Public Health England

Minutes

Title of meeting	National Strategy Group for Viral Hepatitis (NSGVH)
Date	13 September 2017
Time	10.30 to 15.15
Venue	PHE Boardroom, Wellington House

Attendees	Will Irving (Chair) [Clinical Virologist, University of Nottingham] Mary Ramsay (deputy Chair) [Consultant Epidemiologist, PHE] Charles Gore [CE, Hepatitis C Trust] Ray Poll [nurse consultant, Sheffield] Graham Foster [Prof of hepatology, NHS England ODN clinical lead, London] Claire Foreman [Senior programme manager, blood and infection, NHS specialised commissioning NHS England] Matthew Hickman [Prof of Epidemiology and Public Health, Bristol] Mike Gent [PHE – CCDC Leeds, chair of PHE hepatitis leads group] Richard Tedder [PHE blood-borne viruses lead] Peter Kohn [Director in the Office of London Clinical Commissioning Groups (CCGs)] Sarah Hart Samreen Ijaz [PHE, clinical scientist, blood-borne viruses unit, NIS] Sema Mandal [PHE hepatitis consultant lead] Koye Balogun [PHE, clinical scientist, immunisation, hepatitis, blood safety] Helen Harris [PHE clinical scientist – Epidemiology/Research Associate, NIS] Ruth Parry (secretariat) [PHE – scientist/scientific secretariat, NIS] Giri Shankar [Wales observer] David Goldberg [Scotland observer]
Dialed in	Iain Brew [GP at HMP Leeds, General Practitioner with Special Interest in Hepatitis C] Ahmed El Sharkawy [Hepatologist and Chair of BVHG, Birmingham] Sharon Hutchinson [Scotland observer] Noel Craine [Wales observer] Lucy Jessop [Northern Ireland observer]
Invited speakers	Steve Taylor [PHE – Programme manager, alcohol, drugs and tobacco] Ellen Heinsbroek [PHE – Principal Scientist, Drug Use and Infections Team, HIV and STI Department]

Ross Harris [PHE – Statistician, Statistics and Modelling Economics Department]
Ceri Townley [Head of Information and Intelligence, Specialised Services National Support team, NHS England]

Apologies Peter Moss
Eamonn O'Moore
George Leahy
Rosanna O'Connor

1.0 The Chair welcomed all of those in attendance and online.
The Chair requested whether there were any further conflicts of interest and none were declared.

2.0 Minutes and actions of the previous meeting

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

2.2 All actions had been completed; there were no comments on the Terms of Reference.

2.3 SM gave a presentation which provided a further update on the situation with the outbreak of Hepatitis A in MSM and the vaccine supply issues.
MR gave a verbal update on the Hepatitis B vaccine supply issues.

2.4 SI gave a presentation detailing the recent and current situation with Hepatitis E infection in the UK.

2.5 A request from the Hepatitis C Coalition with regard to membership of the group was discussed. Those who voiced an opinion were not in favour as they felt that in the light of the Coalition's funding from Pharma, there would be a conflict of interest. It was agreed that SM and the Chair would communicate this to the Hepatitis C Coalition when they meet on 15 September, 2017.

3.0 Hepatitis C elimination

3.2 (taken first) The meeting agreed that the roles of NSGVH in the context of the HCV elimination goals were:

(i) To receive and monitor data which would allow assessment of progress or otherwise towards elimination goals

(ii) To identify, and then disseminate/recommend, areas of good practice which would enhance the identification of infected individuals and their movement along an appropriate care pathway towards treatment and cure

In order to fulfil the first role above, the NSGVH needed to understand what the WHO elimination targets are, and what data relating to HCV infection in England were available (including the robustness, strengths and weaknesses of those data sources). A series of presentations were then made to the NSGVH:

3.1 The HCV elimination targets and the position in the UK, Helen Harris (PHE)
HH outlined the key WHO GHSS impact targets relevant to HCV in the UK context:

- Incidence – Target: 30% reduction (2020) and 80% reduction (2030).
    - Progress: Data on incident (i.e. new) infections are difficult to ascertain, for a variety of reasons. Trends from 2011 to 2016 show no evidence of any fall in numbers of new infections.
- Mortality – Target: 10% reduction (2020) and 65% reduction (2030).
    - Progress: Data relating to deaths from HCV-related ESLD or HCC in the UK showed a downturn in 2015 and 2016.

and also outlined a number of service coverage targets in relation to:

- Blood safety – targets for 2020 and 2030 already met in the UK
- Safe injections within health-care – targets for 2020 and 2030 already met in the UK
- Harm reduction for all PWID – data showed that the percentage of PWIDs reporting adequate needle and syringe provision (that is harm reduction) was around 50% and unchanging over the last 5 years
- Increasing the proportion of diagnosed individuals – data showed that the percentage of PWID infected with HCV who were aware of their diagnosis was likewise steady at around 50%
- Treatment coverage – treatment coverage had improved significantly in the last 18 months, with over 12,000 patients treated in England in 2016 to 2017

Current best estimates suggest 214,000 people are living with chronic HCV infection in the UK.

Discussion
NSGVH agreed that encouraging progress was being made in terms of increasing numbers of patients accessing treatments since the introduction of all-oral DAA therapy, and in a downturn in transplants in England and deaths in the UK from HCV. However, areas of concern and for possible future action include:

3.1a The WHO targets on reduction on mortality are really designed for low-income countries. We should aspire to figures much higher than those. Scotland has already set targets of a 75% reduction in incident HCV RNA positive decompensated cirrhosis cases between 2015 and 2020 and (to be approved by SG) a reduction in HCV RNA prevalent cases from 34500 in 2017 to 5000 or less by 2027, that is elimination of disease and infection.

3.1b Needle and syringe provision for PWID is suboptimal. There was no further discussion on this, but this should be addressed at a future meeting. (Peter Vickerman and colleagues have a cost-effectiveness model of NSP that could be presented at a future meeting).

3.1c Around 50% of PWID with HCV infection remain unaware of their diagnosis, with no evidence that this is changing or improving.

3.1d Determination of incidence rates is very challenging. Currently used approaches show a disappointing absence of a decline in incident infections. The use of avidity markers may give a false impression and over-estimate true incidence.

3.3 Data issues

3.3.1: Prevalence and rates of diagnosis, Ross Harris (PHE)

RH explained what data sources were available from which to estimate the numbers of infected individuals, and the number already diagnosed. These include: –

- the Unlinked Anonymous (UAM) surveys of PWIDs
- capture-recapture manipulation of NDTMS data on PWIDs
- hospital episode statistics (HES) for ESLD and hepatocellular carcinoma (HCC)
- ONS mortality data
- laboratory diagnoses reported to PHE
- the Sentinel Surveillance study
- HCV treatment data from pharma sales/Institute of Management Services Supply Chain Management data
- Miscellaneous historical data including blood donor screening, antenatal screening, GUM data, household surveys on drug use, disease progression probabilities from cohort studies

He then outlined previous modelling methodologies including multi-parameter evidence synthesis (which yielded an estimate of 142,000 chronic infections in 2003), and back-calculation studies, comparing and contrasting the strengths and weaknesses of each methodology.

He then described current approaches to modelling, taking the optimal parts of the previous approaches, in an “extended” back calculation approach. This utilised data from NDTMS on number of PWIDs, UAM data on HCV prevalence, HES data, lab reports and numbers initiating therapy. Assumptions regarding disease progression probabilities, rates of injecting cessation and non-HCV mortality were adopted. This yielded a current estimate of 111,000 chronic infections. The apparent significant decline from earlier estimates was largely related to a drop in numbers of PWIDs. It was also estimated that around 50% of these infections were diagnosed.

Cautionary note: it was emphasised that these new modelling data are a work in progress, and the figures may change as further analysis is completed.

However, consistent use of the modelling structure should allow monitoring of trends over time.

RH finally provided a wish-list to enhance this work, including correction for under-reporting in HES/mortality data, better estimates of numbers injecting and cessation rates, more population prevalence estimates eg antenatal screening, better data on numbers treated stratified by risk group and disease stage, on numbers in specialist care but not (yet) being treated, and the "black hole" between diagnosis and treatment.

Discussion
Scotland estimate their chronic HCV prevalence to be around 34,000
Wales estimate their chronic HCV prevalence to be around 11,000
The general feeling was that prevalence estimates for England from current modelling work appear too low, and Ross agreed that numbers are likely to increase as revisions are made to the modelling. However, a decline in prevalence since 2005 is not implausible.

It was felt unlikely the National Screening Committee would approve antenatal screening – a suggestion was to invite the Chair of the NSC to an NSVGH meeting.

3.3.2: Numbers in care – numbers receiving treatment, Ceri Townley, Claire Foreman (NHSE)

CT and CF outlined the data being collected from the Operational Delivery Network (ODN) in England. Initially data collection was limited to Blueteq (a prior approval system) designed to facilitate the reimbursement of DAA therapy, but data collection has evolved and expanded to enable the creation of a patient registry using a database solution provided by Arden and GEM CSU. Data collection has been incentivised via a CQUIN payment to encourage all ODN nodes to enter data on all diagnosed patients in their domain. When defining the content and structure of the patient registry and treatment outcome system a number of data fields were defined as mandatory, subsequent to implementation some of those data entry rules have been relaxed to enable incomplete data to be recorded.

Discussion
The potential for the new A&G database to capture all diagnosed patients irrespective of their point on the treatment pathway was recognised and welcomed.
Issues raised included:
<u>Governance.</u> There had been some disquiet at the initial introduction of the A&G data capture system relating to the transfer of individual and identifiable

patient data to PHE, resulting in refusal/delay to enter such data. NHSE had responded to these concerns by arranging a series of webinars for ODN, Trust and IG leads to ask questions about PHE legal permissions for data collection, and processes in place if objections are raised. A patient information leaflet was produced explaining how data are used. It was now hoped that all nodes would now sign up to deliverance of all data including patient identifiers.

Completion of non-mandatory fields. There were concerns that some key public health fields that are not directly related to drug treatment or outcome could be poorly completed, thereby significantly reducing the value of the data in terms of enabling more accurate modelling and prevalence estimates (and hence all downstream activities arising from those) and of enabling assessment of equity of access to care and health outcomes and identification of gaps. This was countered by explaining that data quality reports could be defined to illustrate the incomplete records for updating by ODNs.

Dis-incentive to entering data on all patients as this might impact on achievement of CQUIN targets. As a result of feedback provided by ODNs a small working group has been exploring how the content of the CQUIN can be re-worked slightly to remove the disincentive.

Data entry. RP raised the issue that nurses were being expected to complete data entry, but this was not what they were trained for, nor was it their role.

Linkage to HepCare. A small number of ODN nodes have HepCare up and running and a number of others may follow. Discussions are ongoing between Arden & Gem and HepCare to allow electronic transfer of data.

3.3.3: Treatment failures Will Irving (UoN and HCV R UK)

WI pointed out that even with 95% SVR12 rates for the new DAA regimens, treatment of 10,000 patients per year would result in the accumulation of 500 treatment failures annually. Whilst some of these would be due to loss to follow-up, at least 400 of them would be genuine virological failures.
Data derived from next generation sequencing of treatment failures in the NHSE Expanded Access Programme (EAP) had shown that

(a) Failure was associated with the post-treatment emergence of drug resistance mutations – also known as ‘resistance-associated strains’ (RAS). It is likely these RAS will impact on the likelihood of response to future retreatment regimens.
(b) A surprising number of ‘rare’ or unusual subtypes were identified, including G1l, G3b, G3h, G4r. These were exclusively in African-born patients. Pre-treatment sequences demonstrated natural polymorphism in these strains

at positions known to be associated with drug resistance. These subtypes were not identified by routine laboratory genotyping methodologies.

There was no robust national system for collection of data relating to the prevalence of unusual subtypes which might be naturally drug resistant, or to the emergence of RAS in treatment failures. It was suggested that it might be prudent to address this gap in data collection.

4.0 Case-finding, engagement and treatment best practice

4.1 NHSE case-finding sub-group, Ceri Townley (NHSE)

CT outlined the activities of the NHSE HCV sub-group: case-finding, set up to support NHSE strategic drug procurement and commissioning by providing assurance of likely numbers of treatable patients, but will also identify opportunities to pull patients through to therapy. Stakeholders included PHE, drug and alcohol services, Hep C Trust, NHSE. A document is in preparation outlining possible interventions designed to increase treatment numbers, together with costing implications.

Discussion

It was agreed that the output of this group would be circulated to NSGVH for discussion at future meetings.

Many of the highlighted interventions had already identified by practitioners, but there may be little or no evidence of impact and cost-effectiveness.

4.2 Overview of case finding, Charles Gore (Hepatitis C Trust)

CG identified the issues – maybe 70-100000 undiagnosed, plus a further 30,000 to 60,000 diagnosed but not in clinics – who are they, where are they?

He then outlined issues and potential solutions surrounding the cascade of care in specific patient groups including:

- Prisoners
- PWIDs
- Diagnosed but lost to services
- General population
- Others including migrants, men who have sex with men (MSM), South Asians, East Europeans, PEIDs, homeless, mental health

Discussion

NSGVH will focus on prisoners at a future meeting, and will also discuss the general population and all groups included as “others” above.

Data on PWIDs is presented in the next item.

The question of how, ethically, to re-engage patients lost to follow-up is an important one. There is scope here for a national agreed way forward to discuss with Caldecott guardians.

Further discussion of the issues raised by CG will be informed by the circulation of the conclusions of the NHSE case-finding sub-group (see above).

4.3 Data collected about HCV in PWID, Steve Taylor, Ellen Heinsbrook (PHE)

ST provided an overview of data sources collected by the National Drug Treatment Monitoring System (NDTMS) relating to PWID. The primary purpose of this data collection is performance management of drug treatment and to inform government policy. In relation to HCV infection, the core data set historically has included (i) has the client been tested (Y/N); (ii) date of last HCV test; (iii) HCV test intervention status (offered/accepted/refused/inappropriate), whilst optional collection related to "is the client HCV positive/ referred to specialist care". These latter 2 fields are now discontinued because recent changes (April 2017) to the non-optional data fields include recording of HCV antibody status, HCV RNA status, and referral for treatment (Y/N). It is not yet known how robust these data will be.

EH provided a detailed overview of the Unlinked Anonymous Monitoring (UAM) survey, which annually recruits 2500-3500 people who inject psychoactive drugs across 60+ collaborating drug agencies in England, Wales and Northern Ireland. Participants complete a short questionnaire, and provide a dried blood spot sample, which is tested for HIV, hepatitis B and hepatitis C. To estimate HCV incidence, HCV antibody avidity testing had previously been part of the UAM testing, but since September 2016 HCV RNA testing is routinely done instead. The survey is unlinked and anonymous: participants cannot get their results back and the results of the survey cannot currently be linked to other surveillance systems. The questionnaire includes questions on hepatitis C uptake of testing, individuals' awareness of their hepatitis C status, and if indicated they are hepatitis C positive, whether they have seen a specialist and received treatment. By comparing the dried blood spot results with the questionnaire result, the proportion of people who inject drugs who are not aware of their HCV infection can be estimated (around 50%).

Discussion

ST was asked how data relating to the new NDTMS fields relating to anti-HCV and HCV RNA status was collected. Post-meeting note – the RNA status may be determined by reference to a laboratory result, but may also be dependent on individual client reporting.

The use of UAM data to derive rates of incident infection was discussed. HCV antibody avidity testing had previously been part of the UAM testing, but this may now be abandoned; HCV RNA testing is now routinely done (since September 2016) instead, and discussions to move to HCV antigen testing are ongoing.

The UAM epidemiology and laboratory teams have written a review of the UAM survey, for which endorsement will be sought from the NSGVH in the next meeting.

4.4 Improving the cascade of care for PWIDs, Will Irving (UoN)

WI reviewed data generated from HepCATT (Hepatitis C Awareness Through to Treatment). This was funded by the DH Policy Research Programme. A pilot study of a complex intervention (comprising funding of a half-time “HCV facilitator” in drug treatment clinics was set up. The primary end point was numbers of clients engaged in therapy in the intervention year compared to the previous year. Rates of engagement (and of testing, referral, attendance and treatment) increased significantly in all 3 clinics. No such change was seen in 5 control clinics.

4.5 Is HepCATT cost-effective? Matt Hickman (UoB)

MH presented a cost-effectiveness analysis of the above HepCATT intervention, adapting a dynamic model of the progression of HCV infection from infection through to life threatening liver disease and transmission of HCV between PWID. The preliminary base-case analysis showed a cost-per-QALY of around £14,000. Further sensitivity analysis showed that using more realistic drug costs than the list price resulted in even lower costs per QALY. The cost-effectiveness model will be revised – and some NSGVH members as well as HEPCATT coinvestigators consulted on key baseline parameters and scenarios for sensitivity testing.

Discussion of items 4.4 and 4.5

It is hoped to submit 2 quantitative (plus 1 qualitative) papers on HepCATT for publication. The first, describing the intervention and the results, should be submitted by end September, to be followed by the CE analysis.

Summary of issues identified for further discussion by NSGVH

3.1 Elimination targets:
a) Can we agree a set of indicators specific to England in terms of incidence of ESLD admissions, transplants, and more challenging targets for mortality than the WHO ones?
b) Does needle and syringe coverage for PWID and uptake of other key prevention activity in this group (like OST) need to be improved and if so, how?
c) How can we improve on the 50% of PWID with HCV infection who are aware of their diagnosis?
d) Do we need and how can we derive better estimates of the incidence of new infections?

3.3.1 Data relating to prevalence and rates of diagnosis
a) How can we support/fulfil the wish-list to provide better data – including proper reporting in HES/mortality data, improvement of PWID estimates, better estimates of injecting cessation rates, more population prevalence estimates eg antenatal screening, better data on numbers treated stratified by diseases stage and risk group, on numbers in specialist care but not (yet) being treated, and the “black hole” between diagnosis and treatment.

3.3.2 Numbers in care, numbers receiving treatment – NHSE data
a) Data transfer from NHSE to PHE. Can we receive updates on how ODN nodes are signing up to deliver identifiable data? [Action: CT]
b) Can we have clarity on which data fields are mandatory? Can NHSE provide assurance that key public health fields will be retrospectively completed and prospectively become mandatory, using whatever levers/incentives are available in CQUINs? [Action: CT, HH]
c) Can we have an update on the removal of CQUIN-driven disincentives to submitting complete datasets? [Action: CT]
d) Data entry. Can we see markers of data quality? [Action: CT]

3.3.3 Treatment failures
a) Should we/How can we generate accurate data on unusual subtype infection in the UK?
b) Should we/How can we generate accurate data relating to the emergence of RAS in the UK?

4.1 NHSE Case-finding subgroup and 4.2 Overview of case-finding
a) Circulation of the output of the case-finding sub-group would be extremely informative for discussions on what interventions should be recommended to improve on best practice. Those discussions should include the evidence base plus the health economic analysis (if these exist) of those interventions. NSGVH should aspire to facilitating the evidence synthesis and prioritisation of what should be implemented now/later.
b) NSGVH should review data and evidence of best practice in relation to prisoners and other identifiable population sub-groups at future meetings.

c) NSGVH should push forward the strategy of retrieving patients previously diagnosed but with no evidence of engagement with an appropriate care pathway. This will require a nationally agreed policy on the ethics of such an approach.

4.3 Data collection in PWID

a) How can we use the UAM surveys to improve estimates of incident infection?
b) Review/summarise current best evidence on the number of people injecting drugs in England.

4.4 and 4.5 Improving the cascade of care for PWID

a) The HepCATT data show a specific intervention to be both effective and cost-effective. How can we turn this data into action and commissioning?