

The Egyptian hepatitis C programme: A model of HCV treatment intervention?

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The Egyptian HCV epidemic, and the country's response to it, are unlike any other country to date. Egypt has a very high burden of infection and disease: Egypt ranks 5th amongst all countries for the burden of disease from viral hepatitis,¹ close to 15% of the adult population are seropositive for HCV and over four million individuals remain viraemic.^{2,3} As a lower middle-income country, Egypt is relatively poor with a gross national income per capita of \$3,410 in 2016 according to the World Bank. Yet, it has strong political backing to tackle the HCV epidemic, stemming in part from the role of a national schistosomiasis programme in spreading the epidemic.⁵

As a result, Egypt has one of the largest HCV treatment programmes of any low-income country, with an estimated 330,000 individuals treated between October 2014 and March 2016 with direct-acting antiviral (DAA)-based regimens. In this edition of the *Journal*, El-sharkawy *et al.* describe the development of the Egyptian DAA programme and some lessons learned from this experience, raising the question – what is relevant to other countries, be they rich or poor?

The authors highlight the role of generic medications. Although branded medications were used in the earlier phase of the treatment response, the programme later used domestically produced generics, allowing substantial reductions in cost. The authors show high cure rates (91–98%) from locally produced generics and branded medications, (Table S7). Whether such rapid scale up of treatment could be achieved with imported generic medications is unclear but for countries like India, Bangladesh and Pakistan all with a high burden of disease and with a thriving generics industry, it shows what can be achieved.

The number of patients treated is impressive. But how important is it to know the outcomes of treatment from a public health point of view? There is clearly a balance to be struck between programmes expanding access rapidly and collecting high quality data. Whilst those reporting SVR12 outcomes improved significantly as treatment access expanded (Fig. S2), outcomes were known in fewer than 30% individuals early in

the programme. It is reasonable to think that those without follow-up may be more likely to have failed treatment, so there should be some caution as to the actual cure rates achieved. As countries shift their focus from scaling up treatment access to eliminating infection, finding and curing those who failed treatment and/or become re-infected will be increasingly important.

One reason for the lack of capture of follow-up data was the approach of having centralised treatment centres. When patients had completed treatment, the incentive to return for tests is minimal when they can be performed at local providers. The successful development of an IT platform to allow collection of data and co-ordination of services is an approach that may be helpful in many settings. Even in countries with poor infrastructure, mobile technology may allow such approaches.

How else can follow-up be improved? The authors describe methods to incentivise patients (e.g. the offer of HBV vaccine) which may be helpful, but are unlikely to be as relevant in other parts of the world, especially in endemic areas where people get infected for HBV early in life. Assessing strategies for retention in care should be an operational research priority and could be tested through randomised trials. However, the authors also suggest that public health messages should place greater emphasis on testing for cure and that this is a lesson that may be helpful for other countries.

When looking to scale up services, prioritisation of specific patients or populations is often discussed as a means to both control costs and ensure sufficient capacity for treatment. The ethical principles of prioritisation are complex but put simply, approaches can be categorized into those prioritising (a) equity of access to all e.g. with random allocation or community participation in decisions, (b) social value e.g. offering to healthcare workers (c) maximisation of benefits of treatment, e.g. maximising the number of individuals cured and/or targeting treatment to those transmitting and (d) favouring those worse off medically and/or socially.

Like many countries, Egypt's approach was initially based on the last of these. Between October 2014 and May 2015 treatment was prioritised to those with advanced fibrosis (F3, F4) or at high risk of complications (co-infection with HBV and/or HIV, post-transplant or extrahepatic manifestations), but also rewarding social value (e.g. treatment of healthcare workers). Despite these additional criteria, the numbers of individuals

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accessing treatment without significant fibrosis was very low even in the latest period for which data is presented (Fig. S2).

The authors refer to “moral concerns” with the early prioritisation process, but these are not well documented. The implication is that clinical teams came under pressure from those not eligible to the treatment programme, an experience familiar to clinicians in many settings. However, introducing a system unable to treat those in greatest medical need may also create ethical concerns. The authors conclude that prioritisation should not be part of programmes, but the justification for this is not clear enough. Whilst access to care for all infected should be our goal globally (indeed reaching the WHO targets will require 80% of those infected to be treated), it may be that at the early stage of programme introduction, a phased approach prioritising treatment will be appropriate in some settings. This is not simply about medical prioritisation, but it is also likely that cost-effectiveness will be greater in those with more advanced fibrosis, supported by analysis from resource-limited countries (Côte d'Ivoire, Egypt and Thailand) suggested that focusing HCV treatment on patients with severe fibrosis (F3–F4) delivers the highest number of life-per-year-saved.⁴ However following access to drugs at generic costs and fall of HCV drug prices (three-month course of HCV treatment has dropped by 85% in Egypt over the last years) treatment initiation with DAA regardless of the liver fibrosis stage is increasingly likely to be cost-effective in low and middle-income countries, as observed in high income countries.⁶

Whilst the programme in Egypt is impressive, about 750,000 HCV-infected persons have been treated since 2007, estimates would suggest that only less than 10% of HCV viraemic subjects have been treated to date. More recent data from Egypt reflects the experience in other countries with rapid scale up (e.g. Australia or Germany) where treatment rates have dropped, and case finding has rapidly become a challenge.⁷ Planning ahead for this phase of response is more complex and is likely to require co-ordination across a range of settings. In Egypt access to some public services (e.g. driving licenses) has been linked to hepatitis C testing, but whether such approaches alone will be sufficient to reach those in need is unlikely. In Egypt, patients are given a voucher for free HCV RNA testing 12 weeks after the end of treatment. Most governments of resource-limited countries are currently unable to cover the cost of HCV nucleic acid testing, which also requires high quality laboratories. Simplification of the continuum of HCV care in low and middle-income countries using simple and low-cost diagnostic methods (e.g. HCV core antigen testing) is urgently needed.⁸

While most countries have an HCV epidemic focused in high-risk groups, achieving the WHO elimination targets will require

high screening and treatment coverage, especially in countries like Egypt where infection is more generalised beyond defined high-risk groups. The Egyptian programme suggests that, with strong political and medical commitment, these ambitious targets can be realised.

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Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.jhep.2018.01.021>.

References

- [1] Stanaway JD, Flaxman AD, Naghavi M, Fitzmaurice C, Vos T, Abubakar I, et al. The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. *Lancet* 2016;388 (10049):1081–1088.
- [2] Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. *Lancet Gastroenterol Hepatol* 2017;2:161–176.
- [3] Kandeel Amr, Genedy Mohamad, El-Refai Samir, Funk Anna L, Fontanet Arnaud, Talaat Maha. The prevalence of hepatitis C virus infection in Egypt 2015: implications for future policy on prevention and treatment. *Liver Int* 2017;37:45–53.
- [4] Obach D, Yazdanpanah Y, Esmat G, Avihingsanon A, Dewedar S, Durier N, et al. How to optimize HCV treatment impact on life years saved in resource-constrained countries. *Hepatology* 2015;62(1):31–39.
- [5] Elgharably Ahmed, Gomaa Asmaa I, Crossey Mary ME, Norsworthy Peter J, Waked Imam, Taylor-Robinson Simon D. Hepatitis C in Egypt – past, present, and future. *Int J Gen Med* 2017;10:1–6.
- [6] Deuffic-Burban S, Obach D, Canva V, Pol S, Roudot-Thoraval F, Dhumeaux D, et al. Cost-effectiveness and budget impact of interferon-free direct-acting antiviral-based regimens for hepatitis C treatment: the French case. *J Viral Hepat* 2016;23:767–779.
- [7] Zimmermann R, Kollan C, Ingiliz P, Mauss S, Schmidt D, Bremer V. Real-world treatment for chronic hepatitis C infection in Germany: Analyses from drug prescription data, 2010–2015. *J Hepatol* 2017;67:15–22.
- [8] Mohamed Z, Mbwambo J, Shimakawa Y, Poiteau L, Chevaliez S, Pawlotsky JM, et al. Clinical utility of HCV core antigen detection and quantification using serum samples and dried blood spots in people who inject drugs in Dar-es-Salaam, Tanzania. *J Int AIDS Soc* 2017;20:21856.