Can the United Kingdom control viral hepatitis?

Preliminary meeting conclusions

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How England, Wales, Scotland, and Northern Ireland fit together - decision making -

- The UK harbours four countries in one, including four administrative entities.
- The four Departments of Health share activities and have common advisory bodies.
- Prevention is the responsibility of the health protection centres in each country, and is based on epidemiological information and advice provided by the common advisory bodies.
- Healthcare is delivered on the basis of recommendations of bodies such as NICE, which consider the cost-effectiveness of health interventions.
Current state-of-the-art and practice

- Hepatitis A: risk-group vaccination.
- Hepatitis B: risk-group vaccination (many other countries have risk-group vaccination plus universal vaccination programmes).
- CLD is the 5th cause of death in the UK; mortality rate from liver disease is still increasing.
- Alcohol and obesity are important factors interacting with HCV infection.
- An estimated 250 cases of chronic hepatitis B (CHB) are yearly acquired in the UK; 7000 cases are acquired outside the UK.
- There is no action plan available for CHB; there is a national strategy and action plan for chronic hepatitis C (CHC), which includes the establishment of Managed Clinical Networks.
Epidemiology of hepatitis B in the UK

- The UK is a very low-incidence country:
  - Acute cases of hepatitis B predominantly occur in adults.
  - There is a high proportion in high-risk groups.
  - Ethnic-minority children may also be at risk.
  - A substantial proportion of individuals has no known risk.

- The UK is a low-prevalence country:
  - Low prevalence: < 2% hepatitis B surface antigen (HBsAg).
  - The role of hepatitis B vaccination is limited in the UK, because a large proportion of HBsAg carriers acquired infection in childhood, prior to their immigration to the UK.
  - UK carriage rates are high in ethnic minorities.
  - There is scope for improving current control measures.
Hepatitis B virus virology

- HBV genotypes are unevenly distributed over the world.
- HBV genotypes can be matched to specific ethnic groups and limited geographical regions.
- The hepatitis B core protein (HBcAg) contains amino acid motifs that correlate with ethnic origin rather than with genotypes or subtypes, implying a common immune selection.
- Variability in HBsAg leads to diagnostic insensitivity; current HBsAg assays are still not fully inclusive.
- Lamivudine treatment can lead to non-detection of HBsAg due to overlap of the genes.
- Most persons with HBsAg have detectable HBV DNA – consideration should be given to a more widespread use of HBV DNA as a primary diagnostic test for active liver disease.
- Occult HBV infection occurs, but its clinical / diagnostic importance is unclear at present.
Clinical aspects of hepatitis B: current decision making in the UK

- Treatment of HBV infection is part of the control of the disease (i.e., secondary prevention).
- Hepatitis B is a complex disease:
  - Clinical care of hepatitis B is still evolving.
  - New antiviral drugs are being introduced.
  - Short-term studies show effectiveness of treatment.
  - Longer-term studies show a reduction in complications.
- There are disparities in judgements about treatment decision making.
- Clinical and theoretical paradigms are not always easily reconciled with economic decisions.
Selective immunisation programme in Glasgow includes antenatal screening; IDU programmes; programme in clinics for MSM and female sex workers; HCWs; travel clinics; routine immunisation of the prison population.

The adolescent hepatitis B vaccination study in Glasgow is a two-stage study to assess feasibility and accessibility of a universal approach:
- Focus group study.
- Vaccination campaign.

Focus group study revealed that:
- Knowledge on HBV infection is very limited.
- Most pupils and parents favour hepatitis B vaccination.

The vaccination campaign was a success, with
- A very high vaccine uptake.
- High expectations to continue the programme.
Hepatitis B: public health aspects – London: actions to improve prevention and control

- Improve completeness of laboratory reports and participation in reporting.
- Improve local surveillance.
- Support NEX services and increase the number of free needles to be distributed.
- Ensure agreed care pathway for infants born to HBsAg-positive mothers and full hepatitis B vaccination course.
- Support prisons and GUM services in delivery of hepatitis B vaccine.
- Ensure patients referred to specialist hepatology services.
- Improve screening and hepatitis B vaccination for household contacts of carriers, especially children.
Conclusions based on a cohort model using defined epidemiological and demographic parameters, new assumptions, and cost parameters.

Vaccination will have little short-term impact on burden of HBV-associated chronic disease.

Universal infant / adolescent vaccination is unlikely to be cost-effective, unless a more attractive cost for hepatitis B vaccine is used in the model.

Risk-group hepatitis B vaccination is more likely to be cost-effective than universal vaccination.

Improving a selective immunisation programme (e.g., in prisons) has potential to reduce HBV transmission.
Comments on cost-effectiveness modelling

- Improved disease progression rates were used in the presented model.
- Indirect costs of hepatitis B-related diseases were not taken into account, contrary to what a number of other countries do.
- The calculations were done in LYGs rather than in QALYs.
- The price of a hepatitis B vaccine course (ca. 15 £) does not compare with the prices used by public health institutions in comparable countries.
- Risk strategy as such should also be evaluated economically.
- The mentioned factors may have an impact on the outcome of modelling cost-effectiveness of any public health measure applied or to be introduced. This should be taken into account when evaluating the presented modelling results.
The overall prevalence of hepatitis C in the UK is low.

Many are unaware of their HCV infection.

The burden of HCV infection is the greatest in IDUs.

The incidence of HCV infection among IDUs remains high.

Challenges for the UK:
- Prevention of HCV infection among current injectors.
- Diagnosis of HCV-infected persons who most need therapy, to prevent disease progression.
Cost-effectiveness of case finding for hepatitis C in former injecting drug users

- Model shows that case finding for hepatitis C is probably cost-effective.

- This cost-effectiveness is less striking than that of treatment.

- Data are very limited in specific settings and for the IDUs population.

- Further empirical (probably observational) studies are urgently required.
Current management of diagnosed cases of HCV infection

- **Goals of treatment:**
  - Prevention of long-term sequelae.
  - Reversal of liver damage.
  - Elimination of virus.
  - Resolution of symptoms.
  - Abolishment of the source of infection.

- **Assessment and selection are essential:**
  - 30% of HCV-infected patients are treated.

- **Compliance with therapy is essential:**
  - Full support team required.

- **Outcomes of therapy are limited:**
  - Only 50% of treated patients achieve SVR (sustained viral response rate).
National hepatitis C strategies, action plans, and guidelines

- What do we have?
  - A hepatitis C action plan for England; a proposed hepatitis C action plan for Scotland; BSG guidelines; SIGN hepatitis C guidelines; NICE and SMC; national and international clinical and laboratory guidelines.

- How do we do on strategies, action plans, and guidelines?
  - What is the problem? → done
  - What to do about it? → done
  - How to do it? → still unclear
  - Permission to do it? → done
  - How to measure it is being done? → still unclear
  - How to fund it? → still unclear
  - Who is responsible? → done
HCV infection: monitoring of end-stage liver disease and prediction of disease burden

- HCV-related end-stage liver disease is not uncommon, is increasing, and is usually associated with an alcohol problem.
- The young age of decompensated patients presenting to hospital with both HCV infection and an alcohol problem suggests that the combined effect of these two factors accelerates liver disease progression.
- Thousands of past IDUs (mostly aged 30-49 years) have chronic hepatitis C and are undiagnosed.
- Identifying the above group and considering individuals for therapy should be regarded as a priority.
- If the current low levels of antiviral treatment do not increase in the future, the numbers of individuals developing severe HCV-related disease will increase considerably.
Modelling injecting drug use and transmission of HCV

- Can the UK control hepatitis C?

- Epidemiological evidence:
  - Increase in incidence and prevalence.
  - Increase in injecting frequency and risk.
  - Increase in injecting drug use and crack injecting drug use.
  - Decrease in coverage of syringe distribution.

- Model evidence:
  - Reductions in HCV prevalence (and incidence) are possible.
  - There is a sustained increase in syringe distribution required to reduce HCV transmission; the threshold level needs to be assessed.
  - We need to target recent injectors early after initiation, in order to have the greatest impact.
  - The validity of the model is limited by behavioural and biological uncertainty.
Hepatitis C: economic issues

- The conclusions of the HTA study were presented.
- It is overall more cost-effective to provide antiviral treatment at a mild rather than at a moderate stage.
- Antiviral treatment is not cost-effective at a mild stage for older patients (> 65 years of age) with HCV genotype 1.
- The model is more conservative than previous estimates:
  - Earlier stage of the disease.
  - Lower estimates of disease progression.
  - Lower SVRs based on pragmatic NHS RCTs (randomised controlled trials).
  - Empirical estimates of QOL and cost.
Epidemiology and control of hepatitis A in the UK

- Hepatitis A incidence is at historically low levels in the UK.
- Surveillance is incomplete.
- Utility of HVA genotyping needs evaluating.
- Highest-risk groups are IDUs, MSM, South Asians, and travellers.
- National hepatitis A control policies are based on hygiene and administration of HNIg (human normal immunoglobulin) and vaccine.
- Local practice varies.
More consideration should be given to HCV-positive persons who do not benefit from treatment after screening.

An exhaustive list of subgroups for whom HCV treatment is not cost-effective should be provided.

Balancing the information regarding selective / universal hepatitis B vaccination is important (cautionary words should be used; e.g., ‘universal vaccination may cost more than what the UK is prepared to spend’).
Modelling - Indirect costs should not be taken into consideration according to NICE and similar advisory bodies.

Modelling - If we recommend taking indirect costs into consideration, then it should be applied to all modelling exercises, including those regarding hepatitis C.

Modelling - The range of hepatitis B vaccine prices should be given:

- The cost structure of hepatitis B vaccines in each country should be taken into account (e.g., discounts made when buying several vaccines from the same manufacturer).
- The mentioned 15 £ is the cost of the whole vaccination course (vaccine plus administration).
Prevention of hepatitis B in the British immigrant population: targeting this specific group should be emphasised (cfr USA recommendation 1990s).

The UK should benefit from the lessons learnt in other European countries.

General information on the programmes in the rest of the world should be provided.

It was requested to put the UK data in a broader framework.

Specific groups of HBV-infected persons should be targeted to benefit from antiviral treatment.