# Switching mentality: how "COME" could suggest the way

## Interview with Stefano Fagiuoli

During the last EASL meeting, probably it was the study with the highest number of citation, because it was able to define the burden of HCV infection in our world, let's say in real life. Supported by EpaC – the Italian hepatitis patient based association- the study has as first author Stefano Fagiuoli, director of the Gastroenterology Unit at Ospedali Riuniti, Bergamo. The name of the study is COME, an acronym that sounds a word that is the Italian for "how". How is an ad verb that indicate in what way or manner or by what mean something is going to happen; to what extent or degree; in what state or condition; for what reason; to what effect -with what meaning? How is one to interpret his action?- and the manner or way somebody couldn't figure out how to solve a problem: in this case the problem is HCV infection. I think the name of the study, this acronym, is perfect for your study…

"The idea of our study which is the COME study, which means Costs of Hepatic Disease, it's an Italian acronym, was meant to try to define exactly what was the global cost both in terms of direct cost, indirect cost, medically related cost, liver disease-related cost and anything else that could be necessary to the patient, together with the indirect cost and the quality of life. This is a different approach, because I think that, as physicians, we need to be aware that we probably don't need or are not obliged to take care only of the specific technical medical condition, but overall take care of the patient as a whole".

A medical doctor need to be focused on the best way to treat his/her patient: why he should be interested in an evaluation of the cost of a disease?

First of all, I think we have to define what do we mean with cost of the disease. Most of the data available in literature are dealing with direct cost of the drug or hospitalization. I think it's time to move to a different concept of what costs are. Specifically, cost for a patient means direct cost related to both medical condition, admission, drugs, but also what they usually and routinely spend to reach the hospital, to go and do their testing or to take additional medications or to have somebody taking care of themselves, maybe it's paid assistance. We have also indirect costs, which means they have loss due to disease, absenteeism or loss of productivity. Last but not least, we have to consider quality of life, which is a different cost, that patients have to pay for their disease.

From your study, it seem that hepatitis is a luxury that we cannot afford…

We have to consider several issues. First of all, do we know all the patients that are affected by a viral disease? The answer is of course not. So, we need to make them emerge and be aware of having an infection and define if that infection deserves a treatment. Then, the second question is: do we treat all the patients that are infected and have a condition that needs to be treated? And the answer is no, of course not: we are mainly undertreating those patients. As a consequence, this has by

definition an evolution of the disease, in terms of cirrhosis, development of hepatocellular carcinoma and need for transplantation. The aim of our study was just to show that you can spend much more money when you are treating early disease, but then you are going to save a huge amount of money if you can avoid development of decompensation in end-stage liver disease. Of course this is more a political or a socio-economical issue, rather than a medical issue and we are still in the phase in which we are treating a disease. If these data and this information will be confirmed in more advanced studies with a larger population, we may end up realizing that with a more effective drug could be cost-effective treating earlier disease or maybe even the infection but it means switching mentality from seeing the health system as a cost: if you see it as a cost you have to limit access to cure and contain the cost. But if you see it as an investment in health, then it's an adjunct value to what you are doing. I think we need to have more information to see if we can adjust to a different point of view.

You said early treatment, in the natural history of hepatitis C the infection may be complicated in order to establish what means early.

That is exactly why I am trying to put the discussion to an extreme and discussing about treating disease or treating the infection. We know that most of the infection will lead to a chronic liver disease but not all of this chronic disease will lead to an end-stage liver disease, but we have to consider that times are changing, as always, and metabolic disease and alcohol consumption are actually re-increasing in our society, especially in the Western society, so this may actually imply that having co-factors adding on the same issue, which is viral hepatitis, you may actually see an even more important evolution of the end-stage liver disease. So, my point is if we have effective drugs then we can consider dealing with this disease treating more patients to avoid evolution. Up until now, we didn't have effective enough drugs to achieve this goal and so there was no point in treating everybody having less than 50% success, but if you can reach a higher success rate, then it gets cost-effective to treat everybody and of course it's an investment in health which probably is very difficult to get accepted in this economical period.
The results, some results of the studies presented here

claim that a sustained viral response at 12 could be a measure but we have also 4 weeks of sustained viral response, that means thanks to this different evaluation and the new drugs we can reduce the time and drugs and have a more good economic outcome?

Of course, the issue is very simple in that way, if you have a short treatment which is very effective, and we are very close to this because with hepatitis B we can achieve almost 100% success but we have to treat life-long. Hepatitis C, which was the worst condition because we could achieve success in less than 50% of the overall population, now seems to be aiming towards a situation in which in 4 or maximum 8 or 12 weeks in a few years there will be available drugs that will let us treat a larger number of patients with success. This will change the picture in terms of cost-effectiveness of the treatment because it will cost less and will be more effective and of course we could not afford to treat now for 12 months with these costs all these people, so it needs to be adjusted, of course.

As we said, the name of the study sounds "come" that in Italian means "how", can now you describe the study?

It is a very simple study. We enrolled all consecutive patients admitted in our unit for any condition related to liver disease and with any kind of admission, which could be hospitalization, daily admission or outpatient clinic. At the enrollment patients were asked to fill up an assisted questionnaire -there was a physician assisting them in filling the questionnaire- which was basically building up the 6 previous months history of their liver-related disease and taking into account any possible direct and indirect cost, like we were saying. Then, they were asked to fill up a EQ-5D questionnaire for the quality of life and then to fill up a questionnaire dealing with what was their feeling about their wellbeing, and this was done for a period of about 8 months. We collected more than 1,000 patients and we built a sort of a trend in expense according to chronic hepatitis, cirrhosis, hepatocellular carcinoma and liver transplantation, according to etiology of the disease and being successfully treated or being under treatment. What comes out from the study is that the management of chronic hepatitis who is being treated and is a full time responder to treatment ranges around 3 to 400 Euros, however if you aim at treating a patient which is already transplanted the cost for this patient is going to be 5- or 6-fold higher, so these are the numbers that came out from the study.

This is a policy maker issue. But decision makers need to be advised by expert. There is a study published on Plus One (1) that evaluated the method that politicians or decision makers decide or define the expert to be enrolled in commissions and very often the greatest part of the experts enrolled by politicians are not chosen on scientific evidence, for instance by the number of papers published and so on, but only through direct contact. In your opinion, how could expert be enrolled in the process of decision making? A study like your study –scientifically founded and supported by EpaC, the main community based organization in this field- could be a good tool in order to define where we should to go…

Well, I think it's quite a complicated matter, I don't want to put myself in a bad position, but the habit usually: if you are put by somebody in a position, then you become an expert for that. In an ideal world, you have shown that you have some expertise, then you should be in that position, that is the way it should work. I think what we should choose centers that are dealing with these patients and audit those centers to see who is appropriate in diagnosis, treatment and management. Then when you have done this, combined with people that are publishing results or producing results in that field, then you can select a sort of a population of experts, but that's the ideal world…

In Italy, we are in some way lucky because the Italian Association for the Study of Liver published an expert opinion paper (2) on the direct antiviral agent.

Yes, we are lucky but at the same time it's a little bit confusing the situation, for a very simple reason. If you are dealing with viral hepatitis in any European country, Spain, France, England, Germany, you have a very restricted number of experts which are dealing with that issue. When you are dealing with Italy, you have dozens of experts and that's not a good thing, but is our problem I believe.

Too much is not enough.

Exactly. I mean, in Lombardy, in my Region, we have 91 prescriptor centers for viral hepatitis, so that's not the right way to do it, it should have hub-and-spoke centers to deal with this, if you have a thousand of prescribing centers you can't control quality. ■

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(1) Haynes AS, Derrick GE, Redman S, Hall WD, Gillespie JA, et al. (2012) Identifying Trustworthy Experts: How Do Policymakers Find and Assess Public Health Researchers Worth Consulting or Collaborating With? PLoS ONE 7(3): e32665. doi:10.1371/journal.pone.0032665

(2) It is published on this issue