Response to the letter from the Skipton Fund

Introduction

The question we have been asked is whether the panel can be more precise in it's quantification of the chance that injecting drug use for less than two years has been the cause of the HCV infection in someone who also has a history of blood transfusion. In order to assist the panel in the assessment of balance of probabilities we have addressed three main issues:

1. Estimating the risk of acquiring HCV infection through short term drug use in the UK
2. Additional factors that may influence the estimates of risk from short term drug use in the UK.
3. Estimation of the risk of acquiring HCV infection through the receipt of unscreened blood in the UK

1. Estimating the risk of acquiring HCV infection through short term drug use in the UK

To answer this question we have drawn on two main approaches. The first approach rests primarily on evidence from HCV prevalence and incidence studies in UK injectors. Mathematical models are then used to estimate the force of infection (the incidence in susceptible IDUs) over time. Supporting evidence comes from studies of injecting drug use in other developed countries. The second approach attempts to estimate the risk of acquiring infection from biological information on transmission of infection associated with sharing needles and syringes. Studies of injecting frequency and sharing in London are used to construct mathematical models that will provide estimates for these parameters which would be consistent with the prevalence observed in London.

a) Data on hepatitis C in injecting drug users in contact with specialist services suggest that the overall prevalence of anti-HCV in current injectors has increased from 39% in 1998 and 44% in 2005.[1] This data is obtained from voluntary testing of oral fluid samples from IDUs attending services in England and Wales. Information is also requested on the current age, the age of commencing injection, and for those no longer injecting – on the age of stopping injecting. In 2005, prevalence in those who had been injecting for less than three years (individuals may have been injecting for any period between one day to 2 years and 364 days) was 18%.[2]

To obtain more accurate estimates of the risk of injecting over time mathematical models have also been constructed.[3] These models use the whole data set to provide estimates of the annual force of infection (the incidence of infection in susceptible individuals) over time and by injecting duration. The best fitting model suggests that susceptible individuals have a four times higher a chance of acquiring HCV infection in the first year of injecting than those who have been injecting for more than one year. Between 1999 and 2003, the average annual force of infection in new initiates (injecting

for less than one year) in England and Wales was estimated to be 16%. After this first year, the annual force of infection declines to be closer to 6%. No major change in the force of infection was detected over the period 1999-2003.

Two cohort studies in Australia have confirmed the higher incidence of infection in those who recently commenced injecting, with rates in those injecting for less than one year at least three times higher than the overall rate.[4,5] Those who have recently commenced injecting were also more likely to seroconvert to HCV in Canada[6] and the USA.[7] The high incidence in recent UK initiates is also confirmed by a study in London that suggested that 42% of susceptible IDUs who had commenced injecting in the past three years became infected during a 12 month follow up period.[8]

Using this model, it was not possible to estimate the risk of infecting for periods less than one year but this does suggest that, over recent years, about 16% of injectors in England and Wales acquire HCV infection in the first year of injecting. It is likely, however that even within the first year of injecting, the risk is higher in the earlier months of that period. Data suggests that most injectors are initiated or assisted by friends,[9,10] and that amongst those who initiate others into injecting, sharing of needles and syringes and of paraphernalia is more common than amongst those that have not initiated others.

b) The second approach may allow us to estimate the risks associated with each injecting episode, based on models and data from London.[11] Using estimates for the probability of HCV transmission from needle-stick injuries and the frequency of syringe sharing a model of HCV transmission in London was constructed. Models that were able to fit the observed anti-HCV prevalence in 2002-3 by injecting duration were then constructed using a range of biological and behavioural parameters. The risk of transmission from a single episode of syringe-sharing with an individual with chronic HCV infection was estimated to be between 1.6% and 4.3%. The prevalence of anti-HCV was estimated to be around 44% in those injecting for less than eight years, with between 25-35% "actively infected". Assuming that susceptible individuals share randomly with IDUs in this population, this would generate a risk of transmission of between 0.4% and 1.5% per single sharing episode for IDUs in London in 2002-3.

2. <u>Additional factors that may influence the estimates of risk from short term drug use in the UK.</u>

The estimates of the risk of injecting in 1a) are based on data from IDUs in England and Wales between 1999 and 2003. The risk estimates in 1b) are based on data from IDUs in London in 2002-3. Major geographical differences in prevalence of hepatitis C exist, with London and the north-West of England having particularly high prevalence rates.[1] This suggests that short-term drug use in these areas is likely to be associated with particularly high risks of transmission.

In addition, to geographical variation, prevalence of infection has probably varied over time. Evidence from Scotland suggests that the incidence of infection declined in the mid-1990s[12] and suggests that drug use in the 1980s was associated with higher levels of risk. The evidence for a similar reduction in England is limited but a decline in HCV incidence in the late 1980s is plausible given the investment in prevention activities that took place in response to the HIV epidemic[13] and would be consistent with trends in hepatitis B transmission.[14] Therefore injecting drug use prior to 1990 is likely to be associated with even higher levels of risk of HCV acquisition.

Clearly the risk of HCV transmission in any individual injector will be highly dependent on risk behaviour, most notably sharing of needles and syringes. Many studies of HCV transmission, however, have found evidence of high rates of infection in the face of low rates of syringe-sharing. Injecting with other people's needles or syringes can occur inadvertently during drug preparation.[15] In addition, injectors who share only with close friends and sexual partners often do not report this as "sharing".[16] Although a high proportion of ever-injectors do report syringe-sharing,[17] sharing of other paraphernalia is even more common and usually undertaken more frequently. Evidence is emerging that such sharing may have a major impact on the risk of hepatitis C infection, and therefore that risk of infection in individuals who deny sharing may be important.

In one cohort study of young injectors in the USA in 1997-1999,[18] individuals who denied sharing had 7.7% cumulative probability of becoming infected by twelve months compared to 13.2% amongst those that reported sharing.[18] A similar study in Australia found an annual incidence of seroconversion to HCV of 54 per 100 person years in those who reported using another IDUs syringe compared to 27 per 100 person years in those who denied such sharing.[4] In both studies, indirect sharing, such as use of shared cookers or filters, were strongly associated with seroconversion to HCV with higher risk than those associated with receptive syringe sharing. This evidence suggests that although sharing of paraphernalia may be a less efficient for HCV transmission, injectors may choose to share such items with a wider network of individuals, thus leading to a greater overall risk.

3. Estimation of the risk of acquiring HCV infection through the receipt of unscreened blood in the UK

The risk of transmission by blood transfusion in the UK prior to the use of donor anti-HCV screening was estimated by Soldan et al.[19] Using data on the prevalence of infection in donors at the start of donor screening, it was estimated that around 0.07% of donors were anti-HCV positive in the period 1980-1991. Assuming that infection would follow receipt of all donations from HCV RNA positive donors, this would equate to an approximate risk per transfused donation of around 0.05% in that period. It is difficult to estimate the risk from receipt of blood prior to 1980. Selective deferral of donors, both on the basis of exposure history or markers of other infection, may have reduced the risk from receipt of blood during the 1980s, implying the risk to recipients was higher in the 1970s and before. Alternatively as the incidence

of HCV infection in the UK probably increased from the late1970s, following the expansion of injecting drug use,[20] the prevalence of HCV in the donor pool may have started to increase during the 1980s, suggesting that risks to recipients was lower in the 1970s and before.

Summary

Overall, the risk of hepatitis C infection with short term injecting in the UK is poorly documented, and is likely to have varied geographically and over time. Although data on one-off or casual injectors is absent, evidence from many countries supports the belief that the risk of acquiring hepatitis C in the early period of injecting is high. The estimated probability of transmission from single episodes of needle and syringe sharing also appears to be substantially higher than the risks associated with a single transfusion of unscreened blood. On an individual basis, it will be difficult to assess the risks associated with single episodes of injecting where sharing is denied, but recent studies suggest that the incidence of hepatitis C in injectors who deny sharing is around half of that observed in those that do report such behaviour.

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