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Trends in chronic hepatitis B prevalence in Australian women by country of birth, 2000 to 2016

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Abstract

Routine antenatal screening for chronic hepatitis B (HBV) in countries with high migrant populations provides an opportunity to monitor trends in HBV prevalence and can inform estimates locally and in countries with limited seroprevalence data.

We linked perinatal birth register records with HBV notifications in the largest Australian state, over the period 2000-2016. Among women aged 15-44 years we estimated age-standardised chronic HBV prevalence overall and by country of birth and, also estimated trends in age-standardised HBV prevalence over time using regression modelling. Among 903,831 women, 8001 linked to a chronic HBV infection record (overall age-standardised prevalence 0.76%, 95% CI 0.74-0.78). Prevalence varied by country of birth with the highest estimates among women born in Sierra Leone (11.13%, 95% CI 8.29-13.96), Taiwan (8.08%, 95% CI 6.74-9.43%), Cambodia (7.47%, 95% CI 6.50%-8.45%) and Vietnam (7.36%, 95% CI 6.97-7.75%); more moderate estimates among women from North Korea (2.76%, 95% CI 1.99-3.53) and Samoa (2.64%, 95% CI 1.99-3.29%); prevalence was 0.18% (95% CI 0.17-0.19) in Australian-born women. Over 17 years, there were significant reductions in HBV prevalence among all women (from 0.88% in 2000 to 0.57% in 2016; $p<0.0001$). Among women from high prevalence countries, the greatest absolute reductions were observed among those from Taiwan (10.1%, $p<0.001$) followed by Tonga (5.4%, $p<0.001$), whereas no reductions were observed for women born in Vietnam ($p=0.08$), South Korea ($p=0.41$) and Sudan ($p=0.06$). In conclusion, routine antenatal HBV testing can be used to inform HBV prevalence estimates and vaccine program impact in countries with limited surveillance and high migration to Australia.

Keywords

country of birth, hepatitis B, migrants, prevalence, vaccination

Introduction

Hepatitis B virus (HBV) infection is a major public health problem. Globally it is estimated to be responsible for 43% of all hepatocellular carcinoma cases and 887,000 deaths annually[1] and the World Health Organization (WHO) has set targets to eliminate HBV along with other viral hepatitities by 2030.[2] The prevalence of chronic HBV infection varies significantly between countries.[3] For example, the estimated worldwide prevalence was 3.5%, but ranged from 0.01% in the United Kingdom to 22.7% in Kiribati.[4] A vaccine has been available since 1982 and a 3-dose childhood schedule has been shown to be greater than 90% effective in preventing infection.[5] Since the early 1990s, countries began introducing HBV vaccination into their national childhood vaccination programs with coverage increasing dramatically over the last two decades.[6] By 2018, the WHO estimated global 3-dose coverage was 84% and as high as 93% in the Western Pacific region.[7] The widespread uptake of HBV vaccination has resulted in decreases in chronic HBV infection but this has not been uniform across countries.[8]

Estimating HBV prevalence requires blood sampling and therefore prevalence surveys are expensive and often restricted to small selected populations,[9] these populations may not be representative of the general population and more reliable data are needed to plan control strategies.[4] Although the overall prevalence of chronic HBV infection in Australia is generally considered low (<2%), some populations such as Aboriginal and Torres Strait Islander people and migrants are known to have higher prevalence.[10] In Australia, universal screening for HBV has been recommended for all pregnant women as part of routine antenatal care since 2000[11] with an estimated 98% of women screened for HBV.[12] This routine antenatal HBV screening program provides an opportunity to estimate the prevalence of chronic HBV infection in a large population-based sample. Australia has a relatively high and increasing migrant population, with over a quarter of residents in 2017 born overseas (many from Asia and Western Pacific regions).[13] Estimates of chronic HBV prevalence in different migrant populations can be used in statistical models to project the burden of chronic HBV according to changing migration patterns, and enable the generation of accurate denominator data to track treatment uptake.[14] It can also add to knowledge not only relevant to Australia, but also for some countries with limited population-based data on HBV infection.

Previously, we used HBV screening data from Australian women giving birth between 2000 to 2008, to estimate the prevalence of chronic HBV infection in migrants.[10] While we showed differences between women by country of birth, we did not examine trends in HBV prevalence over time at the country level. Therefore, in this updated report we use 17 years of data on HBV infection (from 2000 to 2016) to estimate HBV prevalence by country of birth, and to examine whether this prevalence has changed over time.

Methods

Study population

Two statutory registries in the largest Australian state, New South Wales (NSW; population 7.5 million)[15], the NSW Perinatal Data Collection (PDC) and the NSW Notifiable Conditions Information Management System (NCIMS) were linked by probabilistic matching of personal identifying details. The study population was all women giving birth during the study period (identified using the PDC), among whom HBV cases were identified by linking the NCIMS to the PDC. The linkage was conducted by the NSW Centre for Health Record Linkage and false positive and negative linkage rates are reported to be less than 0.5%.[16] The PDC contains a record for each woman giving birth in the state to an infant of at least 400 grams birth weight or 20 weeks gestation. Each PDC record includes the woman's date of birth, country of birth, and date of giving birth. The NCIMS records notifications of HBV infection as either newly acquired or unspecified infection according to strict case definitions dependent on laboratory confirmation (Table 1). Notification is mandatory for health practitioners and laboratories under the NSW Public Health Act 1991 and 2000. In addition to basic demographics, the NCIMS also contains the date of notification and estimated onset date.

Analysis

We included the earliest birth record for each woman recorded in the PDC as a NSW resident, who gave birth between 1st January 2000 and 31st December 2016 and was aged 15-44 years, so we only had one record per woman. A woman was considered as having chronic HBV infection if she had at least one linked NCIMS record of an unspecified HBV infection (see Table 1). Women who had a linked record of a newly acquired HBV infection were excluded from the analysis given that acute infection in adulthood is unlikely to lead to chronic HBV infection.[17] All other women from the PDC dataset were classified as not having HBV infection.

The crude and age-standardised prevalence of HBV was calculated overall and by the woman's country of birth. For age-standardisation we used 10 year age groups with the 2011 NSW female population aged 15-44 as the standard.[18] The 95% confidence interval for age-standardised prevalence was calculated by using the normal approximation.

The trend in age-standardised HBV prevalence by the woman's year of giving birth was then modelled with log-linear regression or linear regression. For the calculation of absolute reduction, we used the first minus the last fitted value. The relative reduction was obtained by dividing the absolute reduction by the first fitted value. Models were fitted separately for all women, for Australian-born and overseas-born women, and for women born in countries where there were more than 90 HBV cases. For country-specific trends, age-standardised prevalence was calculated annually for countries with ≥1000 HBV cases, or using the two year average for countries with <1000 HBV cases (and for these countries due to the odd number of years the last three years (2014-2016) were averaged). According to central limit theory, we assumed that the proportions of women with HBV over 17 years followed an approximate normal distribution and thus a student's t-test was used to estimate the prevalence differences between Australian-born women and overseas-born women.

All analyses were done with R version 3.4.2.[19] All statistical tests were two sided, and a $p<0.05$ was considered statistically significant.

Results

Between 1st January 2000 and 31st December 2016 there were 1,586,686 PDC records for women residing in NSW. From this we identified 903,996 unique women aged 15 to 44 years at the time of their earliest record of giving birth. After excluding 165 (0.02%) women who linked to records of newly-acquired HBV, 903,831 remained. The mean age at the time of the earliest birth record was 30 years (median 30 years, interquartile range [IQR] 26-34 years).

Among the 903,831 women, 8,001 linked to an HBV record indicating chronic infection, giving a crude prevalence of 0.89% (95% confidence interval [CI] 0.87%-0.90%) and an age-standardised prevalence of 0.76% (95% CI 0.74%-0.78%) (Figure 1). Among countries with >30 HBV cases (see Figure 1), the highest age-standardised prevalence of chronic HBV was estimated among women born in Sierra Leone (11.13%, 95% CI 8.29-13.96), followed by those born in Taiwan (8.08%, 95% CI 6.74-9.43%), Cambodia (7.47%, 95% CI 6.50%-8.45%), Vietnam (7.36%, 95% CI 6.97%-7.75%), Ghana (6.76%, 4.53-8.98%), Tonga (6.64%, 95% CI 5.43%-7.85%) and China (6.42%, 95% CI 6.16%-6.69%). Of countries shown in Figure 1, Australian-born women had the lowest prevalence at 0.18% (95% CI 0.17-0.19%). However, in terms of absolute numbers of women with chronic HBV the greatest numbers were from China (N=2,242), Vietnam (N=1,457) and Australia (N=1,177).

Figure 2 shows the annual age-standardised prevalence of HBV for all women, and for Australian-born and overseas-born women separately. From 2000 to 2016, among all women there was a significant but small absolute decrease in prevalence of chronic HBV infection over the study period (0.3%; from 0.9% to 0.6%, $p<0.001$). However, the absolute decrease was statistically lower ($p<0.001$) in the Australian-born women (0.2%; from 0.3% to 0.1%, $p<0.001$) than among overseas-born women (1.1%; from 2.5% to 1.4%, $p<0.001$).

Figure 3 shows trends in HBV according to the 12 countries of birth with more than 90 HBV cases. Apart from women born in South Korea, Vietnam, and Sudan, significant reductions were observed among women born in all the other nine countries. The most dramatic decline was observed among women born in Taiwan with a 10.8% reduction from 14.1% to 3.3% or a relative reduction of 77%. This was followed by Tonga with a 5.2% decrease from 8.4% to 3.2%

or a relative reduction of 61%. The third largest reduction was in women born in China with a fall of 3.0% from 8.2% to 5.2% or a relative reduction of 37% over the period.

Discussion

In this study of over 900,000 women giving birth in Australia, the age-standardised prevalence of HBV was 0.76%. However, this differed substantially by country of birth, with the highest prevalence found in migrants born in Sierra Leone followed by Taiwan and Cambodia. Between 2000 and 2016 in this population the absolute reduction in HBV prevalence was 0.3%. This also differed substantially by country of birth with the greatest absolute decreases found among migrant women born in Taiwan and Tonga.

A recent comprehensive systematic review commissioned by the WHO reported HBV prevalence from 161 countries.[4] In general, our estimates of HBV prevalence by country of birth were lower than those reported in the review. However, this is not surprising as our sampling frame included a more recent period (2000-2016) compared to the review (1970-2013), and only women aged 15-44 years, whilst the review had both sexes and no age restriction. Both older age and male sex have been shown to be associated with higher HBV prevalence.[21] The review also specifically excluded studies of migrants whilst our study was primarily focused on migrants who may have different sociodemographic characteristics to the population in their country of birth.[4] However, an earlier study suggested that estimates of HBV prevalence in migrant women from antenatal screening in Australia can reflect HBV prevalence determined by sampling in-country, once age is accounted for.[22] Despite the different methods and populations, our study adds to the findings from the review by providing more contemporary estimates for HBV prevalence. Furthermore, to our knowledge, this is the largest series of its kind ever analysed. The sample sizes obtained in our study for countries such as Sierra Leone, Vietnam, Tonga, Samoa and Fiji were larger than those reported in the review; for example we had 2,357 women from Samoa sampled compared with the 398 participants reported in the review. We were also able to estimate age-adjusted HBV prevalence among women from the Cook Islands (2.37%, see appendix) and North Korea (see Figure 1), countries for which no data were presented in the review.

Previous studies estimating temporal trends in chronic HBV prevalence suggest decreases in countries in the Western Pacific and South-East Asia, but not in Africa.[8] However, some of these estimates may be limited by inconsistencies in the sampling frames with comparisons made between study populations of different ages, sex distribution, sampling methodology and long

periods between sampling.[8] For example a recent study estimated change in HBV prevalence in Tonga by using two studies, one from 1986 which included the general population aged 0 to 60 years and pregnant women,[23] and the other from 1998 which included pre-school children and their mothers.[24] In contrast, our sampling frame was a statutory registry that collects standardised data on all women giving birth in the largest Australian jurisdiction linked with a registry of HBV notifications. This methodology ensures consistency in sampling and case ascertainment over the 17 year period of observation.

The temporal trends in HBV prevalence by country, observed in our study since 2000, are almost certainly driven in part by country-specific HBV vaccination programs. The greatest decreases in chronic HBV infection were observed among women born in Taiwan followed by Tonga. Both countries were amongst the earliest worldwide to introduce universal infant vaccination programs. Taiwan began in 1984, with coverage estimated at 93% in the same year[25] whilst in Tonga, the universal infant vaccination program started in 1989 with coverage of 94% reported.[6] Given the average age of women in this study was 30 years (IQR 26-34), infant vaccination programs with high coverage would need to have been in place for at least 25 to 30 years to detect significant changes in prevalence which was the case for women born in either Taiwan or Tonga.

We also observed smaller but significant reductions in HBV prevalence in women from China, Hong Kong, Thailand, the Philippines, Indonesia and New Zealand. These countries introduced universal infant vaccination programs between 1988 and 1995 but with varying degrees of coverage.[6,26,27] A small reduction was also observed in Cambodia, however Cambodia did not introduce universal vaccination until 2006 with reported coverage of 80%.[6] In contrast, we did not observe any significant trends towards reduction in HBV prevalence in South Korea, Vietnam, and Sudan. For Vietnam and Sudan, universal infant vaccination only commenced in 2003 and 2005 respectively with low coverage.[6] Interestingly, South Korea introduced universal vaccination in 1995 with reported coverage of 99%.[6] It is unclear why we did not observe even a small reduction among women from South Korea in the later years of data given findings from other countries that commenced infant vaccination at similar times. It is possible this was due to an overall low HBV prevalence in South Korea and our limited sample size of women from this country.

We also found a significant fall in prevalence of HBV in Australian-born women and this change is almost certainly due to reductions in prevalence in Aboriginal and Torres Strait Islander women which has been previously reported.[28,29] Nationally, Australia did not introduce universal infant HBV vaccination until 2000, however there were specific programs targeting children born to high risk mothers including Aboriginal mothers and, in the Northern Territory, an Australian jurisdiction with the highest proportion of Aboriginal and Torres Strait Islander people, a universal infant HBV vaccination program was in place from 1988.[28]

The strengths of our study include the large sample size, and our consistent method for sampling both women and HBV prevalence annually over 17 years. The country of birth data is known to be accurate with a recent validation study suggesting good or excellent concordance between NSW administrative data and self-report for 40 countries (Kappa 0.73 or greater).[30] Limitations of our study include a lack of data on age at migration and the reasons for migration that might enable us to determine how similar the migrants in our population may be to the population in their country of birth. For example migrants admitted to Australia for humanitarian reasons may have poorer health and potentially higher HBV prevalence.[31] Also, criteria to gain a permanent residency visa in Australia change over time. For instance, recent changes mean individuals considered to have medical conditions with significant health service costs may be refused permanent residency status[32], and this might reduce the estimated prevalence of HBV among migrant women over time and confound apparent reductions due to vaccination programs alone. In addition, the smaller sample size for some countries of birth also limited our ability to assess trends over time. Finally, our results may not be generalizable to men or other age groups.

Elimination strategies for viral hepatitis,[2] including HBV, will need to be informed by robust estimates of HBV prevalence. We have shown how routine antenatal testing can be an effective method to monitor trends in HBV seroprevalence and have highlighted some countries where vaccination programs have been successful in reducing HBV, and those where continued emphasis on prevention are needed. Additionally, in countries like Australia with high migrant populations, antenatal testing can not only identify high risk groups in-country, but also supplement information on HBV prevalence for countries where data are sparse or absent.

Figure legends:

Figure 1 Crude and age-standardised prevalence of chronic hepatitis B in Australian women aged 15-44 years by country of birth†. †Only countries with HBV case >30 shown.

Figure 2 Age-standardised prevalence of hepatitis B virus (HBV) in Australian women aged 15-44 years by year of giving birth.

Figure 3 Age-standardised prevalence of hepatitis B virus (HBV) in Australian women 15-44 years by year of giving birth and country of birth†. †HBV prevalence estimates are plotted against the average year of giving birth if these were grouped and trend lines estimated using linear or log linear models (see methods).

Appendix. Age-standardised prevalence of chronic hepatitis B in Australian women aged 15-44 years by country of birth†. †Only countries with HBV case ≥5 shown.

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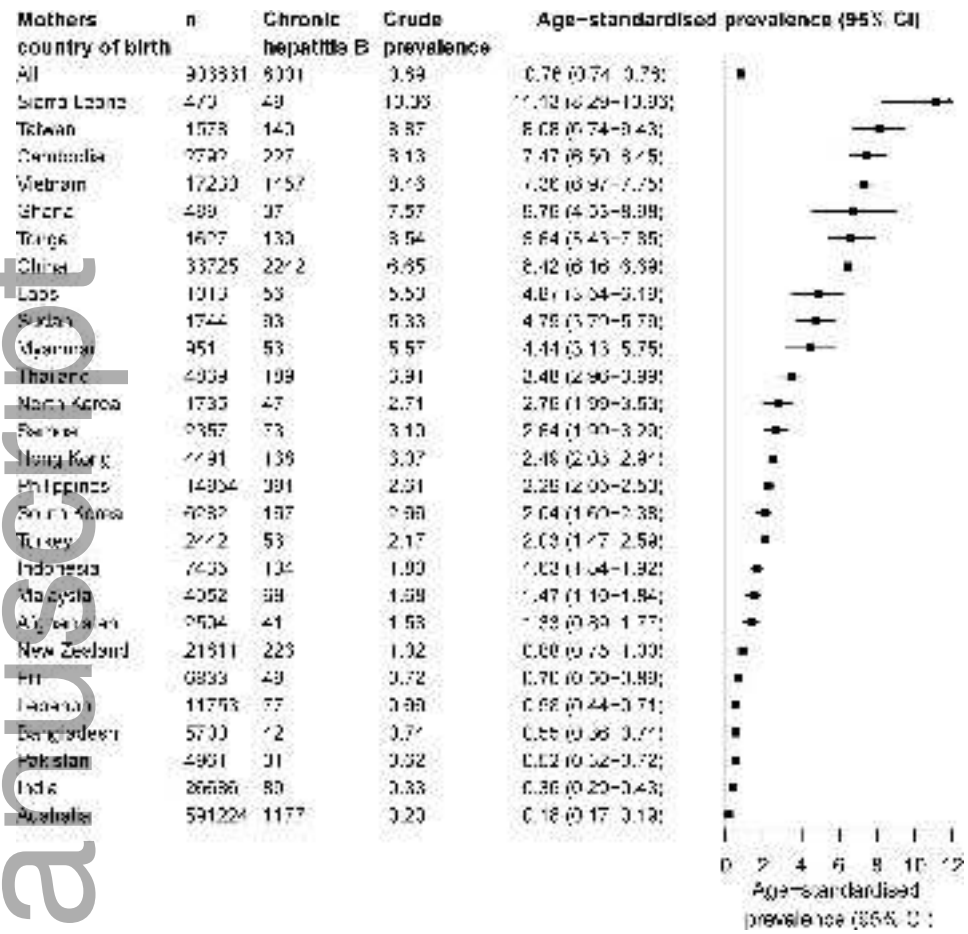
Table 1. Definition of newly acquired and unspecified HBV infection according to the Australia Government Department of Health.[20]

Definition	Confirmed cases	Laboratory definitive evidence
Newly acquired HBV infection	A confirmed case requires **laboratory definitive evidence** only.	Detection of hepatitis B surface antigen (HBsAg) in a patient shown to be negative within the last 24 months. OR Detection of HBsAg and IgM to hepatitis B core antigen, except where there is prior evidence of hepatitis B infection. OR Detection of hepatitis B virus by nucleic acid testing, and IgM to hepatitis B core antigen, except where there is prior evidence of hepatitis B infection
Unspecified HBV infection	A confirmed case requires **laboratory definitive evidence** AND that the case does not meet any of the criteria for a newly acquired case.	Detection of hepatitis B surface antigen (HBsAg), or hepatitis B virus by nucleic acid testing, except where there is prior evidence of hepatitis B infection.



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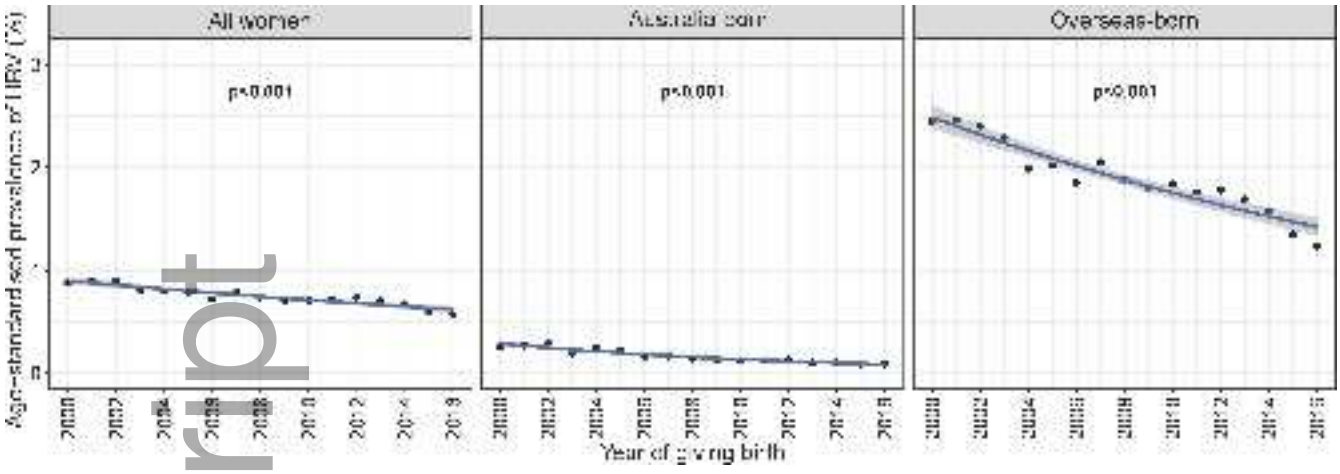

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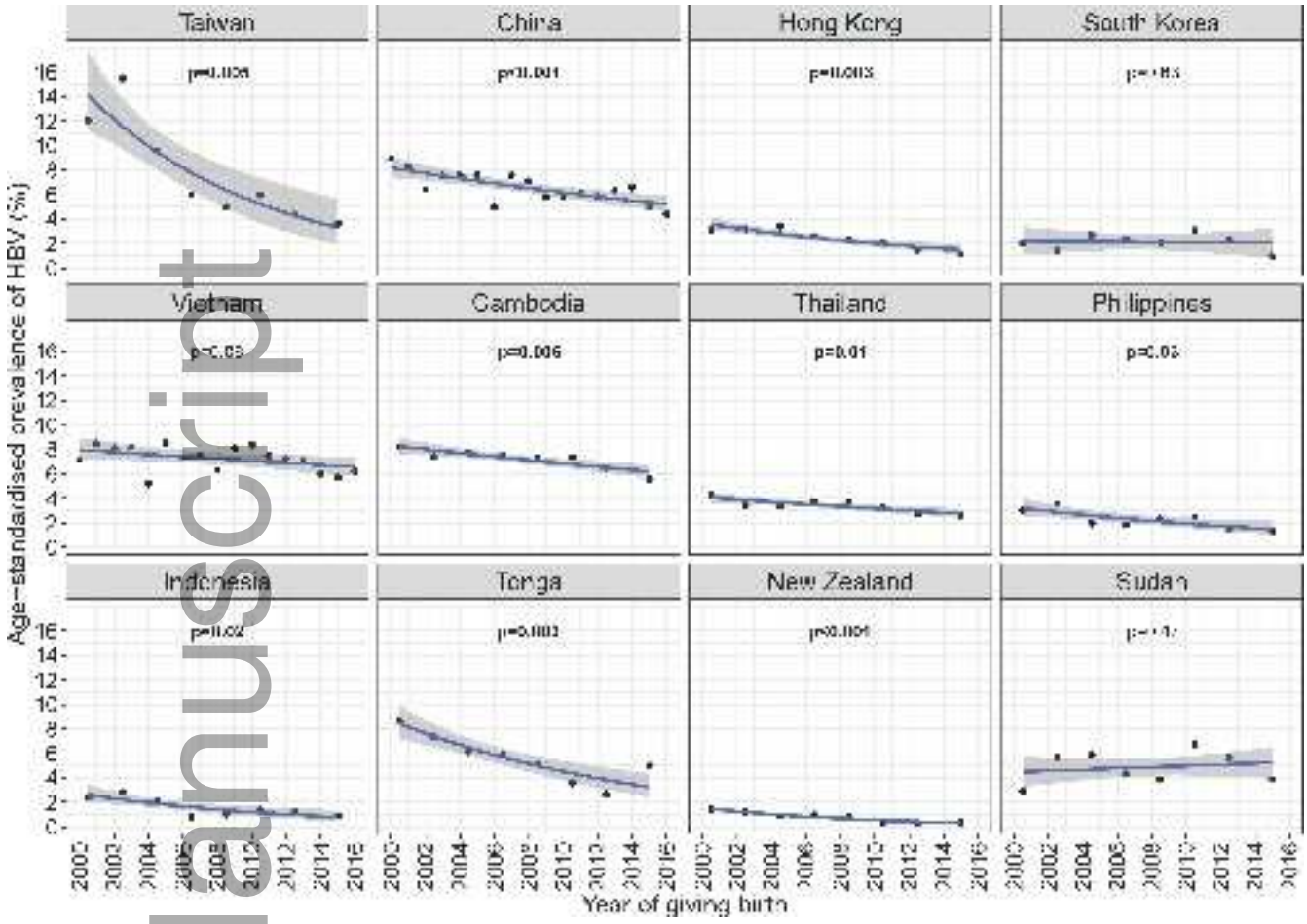

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