

The Global Prevalence of HBsAg by Age in 2016 and the Case for Universal Treatment in Low and Middle Income Countries

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INTRODUCTION

For over thirty years, hepatitis B virus (HBV) vaccination has been available and the vaccination programs have resulted in major reductions in the incidence of HBV and the prevalence in vaccinated cohorts. However, a large cohort of individuals remain who were infected prior to vaccination or were infected in countries with low vaccination rates. To achieve the WHO 2030 target of 65% reduction in liver related deaths, treatment will be required. However, current treatment guidelines may not be practical or effective in low and middle income countries.

AIM

Quantifying the age of the infected population is imperative, as it is evidence of the impact of vaccination, but it is also a harbinger of the coming disease burden that will impact health systems globally. This study aims to examine the age structure of the HBsAg+ population globally in 2016 and examine how this structure will change by 2030 under two scenarios. This then examines what is necessary to meet the 65% reduction in liver related deaths by 2030 in lower middle and lower income countries.

METHOD

120 country-level dynamic disease progression models were built based on literature review and consultation with country experts [1]. The model used historical age-specific prevalence estimates to quantify the prevalence of HBsAg by age in 2016 after taking into account the impact of perinatal prophylaxes measures & treatment. For countries missing data, extrapolation from countries, with data, in each Global Burden of Disease Region was used. Two scenarios were run - The Base assumed that the current prophylaxes and treatment paradigm was maintained through 2030. The WHO 2030 Targets, scaled up prophylaxes to achieve a prevalence of $\leq 0.1\%$ in five year olds in 2030 [2]; and 90% of the HBsAg infected population was diagnosed, and 80% of those diagnosed and eligible were treated.

Since under the current WHO treatment recommendations, the 65% reduction in liver related deaths is difficult to reach in most countries, a third scenario was considered. For the top 8 most populous low & lower-middle income countries (Bangladesh, Egypt, Ethiopia, India, Indonesia, Nigeria, Pakistan, & Philippines), we ran a scenario in which all individuals found to be HBsAg+ were put under treatment (Treat HBsAg+).

RESULTS

In 2016, there were an estimated 292 (UI: 252-341) million individuals chronically infected with HBV. The impact of vaccination is most visible in the <25 year cohorts (Figure 1).

Unfortunately, even with availability of vaccines, there are an estimated 73 million under the age of 25 who are infected due to low or no birth / 3 dose vaccination. In addition, another 219 million were infected prior to, or in early phases of, vaccination. HBsAg prevalence declined in the older age groups due to higher mortality rate. Over 70% of all infections (205 million) are found between the ages of 15 and 54, and this cohort has by and large yet to progress to the later and more expensive stages of the disease. Those aged 25 to 39 accounted for over 30% of the total infections (91 million).

As shown in Figure 2, the HBV infected cohort will age by approximately 15 years by 2030. Under the Base scenario, vaccination will continue to decrease the prevalence in the younger age groups. With a stepwise increase in prophylaxes and treatment under the WHO 2030 Targets scenario, there is an even greater reduction in the prevalence among those born after 2015. This scenario also includes an increase in treatment, which reduces the mortality. This results in a higher number of infections in the older age cohorts as compared to the base.

In the absence of additional interventions, the number of HBV related liver related deaths is expected to increase by almost 25% from 2016 to 2030 in the lower & lower-middle income countries modeled here (Figure 3). By combining increases in prophylaxes measures with diagnosis of 90% of the population and 80% of those eligible under the current WHO guidelines, there is almost a 50% reduction in the annual number of liver related deaths. However, this is not sufficient to achieve a 65% reduction in mortality. The third scenario, treat HBsAg+, utilizes a screen and treat approach, treating any adult found to be HBsAg+.

Table 1. Current testing guidelines for treatment consideration

Guidelines	HBeAg	ALT	Viral Load	Liver Staging	Age
WHO		✓	✓	✓	✓
EASL	✓	✓	✓	✓	✓
AASLD	✓	✓	✓	✓	
APASL	✓	✓	✓	✓	

Figure 1. Overall HBsAg Prevalence by Age Cohort, 2016

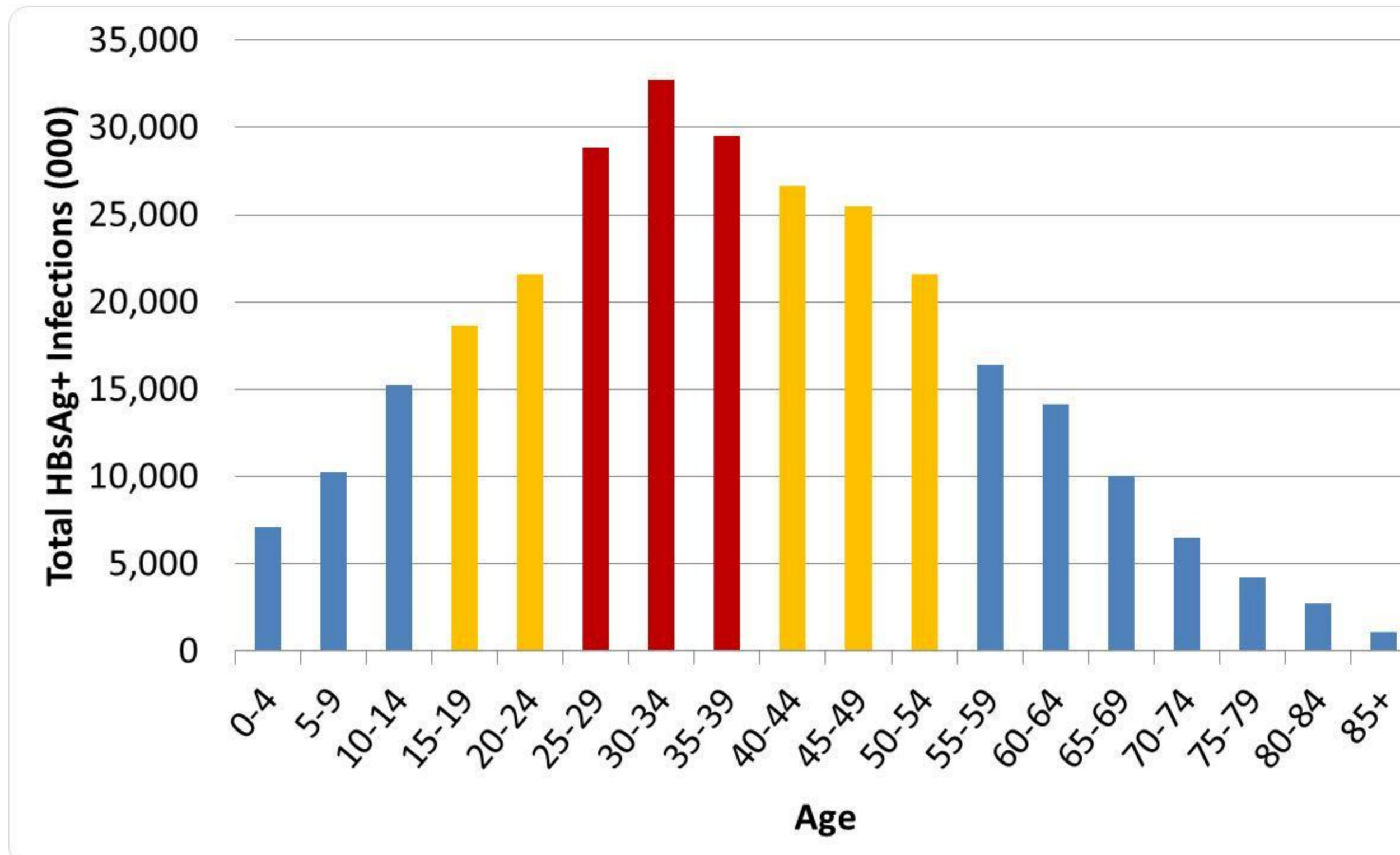


Figure 2. Overall HBsAg Prevalence by Sex Age Cohort, 2030

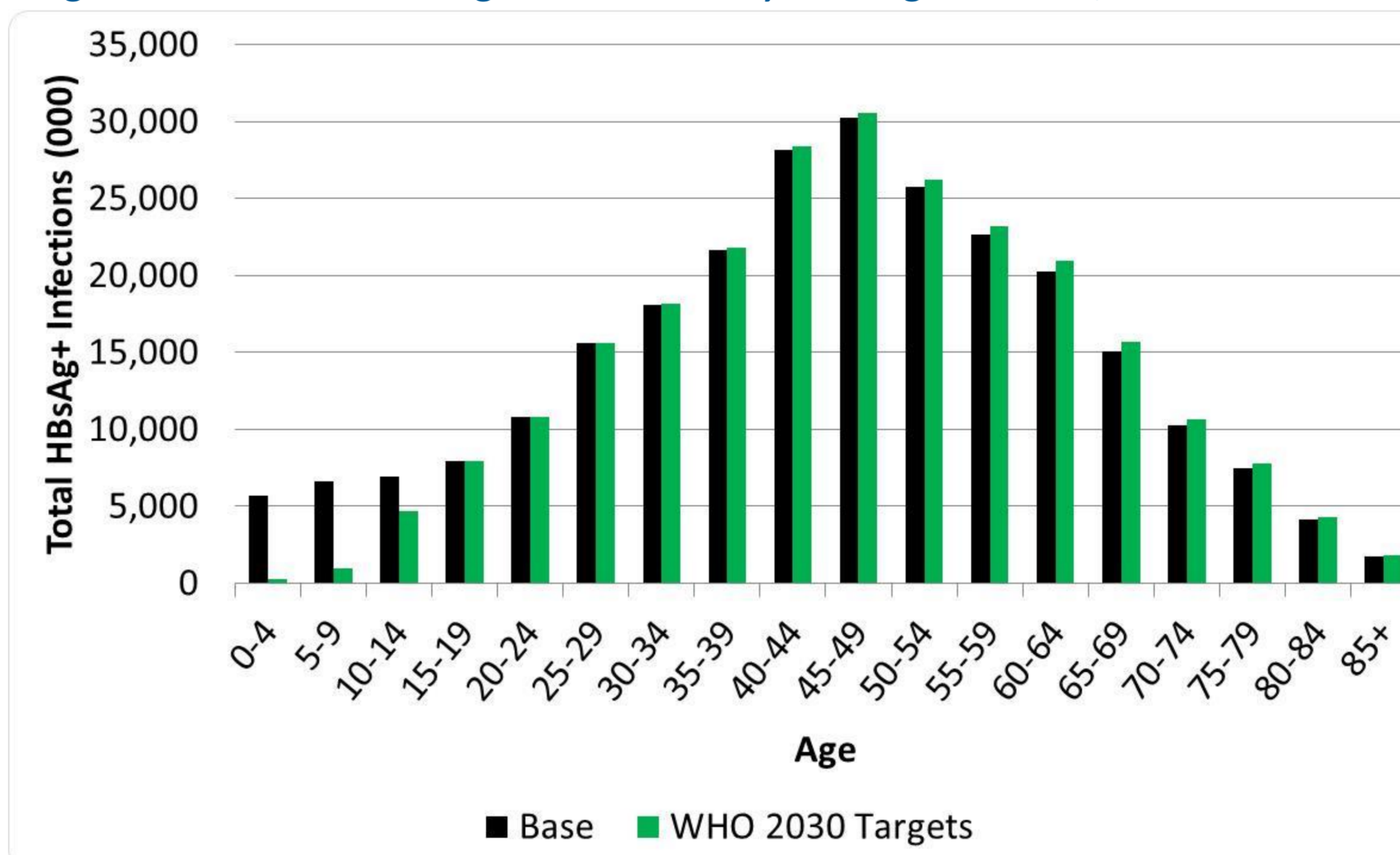
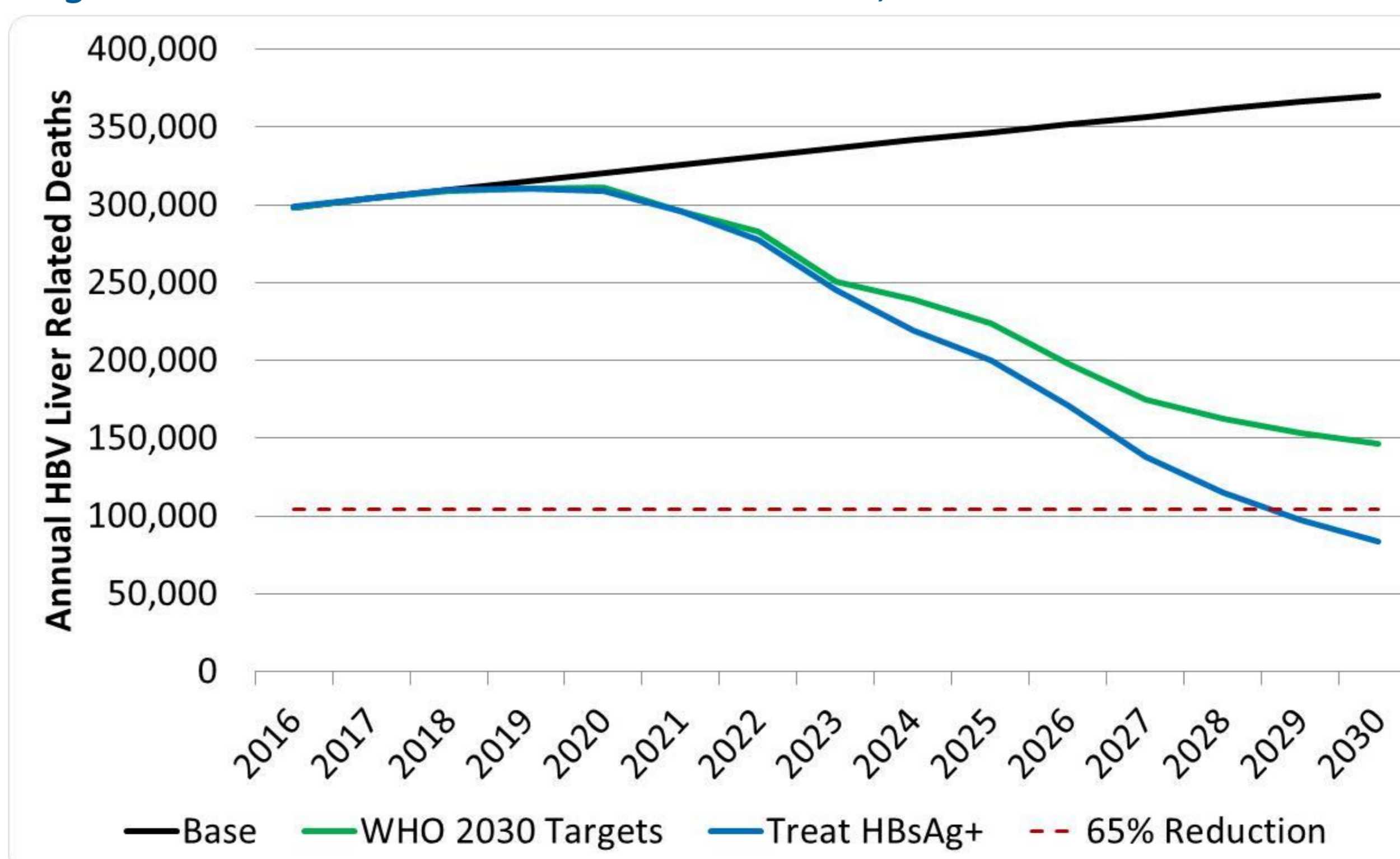


Figure 3. HBV Related Liver Related Deaths, 2016-2030



CONCLUSIONS

HBV vaccination has played an important role in reducing HBV prevalence in younger age cohorts. In addition, if WHO recommendations are implemented, the future prevalence of HBV will be substantially lower in the younger age cohorts. This strategy can leverage current infrastructure that has been used to prevent mother to child transmission of HIV and STIs.

However, HBV related disease burden and liver related deaths will continue to increase as those already infected age. Utilizing the WHO recommended guidelines for diagnosis and treatment, a sizable impact can be seen the reduction of liver related deaths in 2030 when compared to the base scenario. However, these recommendations are not sufficient to achieve a 65% reduction in liver related deaths.

If a test and treat strategy is implemented, in which anyone who tests HBsAg+ is put on treatment, an 80% reduction in liver related deaths can be realized by 2030. This strategy has practical and economic implications as well. Table 1 shows the required testing guidelines before an HBV infected person is eligible for treatment. In addition, annual follow up tests are required for those not eligible for treatment. In low income settings, annual follow up tests are not practical. In addition, with the costs of antivirals dropping below \$60 per year, the cost of annual tests will surpass a test and treat strategy.

We would like to make the case for universal treatment of all HBsAg infected. Additionally, this method can aid in stopping transmission and disease progression. The low cost of antiviral treatments allows for a test and treat strategy in these countries.

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