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Effect of preventive and curative interventions on hepatitis C virus transmission in Egypt (ANRS 1211): a modelling study

Romulus Breban, Naglaa Arafa, Sandrine Leroy, Aya Mostafa, Iman Bakr, Laura Tondeur, Mohamed Abdel-Hamid, Wahid Doss, Gamal Esmat, Mostafa K Mohamed, Arnaud Fontanet*

Summary

Background Most hepatitis C virus (HCV) transmission in Egypt is related to medical injections and procedures. To control the spread of HCV, the Egyptian Ministry of Health initiated awareness and education campaigns, strengthened infection control in health-care facilities, and subsidised anti-HCV treatment. We aimed to investigate the effect of these interventions on the spread of HCV by mathematical modelling.

Methods We developed a mathematical model of HCV transmission in Zawyat Razin, a typical rural community. Our model assumes that each individual has two distinct types of medical procedures: injections and more invasive medical procedures. To quantify the severity of the spread of HCV, we used the notion of the basic reproduction number R_0, a standard threshold parameter signalling whether transmission of an infectious disease is self-sustained and maintains an epidemic. If R_0 is greater than 1, HCV is self-sustained; if R_0 is 1 or less, HCV transmission is not self-sustained. We investigated whether heterogeneity in the rate of injection or invasive medical procedures is the determinant factor for HCV transmission and whether most iatrogenic transmission is caused by a small group of individuals who receive health-care interventions frequently. We then assessed whether interventions targeted at this group could reduce the spread of HCV.

Findings The R_0 of the spread of HCV without treatment was 3·54 (95% CI 1·28–6·18), suggesting a self-sustained spread. Furthermore, the present national treatment programme only decreased R_0 from 3·54 to 3·03 (95% CI 1·10–5·25). Individuals with high rates of medical injections seem to be responsible for the spread of HCV in Egypt; the R_0 of the spread of HCV without treatment would be 0·64 (95% CI 0·41–0·93) if everybody followed the average behaviour. The effect of treatment on HCV transmission is greatly enhanced if treatment is provided a mean of 2·5 years (95% CI 0·1–9·2) after chronic infection and with drug regimens with more than 80% efficacy. With these treatment parameters, preventive and curative interventions targeting individuals with high rates of medical injections might decrease R_0 below 1 for treatment coverage lower than 5%.

Interpretation Targeting preventive and curative interventions to individuals with high rates of medical injections in Egypt would result in a greater reduction the spread of HCV than would untargeted allocation. Such an approach might prove beneficial in other resource-limited countries with health-care-driven epidemics.

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*Dr Mohamed died in August, 2011

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Introduction

Hepatitis C is a blood-borne disease that has been undergoing global spread for over 100 years.[1] However, its causal agent, the hepatitis C virus (HCV), was identified only in 1989.[2] Findings from epidemiological studies revealed large discrepancies in the spread of HCV around the world.[3] In high-income countries, fewer than 2% of adults have anti-HCV antibodies.[3] Because of routine HCV testing of blood products and increased use of disposable material and sterilisation measures in health-care facilities, HCV transmission is low in high-income countries,[4] remaining a major concern only for intravenous drug users.[4–6]

By contrast, HCV prevalence is in excess of 10% of the general adult population in some low-income and middle-income countries (eg, Egypt, Cameroon, and Mongolia).[3] Medical procedures seem to be responsible for most HCV transmission in these countries.[3] The 2008 Egyptian Demographic and Health Survey[7] estimated that 15% of people aged 15–59 years in Egypt have anti-HCV antibodies and 10% (about 5 million) had chronic HCV infection. However, this high figure is related to past transmission events and is not representative of the HCV transmission occurring in Egypt nowadays. The origin of this epidemic has been attributed to mass campaigns of parenteral antischistosomiasis treatment in the 1960s to 1980s, when intravenous injections with antimony salts were given to 3–5 million individuals older than 6 years.[8] Insufficient sterilisation of medical equipment is regarded as the main cause of HCV transmission at that time.[8] Since HCV-infected individuals can survive for

longer than 30 years, many people who were infected are still alive. They form an ageing cohort of HCV-infected individuals from whom HCV is still spreading to the general population through various health-care procedures (eg, injections, intravenous catheterisation, and surgery).[9,10] Similar epidemiological situations have occurred in Cameroon and Gabon, where HCV might have spread greatly during past medical interventions (eg, anti-malaria treatment and transfusions).[11,12]

See Online for appendix

How much HCV is continuing to spread remains poorly understood; there are no reliable nationwide incidence estimates.[13] Field studies have focused on identification of the medical procedures most responsible for HCV transmission.[9,11] Still, whether this spread of HCV is self-sustained and what public health interventions can efficiently reduce HCV transmission in the general population is not known.

To control the spread of HCV in Egypt, in 2008 the Ministry of Health launched an integrated national strategy,[14] including awareness and education campaigns, strengthened infection control in health-care facilities, and subsidised anti-HCV treatment. The present public health strategy of Egypt is to make treatment available to everyone who attends one of 23 national treatment centres and fulfils the eligibility criteria. The treatment consists of a 48-week regimen with pegylated interferon alfa-2a and ribavirin and has a 60% probability of cure.[15] Limited resources prevent treatment of everybody in need: only 40 000 individuals can be treated per year, mostly around 15 years into their chronic phase, corresponding to F2 Metavir fibrosis stage.[16]

To investigate the effect of these interventions on HCV spread, we developed a mathematical model of HCV transmission using epidemiological data from a well-studied, typical rural community in Egypt.[9] Since HCV transmission typically occurred during iatrogenic interventions,[9] our model was specifically designed to investigate how the frequencies at which individuals undergo medical procedures affect the spread of HCV.

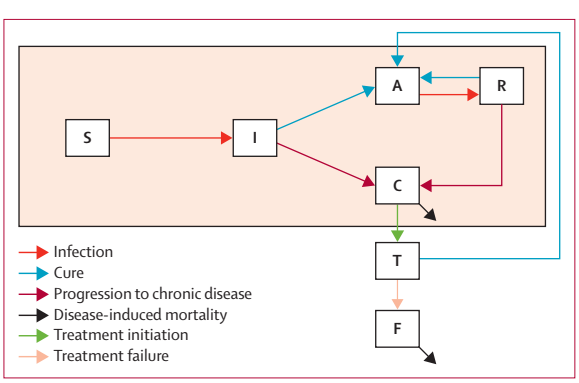


Figure 1: **Flow diagram of the hepatitis C virus transmission model**
The shaded box includes the transmission model in the absence of treatment. A=cured individual. C=chronically infected individual. F=treatment failure. I=acutely infected individuals. R=acutely reinfected individuals. S=susceptible individuals. T=treatment.

Using our model, we investigated various hypothetical interventions, including early anti-HCV treatment—a strategy with recognised success against HIV transmission.[17,18]

Methods

Epidemiological data

We obtained data from two previous epidemiological studies in Zawyat Razin (appendix),[9,19] a typical rural community in the Menofia Governorate with about 20 000 inhabitants and a HCV antibody prevalence of 11·8% in the 3–88 years age group, which is representative of the national level.[9] We also included data from a 2012 study (unpublished), in which we followed up individuals who, in 2002, reported frequent medical injections (appendix). We also included data from the 2008 Egyptian Demographic and Health Survey.[7]

Mathematical model

We constructed a mathematical model describing HCV transmission in the general population of Zawyat Razin, calibrated to epidemiological data collected in Egypt. Our model was inspired by recent modelling work describing intravenous drug user communities.[20] However, injecting drug use is extremely rare, if it happens at all, in the rural area of Zawyat Razin. Therefore, in view of the differences in HCV epidemiology, we carefully reconsidered all modelling aspects (appendix).

Figure 1 shows the population flow of the model. Susceptible individuals become acutely infected; at the end of the acute phase, they either spontaneously clear the virus or become chronically infected. Cured individuals can become reinfected and, at the end of a new acute phase, they either spontaneously clear the virus or became chronically infected. Chronically infected individuals can undergo treatment and recover, or else treatment is unsuccessful and they are no longer eligible for treatment.

In Egypt, HCV is typically transmitted through iatrogenic interventions in the general population,[9] which makes the spread distinct in two regards. First, the population is heterogeneous with respect to their rates of injection and invasive medical procedures. Epidemiological data show that 5% of the adult population takes more than 50% of all injections.[7] Second, transmission of HCV occurs in health-care facilities—an environment where HCV prevalence is higher than in the general population.[21]

To accommodate these features of blood-borne transmission, our model assumes that each individual has two distinct types of medical procedures: injections and more invasive medical procedures; the frequency at which an individual has these types of procedures is henceforth called the rate of access to health-care facilties. Furthermore, the rates of access to health-care facilities are not affected by development of HCV disease—a reasonable assumption for HCV infection, which typically becomes symptomatic only in the late stages of chronic infection.[22]

We stratified the populations in each stage of the flow presented in figure 1 over the rates of access to health-care facilities. This feature also allowed for a parsimonious modelling of the amount of infection in health-care facilities, which takes into consideration that the time scales of the clinical development of HCV infection are much longer than the duration of medical procedures (appendix).

Treatment response rates and other model parameters are according to genotype 4 HCV—the strain responsible for more than 90% of all infections in Egypt (appendix).[23] A decrease in unsafe iatrogenic procedures is modelled as a decrease in the probability of acquiring HCV per iatrogenic procedure after a HCV-infected patient has received treatment.

Calculation of the basic reproduction number R_0

To quantify the severity of the spread of HCV, we used the notion of the basic reproduction number R_0, a standard threshold parameter signalling whether the spread of HCV is self-sustained. R_0 can be understood as the expected number of secondary infections caused by an infected individual in a disease-naive population during the individual's infectious period. Therefore, R_0 does not depend on reinfection, which in the case of HCV remains poorly understood (appendix). Furthermore, if R_0 is greater than 1, HCV spread is self-sustained; if R_0 is 1 or less the self-sustained spread of HCV will stop. R_0 is also widely used to quantify the effect of a public health programme,[18] although it does not specify when the public health programme will have the expected effect.

The R_0 of a compartmental model can be expressed as a function of the model parameters with the next generation methodology. Hence, the value of R_0 and its corresponding 95% CI can be calculated with the parameter values and their uncertainties using the bootstrap method. In which suitable distributions are assigned to the parameters, these distributions are then sampled, and R_0 is calculated for each parameter set to obtain a distribution of R_0 that is used for summary statistics (appendix).

Modelling of whether transmission occurs through a core group

In a population with heterogeneous health-care practices, most iatrogenic transmission is possibly caused by a small core group of individuals who receive health-care interventions frequently. To test for this phenomenon, we modelled a homogeneous population in which everybody accesses health-care facilities at the mean rates. This scenario conserved the total number of iatrogenic exposures, changing only their distribution over the population.

R_0 less than or equal to 1 for the model with a homogeneous population and R_0 greater than 1 for the model with a heterogeneous population suggests that there exists a core group of individuals with frequent access to health-care facilities that maintains the spread of HCV, whereas most individuals remain exposed to HCV without transmitting the disease much. Further R_0 analyses can distinguish whether heterogeneity in the rate of injection or invasive medical procedures is the determinant factor (appendix).

Modelling the effect of interventions when transmission is mediated by a core group

We distinguished two strategic dimensions to HCV prevention interventions when transmission is mostly caused by a core group: (1) targeting the core group with treatment and injection safety programmes, and (2) early testing and treatment (ie, the hit early, hit hard approach), initially proposed for the HIV epidemic.[18] We designed a set of numerical experiments to investigate the multifaceted aspects of prevention of the spread of HCV. First, we compared targeted and untargeted injection management alone. Second, we investigated targeted and untargeted strategies of treatment as prevention, contrasting treat early and treat late interventions by regimens with various efficacies. Third, we explored combined strategies, including both injection management and treatment, addressing both the core group and the general population. In the general Egyptian population, injection safety programmes might be as efficient as those in other developing countries[24,25] and maintaining the present levels of treatment seems feasible. We assumed that the individuals in the core group reached by the intervention programme stop 100% of their unsafe injection practices, but only 80% of this group could be treated because of existing comorbidities. We also assumed that the rest of the population achieves a 10% reduction in the number of unsafe injections and has a 10% chance of being treated if eligible.

Assessment of the rate of leaving the core group

The success of a targeted public health intervention depends also on the rate of joining and leaving the core group—a feature not included in our mathematical model. If the rate is high, then in a short period of time a large number of individuals would be eligible for privileged interventions during the time they belong to the core group. Hence, in this case, the difference between the targeted and untargeted strategies would not be significant. To address some of these concerns, we did a follow-up study in the Menofia cohort (unpublished). At baseline, in 2002, we counted the number of individuals who self-reported regular injection practices for various chronic medical disorders (eg, cardiovascular, metabolic, and rheumatic diseases). In 2012, we re-interviewed these individuals about their injection practices. We excluded self-injections of insulin from the count of injections since they were unlikely to contribute to HCV transmission to others (appendix).

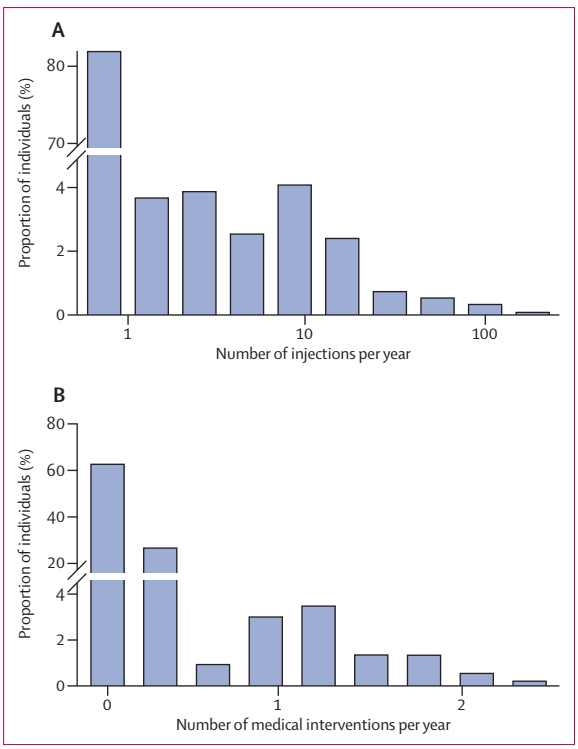


Figure 2: **Yearly rate of injections and invasive medical procedures in Egypt**
Yearly rate of (A) injections on the basis of Egyptian Demographic and Health Survey data[7] covering the rural population and (B) invasive medical procedures on the basis of Zawyat Razin data.[9]

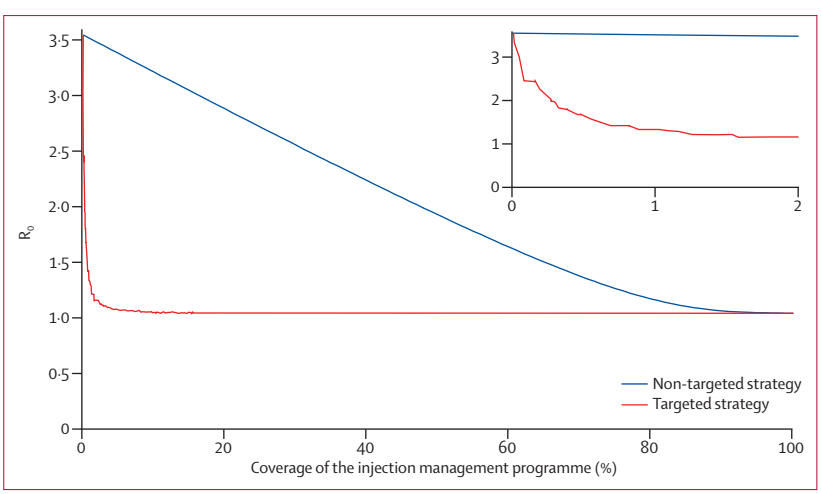


Figure 3: **The potential effect of injection control on the severity of the spread of hepatitis C virus**
The graph shows R_0 (mean of bootstrap distributions) decline versus the coverage of the injection management programme after a non-targeted and targeted strategy. The black graph shows the result of including an increasing number of individuals under injection management, regardless of their health-care practices. The red graph shows the epidemiological effect of injection management when enrolled individuals are prioritised by their injection rates. The inset displays a zoom-in of the main panel in the region of low coverage.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had the final responsibility for the decision to submit for publication.

Results

The R_0 of our model without treatment was 3·54 (95% CI 1·28–6·18). Hence, the spread of HCV would be self-sustained and persist even after the individuals infected during the antischistosomiasis campaigns died.

If everybody accessed health-care facilities at the mean rates calculated in the field studies[7,9] (ie, 2·1 [95% CI 0·0–20·0] injections and 0·23 [95% CI 0·00–1·61] invasive medical procedures per year; appendix), R_0 would be 0·64 (95% CI 0·41–0·93) in the absence of treatment—ie, the spread of HCV would decline without public health intervention if everybody followed the average behaviour. The mean rate of injections is nearly ten times larger than the mean number of invasive medical procedures. However, the probability of transmission by injection is nearly 20 times smaller than that by medical procedures (appendix). Further R analyses showed that an injection rate much higher than the mean is the key feature of individuals comprising the core group, whereas the rate of invasive medical procedures is not a major factor (appendix). Figure 2A shows that the core group is not delimited by a clear cutoff in the injection rate; rather, it occurs because a substantial fraction of the population takes injections at a rate much higher than the mean. This leaves arbitrariness in the definition of the core group, which may be considered, for example, as the 5% of individuals with the highest rates of medical injections (more than ten per year) but also as the 2% of individuals with the highest rates of medical injections (more than 24 per year).

Figure 3 presents modelling results for the decline in R_0 caused by enhanced injection control programmes. R_0 declines nearly linearly with non-targeted programme coverage and then approaches a plateau as almost all unsafe injections are eliminated. The R_0 plateau remains slightly above 1, suggesting that injection control could almost eliminate the self-sustained spread of HCV in Egypt. However, a targeted approach might achieve a substantial decline in R_0 with a much lower coverage; an example of such an approach might be prioritisation of patients with the highest injection rate for enrolment in the injection safety programme (figure 3). In this case, R_0 gets close to the plateau value when the top about 2% of people who receive injections most frequently completely give up their unsafe injection practices. We obtained similar results for less than perfect adherence (appendix).

For Zawyat Razin, our model predicted that the present national treatment strategy had only a slight effect, decreasing R_0 from 3·54 (95% CI 1·28–6·18) to 3·03 (1·10–5·24), which suggests a self-sustained spread. Figure 4A shows that, at 60% efficacy, the present national treatment strategy would not eliminate the

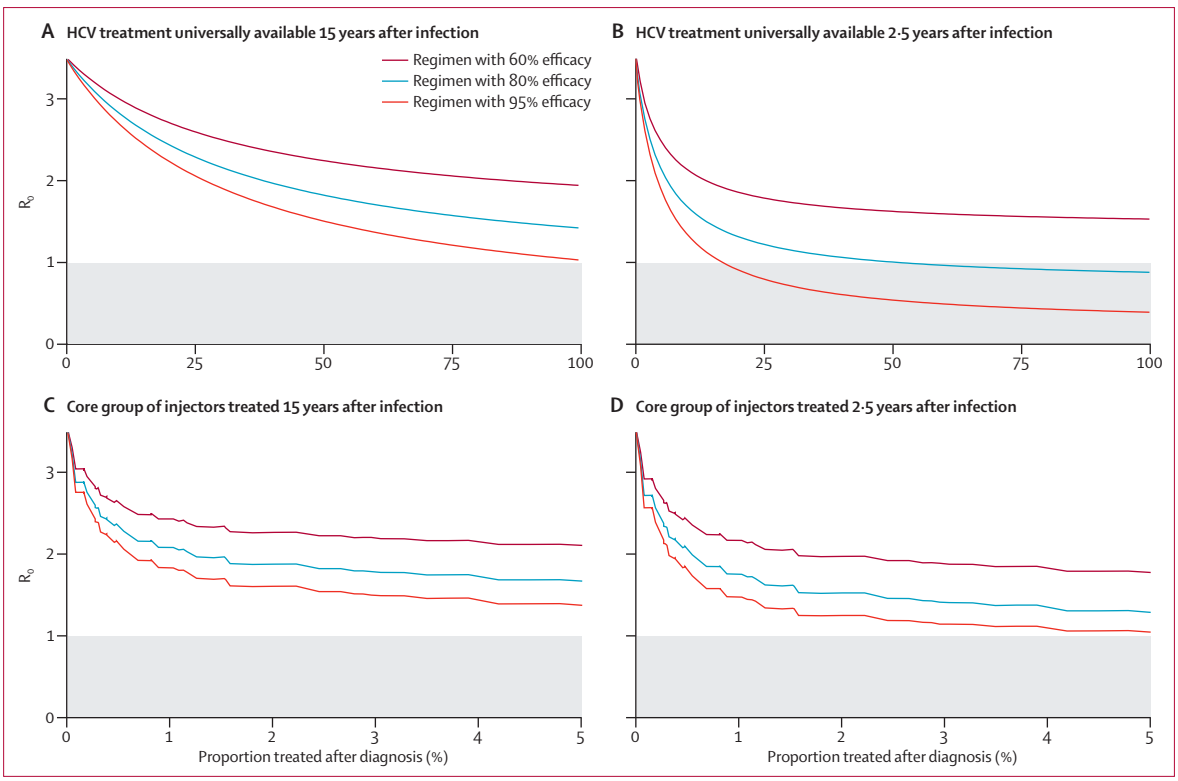


Figure 4: **The effect of various treatment strategies on the severity of the spread of hepatitis C virus**
The graphs show R_0 (mean of bootstrap distributions) versus the fraction of individuals treated after diagnosis according to various public health strategies. The results for making HCV treatment universally available a mean of (A) 15 years (95% CI 0·4–55·3) and (B) 2·5 years (0·1–9·2) after infection and for treating the core group of injectors, on average, (C) 15 and (D) 2·5 years after infection are shown. Since there is no definite cutoff in the rate of injections that delimits the core group, the graphs show the effect on R_0 when the core group is gradually enlarged to include individuals with lower injection rates. HCV=hepatitis C virus.

spread of HCV even if everyone with HCV was treated within an average of 15 years of infection. Regimens at 80% efficacy would reduce the severity of the spread of HCV more but would still be deficient. Regimens at 95% efficacy would need to treat almost every infected individual to stop the self-sustained spread of HCV using the present national treatment strategy. However, our simulations suggest that early treatment would improve the outcome of mass-treatment interventions by reducing the duration of infectiousness of viraemic individuals. Figure 4B shows that, even for regimens with 60% efficacy, a marked drop in R_0 would occur if at least 20% of patients were treated a mean of 2·5 years (95% CI 0·1–9·2) after becoming chronically infected. Interventions with more efficient regimens would not need to treat everybody with HCV to stop the self-sustained spread of HCV. Figures 4C and D show the effect of testing and treatment of the most frequent injectors on reducing the R_0 of the spread of HCV. A marked drop in R_0 could be obtained by treating fewer than 5% of the total eligible population.

We investigated the effect of combining injection management and treatment, covering both the core group and the general population. Figure 5 shows colour maps of R_0 versus the percentage participation of the core group and treatment efficacy. We noted that targeting a restricted core group of 2% of the total population (figure 5B) a mean of 15 years (95% CI 0·4–55·3) after infection would require high efficacy regimens to decrease R_0 below 1. However, targeting a broader core group of 5% of the total population with early treatment a mean of 2·5 years (95% CI 0·1–9·2) after infection shows that the self-sustained spread of HCV could be stopped, even if prevention programmes do not reach everybody in the core group (figure 5C).

In our follow-up study in the Menofia cohort (unpublished), at baseline, in 2002, 82 (2%) of 4020 individuals self-reported regular injection practices for various chronic medical disorders (appendix). The median age of these individuals was 32 years (IQR 15–45), with a male to female ratio of 0·86. 22 (27%) of 82 individuals had HCV antibodies, corresponding to an age-standardised prevalence 1·64 (95% CI 1·03–2·48) times higher than that of the village cohort population. During cohort follow-up (2000–2012), regular injectors were more likely to be hospitalised (age-adjusted rate ratio 1·86, 95% CI 1·01–3·44) and to die (3·10, 1·87–4·85) than the rest of the village cohort population. In 2012, of the 60 individuals who did not die (n=13) or migrate out (n=7) or who were receiving regular insulin injections

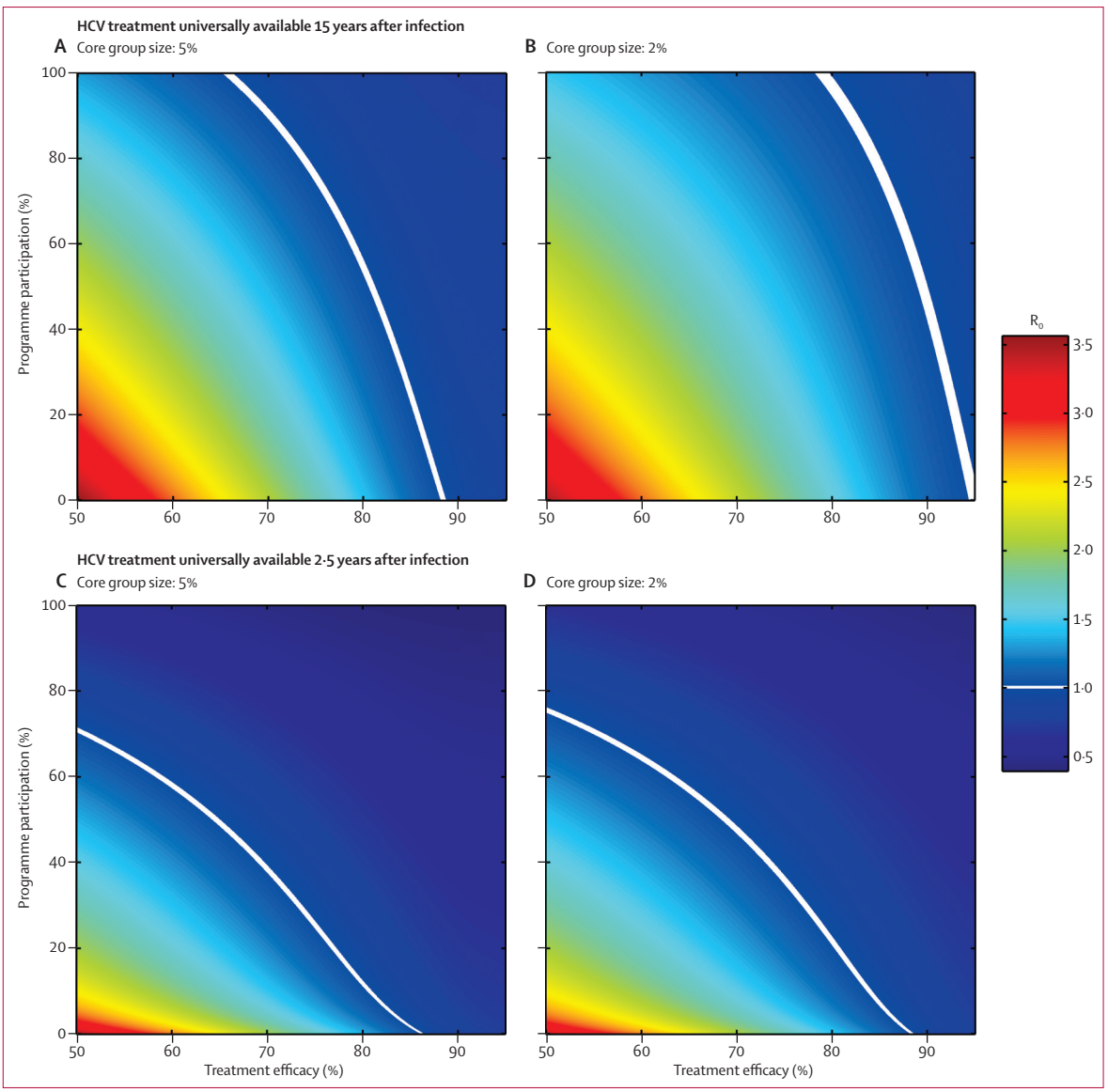


Figure 5: **The effect of combined public health strategies targeting a core group on the severity of the spread of hepatitis C virus**
Colour maps of R_0 (mean of bootstrap distributions) versus treatment efficacy and the fraction of a core group with frequent access to health-care facilities enrolled in the prevention programme are shown. White lines show the HCV spread threshold R_0=1. Interventions with parameters above the white line would stop the self-sustained spread of HCV, whereas interventions with parameters below the white line would just reduce the severity of the spread of HCV. Results are shown for treatment, on average, 15 years after infection of core groups representing (A) 5% and (B) 2% of the total population, and for treatment, on average, 2·5 years after infection of core groups representing (C) 5% and (D) 2% of the population. HCV=hepatitis C virus.

(n=2), 24 (40%) remained regular injectors—ie, receiving more than ten injections per year. Regular injectors reported receiving injections either at home (18 of 19 [95%]) or in health-care facilities (nine of 19 [47%]) from medically trained (16 of 24 [67%]) or non-medically trained (13 of 24 [54%]) personnel. All regular injectors reported having intramuscular injections in the past 6 months; ten (42%) of 24 reported having intravenous injections in the past 6 months.

Based on the follow-up survey, we estimated the mean yearly rate at which individuals quit taking frequent injections. We considered two distinct modelling cases to deal with the fact that 13 injectors died during the study. First, we assumed that all injectors had the same rate of quitting taking frequent injections, which was equal to the rate calculated for the injectors who were interviewed. Hence, we obtained a yearly rate of 8·4% (95% CI 6·3–11·0), corresponding to a median time of 8 years (95% CI 6–11). Second, we assumed that all injectors who were still alive at the end of the study had the same rate of quitting taking frequent injections (equal to the rate calculated for the injectors who were interviewed),

whereas the injectors who died would have never quit taking frequent injections. In this case, we calculated a yearly rate of 6·5% (95% CI 4·7–8·7), corresponding to a median time of 10 years (95% CI 8–14).

Discussion

Mathematical models of HCV have been used to test prevention strategies and address topics relevant to high-income countries where HCV transmission remains essentially confined to intravenous drug users.[20,26,27] These models cannot be used to describe generalised spread of HCV, such as in Egypt, because of stark differences in HCV epidemiology. Indeed, HCV transmission pathways are different in the two cases: social networks mediate HCV transmission in intravenous drug users, whereas for the spread of HCV in the general population of Egypt, injection providers play the key part. Furthermore, annual HCV incidence in intravenous drug users ranges from 6% to 40%,[28] about 100 times higher than estimated incidence in rural communities of Egypt (0·08–0·68%).[13,19]

Here, we have described the first mathematical model of HCV transmission in a high-prevalence setting and calculated the basic reproduction number R_0 using epidemiological data (panel). Our model suggests that, without treatment interventions, HCV transmission would be self-sustained in Egyptian rural communities, maintaining a nationwide spread of HCV. Furthermore, present public health measures including increased access to treatment would not reduce substantially the severity of the spread and would need a large coverage for an effect on the spread of HCV.

Real-world HCV prevention strategies will probably be complex, combining targeted and untargeted interventions, injection control, and treatment. Individuals with high injection rates (ie, more than ten injections per year, representing <5% of the population) perpetuate HCV transmission in Egypt, whereas the rest of individuals remain exposed without transmitting the disease much. Individuals undergoing frequent medical procedures are more likely to become infected early, and, by continuing their practice, transmit HCV to others. In a field study (unpublished), the core group of HCV transmitters consisted mainly of individuals with chronic medical disorders who maintained their injection practices for 8–10 years. Hence, interventions targeting this core group would be beneficial public health strategies and would have nearly the same effect in reducing transmission as untargeted programmes with much larger coverage.

Core groups consisting of sex workers (for HIV) or illicit drug users (for both HIV and HCV) are often difficult to reach because of stigma or the illegal nature of their activities. However, in this case, core group members could be reached easily since they self-identify by accessing health-care facilities to receive care and management. The intervention should therefore consist of raising awareness of health-care providers to HCV testing of individuals with chronic disorders who need frequent medical procedures. If patients are HCV-antibody negative (or HCV-antibody positive but RNA negative), they should be counselled on safe injection procedures and reduction of unnecessary injections. Patient education will therefore be crucial to the success of this preventive intervention. Findings from our survey and those of others[29] on injection practices in Egypt have shown that non-medically trained personnel have a major role in delivering injections. The importance of using disposable injection material should be particularly stressed, both to patients and injection providers.

If individuals are HCV RNA positive, they should be treated as a priority, eventually benefiting from next-generation antiviral treatments with improved efficacy, tolerance, and compatibility with possible comorbidities.[30] We showed that early intervention (~2·5 years after

Panel: Research in context

Systematic review

With the advent of highly effective antiviral therapy for chronic hepatitis C, the strategies to reduce the spread of the hepatitis C virus (HCV) might become more diverse. When a similar situation occurred for the HIV epidemic, findings from modelling[18] and subsequent field studies[17] showed outstanding potential for new prevention strategies to reduce HIV spread in low-income and middle-income countries. We did a PubMed search of titles and abstracts on Dec 5, 2013, with the terms "HCV", "transmission", "antiviral", "treatment" and "model*", which identified 12 reports. Four reports described virus–host interactions and eight reports addressed the effect of hepatitis C treatment on HCV spread among injecting drug users. We did not find studies on people who were not injecting drug users in low-income and middle-income countries—by far the largest HCV infected population worldwide. Therefore, we designed a mathematical modelling study using field data from Egypt—a country with very high HCV prevalence. We used our model to assess the effect on HCV spread of several public health interventions that combine reductions in unsafe injections with treatment of infected individuals.

Interpretation

Our model identified individuals with high rates of medical injections (more than ten per year), representing 5% of the entire population, and receiving more than 50% of all injections, as responsible for the spread of HCV in Egypt. Targeting these individuals with preventive or curative interventions would have a much greater effect on HCV spread than would untargeted interventions—a key parameter to maximise is the eligibility of these individuals to undergo HCV treatment. The effect of hepatitis C treatment on HCV transmission will be much greater if treatment is given early in the course of the infection (eg, 2·5 years after infection) and drug regimens with more than 80% efficacy are used. Such an approach might prove beneficial in other resource-limited settings with health-care-driven epidemics.

infection) in this core group was more beneficial than late intervention (~15 years after infection). However, more effort in the initial phase of implementation would be needed for early treatment since about 90% of infected individuals would qualify for treatment, compared with about 50% in the case of the late treatment strategy. Nevertheless, in the long run, such an endeavour would prove fruitful since HCV-infected individuals would get earlier access to treatment and thus the risk of disease transmission would be reduced. We also showed that treatment for prevention has greater effect with regimens of efficacy higher than 80%, administered early in the course of infection. To implement treatment for prevention would require frequent HCV testing—quite feasible for this population with high rates of medical injections and thus frequent access to health-care facilities.

The main limitation of our approach is that it relies exclusively on the notion of R_0. Although R_0 is crucial for identification of effective public health strategies,[18,31] it does not provide a complete epidemiological description. Reduction in R_0 does not translate into easy-to-read indicators for policy makers (eg, HCV prevalence decline or calendar years left until meeting expected effect of interventions). Also, R_0 is independent of HCV reinfection; hence the effect of reinfection on the efficacy of interventions cannot be revealed by R_0 analyses. However, in a recent meta-analysis,[32] Aspinall and colleagues argue that the incidence of reinfection is probably low in intravenous drug users, with an estimated pooled risk of reinfection of 2·4 per 100 person-years. The reinfection risk is probably negligible in the general population of Egypt, where HCV incidence is much lower than that in intravenous drug users.

After the 2010 hepatitis resolution,[33] WHO released guidelines for viral hepatitis control.[34] An issue that remains crucial for HCV global health policy is the price at which next-generation antiviral treatment regimens will be made available to low-income and middle-income countries. In Egypt, pharmaceutical companies have already started testing some of the new direct antiviral drugs (NCT01838590); price negotiations with the government will follow, provided trial results show high efficacy. Gilead recently concluded an agreement with the Egyptian Government to provide sofosbuvir at US$900 for 12 weeks of treatment.[35] The price is low compared with that offered in the USA ($84000),[35] but is still high for individual patients or government subsidies in low-income or middle-income countries. If, in such settings, HCV is transmitted mostly iatrogenically, then we propose prioritising treatment for patients with advanced disease or who belong to the core group to reduce substantially both HCV mortality and transmission. However, treatment interventions should not overshadow improvements in injection management and infection control, which are likely to be more cost-effective and might also reduce the transmission of other blood-borne pathogens such as HIV and hepatitis B virus.

In conclusion, by developing a mathematical model tailored to a typical rural community in Egypt, we have identified fundamental aspects of HCV transmission and control that might apply to other areas of high HCV prevalence. Offering HCV treatment and counselling on injection use to patients with chronic HCV who receive regular health-care interventions seems to be effective in reducing HCV transmission and is timely and feasible in view of the economic constraints of Egypt.

Contributors

RB and AF conceived and designed the study and wrote the manuscript. RB, IB, MA-H, WD, GE, and AF interpreted the data. NA, AM, MKM, and AF gathered the data. RB, SL, and LT analysed the data. RB developed the models and obtained the modelling results.

Declaration of interests

We have no competing interests.

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