



**Exercise and Physical Activity Intervention in Pediatric Cancer
Survivors: From Clinical Applications to Policy
March 28, 2022, 1:30 – 3:00 p.m., ET**

Webinar Questions and Answers

Moderator:

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Panelists:

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- 1. Is anyone aware of any cancer center school programs that include physical education (PE) as part of the curriculum?**

Betsy Porter, J.D.: I cannot say that I have ever seen it, but that does not mean it's not out there. I think it proves the point that bridging this gap is what is missing and that there is a real opportunity to connect the two. When you look at return-to-school policies, there is a great opportunity to make that transition easier. The result would be that even if a student does end up bouncing back and forth, that student could still end up with a successful PE program in either situation.

Sogol Mostoufi-Moab, M.D., M.S.C.E.: I think parents are equally important advocates for their children interfacing with the school system and the health care system. I would be interested to see how much parents understand the importance of their efforts in advocating to the school system. Most of the time as a clinician, when I talk with families, the whole focus is on academic

reintegration of the survivor with a return-to-school focus; the physical activity aspect at school is hardly ever brought up. Adding the physician activity issues to the academic reintegration process seems to be more overwhelming. There is just no time to dedicate to that.

Jamie F. Chriqui, Ph.D., M.H.S.: Yes, this is a big problem, regardless of whether we're talking about Individualized Educational Plan (IEP), children with cancer, or any sort of condition or not, the focus is on physical activity in competition with reading, writing, and arithmetic. So, I think as best indicated with the return-to-school policies from the pandemic, we're starting to see a broader focus on a wider range of services that might be included, because that's been a real challenge.

2. Can you discuss the long-term contribution of sarcopenia to frailty in this population and the role of supportive physical activity or weight-bearing activities beginning during treatment to attenuate or mitigate sarcopenia?

Sogol Mostoufi-Moab, M.D., M.S.C.E.: A lot of the work in sarcopenia hasn't been focused on bone marrow transplant survivors in pediatrics. There are preliminary studies in adults aiming to evaluate the benefit of improving muscle mass prior to autologous stem cell transplant to improve overall survival by maintaining, or even increasing, muscle mass. In pediatrics, there really hasn't been any focus on addressing sarcopenia before transplant, as the majority of comorbidities that we have focused on are related to cardiovascular and radiation impact in this patient population. So, the sarcopenia picture should become the lens for addressing this issue as the main focus, as it really has not been the main focus in pediatric cancer patients. The musculoskeletal system in some ways is a difficult outcome for many providers to really appreciate and focus on in terms of assessment and interventions. This is why these all lend a hand and why I think the initiative to bring focus on interventions in younger survivor populations could have a significant return on investment in the long run.

Kirsten K. Ness, Ph.D., P.T., F.A.P.T.A.: Sarcopenia or a loss of lean mass in children with cancer is different than a loss of lean mass in the general elderly population because those in the elderly population lose neurologic function first, and then they lose muscle lean mass due to a sort of denervation phenomenon. I mean, not terrible denervation, but they lose some neurological health before they lose their muscle mass unless they're sick, whereas children with cancer lose their lean muscle mass. Although these children may not have abnormal coordination, they don't have any muscle mass. So, I think it's a different phenotype than what we think of in frail elderly people or frail adult cancer survivors.

3. How will VO₂peak be measured in patients in the study?

Sogol Mostoufi-Moab, M.D., M.S.C.E.: Participants will complete a baseline cardiopulmonary exercise test (CPET). Every person will have several fitness variables generated through CPET testing, and we will use the VO₂peak. We will also assess target heart rate to determine the baseline fitness for an individual participant. If a participant is randomized to the exercise intervention arm, then the exercise physiologist will get the baseline CPET data to prescribe the aerobic component of the exercise intervention with a bike. The same process will be applied to determining the resistance strength training component for the exercise intervention. It is important to provide a prescriptive intervention for each participant instead of a one-size-fits-all exercise plan. Hopefully, this approach will help with adherence, as the exercise intervention will slowly increase based on improvements in

a participant's fitness. At the completion of the study (16 weeks), we will repeat the same assessment to determine fitness using VO2max (secondary outcome). The primary study outcome is actually muscle force, evaluated by a Biodex, as well as muscle mass captured by whole body Dual-energy X-ray absorptiometry (DXA). These components together represent overall indices of muscle health.

4. Would children be ready for a physical education component or even community recreation? Would they need a monitor program, or do you have a sense of who needs services?

Sogol Mostoufi-Moab, M.D., M.S.C.E.: Yes, the reason is to intervene early after a bone marrow transplant but not too early, as a patient still has not recovered from the transplant. Medically, there are a lot of additional, overwhelming challenges that a patient must overcome, which we felt might not make an exercise intervention as feasible. So, the earliest time we have proposed for intervention is 6 months after transplant. There are patients who rapidly engraft with minimal graft versus host disease. These survivors do not have a lot of the recognized complications post-transplant. In contrast, there are patients who need immunosuppressive regimens for graft versus host disease, including treatment with steroids that can cause muscle weakness. Because of this, we allowed an interval of up to 2 years after a transplant as the eligibility window to enroll in the study. This way, if at 6 months a patient is not eligible due to steroid treatment for immunosuppression, we can determine if the patient will be eligible in 1 or 2 years. We know, based on Dr. Ness' work, the safety range to introduce exercise after cancer treatment to ensure that we are enrolling participants who show recovery from an active cancer treatment regimen. So, we won't have to actually worry about such conditions as arrhythmias, for which it would be unsafe to deliver an exercise regimen through an iPad with the app that we use to interface with participants. We also decided to focus on pediatric patients after puberty. So, those ages 15 to 18 meet the pediatric age range, but the trial will mostly target young adults up to age 30. We hope to see how quickly these young adults recover from a transplant and hope to push their musculoskeletal rehabilitation to pre-transplant or pre-cancer diagnosis levels.

5. What are your thoughts to move towards PA assessment being incorporated as a standard of care (included in the EHR)?

Kirsten K. Ness, Ph.D., P.T., F.A.P.T.A.: No, they weren't. Nobody who had too much activity was eligible, so we didn't approach people who were too active. Typically, they were not very interested in doing physical activity and had other things to get back to (as our other speakers pointed out), such as school and other activities. They said that they didn't want to do a physical activity intervention right now; typically though, it wasn't for a medical reason. In fact, kids were more likely to have a medical reason. Their parents were more enthusiastic and were looking for answers.

6. When talking to parents, does the fear of being physically active outside the medical center come up as a challenge for you?

Kirsten K. Ness, Ph.D., P.T., F.A.P.T.A.: Sometimes parents can be protective of their child because they've had an ordeal, such as undergoing a transplant, 3 years of leukemia therapy, or a current physical disability because of their brain tumor. Parents might be fearful and want to be protective, so that's sometimes an issue. However, staff members with whom they're interacting for enrollment in this study work at the cancer center, so they're usually trusted staff. In addition, we encourage

them to enroll, and our study team is skilled at adapting what they do, so if they can't ride a bike because, for instance, they don't have strong enough balance, then we suggest other activities for them. We have a lot of educational materials that are cancer-specific based on what outcomes kids might have.

Sogol Mostoufi-Moab, M.D., M.S.C.E: Yes. The other concept that I had never really thought much of, but which has come up more than once, involves parents saying their child is too self-conscious to actually change at the gym or to participate in gym classes. He or she has a lot of stretch marks from treatment side effects, and scars from the cancer treatment (surgery or central line placement/removal) will remain visible throughout adulthood. Similarly, I have patients who are now in college, many years from primary cancer diagnosis, who still feel uncomfortable in using the college wellness center despite costly tuition that readily covers gym memberships. I think we underestimate the strong psychological impact of cancer therapy and that it continues for years afterward, becoming a type of mitigation factor preventing one from engaging in social settings for exercise.

7. Can you discuss the consideration of measuring symptoms and/or measures of anxiety/mood?

Kirsten K. Ness, Ph.D., P.T., F.A.P.T.A.: We're not measuring psychological symptoms; we're using the PedsQL core and multi-dimensional fatigue inventory, both of which might relate to depression and anxiety. However, in this particular study, we're not measuring symptoms, and that's a really good idea.

8. Is there any collaboration in your efforts with physical activity policy research and evaluation network (PAPREN) to move implementation efforts?

Jamie F. Chriqui, Ph.D., M.H.S.: One of my other hats that I wear is as co-PI of CDC's physical activity, policy, research, and evaluation network. We're a network of more than 650 researchers, practitioners, transportation and planning engineers, and advocates, all of whom are focused on the issue of physical activity. One of our workgroups relates to school wellness and physical activity and nutrition. So, the question involves whether we've done any work between Classification of Laws Associated with School Students (CLASS) and PAPREN or have studied adaptive PE and IEPs under PAPREN in our school wellness workgroup; I would imagine that moving implementation efforts. We haven't done that yet, but it's a fabulous idea. Maybe the person who posed the question could reach out to me if you're part of the school wellness workgroup, as we're looking for project ideas for next year. That might be an interesting, PA-related project for next year, which will start in October under that workgroup—great idea. It would totally be relevant under PAPREN, and if they want to learn more PAPREN, go to www.papren.org.

9. Are PE standards governed by school wellness policies?

Jamie F. Chriqui, Ph.D., M.H.S.: So, as we mentioned, PE space is basically governed by three levels of law. There's Federal, which really is silent on PE with the exception of IEPs, but most of the law in this space is at the state and district policy levels. Betsy and I have led the largest nationwide evaluations of school district wellness policies in this country, which this person is asking about, and wellness policies are required of all school districts in the country that participate in any of the Federal child nutrition programs, including the school lunch, school breakfast, afterschool snacks,

and milk programs. So, the authorizing laws relative to and the requirements and standards tend to be at the state level, but as I mentioned, district policies often do one of three things. First, they are [often] silent on the issue, and they basically default to state law requirements; second, they'll embed the state law requirements into their district policies; or third, they will do either the first or second and then go beyond the state requirements. Often, the district policies and actual school practices tend to get into the details of implementation or get into the specifics of how those state laws and/or district policies should be implemented within the unique context of each school within the district.

Just to clarify, part of that Federal mandate for the wellness policies identifies eight different types of stakeholders that must be involved with the adoption and with the ongoing review and revision of the wellness policies. When USDA created regulations in this space a couple of years ago, they added specifically PE, and physical educators needed to be among those stakeholders. Therefore, I think it is a great opportunity, particularly in the context of a conversation we had earlier in this panel about needing to provide more linkages between schools and cancer centers, among other potential policies. That might be a really great avenue for some of these discussions.

Betsy Porter, J.D.: I would also add that one of the USDA Federal requirements that has been updated recently for school wellness policies involves the fact that physical education teachers are now a key stakeholder in wellness policy development and updates. That is a wonderful opportunity to have—a voice who not only knows physical education but also the kids in the district and the kids with whom they are working. This requirement would include anyone who might need adapted physical education.

10. Drs. Mostoufi-Moab and Ness, your studies are unique and spread out across the country. What are the environments for the kids like, and do they have IEPs or anything similar?

Kirsten K. Ness, Ph.D., P.T., F.A.P.T.A.: We could actually query that. I could amend the protocol to query that for the kids who have enrolled so far to find out if they have or if they're getting adaptive PE That would be possible to do.

Sogol Mostoufi-Moab, M.D., M.S.C.E.: After a bone marrow transplant, there is an obligatory period for immune reconstitution during which a survivor cannot go back to school or participate in social events. This period can also change based on other complications, such as graft versus host disease and the degree of immune suppression. Because of this, the need for IEP evaluation can be delayed unless the survivor had cranial radiation prior to the bone marrow transplant as part of acute leukemia treatment. Agree, it is important to capture the learning aspects by incorporating simple data-gathering that may not necessarily be on the investigators' radar.

11. Dr. Chriqui and Ms. Porter, why do you think there is a discrepancy between the general PE educational requirements and those for adapted PE educators within the same state?

Betsy Porter, J.D.: Often, it seems like there is a discrepancy between teacher credentialing for general versus adapted physical education. Many credentialing laws have been the same for years, and now the push is on for adapted physical education. You can see within the states that it seems like the natural first step is simply to add an adapted PE component to the general PE requirement. Some national standards point to the idea that at least our general physical educators should have

an understanding and a few credit hours of adapted PE. However, in a lot of ways, some states are just starting to catch up and expand to create a new credentialing program specific to adapted PE.

Jamie F. Chriqui, Ph.D., M.H.S.: The other issue is really one of advocacy, and this is where the cancer center could come into play in working with partners and advocacy organizations about communicating with staff members from state legislative bodies and state boards of education, who work on standards and regulations about bringing adaptive standards up to a level that is comparable to the national adaptive PE recommendations. That's the data presented; currently, they're pretty far away.

12. Are any of these adaptive policies better implemented in private schools versus public education systems, or is there more of a track record to see what's being implemented?

Jamie F. Chriqui, Ph.D., M.H.S.: Betsy and I and some of our other colleagues did some research looking into whether the state in which a person lives governed private schools as well as public schools. Our findings varied quite a lot, but generally, most of these standards are specific to public schools. In CLASS, we don't have laws governing private schools specifically, so that is an area for further research because there's definitely a distinction.

13. Would either engagement in schools or the community be burdensome for providers and cancer centers, considering there is a transition space for some of these activities?

Sogol Mostoufi-Moab, M.D., M.S.C.E: I think some of it really depends on the support and manpower necessary to help with this request. Imagine a busy clinic day with many different clinical challenges that need to be addressed. This is where partnering with physical therapy to complete common assessments at different time points could give you more objective information. With the objective data, you have details to make a compelling case, and standardized forms will help most of this get completed without the need for the medical provider to write a letter from scratch, which can be time-consuming. Some of this information is more from a policy level. Yet the objective data facilitates a more standardized approach, and the data can give you a range of activities or interventions from which the patient will most benefit.

Kirsten K. Ness, Ph.D., P.T., F.A.P.T.A.: Sixteen years ago, when I started working at St. Jude, the only kids who were getting physical therapy were those with brain tumors, with leukemia who had foot drop, or with osteosarcoma who needed to be taught how to crutch walk. Now, I think that all the kids here get physical therapy at regular time points during their cancer treatment so that when they're done with treatment, their provider knows if they need services. I think that our social work team and the school team does a good job in making sure they get the services or in making sure they at least have contact with the services they need. We also see most of the kids for what I would call research assessments because I'm spoiled; I have a nice lab for the on-therapy kids. I think that after therapy is complete, when your kids are coming back for the first 5 years or so, I think that gets lost because there may not be, unless you're in a place that has extra resources, a physical therapist hanging out ready to assess all the kids who are coming through the survivor clinic. So, I think that, as a physical therapist, I would say that's a really good idea if you have it. I believe that children's hospitals and clinics within Minnesota have that, but I think it would be a good idea. I'm not sure the providers don't know; it could be that they just don't have time.

- 14. With regard to tailored intervention, how would an intervention be tailored with an online platform? Also, we have seen a huge range of resting heart rate, which would greatly affect target heart rate. Are you able to comment on this with regard to developing a tailored intervention?**

Sogol Mostoufi-Moab, M.D., M.S.C.E.: The exercise physiologist at St. Jude will receive baseline fitness data for participants randomized to exercise intervention at each site. Based on the baseline fitness level, each participant will have specific, tailored exercise intervention (aerobic and resistance training) that will be reviewed using the app that allows for interaction with the exercise physiologist and participant. The participant will have formal scheduled intervention sessions throughout the study interval, along with a recommended workout routine in the interim. Although resting heart rate tends to be elevated in many survivors, we will use the baseline information from CPET to provide additional details needed to develop a tailored intervention that is not predominantly based on target heart rate.

- 15. Do you both see a need for health literacy around cytokines (myokines/adipokines) to get buy-in from oncology providers on the need for acute and long-term PA?**

Sogol Mostoufi-Moab, M.D., M.S.C.E.: In general, an improved literacy around musculoskeletal outcomes is important for oncology providers. This literacy would include physical, imaging, and laboratory components, all of which provide complementary information to make a case for both short- and long-term physical activity.