Physics Seminar

March 4, 2019

>>: Okay, well good evening. I'm Walter Thompson. I'm a lecturer here. I know some of you. And I'm subbing for Dr. Garrison, and I want to introduce you to Dr. Yarbough. She is a senior scientist at NASA and a contractor to NASA's Human Research Project. She serves as the principal investigator for the research studies in the human subject studies. She graduated from the University of Houston and in 2017 the College of Natural Sciences and Mathematics honored her as a distinguished alumnae. She serves as (inaudible) Gulf Coast Chapter and on the dean's advisory board.

Please help me to welcome Dr. Yarbough.

(Applause.)

>>: All right. Thank you. Thanks for coming this evening and a special thank you to Dr. David Garrison for actually extending the invitation to me. Dr. Garrison had heard me speak a little bit about the bed rest studies which is what I'm going to talk about today a while back at a during the day physics seminar, and he thought this group might be interested in it. So put your thinking caps on and I'm looking forward to engaging with you in conversation afterwards.

So for a beginning, I start off with this title, which has a bit of a pun to it. "Why on earth should we study the health issues of the space environment?"

So, at NASA, everybody is interested in how to keep our astronauts healthy. And there's a number of ways to go about that and if you think about logistically, in somewhat of an oversimplified way, there is the flight portion of NASA and then the research portion of NASA. And I am actually on the research portion.

And within that organization is a group called flight analogs and our group of scientists and engineers and technicians and others are actually involved in developing analogs that we can use to do all of the research here on earth, almost as a test bed before it goes to the ISS, before it actually goes out in space. And the whole reason behind that is, of course, it'll just be faster and it will be less expensive.

So the basis of the talk tonight is going to be about our ground based studies and those are actually managed ask funded by what is referred to as NASA's Human Research Program and our program is centered right here in Houston at Johnson Space Center because this is the home of the astronauts.

So basic question, what are the health risks of humans living in microgravity and partial gravity? And this becomes important because our astronauts travel into space and that is a microgravity environment. If we go to the moon that is 1/6 the amount of gravity that we have become accustomed to here on earth and when we get Mars, it will be about 3/8. And there's nothing in our life experience that prepares us removal of gravity.

So in a spice environment, a microgravity space environment, if you just think about it, take away the gravity, there's nothing to breathe, there's no air pressure, there's no protection from solar radiation, there's nothing to transmit sound waves, and there's no fluid to transfer heat to and from the body.

And basically, this causes significant changes in the muscular, the skeletal, the digestive, the lymphatic systems. And what we have come to recognize even more recently is to our ocular systems, as well.

So, the likelihood is there's no part of our body that is not impacted by a reduction in gravity.

With that, here's my favorite image of my spaceman, and this is an image that has been created for NASA quite a long time ago but it points out a couple of things and they all have to deal with human adaptations. In a microgravity environment, there is a change in southeaster input and that actually causes disorientation. With the absence of gravity, you're not being pulled down. It's kind of hard to know up from bottom. Kidney filtration rates increase, bone loss is significant and as a result of that, the astronauts are at risk for kidney stones.

Fluid redistribution shrinks the legs and if you look at our astronauts where they are on the ISS, they seem like they have puffy faces. And that's because, we don't have that pull of gravity, we have a shift in the fluids and it rises to the head region. So thus the puffy faces that you typically see on the astronauts on ISS. Touch and pressure sensors, they register no downward force because there's no gravity. The weight bearing bones deteriorate because they need to be loaded in order to be strengthened. And then there's fluid redistribution, but if you think about it, that's going to cause a congestion in the head area. So there's going to be some discomfort with being in space.

Our human spaceflight research is ultimately wanting to create an environment that's going to give the same effect that occurs in space, but here on earth. And the primary effects can be categorized into physiological or cognitive and behavioral. And for those of you who have heard me speak before or for those of you who are watching what is currently going on right now with our HERA program where we put people in isolation, that really refers to the cognitive and the behavioral testing that we're doing where we're asking questions or of, when people are in isolation to just be with each other in the equivalent of mission control, how do they fare over very extended periods of time?

Because the going rate to get to Mars right now is about nine months and you're going to stay about a year, at least. So by the time you're through be the basic math, you know, under which about three years that you're away from friends ask family. But tined the topic is really based upon the physiological changes and how does the human body adapt to this?

So, our ground based analogs that are an analog for the purpose of microgravity is our bed rest analog. So NASA has a number of analogs. Most of them are not on site, which is what is unique about HERA for the psychological studies.

The bed rest studies also were not on site. I will discuss that a little bit later, but those we did in collaboration with our long-term partner at the university of Texas medical branch down on the island in Galveston.

So we develop an analog that we think is going to give us the experience that is comparable to the experience? Space, and then we did a battery of tests and we ask, what can we learn? And then can we confirm that what we're looking at is even relevant by the outcomes being similar to what we observe in astronauts.

By doing it this way, it allows us to do a number of studies because it's very expensive to do each single study. The key is to do a bunch of studies but to schedule them and organize them so that each of the studies gets what they want out of it with respect to the research but that it does not interfere with the other research that's being done. And I will tell you, that is a challenge when you have 20 principal investigators that come with their wish list that is very long and then our team is asked to integrate their studies so that they do not interfere, and then each of those investigators get everything they want. So they never get everything they want, and we always have more drama than we anticipated. But we do get the job done.

So in terms of doing that, then it allows us to actually save money, because it's far less expensive to do research on earth than it is on the ISS. And frankly, we'll do it a lot faster, too, because getting -- getting a new group of crews to the ISS quickly just doesn't happen anymore, right? All right.

And so we need to have a significant number in order to even be able to prove if what we are observing is statistically significant. So it is about using the money wisely and getting as much of the research as we can in the least amount of time.

Once we do that, we kind of establish what the platform is. And then roll forward a couple of years, the hopes is that once we've identified what changes in the body and what changes mic deleterious to the health of the astronauts, we can then try to establish, well what would be a counter measure that would prevent that activity from happening? And those counter measures, we can also study in our ground analog systems. And then we do that before they go to the ISS.

So I like to think of our analogs as being the last stop before our studies go to mission, go to the ISS.

So bed rest is a condition where a subject is placed in a horizontal position with their head 6 degrees lower than the feet. So just imagine being tilted 6 degrees, head down tilt.

This ground analog is the favored analog for studying the physiological changes that occur during spaceflight, primarily because it is the analog where we can induce the fluid shifts that are so critical for the body's response to the absence of gravity.

Bed rest provides a platform that allows us to compare what happens in bed rest, which is a controlled environment, and what has been observed and reported over the many years of all of the past space missions. And it does give us a mechanism for testing a counter measure. And by the time I get to the end of this talk, I will have told you about a counter measure that was studied about four years ago and see recently been published on.

So what happens during bed rest? Well you stay in bed long enough, there will be deconditioning. The weight bearing muscles and the bones of the lower body will unload. Without the pull of the gravity, the bones don't unload. Without the loading, the weight bearing muscles deteriorate. Body fat increases, and muscle and fat deteriorate and change pretty quickly. It can just be a matter of weeks, all right? And depending on the age of the astronaut, it might actually be a matter of days.

Decreases in the bone density occur on average about a percent a month. Where the major impact has been seen in the decrease of the bone in the hip and in the decrease of the bone in the pelvis. And it appears to be the last of the categories of where it is restored after reconditioning.

Decrease mobility, the fluid shift toward the upper body. Cardiovascular deconditioning has actually been observed, that when you look at where the heart is placed in the cavity in a deconditioned position and we've been able to observe it in bed rest, it actually shifts. Literally shifts out of the cavity that it rests in. Okay? Alterations in the immune system and altered cognitive functions but in general we're not using bed rest for cognitive functioning. What we use for cognitive functioning is an isolation system.

With respect to the immune system, in general it has been observed that our immune systems are very robust. In general, most of the changes that are observed in the immune system, it takes between 60 and 90 days of deconditioning in bed rest before those changes are observed. Quite unlike bone and muscle. Well, you'll see it a lot sooner than that.

So, maybe one question is, well, why 6 degrees head down tilt? And it was a question that I first asked when I came to the project. And it has to do with basically the empirical observations that were made in and are cataloged. So back in the early 70s, cosmonauts were coming home from long missions, and they were having difficulty sleeping and they were continuing to say that they felt like they were slipping off of their beds. So after you say something that's unexplained to a scientist, they're eventually going to figure out a way to try and observe that and to see if they can take a measurement that can actually demonstrate that it actually does occur. So this was repeated over several missions.

Finally somebody came up with the idea that they were going to raise the foots of the beds so that the cosmonauts would not feel like they were sleeping and then they adjusted how much they raised it to what their level of best comfort was and their best comfort was at 6 degrees head down tilt. So there's a practical reason why we started there.

And so most of the literature is on 6 degrees head down tilt, and that's what I'm going to talk about today.

So it is currently the accepted model from studying the physiological effects of spaceflight on bone, muscle, and cardiovascular systems. And so all of the international space agencies, whether it's the European agency, the German agency, NASA, the Japanese agency, everybody is doing studies at 6 degrees head down tilt.

So our flight analogs program, which is on the research part of NASA, was actually asked to plan experiments that could answer relevant questions to the human research program. And the question that has been asked is what happens to the body under these circumstances? And then how can we manage the deconditioning that occurs?

So that requires a -- an abundance of subjects. And so oftentimes you will see that NASA has a call out for subjects to actually participate in the studies. And the type of call for the subjects is going to depend on which analog that they're going to be placed in. For our bed rest studies, we were mostly looking for people between the ages of 22 to about 50, 55. We were trying to expand from what the average age of the astronaut is, which is in the late 30s and early 40s, knowing that if we made that range too narrow, we would not be able to recruit a significant number.

And because we wanted to observe the deconditioning under conditions that would be relevant to the astronauts who are very healthy compared to the general population, we had requirements for fitness. All right?

We put a call out. We actually find these people. And when we find them, they are always very pro-science research, and it's one of the reasons why they're willing to do our studies. It does require us as is the case for any time you do human subject studies, is to provide a clear, informed consent briefing so that a person understands precisely what they are -- what they are applying to do. And the bed rest studies in the past have been as short as seven days and what as long as 90 days and a little later in the talk, I will go into details on a study that we manage that was 70 days. So that means our subjects were in bed 70 days. All right.

And yes, the entire time, this is actually done under a physician's care, as well.

So the ultimate goal of the program that I am affiliated with basically is just to develop the best technologies that we can that are going to allow us to have long duration human space exploration. The reality is if we were doing unmanned space exploration, we wouldn't need to do any of this. But at this point in time, our goal is for our astronauts to go to explore, and to return to earth. And when they return to earth, we want them to be healthy. And if they're not exactly how they were when they left, we want to be able to recondition them as quickly as possible. And in most cases, that means that we will have to spend a fair amount of time keeping them conditioned for all of the time that they are outside of the gravitational field.

So our team is a complex one, but I hope you will get an idea of all of the breadth of knowledge that is actually required to pull off the study that I will be talking about a little later. So our team is comprised of scientists and engineers. They come from both the civil service workforce and they are also NASA contractors. As the introducer explained, I am a contractor. I work for KBRwyle. So what that means is a couple of weeks ago when we had the government shutdown, the civil servants couldn't work. But it was our contractors that kept our studies going and frankly for many of us, our contractors actually had more work than ever to do because we were actually covering some of what the civil servants were doing. So it's a team is the point I'm trying to get across here.

So we have campaign scientists, operation planners, data engineers, facility engineers, experiment support scientists, and subject screening coordinators. And it pretty much begins with subject screening coordinators because these are the people who actually help us identify who are going to be the subjects that will come and do our studies. And we have an algorithm for what we're looking for, and it's not easy. I mean it's not the sort of thing that you're going to find every day because we have a lot of criteria that we have to meet.

Then we have the engineers that are oftentimes involved for our bed rest studies on the front end in developing the beds that we actually were using for the duration of the study that have the 6-degree head down tilt. For some of our other studies, like the HERA program, it's the engineers that will actually refitting the isolation unit that was originally at one time placed at (inaudible) Mars but is now on site and is the 636 square foot facility that we actually house our the subjects in.

So the engineers and the scientists work hand in hand. The scientists are the ones asking all of the questions and trying to get all of the answers, too. And for bed rest, because the condition of bed rest deconditions the entire body, we are looking across the full spectrum, cardiovascular, bone, muscle, immunology. I mean, every part of the body, we have specialists in that area that are designing the experiments that will give us the information we need to understand how our bodies actually function and sustain ourselves under very different conditions.

So the unit that we did our bed rest studies in, so I did bed rest studies with NASA for seven years. And then when we ramped down bed rest studies locally so that we could become a part of the international bed rest studies that are now being conducted in Cologne, Germany, at that point I then shifted over to our HERA program. So I've been involved in the behavioral studies for our the subjects.

But between 2010 to 2015, we were conducting the bed rest studies at the FARU, the Flight Analogs Research Unit. So down at the island in the UTMB in the towers, on the top floor, the sixth floor of the children's hospital, the entire floor was a dedicated wing for bed rest studies that was referred to by the acronym the FARU because NASA has an acronym for everything. But this was a partnership as well, too. UTMB put in the dollars, provided the space, provided some of the personnel. And then NASA basically paid for it and the construction was done.

What was really important about this is that that unit on the sixth floor was completely capable of operating. It had all of the resources that it needed there, including a kitchen. So when there was the hurricane that hit, it was actually the FARU was the first research that was conducted at UTMB in completion. It was the first set of studies that was able to be conducted because it was self-sufficient. So it was a great system and we had that for a total of about seven years, even though I was involved in it only for about five of those.

The studies were integrated into what we call study complements and, once again on a non-interfering basis. And the reason why we call them complements is because technically you need the define in advance what sort of statistical significance you are aiming for, and that is going to be driven bit number of the subjects that you can do the number of experiments on. Okay?

Once that's defined, then we split them up into missions. And multiple submissions actually make a complement. All right?

We have standard conditions, which are the control set of variables that we keep consistent across all of the complements. And there were a number of them for bed rest -- the duration of the study, the tilt of the bed, the temperature of the room, very controlled environment.

And standard measures are a battery of tests that are integrated into all of the complements. So NASA gets a large amount of data on a small subset of testing because it's organized that for example, everyone who does a bed rest study irrespective of what the individual studies are being conducted, will do the battery of tests. And if you run tests over a number of years, five to ten years, you then get a large subset of these standard measures. And so that's the definition of the standard measures.

And then those become the measures by which are used to compare what actually happens over the many years of the -- in the astronauts.

The purpose of the standard measures first of all is so that we can actually characterize what actually happens when you put people 6 degrees head down tilt. And then once we figure that out and then we figure out what may be a plausible counter measure, then we test it under those same conditions and see if we get the desired effect.

So the standard conditions, this is a hospital room at UTMB. You see there are two beds in it and each of our rooms housed two the subjects at any one point in time.

Both were at 6 degrees head down tilt. The room temperature was between -- well was approximately 70 degrees. The study duration varied. Which was set for a 60 days study, which was a classic bed rest study length. But, as I said earlier, there were studies that were done as far out as 90 days and the one that I'll talk about at length is going to be 70 days.

What was similar between all of them is that there was a pre-mission phase, there is a mission phase, and then there is a post-mission phase. And the pre-bed rest phase was 13 to 14 days. That was the time where all of the base-line data was actually collected. And because we actually did some studies with diet, it was important for us to have enough time on the front end for our the subjects to adjust to a controlled diet because we actually expected to see some differences. For example if you were eating the bed rest food, there's a good chance that it had a lot less sodium than everyday food would have. And so we would expect to actually see some differences in fluids as a result of that.

And we wanted all of those to actually stabilize before we actually started our study. Then we would put people in bed for whatever the duration was, and then we would have what was called a recovery period. And for the most part studies that were 60 days or more in bed rest, we required 14 days of post-rest. And we had exercise physiologists that were skilled to recreate a reconditioning program that would get our the subjects reconditioned within 14 days. So even if you did a bed rest study and became fully deconditioned, before you went home, you were reconditioned. Okay? Sleep/wake cycle was to wake up at 6:00 in the morning and then lights out at 10:00 p.m.

We had monitoring 24 hours a day. Remember, we're basically doing the equivalent of a clinical study because we need to capture data under controlled environments, which means that we need to be able to demonstrate and to be able to prove, frankly, that if we say that the subject stayed at 6 degrees head down tilt, that they did. So we had complete 24/7 monitoring.

We monitored two ways. There were cameras inside of the rooms and then there was also, what you're seeing here, subject monitors that are sitting outside in the hallway looking into the rooms.

And basically what we were looking for was any subject, once it had gone 6 degrees head down tilt, any subject who would stand up or sit up was in protocol violation and frankly that was the end of the study for them because once those fluids shift, then we have to start all over.

So daily vital signs, blood pressure, heart rate, body temperature, respiratory rate, body weight. Fluid intake and output was measured and there was psychological support provided. But unlike the studies we are doing now, bed rest is not in isolation. You're in a room, you're on a bed. You can't sit up or stand up, but there are -- you have a roommate. You have a phone. You can communicate on your phone. You can connect to the Internet. There is hospital personnel. A psychologist would come and talk to you. There was a physician that would come and talk to you and I would come and talk to you once a week. So it's not isolation.

We did allow our the subjects to stretch and if you actually look at this team member who is posing as a subject, the idea was access to the computer. And it's overhead. So these were swing arms so that the swing arms could move the computer out and away. There's no problem here with the movement of the arms because what we're trying to minimize are the fluid shifts. So the idea is the back and the head stays in contact with the bed. The bed was 6 degrees head down tilt. If you did that, you were in compliance.

So that does mean that all bodily functions have to be managed while you are in bed. So for those that did not know how, yes, there was training on how to use a bedpan, for example. Showers were once a day but the showering was actually done on a gurney that was always designed to be 6 degrees head down tilt so that our the subjects would roll out of the bed on to a gurney, rolled into a shower, were allowed 15 minutes to shower, rolled back, out and then rolled back onto their bed. So when webs strict bed rest, we were serious as a heart attack. And it's one of the things we were very, very good at. And as a result of that, some of the data was more precise than other data had been because there were not the small failures to maintain the 6-degree head down tilt.

No exercise was permitted because what we were trying to understand is what happens in the absence of gravity. And any sort of exercise would have been loading those bones and strengthening the muscles and we did not want to allow that because that would have interfered with the data that we were trying to collect.

Standard diet, it was a diet based on the NASA spaceflight nutritional requirements. And we captured everything. Just think of it as what goes in comes out. So the amount of urine was measured, lots of it. Think about it, the number of the subjects for the number of days. No caffeine. That meant no chocolate, no cocoa, no tea, and no herbal beverages. All right. That was a deal breaker for a few people. So not everybody could do bed rest, but these were the requirements. All of the food was to be consumed. We set the diet based upon wanting the person to not lose or gain more than a 5 percent differential. So our goal was not to starve anybody or fatten anybody up and it was one of the things we were trying to hold as a control. All right.

We had clinical labs that were done on all of the specimens. That meant a huge amount of blood and urine studies that were for the purpose of monitoring the subject's health U because that's the information we wanted. We looked at general immune status, viral specific immunity. A lot of that was either Epstein-barr virus, for example. There was some latent viral information done. And one of the things a came out of that was the immune system did start to get compromised after 60 days and oftentimes that were evidence of if anyone had had a prior chicken pox or hepatitis (inaudible), that was measured.

Anything that was related to the regulation of calcium and also kept track of antioxidants. So a little bit here about the nomenclature. The BR is for bed rest. And if it's a whole number, and they each are because each one of those represents a day. So if it was negative it was pre-bed rest or the baseline period of time, which was up to BR minus 14. And then on this one you're seeing that on bed rest day 28, which was about halfway through for the day 60 is when this measurement was taken. BR plus zero is the day that they stood up. That is the first day they stood up after being in bed for whatever period of time. It was a crucial day for the investigator because, of course, everybody wanted to do all of their analysis on the very day that they are first up.

We got most of it in and it was an extremely busy day for our the subjects, and then plus five is to be able to start to get some idea of what's happening with what naturally reconditions. So that's the nomenclature.

In terms of the amount of studies that were done, it covered everything. I'm giving you just a few examples here with some pictures which will give you an idea. But bone density. Right? We're very interested because probably one of the hallmarks of space travel is the reduction in the density of the bones for the astronauts. And this also turned out to be a great body of research that has provided information for the general public. And in particular for older women over the age of 55 and older men over the age of 65 as naturally their bones also starts to erode in terms of the density. So it's a good example when I say the research that we're conducting in at NASA is of course intended to help us plan for the improved and sustained health of the astronauts. But virtually everything we do also has a value back to the general public, as well.

QCT is a little different, looking for bone density because this is a mechanism by which you can not only look at the mass of the bones but also look at the structure of the bones. And it is many of these scans that gave information with respect to the reconstitution of the bones, particularly in the hip and the pelvis areas, which were the areas that seemed to take the biggest hits with respect to the degeneration of the bone.

Physical fitness, isokinetic testing. You see this gentleman who's actually doing leg lifts. And then overall, (inaudible) activity is overall fitness is observed by cycle ergometry. And during bed rest, there was some cycling that was actually done and those were done on very fancy cycles where a person would cycle on their back.

For the neurological assessment, which is to address what happens to balance, the neural vestibular system and the connection between those two in terms of a person maintaining a good posture so that -- whoops, what I saw over here was an operational tilt test. Yeah. So you stand on this platform and this chamber moves. And you stand on it and it's swaying and it's moving. And so it's actually measuring the balance of the person. And it was very clear that when our the subjects first few days after being in bed and supine for 60 days, they weren't very good with respect to balance. And we were looking actually for indicators of that being improved over time.

Cardiovascular function and operational tilt test to actually look for ortho static tolerance, looking to see if there was the likelihood of a person fainting. Echocardiography which was looking at the actual function of the heart under these conditions.

So now that you're familiar with the data that is collected and, if you think about the fact that we collected the data over five to seven years, and then the concept came of well, now that we know what to expect and we get that routinely every time we get somebody in bed, the idea was to actually test a counter measure. And the counter measure that was actually tested was by a total of eight investigators, but the counter measure itself was one that was designed by our scientists, Laurie Ploutz Snyder.

And the idea was to look at what would be the effects of bed rest on a functional performance. So not just looking at the standard measures and how they vary, but for the outcome to actually be functional based. So how much bed rest will give you what reduction of performance? And how much reconditioning do you need in order to restore that performance to what it was before the person went into the bed rest phase?

Once again, the idea is to actually understand what are the changes and how they impact function, because that's going to be the impact for the astronauts at some point in the future. The longer that they are away, the more deconditioning that there would be. And maybe the likelihood of having that impaired.

So the exercise program which was the counter measure, was referred to as iRAT. And iRAT is an acronym for integrated resistance and aerobic training. And the prescription, the exercise prescription is based on the finding that exercise intensity is the most important factor that determines training effectiveness. So if you actually look at the table, you'll see that there was resistance -- first of all, the subjects exercise six of seven days. They actually didn't exercise on Sundays. Give them a little rest.

And three days a week, there was periodic resistance. So there was a prescription for a number of squats, lifts, legs, knee extensions and, heel raises. And then aerobic exercise was actually done on a vertical treadmill. So that fancy image that you've seen that looks like Spider man. But instead of the treadmill being like this, it's like this so now the person is walking.

That consisted of three days a week of high interval intensity exercise and those alternated with the exercise that was being done.

All right? So Dr. Laurie Ploutz-Snyder designed a prescription and we ran a study that is referred to as our bed rest campaign 11. The fact that it is an odd number would tell those that are familiar with the work that NASA does that this is a head down tilt and not a head up tilt study. This one was 70 days and there is a reason why it was 70 days and it has to do with No. 3. We had one investigator that wanted to ask, what is the impact of testosterone supplementation to the exercise prescription? So that desire, that PI's wish list meant that we had to do two things.

First of all, we were not going to have females in this study because no, we were not going to administer females -- to administer testosterone to females. And it also meant that we needed to come up with a cycling for the amount of testosterone and the investigator wanted us to start off with testosterone to have a period of time where none was given, to have that repeated and then to have it end with testosterone. So we did two weeks on, two weeks off. And we did that five cycles. Thus we had ten times seven, 70 days.

So it's not really magical. Ask a scientist and there's a reason for everything.

All right. So this study was actually six integrated studies and then you add onto it the standard measures that were actually being done in the background always. So we had one investigator that was looking at functional performance and it was really an amazing kind of maize that the subjects would actually go through and that was functional activity to do every step along the way. Those tests were done before they went into bed rest and then after bed rest and then after they were reconditioned.

Then we had the i rat which is the resistance and the aerobic training which is actually done. We had the test on the street roan supplementation. We actually had an investigator that was very curious to what was the effect of a person's ability to smell after they had been at head down tilt for a particular period of time. So this one was coupled with the food study, and they took a lot of study with respect to how much did a person enjoy or not enjoy certain foods after being in head down tilt for so long.

It was our first effort to actually do what was called a detection of attitudes. And this was an investigator who was really interested in a behavioral study, was interested in how did the language, how did the way a person communicated, how did the word usage that they selected change over time that maybe would be indicative of their mood after being in bed for an extended period of time.

And then we actually had an investigator who was looking at cognition changes by doing functional MRIs. No, we could not do MRIs while they were on bed rest because we couldn't get the 6 degrees head down tilt. So it was a pre-MRI functional, then the duration of bed rest, and then looking at what were the MRI scans relative to the -- what was observed before they went to bed rest.

So all of these investigators, and it took us a while to do that. We actually started in spring of 2011, and you can actually see we had to stagger it. Then we got the question to add the testosterone supplementation to the study. And at this point we were recruiting men and women. At this point it was men only.

And we completed the study with the number of the subjects that we needed. We had a three way split of eight the subjects. Those the subjects were controls. No exercise, exercise and exercise plus testosterone. So we had three arms to the study.

And then in spring of 2014 right around the time that we were finishing up, we had an investigator that came in with a new piece of equipment. And we used the bed rest as a mechanism to basically fly wheel was a test bed to actually see how might it work. It was a small piece of equipment that allowed you to do both aerobic as well as resistance.

And so all of these studies were completed at the end of 2014, like, December 30th, something like that. And then there was a couple of years for the data to be analyzed, to be cleaned and, to be shared between the investigators because we had seven, plus an eighth one.

All right. So the outcome of all of this was in an article that came out in 2018. So if you're interested, this could be homework. The title of it was overview of the NASA 70 day bed rest study. And much of what I've described to you here is described in this one article because we had seven investigators who each did an article on the actual science that they were actually responsible for. But because it was a (inaudible) study, the overview actually describes how the study was designed and how the data was captured. Information on the subjects with respect to inclusion and exclusion criteria.

The bottom line here is that there were 24 the subjects that were randomly assigned to these three groups. And what you may want to know is, well what, came out of all of that? Because you guys started that in 2010 and you published it eight years later. And what is the take home message?

So I've tried to put here just what the take home message is, but for the most part, a lot of the data is still being evaluated with new concepts and as more information comes in, and some of the investigators are even doing extension studies. I'll talk a little bit about that because they're not doing them at UTMB anymore.

So the first thing is we were able to demonstrate that doing a 70 day study could actually give us reproducible and row bust data. So the 70 day bed rest study was not the longest study but it was at the time of inception the most complex study that had been conducted by NASA for bed rest. All right?

We were able to demonstrate that we have a suitable platform. And that we have a mechanism where we can evaluate a proposed counter measure.

The second important hallmark was we were able to demonstrate that using the innovation of the studies was a way to support multiple investigators. If you think about it, we had 24 the subjects in a three arm study that did eight different investigative studies. But they were all done one site, right? Not multiple sites. They were all conducted by one team. And they were all analyzed over a five year period. All right?

And the third one is that the research benefits did include the ability for the investigators to share the outcome measures across investigations. And the testosterone is the -- the testosterone study is an excellent example of this. When we first started, it was a two arm. So instead of waiting to do a total other study, which would have been an even longer duration, more money, more subjects, and a later period of time to even be able to start, so it would have delayed the acquisition of the data, we figured out how we could incorporate it.

So the platform has been established and we have been using it now for years and years and years. And our international partners have learned a lot from us. And one of the things that has come out of the all of the research is for the ongoing studies, there are international standard measures. So we talked about what were NASA's standard measures. Now they are international standard measures. So I'm going to be very brief on this one because we usually leave the outcome of the research data to the PI who was actually responsible for it. But there's two of them that I'm going to talk a little bit about because there were so much activity actually at JSC on these. You might remember me saying that Laurie Ploutz Snyder, a doctor who is an exercise physiologist designed the iRAT. So that program actually showed great promise and much of what that exercise program was is actually ongoing on ISS now. For those of you that might be familiar with some of the earlier sprint studies that were done, it's a modified sprint. And it's actually been modified with improvement.

There were multiple outcomes. The one that was probably the most useful with respect to the performance, which is what Jacob Bloomberg was interested in, had to do with the knee strength and aerobic endurance. And those areas were considerably more protected than they had been with other previous exercise prescriptions.

Around the time that we were doing the ocular studies, there was the first breaking news that for astronauts that had been on the ISS for longer than six months, were, some of them, at the time it was thought maybe 10 percent of them, were showing signs of vision issues, aberrations in their vision. And it was not clear what the cause of it, and we still do not know that. And it wasn't clear whether or not somebody was predisposed for it or if it was something that was actually induced on the ISS. What was known is that it was not observed in astronauts that were on the ISS for less than six months.

So our IRB, our institutional review board, was concerned. And rightfully should have been, because we are putting the subjects head down tilt with the desire to mimic what would be the fluid shifts that the astronauts are exposed to. And we actually needed to find out whether or not that process in and of itself was going to be a risk to our the subjects. For those of us who had worked bed rest for about five years before that, inherently thought that probably not because never in the previous bed rest studies had we observed any ocular problems. But we didn't have a study designed to ask the question, were there ocular issues? So we did.

And so for the subjects that were in the 70 day head down tilt, our IRB required us to do monitoring for vision weekly, which we did. And what I'm pleased to say is that for the 70 day study, for the subjects that we did the ocular monitoring on for that entire period of time, there were no clinically relevant visual changes observed during bed rest. So it was very consistent with what we had before.

The down side of that, though, is bed rest did not appear to be a model for studying what is very real. And it goes by the acronym of a visually impaired activity. So it's referred to as VIP. And there's a lot of continued research on VIP now and still to this day, we still don't know exactly what the issues are. But we're hoping that with joining with our international partners, being able to do our studies? Germany, because the German facility has dedicated rooms where you can pump in carbon dioxides that will be at levels similar to what's on the ISS. Maybe it's a result of the environment. So then you start picking apart and looking at everything that's in that environment.

All right. The last thing -- oh, okay. The last thing I'm going to speak about, I think I'm reasonably on time, is on our international bed rest studies. So how are these different? So the whole concept behind the facility in Cologne, which has been up and running now for just about two years, is that everybody was doing bed rest studies based upon their programming and their planning, which means that we weren't able to make perfect comparisons.

For 6 degrees head down tilt was certainly maintained, but the duration of the studies, the room temperature, now carbon dioxide, the monitoring -- you know, how intense are you with respect to monitoring and being sure that there's no moving of your the subjects? And so now we have what are international bed rest studies where all of the partners, the primary ones are NASA for the U.S., ESA for Europe and DLR -- Germany. Those three agencies are the primary ones that are moving forward with the international bed rest studies.

The idea is similar to what we had used here, and that is recruiting the subjects that meet certain criteria of age and fitness, and then doing the conduct of the study in a very controlled environment where there are scientists and engineers and staff that actually monitor all of the daily activity.

So with that, I'm just going to tell you that what you need to be paying attention to is there is a study that NASA is a part of that will start at the end of this month. And this study is entitled the physiological and behavioral responses in humans to intermittent artificial gravity during 60 days of head down tilt. It also goes by the acronym (inaudible) and that is because it was a European Space Agency study that was looking at asking the question that if you apply the equivalent of artificial gravity by using a small radial centrifuge and spinning the subjects, can you mitigate, will it act as a counter, to what would be the deconditioning of the body?

And what little details that I can share is that there's basically going to be three arms of this study where there will be no centrifugation, and then centrifugation under two conditions where one will be for a fixed amount that I believe will be 30 minutes a day, don't quote me on that, and then the other one will be intermittent. Six times five for your 30 minutes but with five minute breaks in between.

So that will start at the end of the month. Even though we're no longer conducting bed rest at NASA and at UTMB and it's not being conducted -- strict bed rest is not being conducted the way I've described to you in the states anymore, it is now a part of the international studies that are being done at -- (inaudible) and (inaudible) is in Cologne.

So this is what I've described. There's a continuous artificial gravity group and then an interval artificial gravity group with medical monitoring and with this set of international standard measures. So just like we had our standard measures, the other agencies have theirs as well. And you get a leader from each of those agencies and collectively they nailed town a smaller subset of measures. And just once again to give you some idea in terms of what those measures are directed to, sensorimotor, muscle, bone, nutrition, immunology, and now even a little bit more psychology also because of the duration of the studies. And cardiovascular.

So with that I'm going to end just by saying that if you think in terms of all of the elements that are necessary to carry out a mission like this, the part of it that is really the most complex is the human element, right? And we continue to do this because it still appears at this point that we need for the sake of being able to capture the best and the most data on any exploration is for that to be a manned mission. And so for that reason, if we're going to continue to do manned missions, we need to continue to do the biological research that will be necessary to inform us how to keep our astronauts happy. Because it's not likely that the human public will want U.S. dollars going to studies where we can't keep our astronauts safe.

So at that, I am going to close and I will take any questions that you may have.

(Applause.)

Yes?

>>: So I'm curious, you said that, you know, obviously your the subjects violate protocol, they're kicked out of the study. What percentage of your the subjects actually make it all the way through, say, a 60 or 70 day study versus being kicked out for protocol violations or dropping out voluntarily?

>>: About 90 percent actually we were amazingly pleased. And I attribute it to the selection process. All right? So the selection process is very different depending on what your analog is and what it is that you want to measure. So, the biggest component for

compliance on the bed rest studies is for the persons that are avid exercisers, which is going to be very astronaut-like, but if you think about it, some of those people aren't going to want for their bodies to be deconditioned. They just aren't going to want to do that. And so we had to identify those, and not recruit them. It was just as simple as that. And we got better and better at it over time.

But I will tell you, I had one subject -- because in fairness, on the 70 day study, there were three arms to the study. So you could end up being a control where you did no exercise, or a control that exercised, a control with no exercise and exercise -- or an exerciser who had testosterone or placebo. Everybody got an injection, they just didn't know which one it was.

We could not tell the person before they signed the consent form which group they were assigned to. Because that would have built in bias into the study.

But they were told that whatever they were selected for, that they had to want to do it. Right? Not a single time did we tell somebody which arm they were in and then they immediately checked out. Nobody did that. There were of a that didn't make it for true compliance reasons. I just -- you know, I just kind of got sick of it or I just couldn't do it for that long. But I was really impressed. Very few. And I think many of those had thought process that, once I understood it, was something that I started to mention as a way to think about it.

One of the subjects said to me that when you come in and you are exercising, your goal, your personal goal, is how fitter can you become than what you started? So it starts right on day one for you and you're exercising. And you have some preferred or proposed focus or goal. And then it's how fast can you get there?

But he said to me that if you are a non-exerciser, you have a goal, too. Your goal isn't the exercising. Your goal is how short a time can you get to reconditioning? You've got 14 days. Can you do it in less than 14? And so that mind frame is what made many of them want, frankly, to do the study even though they weren't exercising because they really wanted to understand even more about their amazing bodies.

>>: Are there any, like, specific technologies that are being developed through your research (inaudible) to be used on Mars? Like, any specific one thing? I mean, I know all of it is going to be used because they're going to have to use (inaudible) Martian environment or lunar, whichever one. Do you know how exactly that might -- how exactly that information might be implemented in those technologies?

>>: So it's not very obvious. So with respect to the bed rest analog, no is really the fair answer at this point. There's nothing that we're doing that we can actually say is going to be directly related to the design of those suits. All right? Because what we were looking at in the bed rest studies is the deconditioning of the body and then the reconditioning of it.

However, on some of the -- on the HERA, for example, where we're looking at behavior and we're not only looking at behavior of people when they are away from their friends and family, we're also asking two really important questions in our current campaign.

And one is, how do people respond to a significantly reduced workable space? And, how do they respond to a significant increase in the lack of privacy?

So on that first one, it's very much related to what's called habitability. So how well can a person maneuver or not injure themselves or move around and be efficient in a small space? And that information is going to directly inform your suit. You know, how big can it be? How thin is the fabric? And all of that is going to be driven by how you're going to work in this dedicated space.

>>: (inaudible) specific psychological (inaudible) so they don't just get bored because that (inaudible).

>>: Yeah, no. That's a great question. And I failed to mention that up front. So for the people that are in bed, remember the key is just to stay on the surface of the bed. It sounds like it's really easy but I'm sure it's really hard, right, to do that for that period of time. So we're not limiting the brain. And frankly what we wanted is for people to be engaged and to have some quote, unquote work to do. But they weren't going to be able to work like they were typically working. So they were all encouraged to take on a project. And you see these tiles that you have in the ceiling? At UTMB for the five years that we were there, each of the subjects were given a tile and then they actually designed that tile, painted something on it, drew something on it that was representative of how they spent their time.

We had a variety of things they did. Some were students that were prepping for medical school, used that time to actually study. Others wanted to learn a new language. Some of it was a little for practical. You know like you just become a project manager for your wedding. I mean -- but they needed -- and they really needed to stay engaged because what we weren't doing was looking at the impact of behavioral changes on the physiology. We weren't doing that in our bed rest studies. So we needed to feel that that was being maintained and staying intact so that the changes were mostly as a result of the not being able to move and the fluid shifts. Right. And so that was the reason for the psychological support. And so psychological support kept an eye, just to be sure, that they weren't too moody, if you will. Yeah.

>>: So (inaudible) I guess just kind of what are your parallels between your bed rest studies and now that Scott Kelly has come back home and (inaudible)?

>>: Yeah, I haven't finished reading the book yet but I have started it. So, Kelly's the astronaut, so it's the real thing. You know? And what we have in our the subjects is at the end of the day, it's an analog. Everything that we talk about now on the HERA project with respect to behavior is being done in an environment where we are doing nothing to reduce the gravity. So we've isolated, if you will, wanting to study the behavior in a confined isolation module on earth. And we just accept the fact that we aren't doing it in conditions where we've removed the gravity and have maybe stressed the body in a way that it would naturally be maximally stressed.

But, Scott Kelly had a whole lot to say with respect to the livable space, with respect to the privacy, with respect to things like -- that bring like comfort. You know, how much of what is personal that you can bring with you.

Also, how much free time can you have? And mechanisms so that you can have some separation. And so that has informed us for what we're doing in campaign five, which is not a part of this talk. But for those of you that are following HERA, the amount of livable space on the first floor of our two floor module has been reduced about 35 percent. And it was small to start off with. So we feel like we've become more closely related to mission fidelity there.

The hygiene module, which was something that was an add-on to the module for the purposes of the first couple of campaigns of HERA, because we were doing a study on site and the IRB required us to provide just some basic privacy and mechanism for bodily function. But as we've gone on, we knew from the very beginning that that space was not in line, spice-wise. It was very low (inaudible). The shower was incredible. It was really big. And that's just the way it was designed.

So had the habitat been designed from the bottom up, it wouldn't be looked like that. Now we're doing in and making the changes. Part of the push for campaign five is to get information on space because the contractors are already envisioning what sort of capsule is going to be used for transport and how small is it going to be? And so we were actually tasked on our fifth campaign, which is our first mission, which just started a couple of weeks ago, so try and understand how small is too small? And so it's designed to actually provide direct information.

Yes?

>>: Okay, so two part question. At the beginning you mentioned something about problems with being in a microgravity environment, and one of the things was (inaudible) production. Now, is that because there's fluid flowing up and they want to work in a top-down fashion, (inaudible) or does being in microgravity do something to the kidneys to make it (inaudible)?

>>: It has to do with the calcium absorption. So it's related to the bone loss.

>>: So as long as your -- so the second part is does compression stuff help combat the movement of fluids? Like stuff that squeezes tight like (inaudible)?

>>: Yes, it does.

>>: You can keep the pressure on the legs (inaudible) but what about, like, rubber bands? You know how they have the exercise rubber bands that keep your bones under constant pressure (inaudible) bone under pressure and hopefully not have the calcium (inaudible)?

>>: Yeah. It would be. It was not a part of our bed rest studies, and I'm sure that there is some investigator that was looking specifically at that. For the bed rest studies, what we did is for anybody that had a history with filtration issues, we did not want to place them

at a greater risk. So it was one of the exclusion criteria for our studies. But it's a real problem, and the concern becomes that with the longer the distance, there's an even greater chance that you could have for example, the development of kidney stones. And so what are going to be the counter measures against that?

A lot of it right now what about preventive in terms of the selection of the astronauts that no family history of it. Right. So on compression -- and that's really all I can say on that because I'm just not very knowledgeable about what other things are being manifested. I would imagine some of it would come down to nutrition, as well. The selection of what they would eat over a period of time so that they could maintain the calcium levels.

What ill say is that for the first two years when I was at NASA was actually the study that brought me to NASA because I'm an immunologist by training and so I was very interested in the immune system. But a couple of years ago when we were going to the moon and not going to an asteroid, NASA had launched a lunar project and the purpose for the lunar project was to ask, well, what happens when you've got the modify gravity that's different from the one you have on Mars? 1/6 instead of the 3/8. So for that it was a head up tilt and the subjects actually wore very height compression hose. And we were able to demonstrate that we could control the body fluid shifts in a comparable way.

That study was only a pilot that was done initially. And I was on that study. And we were very proud that our first pilot we were able to demonstrate the efficacy that was expected. But then the study was deconditioned because we were no longer going to the moon. We were annoy going to an asteroid. And so that portion of the lunar head up tilt, which went by the acronym HUT, instead of HDT, was decommissioned.

There's been questions on if we want to resurrect that now, particularly because of the lunar gate way because there would be travel to an inbetween spot to resupply, and then launching from there to a -- launching from there to Mars. So the way we've managed that for our campaign five, our simulated mission is also a lunar gate way. And the final destination is Phobos, which is the moon of Mars. That's really all that I am aware of at this point in terms of what's being done for mitigation.

>>: So I have a friend who passed a kidney stone once (inaudible) or can be a thing.

>>: It's a big thing, yeah.

>>: How (inaudible) is dialysis (inaudible) especially for, like, long-term trips?

>>: So I think I am going to answer that cautiously because I have a P in front of my D and not an M. (laughter).

But I'll speak a little bit from experience, because in one of the other analogs that we were engaged in, we actually had a subject that passed a kidney stone. And it was excruciatingly painful. We released that subject from our study as we took them to the hospital. They passed the stone before getting to the hospital and was perfectly fine thereafter. But unfortunately at that point they had been removed from our study.

So it is -- it's critical, and the prevailing opinion at this point is that it has to be preventative because depending on where the stone is in the tract and how long it stays there is what causes the severe pain. So if you can imagine if it gets in and gets obstructed and then you don't have a physician who is on your flights, and even that has raised a number of questions about do we even need to have physicians on these long duration flights? Which will be a different process to actually always ensure that you select for them.

But much of it is trying to address the question of, what sort of medical help could you instruct long distance? But that's not going to work for Mars, because you're going to have a very delayed communication time.

>>: One more.

>>: Yes?

>>: You said that people stood up or sat up they would be disqualified. But you roll out of bed to a shower (inaudible) that you allow them to roll around in the bed before kicking them out as well?

>>: Good question. Good question. So we really didn't kick them out. They kind of kicked themselves out and I can only think of maybe one case where, you know, a person just sat up and so -- that subject was ready to go, and it is what it is. I mean, you know, those were just the rules. But I do want to be sure that you understand that when our the subjects were in bed rest that they were not mummified where they just had to -- they could move. I mean they had a lot of flexibility. They could use their upper bodies, their arms. We had people who were crocheting. They were doing all sorts of things. The key was to maintain the contact with the bed so that we could actually minimize the fluid shifts, because any amount of fluid shift was going to be take us back to square one.

>>: So they were allowed to lay on their sides?

>>: Yes, yes, yes. And when it came to eating, I should have mentioned this, that because we were concerned about maybe the choking hazard, if you're eating in a -- in a head down tilt, right? So they could prop up on their elbow for -- not one minute more than 30. Okay? And so once again it was another controlled thing that for each meal, 30 minutes. So one out of 24 hours they could be propped up. There were all of those additional things that we did. Right?

The other thing is maybe to just give you a little bit of a better view that may be a little bit more humane that, you know, the subjects were not confined to their rooms, either. Because their beds were on wheels -- (laughter) -- so they were able to roll around to a common area and have happy hour. You know? And I tell you, I saw some fierce Monopoly games as a result of that. (laughter).

All right. Thank you.

(Applause.)

Thank you.

(End of class)

DISCLAIMER