Evaluation of the seroepidemiology of hepatitis A and B in the general population for informing the development of new hepatitis vaccination strategies in Hong Kong

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Background

- hepatitis A virus (HAV) and hepatitis B virus (HBV) infections are vaccine-preventable

- A universal neonatal hepatitis B vaccination programme has been routinely implemented since 1988

- no government-run programme for hepatitis A vaccination

- A gradual decline of age-sex specific HBsAg prevalence in the community has been observed, from 9.5% in 1983/84 to 8.8% in 2001, and further to 7.2% in 2015/16 [1-3].

Aim: to update on hepatitis A and B epidemiology, assess population susceptibility and transmission potential of the viruses in Hong Kong

Methods

A prospective territory-wide cross-sectional household survey

There were 3223 defined Building Groups covering 41 327 residential buildings. In this system, buildings are grouped in the way that each Building Group has approximately similar populations, who are socially homogeneous, in terms of geographical location, building type, building age and number of residential storeys. Each Building Group has at least 1000 residents for ensuring protection of confidentiality of individual's identity. With the building information available in the website of Centaline Property Agency Limited, 10 households were randomly selected from each Building Group.
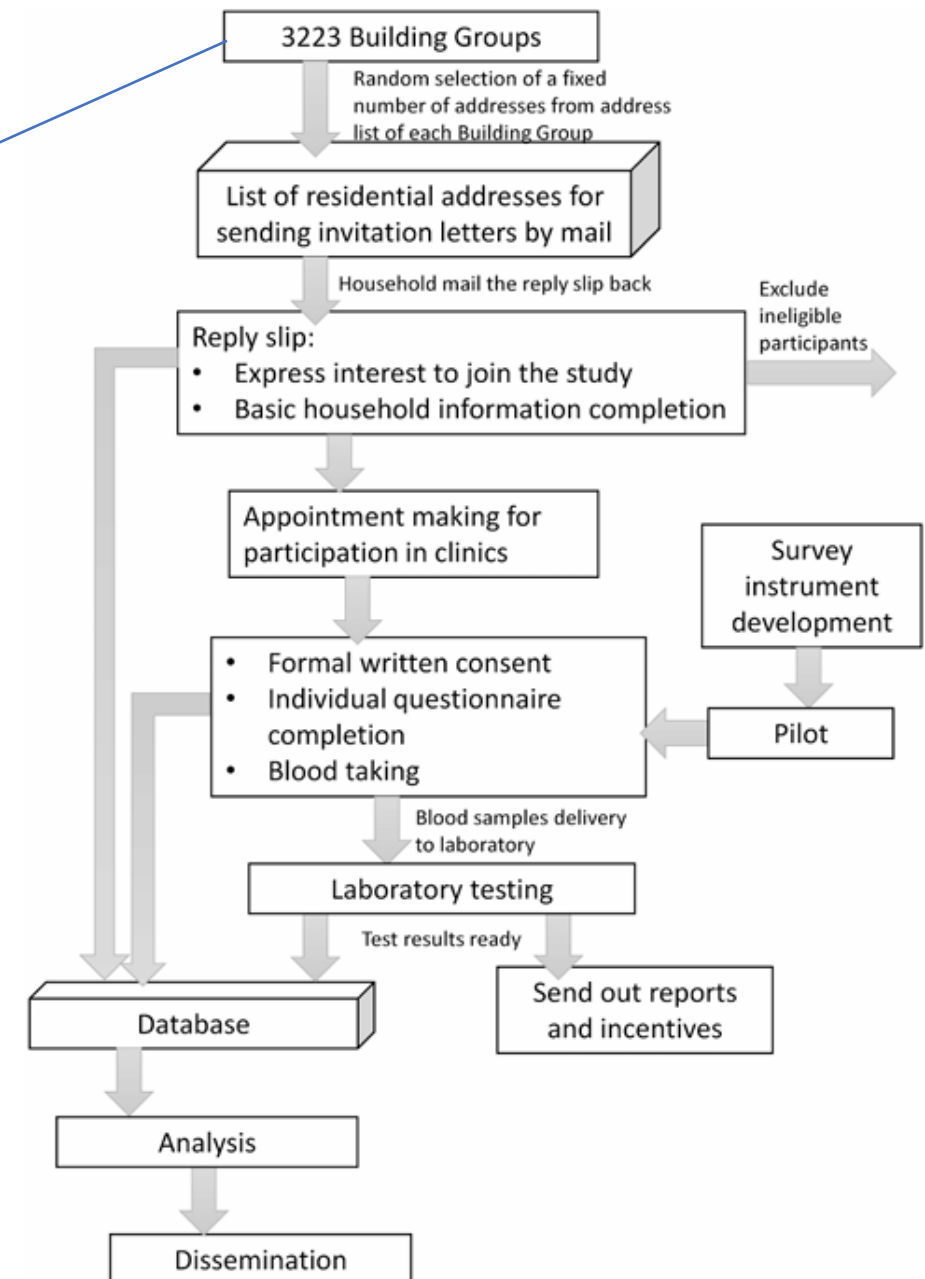
Poon et al., 2021 [4]

Figure 1 Study flow diagram.

Laboratory testing

anti-hepatitis A virus (anti-HAV), hepatitis B surface antigen (HBsAg), hepatitis B surface and core antibody (anti-HBs, anti-HBc)

Data analysis

Outcome variables: HAV infection, HBV infection, vaccination coverage

Prevalence of infection and vaccination coverage were calculated

Factors associated with anti-HAV and HBsAg positivity were identified in bivariable and multivariable logistic regression models.
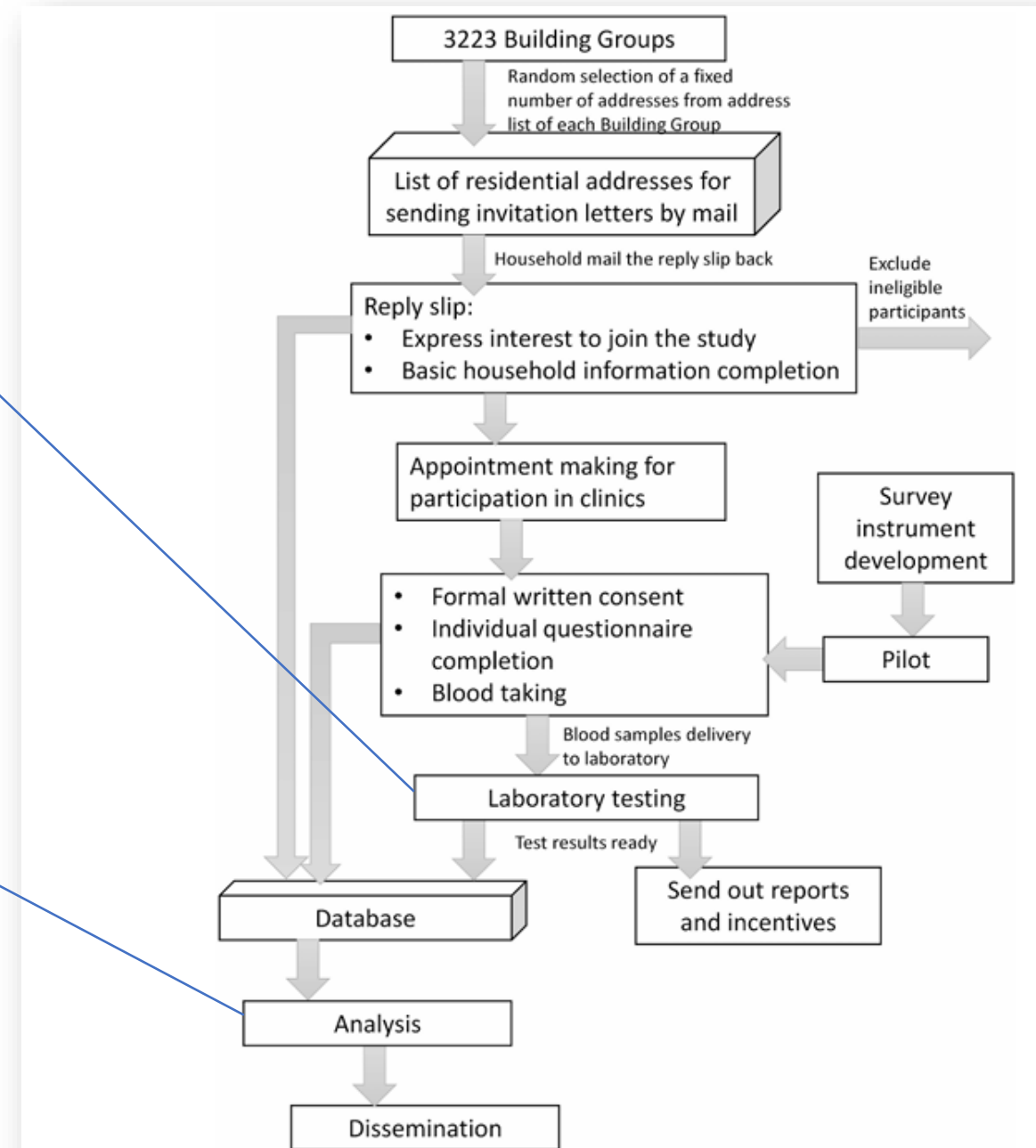

Figure 1 Study flow diagram.

Mathematical modelling

- An age structured catalytic HAV model [6], 2001-2030
  - Diverse exposure risk and could be non-local, so we assume individuals were infected at an age-dependent rate using catalytic modelling approach

- An age-gender structured HBV epidemic model, 1981-2030
  - Included mother-to-child transmission and sexual transmission
  - The key model compartments: susceptible persons without vaccination, vaccinated persons, persons with acute HBV infection, patients with chronic HBV infection, those on treatment, and recovered individuals
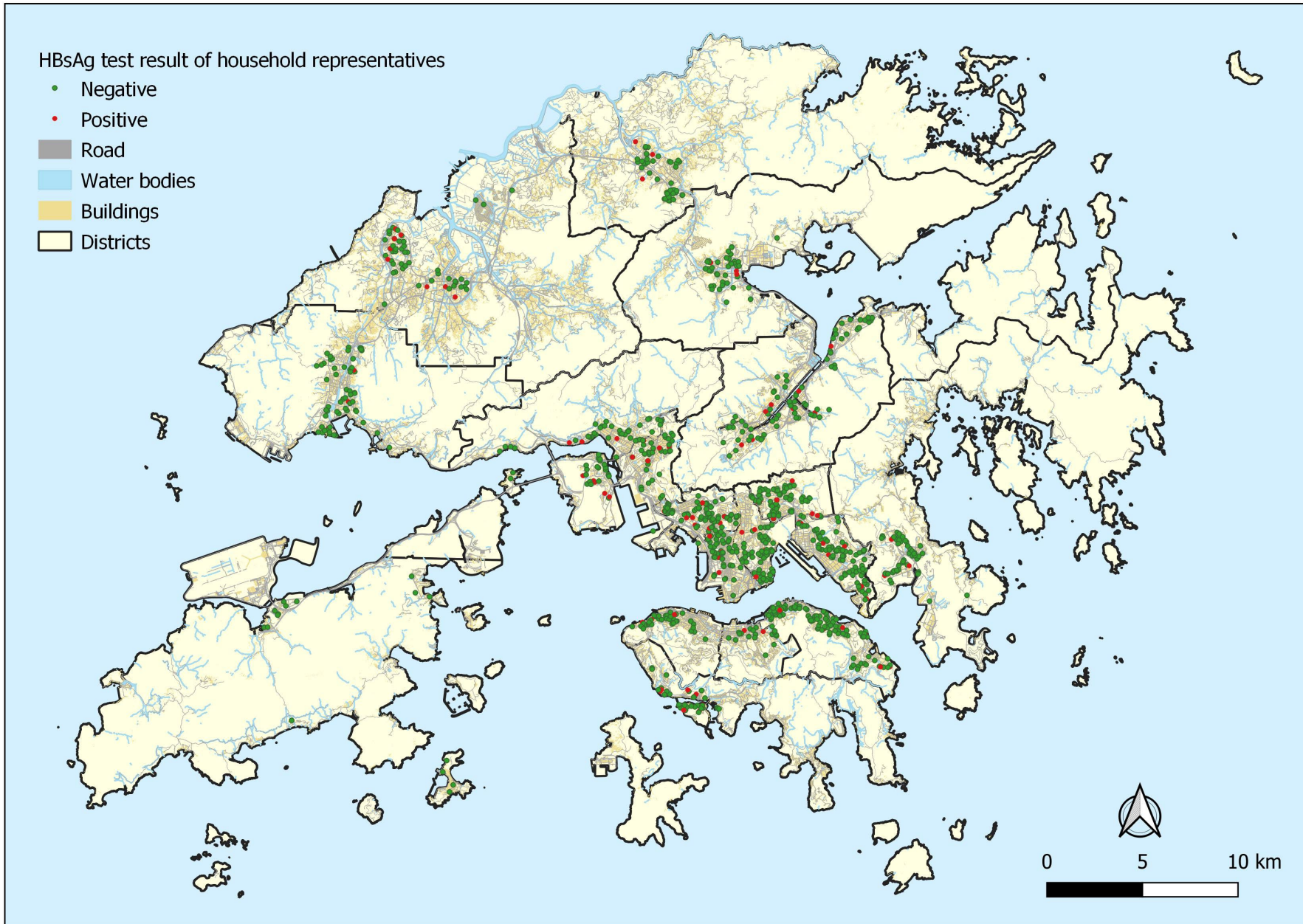
Mathematical modelling

- Data source for model parameterization:
  - Demographics from Hong Kong Census and Statistics Department
  - Prevalence of anti-HAV and HBsAg from previous and current studies [1,3,5]
  - HBV vaccination coverage from annual surveillance reports
  - Other parameter values from literature [7-8]
- Key assumption: life-long immunity after vaccination or recovery from infection
- One-way sensitivity analyses around key parameters were performed

Main findings

HBsAg test result of household representatives
- Negative
- Positive
- Road
- Water bodies
- Buildings
- Districts

Prospective territory-wide cross-sectional household survey:

❖ October 2018 – August 2021

❖ 2267 respondents from 1325 households

Wong et al., 2021 [5]

Characteristics of participants

Characteristics comparison among all participants, household representatives, and census population in 2016

	All participants, n=2085 (%)	Household representatives, n=1143 (%)	Population by-census 2016 (%)#
Gender			
Female	56%	55%	52%
Male	44%	45%	48%
Age group (yo)			
0-14	3%	0%	12%
15-34	16%	9%	25%
35-64	60%	67%	47%
>64	21%	24%	17%
Ethnicity			
Non-Chinese	1%	0.4%	4%
Chinese	99%	99.6%	96%
Education level&			
Primary and below	11%	13%	21%
Secondary	45%	45%	46%
Post-secondary	44%	42%	33%

#population excluding foreign domestic helpers; data source: Census and Statistics Department, Hong Kong SAR Government.

&highest level of educational attainment for individuals aged 15 or above

	n	%
	2267	100
Gender, n=2267		
Male / Female	1175 / 1092	52% / 48%
Median age (IQR), n=2267	52	36-62
Year of birth group, n=2267		
<=1950	224	10%
1951-1960	527	23%
1961-1970	474	21%
1971-1980	368	16%
1981-1990	329	15%
>1990	345	15%
Ethnicity Chinese n=2255	2236	99%
Born in Hong Kong, n=2266	1642	72%
Marital status, n=2181		
Never married	673	31%
Widowed	104	5%
Separated / Divorced	158	7.3%
Married	1246	57%
Education level, n=2260		
Secondary and below	1205	53%
Post-secondary	1055	47%
At work	1313	60%

HAV epidemiology in Hong Kong

Prevalence of anti-HAV positive by year of birth and gender (individual level)
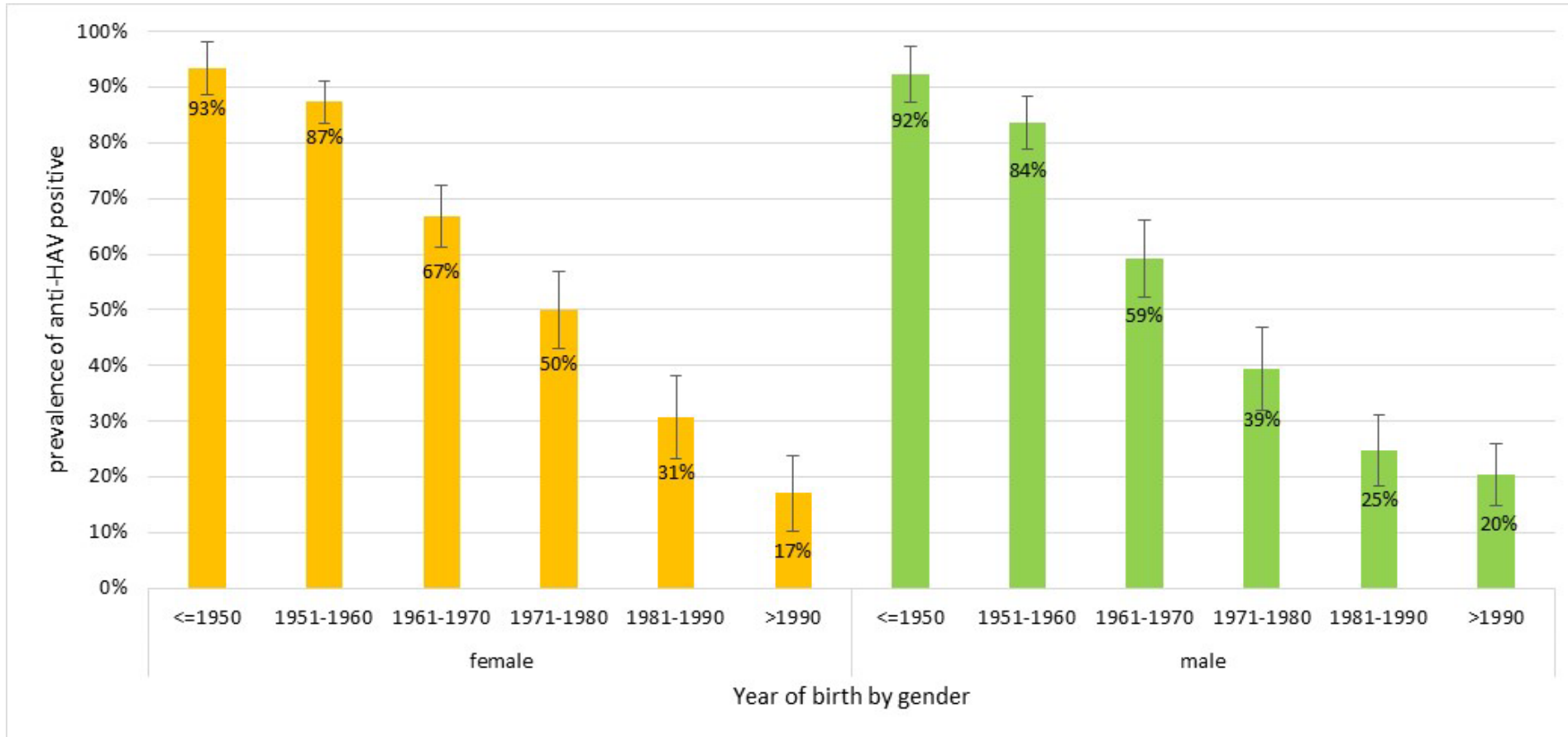
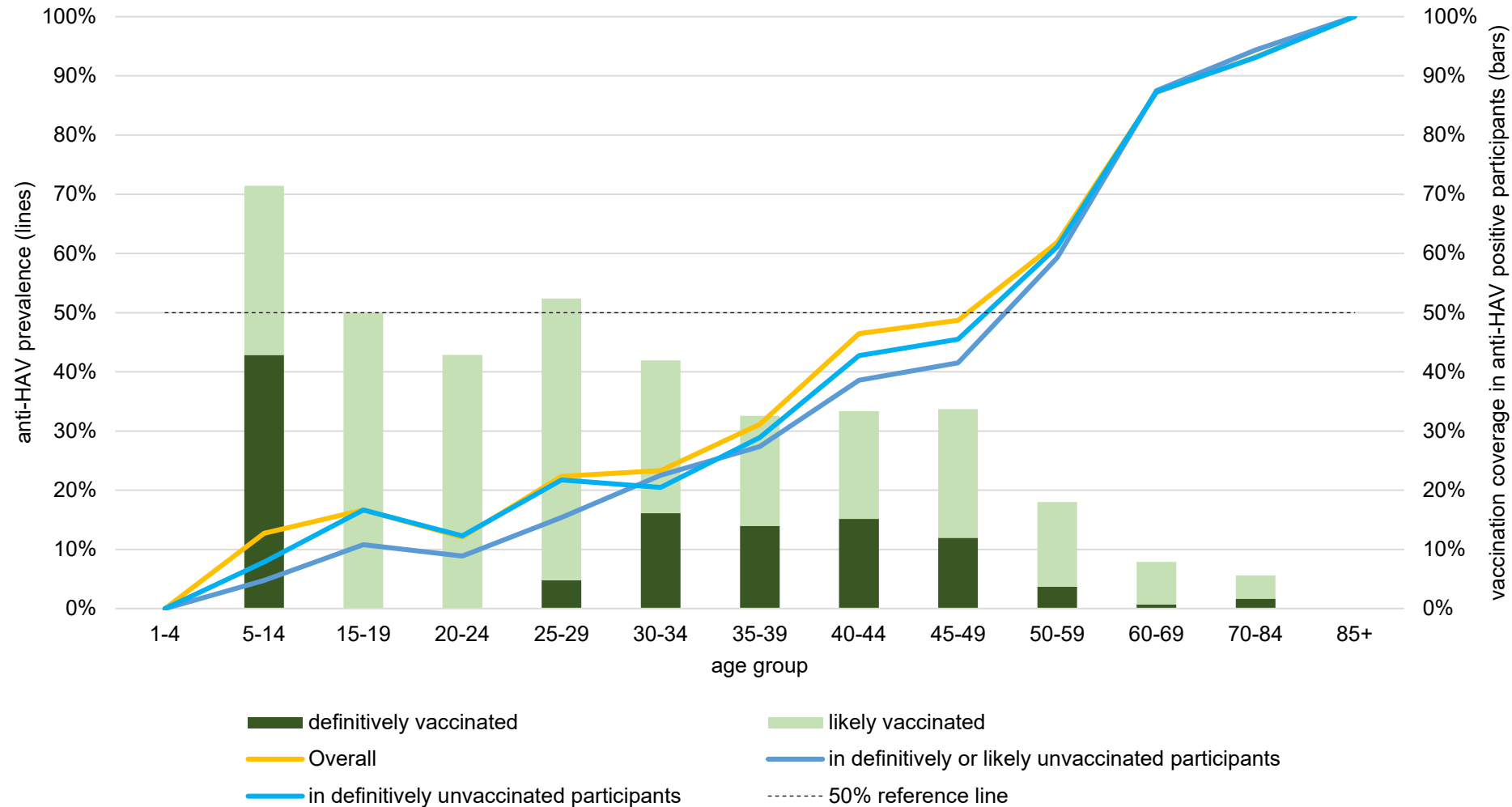The age- and sex-adjusted prevalence of anti-HAV was 49.88% (95%C.I.=47.8%-52.0%) in this study.
Factors associated with anti-HAV positivity: age, female, non-local, lower education level attainment
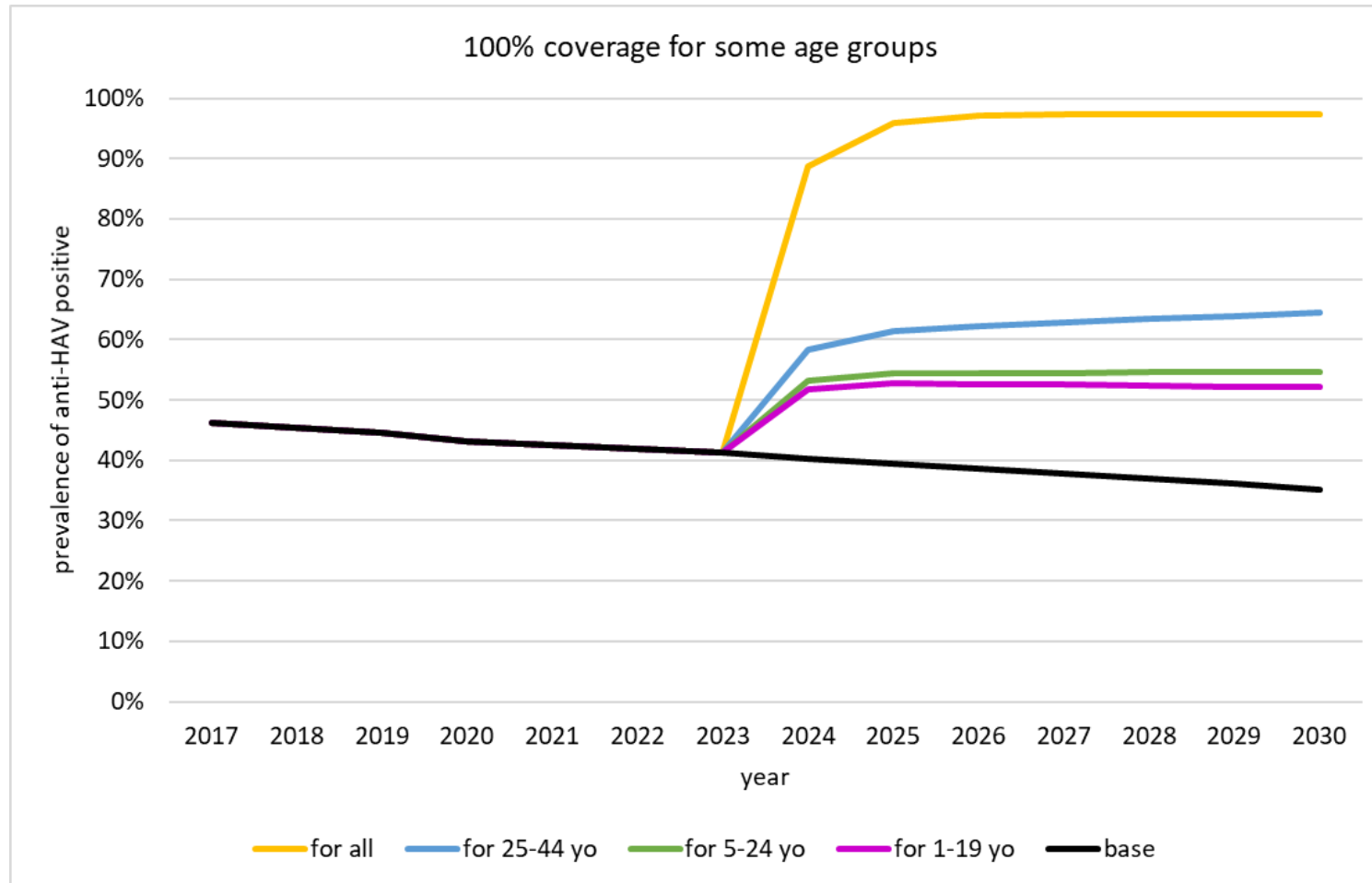
Self-reported HAV vaccination coverage: 20%

HAV vaccination history and anti-HAV antibody prevalence in study population according to age

Impact of expanded HAV vaccination coverage from 2023

100% coverage for some age groups

- ❏ Anti-HAV prevalence would drop from 43% in 2020 to 35% in 2030 in basecase;
- ❏ annual incidence of HAV infection would be very low, decreasing from 0.05% in 2020 to 0.01% in 2030.
- ❏ Scaling up vaccination uptake would effectively reduce the HAV susceptible population

We fitted model predictions of anti-HAV prevalence with the estimates (52%) in 2015 [5] and in 2020 of this study with slight adjustment of study population (39%), using maximum likelihood estimation under a beta-binomial distribution in R (bbmle2 package).
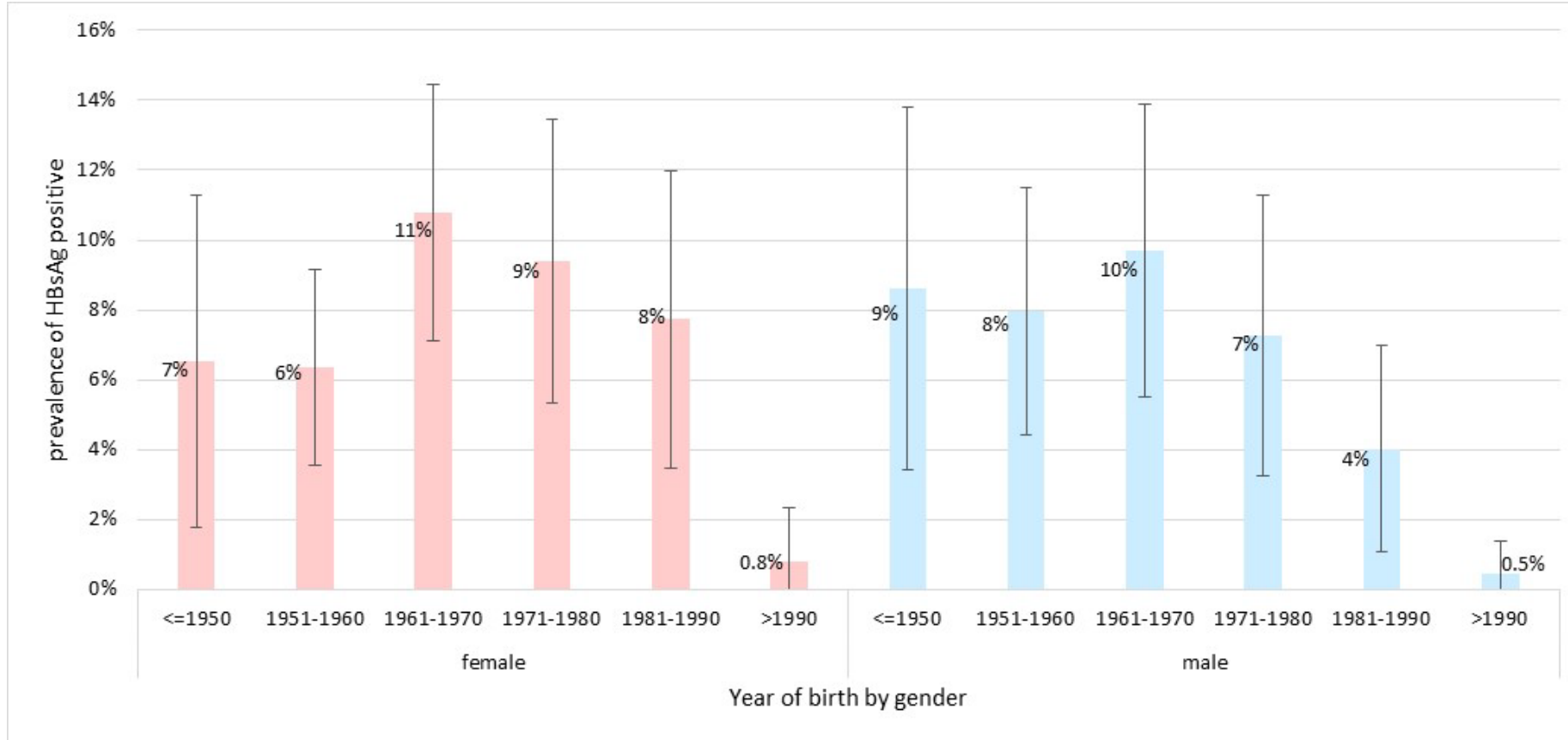
HBV epidemiology in Hong Kong

HBsAg prevalence by age groups and gender

Age groups	Male			Female			Population (mid-2019)#	
	n	HBsAg prevalence	95%CI	n	HBsAg prevalence	95%CI	Male (%)	Female (%)
<29	120	0.8	(0-2.4)	114	0.0	(0-0)	13.06	13.04
29-38	108	6.5	(1.8-11.2)	160	8.1	(3.8-12.4)	6.21	9.15
39-48	135	8.1	(3.5-12.8)	186	9.7	(5.4-14)	6.23	9.15
49-58	189	10.1	(5.7-14.4)	276	10.1	(6.6-13.7)	7.29	8.92
59-68	223	7.2	(3.8-10.6)	306	6.9	(4-9.7)	6.95	7.19
>68	130	10.0	(4.8-15.2)	123	6.5	(2.1-10.9)	5.87	6.96

Anti-HBs	HBsAg	Anti-HBc	n	%
-	-	-	802	36%
	-	+	146	7%
	-	+	61	3%
	-	NA	8	0.4%
	+	NA	86	4%
+	-	-	306	14%
	-	+	222	10%
	+	-	1	0.0%
	+	+	7	0.3%
	0	NA	607	27%

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HBV epidemiology in Hong Kong
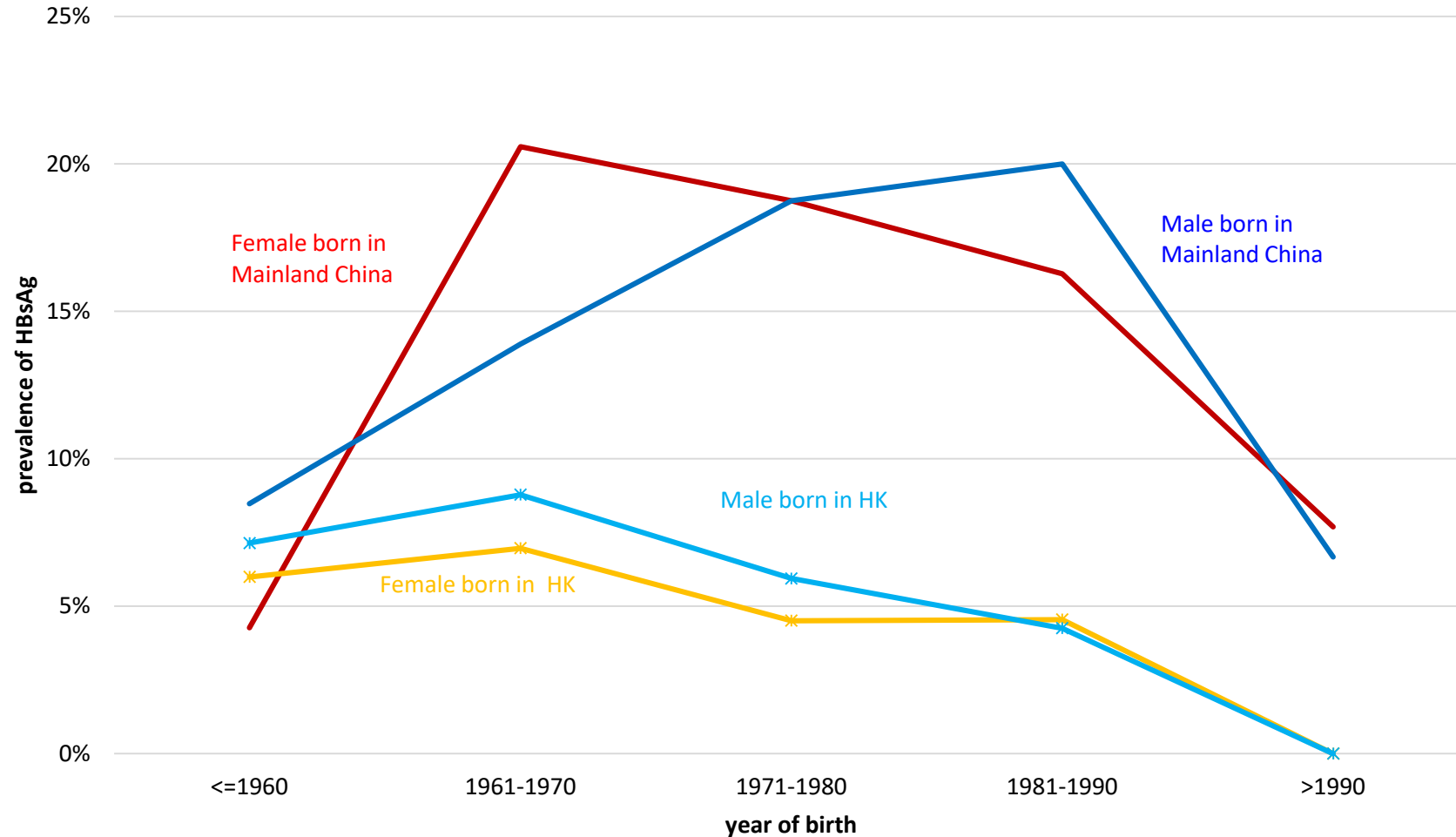## Prevalence of HBsAg positive by year of birth and gender (individual level)

- ❑ The age- and sex-adjusted prevalence of HBsAg was 6.0% (95%C.I.=5.0%-7.0%) in this study.

Self-reported HBV vaccination coverage: 41%

HBV epidemiology in Hong Kong
Local born versus non-local born

Factors associated with HBsAg positivity:

age, non-local, lower education level attainment, known family members with HBV infection, received intravenous injection

Projected prevalence of chronic HBV infection to 2030

Sensitivity analysis of varying chronic HBV prevalence (from 5% to 30%) in immigrants [10% in basecase]

❑ The prevalence of chronic infection will fall from 4.9% in 2020 to 4.2% in 2030.

❑ The HBsAg prevalence in 2030 could be lower at 3.5% (scenario of 5% in immigrants), but could be high at 7.1% (scenario of 30% in immigrants)

prevalence of chronic HBV infection in immigrants:
— 0.05   — 0.1   — 0.15   — 0.2   — 0.25   — 0.3

basecase

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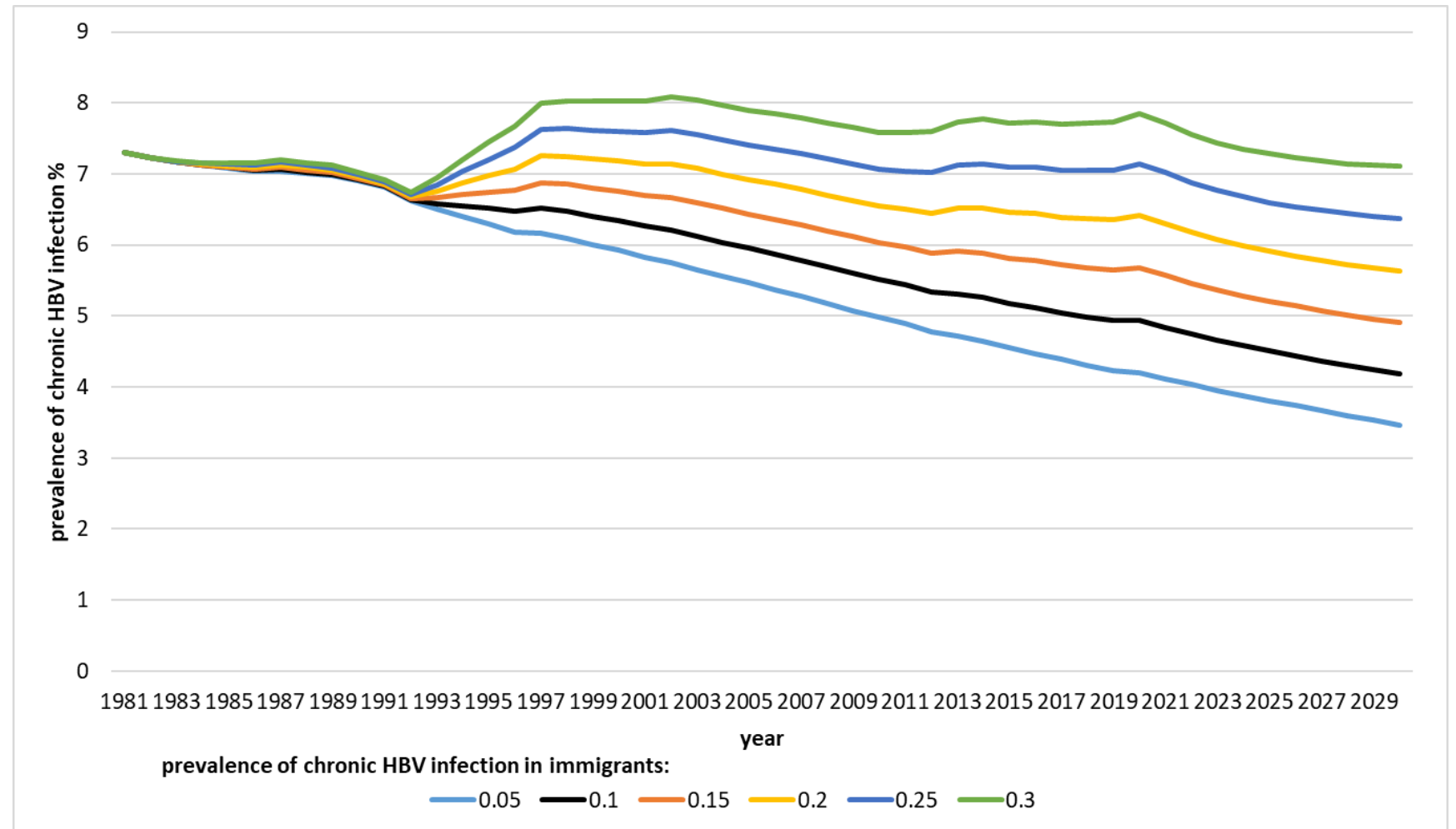
Implications on hepatitis vaccination

❑ Public **health burden** of diseases arising from HAV and HBV are declining

❑ For **hepatitis A**

  ▪ The risk of HAV outbreaks in terms of episodic outbreaks in adults with symptomatic diseases could be high

  ▪ HAV vaccination coverage should be enhanced to boost up community immunity level

❑ For **hepatitis B**

  ▪ Transmission risk is low, but the rate of HBsAg decline would be slow

  ▪ The burden of HBV could be affected by imported infections from immigrants

  ▪ Targeted HBV screening with provision of affordable and sustainable treatment

  ▪ HBV vaccination not a major public health strategy

Outputs

❑ Conference presentation

- Chan CP, Poon CM, Wong NS, Chan DPC, Lee SS. Seroprevalence, seroprotection and risk factors of hepatitis B infection: a territory-wide study in Hong Kong. [oral] *Hong Kong College of Community Medicine Annual Scientific Meeting*. 26 September 2020, HONG KONG.

- Wong NS, Lee SS, Poon CM, Chan DCP. Awareness of hepatitis B virus infection status in the general population in Hong Kong*. International Congress of Infectious Diseases* 2020 [published abstract]. Kuala Lumpur, MALAYSIA. *Int J Infect Dis* 2021; 101(S1):464-486. https://doi.org/10.1016/j.ijid.2020.09.1233

❑ Publications

- Poon CM, Chan PC, Lee SS, Wong NS. Seroepidemiology of hepatitis A and B in the general population in Hong Kong – protocol of a cross-sectional survey using spatial sampling in a highly urbanised city. *BMJ Open* 2021;11:e042065.

- Wong NS, Chan DPC, Chan CP, Poon CM, Lee SS. Community burden of hepatitis A infection and risk of transmission in Hong Kong. *Hong Kong Med J.* 2023;29 Suppl 7(6):41-46.

- Wong NS, Chan DPC, Poon CM, Chan CP, Lau LHW, Yeoh EK, Lee SS. Hepatitis B burden and population immunity in a high endemicity city - a geographically random household epidemiology study for evaluating achievability of elimination. *Epidemiol Infect* 2023;151:e22. https://doi.org/10.1017/S095026882300002X.

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[4] Poon CM, Chan DP, Lee SS, Wong NS. Seroepidemiology of hepatitis A and B in the general population in Hong Kong: protocol of a cross-sectional survey using spatial sampling in a highly urbanised city. BMJ Open. 2021;11(3):e042065.

[5] Wong NS, Lee SS, Poon CM, Chan DCP. Awareness of hepatitis B virus infection status in the general population in Hong Kong. Int J Infect Dis 2021; 101(S1):464-486.

[6] Vynnycky, Emilia., and Richard G. White. An Introduction to Infectious Disease Modelling. Oxford: Oxford UP, 2010.

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CUHK Research Team

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- DCP Chan
- CM Poon
- NS Wong
- CY Poon
- KY So
- CQ Ye
- SF Wong
- HY Wong

Acknowledgements

Staff at Parkes Medical Centre