHAC, 2012[13]; Sievert et al., 2011[14]; Vriend et al., 2012.[15]

HCV-Related Mortality

- In 2010, there were estimated to be 499,000 deaths globally related to HCV, making HCV-related complications the 25th most common cause of death and a significant global health problem.[16]
- HCV infection now has a higher mortality rate than HIV (Figure 2).

Figure 2. Annual Age-Adjusted Mortality Rates From Hepatitis B and C Virus and HIV Infections Listed as Causes of Death in the US Between 1999 and 2007



Source: Ly et al., 2012.[17]

- The breakdown of all-ages deaths attributable to HCV demonstrated an increase in the number of deaths from 1990 to 2010:
  - 97.1% increase in deaths due to acute HCV (from 8,100 to 16,000 deaths)
  - 73.3% increase in deaths due to liver cancer secondary to HCV (from 113,000 to 195,700 deaths)
  - 35.6% increase in deaths due to cirrhosis of the liver secondary to HCV (from 211,900 to 287,400 deaths)

Prevalence of HCV Genotypes

- The prevalence of HCV genotypes varies geographically.
  - G1 is the most prevalent genotype in North and South America (59%-86%), Europe (45%-99%), and the Asia-Pacific region (48%-68%).
  - G3 is most prevalent in South Asia (Pakistan, India, and Thailand) (53%-67%).
  - G4 is most prevalent in the Middle East (Egypt, Syria, and Saudi Arabia) (59%-63%).
- Figure 3 shows HCV prevalence and genotype distribution by key countries and region.
- There is a lack of detailed data on genotype distribution for the majority of African and some Middle Eastern countries; however, recent data[10] suggest the following:
  - G1-G3 are most prevalent in West Africa and some East African countries (Eritrea, Ethiopia, and Kenya).
  - G1b is most prevalent in Tunisia and Morocco.
  - G4 is most prevalent in Central Africa and some North African countries (Egypt, Sudan, Libya).
  - G5 is most prevalent in South and East Africa, including South Africa, Tanzania, and Zambia.

DISCUSSION

- HCV infection shows a high degree of interindividual variability, and the risk of HCV-related liver morbidity and mortality depends on a number of factors, including the duration of HCV infection, HCV genotype, presence of cofactors for liver fibrosis, access to treatments, and competing mortality risks from factors such as intravenous drug use.
- The global prevalence of HCV increased from 2.3% to 2.8% between 1990 and 2005, which equates to an additional 63 million people living with HCV.[6] Furthermore, HCV screening programmes and mandatory reporting are present in only a few countries, so actual prevalence is likely to be even greater. Thus, the burden of disease for HCV infection and the subsequent hepatic diseases continues to increase.
- The increasing prevalence of HCV over time is mirrored by an increase in the number of deaths due to HCV infection. HCV, combined with diseases secondary to HCV, is ranked as the 25th most common cause of death (if these deaths were counted in the main global burden of disease cause list).[16] HCV infection poses a significant global health problem.
- Across countries, it is recommended that HCV genotype should be considered when selecting therapy.
  - The recommended mainstay of therapy for G1 HCV is PEG-IFN alfa plus ribavirin, with directly acting anti-virals now being recommended, particularly in the US and the UK.
  - In many markets, tailoring length of treatment according to the patients' response is recommended. Doing so has the benefit of reducing the cost of therapy while minimising the risk of adverse events to treatment in patients with HCV infection.
  - New drugs in development target specific HCV genotypes; as such, it is important to know patients' genotypes prior to treatment.
- Epidemiological data on genotype distributions may help ensure appropriate therapy for patients in different parts of the world.

CONCLUSION

- In light of upcoming treatment alternatives, detailed epidemiological studies will help ascertain more accurately the prevalence of each HCV genotype and subtype, so that the true burden of HCV can be understood and treatments targeted appropriately.

REFERENCES

Please see handout for complete reference list.

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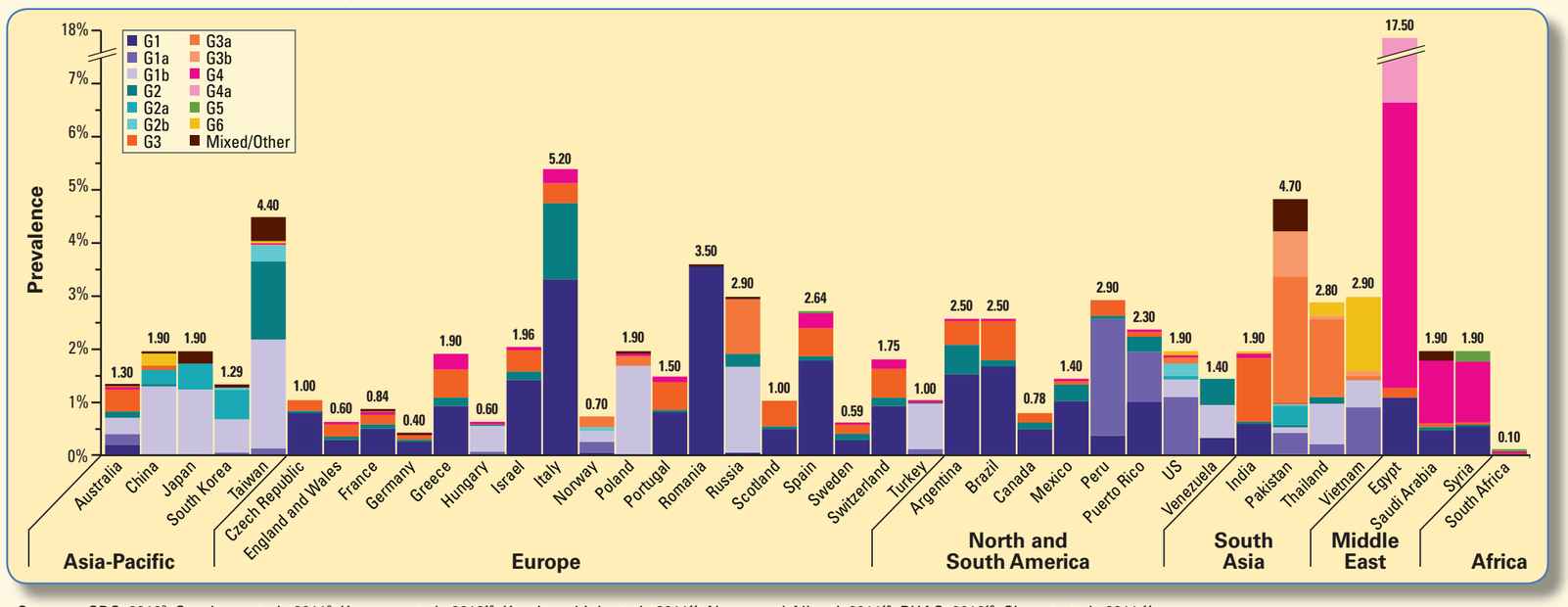
Figure 3. Prevalence and HCV Genotype Distribution by Country and Region



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