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Hepatitis B – priority areas

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National Infection Service -Colindale

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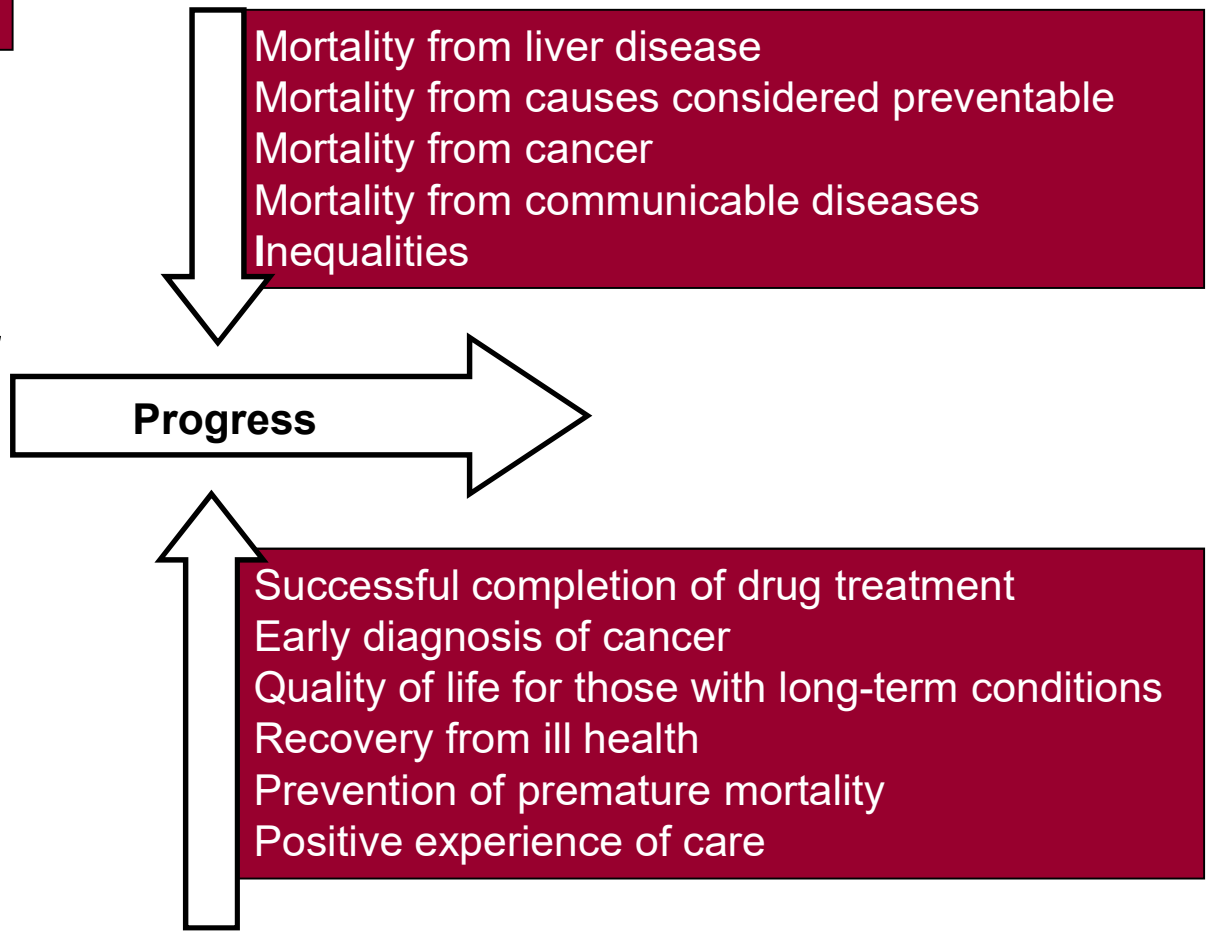
Tackling hepatitis B

Four action areas

- **Prevention of new infections**
- **Increasing awareness of infection**
- **Increasing testing and diagnosis**
- **Getting diagnosed individuals into treatment and care**



Tackling hepatitis contributes to reducing inequalities and morbidity and mortality - all goals of Public Heath Outcomes Framework

WHO Global Hepatitis Strategy – targets to achieve elimination

TARGET AREA	2020 TARGETS	2030 TARGETS
Impact targets		
Incidence: New cases of chronic viral hepatitis B infection	30% reduction	80% reduction
Mortality: Viral hepatitis B deaths	10% reduction	65% reduction
Service coverage targets		
Blood safety:Proportion of donations screened in a quality-assured manner	95%	100%
Hepatitis B virus vaccination: childhood vaccine coverage (third dose coverage)	**90%**	**90%**
Prevention of mother-to-child transmission: HBV birth-dose vaccination coverage or other approach to prevent mother-to-child transmission	**50%**	**90%**
Safe injections:Percentage of injections administered with safety engineered devices in and out of health facilities	50%	90%
Harm reduction: A comprehensive package of harm reduction services to all PWID	At least 200 sterile needles and syringes provided per PWID per year	At least 300 sterile needles and syringes provided per PWID per year
Proportion of people with HBV diagnosed and aware	30%	90%
Treatment coverage	75%	80%

✓ ✓ ✓ ✓

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High level summary of functions
Other than surveillance

- Scientific secretariat to JCVI and NSGVH
- Implementation of vaccination programmes
- Clinical guidance (including Green Book)
- Clinical vaccine advice and incident support
- Modelling and economic analysis
- Immunoglobulin issue and stock control
- Research (including MRC, NIHR, HPRU)
- Teaching and training
- Clinical testing service: DBS
- Development and application of molecular tools
- Media and communications

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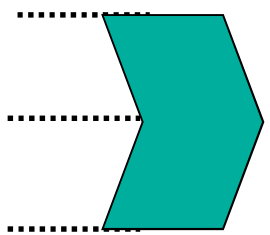
Surveillance of hepatitis B – sources and modelled use of data

- Reports of laboratory confirmed chronic HBV infections

  ~ Testing trends, not incidence (notifications of limited/no use)
- Enhanced molecular surveillance of acute hepatitis B ~ incidence, risk factors
- Blood donor testing ~ Routine screening of low risk population
- Sentinel surveillance ~ Testing in different settings/risk groups
- UAM testing of drug users in contact with drug services

  ~ Prevalence in risk group
- Universal antenatal screening ~ proxy for prevalence in general population
- Babies born to hepatitis B infected mothers – high risk infant post exposure follow up
- Hospital episode statistics
- UK transplant data
- ONS death registrations

MPES prevalence estimates



~ Burden of disease

Impact of strategies on predicted burden

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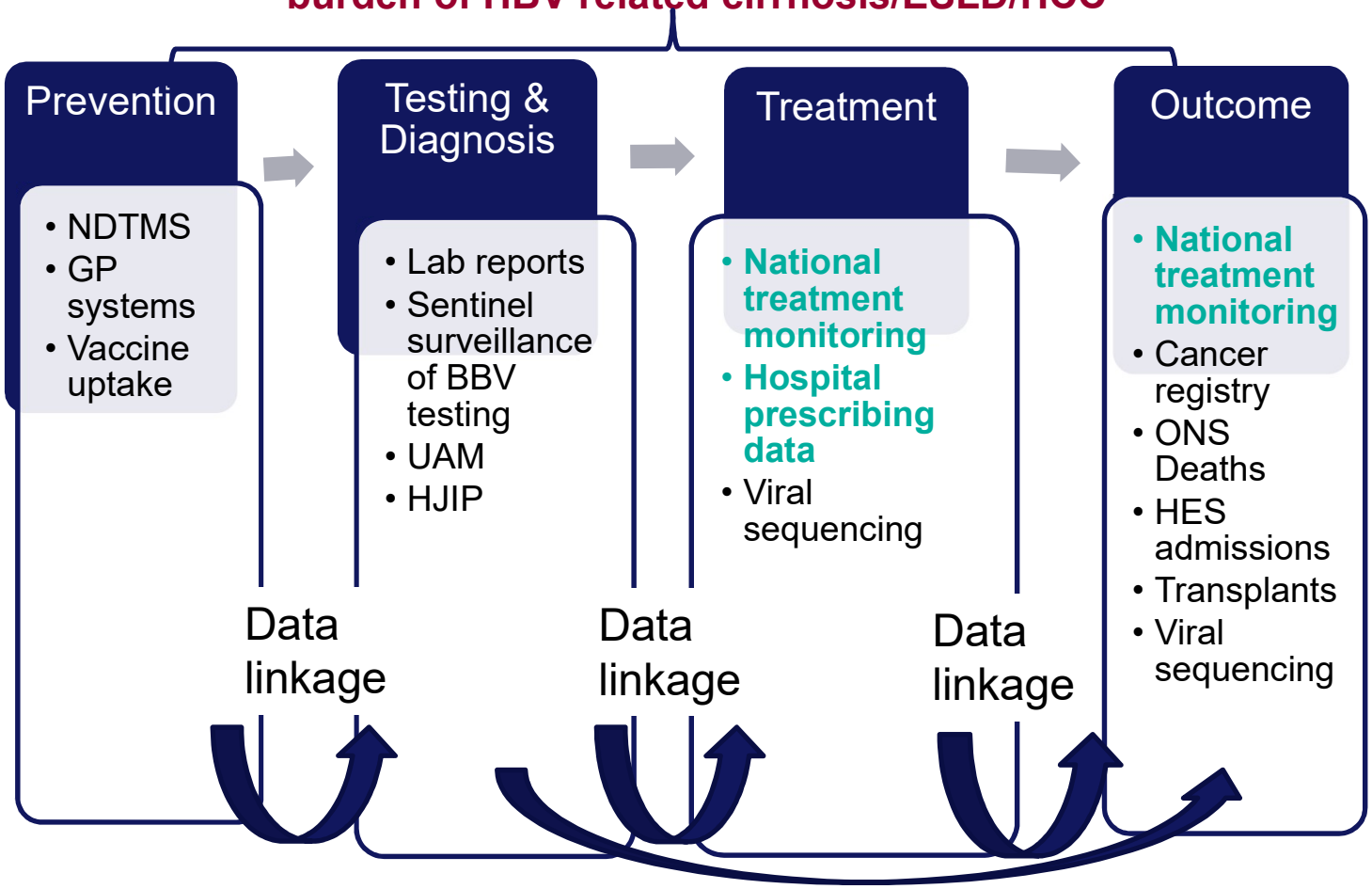
Data linkage across surveillance systems

Parameterise models to estimate HBV prevalence and burden of HBV related cirrhosis/ESLD/HCC



Assess equity in access and outcomes
Monitor performance of commissioning and provider services
Identify vulnerable groups and opportunities for interventions

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Prevention: Introduction of hexavalent infant vaccine into UK programme

News story

Hexavalent 6-in-1 vaccine to be made available to newborn babies

From: Public Health England
Published: 1 August 2017

The hexavalent vaccine replaces the existing 5-in-1 pentavalent vaccine, which infants are routinely given at 8, 12 and 16 weeks.

All babies born on or after 1 August 201 hepatitis B as part of our universal child Public Health England has announced. protection against diphtheria, tetanus,

The hexavalent vaccine replaces the ex routinely receive. It is already widely us having been given in 97 countries in Eu

There has been no change to the immu

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Hepatitis B

Hepatitis B jab to be added to immunisations of babies born in UK

Babies born from the 1 August will be offered new 'hexavalent' jab in effort to clamp down on infections that cause cirrhosis and liver cancer

This article is 5 months old

Ian Sample Science editor

@iansample

Sunday 9 July 2017 16.24 BST

The World Health Organisation (WHO) recommended in 1992 that babies should be immunised against the virus. Photograph: Sean Gallup/Getty Images

All babies born in the UK will receive the hepatitis B jab as part of their routine immunisations from the autumn in an effort to drive down viral infections that cause cirrhosis and liver cancer

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Prevention –evaluation of hepB immunisation programmes

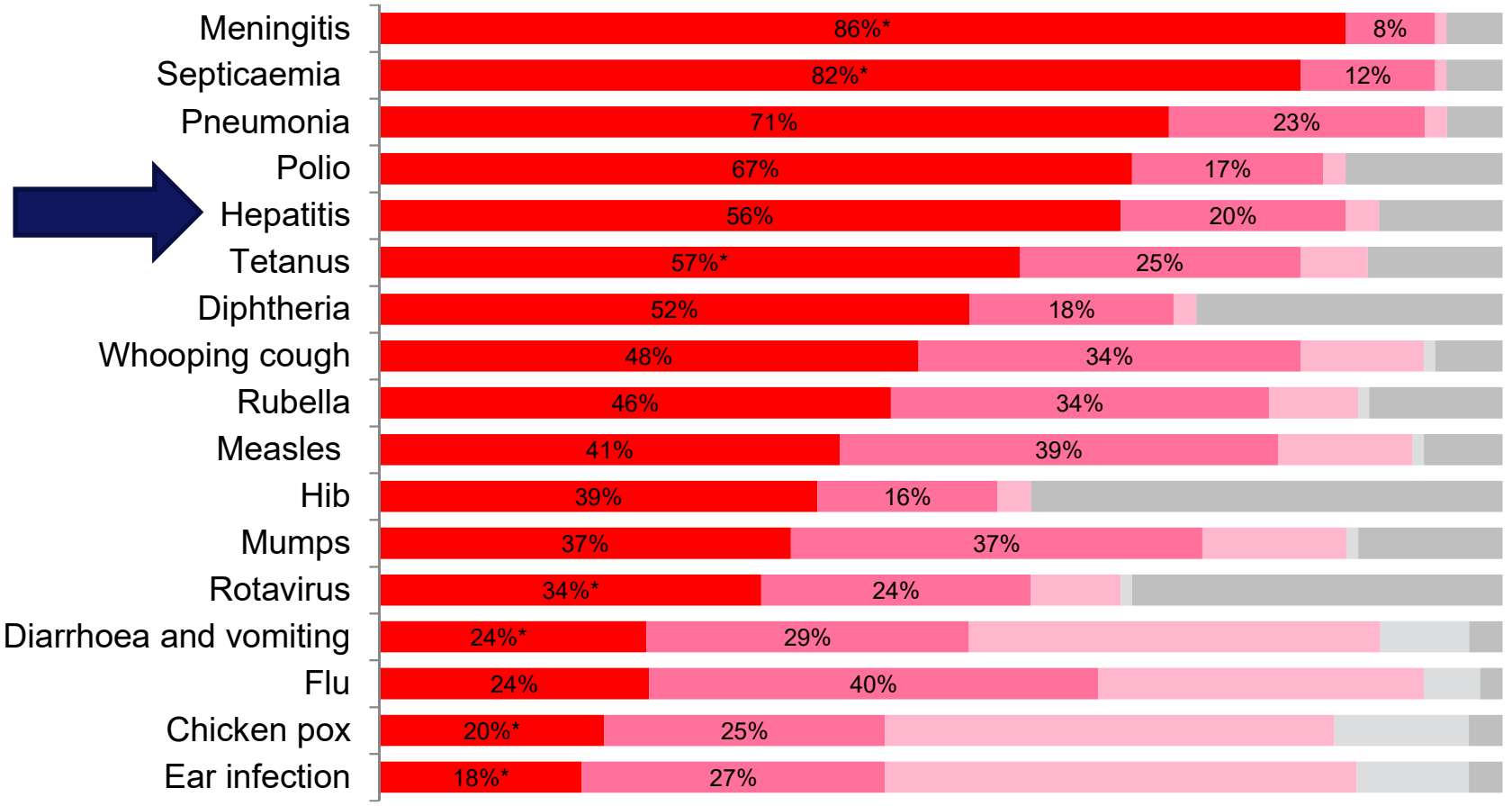
PRE-EXPOSURE

- Universal immunisation programme with hexavalent vaccine
  - Vaccine uptake
  - Efficacy, safety and impact
  - Enhanced molecular surveillance
  - Need for booster / reinforcing doses

POST EXPOSURE

- Selective immunisation programme – babies born to infected mothers
  - Timeliness of doses
  - Optimising schedule post hexa introduction (immunogenicity and durability)
    - ?drop 4 week dose and/or 12 month dose
  - Impact of anti-viral treatment in pregnancy
  - Contribution of *in utero* transmission
- PEP guidelines

Attitudinal research: what infections parents are most concerned about



Base: All Parents (n =1683)

bmg research Understanding People.

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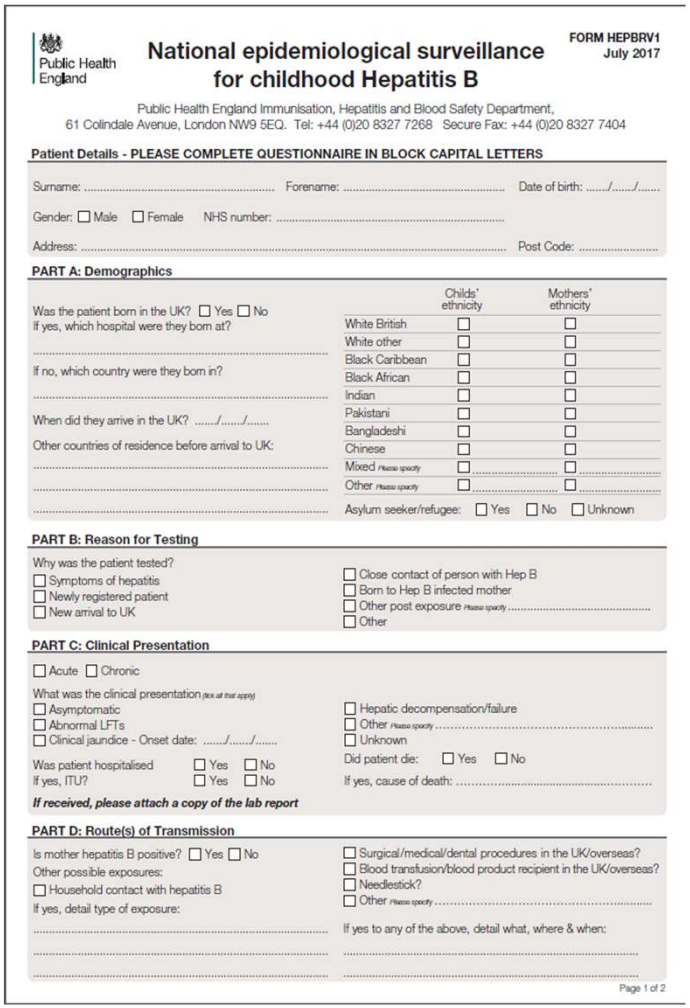
Monitoring the new universal programme

- Enhanced surveillance of hepatitis B in childhood
  - Prompt is new laboratory diagnosis
- Monitor efficacy of vaccine programme
- All children under 10 years old with hepatitis B will be followed up via letter to GP
- Residual sample of blood will be requested for genotyping and sequencing
- Linked into existing surveillance for hepatitis B
  - High risk babies
  - Acute hep B



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National epidemiological surveillance for childhood Hepatitis B

FORM HEPBRV1
July 2017

Public Health England Immunisation, Hepatitis and Blood Safety Department,
61 Colindale Avenue, London NW9 5EQ. Tel: +44 (0)20 8327 7268 Secure Fax: +44 (0)20 8327 7404

Patient Details - PLEASE COMPLETE QUESTIONNAIRE IN BLOCK CAPITAL LETTERS

Surname: ..... Forename: ..... Date of birth: ...../...../.....

Gender: ☐ Male ☐ Female NHS number: .....

Address: ..... Post Code: .....

PART A: Demographics

Was the patient born in the UK? ☐ Yes ☐ No
If yes, which hospital were they born at?
.....
If no, which country were they born in?
.....
When did they arrive in the UK? ...../...../.....
Other countries of residence before arrival to UK:
.....
.....
.....

	Childs' ethnicity	Mothers' ethnicity
White British	☐	☐
White other	☐	☐
Black Caribbean	☐	☐
Black African	☐	☐
Indian	☐	☐
Pakistani	☐	☐
Bangladeshi	☐	☐
Chinese	☐	☐
Mixed (Please specify)	☐	☐ .....
Other (Please specify)	☐	☐ .....

Asylum seeker/refugee: ☐ Yes ☐ No ☐ Unknown

PART B: Reason for Testing

Why was the patient tested?
☐ Symptoms of hepatitis
☐ Newly registered patient
☐ New arrival to UK
☐ Close contact of person with Hep B
☐ Born to Hep B infected mother
☐ Other post exposure (Please specify) .....
☐ Other

PART C: Clinical Presentation

☐ Acute ☐ Chronic

What was the clinical presentation (tick all that apply)
☐ Asymptomatic
☐ Abnormal LFTs
☐ Clinical jaundice - Onset date: ...../...../.....
☐ Hepatic decompensation/failure
☐ Other (Please specify) .....
☐ Unknown

Was patient hospitalised ☐ Yes ☐ No
If yes, ITU? ☐ Yes ☐ No
Did patient die: ☐ Yes ☐ No
If yes, cause of death: .....

If received, please attach a copy of the lab report

PART D: Route(s) of Transmission

Is mother hepatitis B positive? ☐ Yes ☐ No
Other possible exposures:
☐ Household contact with hepatitis B
If yes, detail type of exposure:
.....
.....
.....
☐ Surgical/medical/dental procedures in the UK/overseas?
☐ Blood transfusion/blood product recipient in the UK/overseas?
☐ Needlestick?
☐ Other (Please specify) .....
If yes to any of the above, detail what, where & when:
.....
.....

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Testing and Diagnosis

- Support implementation of NICE guidance
- Feasibility of testing in A&E and other settings
- Expanded use of Dried Blood Spot testing
  - Clinical service for 12 month testing of infants born to infected mothers
  - Evaluation of use in community settings with at-risk populations: household contacts, migrants, PWID
- Economic evaluation of interventions (with LSHTM and UoB)

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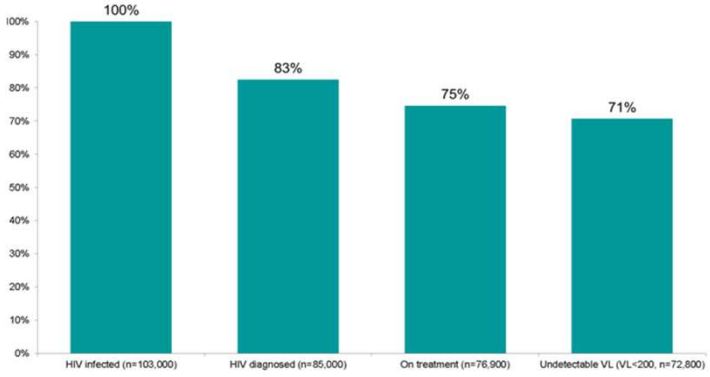
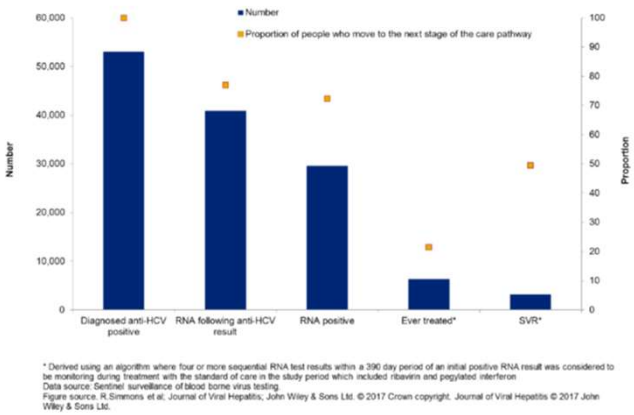
Treatment and care

- Cascade of care –compare to HIV (L) and HepC (R)
  - SSBBV: only 25% of new HBsAg positive patients have evidence of HBV DNA test done
  - Validate treatment algorithm in SSBBV against clinical databases
- Linkage and engagement in care: EMPACT-B: nurse-led enhanced management of patients and contacts
- Characteristics of patients in care (CUSHI-B) vs diagnosed and undiagnosed in community





* Derived using an algorithm where four or more sequential RNA test results within a 390 day period of an initial positive RNA result was considered to be monitoring during treatment with the standard of care in the study period which included ribavirin and pegylated interferon
Data source: Sentinel surveillance of blood borne virus testing
Figure source: R Simmons et al. Journal of Viral Hepatitis, John Wiley & Sons Ltd. © 2017 Crown copyright. Journal of Viral Hepatitis © 2017 John Wiley & Sons Ltd.

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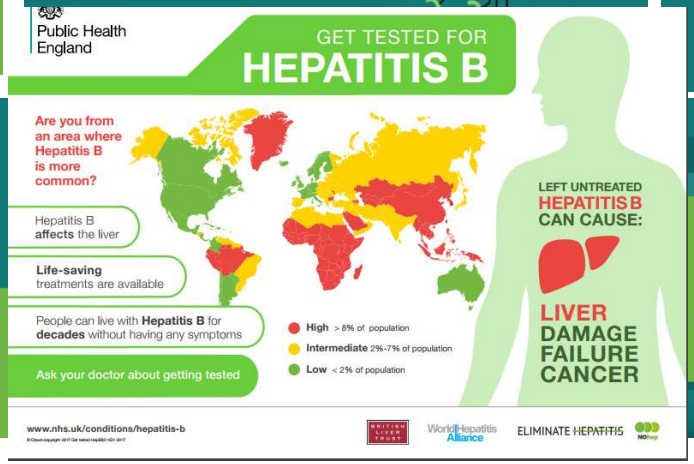
Awareness raising – public and professional

RCGP/PHE course

Social media banners, posters, videos



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Population based Hepatitis B virology

- Enhanced surveillance programmes
  - Acute hepatitis B (virus characterisation and epidemiology)
  - Mother to Child HBV interface

- Poor broad, cross sectional data on persistent, chronic hepatitis B infections

- Development of tools for characterisation, phenotyping, diagnosis and monitoring
  - Future tools for defining biomarkers and monitoring response to new agents

- Better linkage of data

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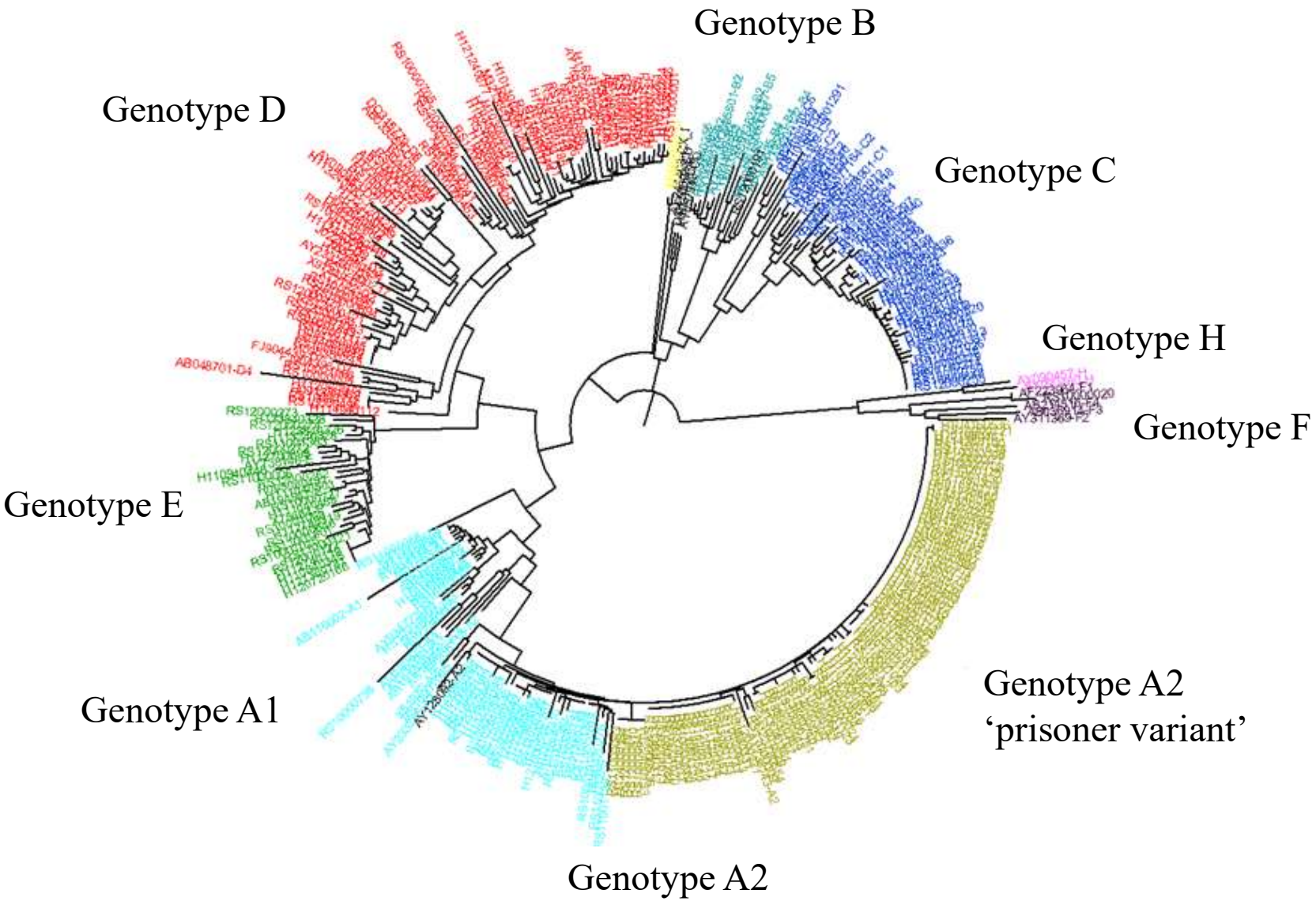
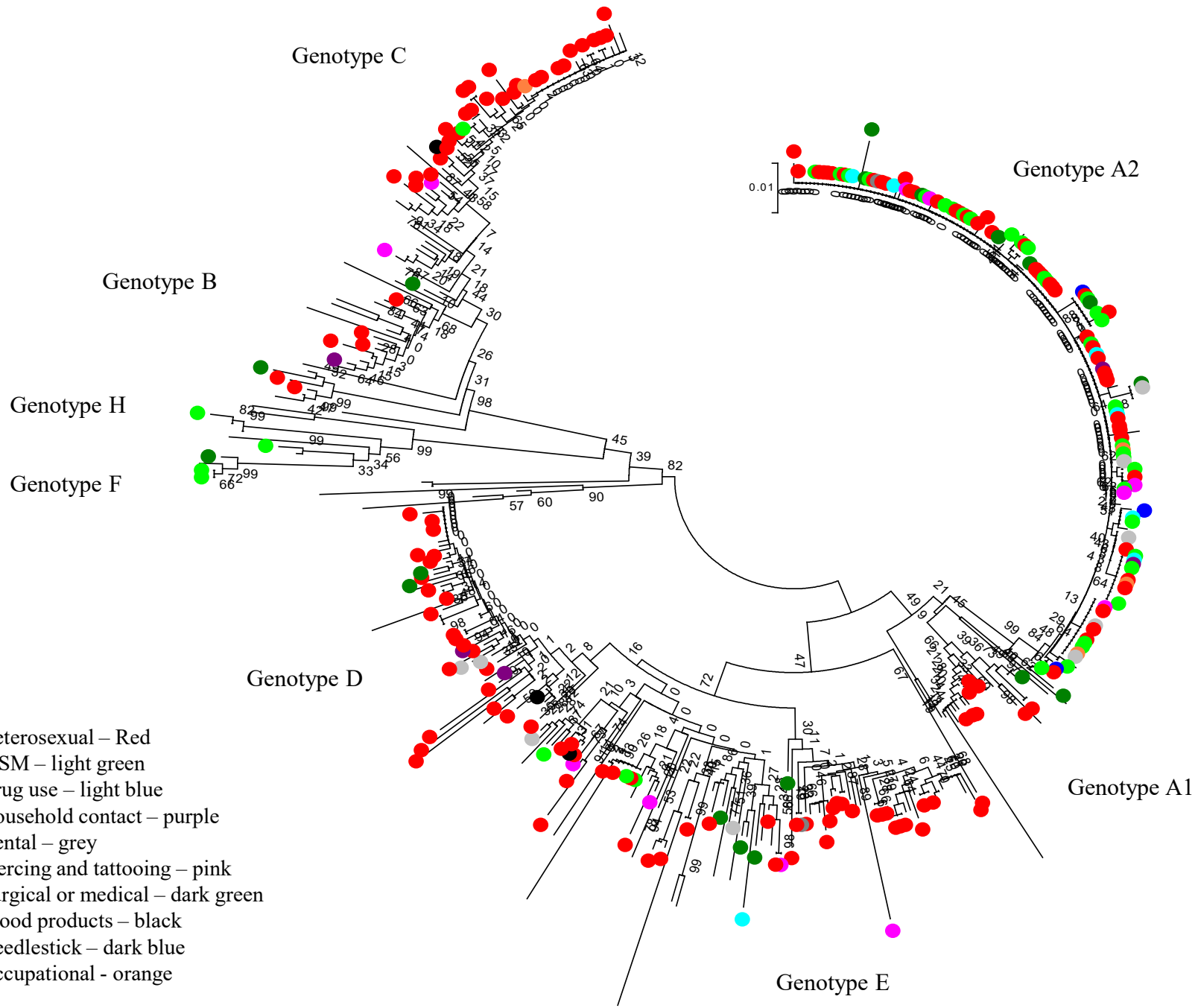
Phylogeny of acute Hepatitis B




Genotype C
Genotype B
Genotype H
Genotype F
Genotype D
Genotype A2
Genotype A1
Genotype E
0.01
Heterosexual – Red
MSM – light green
Drug use – light blue
Household contact – purple
Dental – grey
Piercing and tattooing – pink
Surgical or medical – dark green
Blood products – black
Needlestick – dark blue
Occupational - orange

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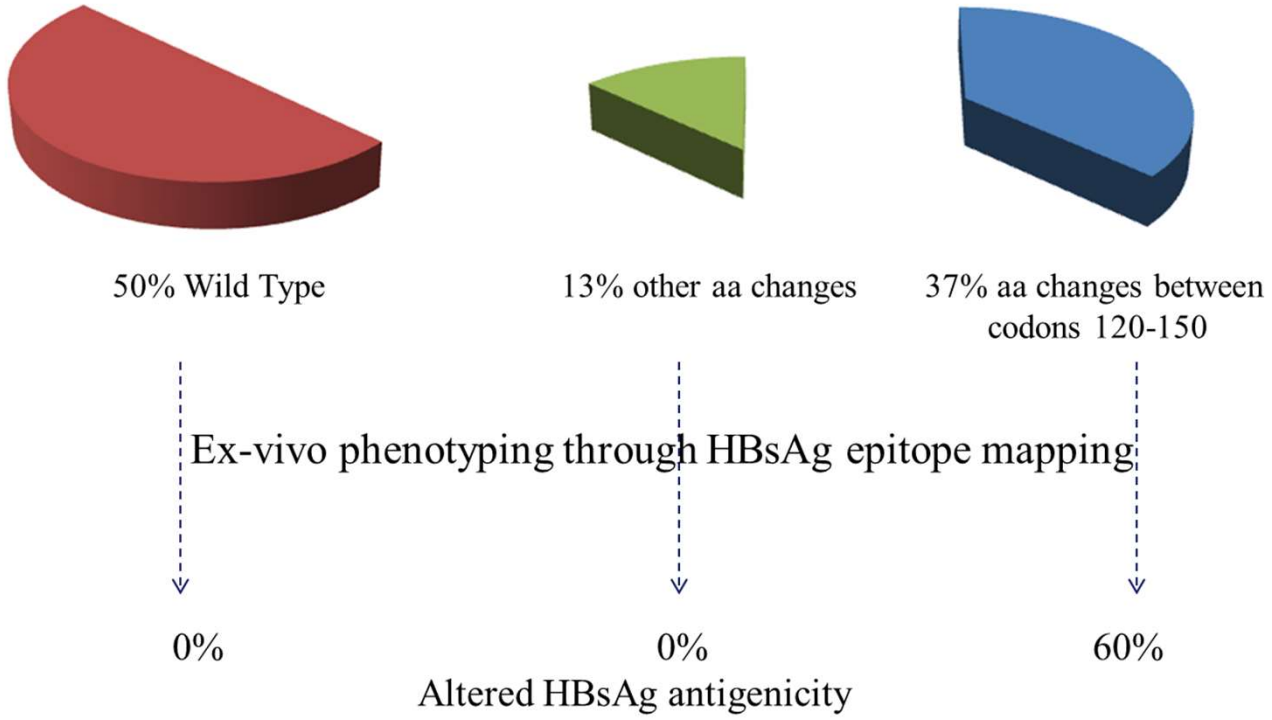
The Mother/Child HBV interface

- Testing undertaken at 12 months, 69 infected infants identified between 2003 and 2015
- Maternal viral load important factor
- Presence of HBsAg amino acid changes in infant samples



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Enhanced surveillance of HBV MTCT

- Better monitoring of dynamics of HBV infection in infected mothers and markers associated with vaccine failure in HBV-infected infants
- Maternal samples
  - VL at screening and at delivery
  - Characterisation of HBsAg
- Collecting DBS at time of birth from babies born to ‘high risk’ mums
  - HBV DNA testing
  - Comparing markers at birth to markers at 12 months

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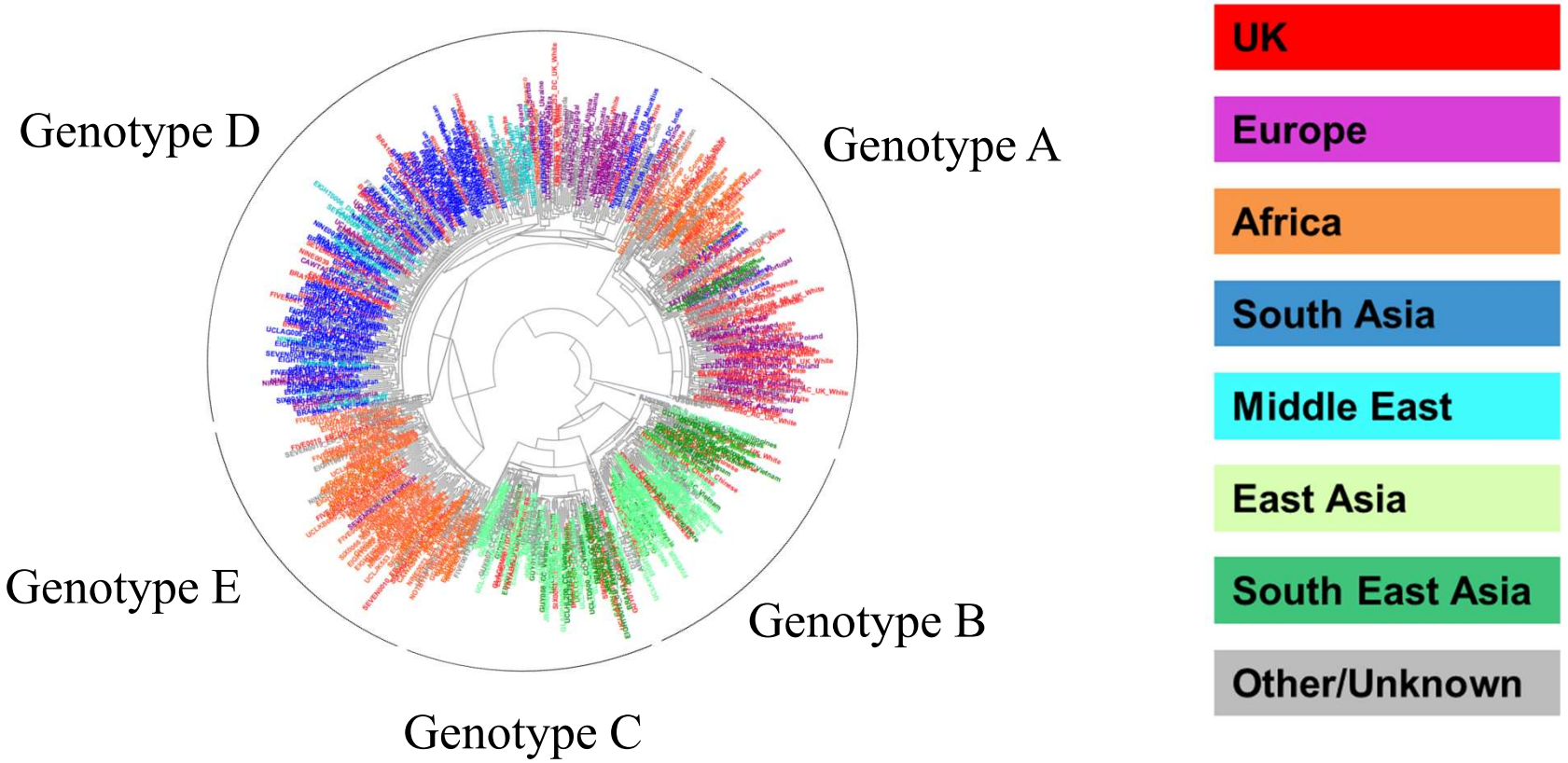
Cross sectional study on chronic hepatitis B – CUSHI B

- 80% were born outside the UK, in 61 different countries
- Association of genotype and place of birth



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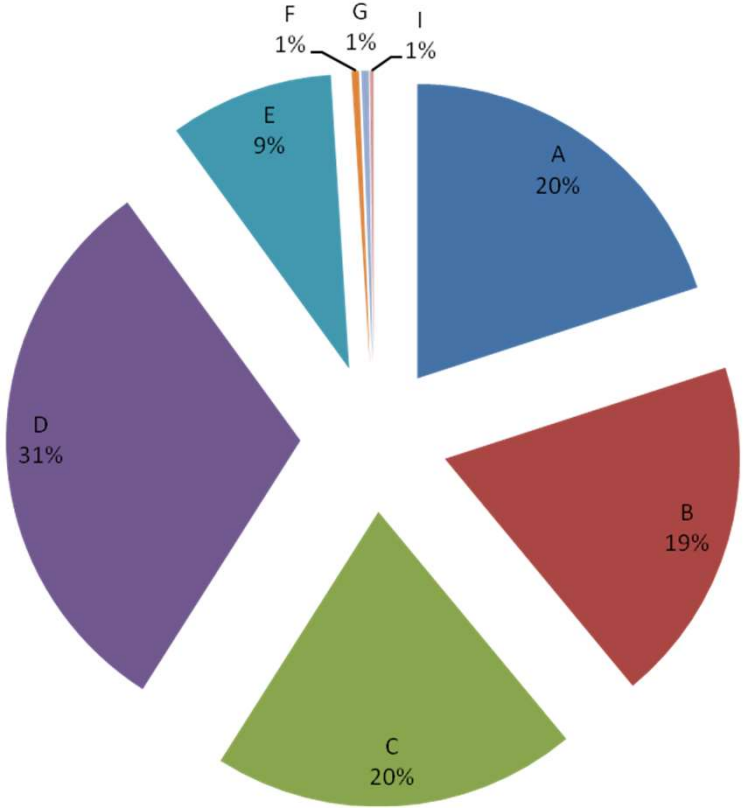

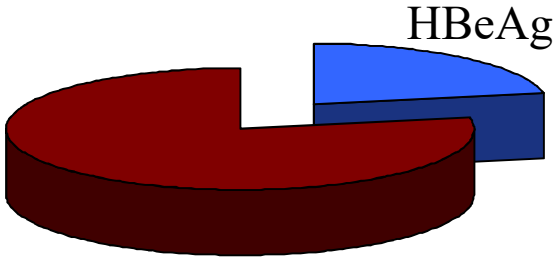

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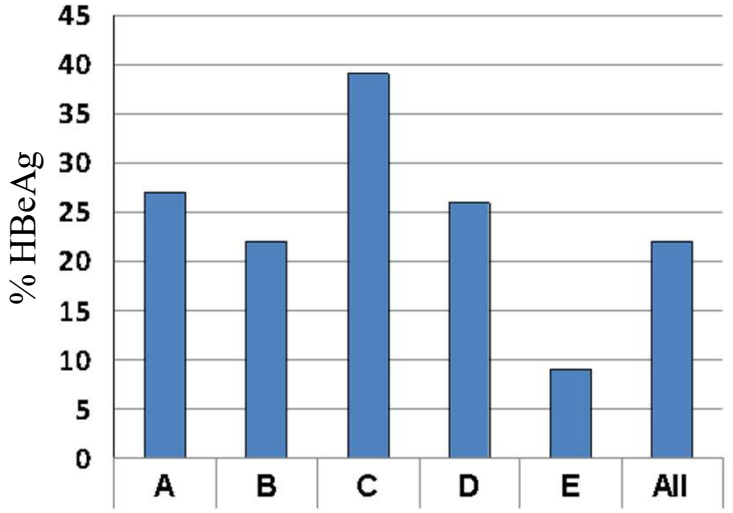

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Tools for investigating HBV

- Conventional serological and molecular markers plus [HBsAg]
- HDV RNA quantification
- Avidity testing - ~25% misdiagnosis
- DBS - HBsAg, anti- HBc, (anti-HBs in development)
  - HBV DNA, sequence/phylo analysis
- Partial sequence analysis (HBsAg and X/precore/core regions)
  - Genotype/subgenotype and phylogeny
  - HBsAg variants, Precore/BCP mutations

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Novel tools for investigating HBV

- Phenotyping of HBsAg based on epitope mapping
  - Defines alteration in HBsAg antigenicity
- Expression of recombinant HBsAg and PreS1/S2/S proteins
  - Dissect immune response
  - better understand genotype specific antibody
  - Role of genotype backbone on phenotype
- Expressing NTCP
  - Investigate reactivity against generated envelope recombinant proteins

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Novel tools for monitoring HBV

- HBV RNA
- Core-related antigen (HBcrAg)
- eAg quantification?
- Bioinformatic tools
  - Define ‘normal’ variation’ allows better definition of important/significant amino acid changes
  - PreS1/S2 sequence generation
  - Core sequence analysis
  - Better use of bioinformatic tools eg co-variation

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Linkage with sequence data