**TITLE PAGE**

# Treatment as prevention: The breaking of taboos is required in the fight against hepatitis C among people who inject drugs

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**FOOTNOTE PAGE**

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**List of abbreviations:**

PWID: people who inject drugs

HCV: hepatitis C virus

DAA: direct acting antivirals

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High prevalence and incidence rates contrast starkly with low detection and treatment uptake rates and that makes the hepatitis C epidemic among people who inject drugs (PWID) a serious public health issue. In expectance of new interferon-free hepatitis C treatment regimens, Martin and co-authors present in this issue of Hepatology mathematical model calculations on an approach which is already well documented in the field of HIV: Treatment as prevention (1). As future treatment regimens will be much better tolerated and even more efficient than current interferon-based dual or triple therapies, they have the potential of being widely used to treat PWID. Taking this into account, the model described in this study suggests that scaling up treatment uptake rates for people who inject drugs with the new direct-acting antivirals (DAA) has the potential to, over time, significantly reduce the prevalence of chronic hepatitis C in this so far heavily underserved population. However, in order to increase treatment uptake rates in this major at-risk group requires drastic changes on several levels, and the breaking of some taboos.

Martin et al calculated the necessary scale up rates among PWID to half the prevalence of HCV infections within the next fifteen years (1). Their mathematical model has been applied to a variety of settings and takes into account different levels of baseline prevalence and treatment uptake and the varying levels of primary prevention measures such as the provision of sterile injection equipment and opioid substitution therapy. In settings with a high baseline chronic prevalence, like in Melbourne, Australia, (50%) and Vancouver, Canada, (65%), the use of future DAAs over the next fifteen years would, at the current treatment rates, only have a very low impact on the prevalence (less than 2%). A 13- to 15-fold increase of treatment uptake would be needed to half the prevalence in these settings. With a chronic baseline prevalence of 25%, like in Edinburgh, Scotland, a mere 3-fold increase in treatment provision could reduce the chronic HCV prevalence to less than 7%. As discussed by the authors, various programmes have proven that such annual numbers of treatment uptake rates are in fact feasible. However, from a more global point of view, such programs remain isolated examples of best practice in their respective regions and have so far had no relevant impact on the epidemic.

Many western countries show similar hepatitis C prevalence levels to the ones in Melbourne and Vancouver (2) with similarly low levels of treatment uptake rates, but with reasonably high coverage of primary prevention measures. To achieve nation-wide treatment uptake rates among PWID that relevantly affect prevalence, ground-breaking changes in the currently inefficient HCV care system for this vulnerable population are urgently needed.

First of all, and easiest to achieve: Treating patients irrespective of their liver fibrosis stage, which is in effect treatment as primary prevention. Today in many countries, fibrosis stage of at least F2 is a prerequisite to obtain antiviral treatment.

Secondly, a paradigm shift concerning reinfection must be made: The risk of reinfection is one of the most mentioned reasons why PWID are not treated. Looking closely at the model of Martin et al, the risk of reinfection actually becomes an indication for treatment since people at risk of reinfection are also the most likely ones to further spread the virus. From a public health perspective, treating those at high risk of reinfection should be a priority and, if indicated, they should be treated repeatedly. Similar model calculations for dual combination therapies with pegylated interferon and ribavirin have shown that this is a cost-effective approach and, in many settings, even more cost-effective than treating patients without intravenous drug use (3).

Thirdly, a relevant scale up of treatment among people who inject drugs is impossible without massively reducing the barriers to hepatitis care. Low awareness, low hepatitis and addiction literacy among healthcare professionals, discrimination and stigmatisation of drug users are all major barriers for PWID to access HCV care (4). Many of those barriers are a result of the criminalisation of drug use (5), one of the taboos that need to be broken. The global war on drugs of today is hindering effective public health measures for PWID and therefore fuelling the HCV and HIV epidemic in this population. Decriminalising drug use would therefore be an important step towards eliminating hepatitis C.

As discussed by Martin et al (1), another taboo that has to be looked at is the highly limited access to HCV standards of care all over the world due to financial restrictions. The cost of today's standard of

care HCV treatment is prohibitively expensive for middle- and low-income countries. Even in Western European countries, access to triple therapies is restricted due to the exorbitant cost of the medication. Prescriptions of interferon-free HCV treatment regimens at similarly high prices will inevitably be restricted by health authorities. High tolerability of those regimens will bring the potential of high applicability. But their short- to medium-term extortionate cost will exceed even the health care budgets of rich countries. Offering hepatitis C treatment at affordable prices is crucial in the fight of the global hepatitis C crisis.

If interferon-free treatment regimens were to be made available at reasonable prices, i.e. only at only a fraction of today's cost, the number of patients eligible for treatment would rise accordingly. Millions of HCV patients in low- and middle-income countries could receive adequate treatment. While it makes no difference to the pharmaceutical companies whether they get their money from a limited number of treatments at a very high cost or whether they make their profit from a much wider use globally at affordable prices, for the global burden of the disease, this could make all the difference.

If pharmaceutical companies don't take decisive steps to offer their medication at affordable prices, governments all over the world will face a HCV induced public health emergency and will be permitted by the World Trade Organization Agreement on 'Trade Related Aspects of Intellectual Property Rights' (TRIPs) to use patent flexibilities. These flexibilities include the issue of compulsory licenses for the import or production of cheaper, generic versions of these urgently needed drugs, despite them still being under patent. This has already been successfully done to improve global access to HIV medication(5).

The excitement about the new, highly efficient and well tolerated treatment will reduce some of the current barriers to hepatitis C care. Testing rates and hepatitis C awareness will increase with the arrival and promotion of the new medication. But to achieve the required treatment uptake rates to

have any relevant impact on prevalence, as calculated by Martin et al(1), drastic actions, coordinated by comprehensive national and regional plans, are now needed in the fight against hepatitis C.

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