Hepatitis B vaccination in England and Wales

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Hepatitis B: what should we do?

Current policy:

- Selective vaccination of high risk groups
- Antenatal screening and vaccination of infants born to positive mothers

Additional policy options examined:

- Universal vaccination of adolescents
- Universal vaccination of infants
  - Assumed this was added to current antenatal screening and vaccination

Hepatitis B in ethnic minorities

- Prevalence of hepatitis B is highest in those born in high prevalence countries
  - Not preventable by UK vaccination
- Universal antenatal screening and vaccination will prevent vertical transmission
- But, emerging evidence that individuals born in the UK to parents from endemic countries are at higher risk of **post-perinatal** transmission

Possible options for vaccination of infants at higher risk

- Selective vaccination of those from ethnic minority populations
  - the “Dutch” approach
- Universal vaccination of infants in areas with high proportion of ethnic minorities
  - the “BCG” approach
- These options included in economic analysis

Hepatitis B vaccination
data needed to inform UK policy

- Incidence of acute infection
- Incidence of new chronic infection acquired in UK
- Burden from acute symptomatic and new chronic infection
  - By age, sex and other demographics

- Current overall burden of chronic infection
  - Reflects past UK and overseas exposure
  - Limited bearing on current UK vaccination policy

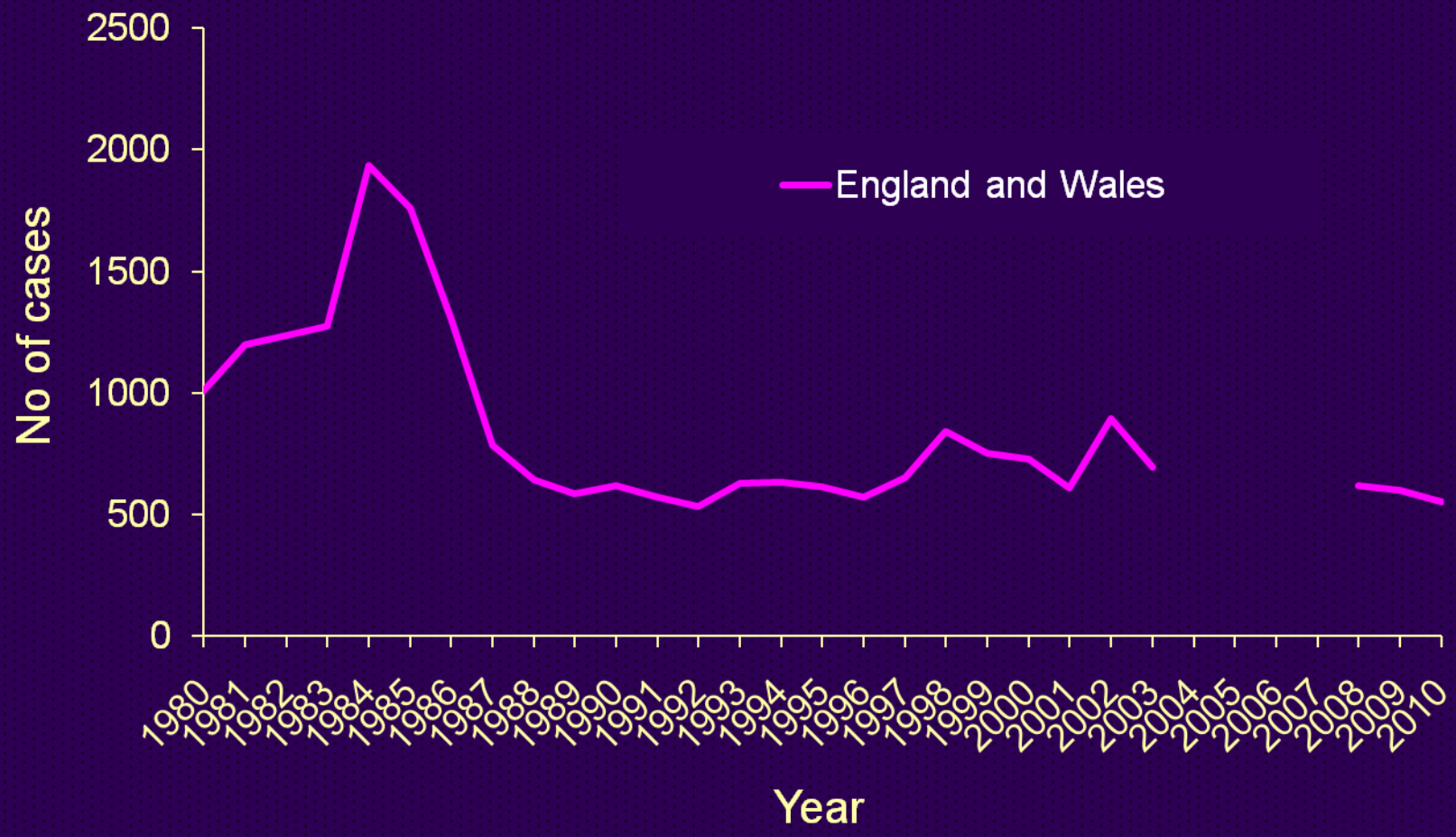
Data sources used for economic analysis

- Laboratory reports of acute infection
  - Used to estimate current incidence
  - Adjusted for under-reporting
  - Adjusted for asymptomatic infection

- Prevalence of anti-HBc
  - Marker of past infection
  - Used to estimate past / cumulative incidence in UK born individuals

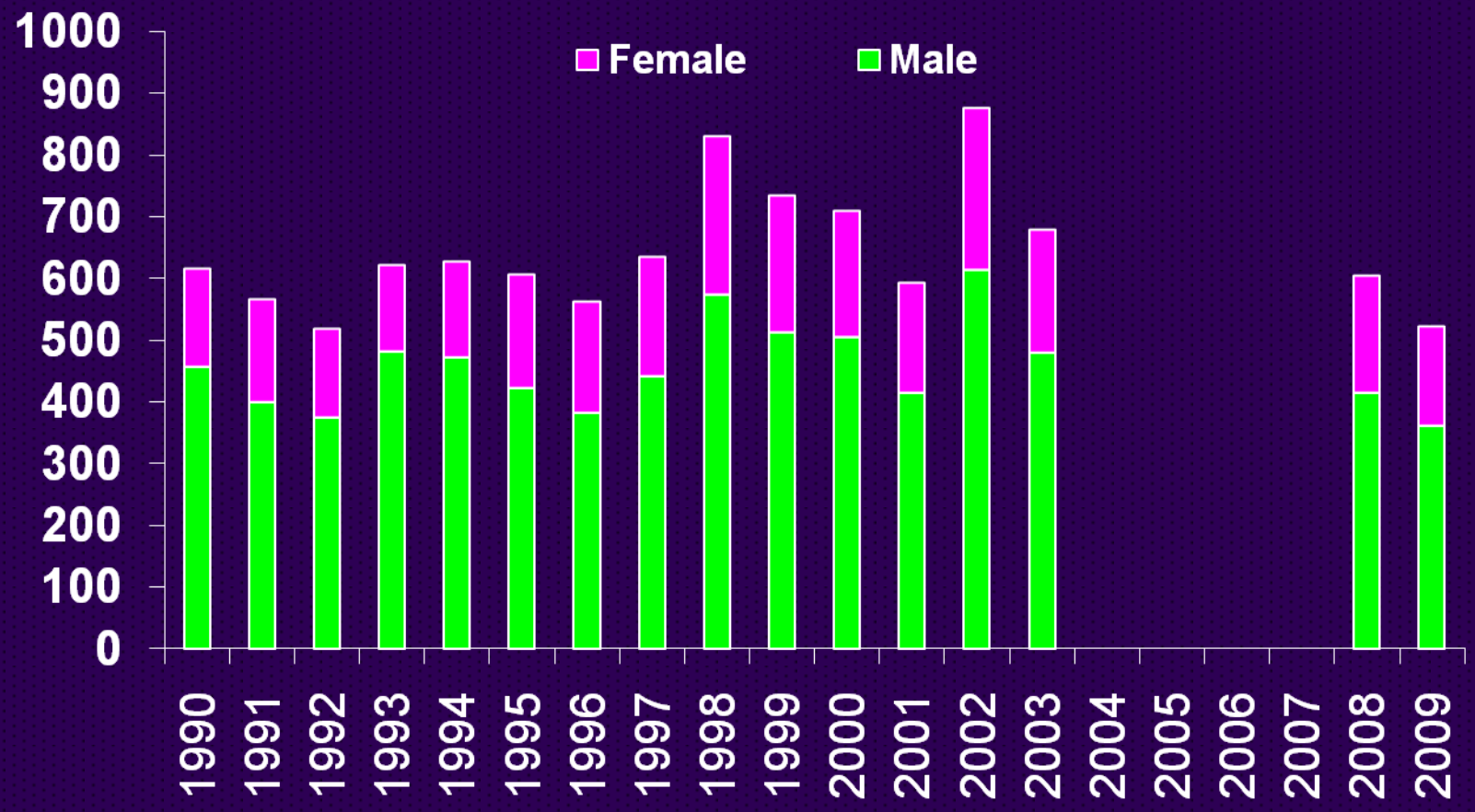
Laboratory reports of acute hepatitis B

England and Wales, 1980-2003, and 2008-10



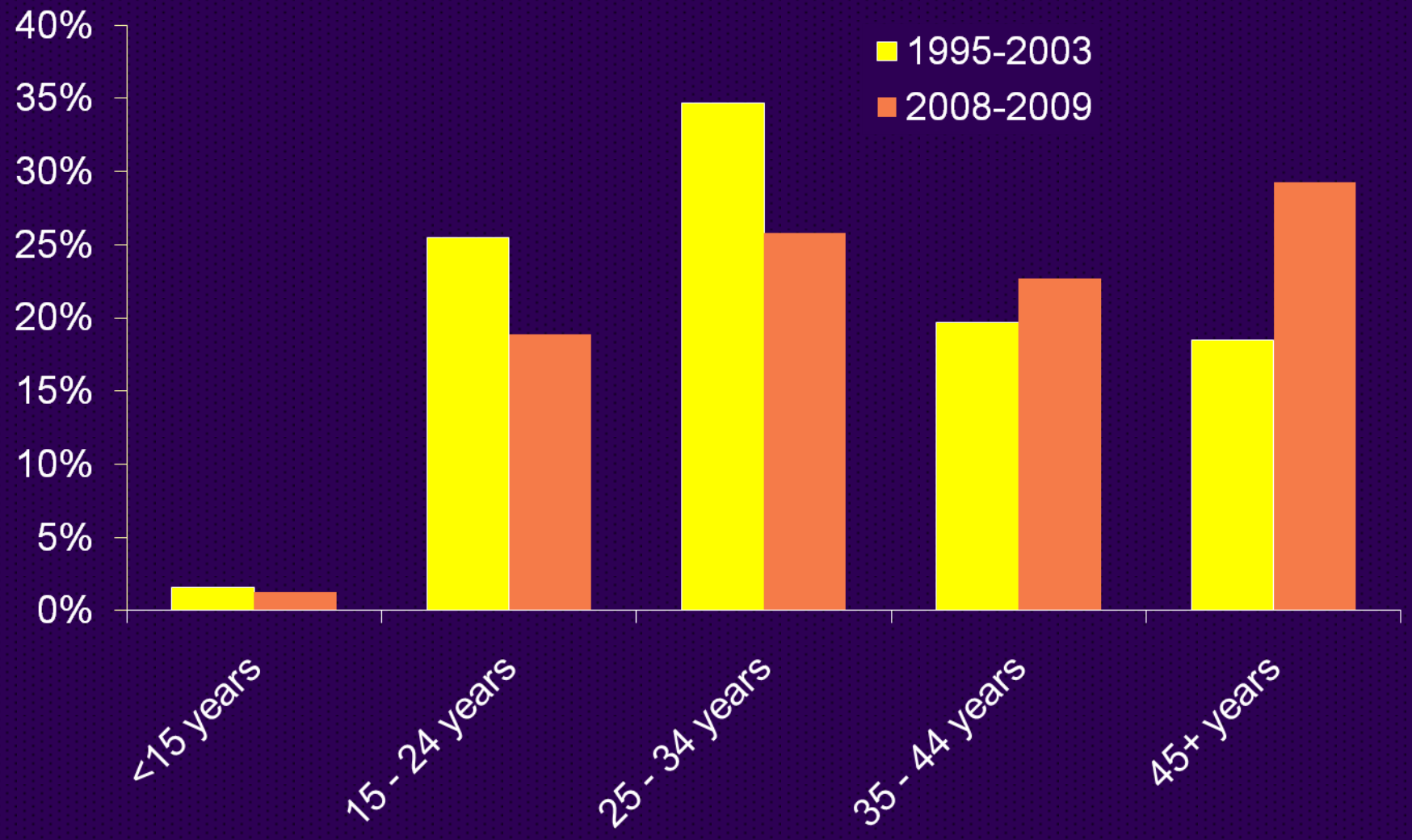
Acute HBV laboratory reports to CfI

By sex, 1990-2003 (2008-09)



Age distribution of acute HBV laboratory reports

England and Wales, 1995-2003, 2008-09

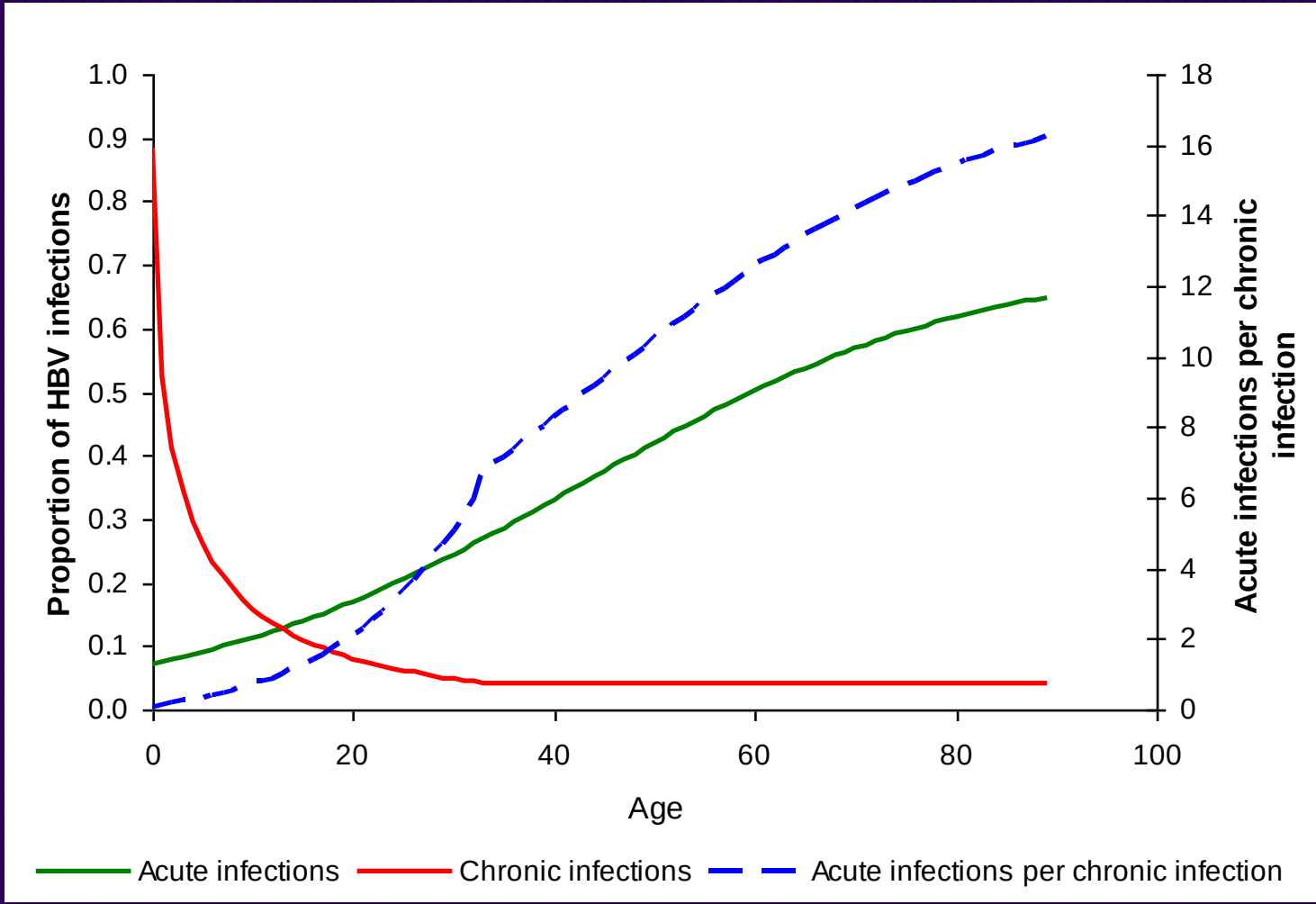


Estimating the true incidence of acute and new chronic hepatitis B

- Incidence of infection estimated from laboratory reports
  - Allowing for under-reporting
  - Allowing for age dependent chance of being symptomatic (ranging from 5 to 60%)
- Incidence of chronic infection
  - Allowing for age-dependent risk of becoming a chronic carrier (ranging from 4 to 90%)
- Incidence in populations with origins in high prevalence areas
  - Anti-HBc survey of inner city children in four areas
  - Analysis of laboratory reports using “names”

Number of chronic infections per acute infection by age

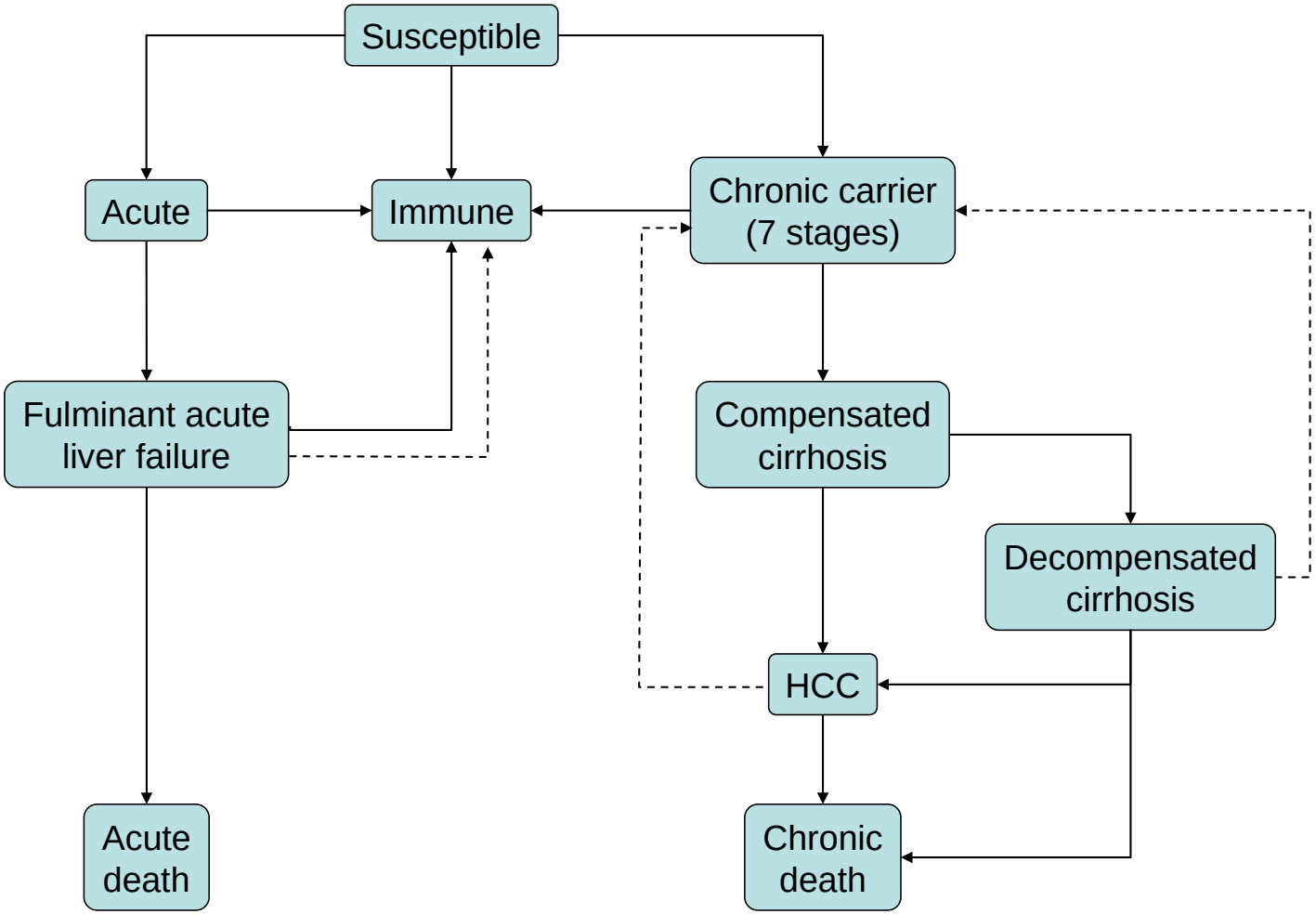
Accounting for proportion asymptomatic and proportion cleared



Incidence of hepatitis B in ethnic minority children

- Oral fluid study of inner city children in four localities (aged 8-11 years)
  - Bury, Birmingham, Camden, Haringey
- Overall 14/5334 (0.26%) confirmed anti-HBc positive
  - 8 born overseas (migrated between 5-10 years of age)
  - Of remaining 6 all born to parents from endemic areas
  - Of the 6 children, 1 had mother who was HBsAg positive, 3 had mothers with resolved infection
- Estimated annual post-natal incidence preventable ONLY by a universal programme
  - Maximum of 12.49 per 100,000 person years
  - Agrees with analysis of laboratory reports based on “names”

HBV Markov model structure



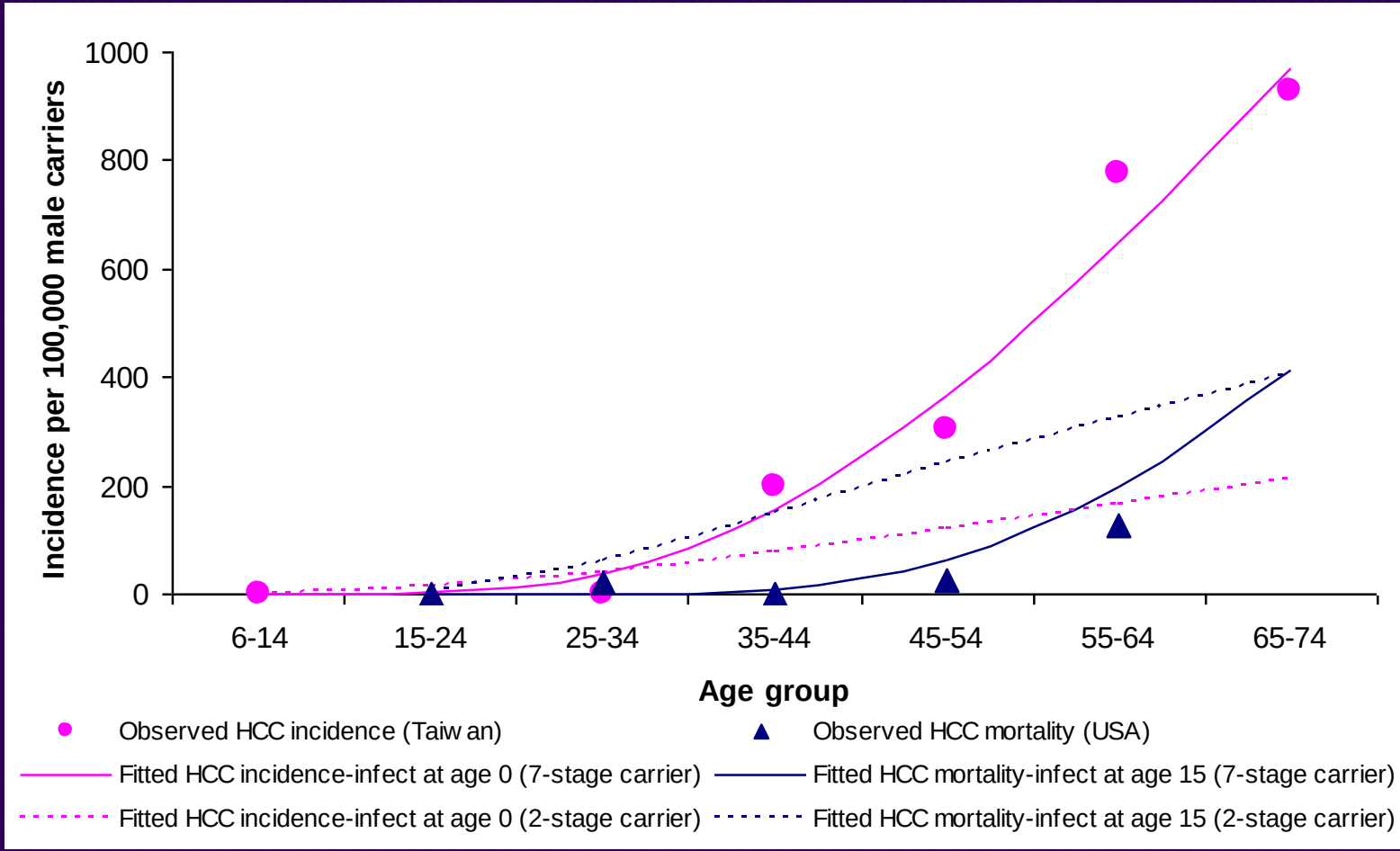
Economic models for hepatitis B

- Highly dependent on assumed rate of progression from chronic infection to cirrhosis and other end-states
- Observed progression rates vary dramatically
  - Taiwan (high) and USA (low)
- Model developed by CfI that fits to both datasets
  - Use six stage progression model (rather than two stage model used by other groups)
  - Allowing for older age at acquisition in USA than Taiwan

Estimating progression to cirrhosis

Fitting data from carrier cohorts to:

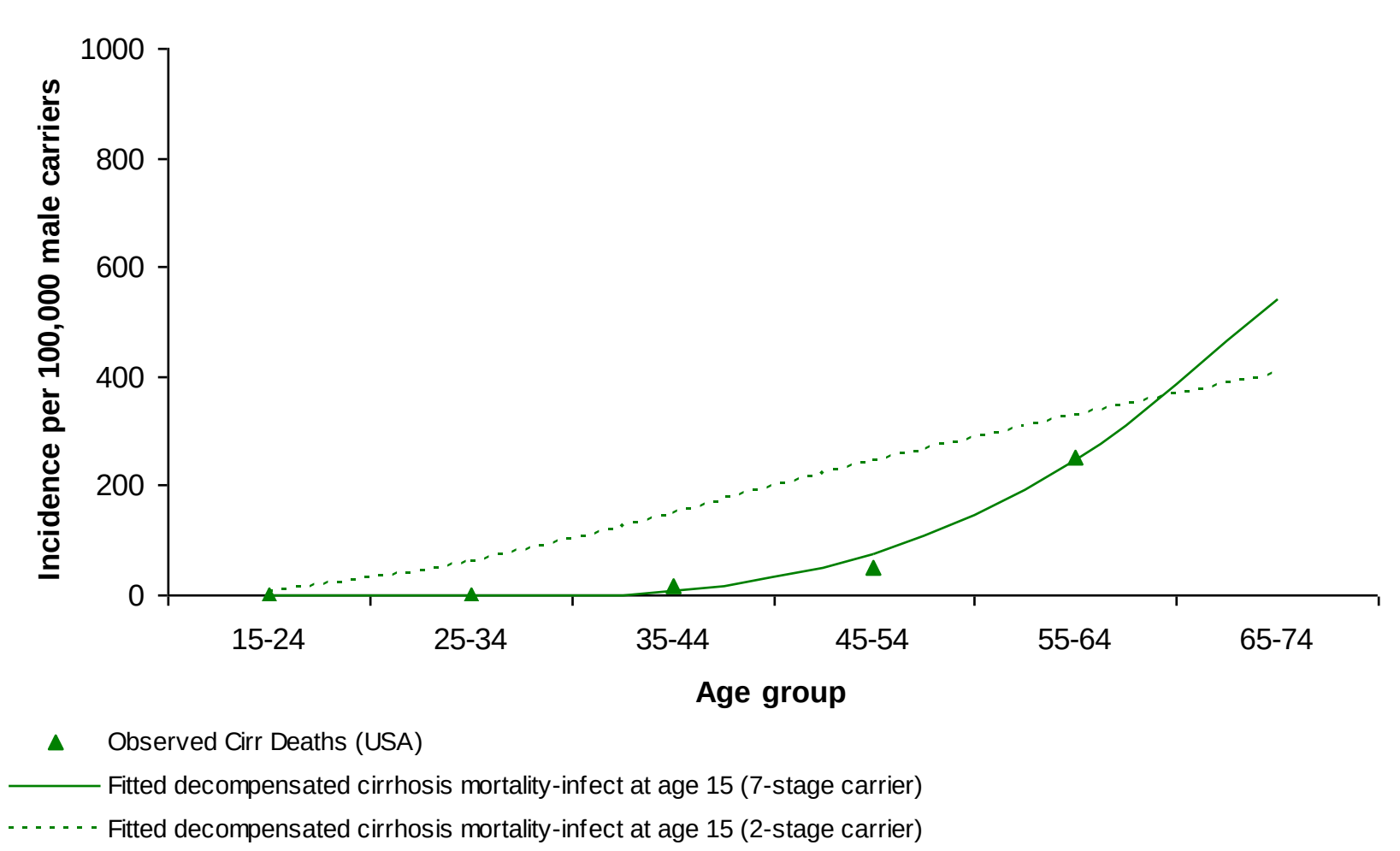
i) HCC incidence in Taiwan and USA



Estimating progression to cirrhosis

Fitting data from carrier cohorts to:

i) HBV related mortality in the USA



Cost and Health Utility estimates

HBV Status	Annual Costs (£2007)	Mean reduction in health utility
Acute hepatitis B (no liver transplant)	£2,279	0.01
Fulminant hepatitis	£5,451	0.50
Chronic HBV (carrier)	0	0.04
Compensated cirrhosis	£1,270	0.07
Decompensated cirrhosis	£10,179	0.45
Hepatocellular carcinoma	£9,071	0.50
Liver transplant (surgery + 1st year)	£52,076	0.49
Post-liver transplant (remaining life)	£1,889	0.29

Vaccine Costs – base case

Vaccine Costs

Infant – 3 doses @ £9 per dose

Adolescent – 2 doses @ £12 per dose

Administration Costs

Infant - £0.00 assumed (combined vaccine)

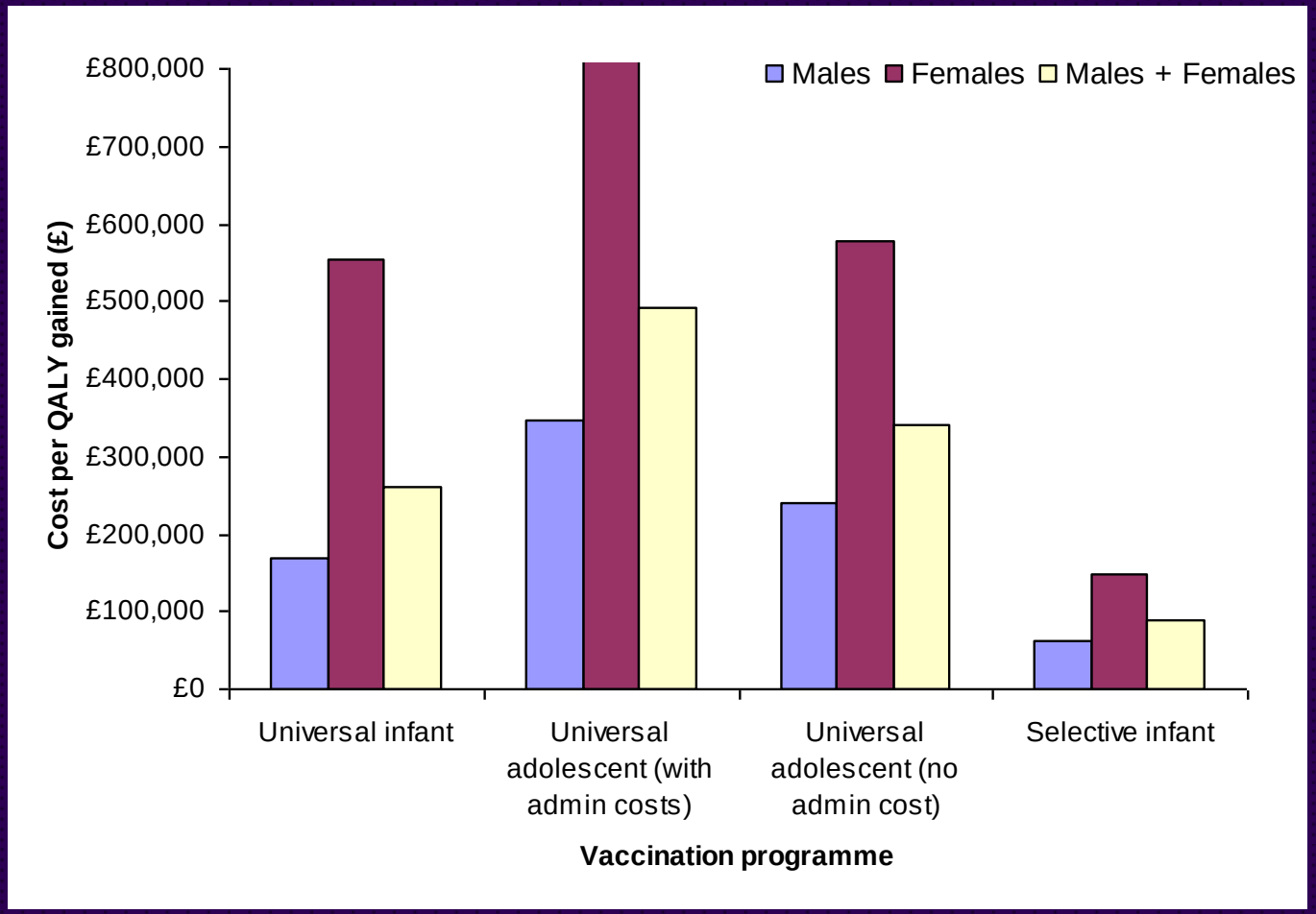
Adolescent - £4.48 per dose

Model-estimated HBV burden

Annual birth cohort (334k males, 319k females)

HBV state	Number of cases			QALY loss (discounted)		
	Male	Female	Total	Male	Female	Total
Acute case	640	264	904	2.7	1.3	4.0
Fulminant Liver Failure	12	5	17	0.2	0.1	0.3
Fulminant Liver Transplants	2	1	2	0.2	0.1	0.4
Acute Deaths	3	1	4	20.1	10.5	30.6
Total Acute	**656**	**271**	**927**	**23.2**	**12.1**	**35.2**
Carriers	179	100	278	0.0	0.0	0.0
Cirrhosis	50	11	61	2.7	0.5	3.1
Decompensated Cirrhosis	21	4	26	2.5	0.4	2.9
HCC	13	3	16	1.0	0.2	1.2
Chronic Liver Transplants	3	1	3	0.7	0.1	0.8
Chronic Deaths	27	5	32	25.4	3.5	28.9
Total Chronic	**293**	**123**	**417**	**32.3**	**4.7**	**36.9**
Total	**950**	**394**	**1344**	**55.4**	**16.7**	**72.2**

Cost-effectiveness of vaccination strategies
Base case analysis



Summary: No approach is cost effective at current vaccine prices

Sensitivity analysis

Threshold costs per vaccinated child

	Universal infant	Universal adolescent	Selective infant
Base case	**£4.09**	**£3.53**	**£10.73**
Incidence of infection (200%)	£8.26	£7.07	£21.70
Outcome of infection (Low % acute High % chronic)	£4.35	£3.78	£11.12
Discount rate			
0%	£22.99	£14.90	£73.81
6%	£1.69	£1.84	£3.87

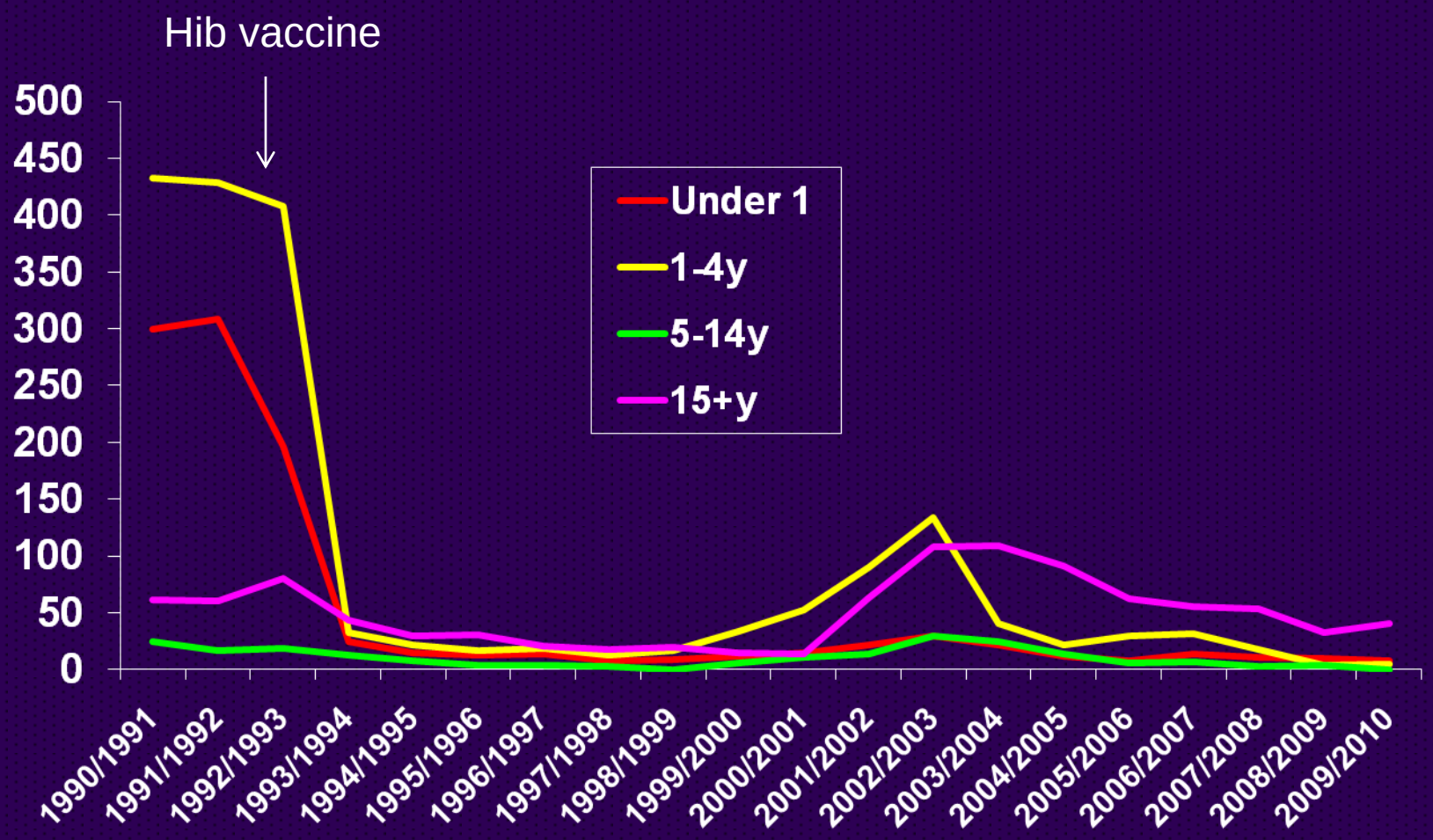
Assumptions / uncertainties

- JCVI paper reviewed by 6 hepatitis experts / 6 modellers
- Main issues raised were:
- We have not accounted for onward transmission
  - Unlikely to be major importance given existing prevalence
- Cost of treating chronic infections
  - CEA is not affected by this - subject to own assessment
  - If treatment is cost-effective – likely to reduce CE of prevention
- Main influences on cost-effectiveness are
  - Incidence (most recent estimates are LOWER)
  - Progression rate (our approach fits to existing data better than previous models)
  - Discount rate (we use 3.5% as recommended by NICE)

Conclusions

- No strategy is cost effective at current vaccine costs
- Universal infant programme could be offered at an additional cost £4 per vaccinated child
  - Would need to include vaccine AND administration costs
- The selective programme in inner city / specific ethnic populations could be offered at higher cost of £11 per vaccinated child
- Either approach could only realistically only be achieved with infant combination
  - UK has concerns about the currently available combination vaccine (DTaP-IPV-Hib-HepB)

Invasive Hib infections by age and epidemiological year (July-June)



HPA data to inform hepatitis B and C testing

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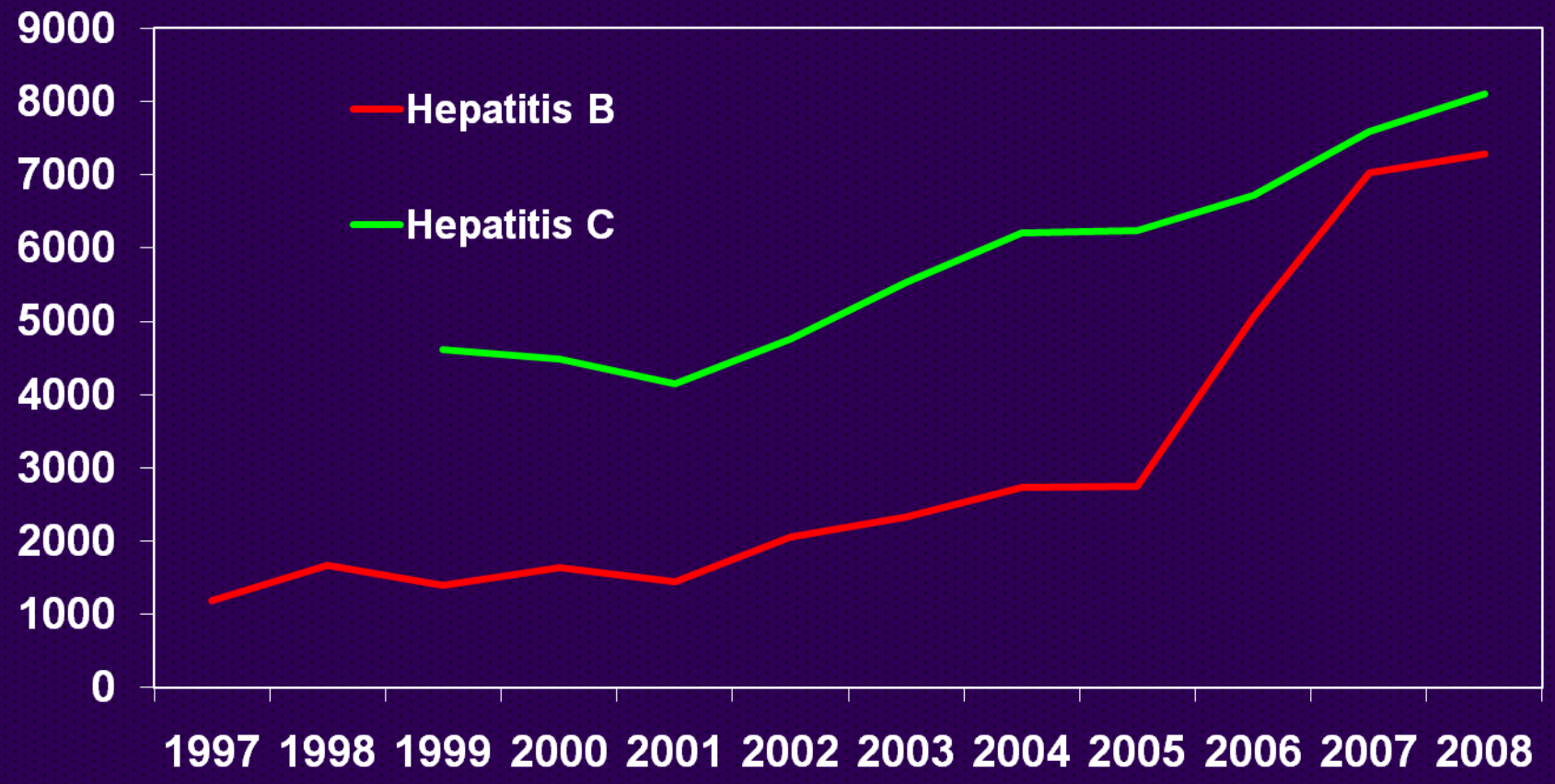
Sentinel Surveillance Laboratories

HPA information on testing and diagnosis of hepatitis B and C

- Statutory notifications from registered medical practitioners (changed in April 2010)
  - Massive under-reporting
- Voluntary reporting from around 200 labs
  - Chronic hepatitis B and C reportable from mid 1990s
  - Moved to electronic reporting since mid 1990s
  - Statutory reporting since October 2010
- Sentinel surveillance of hepatitis testing
  - Collects information on test negatives and positives

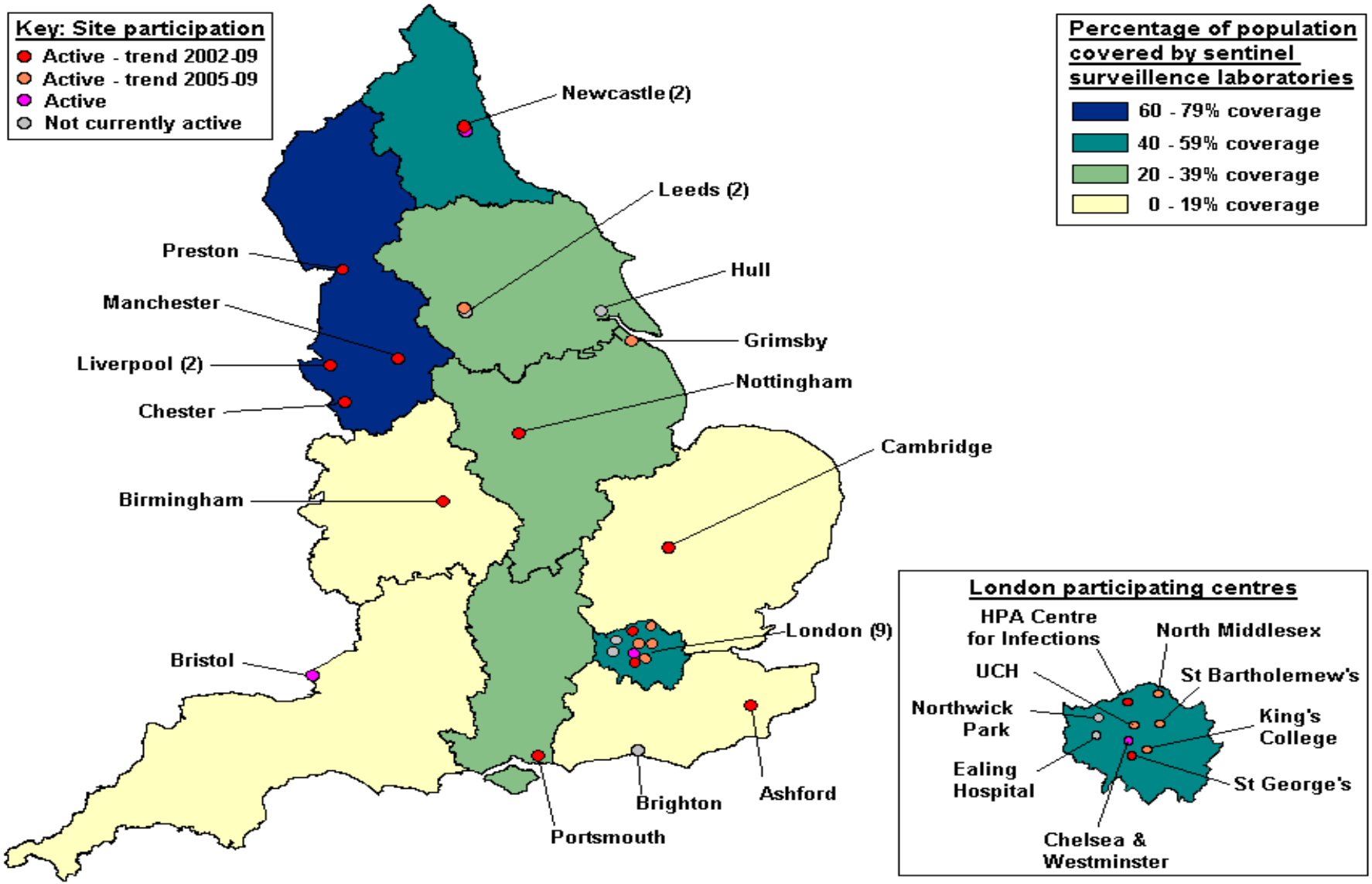
Laboratory reports of confirmed hepatitis B and C infections, England and Wales, 1997-2008



Sentinel surveillance of hepatitis testing

- Running in between 18 and 27 centres since 2002
- Hepatitis testing data electronically extracted from laboratory system
- Most hepatitis B and hepatitis C markers collected
  - HBsAg, total anti-HBc, anti-HBc IgM, HBV DNA
  - anti-HCV, HCV RNA
- Analysis by basic demographics, requesting service type, laboratory markers etc.

Coverage of sentinel surveillance



Overview of 2010 HCV data

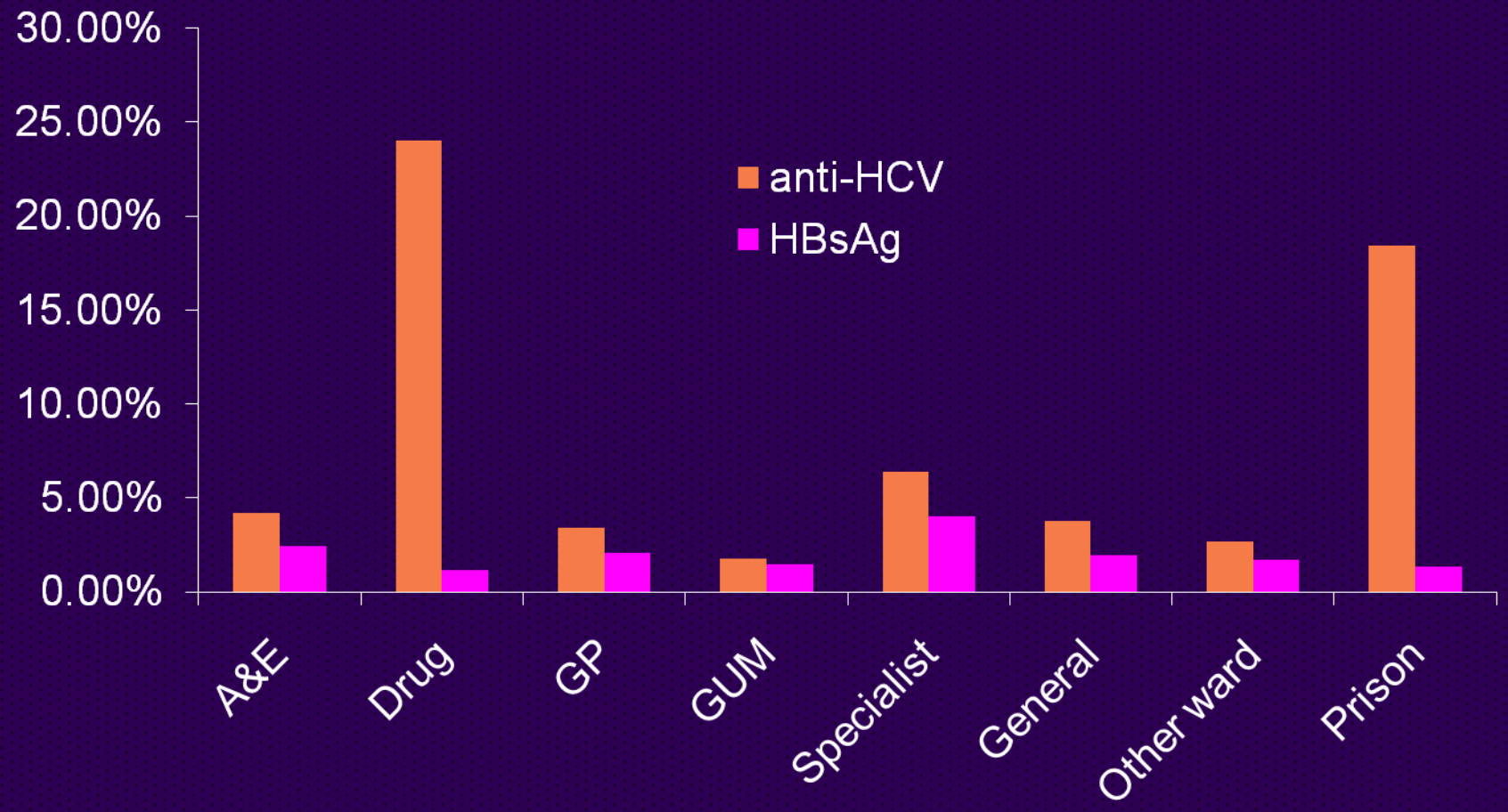
- Total of 162,119 individuals had primary diagnostic test for anti-HCV by venepuncture
  - Children under one year excluded
- A further 3,054 individuals tested by DBS in 3 sentinel laboratories (mainly from drug services)
- Aggregate data also supplied from 6,733 OF/DBS tests done by Concateno (also mainly drug services)

- Additional 18,063 individuals tested in sentinel labs but samples referred from other labs
  - 8,332 for primary test, 9731 for confirmatory test

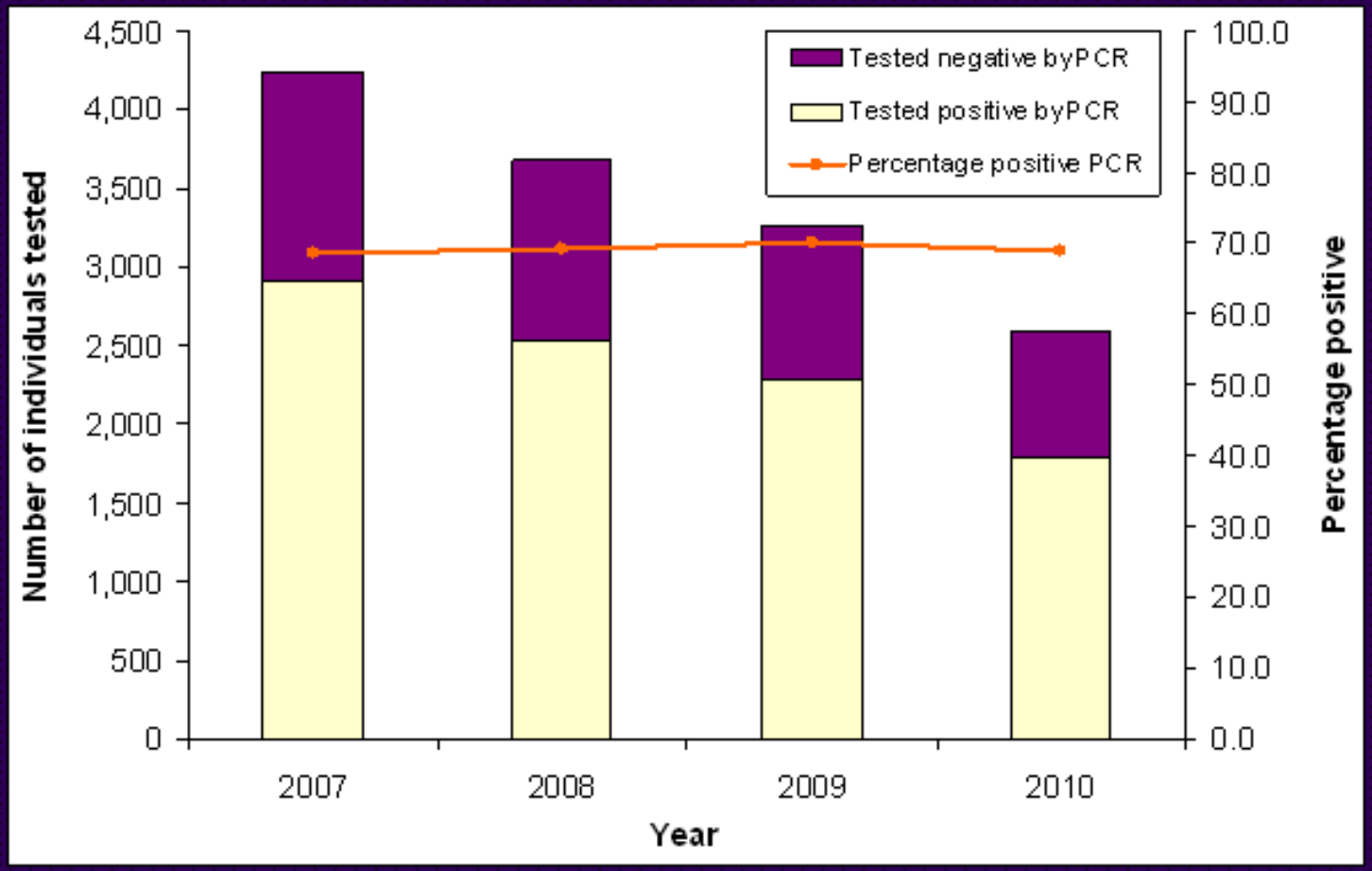
Trends in anti-HCV and HBsAg testing, sentinel laboratories 2007-2010

Trends in numbers of anti-HCV tests by selected service types

Proportion of individuals testing positive by selected service type



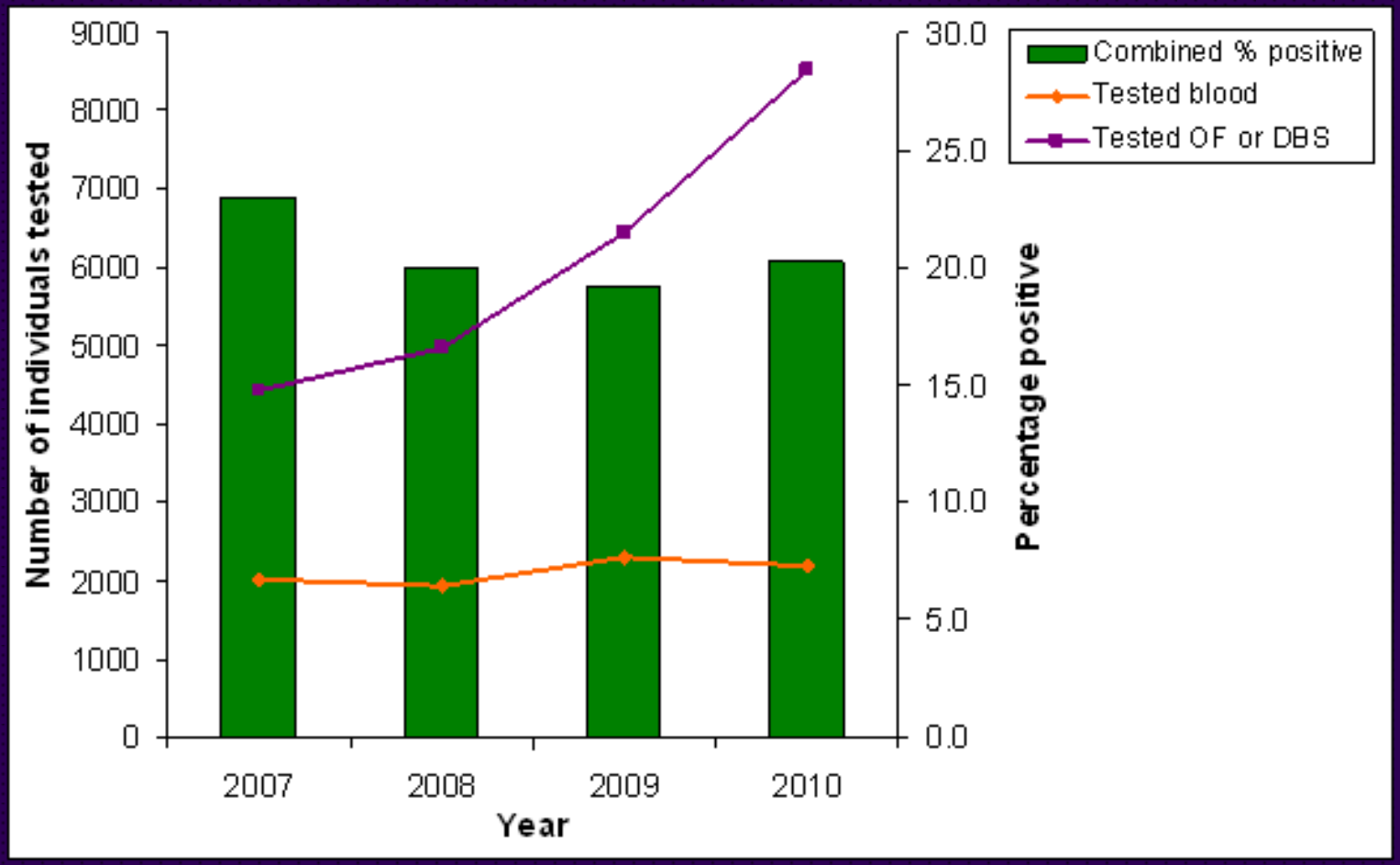
Trends in RNA testing in anti-HCV positive individuals



Injecting drug use and HCV testing

- Clinical/exposure details collected very limited
  - Some clinical information for around 36%
  - Around 3% of those with clinical information specify IDU (mostly not from drug services)
  - Of total of 5,679 with IDU specified, 1,890 (33%) anti-HCV positive
- Also 8,439 individuals tested from drug services
  - 2,027 (24%) of these are anti-HCV positive
  - Also have data from DBS and OF testing

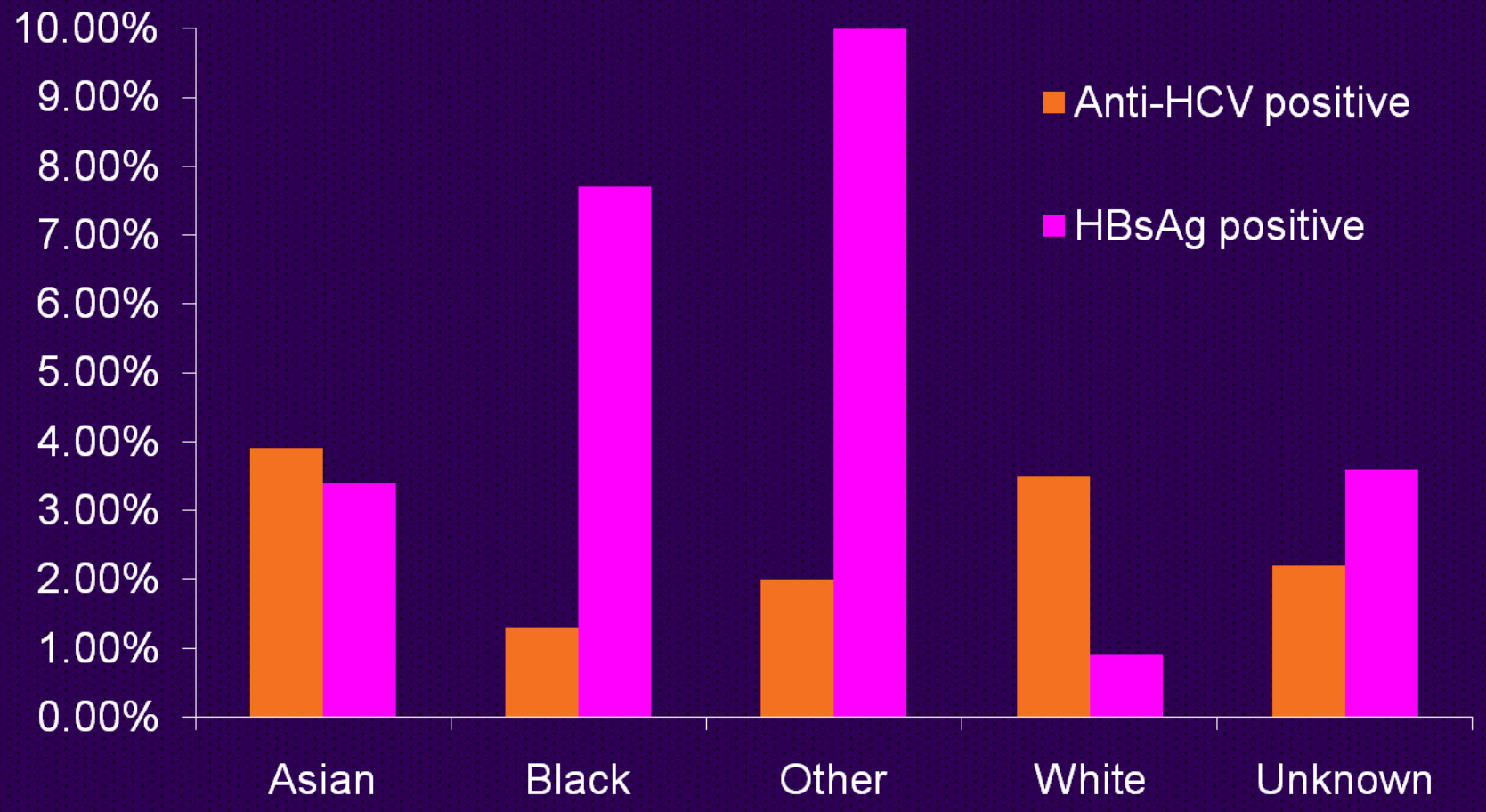
Trends in sample type tested, combined data from drug services



Ethnicity analysis

- Ethnic status not routinely available in lab systems
- Name is available for most (75%) samples
  - Exception is GUM clinics
- Able to classify ethnicity based on name
  - Initially used Nam Pecham
  - Now using Onomap
- Analysis by ethnic group and service type

Proportion testing positive by ethnic status - general practice



Other HPA data / resources

- Routine national collection
  - Prevalence of anti-HBc and anti-HCV in IDUs
  - Prevalence of HBsAg and anti-HCV in blood donors
  - Prevalence of HBsAg in antenatal women
  - HBsAg in babies born to HBeAg positive women
  - Acute hepatitis B surveillance
- Potential future data collected could include
  - Chronic hepatitis B follow up in local HPUs
  - DBS testing for all babies born to HBsAg positive women