

Can the United Kingdom control viral hepatitis?

Preliminary meeting conclusions

Guido François

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).
- Hepatitis B and C – chronic liver disease (CLD): prevention and treatment.
- 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.

Hepatitis B: public health aspects – Glasgow

- 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.

Hepatitis B in the UK: economic aspects

- 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.

Epidemiology of hepatitis C in the UK

- 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.

Discussion and additional comments (1)

- 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’).

Discussion and additional comments (2)

- 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).

Discussion and additional comments (3)

- 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.