Please find my comments as a clinical expert to the NHS England responses to the Single Technology Appraisal (STA) on Ledipasvir-sofosbuvir for treating chronic hepatitis C [ID742].

I look forward to the discussions on this and the additional STA's for daclatasvir (Daklinza®) [ID766], and paritaprevir/ritonavir/ombitasvir (Viekirax®) +/- dasabuvir (Exviera®) [ID731] being held on 23rd June.

The remit of the STA was to appraise the clinical and cost effectiveness of ledipasvir-sofosbuvir within its licensed indication for treating chronic hepatitis C and it has done this. The responses from NHS England indicate that in their view the NICE STA recommendations should additionally take into account a much broader perspective of affordability of a treatment within the context of limited overall NHS resources. This runs counter to the long held use of cost per QALY as the benchmark for cost effectiveness.

A detailed rebuttal of many of the arguments put forward by NHS England has been provided by BSG, BASL and other organisations representing clinicians specialising in this field.

The advent of directly acting anti-viral therapies for hepatitis C represents a very significant clinical advance with the opportunity to now cure most people infected with HCV, if identified and treated. Whilst the evidence base continues to grow rapidly, with the data from large clinical trials increasingly supported by real world experience of using these medications, the evidence behind the appraisals for the use of these treatment options was already large and comprehensive. Deferring recommendations for 18 months to allow a multiple technology appraisal to take place at this stage is both inappropriate and unfair to patients with HCV infection.

The debate over how to implement recommendations and how to fund them is clearly pertinent and challenging. We all recognise the need to work within financial constraints, but it is unfair to apply a different threshold for cost-effectiveness to hepatitis C than other disease areas. There will be a number of constraints on the use of these treatments in the next 12 months, importantly including current service organisation and capacity, as well as finance. Inevitably there will be some clinical prioritisation of those treated, and the recent confirmation of the extension of the NHS England treatment programme to include all cirrhotic cases is very welcome. This will keep many treatment centres working at or close to capacity for some months to come. However, treating only cases with advanced fibrosis misses the opportunity of preventing disease and leaves those patients successfully treated still at risk (albeit reduced) of encountering complications subsequently. Previous work makes it clear that treating HCV early is effective and clearing HCV RNA is a cure that will prevent liver disease developing in the absence of other disease drivers. It was not in NICE's remit to identify a strategy for phased implementation of its treatment recommendations, but this could be part of the work of the CRGs and specialist bodies to guide this. Any decisions need to take into account multiple factors that would make early treatment appropriate, not just liver fibrosis severity. The recent call for HCV Operational Delivery Networks that will cover the whole of England potentially provides a platform for oversight of treatment.

I hold the view that the evidence base for the clinical and cost effectiveness of the new HCV treatments is compelling and that the NICE review has been robust and thorough. NHS England's concerns over possible budgetary impact on treating a prevalent condition such as HCV are understandable, but the process of planning for the implementation of NICE recommendations falls

within the remit of specialised services and the CRGs and should not be used to prevent NICE sticking to its remit of appraising the clinical and cost effectiveness of the new HCV treatments within their licensed indication for treating chronic hepatitis C.

Matthew Cramp