2015 Applications Award Announcement for Winner:

"Biomedical System Dynamics to Improve Anemia Control with Darbepoetin Alfa in Long-Term Hemodialysis Patients," published in the Mayo Clinic proceedings in January 2014.

Good evening, my name is Brad Morrison. I am the chair of the selection committee for the System Dynamics Applications Award. The Applications Award is presented by the society every other year for the best real world application of System Dynamics. The best application is based primarily on demonstrated, measurable benefit to an organization through the use of System Dynamics, and secondarily for new ideas that improve the art of applying System Dynamics or for relating work to existing System Dynamics literature and/or other disciplines. The work must have been conducted within 10 years of the submission deadline. Eligible papers must be full-length in English, either originally or translated, at least one author must be employed by the organization whose performance has been improved. Papers may be self-nominated and there are some other criteria but I encourage you all to refer to the society website. There are instructions there for making nominations and we are always eager to see more and more nominations, so please, look for good work and let us know about it and send these nominations in.

I'm the chair of the committee, but I'd like to thank the other members of the committee for their service. They are Jack Homer, Mark Paisch, Kim Warren, Eric Wolstenholme, and Erich Zahn; and I would also like to thank all of the people who have made the nominations. You know who you are. Thank you very much, you will remain anonymous but thank you to you nominators out there. They're very important to keep this happening.

I am delighted to present the 2015 System Dynamics Applications Award to the paper "Biomedical System Dynamics to Improve Anemia Control with Darbepoetin Alfa in Long-Term Hemodialysis Patients," published in the Mayo Clinic proceedings in January 2014. If you thought that was a long title the list of authors – it's a medical paper – are James McCarthy, Craig Hocum, Robert

Albright, James Rogers, Edward Gallaher, David Steensma, Steven Gudgell, Jay Bergstrahl, John Dillion, LaTonya Hickson, Amy Williams, and David Dingli.

It is my great pleasure to introduce the three people most responsible for this System Dynamics, at the center of this work, Ed Gallaher, Craig Hocum and Jim Rogers and I hope you will please come up.

It's traditional when we give out this award to have them stand here while I say a few embarrassing things about the awesomeness of their work so that's what I'm going to do right now.

This paper describes how an interdisciplinary team used System Dynamics to design, implement, and validate a new protocol for treating anemia patients in hemodialysis situations. This work showcases the path breaking capability of System Dynamics to do what we're starting to call modeling under the skin. You heard Ken Cooper talking a little bit about that today and Jay just recently mentioning the awesome capability to do that. We have here in front of us a powerful example of the success of this kind of work in actually helping. The authors built a System Dynamics model that is the core of what is known now as the Mayo Clinic Anemia Management System. Red blood cells, as you all know, carry hemoglobin which carries the oxygen from our lungs to the cells in the body that need it. If you don't have enough of those red blood cells we call that anemia. Well patients with kidney disease, especially hemodialysis patients, have very high risks of anemia. So clinicians who are taking care of them actively manage their red blood cell levels. The standard approach to doing this is to administer doses of drugs called Erythropoiesis-Stimulating Agents, which fortunately is abbreviated ESA, so I won't have to say it again. The ESAs stimulate the process of manufacturing red blood cells aiming at keeping the blood hemoglobin levels within an acceptable range.

Two things make this very difficult. First is that the hemoglobin levels need to be regulated within a fairly narrow range. Low levels might starve you of oxygen and high levels increase the risk of cardiovascular disease, thrombosis and stroke. The second thing that makes it challenging is that there are considerable delays, often on the order of a month or so, between the administration of the treatment and

the resulting changes in the hemoglobin levels. Consequently, and not surprising to this audience, I guess, hemoglobin dialysis patients often experience very dangerous cycles, what we would call oscillations, in their hemoglobin levels, often with very large and dangerous amplitudes. This sure sounds like a System Dynamics problem, even reminiscent of the beer game for some of us.

This model simulates the dynamics of red blood cell production and its response to ESA drug therapy in hemodialysis patients. Here's the really cool thing about it, I think. This model is calibrated to each individual patient in order to generate recommendations for the ESA dosing. To do that, they collect time series of blood hemoglobin levels and ESA levels for individual patients and then use Monte Carlo's simulation techniques to define a patient's specific profile that can then be used to design the optimal protocol customized for that particular patient.

The results have been spectacular. The paper reports results from a 2009 study with more than 300 patients in 8 different out-patient clinics showing that the rates of high hemoglobin fell from 30% to 11% of the patient population and patients within range increased from 62% to 78%. Since the system was implemented in the spring of 2009 there have been about 1200 to 1300 patients cumulatively enrolled, currently about 700 currently enrolled and this work has made a major impact in the lifestyle and quality of life of those patients.

The care treatment team has actually reported that now that they have gained more and more familiarity with this model, they're actually able to now detect small changes in hemoglobin, which were previously lost in the noise, because of these cycles and have begun to associate meaning with those small changes so they're now able to actually detect other consequences such as iron deficiency, folic deficiency, occult bleeding, bleeding, and so on. So providers say this model has really given them a window into the individual patient's needs.

These quality of care improvements have been fabulous and they also come with fabulous cost reductions. The reduced drug costs and reduced hospitalizations alone have generated an estimated 25-30 million dollars savings just for the Mayo Clinic in these 8 facilities over the 6 years that the new system has been in place and that does not include additional savings such as the reduction of staff time in

managing these patients. Dr. Jim McCarthy, one of the authors of the paper, and the then head of the Nephrology Department at Mayo estimated that if this method were rolled out nationally it would be worth about 2 billion dollars in savings in our U.S. Medicare costs because we pay for kidney patients. So if you're an American tax payer, which I would imagine would be anybody who is an American, you should be really interested in getting this out to your local facilities so that our Medicare bills can go back.

Anyway, this work is rigorously grounded in medical and clinical data. It was developed with a very interactive and integrative process by a highly interdisciplinary team. The Mayo Clinicians were so convinced that they were compelled to implement this new treatment with real patients and that's testimony to the rigor and quality of the model as well as the thoroughness and effectiveness of the process that the team used to develop it along with these clinicians. So Jim, Ed and Craig, it's clear that your work has made and will continue to make the powerful impact through improvement in patient outcomes, quality of care and costs and we're quite pleased to recognize this. Congratulations.

I just want to say one other thing really quickly. The authors tell me there's a lot of really interesting stories associated with the process of getting to where they are here today and they're going to tell some of those stories in the Biomedical SIG meeting, the special interest group meeting tomorrow at 12:30 in the Cambridge Room. The Biomedical SIG group is going to be meeting and some of that time is going to be spent reviewing this work so if you're interested go check it out. To everybody out there if you're not familiar with this work please go check it out, it's really awesome. Congratulations guys!