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Conversation with Bill Byrom & Mariana Fontana: Measuring Meaningful Aspects of Health in Heart Failure Research

Dr. Bill Byrom, Principal, eCOA Science at Signant Health, recently had the pleasure of sitting down with Professor Marianna Fontana, Professor of Cardiology and Honorary Consultant Cardiologist at the National Amyloidosis Centre, at University College London (UCL), and a member of the Signant Health Scientific Advisory Board. They discussed current and future opportunities for measuring aspects of health that are particularly meaningful for increasing the usefulness of clinical outcome assessments (COAs) measures in heart failure clinical trials.

Byrom: Professor Fontana, it's a real pleasure to be speaking with you today. Please could you first tell me a little about your research interests?

Fontana: At UCL, my research involves patients with cardiac amyloidosis. This is a condition caused by a buildup of amyloid in the tissues of the heart that affects its function. It's a progressive and fatal condition. I am interested in the delivery of efficient and effective care for patients with cardiac amyloidosis, with a particular focus on new technologies including new treatments.

Byrom: I know you're very involved in clinical trials, and we've talked before about some of the clinical outcome assessments typically used in trials. One such measure commonly used is the six-minute walk test (6MWT) – what are your observations in using that test in this population of patients?

Fontana: The 6MWT has been widely used in cardiology trials, including studies of treatments for heart failure and pulmonary hypertension. Trials in cardiac amyloidosis have only occurred in the last 10 years or so, as before that we didn't have any treatments for this condition. In these, the 6MWT has been used as an endpoint, and in some studies as a primary endpoint. It's an important test that measures something that matters to patients – their functional capacity.

But, there are also many limitations. For example, we want to use the same cut-offs across a broad range of patients, and we find that factors such as age have a huge effect on the measure, independent of the status of the condition. Further, the test only measures distance walked – it fails to provide any information about how the patient felt during and after the performance of the test. For our patients, who typically have an average age of 75 years, it's not only important to be able to do certain activities – like daily activities in and around the home – but how they feel whilst doing these activities is very important. So, the distance walked during the 6MWT is only one aspect of what is meaningful and important to patients.

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We also need to collect information about how the patient felt during the exercise. So not just how far they walked in 6 minutes, but how it was for them performing the exercise, how breathless they were, how this compared to the previous time, how many times they had to stop – information about their overall experience of the test.

Byrom: The 6MWT is really a surrogate for how patients might be able to cope with physical activities at home. Would you see an opportunity to measure at-home physical activity more directly?

Fontana: Measuring at-home physical activity using, for example, a wearable sensor, may be significantly more meaningful. The 6MWT is performed in hospital, after a day of travelling to the clinic – some patients have to travel many hours to get to the UCL Amyloidosis Centre – and translating the results of a test conducted in these conditions to physical activity abilities at home means we have to make a lot of assumptions. Alternatively, performing a test which measures a collection of daily physical activity data using a sensor worn by the patients at home could generate a more meaningful measure for the patients. It may give a much better assessment of what has changed in the daily life of the patient.

Byrom: If we think about what we can measure using actigraphy – physical activity can certainly be measured, but we can also assess aspects of sleep. We know in heart failure patients that sleep disturbance is a common problem. Is measuring sleep using a wearable also important in your view?

Fontana: Definitely. How they sleep, how long they sleep, how many times they wake up, do they sleep flat or with 3 or 4 pillows – or sometimes on a chair – it's not just understanding the length of the sleep but also the quality of the sleep. Sleep monitors can provide a lot of valuable detail including sleep disturbance, awakenings, sleeping position, heart rate, all of which give a lot of information about the nature and quality of sleep that is important to the patient.

Byrom: Are you seeing any of these sensor-derived measures in clinical trials?

Fontana: Not yet. While this technology has become well adopted and utilized in personal health outside the clinical trials, none of this has been adopted yet in the trials that I'm seeing. Even in routine care, we don't really see patients bringing in their activity data – but this is likely a result of the demographic – the average age of our patients is 75 years old. Of course, as time goes on, we may start to see that change. For clinical research, we could do better by improving trial designs by including these technologies and collecting better outcome measures that really matter to patients.

Byrom: Thank you, Marianna, that was really interesting and insightful.