The Hepatitis C Trust

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Submission to NICE for the partial review of existing guidance no. 75, assessing the use of interferon alpha and ribavirin in the treatment of mild chronic hepatitis C.

This short submission by The Hepatitis C Trust will not address the issues of clinical effectiveness or cost effectiveness, except peripherally, since other submissions will be doing that. Instead it will set out the patient perspective as well as touching on issues of public health and equity of access to treatment.

We would like to begin by asking NICE to include in its introduction to hepatitis C (set out under 'Clinical needs and practice' in TA 75) a number of points:

1. The public health aspect of hepatitis C. Hepatitis C affects not just individuals but also the public health of the country, because it is infectious, large numbers are infected with the chronic stage of the disease and there is no vaccine.
2. The prevalence range (300,000 – 600,000) from the report of the Royal College of Physicians, Edinburgh Consensus Conference on Hepatitis C of April 2004 and the result of the latest prevalence modelling by Southampton University[i].
3. The numbers currently receiving treatment. We believe this to be around 3,000 patients in 2004 but we do not have reliable data. This compares with a similar figure for 2003, before the results of NICE's TA Guidance 75. This is important both because it highlights the public health facet of hepatitis C and what is or is not being done to decrease the pool of infection and because it suggests there may be barriers to treatment, one of which – biopsy – is central to consideration of mild disease.

Public health *is* an issue in the case of an infectious disease. The less people that are offered treatment, the greater the pool of infection that remains and the greater the chance that infection is passed on accidentally. Three obvious ways this can happen are from mother to baby at birth, through unintentional sharing of household implements such as razors and via needlestick injury (continual monitoring with blood tests is typically required for those whose disease is currently too mild to allow them treatment). The costs associated with this do not feature in assessments of cost effectiveness. We would therefore like to urge NICE, should cost effectiveness be a borderline decision, for example for genotype 1 patients, to take this into account and recommend treatment.

Current NICE guidance requires the use of biopsy to determine eligibility for treatment, yet biopsy is a significant barrier to treatment, which we believe is one of the reasons the UK is treating 3,000 patients a year while France, Germany, Italy and Spain are each treating between 10,000 and 20,000 annually. Biopsy is an invasive, frightening, often painful and occasionally dangerous procedure. We asked 50 patients, who did not want to do treatment, their reasons and 19, more than a third, cited biopsy as at least one of the reasons. In addition, we have continually come across instances where waiting times for access to biopsy have been so long that they have permitted what amounts to a flouting of NICE guidance. The extension of treatment to those with mild disease would remove this problem. Conversely, the continued restriction of it to those with moderate to severe disease means, for someone anxious to have the treatment as soon as possible for one of the reasons discussed below, the need for repeated biopsies until a sufficient degree of fibrosis or necrotic inflammation is visible.

There are many reasons for patients to want to 'cure' hepatitis C, aside from issues of morbidity and mortality, and therefore for NICE to give them the opportunity to access treatment regardless of the stage of their liver disease:

1. Having children. There is a 6% risk of an infected mother passing hepatitis C to her child at birth[ii]. This is worse than a 1 in 17 chance and is not acceptable to some. For example, one patient (who is making a TV documentary with us) is currently undergoing treatment precisely because she is 38 years old and wants to have another child *and her first child was born with hepatitis C.* Women with mild disease currently do not have this option. If a women has become infected at say 25 years old, has mild disease and no symptoms and does not want to risk giving birth to an infected child, is it right to deny her available treatment quite possibly until she is past child-bearing age (women's liver disease seems to progress more slowly than men's[iii])?
2. Being infectious. There is a tremendous stress for some in knowing that their blood is infectious (this has emerged from a questionnaire we are carrying out into many aspects of hepatitis C). This is particularly true in the home and around partners and children with the need to be constantly vigilant about blood spillages. For example, diabetes is a recognised if poorly understood co-morbidity (we have 3 HCV+ diabetics in the office and the Chelsea and Westminster hospital screens all diabetics with raised ALTs for HCV) and requires frequent daily use of potentially infectious articles, such as finger pricking implements and blood soaked test strips.
3. Sexual transmission. The single most commonly asked question to our helpline about infectivity is whether hepatitis C is transmissible sexually. This is a major source of anxiety both for those infected and for their partners. Even though we do not believe there is any significant risk for sex between monogamous couples where blood is not involved[iv], this is not yet definitive (a presentation at the European Association for the Study of the Liver (EASL) conference 2005 claimed the risk of sexual transmission was 15%).
4. Discrimination. We have come across people who have lost their jobs as a result of their hepatitis C status becoming known. Perhaps even more disturbingly, we have come across 2 cases this year where hepatitis C infection is being used by one partner to deny access to children to the other, infected partner. One of these went to court in March 2005 and the judge ruled that an infected father could only see his children under supervision in a neutral environment on the grounds that his entire house was potentially infectious because bleach cannot be 100% guaranteed to kill the hepatitis C virus.

5. Stigma. This is still a highly stigmatised disease. Interestingly, in a brief survey we are carrying out because of the rise in HCV/HIV co-infection amongst gay men, we found that most were unwilling to disclose their HCV infection while quite willing to disclose their HIV status. This is because HCV is linked with intravenous drug use (being a 'dirty junkie'). In an ONS survey for the Royal College of Psychiatrists, drug addiction was found to be the most stigmatised of the 7 mental illnesses they looked at[v].
6. Financial costs. There is a significant financial cost to having hepatitis C and therefore a corresponding gain to having successful treatment. For example, life assurance may be unobtainable or only available with a large weighting. This may make it impossible to obtain a mortgage.
7. Clinician discretion. Currently, treatment for mild disease is permitted if extra-hepatic symptoms are sufficient to impair quality of life. Given that many of the symptoms are hard to differentiate from those that could be the product of middle age, overwork or stress, we believe clinicians currently have too much discretion over who has access to treatment. In our patient advocacy work we are continually encountering payment arrangements whereby PCTs have a block contract with a hospital trust. This allows any under-spend allocated to hepatitis C treatment to be used in other ways, such as improving the A & E waiting times. We are extremely concerned that hospital managers may pressure clinicians to postpone or even deny treatment to patients with symptomatic mild disease in contravention of NICE guidelines. A clear policy of extending treatment to all with mild disease would prevent this.
8. Evidence is emerging that older age, as well as increased liver disease, at the time of treatment leads to lower SVRs[vi]. In a paper at the American Association for the Study of Liver Disease (AASLD) conference 2003, Foster and Others estimated that SVRs decline by some 8% every 10 years that treatment is delayed. How can it be justifiable to refuse access to treatment until it is likely to be less effective, especially since it is such a difficult treatment and guidelines only permit one attempt with no retreatment option?

These are extremely good reasons, in our opinion, to offer treatment to people with mild disease. Many, indeed, are so compelling that we urge NICE, in the event that cost effectiveness is not demonstrated, to nonetheless make it available to those with mild disease for a specified set of 'compassionate' reasons, in a similar way to that done for those with extra-hepatic symptoms.

We would also like to emphasise the benefits of achieving an SVR after treatment. We have spoken to 7 patients with mild disease who did PEGIFN/RBV treatment and achieved an SVR. They did not have significant symptoms and so fell outside current guidelines but would be automatically included if treatment was extended to those with mild disease. 5 were type 2 or 3 and 1 was type 1 and were given treatment without biopsy. The remaining case was type 1, was found to have mild disease on biopsy but was offered treatment anyway. All reported benefits – improvements to health and some of those listed above, including an end to discrimination and financial benefits – from treatment and were pleased they had done it, *although the benefits were not always immediately apparent*. One patient, who had had no symptoms before treatment, not surprisingly felt much worse during its course and did

not recover fully for over 18 months. Interestingly, 2 patients reported that they had believed they had had no symptoms. Only after completing treatment and feeling so much better, did they realise that they had previously simply adjusted to low energy and low levels of depression. One person reported that it was only a year after the end of treatment and seeing a nurse write 'no known infection risk' on a vial of their blood that it suddenly hit them what an extraordinary freedom they now enjoyed – freedom from the risk of infectivity, from 'being some kind of leper'.

We would also like to emphasise the importance of NICE. Firstly, the stigmatisation of hepatitis C has meant that patients do not have a strong voice and it is therefore much easier to ignore them than say oncology, HIV or heart disease patients. Secondly, many PCTs are under financial pressure and will spend only where they have to. In this environment hepatitis C patients have virtually no chance of getting treatment unless there is clear guidance from NICE that they are entitled. This applies to hepatitis C patients generally but also particularly to current drug users. Although in TA 75 NICE took notice of our comments and changed its wording so as not to exclude current drug users and this was much appreciated, we would like stronger support as very little is currently being done. We are therefore in the most extraordinary situation at present where an infectious disease is being ignored at the most important point of incidence and where it is necessary to get ill in order to receive treatment. We very much hope that NICE, in its new role with responsibility 'for providing national guidance on the promotion of good health and the prevention …of ill health' will address this in this partial review.

In summary, we believe that for a whole range of reasons treatment offers benefits both to individual patients and to the nation's public health and that it should therefore be available to all, regardless of the stage of their disease, subject only to a case-by-case clinical decision on their ability to tolerate and adhere to it.

On behalf of The Hepatitis C Trust

Charles Gore, Chief Executive 24.04.2005

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[i] J. Parkes and Others. This is awaiting publication. However, the authors have offered to make a copy available to NICE on request.

[ii] NICE HTA 75

[iii] E.g. Salomon and Others. Empirically Calibrated Model of Hepatitis C Virus Infection in the United States, American Journal of Epidemiology, Vol.156, No.8, 2002, 761-773

[iv] Carmen Vandelli and others. Lack of Evidence of Sexual Transmission of Hepatitis C among Monogamous Couples: Results of a 10-Year Prospective Follow-Up Study. *American Journal of Gastroenterology* 99(6): 855-859. May 2004.

[v] Report of the research carried out in July 1998 and July 2003
by the Office for National Statistics (ONS) on behalf of the
Royal College of Psychiatrists' Changing Minds Campaign, page 3

[vi] E Gane and others. AGE AND SUSTAINED VIROLOGICAL RESPONSE IN PATIENTS WITH PERSISTENTLY 'NORMAL' ALT AND CHRONIC HEPATITIS C TREATED WITH PEGINTERFERON ALFA-2A (40KD) PLUS RIBAVIRIN. Abstract 562. 40th EASL. April 13-17, 2005. Paris, France.