UK Health Security Agency

National Strategic Group for Viral Hepatitis (NSGVH)

Minutes of meeting held on 16 November 2022
Nobel House, London, 10:30am to 2:30pm

Attendees

Members:	Will Irving (WI, Chair)	**Invited presenters and observers:**	Daniel Bradshaw (DB) *
	Mark Gillyon-Powell (MGP)		Ruth Simmons (RS)
	Samreen Ijaz (SI)		Koye Balogun (KB)
	Peter Vickerman (PV)		Ross Harris (RoH) *
	Caroline Sabin (CS)		Stuart Smith (SS)
	Sema Mandal (SM)		Graham Cooke (GC)
	Chantel Edge (CE) *		Georgia Threadgold (GT) *
	Rachel Halford (RH) *		Patrick Kennedy (PK) *
	Mike Gent (MG) *		Noel Craine (NC) *
	Sarah Hart (SH) *		Gabriel Gurmail Kaufmann (GGK)
	Iain Brew (IB) *		Philippa Matthews (PM)
			Emmanuel Musah (EM) *
			Eimhear Rainey (ER) *
			Annelies McCurley (AM) *
			Ahmed Elsharkawy (AE) *
			Douglas Macdonald (DM) *
			Najla Basketfield (NB) *
Secretariat	Iain Hayden (IH)		

* = virtual attendance

Apologies

Graham Foster, Neil McDougall, Giri Shankar, Claire Humphrey, Mark Aldersley, Monica Desai, Matthew Hickman, Peter Moss.

1. Welcome and introductions

The chair welcomed all those in attendance and apologies were given.

It is likely meetings will continue to be hybrid and therefore the group may not need to be as limited on membership size due to physical space constraints as pre-coronavirus (COVID-19).

The current membership of the group was summarised highlighting gaps in GP, HBV patient and sexual health service representation. It was agreed a current membership summary will be circulated, and the group should feedback other potential key stakeholders to be invited.

Discussions are underway to set up an HBV patient group. Ahmed Elsharkawy, Phillipa Matthews and the British Liver Trust are involved and can feedback in the future. British Liver Trust themselves could be invited.

Action: PM/AE to feedback on creation of HBV patient group and provide contact to attend NSGVH.

MGP suggested the association of directors of public health could be contacted for access that network.

A BASSH member could join the group to represent sexual health services.

Several GPs were put forward as potential representatives, Rachel Hill Tout, Wener Leber and Helen Jarvis.

MGP suggested an antenatal physician could attend and Ashley Brown was suggested.

WI introduced Sema who has taken up the role of deputy director of Blood Safety, Hepatitis, STI and HIV Division in UKHSA and Monica Desai Is now Interim Hepatitis Section Head.

It was raised the strategy group's terms of reference needed a review and re-circulation to refresh everyone on the strategy group's objectives.

Action: IH to circulate membership summary, group to feedback on other stakeholders that should be included after reviewing the group's terms of reference (ToR) and objectives.

Action: IH to contact representatives from GP, Directors of Public Health and other groups.

Action: IH to review and circulate the Terms of Reference.

2. Update and minutes

2.1 The minutes of the previous meeting were agreed as an accurate record.

2.2 Update on actions not appearing as agenda item

Action 1 on agenda: Submit a paper outlining suggested HEV work programme.

SI mentioned the paper is almost complete with comments received from other stakeholders. Sources of data are being explored and a data anomaly is being investigated before further circulation.

Action 2 on agenda: Interim results of HCV case finding fed back to NSGVH to advise how much to invest into primary care HCV testing.

This item will be raised under HCV updates.

3. Updates on projects and programmes

HCV elimination initiatives from NHSE

MGP summarised updates on NHSE elimination initiatives:

- 'Needs assessment' testing is in its final week, almost 11,000 individuals have been tested in drug services and needle exchanges. There is variability between ODNs in current HCV prevalence. The study will help in targeting resources where they are needed. Those in homeless hostels were highlighted as a particular risk factor. Results will be shared more widely in the New Year.
- Drug services are now working to micro elimination criteria, and this is progressing well.
- The national web testing portal contract has been awarded to PreventX, this is being evaluated now with various stakeholders. A beta version is expected in the new year. It will be live before 1 April 2023.
- There are still barriers progressing with opt out antenatal HCV testing. Work is ongoing to ensure this is viewed by other stakeholders as a time limited project to investigate effectiveness as a future screening programme, funded by the national HCV team. There is a need to demonstrate this will not impact on current screening programmes.
- ED opt out testing is being evaluated by UKHSA which is almost rolled out across all of London. It is finding many positive cases of HIV, HCV but especially for HBV, that would otherwise not have been found. Rollout is being facilitated in Brighton and Blackpool. There are other areas interested and now approaching with business cases NHSE.
- Primary care testing of 100,000 people is being carried out and testing of samples is ongoing. Similar investigations on Birmingham are finding lower number of positives than originally expected. A GP is championing rollout across London working with ICBs to increase engagement. There are early approvals to use the national primary care data set to query and feedback to ODNs or at GP level to guide action.
- Cheshire, Mersey and Manchester are considering using the ED opt out testing model in primary care in certain communities with higher risk populations.
- Inequalities in a thread running through all initiatives.
- ODNs are to be offered a winter programme to incentivise testing and diagnosis in hostel and street homeless populations.

Several members raised ED testing initiatives were identifying large numbers of positive cases and clinics are struggling to cope with referrals. MGP clarified funding for hepatitis testing and clinical capacity for HCV is funded by the HCV elimination budget through the ODNs. There is no funding for HBV clinical capacity which is what is causing pressure. This funding is devolved to regions and ICBs, so discussions need to happen with ICBs to ensure appropriate funding is available. This issue needs picking up at the national meeting on Friday.

Other pathway options were discussed to help divert pressure, however manpower for initial diagnostics to place on suitable pathway is lacking.

PM raised issues screening refugee populations who are mobile and can move out the area before being seen in clinic due to waits.

The group concluded that with drives around case finding, it is important to ensure adequate resourcing for follow up. DHSC policy team are invited as observers, these points need to be raised to get their take on the issues. They need to be aware if local teams are considering not engaging with initiatives due to capacity worries, as this will risk elimination goals not being achieved.

Wales will have evaluation data on a system that automatically flags HCV positive patients to specialist nurses. Similar challenges are being faced on capacity to triage.

SS highlighted the HCV Trust has surveyed staff undertaking testing for the needs assessment. Results will be fed back to NHSE and it was recommended similar surveys are undertaken by them directly. The drop in HCV prevalence seen through ED testing initiatives needs to be maintained with good needle exchange programme maintenance.

MGP summarised some additional data being collected through roaming vans, which would be presented when available.

3.2 Monitoring and evaluation of HCV elimination

SM presented on ongoing monitoring and evaluation programmes for HCV at UKHSA.

- The HCV testing and treatment dashboard used to monitor progress at ODN level has had good engagement. An updated version is in development. The dashboard includes local re-infection and prevalence estimates which are due for an update shortly.
- Antenatal testing: more evidence is being collected to put to the national screening committee. This includes a literature review and results of a survey of HCV testing in maternity services. Evaluation of current routine data highlighted missed opportunities to test on key risk factors. Evaluation from 3 pilot centres found little opt out and no impact on uptake of other screening programmes.
- An antenatal HCV care cascade has been mapped to audit provision of such services.
- The initiative has been submitted to IDPS research advisory group who are currently working through their concerns
- ED testing is being evaluated by UKHSA for public health monitoring, HPRU are leading on implementation optimization and economic evaluation. Logic models are being drafted for each infection and will be shared.

It was suggested that the Clinical Virology Network (CVN) should be consulted on antenatal HCV testing initiatives, as they will be completing the testing.

Action: GT/MGP to ensure the CVN are on working groups for antenatal HCV testing.

3.3 Estimating HCV incidence and re-infection

RS presented work estimating HCV incidence and re-infection through the UAM and Sentinel surveillance data. There was no indication of a fall in incidence in PWID. A small decline might be observed in young adults through laboratory reports. Due to the declines in testing through COVID-19, more data is needed to confirm this trend.

Criteria for re-infection were provided and re-infection risks presented by risk groups. Particularly high rates of seroconversion were identified in women in prison which needs investigating further.

Challenges were raised in measurement of incidence and triangulation with other data sets is needed.

It was suggested that investigating by year would be a good next step and praise was given on the value of re-infection data.

3.4 Other HCV research project updates

Epitope and the case finding model will be discussed further next meeting.

Reception testing in prisons was flagged as a concern, with lower post pandemic recovery in testing compared to other settings. MGP commented NHSE have tried to increase uptake by providing targeted temporary resource but further work is needed in areas facing low uptake. It was recommended the bottom quartile is investigated to see what actions are needed.

4. Incidents and outbreaks

4.1 Hepatitis A clusters

KB presented on clusters of HAV strains seen recently including:

- strain HAV055 with 76 confirmed cases
- HAV strain 040 and 041 with 14 cases – associated to fruit berries and the MSM community in Hungary
- strain 067 has been seen in 4 MSM cases linked to sex on premises venues (commercial venues for engaging in public sex); there are concerns HAV vaccination might have dropped in GUM settings throughout the monkeypox outbreak as efforts were focused on this programme

4.2 Outbreak of acute hepatitis in children

SM gave an update from the outbreak, an association was found primarily with adenovirus, adeno associated virus 2 (AAV2) was also detected in some cases, however significance is

not clear. A multi hit of viruses following lack of mixing during COVID-19 was thought to be the cause.

Gastrointestinal Adenovirus isolates will be used as a signal going onwards.

5. Hepatitis B updates

5.1 Hepatitis B elimination goals and progress report

SM presented highlights from a draft Hepatitis B elimination progress report asking the NSGVH for comments and feedback.

- WHO elimination impact and programmatic targets for HBV were summarised and can be seen in Appendix 1 of the report.
- Modelled estimates of prevalence and undiagnosed proportion are still in progress. Current estimates suggest about 200,000 people living with HBV in England.
- There is good progress on elimination of mother to child transmission (MTCT) metrics, a sero-epidemiology study is underway to demonstrate seroprevalence in children. The rate of MTCT has consistently achieved the WHO target. Whilst currently not fully representative of all those at risk, there are plans to improve coverage of this metric through data linkage with Infectious Diseases in Pregnancy Screening (IDPS) team chasing the 12 month outcome of unreported infants.
- There is no data on chronic infection incidence, only acute through Notifiable Infectious Diseases (NOIDS) and SGSS.
- For mortality metrics, England is meeting the absolute targets for deaths from End Stage Liver Disease (ESLD) or hepatocellular carcinoma (HCC) with HBV mentioned on death certificates. England is not on trajectory to meet relative targets from the 2015 baseline, an increase of 2.0% has been seen by 2020.
- Incidence of ESLD and HCC have data quality issues for 2017-2018, more data is needed to confirm the downward trend seen recently. Liver transplants are on a downward trend.
- Targets for antenatal screening and birth dose coverage to prevent MTCT are all consistently achieved.
- Data is missing on antiviral treatment in pregnant women, with hopes this will be available form IDPS soon.
- HBV vaccine uptake from injecting drug users is on a decline and limited data is available on vaccine uptake in prisons yet.
- Positivity of laboratory diagnosis from Sentinel Surveillance have remained around 0.9%, although positivity rates vary by ethnic group.
- Data gaps in progress include data from prevalence and incidence/transmission models, serosurveys, vaccine uptake in high risk groups and testing in prisons and drug services.

The group discussed the difficulty in reaching relative mortality metrics, especially when testing and diagnosed proportion is increasing. There was a suggestion that rates could be

controlled by proportion diagnosed. WHO do give flexibility in how these are reported as long as there is suitable justification.

PV raised the challenge of estimating HBV incidence, which is usually estimated from modelled prevalence. With migration being such a large driver for prevalence, estimating the proportion change in prevalence due to incidence rather than migration will be difficult. Using acute HBV incidence could be a method around this if the symptomatic proportion is known.

The report will be shared with the NSGVH in confidence so feedback and comments can be provided ahead of publication.

Action: Members to feedback on contents and recommendations from the report and suggestions of data that could be included.

5.2 HBV prevalence estimation

RS presented on data sources that could be used in HBV prevalence models and estimations of HBV prevalence from routine laboratory surveillance data using methods from Schnier et al.

An estimate of 210,000 individuals chronically infected with HBV across England was achieved with this method, with a population prevalence of 0.46%. The appropriateness of using 12 to 29-year-old women as the baseline was raised for discussion.

The group discussed the error margins around the estimates and suggested that bootstrapping the data would be worthwhile.

5.2.1 HPRU HBV projects from Bristol

Item 5.5.2 was brought forward in the agenda due to its relevance alongside the previous agenda item.

PV presented on work being undertaken at Bristol:

- A systematic review from 2017 is being updated on national prevalence estimates of chronic hepatitis B in EU/EEA/UK.149 new prevalence estimates were found much of which was identified from grey literature from EU country focal points. Finite mixture models were used to estimate HBV prevalence for populations groups where no data exists in a country.
- A transmission model is being developed including dynamics of migrants and HBV for different European countries. Model is currently focused on the Netherlands and there is hope to develop UK model in the future. The plan is to firstly develop the model to just capture migration and secondly develop to incorporate vertical and horizontal transmission.
- Using antenatal prevalence estimates by country of birth, estimates of England’s prevalence are to be estimated by year building on the estimates presented earlier by RS. The largest challenge is to estimate the uncertainty around these estimates.

The group discussed the proportion of HBV cases that have been diagnosed in England in relation to the estimated prevalence. These can be estimated from new diagnoses sent to UKHSA from laboratory surveillance and after linking to ONS death registry, estimates could in theory be produced.

5.3 Treatment monitoring general discussion

This agenda item was discussed later in the meeting, with a decision to continue the discussion offline and a subgroup meeting to be set up.

5.3.1 HBV treatment and care audit

WI presented data from audits collected at Nottingham University Hospitals. Around 1600 chronic hepatitis B cases since 2007. The audit was still incomplete and some missing data was noted.

There was discrepancy between cirrhotic scoring of APRI and FIB4 from laboratory criteria vs those recorded by hepatologists.

From pharmacy records, they have identified who is on treatment but are unable to tell who needed treatment. 46% of apparently cirrhotic patients received treatment.

The audit found many patients apparently meeting EASL guideline criteria for treatment untreated. Hepatologists in practice are using other criteria to make decisions.

The low numbers on treatment who were cirrhotic by laboratory, rather than clinical, criteria or meeting guideline-driven criteria for treatment were likely due difficulties interpreting or applying EASL guidelines and their appropriateness in clinical practice.

The group flagged common weaknesses when analysing local clinical management databases, that it is challenging to quantify biases if the criteria for interventions or diagnostics is unknown.

PK suggested anyone with a HBV DNA level >2000 iu/ml should be offered antiviral therapy, as it would remove a lot of ambiguity about treatment. This behaviour can retain engagement in clinics and form a cohort of virally supressed individuals when a functional cure is available.

It was raised the evidence base for a change in treatment recommendations is likely achieved and it needs support from policy makers to move this forward. The group discussed the benefits of the treatment strategy including reduction in inequalities.

5.4.2 HIC data sets

PM presented an overview of the NIHR Health Informatics Collaborative (HIC) on HBV, data held by the group and projects underway. Currently data is held on over 8000 HBV positive individuals in secondary care across 6 NHS Trusts in England from 1994.

Key projects include:

- parameters associated with surface antigen loss
- risks and outcomes of antiviral therapy use, exploring treatment eligibility and complications.
- impact of COVID on clinics and treatment.
- natural language extraction from free text reporting.
- risk factors for cirrhosis and HCC is under development along with exploring links with fatty liver disease.
- assessment of loss to follow-up in clinics is also under development

This is not an automated system of data collection and requires data to be collated and submitted from each trust.

The group discussed some biases of the data set, being largely from tertiary trusts and clinic data and other potential uses of the data set for public health objectives.

GC raised the programme is being run with little finance and suggested if the group sees value in it, to make the case to continue in face of upcoming cuts. There is an ongoing collaboration with GSK where they receive some of the data.

The group discussed whether this data set could be used as an equivalent database to Hepcare and the Arden and Gem registry (which is used for HCV treatment) for HBV.

There were discussions around information governance issues, data sharing restrictions and if these were similar to what was experienced with HIV treatment data sets.

SM stated that sharing of patient level and identifiable information is key to ensure linkage between surveillance systems and that for public health objectives a data set needs to be population representative. UKHSA does not have funding to give for surveillance but will be happy to discuss further and collaborate where possible as UKHSA has legal grounds to collect unconsented sensitive data for public health purposes.

5.5 HPRU projects: University College London

CS gave a summary of HPRU themes and updates on work relevant to HBV.

Theme B has many projects largely around tapping into the surveillance data sets UKHSA hold and linking them or using novel methods to produce insights.

A systematic literature review was completed on HBV prevalence in different populations which can feed into population prevalence models.

A systematic review of case-finding and care linkage has also been completed calculating mortality rates in the HBV diagnosed population. This identified whilst hepatitis associated mortality has decreased, liver cancer mortality did not.

Other projects still underway include:

- vaccination strategies for hep A and B attending sexual health services
- assessing COVID-19 coverage and impact of COVID-19 vaccination among those with hepatitis
- HTLV seroprevalence in pregnant women with HBV
- unlinked anonymous testing of samples to estimate HBV seroprevalence

Under theme C:

- developing novel biomarkers for HBV
- understanding epidemiology and management of HBV infection in the UK

Whilst the HPRU is intended to be flexible, the approvals process to change and re-prioritise work is cumbersome and time consuming in practice.

The group discussed differences between mortality figures presented and those from the HBV in England report, concluding differences in methodology, outcome measurement and captured population explain these.

SM raised the EMPACT-B study which found nurse led contact tracing and referral of hepatitis B cases which increased management of contacts. There is a need to assess the cost effectiveness of this as an intervention. The group discussed the current process and roles for contact tracing cases of HBV, which can vary across England.

Audits have shown contact tracing and follow up of cases is poor and conversations with commissioners are needed to improve this.

6. Any other business and close

PM asked how the group can influence policy and guidance on HBV treatment. It was stated the NSGVH was a non-statutory body which is limited to providing advice and recommendations. Members gave examples of success influencing treatment policy in HIV and HCV through professional bodies issuing independent guidance, which can then be endorsed by other agencies.

The BVHG was raised as a suitable group to issue guidance and the group discussed financial implications that need considering if guidance increased the number of people on hepatitis B treatment. ICBs and regional NHS hubs were suggested as the suitable audience to take any modelling costs to decide to adopt recommendations.

The group asked if Bristol HPRU could undertake an economic analysis of a change in treatment guidance by the next hepatitis B focus meeting. This will be taken away for discussion with the team to devise a possible timescale, as 6 months would be very difficult. SM said this can become a recommendation in the HBV report which will be seen by senior officials and DHSC policy teams.

Action: Bristol HPRU to feedback on duration needed to undertake an economic analysis of changing treatment guidelines to all patients with a HBV DNA >2000 iu/ml.

The need for a HBV treatment and monitoring subgroup was raised that can discuss these issues and how to take them forward in more detail.

Action: Set up an HBV treatment and monitoring subgroup.

The Chair thanked all presenters and closed the meeting suggesting the next would be held in early March with a focus on HCV.

Actions arising from meeting

Action		Tasked to
1	Feedback on the creation of a HBV patient group and provide contact to attend NSGVH.	Philippa Matthews or Ahmed Elsharkawy
2	Circulate membership summary and group to feedback on other stakeholders that should be included after reviewing the group's ToR and objectives.	Iain Hayden and All
3	To contact and invite un-represented stakeholders to the NSGVH. Primarily ADPH and GPs.	Iain Hayden
4	Review and circulate group ToR.	Iain Hayden
5	NHSE to ensure the CVN are on working groups for antenatal HCV testing.	Georgia Threadgold and Mark Gillyon-Powell
6	Members to feedback on contents and recommendations of the HBV elimination report and provide suggestions of data they think could be included.	All
7	Bristol HPRU to feedback on duration needed to undertake an economic analysis of changing treatment guidelines to all patients with a HBV DNA >2000 iu/ml.	Peter Vickerman
8	Set up an HBV treatment and monitoring subgroup.	Secretariat