WHO hepatitis B elimination targets: how are we doing?

Ruth Simmons

Public Health England

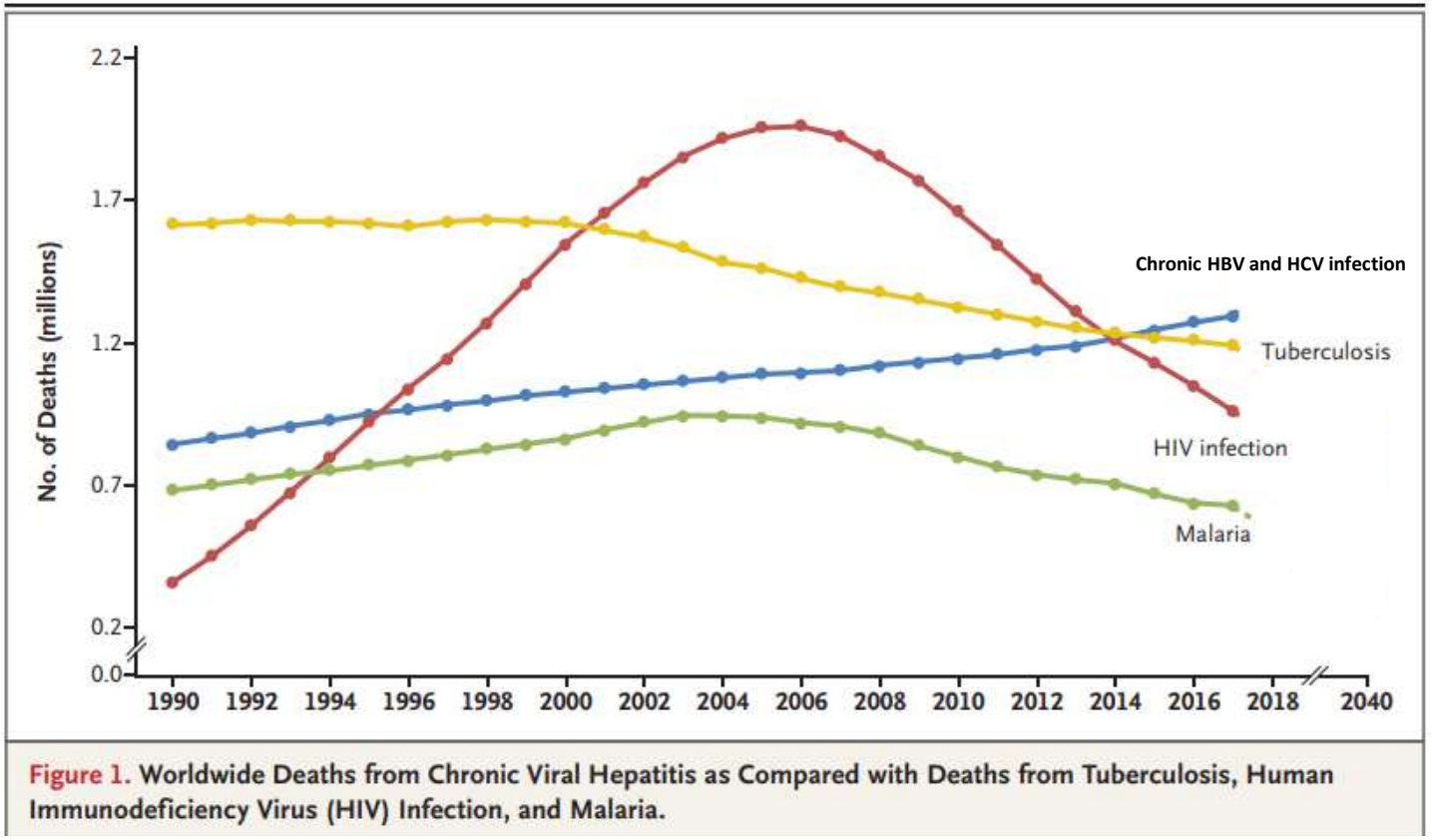


Figure 1. Worldwide Deaths from Chronic Viral Hepatitis as Compared with Deaths from Tuberculosis, Human Immunodeficiency Virus (HIV) Infection, and Malaria.

Thomas DL. New England Journal of Medicine 2019; 380: 2041-50

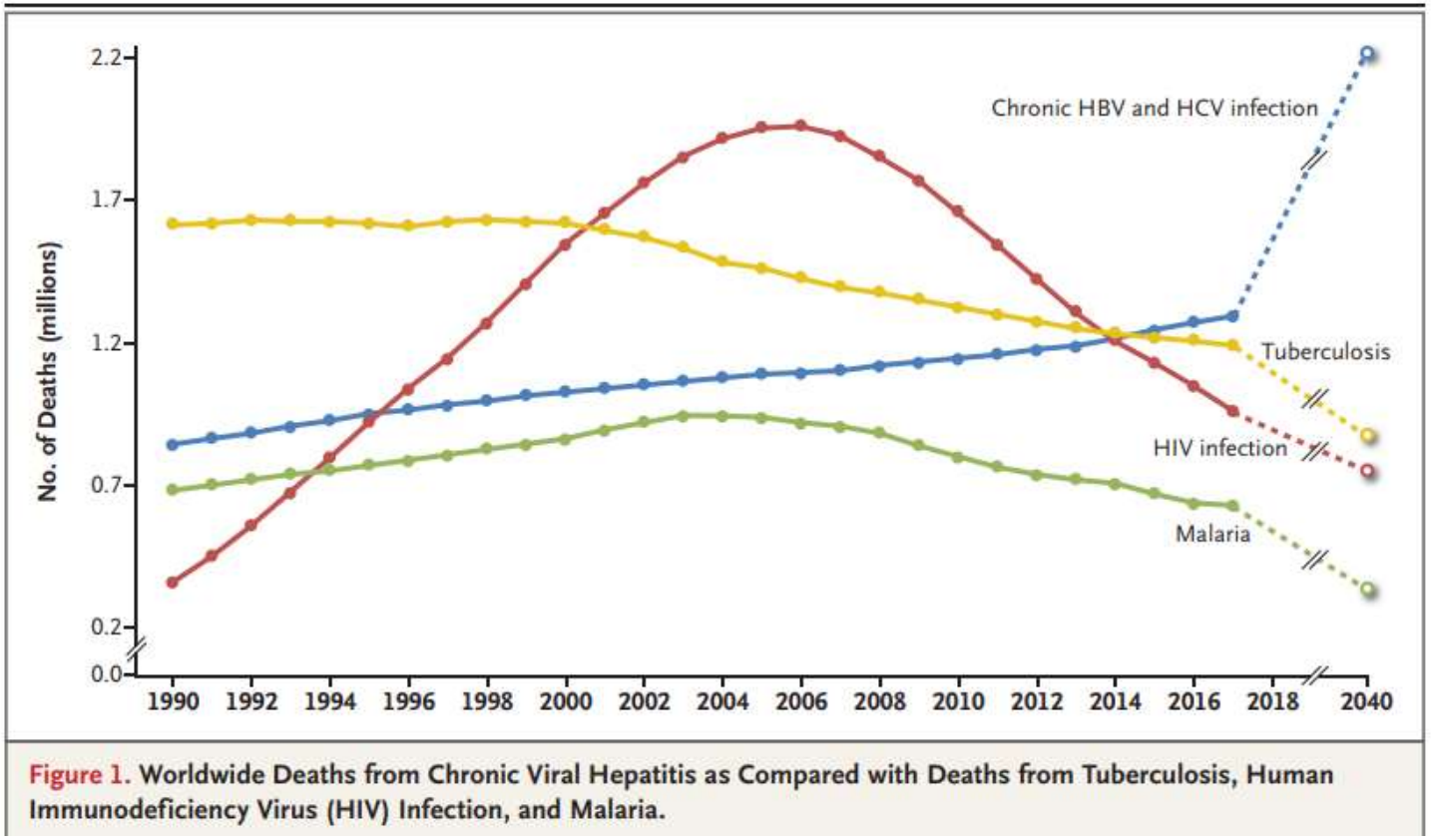


Figure 1. Worldwide Deaths from Chronic Viral Hepatitis as Compared with Deaths from Tuberculosis, Human Immunodeficiency Virus (HIV) Infection, and Malaria.

Thomas DL. New England Journal of Medicine 2019; 380: 2041-50

May 2016:

World Health Organization

Make the elimination of viral hepatitis our next greatest achievement

Video animation rallying for the first ever Global Viral Hepatitis Strategy
May 2016 | Video, [duration 01:59]

On 28 May, 194 Member States made a historic commitment to eliminate viral hepatitis by 2030. At the 69th World Health Assembly, governments unanimously voted to adopt the first ever Global Viral Hepatitis Strategy, signalling the greatest global commitment in viral hepatitis to date. The Strategy sets a goal of eliminating hepatitis B and C by 2030 and includes a set of prevention and treatment targets which, if reached, will reduce annual deaths by 65% and increase treatment to 80%, saving 7.1 million lives globally by 2030.

https://www.who.int/hepatitis/news-events/ghss-hepatitis-video/en/

- Elimination:
  - As a public health threat ….Falls between eradication and regional control
  - Is defined as 90% reduction in incidence and 65% reduction in number of related deaths from a 2015 baseline

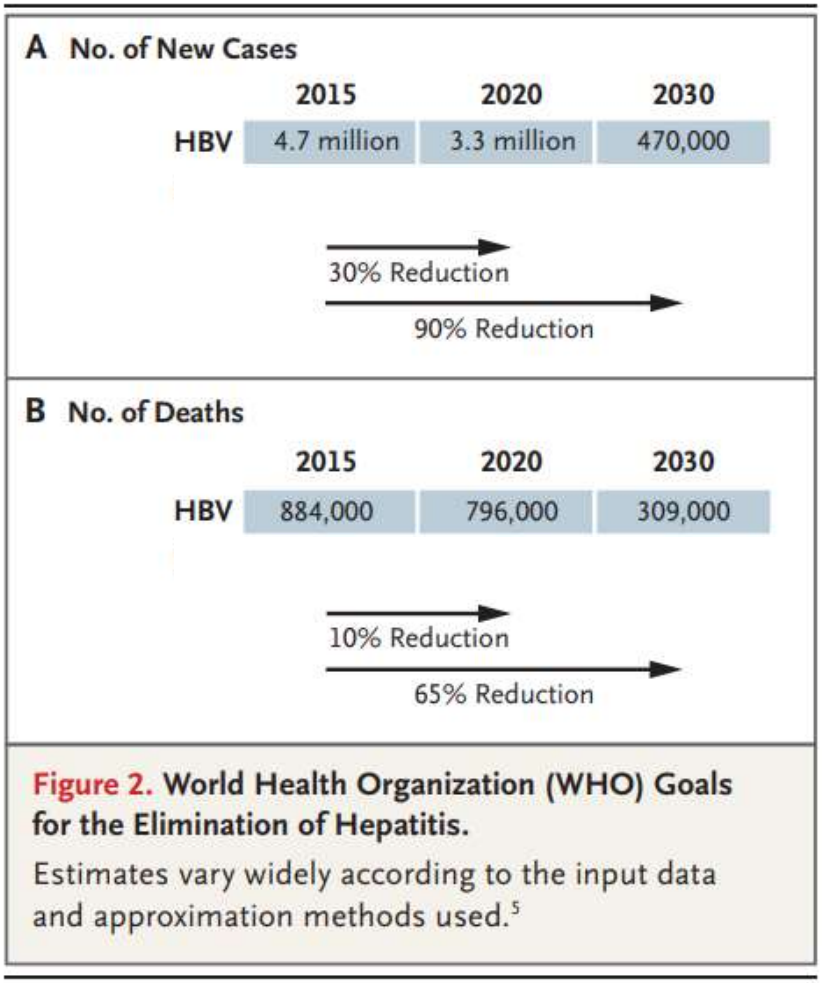


Figure 2. World Health Organization (WHO) Goals for the Elimination of Hepatitis.

Estimates vary widely according to the input data and approximation methods used.[5]

Thomas DL. New England Journal of Medicine 2019; 380: 2041-50

How can we prevent new HBV infections?

- Progression to chronic HBV infection is age-dependent

Age at infection	Progression to chronicity
Infancy	90%
Early childhood	50%
Adulthood	5%

- Therefore target prevention at MTCT and early-childhood infection
- Vaccination

Vaccination strategies

- Selective or Universal?

- Selective immunisation in high risk groups
- Selective immunisation of babies born to mothers infected with the hepatitis B virus (Pre August 2017)
- Universal infant immunisation since August 2017
    - Infanrix hexa® contains *DTaP/IPV/Hib/HepB* in combination

Vaccination of other at-risk groups

PHE recommended high risk groups for HepB selective immunisation

- Post exposure including babies born to HBsAg positive women
- People who inject drugs
- People who frequently change sexual partners
- MSM
- HIV positive individuals
- Close family contacts; families adopting; emergency foster carers
- Recipients of regular blood transfusions/products
- Patients with chronic renal failure and chronic liver disease
- People at occupational risk: health care workers (students & trainees), laboratory staff & other occupational groups e.g. prison staff
- Staff and clients in residential accommodation for those with LD
- Prisoners
- People travelling to or moving to endemic countries
- Aligned with other guidelines: PHE, NICE, BASHH/BHIVA, DHSC, Renal Association, NaTHNaC as appropriate

Source: PHE Immunisation against Infectious Disease (Green Book) 2017

Universal infant HepB immunisation

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 2017 will be c
hepatitis B as part of our universal childhood imr
Public Health England has announced. This is in
protection against diphtheria, tetanus, pertussis

The hexavalent vaccine replaces the existing 5-ir
routinely receive. It is already widely used with a
having been given in 97 countries in Europe and

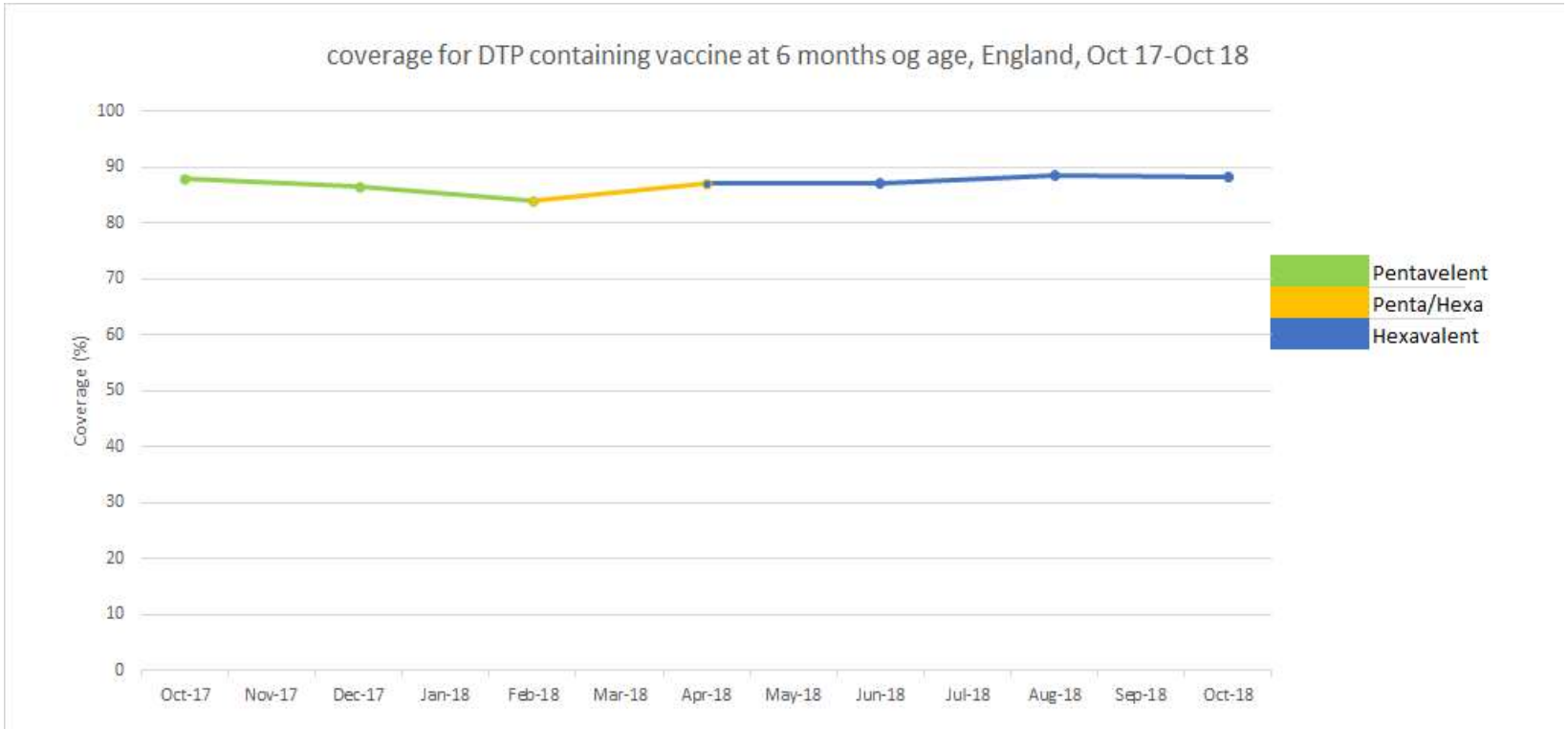
There has been no change to the immunisation s

Hepatitis B vaccine schedule for routine and at risk infant immunisation programmes

Age	Routine childhood		Babies born to hepatitis B infected mothers	
Birth	X*		✓	Monovalent HepB (Engerix B or HBvaxPRO Paediatric) (with HBIG if indicated)
4 weeks	X		✓	Monovalent HepB (Engerix B or HBvaxPRO Paediatric)
8 weeks	✓	DTaP/IPV/Hib/HepB (Infanrix hexa)	✓	DTaP/IPV/Hib/HepB (Infanrix hexa)
12 weeks	✓	DTaP/IPV/Hib/HepB (Infanrix hexa)	✓	DTaP/IPV/Hib/HepB (Infanrix hexa)
16 weeks	✓	DTaP/IPV/Hib/HepB (Infanrix hexa)	✓	DTaP/IPV/Hib/HepB (Infanrix hexa)
1 year	X		✓	Monovalent HepB (Engerix B or HBvaxPRO Paediatric) Test for HBsAg

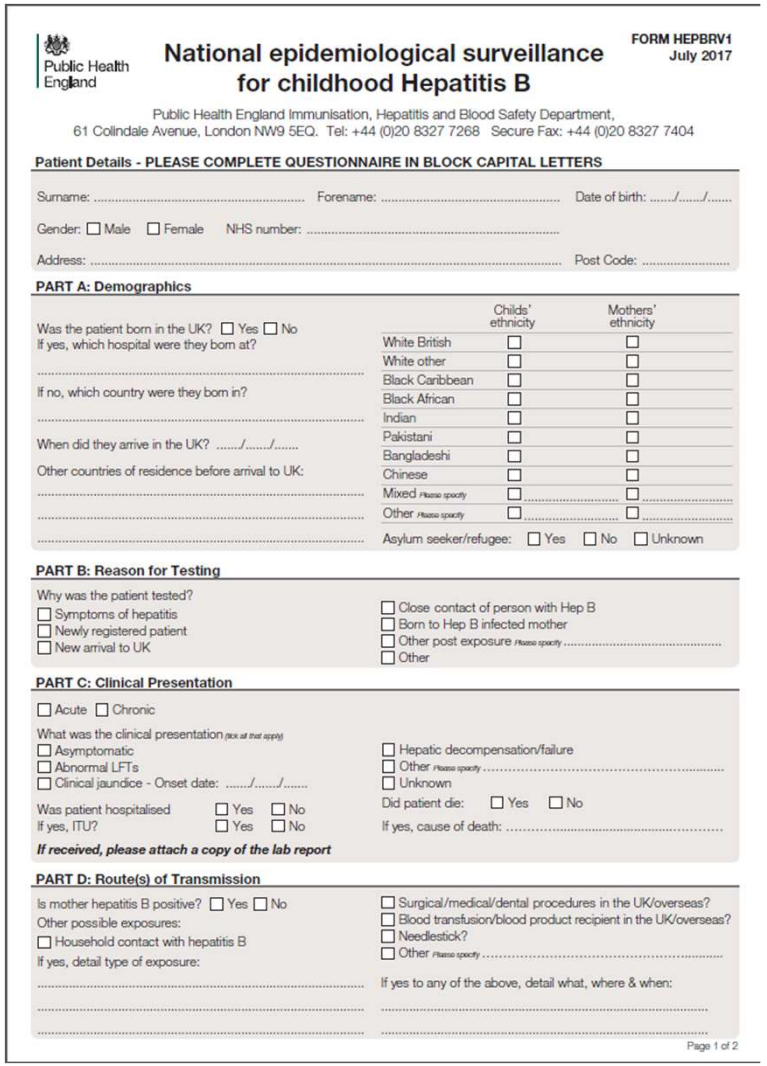
*Babies born to hepB negative mothers but going home to a household with another hepatitis B infected person may be at immediate risk of hepatitis B infection so should be given a monovalent dose of hepatitis B vaccine before discharge from hospital

Immunisation – coverage of 3 doses of DTP/IPV-HiB containing vaccine after switch to hexavalent vaccine



Surveillance to monitor the new hepB universal infant immunisation programme

- **Enhanced molecular surveillance of hepatitis B in childhood**
  - Prompt is new laboratory diagnosis (SGSS)
  - Aim: monitor 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
- **Vaccine uptake**
  - Neonatal (at-risk) HepB coverage (from Child Health information systems)
  - Hexavalent coverage (from Child Health information systems and primary care)



Public Health England

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:
.....
.....

Page 1 of 2

Prevention of HBV Infection: Vaccine Coverage

Target area	2020 targets		UK 2019	2030 targets
	Global	Europe	UK	Global
Childhood vaccine coverage (third dose)	90%	95%	>90%	90%

Prevention of MTCT HBV

- Requires antenatal screening for HBV infection
- Birth-dose of vaccine with completion of vaccine course
- Passive immunisation – HBIg
- Combined active/passive
- Antiviral therapy to mother

Table 18.4 Vaccination of term babies according to the hepatitis B status of the mother

Hepatitis B status of mother	Baby should receive	
	Hepatitis B vaccine	HBIG
Mother is HBsAg positive and HBeAg positive	Yes	Yes
Mother is HBsAg positive, HBeAg negative and anti-HBe negative	Yes	Yes
Mother is HBsAg positive where e-markers have not been determined	Yes	Yes
Mother had acute hepatitis B during pregnancy	Yes	Yes
Mother is HBsAg positive and anti-HBe positive	Yes	No
A woman who is HBsAg seropositive and known to have an HBV DNA level equal or above $1x10^6$IUs/ml in an antenatal sample*	Yes	Yes

* Where viral load testing has been performed to inform the management of the mother.

Prevalence: hepatitis B among pregnant women

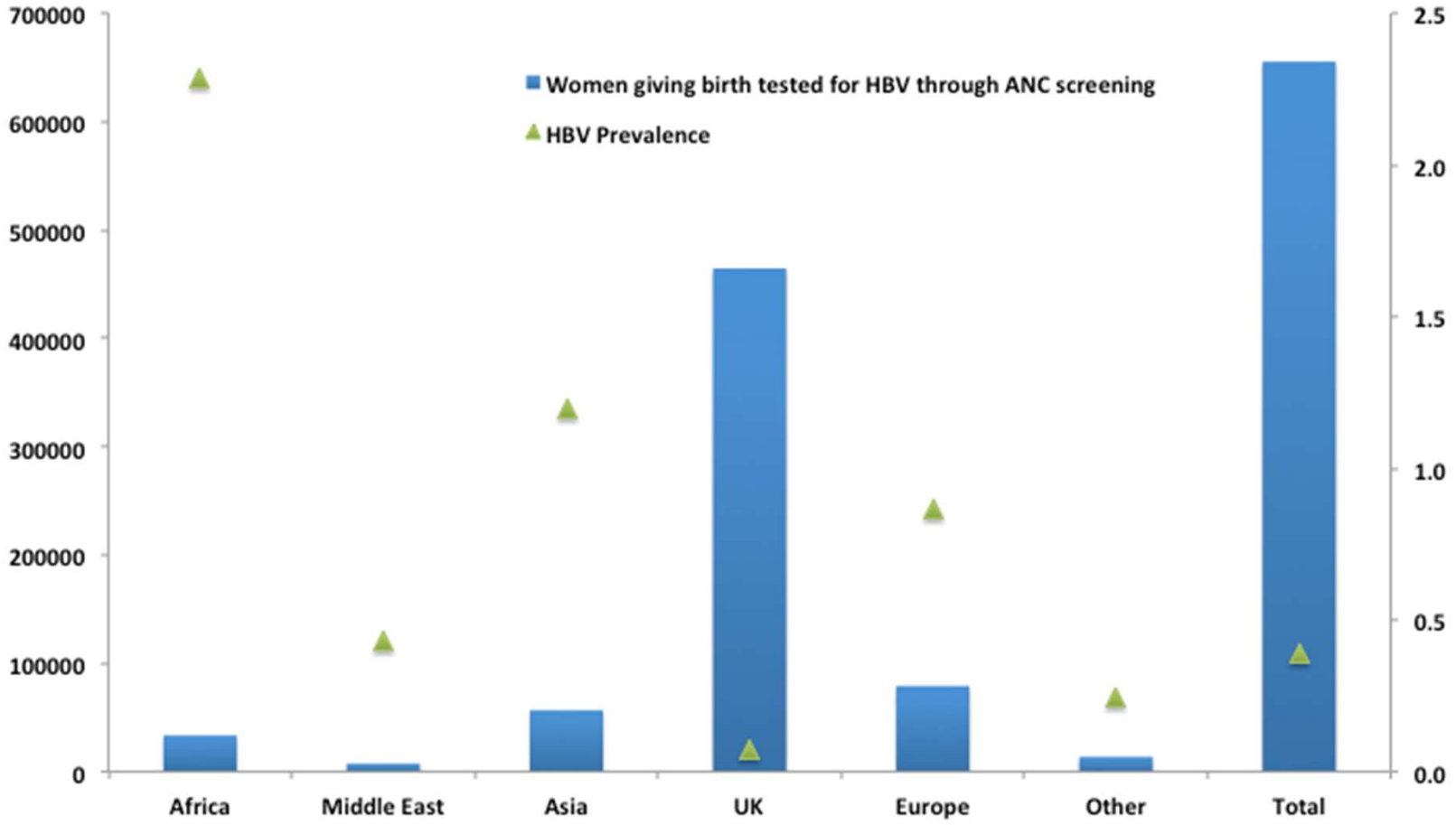
England, 2013

Region	Number screened	Antenatal prevalence %
East Midlands	40,315	0.26
East of England	80,770	0.44
London		
North East	30,702	0.17
North West	91,970	0.34
South East	105,810	0.29
South West	57,286	0.16
West Midlands	66,922	0.55
Yorkshire & Humber	68,301	0.32
ENGLAND	690,760	0.58

About 3000 pregnant women per year

Source: Data Tables for National Antenatal Infections Screening and Monitoring (NAISM) Programme 2013 (PHE IDSP & CIDSC)

Prevalence: hepatitis B among pregnant women by country of birth – preliminary data linking ONS live births data to HBV diagnoses



Monitoring: HBsAg positivity at 12 months (DBS) in infants at risk of vertical transmission

Financial Year	Tested	HBsAg positive (%)
2013/14	**222**	**1 (0.5)**
2014/15	**432**	**4(0.9)**
2015/16	**788**	**1(0.1)**
2016/17	**914**	**1(0.1)**
2017/18	**1,127**	**4(0.4)**
Total	**3483**	**11*(0.3)**

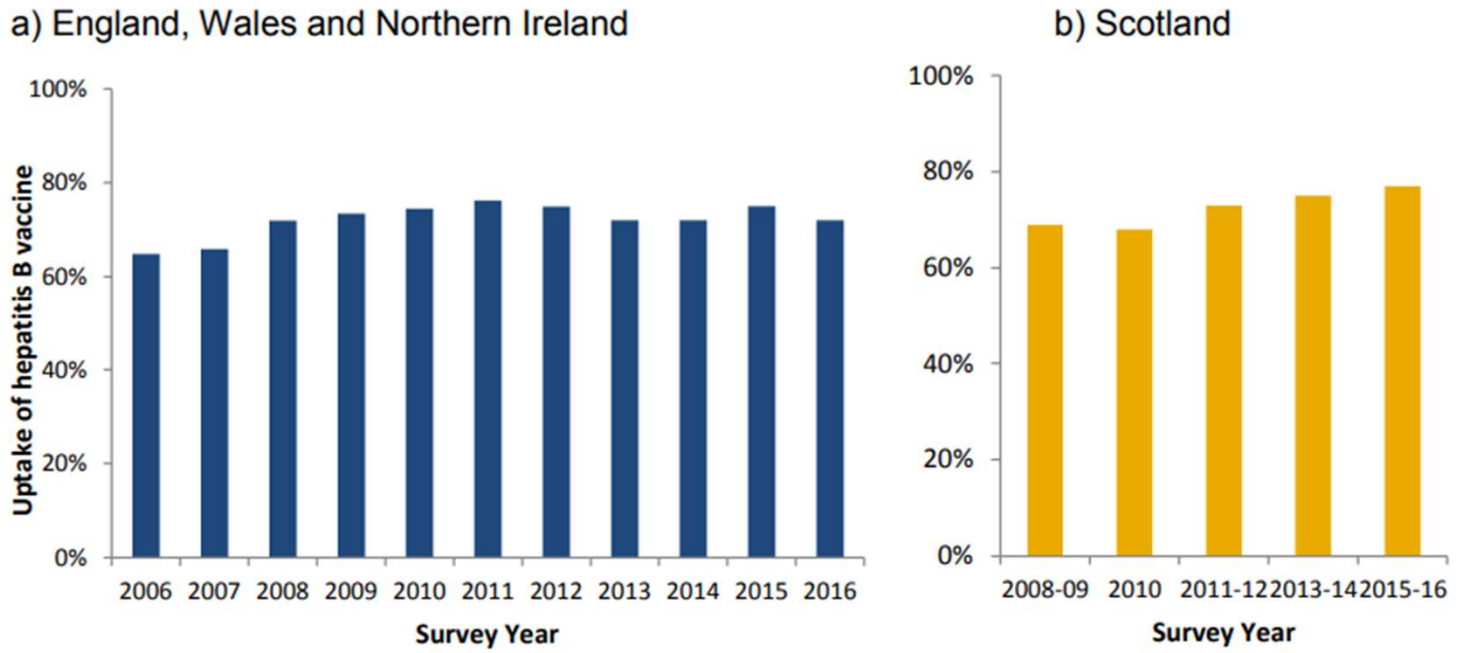
* Provisional data suggests these are high infectivity risk babies

Prevention of HBV Infection: prevention of MTCT

Target area	2020 targets		UK 2019	2030 targets
	Global	Europe	UK	Global
Childhood vaccine coverage (third dose)	90%	95%	>90%	90%
Interventions to prevent mother to child transmission (vaccination or other approaches)	50%	90%	>95%	90%

Vaccination of other at-risk groups

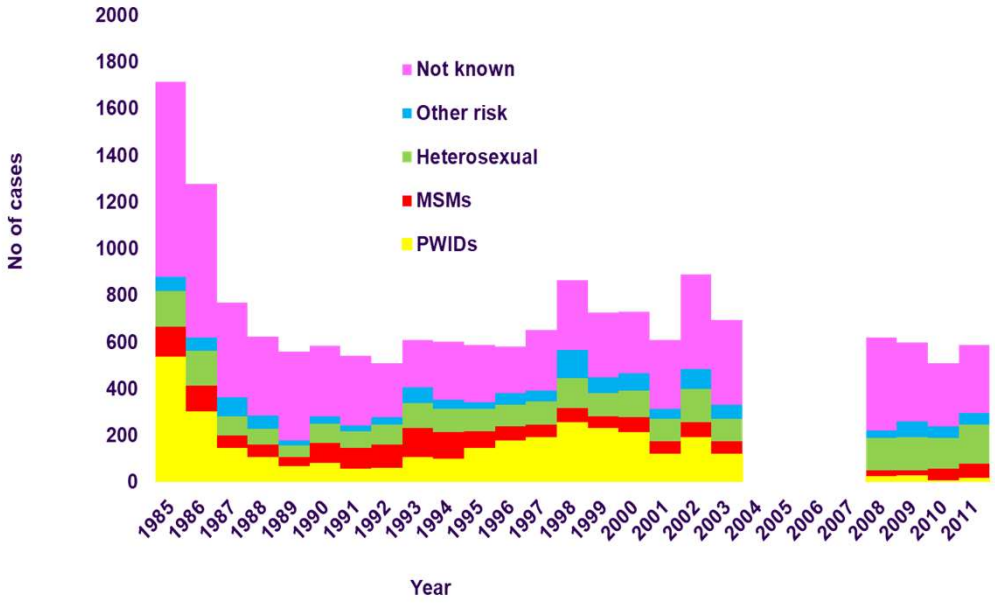
Uptake of the vaccine against hepatitis B among people who inject drugs: a) England, Wales and Northern Ireland, and b) Scotland



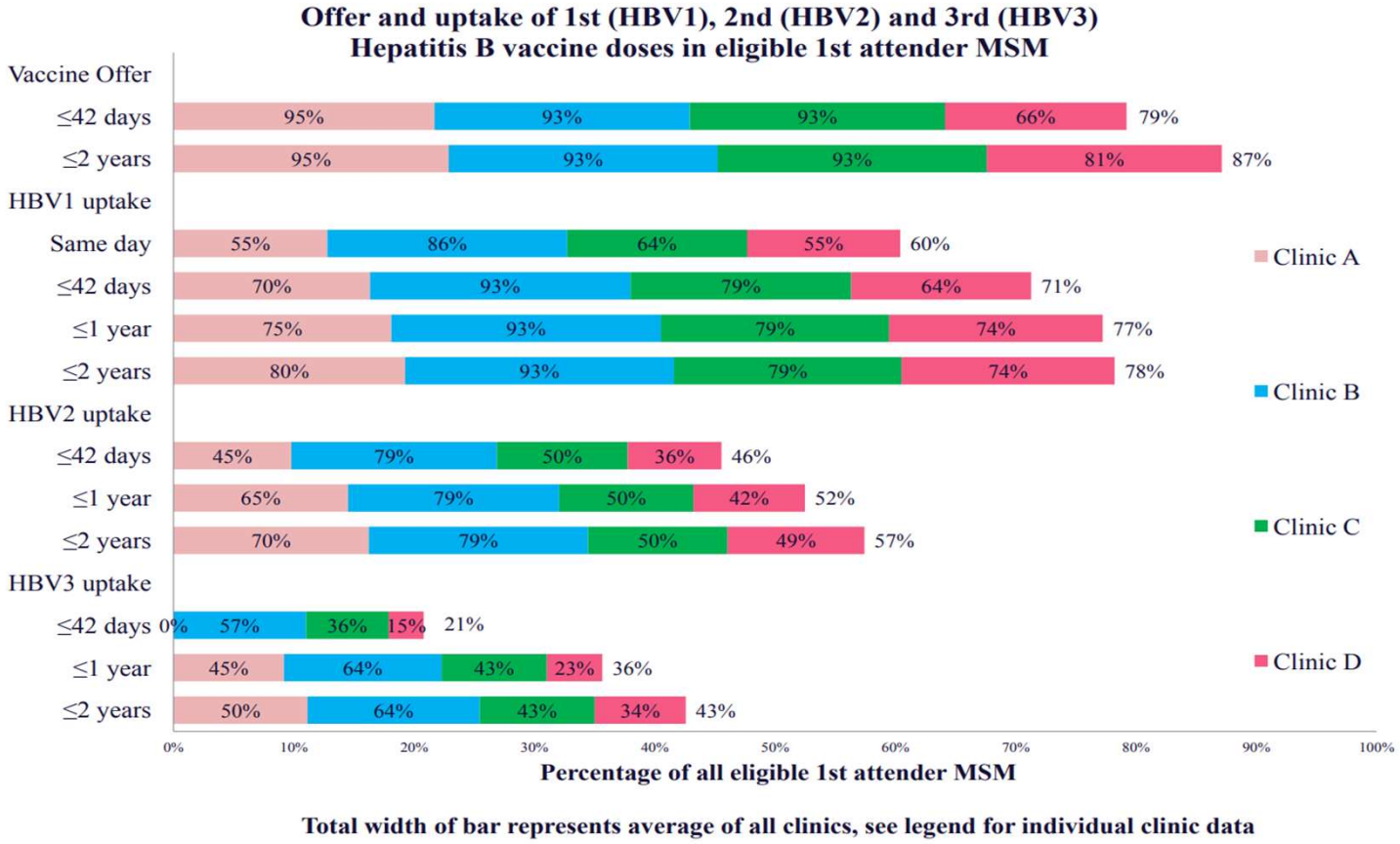
Data source: Unlinked Anonymous Monitoring survey of people who inject drugs (England, Wales and Northern Ireland) and Needle Exchange Surveillance Initiative (Scotland).

Impact of prison HepB immunisation

- **Major increase in vaccines provided in prisons**
  - Around 50% new receptions were immunised in 2010
- **Led to increase in PWIDs self-reporting receipt of HepB immunisation (UAM)**
  - Around 76% immunised by 2011
- **Major decline in incidence of acute HBV in PWIDs**



Hepatitis B vaccine coverage in MSM, a south West London Audit. GUMCADv2

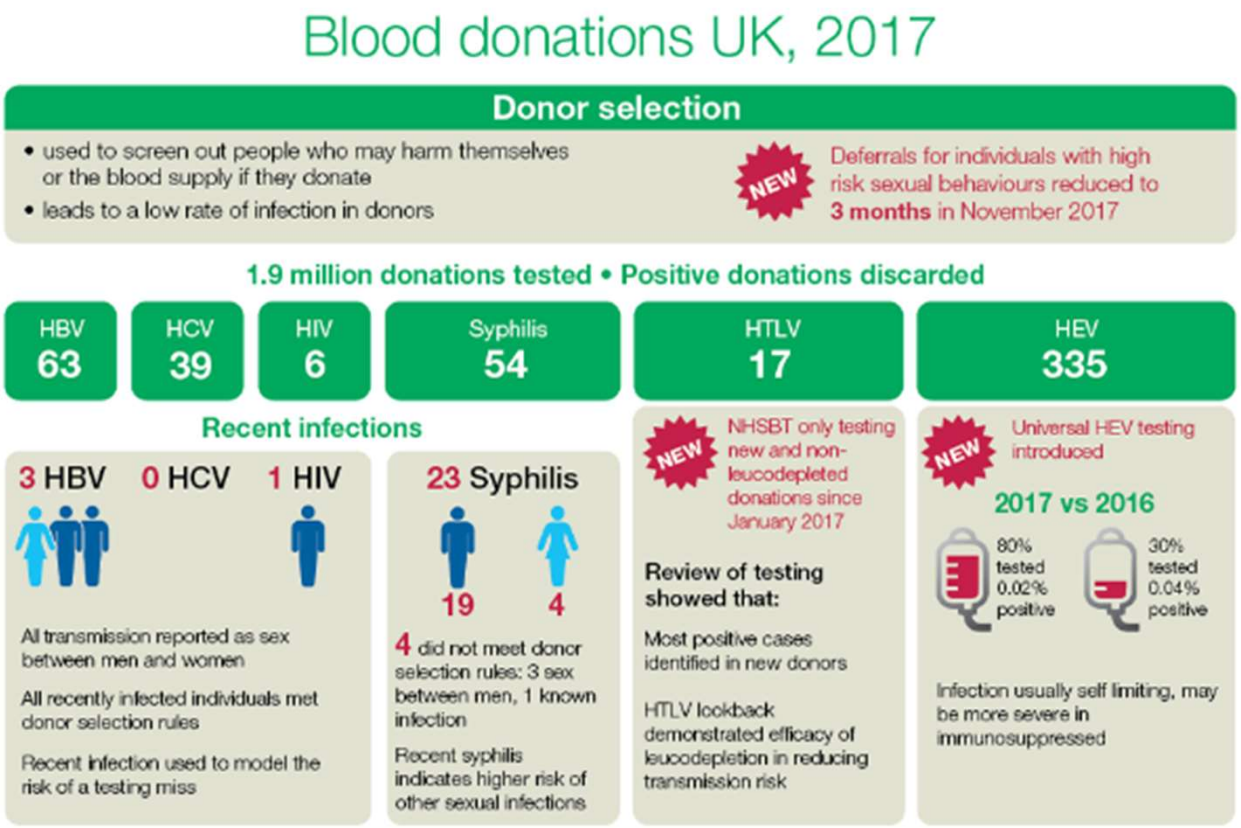


Coding of HBV immunity and HBV vaccine delivery is suboptimal, falling below national targets.

Low HBV vaccine coverage rates from GUMCADv2 coding relate to:

- poor coding of vaccine delivery,
- poor coding of immunity,
- And a true drop in vaccine coverage since 2008.

Safe supplies 2017 – Blood safety



Not with standing that blood donor screening doesn't guarantee zero risk of transmission
e.g. donor occult HBV infection may transmit to recipient

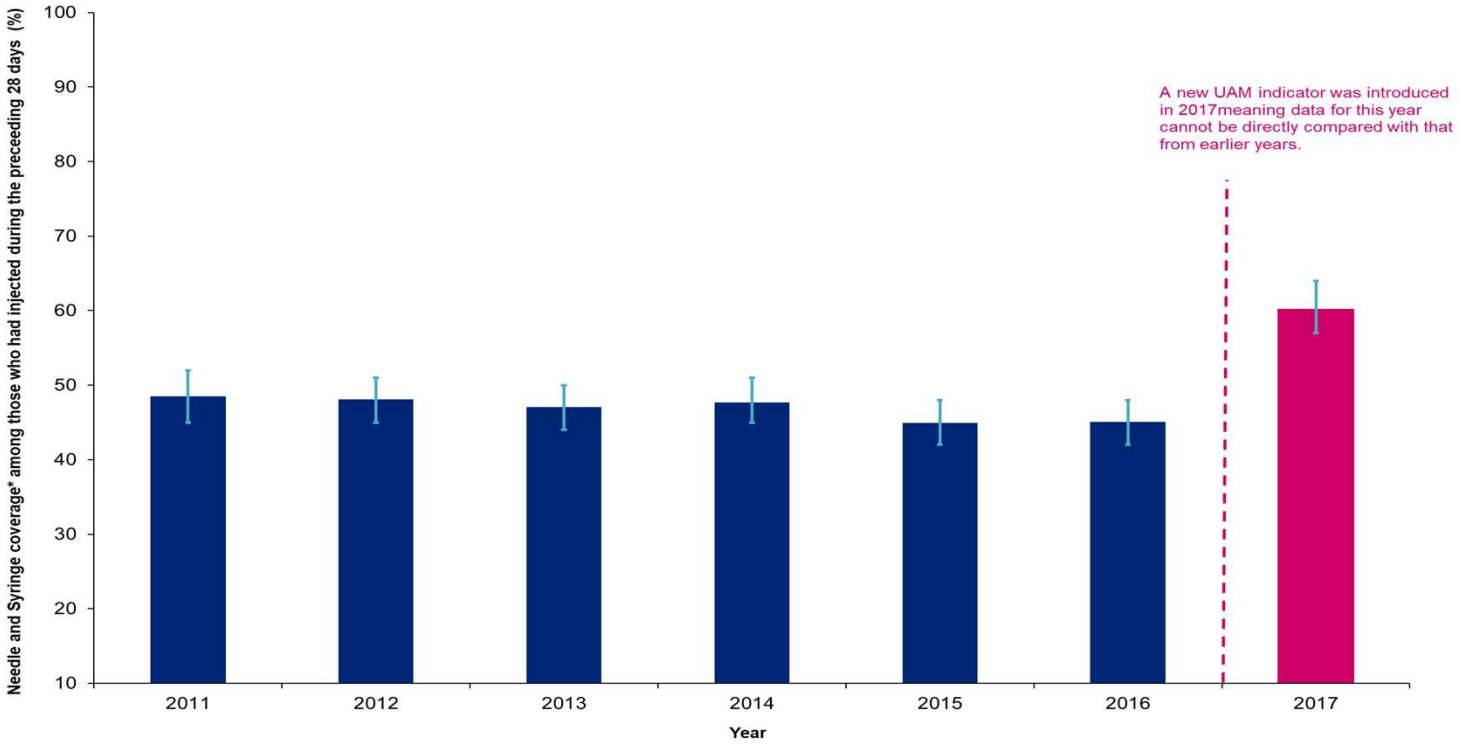
Prevention of HBV Infection: Blood Safety

Target area	2020 targets		UK 2019	2030 targets
	Global	Europe	UK	Global
Childhood vaccine coverage (third dose)	90%	95%	>90%	90%
Interventions to prevent mother to child transmission (vaccination or other approaches)	50%	90%	>95%	90%
Blood safety – screening of blood donations screen using quality-assured methods	95%	100%	100%	100%

Prevention of HBV Infection: Iatrogenic

Target area	2020 targets		UK 2019	2030 targets
	Global	Europe	UK	Global
Childhood vaccine coverage (third dose)	90%	95%	>90%	90%
Interventions to prevent mother to child transmission (vaccination or other approaches)	50%	90%	>95%	90%
Blood safety – screening of blood donations screen using quality-assured methods	95%	100%	100%	100%
Safe injections – percentage of injections administered with safety engineered devices in and out of health facilities	50%	50%	Not monitored	90%

Proportion of PWID reporting adequate needle and syringe coverage



* Needle and syringe provision is considered 'adequate' when the reported number of needles received, met or exceeded the number of times the individual reported injecting.

Data source: Unlinked Anonymous Monitoring survey of people who inject drugs: people injecting psychoactive drugs.[18]

Prevention of HBV Infection: PWID

Target area	2020 targets		UK 2019	2030 targets
	Global	Europe	UK	Global
Childhood vaccine coverage (third dose)	90%	95%	>90%	90%
Interventions to prevent mother to child transmission (vaccination or other approaches)	50%	90%	>95%	90%
Blood safety – screening of blood donations screen using quality-assured methods	95%	100%	100%	100%
Safe injections – percentage of injections administered with safety engineered devices in and out of health facilities	50%	50%	Not monitored	90%
Harm reduction: number of sterile needles and syringes provided per PWID per year	200	200	60% reported adequate provision	300

- Reduction in HBV deaths will require increase in diagnosis and treatment

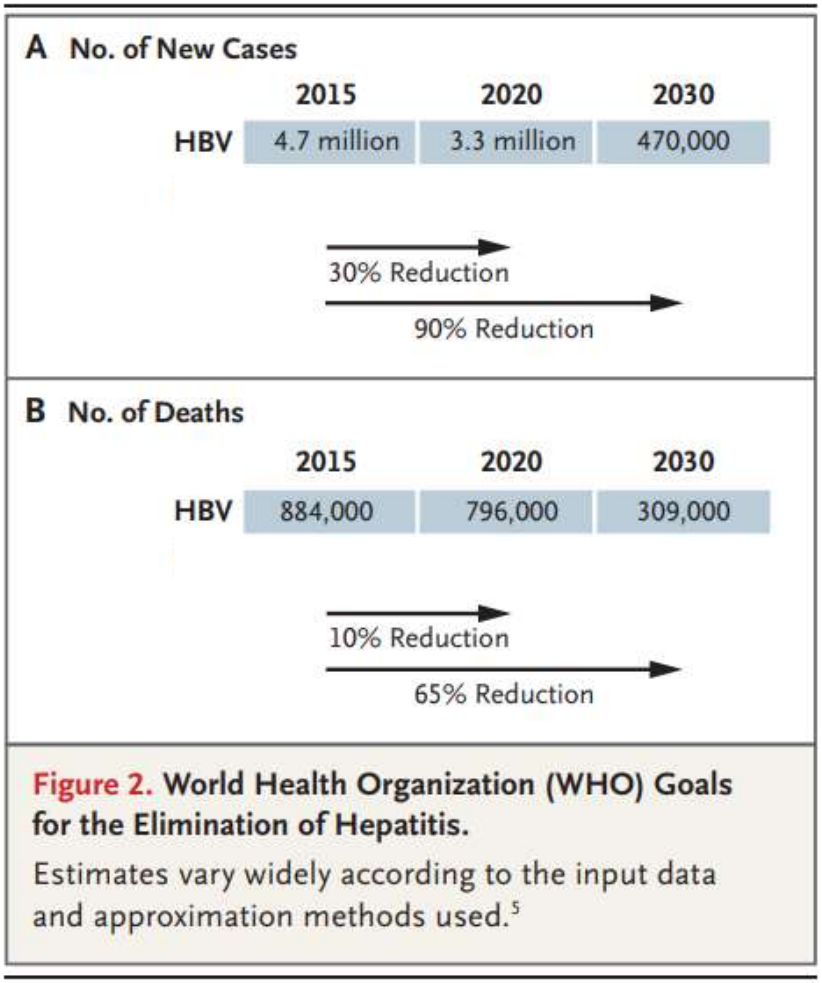


Figure 2. World Health Organization (WHO) Goals for the Elimination of Hepatitis.

Estimates vary widely according to the input data and approximation methods used.[5]

Thomas DL. New England Journal of Medicine 2019; 380: 2041-50

NICE guidelines: improving uptake and offer of hepatitis B and C testing in people at risk of infection

- **Recommendations on:**
- Raising **awareness** about hepatitis B and C among people at increased risk
- **Education and training** for professionals who provide services for people at increased risk of infection
- **Testing** for hepatitis C in **primary care, prisons and immigration removal centres, drugs services, and sexual health and GUM clinics**
- **Commissioning integrated services** for testing and treatment

- **HOW** to increase testing
- **WHAT** case finding and linkage to care interventions are effective and cost-effective

nice.org.uk/guidance/ph43

Current diagnostics: all laboratories

- HBsAg – marker of infection
- IgM anti-HBc – marker of recent infection
- IgG anti-HBc – marker of past infection
- Anti-HBs – marker of past infection, response to vaccine
- HBeAg/Anti-HBe – helps to characterise disease stage
- HBV DNA – helps to characterise disease stage, response to Rx

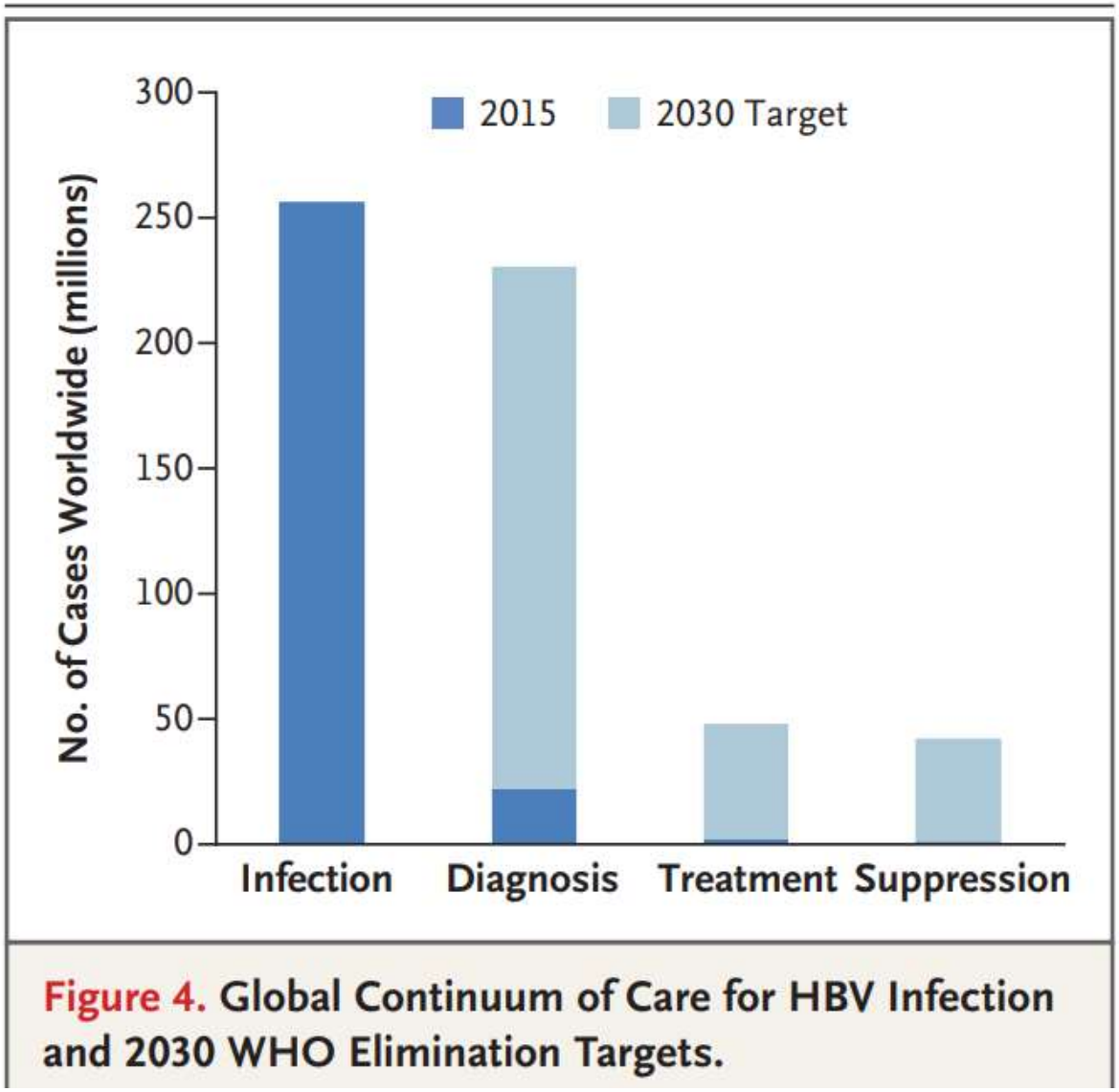


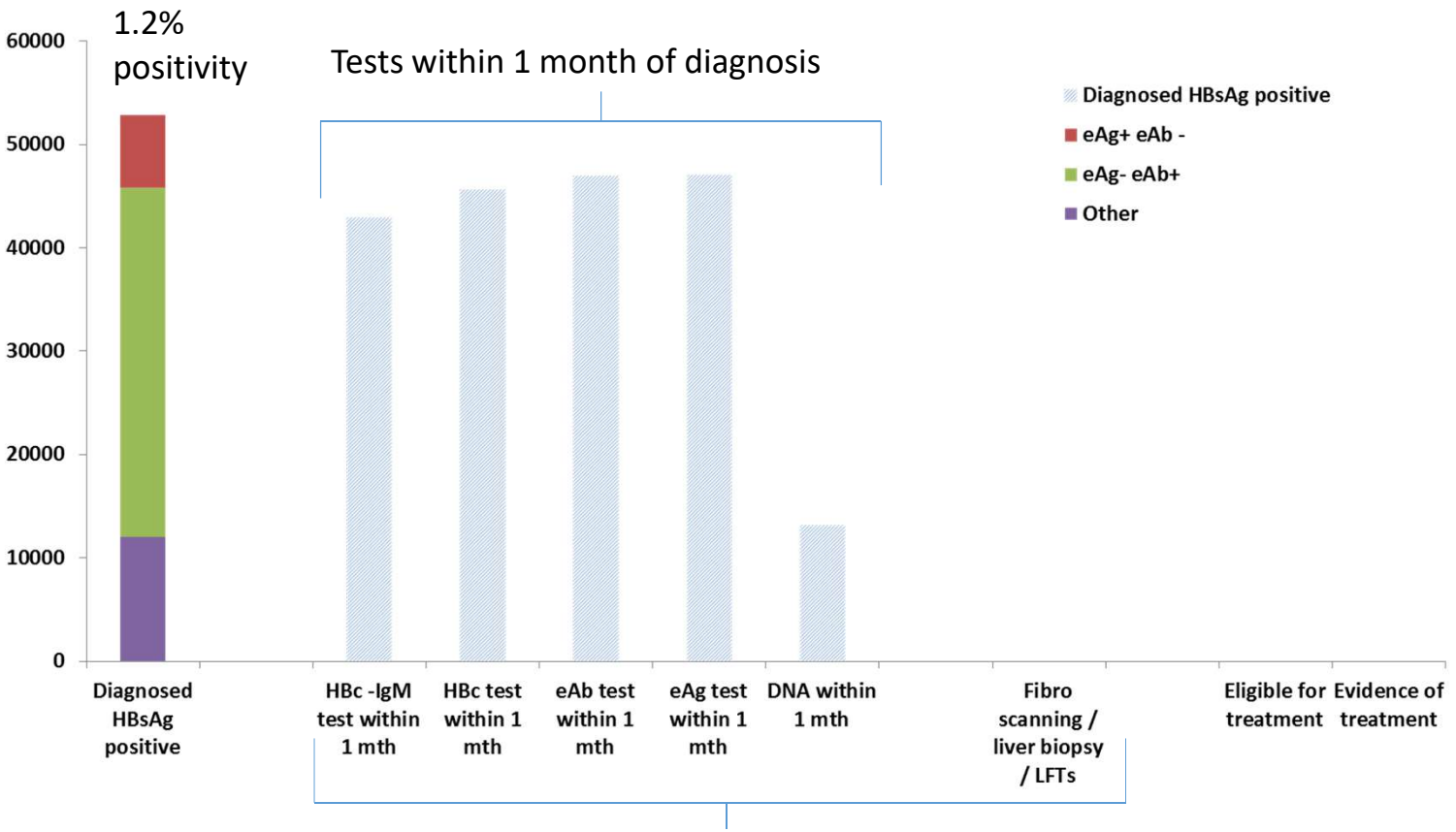
Figure 4. Global Continuum of Care for HBV Infection and 2030 WHO Elimination Targets.

Thomas DL. New England Journal of Medicine 2019; 380: 2041-50

2015 global estimates

- 9% of persons with HBV had been diagnosed
- <10% in need of antivirals had been treated.

Can we map the care pathway for HBV using surveillance data?



Prevention of HBV Infection: % Diagnosed

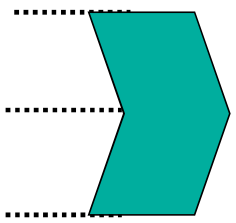
Target area	2020 targets		UK 2019	2030 targets
	Global	Europe	UK	Global
Childhood vaccine coverage (third dose)	90%	95%	>90%	90%
Interventions to prevent mother to child transmission (vaccination or other approaches)	50%	90%	>95%	90%
Blood safety – screening of blood donations screen using quality-assured methods	95%	100%	100%	100%
Safe injections – percentage of injections administered with safety engineered devices in and out of health facilities	50%	50%	Not monitored	90%
Harm reduction: number of sterile needles and syringes provided per PWID per year	200	200	60% reported adequate provision	300
Percentage of chronic hepatitis B diagnosed	30%	50%	Not monitored	90%

Diagnosing HBV infection

- Estimated 180,000 in UK, 95% immigrant-imported
- Low prevalence country - estimated 0.3-0.4%
  - We need more precise estimates of prevalence
  - We need data on numbers diagnosed

Data sources for surveillance and modelling

- Reports of laboratory confirmed chronic HBV infections
  ~ Testing trends, not incidence (notifications of limited/no use)
- Enhanced molecular surveillance of acute HBV ~ incidence, risk factors, outbreaks
- 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
- Surveillance for childhood hepatitis B ~ impact of universal infant immunisation
- Hospital episode statistics
- UK transplant data
- ONS death registrations



~ Burden of disease

National HBV disease prevalence estimates

Received: 18 September 2018 | Accepted: 19 December 2018
DOI: 10.1111/jvh.13063

ORIGINAL ARTICLE

WILEY JVH

Monitoring the hepatitis C epidemic in England and evaluating intervention scale-up using routinely collected data

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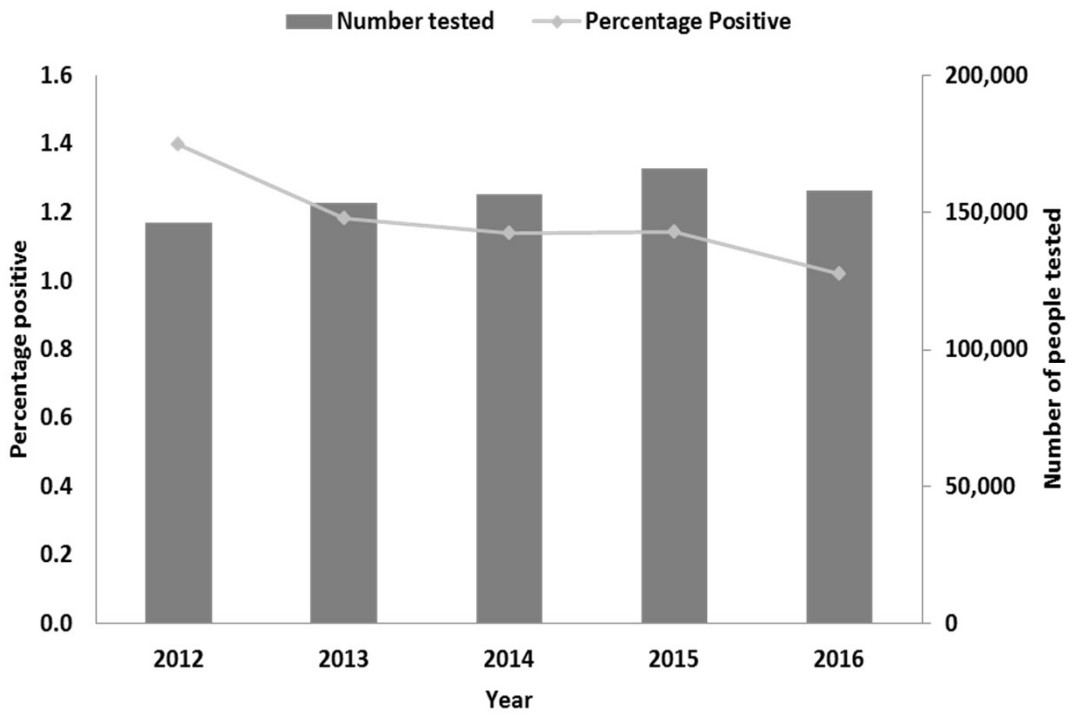
Summary

In England, 160 000 individuals were estimated to be chronically infected with hepatitis C virus (HCV) in 2005 and the burden of severe HCV-related liver disease has increased steadily for the past 15 years. Direct-acting antiviral treatments can clear infection in most patients, motivating HCV elimination targets. However, the current burden of HCV is unknown and new methods are required to monitor progress. We employed a Bayesian back-calculation approach, combining data on severe HCV-related liver disease and disease progression, to reconstruct historical HCV incidence and estimate current prevalence in England. We explicitly modelled infections occurring in people who inject drugs, the key risk group, allowing information on the size of this population and surveillance data on HCV prevalence to inform recent incidence. We estimated that there were 143 000 chronic infections in 2015 (95% credible interval 123 000-161 000), with 34% and 54% in those with recent and past injecting drug use, respectively. Following the planned scale-up of new treatments, chronic infections were predicted to fall to 113 400 (94 900-132 400) by the end of 2018 and to 89 500 (71 300-108 600) by the end of 2020. Numbers developing severe HCV-related liver disease were predicted to fall by at least 24% from 2015 to 2020. Thus, we describe a coherent framework to monitor progress using routinely collected data, which can be extended to incorporate additional data sources. Planned treatment scale-up is likely to achieve 2020 WHO targets for HCV morbidity, but substantial efforts will be required to ensure that HCV testing and patient engagement are sufficiently high.

KEYWORDS
back calculation, direct-acting antiviral treatment, disease burden, people who inject drugs, surveillance data

HBsAg tests and positivity in 23 sentinel laboratories: 2012 to 2016

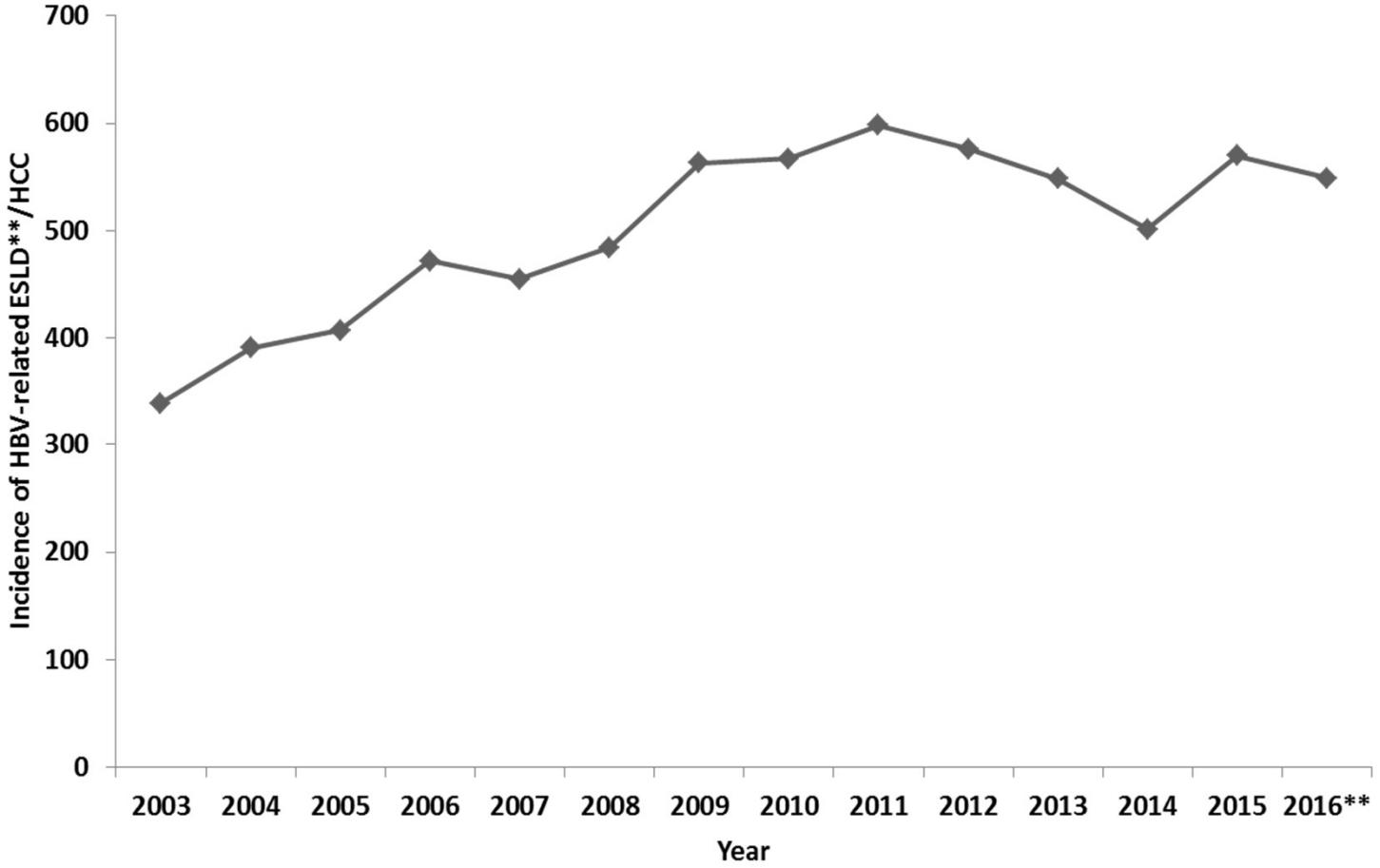
2012 to 2016



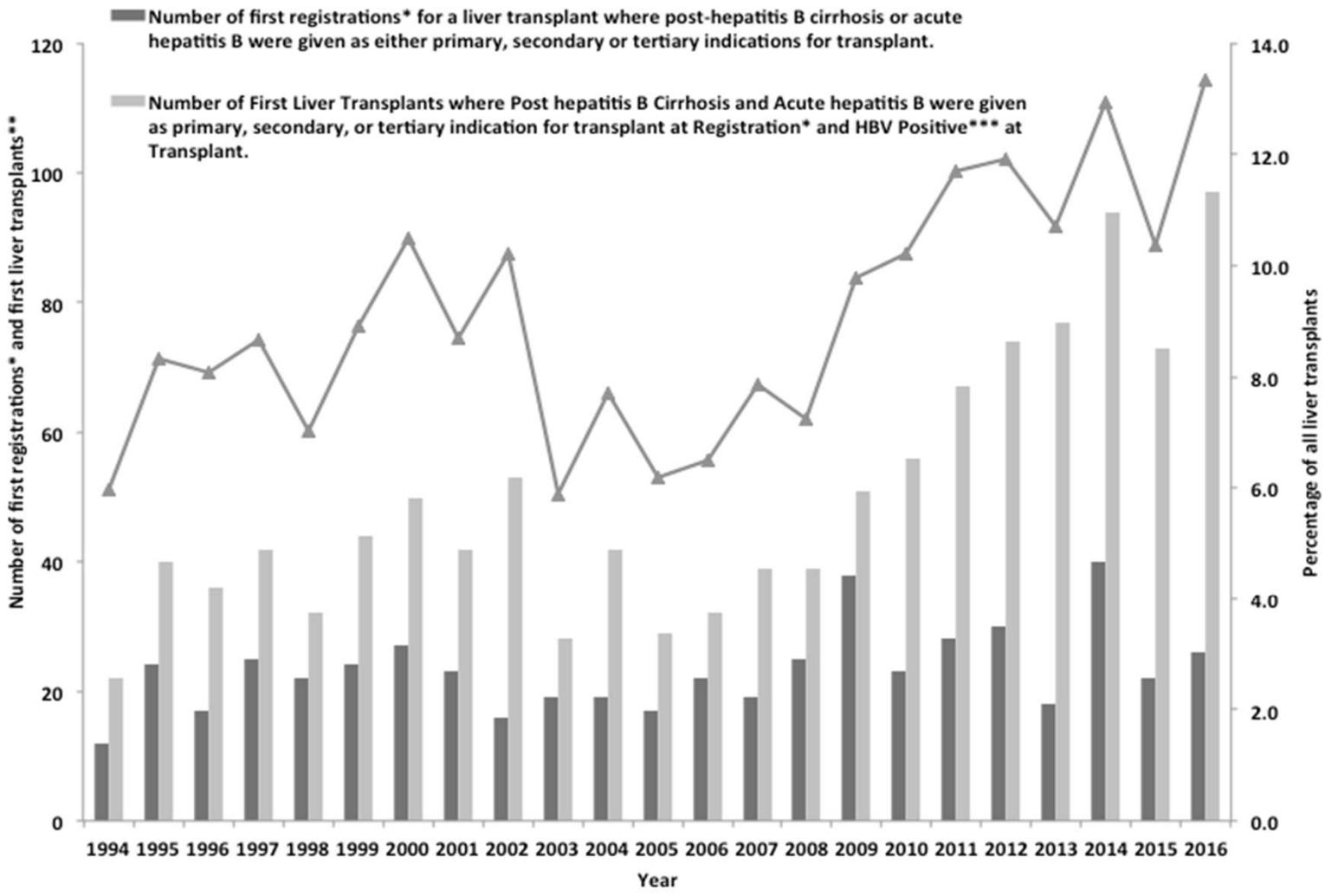
2017

Service type	Number of tests	Number of individuals tested	Number positive (%)
Primary Care			
Accident and emergency	23,180	20,538	147 (0.7)
Drug dependency services	1,440	1,311	6 (0.5)
General practitioner	106,452	99,731	1,108 (1.1)
GUM clinic	42,530	40,255	490 (1.2)
Occupational health	18,108	17.383	82 (0.5)
Prison services	9,345	8,575	115 (1.3)
Pharmacy	25	17	0 (0.0)
Total primary care	201,080	187,810	1,948 (1.0)
Secondary Care			
Fertility services	22,892	20,270	117 (0.6)
General medical / surgical departments	16,005	12,589	84 (0.7)
Obstetrics and gynaecology	22,558	20,576	82 (0.4)
Other ward type (known service)†	86,884	72,592	612 (0.8)
Paediatric services	5,951	5,123	54 (1.1)
Renal	52,999	17,058	99 (0.6)
Specialist HIV services	778	692	13 (1.9)
Specialist liver services	16,227	13,114	402 (3.1)
Unspecified ward§	10,284	8,801	127 (1.4)
Total secondary care	235,005	170,815	1,592 (0.9)
Unknown#	280	259	3 (1.2)

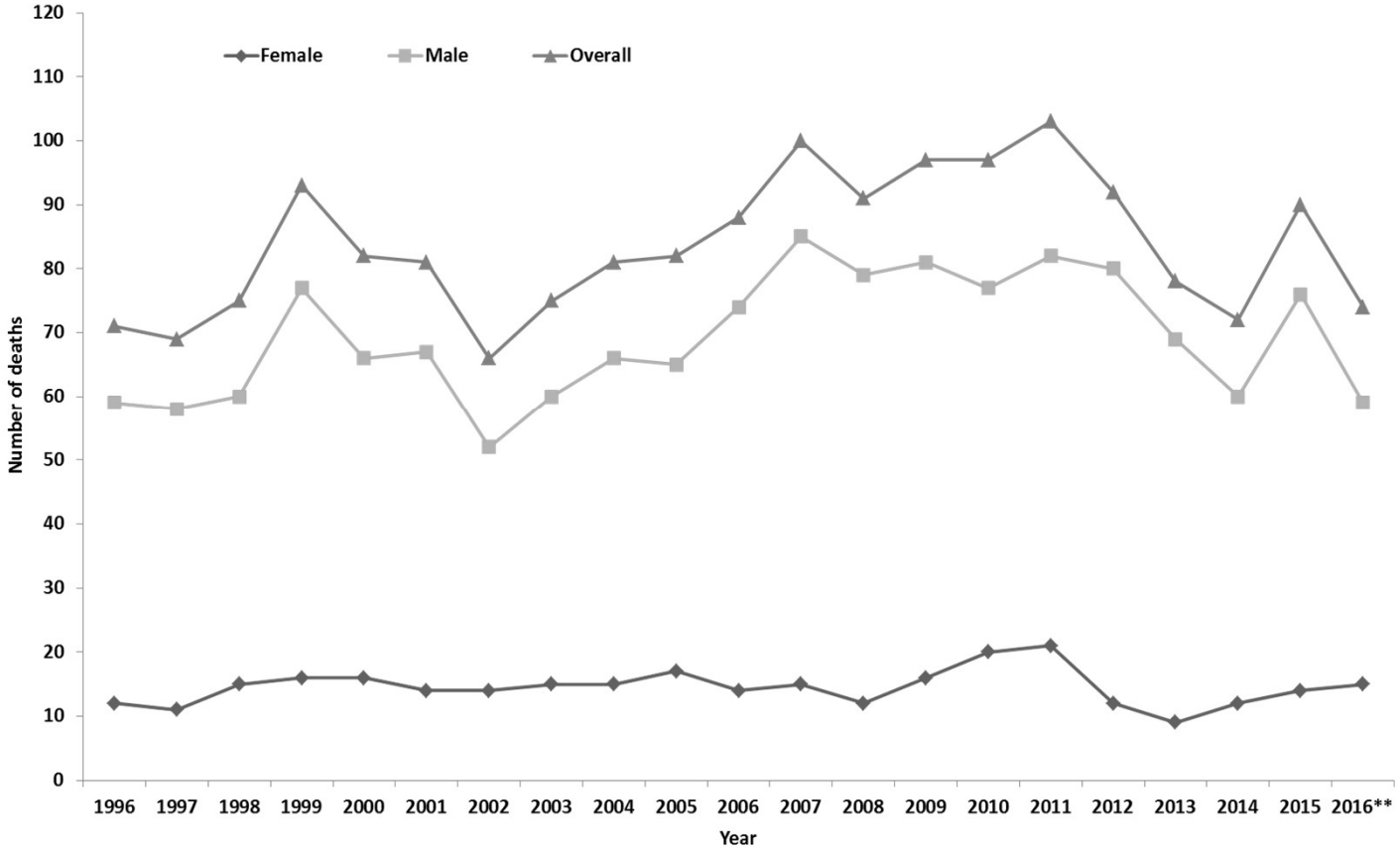
Preliminary estimates of incidence* of HBV-related ESLD**/HCC in the UK: 2003-2016



First liver transplants or registrations associated with HBV, 1994 to 2016**



Deaths from ESLD or HCC in those with HBV mentioned on their death certificate in England: 1996 to 2016



PWID and Prisoners

People who Inject Drugs (PWID)

- Unlinked Anonymous Monitoring (UAM) Survey:
  - decline in anti-HBc positivity from 29% (95%CI 27%-31%) in 2006 to 15% (95%CI 13%-16%) in 2016
  - HBsAg positivity now <1%

Prisons

- Health and Justice Indicators of Performance (HJIPs)
  - Prior to opt-out programme testing in 2013/14 uptake of testing In English prisons of new receptions approx. 4%
  - In 2017/18 opt out testing programme uptake of new receptions for hepatitis B risen to 28%

Diagnosis: Can we do better?

Evaluation of BBV testing in A&E

Systematic review – seroprevalence, feasibility, acceptability, linkage to care
Hepatitis B Virus Surface Antigen (HBsAg) Seroprevalence

Source	Year	Country	Setting	Time Frame	Design	Sample Size	Study Pop.	HBsAg Prev. (%)
Jui et al, 1990(55)	1988	USA	7 US Emergency Departments	Four Days	Prospective, anonymous sero-prevalence.	444	All patients attending the ED with excess serum taken for routine care.	0.6
Kaplan et al, 1992(35)	1990/1991	USA	Level 1 Trauma Centre	Six Months	Prospective, cross-sectional seroprevalence	286	Consecutively approached trauma patients, aged 18+ years.	1.7
Kelen et al, 1992(36)	1988	USA	Emergency Department	Six Weeks	Prospective, cross-sectional seroprevalence.	2523	All patients aged 15+ years, presenting to the ED and had blood drawn.	5
Sloan et al, 1995(56)	1988	USA	Urban Level 1 Trauma Centre	108 Days	Prospective, blinded point prevalence	994	Consecutive trauma patients aged 16+ years, treated in trauma centre.	3.1
Hall et al, 2010(37)	2005	USA	Emergency Department	Four Months	Prospective, anonymous, cross-sectional seroprevalence.	404	Extra blood samples from patients aged 15-50 years, previously obtained through the course of normal ED operations.	0.7 95% CI 0.1-1.6
Bradshaw et al, 2017(57)	2018	UK	Emergency Department	NR	Retrospective unlinked anonymous seroprevalence	500	Randomly selected, irreversibly-unliked samples from individuals who had tested HIV-negative as part of an ED testing program.	**1.6**
Cieply et al, 2016(38)	2015	UK	Emergency Department	Four Months	Unlinked, cross-sectional seroprevalence.	1249	Patients aged 17+ years attending the ED having their blood taken for routine biochemistry.	**1.2**

Evaluation of BBV testing in A&E

'Just another vial…': a qualitative study to explore the acceptability and feasibility of routine blood-borne virus testing in an emergency department setting in the UK

Lucy Cullen,[1,2] Pippa Grenfell,[1,2] Alison Rodger,[2,3] Chloe Orkin,[4] Sema Mandal,[2,5] Tim Rhodes[1,2,6]

- *Opportunities and constraints of ED as a site for testing*
- *Notions of acceptability and responsibility of status knowledge*
- *Value of test offset by perceptions of health need and justification of test expense*
- *Opt-out testing assumes an understanding of hepatitis and HIV – but little awareness of hepatitis*
- *Patients did not notice posters but these were a reminder for staff*

Serosurveys among MSM

- ***Response to recent clusters of acute HBV in MSM***
- Vaccine uptake data from GUMCAD insufficient for monitoring coverage
- Serosurveys to monitor and inform testing and vaccination in MSM
- **HBV susceptibility among MSM testing for HIV or syphilis in GUM clinics**
  - 6 labs mainly serving London GUM clinics; ~600 samples per lab
  - analysis in progress
- **HBV prevalence and susceptibility in at-risk individuals negative for HIV**
  - residual samples from HIV self-sampling project (n=2760)

Preliminary results	Anti-HBc only	Anti-HBs only	Anti-HBc and anti-HBs	HBsAg positive and anti-HBc
Reactive n (%)	39 (1.4)	690 (25)	53 (1.9)	11 (0.4)
Interpretation	Past exposure	Immunisation	Cleared infection	Current infection

Case Finding: Ethnic minorities in primary care – the HepFREE trial

	Numbers screened of the number eligible, n (%)/N	Incidence rate ratio* (95% CI)	p value
All participants†			
Standard	543 (1·7%)/31738	..	..
Interventional	11386 (19·5%)/58512	3·7 (1·3–10·5)	0·014
Participants registered at the start of the study‡			
Standard	271 (1·0%)/26046	..	..
Interventional	10524 (20·3%)/51773	5·2 (1·9–14·3)	0·001

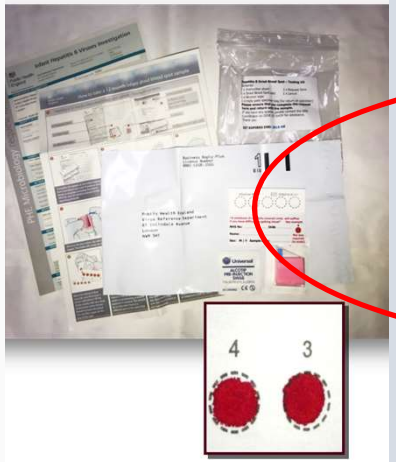
Intervention = sending letters to all ethnic minority patients on GP lists

Flanagan S et al. Lancet Gastro Hepatol 2019; 4: 32-44

Case Finding: use of DBS

- Enhanced nurse-led support for chronic HBV management in primary care
- Greatly improves the identification and testing of contacts
- Limited impact on improving referral rates
- Proportion of contacts receiving at least 3 doses of HepB vaccine improved as a result of research nurses actively booking appointments
- Impact likely due to consistent support provided by nurses along care pathway

EMPACT-B

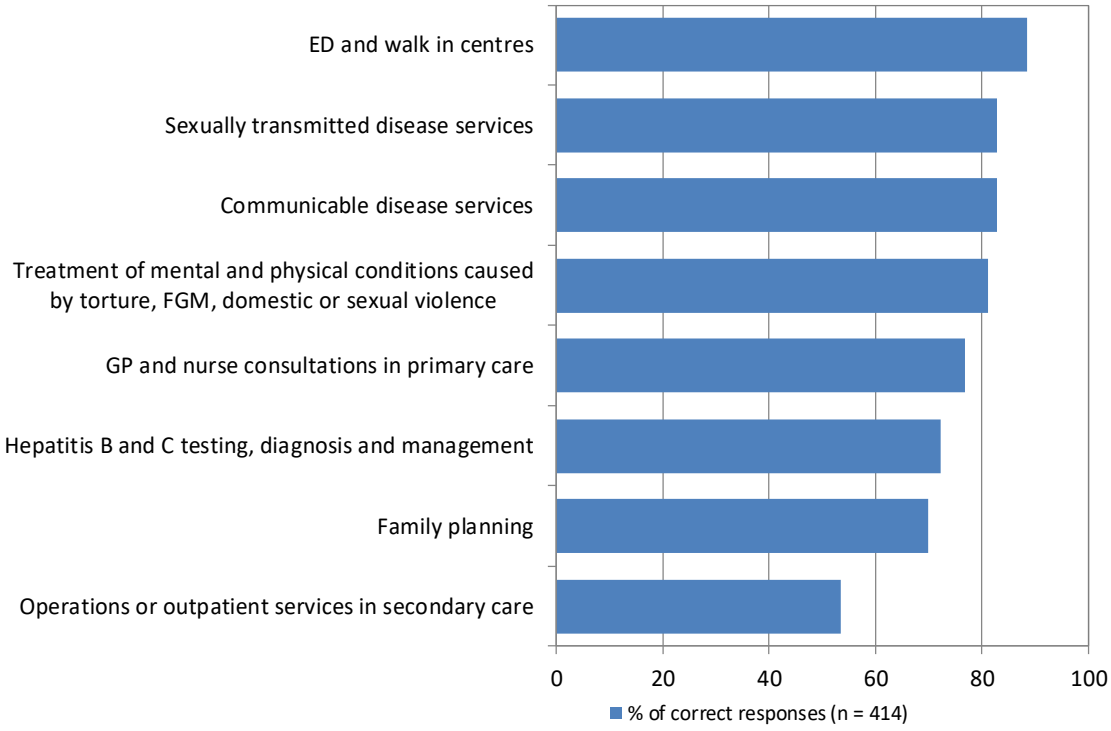


A pilot study in North Middlesex and Newham Hospital NHS Trusts, where the antenatal prevalence of CHB is high, demonstrated that nurse-led enhanced follow-up of HBV positive pregnant women, and home sampling by DBS improved close contact testing uptake, in particular among their partners where testing increased from 43% to 90%.

KEEL, P., EDWARDS, G., FLOOD, J., NIXON, G., BEEBEEJAUN, K., SHUTE, J. POH J, MILLAR A IJAZ S, PARRY J, MANDAL S, RAMSAY M and AMIRTHALINGAM, G. (2016). Assessing the impact of a nurse-delivered home dried blood spot service on uptake of testing for household contacts of hepatitis B-infected pregnant women across two London trusts. *Epidemiology and Infection, 144*(10), 2087-2097.

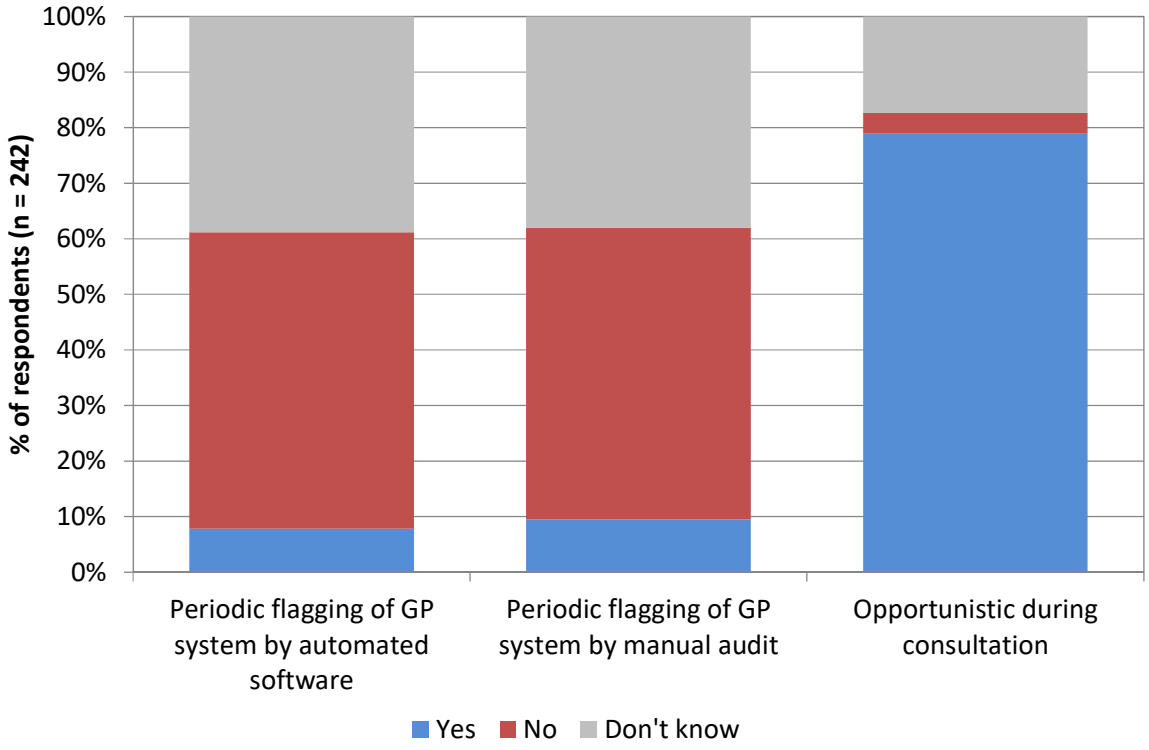
Primary care staff knowledge, policy and practice about BBV testing and care for migrant patients: survey

- 236 - 414 respondents (depending on question)
- 18% had universal opt-out HBV / HCV testing for new migrant patients
- Only 77% knew that GP and nurse consultations in primary care are free to all
- Most requested correct serology tests
- Language most commonly perceived barrier to accessing care



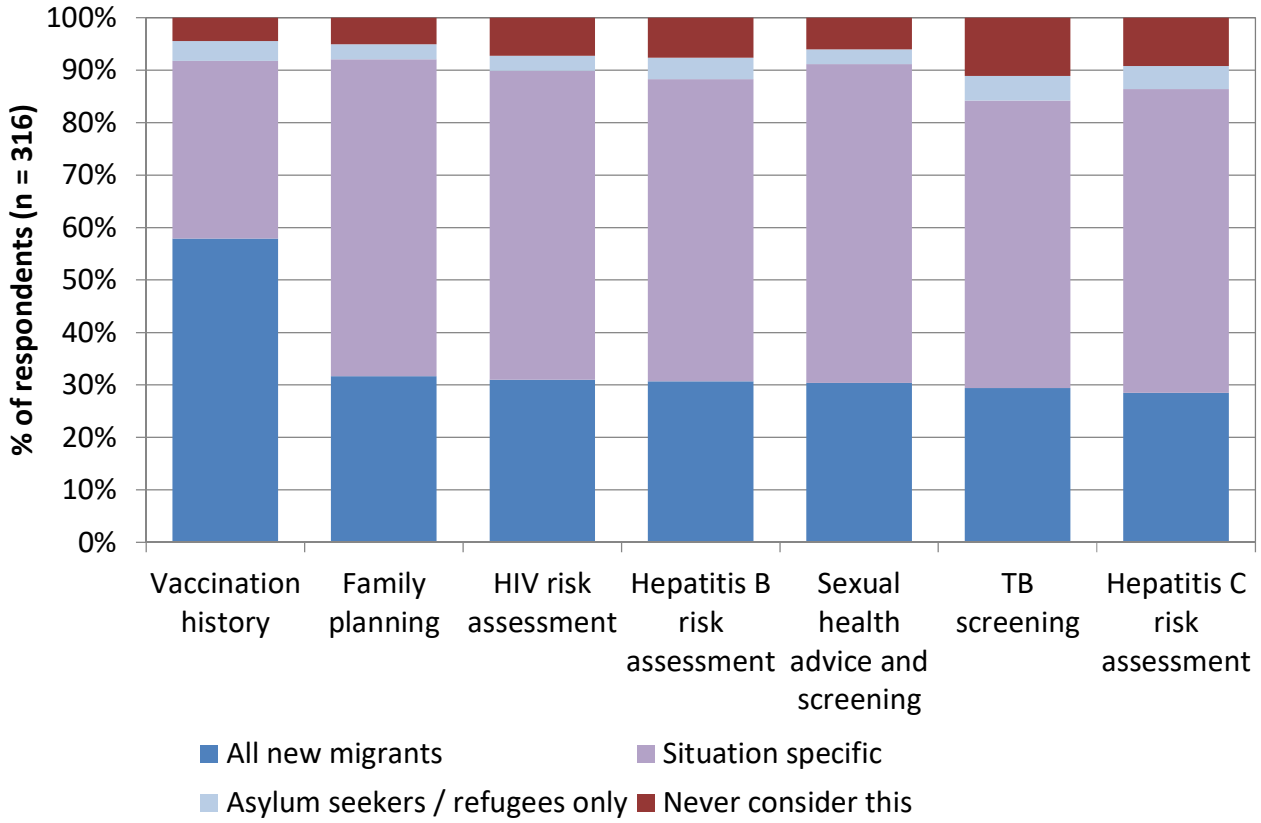
Identifying migrant patients for BBV testing

- 13% reported systematically identifying migrant patients for BBV testing
- 79% identified migrant patients for BBV testing opportunistically during consultation



Health issues considered for new migrant patients

- Vaccination history most common issue addressed for all new migrants (58%)
- All other issues more often addressed on a situation specific basis
- 31%, 28% and 31% would consider HBV, HCV and HIV risk assessments
- 29% would consider TB screening



Cost-effectiveness analyses in testing and diagnosis and linkage to care

Intervention / Description	Results
Routine HBV and HCV testing in A&E	• Highly likely to be cost-effective across the UK (ICERs <£10,000 /QALY for both) • Testing likely to remain cost-effective at low prevalence (0.24% or higher) – much higher than observed A&E attendee prevalence (up to 2% for HBV and HCV)
HBV case finding in UK migrants – primary care recall and testing	• Intervention cost-effective for those born in countries with intermediate or high HBV prevalence (≥2%), at £13,600/QALY. • Intervention still cost-effective at 1% prevalence.
EMPACT-B: Case management and contact tracing for chronic HBV	• Analysis being planned

Using GP data to get information on BBV testing and epidemiology among migrants

- 31% HBV and 26% HCV infections are diagnosed in general practice (2017)
- NICE guidance recommends testing migrants in primary care (2012)
- **Aim:** find out whether GP records can be used to help case-finding in migrants

Possible data sources:

Primary care research databases (THIN, CPRD): country of birth, hepatitis testing and diagnosis Read / Snomed codes exist **BUT** recording of country of birth very low, <2%

Sentinel network of GP practices: obtaining data from individual practices that routinely test new migrant patients for BBV and record country of birth:

- 4 practices signed up, currently going through IG processes
- mainly asylum seeker focused practices, still lacking data on wider migrants

•Wider work needed to improve recording of country of birth and other risk factors in health records

Enhance surveillance using established healthcare datasets through data linkage.

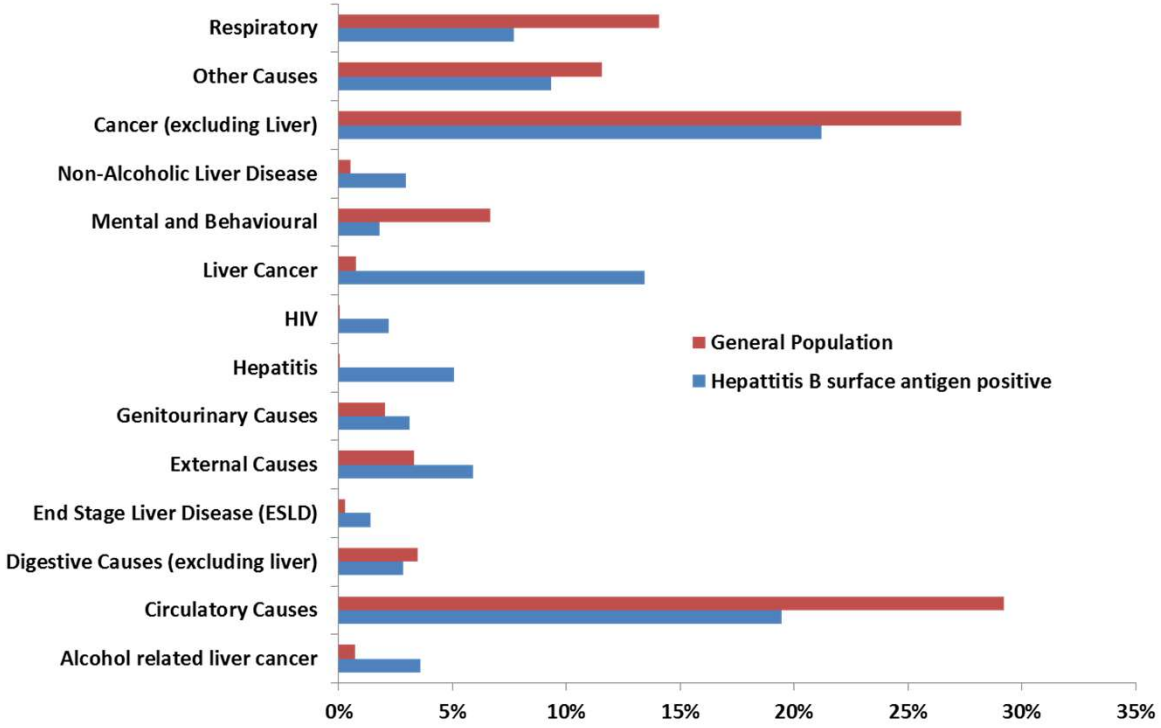
- Enhance surveillance using established healthcare datasets through data linkage.
  - •Cancer register ✓ Transplant register ✓ hospital episodes ✓
  - •ONS deaths ✓ Treatment register ✓ NDTMS ✓
  - •National HIV database ✓ TB✓
- Used both sentinel surveillance and routine laboratory diagnoses of hepatitis depended on the question.
- What else?
  - Disease staging (fibro scanning or liver biopsy, LFTs)
  - Risk factor information
  - Prescribing data

Linkage to national HIV database: HBV co-infected with HIV

- 3.9% (1,129/28,789) of HBsAg positive co-infected with HIV
- Females - 95% heterosexual
- Males - 32% heterosexual 62% sex between men

- Predictors of HIV positivity
  - older age (aOR:1.1),
  - black ethnicity (male aOR:15.5, female aOR:16.4) or
  - male of white ethnicity (aOR:8.2) compared to white females.
- HBV diagnosis was higher in
  - sexual health (aOR:55.0),
  - specialist liver (aOR:6.7),
  - emergency department (aOR:5.3) and
  - renal services (aOR:2.8) compared to general practice.
- 60.4% co-infected persons were diagnosed with HIV more than six months before HBV diagnosis.

Linkage to ONS death register
Causes of death among persons diagnosed with HBV: England 2008-2016



- 3.7% HBsAg died.
- Cancer (excluding liver) was the leading cause of death
- Liver disease on the death certificate for 26.4%.
- 52.1% for those who died of liver disease had HCV reported.
- Higher proportion of persons with HBV died of external causes, liver disease, genitourinary causes and HIV compared to the general population.
- HBeAg positive - alcohol related liver disease, digestive, external and HIV
- HBeAg negative – cancer (excluding liver).

Still to come……

Using GP data to get information on BBV testing and epidemiology among migrants

- **Aim:** find out whether GP records can be used to help case-finding in migrants

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Continue data linkage work for HBV

Assess the Blood Borne Virus (BBV) Burden among underserved populations

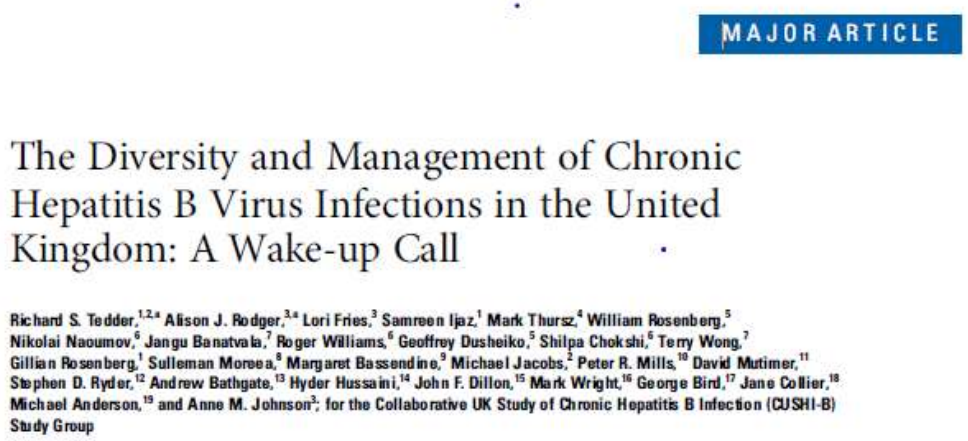
- Systematic review of HCV prevalence estimates, and on HBV case-finding and linkage to care
- Identify and characterise underserved populations, determine how these populations differ from those attending services, and monitor testing, positivity, and referral to care
- Consider how surveys or enhancing existing surveys among at-risk populations will fill data gaps, improving disease prevalence and burden models.

Prevention of HBV Infection: % treated

Target area	2020 targets		UK 2019	2030 targets
	Global	Europe	UK	Global
Childhood vaccine coverage (third dose)	90%	95%	>90%	90%
Interventions to prevent mother to child transmission (vaccination or other approaches)	50%	90%	>95%	90%
Blood safety – screening of blood donations screen using quality-assured methods	95%	100%	100%	100%
Safe injections – percentage of injections administered with safety engineered devices in and out of health facilities	50%	50%	Not monitored	90%
Harm reduction: number of sterile needles and syringes provided per PWID per year	200	200	60% reported adequate provision	300
Percentage of chronic hepatitis B diagnosed	30%	50%	Not monitored	90%
Percentage of eligible persons with chronic HBV infection treated	(5 million)	75%	Not monitored	80%

Chronic HBV infections in tertiary care: the UK – CUSHI B

- No comprehensive, national data on the management of chronically infected patients, treatment, outcome or how viral diversity impacts
- Collaborative study of 698 chronically-infected individuals from 13 liver-referral centres across the UK in 2008/9
- National cross-sectional study



MAJOR ARTICLE

The Diversity and Management of Chronic Hepatitis B Virus Infections in the United Kingdom: A Wake-up Call

Richard S. Tedder,[1,2,a] Alison J. Rodger,[3,a] Lori Fries,[3] Samreen Ijaz,[1] Mark Thursz,[4] William Rosenberg,[5] Nikolai Naoumov,[6] Jangu Banatvala,[7] Roger Williams,[6] Geoffrey Dusheiko,[5] Shilpa Chokshi,[6] Terry Wong,[7] Gillian Rosenberg,[1] Sulleman Moreea,[8] Margaret Bassendine,[9] Michael Jacobs,[2] Peter R. Mills,[10] David Mutimer,[11] Stephen D. Ryder,[12] Andrew Bathgate,[13] Hyder Hussaini,[14] John F. Dillon,[15] Mark Wright,[16] George Bird,[17] Jane Collier,[18] Michael Anderson,[19] and Anne M. Johnson[3]; for the Collaborative UK Study of Chronic Hepatitis B Infection (CUSHI-B) Study Group

- Of the 289 biopsied, 20% had evidence of cirrhosis
  - 24% men and 8% of women
  - Cirrhosis more common (18%) in genotypes A and D
- 451 (66%) were not on anti-viral treatment
  - Men 2.5 x more likely to be treated than women

Treatment of HBV

- **Current therapies: IFN or NA**
  - Mostly achieve Partial cure; Functional cure is very much the minority
  - HBsAg loss with IFN – 3-7%; with NA – 0-3%
  - New approaches - 10 different trials in phase I/II
  - Change to the treatment landscape of the next 5 years
- **Sterilising:**
  - HBsAg –ve;
  - Eradication of intrahepatic HBV DNA, cccDNA and integrated DNA
- **Functional:**
  - HBsAg –ve; serum HBV DNA –ve; cccDNA persists
  - ↓ risk of HCC over time
- **Partial:**
  - HBsAg +ve; serum HBV DNA –ve

Revolution in treatment - *Hepatitis B cure: from discovery to regulatory approval. Lok AS, Zoulim F, Dusheiko G, Ghany MG. Journal of Hepatology 2017; 67: 847-861*

Elimination – how are we doing?

- We are broadly on target towards elimination of HBV as a public health threat in terms of preventative interventions – harm reduction, blood donor screening, immunisation and infection control and safe injecting policies.

- Challenges remain with diagnosis and treatment/care cascade, both in delivery and monitoring.

- Looking forward we need:
  - Improved estimate and characteristics of infected population
  - Improved estimate of proportion diagnosed
  - Improved case finding and referral to treatment and specialist care
  - Monitoring of treatment cascade

•… in the context of anticipated treatment advances

Acknowledgements

- Will Irving
- Sema Mandal, Ellen Pringle, Koye Balogun, Samreen Ijaz and others in PHE