

Resolve to Save Lives – LINKS Webinar
“Making the List: Why now is the time to declare that SPC therapies are essential”
Thursday, October 25th, 9AM – 10AM ET

Questions and Answers

1. Combination therapy is better indeed but in Bangladesh, the price is still a bit high. So, regarding socio economic conditions, will the patients of middle and low-income groups be able to continue the medication? This is our concern. (Q1)

- Tom: This is an excellent question and reality. What we hope is that by putting these FDCs onto the WHO EML, they will then get onto country EMLs. As Sunny showed, that tends to result in a reduction of costs. As programs to treat hypertension scale up and standardize medications, there is an opportunity to identify specific drugs with specific dosages and purchase them in bulk. We would be able to benchmark a cost then drive down that cost so that we can get more affordable drugs. What we could see is a cost as low as \$2, \$5, \$10 per year for some of the best quality antihypertensive combinations.
- Sunny: If we go back to the HIV/AIDS experience and what we've seen in other settings, that is exactly what Tom is arguing. This is precisely why it needs to be on the essential medicine list. If you focus attention, you can apply government pressure, but you also get economies of scale. It is a very important question that fuels the rationale behind trying to add FDCs on the EML.

2. Like in HIV, probably India could play a major role in providing the cheapest generics in htn too. Will this scenario come true? (Q2)

- Tom: We don't know. It will be interesting to see. I will say that in Resolve to Save Lives, as an organization, we generally do not purchase or provide medication. However, we are in a couple of jurisdictions where they are scaling up and they need a starter set of medications. We are doing bids to see what the market is like and we have provided one-time medications for a couple areas. We are still trying to understand the market, quite frankly. We do not know what it will be like or who the major suppliers are. It is certainly possible you will see some of the major manufacturers of generics or brand of generics providing high quality at low costs. Remember, we're talking about 1.4 billion people who have an indication of treatment, of whom, only 200 million or so are on treatment. There is an untapped market of a billion people. Some people might say it is impossible to treat that many people, but people thought it was impossible for there to be HIV treatment for tens of millions of people and that cost many times more and was much more complicated. This is something that has been standard of care in high income countries for more than half a century and is not yet present in many other countries.

3. I would like to highlight some challenges with the EML – I understand that a particular medicine has to be on the WHO EML which is necessary but not sufficient – because the medicine should also be listed in country EMLs (Q3)

- Tom: That's exactly the case. What we have done at Resolve to Save Lives is convene a series of stakeholder meetings in the countries, states, and provinces where we are working.

We bring in their experts and we bring in international experts. We say it's your decision. You decide what to choose as your algorithm. And what we've heard over and over again is "we would like to use a fixed drug combination but it's not on our EML, and it's not on our EML because it's not on the WHO EML". So, given that dynamic that all of the jurisdictions we've been working in so far have chosen mono-therapy, we support whatever the jurisdiction wants to do. But we've heard them loud and clear that what they want is for FDCs to be on the EML so that they can then have it on their state or country EML. That would result in a greater comfort of using it as well as lower costs and the ability to get quality up.

- Sunny: I would just add that we know there are 134 countries that effectively use national essential medicines lists to influence procurement. But what we don't yet have is the same sort of scaled process whereby practitioners and citizens are monitoring the national essential medicines list. And then making the point that Tom made, it is possible for these fixed dose combinations or modern hypertension treatments to be on a national essential medicine list. And so, I think it's a brilliant question, but I would also say it's an opportunity to do the same kind of work we have done on an international level and at the national level to standardize the list.

4. Does a real possibility exist to introduce these drugs into the WHO EML, specifically after the last rejection? (Q4)

- Tom: We're optimistic. We think that we addressed the concern that the committee had. There's a greater understanding. There are concerns that the cost may be too high, but we think that, if it's on the EML and we standardize the doses in drugs, we can reduce those costs substantially.

5. In a primary health set up where lab investigations are not available in the primary health centres, is biochemical monitoring feasible if the patients are kept on FDC when compared to monotherapy? Since its easier to diagnose any abnormalities when the patient is on monotherapy in a set up where investigations are limited. (Q5)

- Tom: This is one reason why several jurisdictions have selected as their algorithm: amlodipine- 5 mg, amlodipine – 10 mg, and then add either a diuretic or RAS-inhibitor or both. Because you are minimizing the potential metabolic abnormalities, what we're finding is that in many contexts where patients need treatment, regular biochemical monitoring is very unlikely to occur. Now it's been studied that even in high income countries biochemical monitoring, even when recommended, generally doesn't occur and there's no worse outcome in patients whom it doesn't occur. Never the less, as it is recommended, it is something to understand. This is an area for further investigation and further evaluation. For example, if you added an ACE or an ARB with a diuretic as the FDC after amlodipine, as one country has suggested to do, that might balance the abnormalities in potassium. This is an important issue.

6. Vietnam. Interesting and important presentation – I hope to introduce it to the country. (Q6)

- Tom: This is an important point. Thailand and some other countries are saying, "we don't have to wait for the WHO to put it onto our EML." You can download from the links Sunny

that showed the full justification of this and countries can add to their EML. We began this process more than 6 months ago and it will be another 6 months before the WHO EML actually considers it – Apr 2019. So, we will see.

7. One hurdle to overcome is misconceptions of influential physicians. (Q7)

- Tom: Interestingly, what we've seen in other countries is they all use the combination drugs in their private practices. So, there is actually a disadvantage to the public sector if it's not using FDCs because it's seen as better for all the reasons Sunny went into. There's a much bigger issue of impact by adding a low dose of a second agent than by doubling the dosage of the first agent and, probably, a lower level of adverse events. For example, when you double amlodipine, you get a lot of edema. There are also lots of misconceptions about anti-hypertensive treatments and something we might do in the future in a webinar is go through some of those misconceptions. We see this repeatedly around the world in terms of the role of beta blockers; who should get an ACE-inhibitor; ACEs and ARBs, etc. Some of the things are still debatable but some are pretty clear and the knowledge lags behind the reality.
- Sunny: This hurdle of the misconception of influential physicians is important. I was talking to my mother, who is also a physician, about changes in practicing that some physicians have done for 30 or 40 years. For me, what I use in those settings is guideline support. And so, if physicians are raising those questions and they do have influence on treatment policy, I would say the European guidelines in 2018 are very important because they affirm in a very strong way the role of FDCs.

8. A number of initiatives aimed at increasing access to NCD meds are underway – Defeat NCD Marketplace and the PATH coalition comes to mind. Is this important work by Resolve interacting with work of other NCD coalitions' partnerships? (Q8)

- Tom: Absolutely. We will work with anyone who is helping to improve care and treatment. So, this is an important area to be in. Some of these groups are just scaling up and I think some of what we have to do is work with countries because ultimately, it will be the countries that are purchasing the drugs. They will be spending the money. They'll maybe make a decision based on where national manufacturers are or at the most cost-effective. We hope these decisions will always be evidence-based and for the maximum benefit of patients and reducing to the greatest extent possible any co-payments patients have to make.

9. In Bangladesh, it will be hard to make everyone follow the same protocols. (Q9)

- Tom: Well, I think that's true not just of Bangladesh but for every country in the world. One of the challenges we have is that doctors tend to be quite reluctant to follow protocol. This is one of the reasons we strongly encourage task sharing. We strongly encourage the involvement of nurses, pharmacists, community outreach workers, and the rigorous evaluation of outcomes. It's been shown now, for more than 40 years, that protocol driven care does better. Patients are more likely to have disease control. They're less likely to have adverse events. They're less likely to have heart attacks, strokes, and other complications of

hypertension. So, in those situations, it's really important that we see what the outcomes are and then use that to improve performance.

10. Thanks. Are the country EMLs updated routinely? (Q10)

- Sunny: That's a great question. I will be honest with you. So, I am part of a consortium with the World Heart Federation called GLO-PRO and its looking at exactly this question. The honest answer is we don't know. In some countries, e.g., if you look at sub-Saharan Africa, the country level essential medicines list have not been updated in the past five, in some cases ten years. And so, who's asking those questions? What are the protocols? Where can you find to dig into some of those processes now?

11. At least in Chile, it is very important the introduction in the WHO list, because our national health public system always is seeing what the WHO says. Our local initiatives are always supported by personal efforts and not by the system itself (Q11)

- Tom: That's why we're very hopeful that this will get approved by WHO and I really want to emphasize as strongly as I can that all of these medications are generic. Yes, there are multiple manufacturers for all. They're all safe. They're all effective. They're all evidence-based. They're all standard of care. They would be used for the treatment of any patients in any country, regardless of income level.

12. Guinea allocates few funds for health. How can you involve the government in implementing this treatment plan in the national protocol to treat htn in countries that allocate little funding for healthcare? (Q12)

- Tom: It's a great question. Some of this is going to involve advocacy for countries to spend more on health. Someone who will involve good procurement so that if the government can't pay for the anti-hypertensive drugs, at least you could get high quality drugs that wouldn't have to cost more than a couple dollars a year. We would rather it be completely free to the patient, but we recognize that may not be possible in all countries immediately. In Africa, most countries have hypertension control rates in the low single digits (<5%) and because of that, what we're seeing is a large number of strokes, heart attacks, and large expenditures on trying to scale up dialysis and even kidney transplants. But prevention is going to be much more cost effective.

13. Regarding drug forecasting, if we go for FDCs, will it yield the same level of accuracy as monotherapy and yield the expected level of stock-out-free situations? (Q13)

- Tom: What I have seen in multiple countries is one month they have one drug, the next month they have another drug, the next month they may have the first drug or a third drug and that's really difficult for the patients and doctors. So, if you put the drugs together, you are going to have a lower rate of stock-outs and you also simplify the logistics of the pharmacy. You can't have one without the other. What we have seen with HIV and TB with FDCs is that it really reduces stock-outs.
- Sunny: Yeah. I think that's spot on and I think the moment you clarify and focus, it becomes a global issue to where everyone is actually aligned on a common set of treatments and that actually starts to ensure that there is more attention paid to it. If you have too many

treatments, too many doses, it splinters attention and splinters focus. So this sort of brings it together and centralizes it on a common set of priorities.

- Tom: Also, as we gain more experience with these, we hope there will be more price transparency. So, it's openly stated what the prices are. We've seen, and Sunny mentioned, 100-fold variation in prices for the same chemical but all of high GMP quality.

14. What's your assessment about the current practice/situation regarding the use of brand vs generics hypertension drugs in LMICs – given that the price and affordability, and maybe availability differ significantly? (Q14)

- Sunny: It's a very important question. So, I will just go back to the point that all of the current treatments for hypertension and, many for cardiovascular disease in general and hopefully for FDCs, are on the essential medicines list. So, I do think that using generic treatments is actually very, very important. In the case of FDCs, we have seen that some of the innovator companies have started to combine these treatments and then they have what's called evergreening. So, then they say that this is a fundamentally different molecule, so the price should be high. And in my view, that is not good for FDCs or hypertension therapies in general. All of these are essential. All of these are generic. I do think putting a focus on using those treatments will be critical.

15. In Latin America, the medical community is against many other health professionals participating in the treatment of high blood pressure. Any suggestions for how we might change this? (Q15)

- Tom: Well, this is a great question. It's the case all over the world. In fact, you can kind of think about the evolution of health care. Early on, before professionalization, you have everyone doing treatment and then the doctors try to control everything. If you look at the most advanced health system, you see more task-sharing. More involvement of nurses and pharmacists and the evidence is very clear. The evidence is incontrovertible that you get higher control rates, lower costs, and better outcomes if you have a task-sharing approach. But you have the doctors' association which is quite against it. One of the things to emphasize is that what we're trying to do here is to scale up the number of patients on treatment. When you scale up the number of patients on treatment, you can make a big difference by basically getting a higher volume and then the doctors can be reserved for those patients with complications or with resistant type hypertension. So, what the doctors do, which they do best, is take care of the complicated patients. Meanwhile the nurses and pharmacists are not working independently. They are following the doctor's orders. They're following the protocol that the government has established. And in different countries, there will be different possibilities of doing this. Sometimes, it's a systematic way, one step at a time. This is another area for possible work or a possible future webinar topic.

16. Do you suggest a country place ALL potential doses of FDC on their EML list or limit to 1 or 2 SPCs with 1 or 2 doses on their EML – and why? (Q16)

- Sunny: I have a personal preference for focus. We applied previously for the ACE inhibitor and thiazide. So, I do think that is a very important one, with the other one being the CCB

- plus ARB - at least those two is what I would say. When you look at prescription volumes and you look at the efficacy and safety data, we know that many of those are already in play right now globally. The dose question is an important one. I think at least two doses, if not three. If going with one, there is an argument to be made for using half pill, one pill, two pills and I think that's a possibility, but I do think having at least two doses and at least two combinations would be an appropriate approach that satisfy everyone.
- Tom: I guess, I would say if I were in a country where there's a question of what's on the EML and there's a question of what I purchased and since the drugs are therapeutically equivalent, I'd want to get the lowest rates for high quality drugs possible.

17. In Nepal, only ~35% of those on hypertension treatment have their blood pressure controlled. Apart from the question on drug efficacy, I think patients' low perception on risks of hypertension, low health literacy is also hindering factors to get the desired results. Do you see or propose any new tailor-made strategies in increasing awareness among the general population because awareness is as important as treatment and control? (Q17)

- Tom: Very important point. One of the things that is quite important, and Norm Campbell has made this point very eloquently, is that every doctor at every visit should be emphasizing that this is the leading preventable cause of death. The communication from the health workers is a certainly role that everyone in the health system should be playing, emphasizing that hypertension is a silent killer, and that treatment is likely to be lifelong and also life-saving. There's also the possibility of working with media, more specifically earned media where a newspaper, radio, television, or articles provide information about hypertension to increase health literacy. This probably not an area where paid advertising, e.g., the kind that is done in the anti-tobacco context for example, is likely to make a big difference simply because it is such a long-term issue. But by getting journalists and other members of civil society involved, we have the ability to increase awareness.