UK Health Security Agency

National Strategic Group for Viral Hepatitis

Minutes of meeting held on 30 June 2023

Virtual only: 10:30am to 3pm

Contents

Attendees and apologies

Attendees

Members

Will Irving (WI, Chair)
Rachel Halford (RH)
Samreen Ijaz (SI)
Patrick Kennedy (PK)
Sema Mandal (SM)

Invited presenters and observers

Georgia Threadgold (GT)
Gabriel Gurmail Kaufmann (GGK)
Sameera Lyons (SL)
Stuart Smith (SS)
Lesley Wallace (LW)
Rebecca John (RJ)
David Leeman (DL)
Monica Desai (MD)
Simon Packer (SP)
Daniel Bradshaw (DB)
Aneesha Noonan (AN)
Simon Packer (SP)
Daniel Bradshaw (DB)
Aneesha Noonan (AN)
Daniel Thomas (DT)
Matthew Hibbert (MH)
Koye Balogun (KB)
Ruth Simmons (RS)
Rhiannon Drakeley (RD)
Philippa Matthews (PM)
Heli Harvala (HH)
Ross Harris (RH)
Ahmed Elsharkawy (AE)
Vanessa Hebditch (VH)
Neil McDougall (ND)
Zoe James (ZJ)
Emmanuel Musah (EM)

Secretariat

Amber Newbigging-Lister (AL)

Apologies

Ellie Barnes
Chantal Edge
Beatrice Emmanouil
Sarah Hart
Matthew Hickman
Sharon Hutchinson
Zoe James
Annelies McCurley

1. Welcome, introductions and membership discussion

The chair welcomed all those in attendance, there was a round of introductions and apologies were given.

No issues raised with terms of reference. WI raised need to invite Ashley Brown, NHS England (NHSE), to future meetings in place of Graham Foster.

Action

Action 1: AL to invite Ashley Brown to the group and future meetings.

2. Minutes of previous meeting

WI raised that point 5.7 should be updated to reflect that WI thanked Iain Hayden in his last meeting as the secretariat for the National Strategic Group for Viral Hepatitis (NSGVH) for his efforts and the fantastic job done.

Actions not covered elsewhere in the agenda

The remaining actions have all been completed or are on the agenda as items.

3. Updates on hepatitis B

3.1 Impact targets and achievements to date

SM presented on the World Health Organization (WHO) impact targets and definitions for hepatitis B virus (HBV) and highlighted the progress made in England in reaching these.

Incidence impact targets

Mother-to-child transmission (MTCT) target has been met, however systematic data collection is needed for local venepuncture screening among children not receiving dried blood spot testing (DBS) and work is being done to improve uptake of DBS among children. Data not yet available for prevalence in under 5's but seroprevalence studies are ongoing and there should be data later this year. There is modelling work being carried out to understand reduction in incidence of chronic HBV infection.

Mortality impact targets

These targets focus on relative and absolute reduction in HBV-related deaths. There has been a small increase in mortality compared to 2015 baseline and absolute mortality rate target has been met.

Incidence programmatic targets

These targets focus on coverage of antenatal screening, coverage of antivirals in pregnant women, coverage of timely birth dose of vaccine for new-born, and coverage of HepB3. All of these targets have been met except there is currently no available data on antiviral coverage in pregnant women and work is being done to systematically collect this.

Treatment programmatic targets

These targets focus on coverage of treatment and diagnosis of people with chronic HBV. The proportion of people diagnosed or on treatment is not currently known and modelling work is in progress in collaboration with the University of Bristol to look at this.

In summary, where there is available data good progress is being made against the targets, aside from relative mortality. Where the data is not available, work is being done to get this data.

3.2 Programmatic targets: HPRU modelling - prevalence and problem solving

RH presented on HBV modelling giving an overview of HBV prevalence modelling with ideas from hepatitis C virus (HCV) and HIV. Population surveys pose difficulties as a method and so

the multi-parameter evidence synthesis (MPES) method, focusing on combining multiple sources of risk group-specific information, is preferred. The principles of this approach have been applied to initial HBV prevalence modelling using antenatal testing population and Sentinel Surveillance data. This will be expanded to include further data sources, such as emergency department (ED) testing, overall numbers of new HBV diagnoses, testing in specific risk groups, GP testing, prison testing. There is good progress being made towards getting national prevalence estimates but there are questions around whether there are other data sources that can support or replace the assumptions for representative relative risks from Second Generation Surveillance System (SGSS) positivity.

Members discussed the numbers of HBV diagnoses in England with a view to better understand the undiagnosed population. Points were raised about the large numbers of HBV being diagnosed in the ED testing pilot and the possibility of including in MPES. It was highlighted that there is a need to consider the risk profiles of people attending ED and the differences in risk profiles of people being diagnosed with HBV compared to HCV.

There are large numbers of HBV being diagnosed in migrant populations. It was raised that work is being done to understand the characteristics of people using ED as a primary care contact and that disproportionately people using services are from vulnerable groups. There are issues collecting data on country or region of birth and a need to collect this data systematically. UKHSA is receiving ED blood-borne virus (BBV) testing pilot data. There is an ED BBV testing evaluation group within UKHSA led by Rachel Roche and this is the forum to discuss co-ordination of benefits (COB) and ethnicity data. DL and RS are focusing on HBV treatment monitoring.

Action for next meeting

RR to give overview on ED Evaluation and RS and DL to present on HBV diagnoses and treatment monitoring work.

3.3 WHO revised treatment guidelines

PK presented on the WHO revised treatment guidelines. There is a push globally to change treatment guidelines due to estimated figures on deaths from complications including hepatocellular carcinoma (HCC).

The WHO guidelines are likely to be simplified so that anybody with a HBV DNA above 2,000 IU/ml or anybody with surface antigen in the absence of HBV DNA and evidence of fibrosis will be considered a treatment candidate. Earlier this year the Chinese guidelines were updated so that anyone over 30 who is HBV-positive will be offered treatment. There is hope that the European Association for the Study of the Liver (EASL) guidelines will also be simplified. As a result, more patients will be accessing treatment and smarter ways of delivering HBV care need to be developed to cope with increasing numbers, especially as diagnoses increase through routes such as ED testing. The specialist care model is not seen as sustainable to cope with the

number of patients but there are possible simple solutions that could be addressed such as repeat prescriptions without secondary care attendance.

Members discussed the need to have conversations with NHSE around care pathways and access to generics. The point was raised that although treatment barrier may be lowered, not all patients will take up the offer of treatment or other barriers will persist such as difficulty attending clinics. HBV treatment needs to be framed as chronic disease management. Treatment initiation is not the issue in specialist care, it's the monitoring and the model needs to change to ensure people get access to the drugs that prevent HCC.

It was raised that there is a lack of patient representation, patient voice and advocacy for HBV. There needs to be patient support to get the information and awareness out to patients. There have been attempts to put a patient group together but it is all anonymous at this point and getting advocates is a slow process. The British Liver Trust is developing materials and trying to get messages out but need the support of ambassadors.

Three actions from conversation identified for NSGVH members:

1. UKHSA BBV programme managers to work with local networks or health economies to improve awareness and address issues of stigma.
2. NSGVH HBV treatment and care monitoring subgroup to work out what the increased demand on services will be so we can provide policy makers with evidence to inform resource allocation and service planning.
3. NSGVH HBV treatment and care monitoring subgroup to consider what the model of care might look like and discuss with NHSE.

There was a discussion around the goal of primary care being involved to take on prescribing. There was not a clear answer but it will need to involve collaborative working and a shared care model. GP, engagement guidance and education will be key. There will need to be peers and nurse training and support, so not relying exclusively on doctors or primary care. For non-specialists, it should be framed as cancer prevention to fit with long term planning.

There was a discussion around NHSE's investment in HCV and NSGVH would like to see the same for HBV. NSGVH to write a co-signed letter to escalate the concern.

Action for next meeting

Co-signed letter from NSGVH on HBV which will identify the need for HBV leadership in NHSE.

3.4 Treatment registry: HBV care and treatment subgroup

RS presented on the development of the HBV treatment registry. There are ongoing meetings. The main aim is to understand who is in a centre, in care, on treatment, and what that treatment is. There is intention to hold a pilot study to refine the data, RS will present data from Barts to

the subgroup to understand how much work will be involved and what UKHSA can look at through the linkage of data sets.

RS raised question of what UKHSA's role is and highlighted how helpful personal identifiable information (PII) is in monitoring inequalities and ensuring that the right people are being reached. The need for a collective voice was emphasised.

DL raised that any revised treatment guidelines will have impact not only on care and care pathways but will also impact surveillance. Better routes are needed for data sharing and integrated pathways. It would be good to build surveillance needs into the system designed to cope with treatment needs.

RS highlighted success in hepatitis D virus (HDV) treatment registry and the potential to learn from this.

3.5 Enhanced pathway of HBV-infected mothers and infants

SI presented on the surveillance programme for HBV-infected women and their infants. The programme was set up as gaps and areas for improvement were identified. This led to guidance for providers and commissioners to support timely screening and entry to care for HBV-infected mothers as well as updated clinical guidelines.

Investigating MTCT found approximately 70 babies to be positive over a 10-year period. A major factor related to incidence was a high viral load in mothers. To understand pathways associated with MTCT DBS cards were used to test for HBV DNA and found that some infants were likely to be infected in utero so infection in that subgroup was not associated with primary vaccine failure.

The enhanced surveillance pathway launched in 2021 and the aim is to get better characterisation of infection in the antenatal setting and look at what factors impact on outcome. There is ongoing sample collection at an antenatal stage for all mothers and further collection at delivery for those at high risk of transmission. Baby or infant samples are also taken.

Overall, the programme has found there is diversity in the HBV infected population and diversity in their viruses . The programme will see how this impacts transmission and outcome. UKHSA is currently working with Integrated Screening Outcomes Surveillance Service (ISOSS) to get the data on how many with a high viral load are on treatment or will be going on to treatment.

There was a discussion around WHO concerns about treatment during pregnancy and role of hepatitis B e-antigen (HBeAg) in surveillance and treatment guidelines.

Members discussed vaccinations for household contacts and people at risk. There is a lack of data on vaccine coverage for household contacts. This is exacerbated by barriers to GP access and inequalities. There are 2 issues in vaccine provision:

1. Funding, commissioning and responsibility. GPs are pushing back on whether it is their responsibility to provide this, and there is currently no contractual or commissioning responsibility.
2. Data or monitoring of vaccination. There have been audits showing variation of recording and data.

Community stigma issues are also feeding into barriers to vaccines. There is indirect evidence of household transmission occurring but limited. Members raised previous studies which have occurred: The EMPACT-B project (Enhanced management and contract tracing among antenatally screened HBV-infected women and chronically infected individuals) which was enhanced contract tracing and vaccination for HBV, and also a study on DBS of household contacts of pregnant women diagnosed with HBV. There are evidence-based interventions that improve contact tracing and support from an NHSE member with overall responsibility for HBV would be key to driving this forward.

3.6 Occult hepatitis B virus infection (OBI) headline figures

HH presented on screening of anti-HBc (hepatitis B core antigen) for blood donations. Screening has found around 4,000 repeat anti-HBc reactive blood donors with confirmatory testing finding a total of 12 donors with occult HBV infection (that is, HBV DNA in their blood without detectable hepatitis B surface antigen (HBsAg). All confirmed anti-HBc positive donors are subsequently excluded from blood supply and any recipients from donors with occult HBV are being followed up. The screening aims to make the blood supply safer.

DB presented on plans for dialysis guidance. There have been 3 reports from trusts where HBsAg-negative patients had dialysed with other negative patients but were subsequently found to be HBV DNA positive at different levels. Trusts have asked for support for how to deal with these incidents but there is a gap in the guidance so to manage better there will be an audit of practise, review of existing literature, and then pragmatic guidance produced. There have also been a number of cases over the last year of surface antigen positive patients dialysing with HBV susceptible patients but this is a failure to follow established guidance as they were only realised to be positive after dialysis. A briefing note is going to be put out to remind units of current guidance. There was a discussion around referral for hepatologist management of people with occult hepatitis B virus infection (OBI) as there would be nil to treat at this stage, there is no consensus about whether they are at an increased risk of liver cancer, and bigger priorities around increasing treatment and care of those with chronic HBV infection.

4. Break

5. Update on projects and programmes: quick-fire updates

5.1 Hepatitis A

KB presented updates on hepatitis A. A novel strain (HAV 055) identified last year has appeared again this year and has led to a mass vaccination programme due to a cluster of cases leading to an outbreak. Previously, last year the majority of cases were in England, among people of white ethnicity, 60% male, and age 6 to 89, median 58. There was no obvious risk acquisition and no history of travel so it wasn't clear how people had acquired the strain. A contaminated food item was suspected although no specific product was identified.

There were 17 confirmed cases in the East of England between December 2022 and April 2023. These have links to a school and nursery which led to a targeted vaccination programme in the reception class of the school, extending to the whole school and adjacent nursery and coverage of the vaccination programme reached 70%. Cases were still being seen in adults which led to a community-based mass vaccination programme. Community vaccination coverage was fairly low and this might be an issue of COVID-19 fatigue. The local vaccination programme will finish on 21 July if no more cases are detected. This particular outbreak was caused by person to person spread and surveillance of the strain continues.

5.2 Hepatitis E

SI presented an update on hepatitis E. The monitoring of acute hepatitis E continues with nothing remarkable or concerning in the trends. Cases have plateaued and there is no change in the phylotype. In chronic hepatitis E, there are small numbers of relapses in patients with treatment failure and developing resistance. There is a need to better understand what is happening and whether there can be any adaptations to treatment guidelines so a small piece of work is being taken forward to support these patients. The cross government working group hasn't met since the last NSGVH meeting. The British Liver Trust have updated their pages about Hep E. There was a discussion around effective screening and transmission risk in transfusions but the working group have made the point that transmission is low in transfusion and most transmission is in food and this sits with the Department for Environment, Food and Rural Affairs (DEFRA).

The study on rat hepatitis E has not yet started. The assay has been developed and optimised. Ribonucleic acid (RNA) transcripts to act as control material have been generated as there is an absence of readily available rat hepatitis E virus (HEV) material. UKHSA is putting in a proposal to the Research ethics and Governance Group (REGG) to test samples received in the Blood Borne Virus Unit (BBVU). The proposal will be for unlinked or anonymised testing of these samples. The study will test samples that are (a) HEV immunoglobulin M (IgM) and

immunoglobulin G (IgG) reactive, HEV RNA not detected on current assay and (b) hepatitis screen sample which are HEV RNA not detected on current assay. There has been a discussion with Zoe Gibney about accessing samples from specific occupational exposure groups but this may not be easy.

5.3 Hepatitis C

GT presented an update on hepatitis C.

Data needs assessment

NHSE is currently preparing for the second year of the needs assessment and BE is working on analysing year 1 data further and will present when done. Needs assessment data will be written up and published, there has currently been basic analysis and deeper analysis is being undertaken.

Web testing portal

Extensive alpha and beta testing has been carried out and the portal has received cabinet and Department of Health and Social Care (DHSC) sign-off. The website is available in English and Urdu and there are online PDFs in other languages but the website may be extended to include other languages if required. Currently the portal asks for name, postal address, contact number (for order confirmation and negative results via text and for positive patients to be contacted by operational delivery networks (ODNs)), and date of birth (DOB). There are optional data requirements for gender and possible route of transmission but not sure how reliable that information is. The test is a capillary blood test with reflex polymerase chain reaction (PCR). All positive results come through ODNs who contact patients.

The portal went live on 24 April 24 and there was a press release on 13 May. There were nearly 4,000 orders between 2 May and 16 June. Following the press release there were over 1,000 test orders with a 65.3% return rate. There is a need to work on the return rate as currently around 54%. Targeted marketing is being used to encourage people to access the portal and return tests.

Orders and returns by gender are at an almost 50:50 split and there is a good age range. A heat map has been produced on countries of birth. Other than the UK, the next highest country of birth for orders is Pakistan followed by Poland so the portal is capturing individuals from countries that it is trying to target. There had been fears that the ‘worried well’ would be the main audience but orders by deprivation decile suggest that this is not the case but NHSE will continue to monitor.

Antibody results found 88% non-reactive and NHSE are developing a protocol to reduce number of insufficient samples. A total of 11 reactives have been found (rate of 0.5%).

For the next steps, NHSE are continuing to adapt the web testing portal to be as effective as possible. There will be targeted marketing for high risk groups, work is being undertaken with the Hep C Trust to develop case studies for marketing and encouraging testing, the portal is being adapted depending on need, for example, different languages, and NHSE is ensuring there are protocols in place for insufficient samples or people who are positive but not possible to contact.

Members discussed targeted marketing to encourage response rates by looking at whether the data differs in different demographics. Preventx are working on providing this information. There were questions asked around whether people testing have attended services before or not and whether the positive diagnoses are occurring in people who are not being captured in other services. There is more work to be done, especially with ODNs who are contacting patients and seeing if they have come through the system before. It would be useful to link to SGSS and sentinel data to see if people are testing again or if this initiative is reaching people who aren't in touch with other services, such as drug services (as many had written paraphernalia as possible route of transmission). And then for those who do not return kits, it may be possible to see if they then test elsewhere to get an idea of risk profile of those who aren't returning tests kits and whether they are receiving a test elsewhere.

There was a discussion around the positivity rate which is similar to the general population rate but currently there is low sample size. There is now a need to make sure that positives can be linked to care. There is potential for a health economic analysis on diagnosis and cost per quality-adjusted life year (QALY). There was also a question around whether it's possible to look at positivity rate over time as when there is general media coverage, may get more of the 'worried well', whereas this may differ when there is more targeted marketing. This could be looked at in the data.

Antenatal testing

Last year a joint request submitted to the Research and Innovation Development Advisory Committee (RIDAC) for service development of opt-out testing in antenatal settings was rejected. NHSE has worked closely with NHSE infectious diseases in pregnancy screening programme and UKHSA to form a response to the outcome letter and RIDAC has until 14 July to respond. In the meantime, NHSE is continuing conversations with ODN teams that are interested and have buy-in from their maternity screening teams. Meetings are taking place with London ODNs and there is interest from Sheffield, Leeds, Liverpool and Thames valley. Bradford have started doing opt out testing on their own accord. The hope is to still receive support and approvals from RIDAC but currently continuing to work outside of this.

There was a discussion around ability to support sites that want to do it and NHSE highlighted that it requires buy in from the treatment and testing side and needs funding for tests and training. ODNs are aware that they can take part in the screening programme and many have tried to speak to their maternity teams but in the absence of it being a national screening

programme many maternity teams are not interested at this time. WI to put messages on the clinical virology message board to assess lab willingness to undertake the testing.

Members discussed the need for patient facing information to support screening in antenatal settings with a need for clear and simple information in multiple languages. No national patient facing resources available but some sites have developed them and it may be possible to link in with UKHSA colleagues as leaflets already available for HBV antenatal screening.

Issue raised around equity of access as testing being offered in some areas but not others, attempts being made to go through routes which would support a more equitable offer and current work being done to get the data to show the need for the programme.

Action for next meeting

WI to advertise opt out antenatal screening on message board for clinical virology network.

5.4 Health Protection Research Unit (HPRU) modelling update and 4 nations deep dives: high-level overview

MD presented on the HCV 4 nations deep dive held by UKHSA. The deep dive was focused on the metrics for HCV elimination with representation from devolved administrations, the Hepatitis C Trust, academic colleagues, NHSE, and WHO. Aim of the meeting was to:

1. Understand from WHO colleagues the progress that has been made in developing metrics to measure progress against programmatic and impact targets (WHO aim to published technical guidance on world hepatitis day to show preferred methods).
2. Discuss metrics currently used by 4 nations and any future plans. Discuss any additional metrics needed, with a focus on inequalities.
3. Discuss current data completeness and quality and any additional work needed to support monitoring progress to elimination.
4. Discuss the governance progress for verification of elimination and the path to elimination approach from WHO. Explore views towards each of these from 4 nations.

Validation will be assessed by independent verification committee. MD gave an overview of the discussions around impact (incidence and mortality) and programmatic (testing and treatment) targets:

Mortality

Discussed how this is currently measured and whether the target is ambitious enough. There were presentations on different measurement options with different sensitivity analyses. The deep dive attendees discussed the possibility of using wider definitions for death, for example, decompensated cirrhosis and liver cancer. There was a discussion around presenting different

estimates using different definitions as well as the use of attributable fractions. There was a reminder that inequalities should be presented throughout.

Incidence

WHO presented on the preferred measures. RS mapped the data sources available in England that could feed into estimates of incidence and into a modelled approach. There was a discussion around using periodic surveys to test surveillance estimates, the need to synthesise data for modelled estimates, the need to ensure maintenance for robust systems, and a discussion around reinfections as an indicator of incidence.

Proportion diagnosed

WHO target of 90% of people living with HCV diagnosed. There was a discussion around using a cumulative or annual denominator and the difficulty of estimating the numerator. It was agreed that the cumulative proportion from baseline year of 2015 would make sense and there was a discussion around how to do this and the possibility of using imputation. It was agreed that the current markers used are useful additional national metrics. It was felt that it may be useful to have additional national metric for late diagnoses to see if targeted testing is picking up these individuals.

Proportion treated

WHO definition was the proportion of people living with chronic HCV that have completed treatment. However, there was recognition that this is difficult to measure and that treatment initiation using Blueteq and Treatment Registry data could be used. There was also a discussion around whether those without an NHS or community health index (CHI) number are included in the denominator and the potential to look at sustained virologic response (SVR) with imputation.

There was a discussion around the governance process and path to elimination. WHO technical guidance has defined path to elimination with multiple tiers linked to programmatic targets. No consensus was reached on whether UK should aim for path to elimination or full verification as there is a need to look at the evidence with the revised metrics to see if UK would have evidence in place for a verification dossier. There was agreement that a national approach would be taken for validation with the ability to pull out sub-national areas for improvement.

It was evident that there was lots of rich data and lots of evolving data. There were variable approaches to measurement but strength in data sources and methods used and there is further agreement needed on detail to align measurement for verification. The plan will be to develop working groups and think about verification dossier versus path to elimination.
A question was raised about access to treatment without NHS or CHI number and it was clarified that the difficulty is the mismatch of data sets and how to link so not under or overreporting. The issue sits with the test request.

Members discussed injection safety in programmatic targets and that 100% is achieved due to policies in place but the UK will need to provide evidence of this. This target is within healthcare settings so there will be device procurement data to support. There are separate criteria for persons who inject drugs (PWID).

There are plans for a HBV deep dive towards the end of the year.

6. Any other business

It was agreed that next meeting to take place in late September or early October 2023.

SS raised question about the risk of HCC development post HCV treatment and whether the risk is increased if genotype 3. It was clarified that if HCV is treated then the risk reduced but doesn't go back down to level in general population due to cirrhosis, if a patient hasn't developed cirrhosis then the risk should be similar to the general population. There was no awareness of an increased risk in genotype 3 among someone who has been treated.
MD raised the work around monitoring stigma and development of stigma index. UKHSA are holding a workshop in August to hear about work that has happened in Australia and in other groups to begin a discussion around monitoring and measuring hepatitis related stigma.

The chair thanked those who presented and everyone for their contributions to the meeting.

Actions arising from meeting

Action		Tasked to
1	Devolved administrations (DA's) to be invited to HBV/HCV incidence and prevalence modelling meetings once agendas are firmed up.	MD

About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation health secure.

UKHSA is an executive agency, sponsored by the Department of Health and Social Care.

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