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Hepatitis B virus prevalence:

implications for a tenofovir-based HIV prevention strategy

Gonasagrie Nair

On behalf of the CAPRISA eThekwini VOICE team

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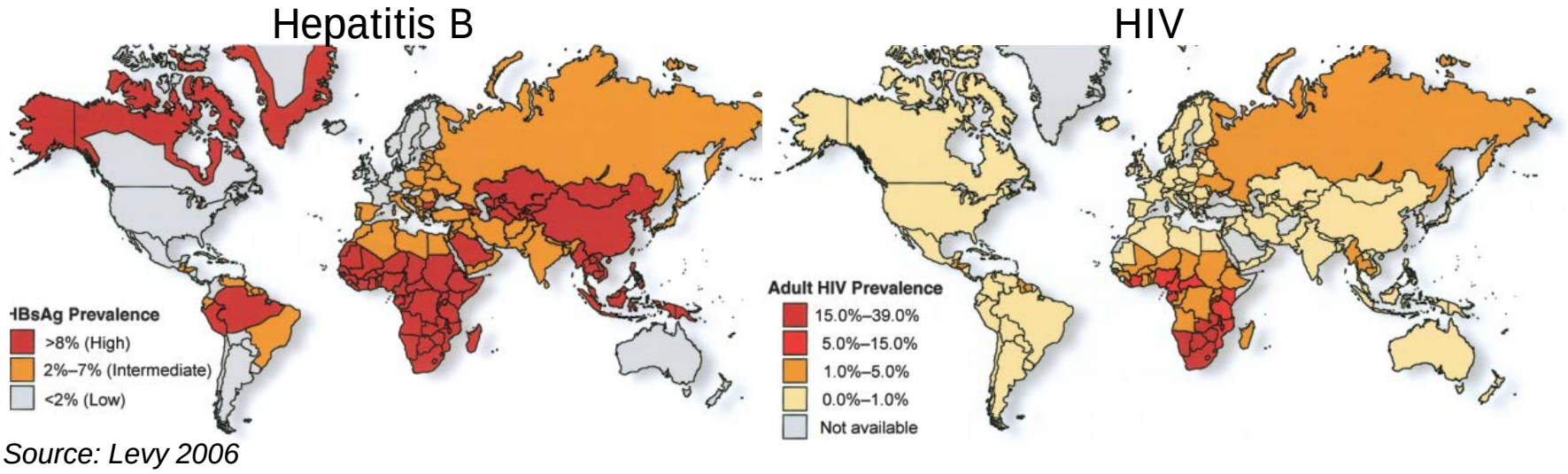
Introduction

- **Hepatitis B virus (HBV) infection is a significant global public health problem**
  - Over 2 billion have been exposed to HBV
  - ±350 million are chronically infected
  - 60% of global population reside in highly endemic HBV areas (Africa/Asia)
  - Prevalence in Sub-Saharan Africa: 0.3 –15%
- **South Africa**
  - 76% of adult population have had past HBV exposure
  - 9.6% have chronic infection
  - HBV prevalence highest in Gauteng (18% of 2077 reported between 1998-2007) and KZN (17,6%)

Global distribution of chronic HBV and HIV infection



Source: Levy 2006

- HBV and HIV share common modes of transmission
- Dual infection is common in high/intermediate prevalence areas of HBV infection
- Occult infection (sAg negative, HBcIgG positive, low levels of HBV DNA) estimated to be 10.6 and 23 % in HIV-HBV infected individuals

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Preventing Hepatitis B infection

- **Immunization most effective strategy in HBV prevention**
- **In South Africa: HBV vaccination incorporated into EPI in 1995**
- **In 2005 – vaccine coverage in Africa was 39%**
  - South Africa: 94%
  - Uganda: 84%
  - Zimbabwe – 90%
- **In July 2010: WHO/UNICEF estimates coverage to be 67% in South Africa**

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Treating Hepatitis B infection

- **Tenofovir is licenced for the treatment of chronic HBV and HIV**
  - When tenofovir is discontinued in HBV-infected individuals they may experience severe, acute post treatment exacerbation of hepatitis (hepatic flares)
  - these patients need to have their hepatic function closely monitored
- **PrEP trials generally exclude HBV carriers (HBsAg+) to avoid potential :**
  - hepatic flares, and
  - HBV resistance on discontinuation of PrEP
- **Safety of tenfovoir as PrEP in HBV-infected individuals unknown**

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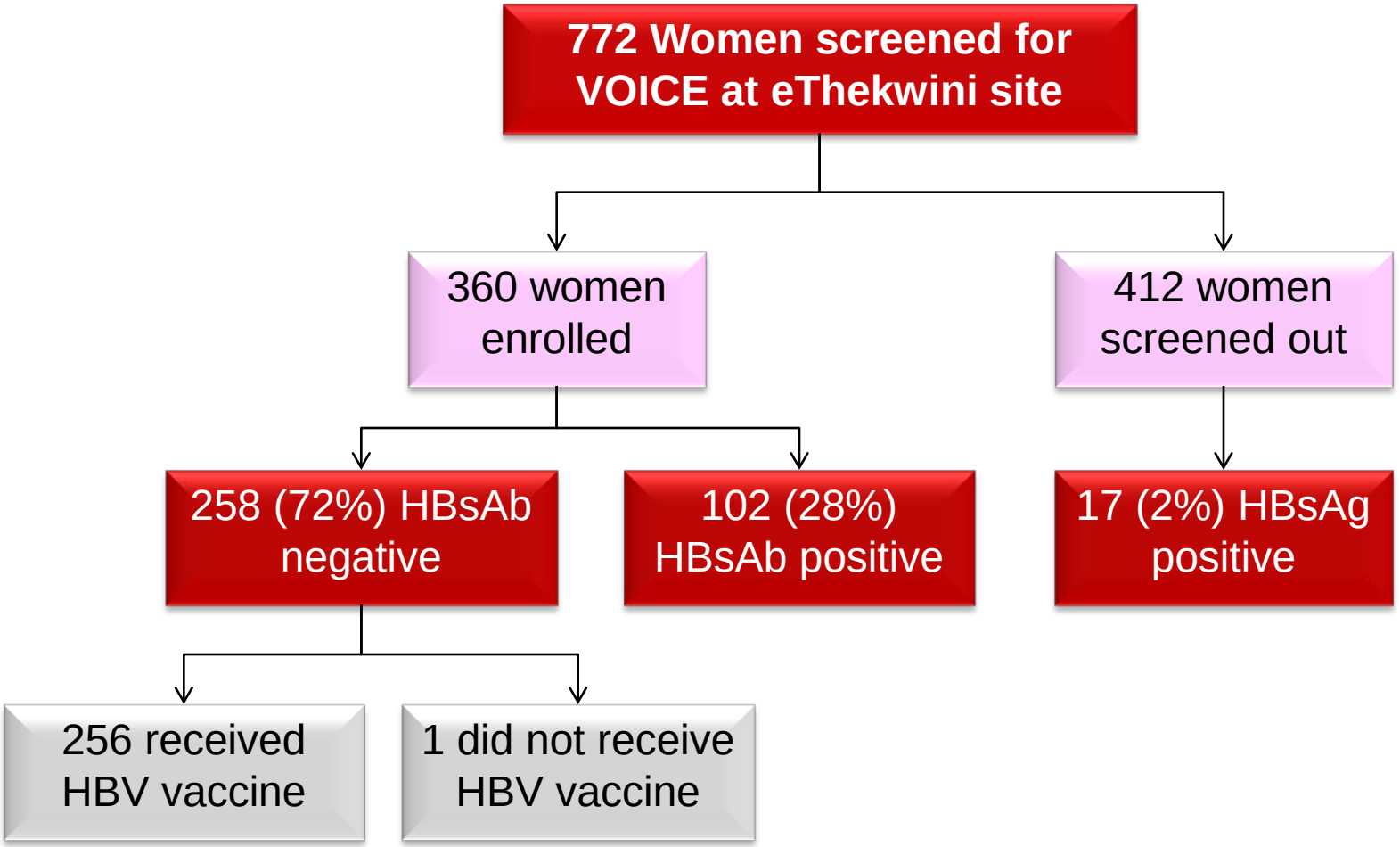
Risk factors for hepatic flares and HBV resistance

- **Hepatic flares associated with:**
  - raised transaminase levels
  - severe liver fibrosis
  - presence of HBeAg
- **HBV resistance:**
  - higher risk with nucleoside analogues (FTC/ 3TC)
  - lower risk if nucleoside and nucleotide analogues are combined (TDF and FTC)

Rationale for chart review

- **To determine whether there would be a public health impact in excluding carriers of HBV, should PrEP be made available as an HIV prevention strategy by:**
  - Establishing the prevalence of HBV carriers (HBsAg positive) in women screened for the VOICE study
  - Determining the extent of existing immunity (HBsAb positive) at the eThekwini site
- **Secondary objective: to determine the severity of liver disease in HBV carriers amongst women screened.**

HBV status of participants at enrolment



Results

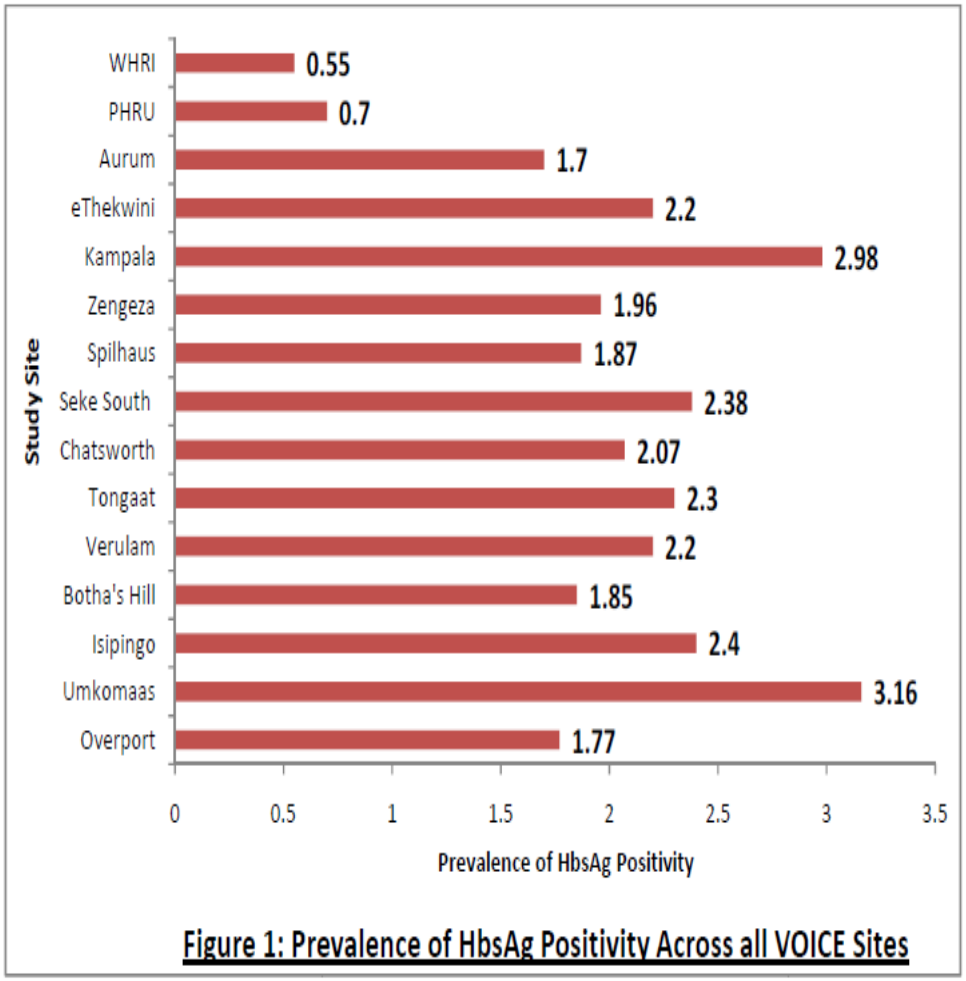


Figure 1: Prevalence of HbsAg Positivity Across all VOICE Sites

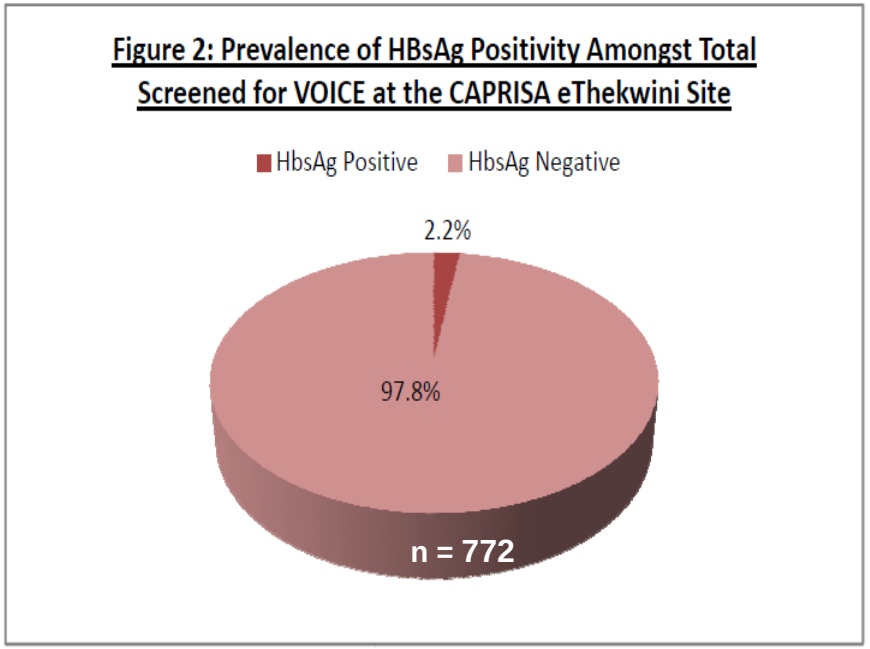


Figure 2: Prevalence of HBsAg Positivity Amongst Total Screened for VOICE at the CAPRISA eThekwini Site

- **Prevalence of HBV carriers : 0.55 – 3.16%**
- **No geographic variation noted**

Past Exposure to HBV amongst eThekwini VOICE participants

Figure 3: Prevalence of HBsAb Positivity Amongst Participants Enrolled in VOICE at the CAPRISA eThekwini Site

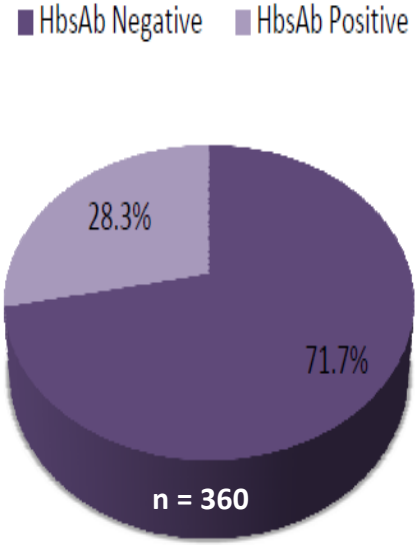
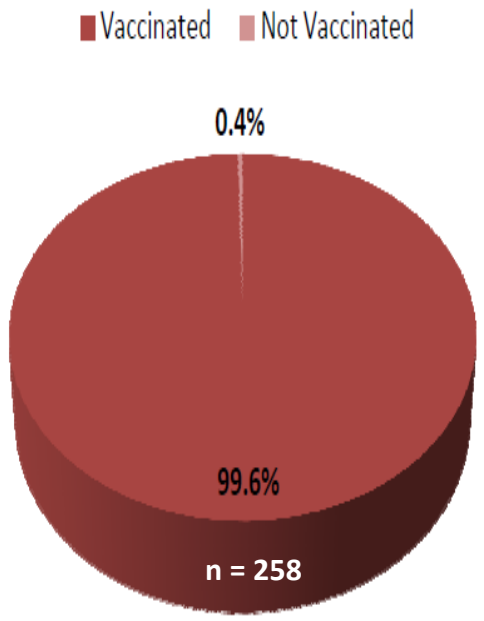


Figure 4: HB Vaccination Status Amongst Enrolled VOICE participants at the CAPRISA eThekwini Site



AST/ALT in HBsAg positive screeners

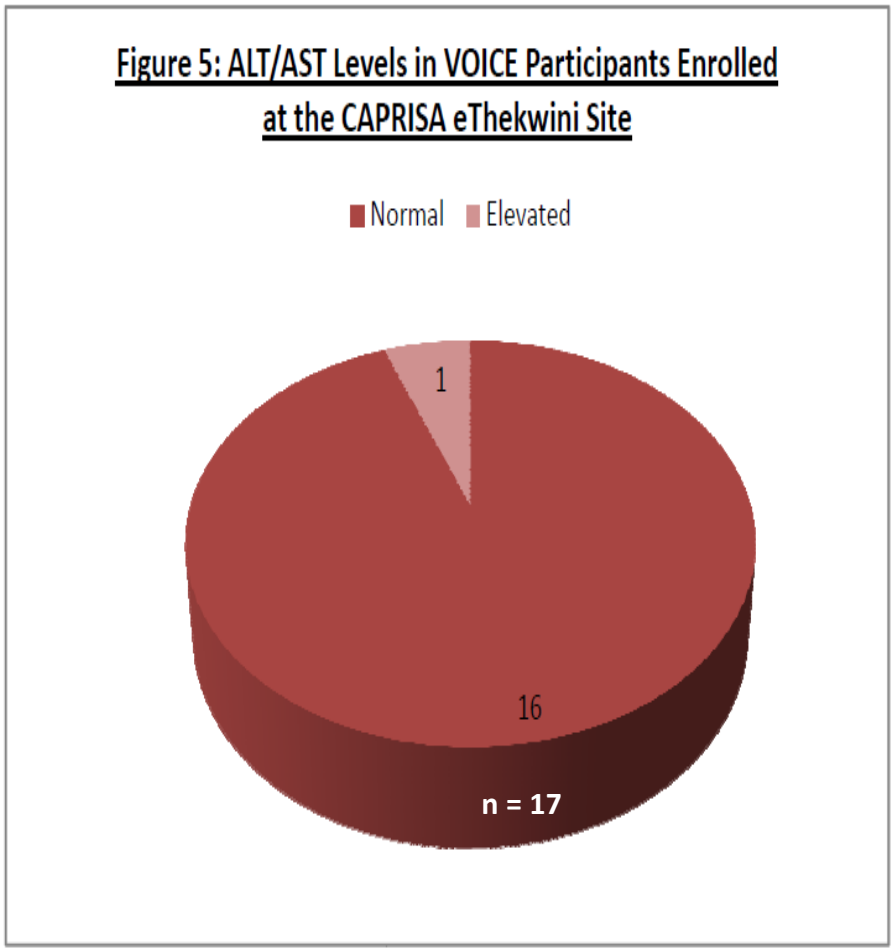


Table 1: ALT / AST Levels of HbsAg Positive Participants

No.	ALT	AST	Site Upper Limit of Normal
1	29	26	35
2	27	21	35
3	22	19	35
4	12	19	35
5	15	21	35
6	11	15	35
7	18	21	35
8	15	20	35
9	21	20	35
10	42	36	35
11	17	18	35
12	21	21	35
13	34	30	35
14	28	18	35
15	29	43	35
16	17	19	35
17	22	28	35

Discussion

- **Only a third of enrolees had HBsAb**
- **2/3 required HBV vaccination**
- **Impact of oral tenofovir use on HBV-infected remains unknown**
- **Exclusion of HBV-infected individuals may have minimal public health impact for PrEP implementation:**
  - Prevalence low amongst women screened out (2%)
  - Prevalence likely to decrease further as vaccine coverage increases and due the cohort effect of infant vaccination
- **Implementation of tenofovir-based regimens for PrEP will need to include screening for HBV and vaccination of HBsAg negative until more safety data is obtained**
- **Should we consider including HBV infected in future PrEP trials with close clinical monitoring for flares?**

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- VOICE protocol chairs