

Commentary

Mortality due to viral hepatitis in the Global Burden of Disease Study 2010: new evidence of an urgent global public health priority demanding action

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The recently published Global Burden of Disease Study 2010 (GBD 2010) contains accurate, contemporary estimates of human morbidity and mortality, with substantial changes in the patterns of illness observed over the last two decades. One of the most significant alterations to these estimates has been the recognition that viral

hepatitis is a leading cause of human mortality, with an estimated 1.29 million deaths worldwide in 2010. The global community must act to address emerging health priorities identified by GBD 2010, including the need to provide treatment and care to people living with viral hepatitis, especially in resource-poor settings.

In December 2012, for the first time in the Lancet's history, an entire issue was devoted to a single body of research – the Global Burden of Disease Study 2010 (GBD 2010) [1]. Supported by the Bill and Melinda Gates Foundation, GBD 2010 was a collaboration of 486 researchers from 50 countries, led by a consortium of institutional partners coordinated by the Institute for Health Metrics and Evaluation at the University of Washington, Seattle, WA, USA.

The aim of GBD 2010 was to provide more accurate estimates of human disease, injury, disability and risk factors globally, in order to inform the setting of new priorities in allocation of public health efforts and resources. It has been a huge undertaking, with estimation of the impact of 291 diseases and injuries and 67 risk factors, and trends from 1990 to 2010, for the entire global population [2].

GBD 2010 shows that global life expectancy has been increasing and that the burden of childhood mortality has dropped significantly. The burden of many infectious diseases has reduced, particularly diarrhoeal disease, lower respiratory tract infections, measles and tetanus; but huge challenges remain in many parts of the world [3].

HIV/AIDS remains a leading cause of human mortality, having moved from 35th position in 1990 (300,000 deaths) to 6th position in 2010 (1.47 million deaths). It is testament to the impact of global political will, donor

funding and engagement with affected communities that HIV/AIDS mortality has steadily decreased since 2006, reflecting declining incidence, enhanced prevention of mother-to-child-transmission and the rapid increase in access to antiretroviral therapy in some high-prevalence settings [4].

The last 20 years have also seen a 20% rise in malaria mortality, with 1.17 million people dying as a result (11th position); a similarly large burden of human death (1.20 million people) resulted from tuberculosis in 2010 (10th position) [3].

One of the major changes in methodology for GBD 2010 was to assess deaths attributable to viral hepatitis (and other causes of liver disease) as separate causes of subsequent outcomes. Earlier GBD studies had not categorically assigned deaths from cirrhosis and liver cancer to their ultimate causes, including viral hepatitis. This has arguably contributed to a profound underestimate of the impact of viral hepatitis on human mortality [5], reflected in the significant lack of public health priority for viral hepatitis globally [6,7], particularly given many of these deaths are preventable [3].

In GBD 2010, the total number of deaths attributable to hepatitis B was estimated to be 786,000 and for hepatitis C, 499,000. If these chronic viral infections were represented in the main causes of death listing, they would respectively be ranked 15th and 25th [3]. Considered together, viral hepatitis resulted

in 1.29 million deaths, ranking 9th as a cause of human mortality, comparable to the diseases targeted by the Global Fund to fight AIDS, Tuberculosis and Malaria [3].

Comprehensive responses that strengthen balanced health systems are necessary if we are to learn from successful global responses to previously identified health priorities such as HIV/AIDS. In some cases funding vertical programmes has the potential to distort priorities [7,8], with greatest impacts in resource-poor settings.

The imperative to develop balanced, comprehensive programmes to address viral hepatitis is increasingly recognized by the international community. Examples include the World Health Assembly's Viral Hepatitis resolution WHA 63.18 in 2010 [9] and the WHO Global Hepatitis Programme's Framework for Global Action in 2012 [6]. The Framework outlines four axes for global action: raising awareness, promoting partnerships and mobilizing resources; developing evidence-based policy and data for action; prevention of transmission; and increasing access to screening, care and treatment.

This last axis in the WHO Viral Hepatitis Framework calls for increasing access to treatment for people with chronic hepatitis B and hepatitis C, especially in resource-constrained settings [6]. The evidence of the real-world impacts of these treatments is mounting – for example in the case of hepatitis B, appropriate antiviral therapy has been shown to reverse liver cirrhosis [10,11] and to reduce the incidence of liver cancer by 50–70% over approximately 5 years [12–14].

It is however, a stark reminder of the low priority given to the health-care needs of people living with viral hepatitis that an effective antiviral agent for the treatment of hepatitis B – tenofovir – remains inaccessible even for those with advanced liver disease in many countries where it is saving lives as part of low-cost antiretroviral therapy for people living with HIV/AIDS. This disparity has recently been described where ‘not being HIV-positive is ironically a disadvantage’ [7].

How the global community and major donors respond to this new evidence that viral hepatitis is a major cause of human death – on a comparable scale to HIV/AIDS, tuberculosis and malaria – will be illustrative of the degree to which the discussions of global policy and prioritization generated following GBD 2010 will be evidence based [1].

We must ensure that this unprecedented opportunity for action to reduce the burden of viral hepatitis is realized. Properly funding and implementing the WHO Framework for Global Action, especially in resource-poor settings, would be a fundamental step towards comprehensively addressing one of the major causes of global mortality.

Disclosure statement

The authors declare no competing interests.

References

- Horton R. GBD 2010: understanding disease, injury, and risk. *Lancet* 2012; **380**:2053–2054.
- Murray CJ, Ezzati M, Flaxman AD, *et al.* GBD 2010: design, definitions, and metrics. *Lancet* 2012; **380**:2063–2066.
- Lozano R, Naghavi M, Foreman K, *et al.* Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380**:2095–2128.
- Ortblad KF, Lozano R, Murray CJ. The burden of HIV: insights from the GBD 2010. *AIDS* 2013; **27**:2003–2017.
- Cowie BC, Dore GJ. The perpetual challenge of infectious diseases. *N Engl J Med* 2012; **367**: 89; author reply 90.
- Prevention & Control of Viral Hepatitis Infection: Framework for Global Action. Geneva: Global Hepatitis Programme, World Health Organisation, 2012.
- Lemoine M, Nayagam S, Thurs M. Viral hepatitis in resource-limited countries and access to antiviral therapies: current and future challenges. *Future Virology* 2013; **8**:371–380.
- Cavalli F. An appeal to world leaders: stop cancer now. *Lancet* 2013; **381**:425–426.
- Viral hepatitis. (WHA63.18). Geneva: World Health Organisation, 2010.
- Chang TT, Liaw YF, Wu SS, *et al.* Long-term entecavir therapy results in the reversal of fibrosis/cirrhosis and continued histological improvement in patients with chronic hepatitis B. *Hepatology* 2010; **52**:886–893.
- Marcellin P, Gane E, Buti M, *et al.* Regression of cirrhosis during treatment with tenofovir disoproxil fumarate for chronic hepatitis B: a 5-year open-label follow-up study. *Lancet* 2013; **381**:468–475.
- Hosaka T, Suzuki F, Kobayashi M, *et al.* Long-term entecavir treatment reduces hepatocellular carcinoma incidence in patients with hepatitis B virus infection. *Hepatology* 2013; **58**:98–107.
- Kumada T, Toyoda H, Tada T, *et al.* Effect of nucleos(t)ide analogue therapy on hepatocarcinogenesis in chronic hepatitis B patients: a propensity score analysis. *J Hepatol* 2013; **58**:427–433.
- Papatheodoridis GV, Lampertico P, Manolakopoulos S, Lok A. Incidence of hepatocellular carcinoma in chronic hepatitis B patients receiving nucleos(t)ide therapy: a systematic review. *J Hepatol* 2010; **53**:348–356.