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Getting Smart in how we pay for HCV drugs: KAOS versus CONTROL

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Dear Editor:

Over the last two years a therapeutic revolution has been occurring for the treatment of Hepatitis C virus (HCV) infections. Direct acting antiviral (DAA) agents that allow all-oral regimens have been released. These regimens replace the use of injectable peginterferon, which markedly reduce side effects, significantly reduce the duration of treatment (e.g., from 48 weeks to 12 weeks), and increase cure rates from 60 -70% to greater than 95% in most clinical scenarios (1). Based on this set of facts alone, a clear message is that virtually every patient with chronic HCV should be treated (2). Now.

As the new HCV agents were released, however, the price-tag of the drugs created sticker shock, especially among the payers who were not fully prepared to treat so many patients at one time with such expensive medications. To keep expenditures under control, payers questioned the need to treat patients with less advanced disease (e.g., those with F0- F2 fibrosis), owing to the uncertainty of who will progress (less than 50% of patients develop cirrhosis over 30 years) and the relatively slow progression of disease among those who do progress. The payer's reluctance to pay for drugs created barriers for patients and providers to gain access to therapy. All involved called out for data on the cost-effectiveness of the new all oral regimens, which heretofore did not exist.

In this issue of *CID*, Rein and colleagues provide, for the first time, the cost-effectiveness data for the newer HCV drugs compared to use of the older, PEG-interferon containing therapy and to no therapy at all (3). Their results are informative, timely, and most welcomed. For their analysis, the investigators used a combination of simeprevir + sofosbuvir as the primary all oral DAA regimen, which has a wholesale acquisition cost (WAC) of $150,360. Using sophisticated models they determined that, compared to no treatment, the incremental cost-effectiveness ratio (ICER) of both PEG-based and DAA only treatments was sensitive to the fibrosis stage at the time of treatment, ranging from $173,800 per quality adjusted

life year (QALY) gained for DAA use at stage F0 to $13,000 per QALY gained for PEG-based therapy in patients with cirrhosis. The investigators went on to determine what the cost of DAA treatment would need to be in order to achieve an ICER of $50,000/ QALY gained, a value typically judged to be 'cost-effective.' This threshold was reached at a WAC of $139,000 or $136,000 when DAA treatment was compared to no treatment or PEG-based treatment regimens, respectively. In the treatment of patients with no fibrosis (F0), the cost of a treatment course with DAA therapy would need to be $47,000 per treatment course to achieve an ICER of $50,000 per QALY gained. With the release of the newer DAA agents, the team evaluated the cost-effectiveness for sofosbuvir-ledipasvir ($94,500 /treatment course) and the new Abbvie drug combination ($83,000 / treatment course) and determined that, compared to no treatment, the ICER was $35,100 and $31,828 per QALY, respectively.

The take home point of the analysis is obvious: Cost-effectiveness is dependent on the cost of treatment. With the release of several DAAs, and many more slated for release over the next 18 – 24 months, the hope is that market-based competition will drive the cost of regimens down, thereby improving the cost-effectiveness proportionately. This is how a free market works. But the question remains, does the pharmaceutical industry operate as a free market?(4)

Just in the last 6 months, evidence exists that free market forces are at play in the realm of HCV drugs, at least at the level of the pharmaceutical companies. With the release of Abbvie's '3D' combination therapy, reductions off of WAC were granted to gain 'exclusivity' within a certain pharmacy benefits manager (PBM) entity, whose job is to serve as an agent for a payer or care delivery system(5). This was countered by Gilead creating special deals with other PBMs for the exclusive distribution of their combination regimen. On first glance, it seems that the market is working and the payers (and their patient constituents) are paying less for HCV drugs. But are they? And if so, how much less?

Unfortunately, the chaos in the system prevents us from being able to answer these questions. Here's the way it works: Drug company A offers a rebate to PBM 'X' in exchange for exclusive distribution of company A's product. The amount of this rebated discount is not in the public domain and therefore unknowable to patients, providers, and, in some cases, payers. Therefore, it is unclear how much benefit is accrued to payers and how much reduction, if any, there is in co-payments for patients. What's worse, the PBM makes its 'profit' based on a percentage of WAC, not on the net price after rebate. In this way, the PBMs are assured maximum profits regardless of the discounted rebate and, since the payers may not know the amount of the negotiated discount, extra profit may accrue to the PBM if the rebate benefit is not passed along to the payer or the patient.

Yet, the worst outcome of the occult dealings of the PBMs is that it impedes drug company B, who might be releasing their HCV drug at some point in the future, from pricing the WAC of their new regimen substantially below the WAC of other drugs in the market. If they were to price their new drug, for example, at 50% of the WAC of the competition, the PBM would make half as much. The PBM, therefore, might choose not to carry the newer drug as a 'preferred' drug (or perhaps not at all) even though the cost to the payer could be less. Rather, company B is encouraged to price the WAC at nearly the same level as the other drugs and attempt to gain market price advantage through provision of a more substantial rebate to the PBM. Not exactly a "free market."

In every industrialized country outside of the US, pharmaceutical companies negotiate pricing directly with the payers (usually a nationalized system) and the actual cost of drugs to the payer is in the public domain. Using cost-effectiveness data such as those provide in the article by Rein, et al, these countries can make informed decisions about use of the drugs in all patient populations. In the US, however, such direct decision-making is impossible owing to the absence of information about the true expenditures made by payers for drugs.

In Mel Brooks' sitcom from the 1960s, *Get Smart*, CONTROL agent 86 (Maxwell Smart) and his colleagues fought against their nemesis KAOS. Working under the tagline, 'the international organization of evil,' KAOS was run by an amorphous cabal whose leadership was always referenced but never seen. As would be portrayed in Brook's *Get Smart,* HCV (and other expensive) drugs, as distributed through PBMs, are negotiated under a 'cone of silence,' thereby creating KAOS and corrupting the workings of true free-market forces. By exposing these business practices, we can gain CONTROL of the situation, lift the cone of silence, and eliminate some of the KAOS in our healthcare system. If we fail to do this, we will have 'missed it by *that* much!'

REFERENCES

1. Webster, DP, Klenerman, P, Dusheiko, GM. Hepatitis C. *Lancet* on line (14 Feb 2015) pii: S0140-6736(14)62401-6. PMID: 25687730

2. AASLD, IDSA, IAS-USA. Recommendations for Testing, Managing, and Treating Hepatitis C. Available at: http://www.hcvguidelines.org/full-report/hcv-testing-and-linkage-care. Accessed 3/2/2015.

3. Rein, DB, Wittenborn, BS, Smith, BD, Liffmann, BA, Ward, JW. The Cost-effectiveness, Health Benefits, and Financial Costs of New Antiviral Treatments for Hepatitis C Virus. *Clin Inf Diseases* (2015) (this issue)

4. Saag, MS. Quantum Leaps, Microeconomics, and the Treatment of Patients with Hepatitis C and HIV Co-infection. *JAMA (*2015) 312:347-48.

5. Eban, K. Painful Prescription: Pharmacy Benefit Managers Make Out Better than their Customers. *Fortune* (2013) http://fortune.com/2013/10/10/painful-prescription/