Chapter 4. Discussion

General Population

Overview

Many Americans are inactive. Three-fourths of adults and over a third of children and adolescents do not meet national recommendations for physical activity. Understanding how to make us more active and stay active is therefore an important task. Interventions that increase activity while individuals are within the intervention but have no ability to keep people exercising when the intervention is concluded will not solve this problem. Therefore, in this systematic review we chose to focus on the effects of interventions sometime (i.e., three months) after the intervention was concluded. Three months was chosen not because it is clear that physical activity at three months post intervention is predictive of long-term maintenance. Rather we felt that it was a reasonable interval for a first look at this question of whether physical activity interventions alone, or in combination with diet modification or smoking cessation, are effective in helping individuals increase their aerobic physical activity or maintain adequate physical activity.

Overall, the completed research on promoting physical activity has not focused on measurement of physical activity behavior after the end of the intervention. Proof of this lies in the observation that 'lack of 3 month followup' was the most common exclusion criteria for this review, accounting for 50 percent of the exclusions. The more common approach in promoting physical activity has been to 'fade' an intervention, moving from higher to lesser intervention intensity (e.g. interventionist contacts) over time. Though this is important work, it could be argued that it will never be possible to intervene on a constant basis, even minimally, across an entire population. Therefore, interventions that alter physical activity behavior in a way that results in long term maintenance are of great public health interest. We do not claim that this review answers the question of what intervention components will result in long-term physical activity behavior changes in the general population. In fact, our review points out the lack of research attention to this important question. Perhaps the most important outcome of this review is the empirical statement regarding the paucity of data on how physical activity behavior is maintained after the end of a behavior change intervention.

In all of the discussion that follows it is important to keep in mind the diversity of this literature. The major criteria for exclusion from this review were size of the study, a concurrent control group, and followup of greater than or equal to three months (see Figure 2). Hence, the review contained studies that varied on many other important dimensions including demographics of the subjects, settings and types of interventions, and outcomes measured. With this many important variables and only 47 studies, conclusions about the role of specific factors on the outcomes of interventions are clearly limited. Any one dimension that is examined is still likely to contain significant variation that cannot be subdivided due to small numbers. For example, even when the analysis is limited to one setting such as healthcare, the studies still have important differences in populations examined, types of interventions, and outcomes measured. Therefore, all of the results should be interpreted as the distribution of effects within the group rather than as some specific or average effect. For this reason, further mathematical analysis, such as meta-analysis, was not done.

Key Questions

What is the evidence that physical activity interventions alone, or combined with diet modification or smoking cessation, are effective in helping individuals in the general population change their aerobic physical activity and maintain an active lifestyle?

Overall results at the study level. We did find evidence that it is possible to intervene on subjects to increase their physical activity in a manner that can be at least partly maintained for at least three months after the intervention stopped. However, the majority of the studies we examined did not demonstrate any effect on physical activity at the first followup three months or more after the end of any intervention activities. This does not bode well for the long-term maintenance of physical activity behaviors after the end of interventions as they are currently designed.

Of the studies examined, 45 percent demonstrated a positive effect (significance level of less than 0.05) of at least one physical activity outcome from at least one intervention at a followup time point at least three months after the end of interventions. However, the overall magnitude of the effects found was generally modest. Only four of the studies had an effect size greater than 0.5 at followup. In one of these studies, an effect size of 0.932 at six months post intervention translates into a 15 percent higher maximal aerobic capacity (compared to controls) in older women. This was observed six months after the end of a four month community-based intervention that included health education and supervised exercise.[63,79,115] This study was clearly a success from a public health standpoint. In the second study, the effect size of 0.597 was reported 12 months after a five-session school-based health education intervention in children. The outcome for which the effect size was 0.597 was related to the percentage of treatment versus control children who reported that most of their physical activity was running one year after the end of the intervention.[56] It should be noted that there was no intervention effect on self-reported frequency of physical activity or the fitness measure in this same study.[56] Therefore, despite a large effect size for one outcome, this intervention is of questionable value for public health interests. In the third study, an effect size of 1.84 at three months post intervention translates into an increase of 50 percent of participants meeting the current CDC/ACSM guidelines for physical activity, in an adult worksite based intervention group that received frequent phone calls compared to a 50 percent decrease in the comparison group.[69] Further, this third study showed consistent improvements for all reported physical activity outcomes. Like the successful intervention in older women described above, this study can also be considered successful, at least at three months followup.

Finally the fourth study[72] showed an increase in leisure time physical activity (with an effect size of .527 at 12 months) for female farmers who underwent two and a half months of aerobic physical training. This study, although successful, had an effect size of only .103 when the subjects were assessed at a 36 month followup.

The diversity of settings, interventions, populations, and outcomes in this set of three physical activity behavior interventions with large effect sizes underscores the difficulty of translating the results from the 47 included studies into something that can be said to have (or not have) public health significance. Greater standardization of reporting time frames and outcomes measured in the physical activity literature is needed to facilitate comparison across studies, settings, interventions, and populations.

Results at the intervention and outcome levels. Within the 47 studies reviewed, there were 72 interventions and 166 outcomes. We envisioned the possibility of variability of success of unique interventions within studies that might be informative regarding specific intervention components that would be associated with increased physical activity behavior. As it turned out, the variability of intervention success was far greater across than within study. For example, in the study described above with an effect size of 1.84 at three months post intervention,[69] the effect sizes for the four interventions ranged from 0.65 to 1.84. Though this is a wide range, all four of the interventions from this study were more successful than interventions from any other study for which effect sizes could be calculated (except for one[115, 63, 79]). We also envisioned the possibility of variance across outcomes within interventions, but found that variability of outcome success was far greater across than within study. Therefore, the remainder of this discussion will focus on the study level results.

Are interventions that use behavioral theories more effective in changing aerobic physical activity than those that do not?

One surprising finding of the review was that there did not appear to be an effect of the use of theory in the effect of the interventions. Interventions that used theory did not appear to be any more effective than those that did not explicitly use theory. One cannot necessarily conclude that the use of theoretical constructs is ineffective. The studies varied in multiple critical areas that may influence the effects of the intervention. It is very possible that we do not observe an effect of theory because other aspects of the studies confound any possible effect. It also may be that theory based interventions differ from other interventions in other important ways that affect outcome apart for the use of theory itself. For example, it appears as though there may be a relationship (not statistically significant in this review) between the intensity of interventions and whether they used theory. Such differences could obscure any effect of a theoretical underpinning to the intervention.

Do hypothesized moderators affect the results of these interventions? Do these interventions affect theoretically hypothesized mediators? In these interventions, is there a relationship between changes in theoretically hypothesized mediators and changes in physical activity?

These three questions were among the originally proposed key questions. The goal was to examine the role of moderators and mediators of the effects of the physical activity interventions within studies as well as across studies. Unfortunately, this literature did not prove to be particularly rich in this information. Only one study included in this review examined a moderating variable within study.[75] The results showed that self-reported baseline levels of support from family and friends, having a partner who exercised, and perceiving greater benefits and fewer barriers to exercise moderated the effects of the intervention. There were nine studies that examined the effect of an intervention on a hypothesized mediator. Only one reported a statistically significant effect on a hypothesized mediator (intention to exercise).[116] Only one study examined whether a hypothesized mediator affected the physical activity outcome. This study reported that partner support and self-efficacy mediated the intervention effect of the physical activity intervention.[78] This paucity of results within the current review does not mean that these questions have not been examined in the physical activity literature, only that they have not been well addressed within the subset of the literature that examines physical activity behavior three months or more after the intervention. Further, none of the studies used robust methods for examining mediation, such as structural equation modeling. It is important that more

attention be paid to this area, as there is no guarantee that what might be understood as a mediator of physical activity behavior during an intervention would hold up as a mediator after the end of an intervention.

Moderators across studies.

Setting. Within this literature we found that it is possible to intervene in a number of different settings and successfully increase physical activity. Because of the small numbers of studies and the variations in specific interventions and populations, it was not possible to isolate the effect of setting to conclude that one was better than another. In all of the settings only a quarter of the trials resulted in a statistically significant increase in physical activity on at least one measure three or more months after the end of the intervention. There was no clear pattern of effect sizes within the different settings, but this analysis is limited by the small number of studies within each setting and the diversity of the interventions themselves.

Population. Most of the studies in this literature intervened on adult men and women. Although a few focused on children (four studies) or older adults (three studies) these numbers were too small to make any meaningful comparisons of outcomes by population and therefore all of the studies were examined together. None of the conclusions would have changed by excluding the studies of these populations.

Outcome type. We found that outcomes that fit into the moderate outcome group were more likely to be statistically significant than outcomes that assessed total activity. Although the comparison did not reach statistical significance, more moderate outcomes than vigorous outcomes were statistically significant. This may well reflect an order effect within the outcomes. That is, if one has increased total activity group, one has also, by necessity, had an increase in some moderate activity. However, the reverse is not necessarily true. One can increase a moderate activity, such as walking, without increasing total activity by reducing activity in some other way. Hence, it would be expected that interventions would change moderate activity before they change total or vigorous activity as observed here.

Intervention intensity. It was not necessary to have an intensive intervention to get an effect. A wide range of intervention types were included in this review. The intervention intensity varied widely, everything from one mailing to multiple personal interactions per week for years. We found that there were successful interventions at all levels of intensity; in fact there was not a clear trend that more intensive interventions were more successful. Even a number of the least intensive interventions had at least one statistically significant outcome at followup. This suggests that it may be possible to increase physical activity with relatively modest efforts. There also was not a clear pattern in the size of the effect with the intensity of the intervention.

Length of followup. Physical activity behaviors are difficult to maintain after the end of an intervention. Approximately 25 percent of the studies with data at one year or more reported statistically significant increases in physical activity. It is not possible from these data to get an accurate assessment of how long the behavior change may last, but some studies, such as Periera et al. in which statistically significant differences in physical activity behavior were evident ten years after at intervention, suggest that long-term changes may be possible.[64] The limited data that is available from this literature on effect size over time is perhaps more sobering. Three-quarters of the studies for which an effect size could be calculated at two points in time showed a decrease in effect size from first to last followup. This data is not sufficient to accurately

understand the pattern or magnitude of the changes over time, but it is clearly an important issue to be addressed if interventions are to achieve long-term benefit in populations.

Combined interventions and access to physical activity. We examined other possibly important intervention factors, including whether interventions addressed issues with access and whether interventions combined with diet and smoking cessation had different effects on physical activity. Again, we were not able to show that the effect sizes differed in meaningful ways when comparing studies that intervened on physical activity only versus physical activity with diet and/or smoking cessation. There were also no differences in the results of studies that did versus did not address the issue of access to physical activity equipment, facilities, or classes. As said before, the issues with this literature means this cannot be taken as firm evidence that these are not important factors.

Study quality. We found the quality of this literature to be extremely variable. Some of the issues with quality may be very difficult to address; for example, it is difficult to blind subjects to the intervention. Yet more could be done to blind the outcome assessment such as using accelerometers with blinded reading. In these studies, even when some other measure of outcome was used besides self report, there was never any indication of blinding of that assessment.

Other quality issues may be difficult to address but unlike blinding may be possible. A large number of the studies suffered from attrition, which may bias the results either positively (if only those who stay in the trial are analyzed) or negatively (if all of those who withdraw are assumed not to change). This can be partially addressed by looking at the results both ways but would be of most benefit if means could be devised to reduce the attrition in these trials. Finally, some pervasive quality issues such as poor attention to the specifics of randomization could and should be easily addressed.

Adverse events. Understanding the overall benefits of these interventions requires an accounting of any harms that they may cause. It is certainly plausible that the risk of injury may increase as one becomes more active. Given the relatively small effects noted from the majority of these studies, it would not take many significant injuries to outweigh any health benefits that may occur. Unfortunately, there was almost no information in this literature on adverse events.

Future Direction

After this exhaustive review of the physical activity literature, it is still not possible to answer the question of what works and what does not work to increase individuals' physical activity and have them continue to be active at least three months later. Further we are even less able to judge the net benefits of programs to increase physical activity because harms have rarely been examined. To be able to answer this important question in the future, a number of issues need to be addressed:

- Examine longer outcomes
- Standardize followup intervals
- Standardize the domains of physical activity measured
- Standardize, if possible, the outcome measures
- Use, where possible, blinded measures of outcome rather than self-report
- Reduce attrition from studies
- Standardize reporting of study results

- Use appropriate statistical methodology to examine moderators and mediators of effect
- Examine harms

Examine longer outcomes. We could be criticized for the fact that the majority of the physical activity literature was excluded by our modest criteria of followup three months after the end of the intervention. Yet, as the ultimate goal is to help people change their lives and become more active, one could be equally critical of a literature that has largely ignored what happens to the subjects when the intervention ceases. This significantly limits the conclusions that can be drawn. Obviously, looking at followup after the end of the intervention adds to the time and complexity of studies, but it is time and resources that would be well spent. Further, there may be natural opportunities to identify and follow up on past intervention trials such as was done by of Periera et al.[64] and MacKeen et al.[157] If we are ultimately going to be able to improve the physical activity habits of the American people, we are going to need to have a better idea of what works over time.

Standardize followup interval. Making sense of this literature also suffers from a lack of standard followup intervals. As we showed, the effects of the interventions do seem to decrease over time. Therefore, one important factor in the results of any study will be the length of time since the intervention ended. To be able to compare interventions in the future, it would be beneficial to have standardized followup intervals. We do not have firm recommendations as to what these intervals should be; this could be defined through consensus of experts in the field, although both a shorter interval of a few months and a longer interval of a year or more would be most informative as to the true effect of the interventions.

Standardize the domains of physical activity measured. We attempted in this review to define some domains of physical activity. We do not claim that these particular categories are the best at capturing the true underlying domains of physical activity measurement. Yet, they are illustrative of two important principals. First is that the domain measured is the only domain measured. For example, a measure of leisure time activity is not a measure of total activity. An intervention that increases leisure time activity may, at the same time, decrease total activity. So, if one is interested in total activity, it must be measured, as it cannot necessarily be extrapolated from other measures. This leads to the second principal. In order to compare two studies they need to be measuring the same underlying domain, so, in order to fully understand the effect of these interventions, some standardization of the domains to be assessed needs to occur, as well as means for assessing each domain.

Standardize the outcome measures. Examining the results across studies would be most comparable if the same outcome measure is used across studies. This is less important than assuring that the domains are the same, but would further enhance the comparison of future studies.

Use blinded measures rather than self-report. We do not have any independent evidence from this review that the use of almost exclusively unblinded self-report as an outcome measure biases the results, but the possibility cannot be excluded. There are circumstances where other blinded measures could be used and should be considered.

Reduce attrition from studies. This may be easier said than done, but many of these studies failed usual criteria for attrition (80 percent followup with one of our quality measures and 85 percent with our other quality measure). Clearly, improving this would strengthen the conclusions that could be drawn from the studies.

Standardize reporting of study results. Accurate effect sizes could not be calculated for many of the studies in this review. Frequently what was missing was a variance estimate or an exact p-value. Occasionally the problem was that only a multivariate model was presented without enough information to assess the independent effect of the variable of interest. To the extent that it would be beneficial to compare studies, providing sufficient information (means, variance estimates, and correlations) would be beneficial.

Use appropriate statistical methodology to examine moderators and mediators of effect. Although a number of studies made some attempt to examine mediators of effect, none of them used techniques that can account for the complexity of relationships between the variables such as Structural Equation Modeling. This is important because any one model or combination of individual models can miss important relationships between the interventions, mediators, and outcomes.

Examine harms. Ignoring whether subjects suffer any harm from these interventions leaves open the question of the overall benefit of the interventions. Addressing this deficiency in the literature will allow a better accounting of the full effects of these interventions.

With attention to these areas, there is hope that we may learn how we may intervene to increase individuals' physical activity in a manner that can be maintained after costly intervention activities have ended.

Cancer Survivors

Magnitude of Effects by Outcome

The presentation of mean effect sizes for each outcome category (Tables 18 and 19) allows for discussion of the relative impact on each outcome category of physical activity interventions on cancer survivors. However, because the effect sizes were calculated based on post intervention between group differences only, interpretive caution is urged. For example, the mean effect size of 2.93 for physical activity behavior is mostly driven by between group differences that existed at baseline and persisted to the end of the intervention.[99] Other categories for which effect sizes may be overestimates include body image/dissatisfaction and body size (goal to reduce), since both of these are also reflective of baseline between group differences from studies that showed large effect sizes. By contrast, there are several categories for which the mean effect sizes reported in Table 18 may be underestimates, including quality of life, self-esteem, and anger/hostility. In all three of these categories, the mean effect sizes were influenced by between group differences at baselines: the treatment groups started out worse than the control group in several studies that included these outcomes. Thus, the intervention effect was larger than what can be reflected by a post-intervention comparison of groups. Finally, there are three outcome categories for which values for more specific individual variables might be more useful than the mean effect size for the entire categories: physiological outcomes, immune parameters, and the 'multiple constructs' portion of the mental/emotional/psychological well-being category. These three categories are discussed in greater detail below. Beyond these caveats, the conclusions that can be drawn from a review of the literature on the efficacy of physical activity interventions to positively impact physiologic and psychosocial outcomes are outlined below.

Controlled trials in cancer survivors consistently report mean post test effect size $\geq$ 0.2 and consistent (five or more studies) positive effects of physical activity (usually aerobic exercise) on the following outcomes:

- Vigor and vitality (effect size 0.850)
- Cardiorespiratory fitness (effect size 0.647)
- Quality of life (effect size 0.427)
- Depression (effect size 0.418)
- Anxiety (effect size 0.333)
- Fatigue/tiredness (effect size 0.217)

The outcomes with the greatest consistency across the cancer experience are cardiorespiratory fitness and fatigue/tiredness. The exercise prescription associated with these positive outcomes in cancer survivors was generally moderate to vigorous intensity aerobic activity on three or more days per week, for 10-60 minutes per session. For many of the other variables there are too few studies to evaluate whether the findings differ for survivors during compared to post treatment. The findings for some categories, such as cardiovascular fitness, strength, flexibility, body size, and anxiety and depression parallel results reported from exercise interventions in generally healthy populations.[12] For example, the lack of weight loss associated with exercise only interventions parallels the results in generally healthy populations. Studies designed to produce weight loss are typically designed differently than studies designed to test the independent effect of exercise on physiologic or psychosocial outcomes. Further, physical activity has been shown to improve symptoms of mild to moderate depression in generally healthy adults.

Other variables for which there is either consistent evidence that is either less strong or results from fewer studies include:

- Confusion (effect size 0.402)
- Symptoms/side effects (effect size 0.400)
- Psychosocial outcomes (effect size 0.191)
- Body size (goal to reduce) (effect size 0.187)
- Self-esteem (effect size 0.100)
- Mental health quality of life (no effect size available)
- Strength (no effect size available)

Variables for which there is less consistent evidence include:

- Body image/dissatisfaction (effect size 0.310)
- Anger hostility (effect size 0.070)
- Physical activity behavior (no valid effect size estimate available)
- Body size (goal to gain or avoid muscle mass loss) (no effect size estimate available)
- Pain (no effect size estimate available)

In addition, there is an assortment of mental/emotional/psychological well-being variables (e.g., emotional well-being, impact of medical illness on subject, psychological distress, well-being with breast cancer, global psychological distress, total mood disturbance, avoidance, fatalism, fighting spirit, hopelessness) that have each been measured in one or two studies, and this group of variables shows a mean effect size of 0.356. One perspective might be to note that these constructs are all related to anxiety and depression, which have mean effect sizes of 0.333 and 0.418, respectively. To the extent that these constructs are similar to anxiety or depression, this might be further consistent evidence that physical activity has a consistent and positive effect

on anxiety and depression among cancer survivors. Another possible interpretation would be that these variables differ from anxiety and or depression enough to require further studies prior to interpretation.

Physiologic Outcomes

The nine studies that measured non-fitness and non-anthropometric physiologic outcomes were placed into one of three categories: immune parameters, symptoms/side effects, or physiologic outcomes. The last category was created for physiologic variables that did not fit into the first two. The outcomes from studies with outcomes in these three categories were disparate and reflected goals of evaluating the safety of exercise during active cancer treatment, the efficacy of exercise to prevent muscle loss or assist patients in recovering from active cancer treatment, and two studies specifically interested in whether exercise could favorably alter physiologic parameters hypothesized to be associated with breast cancer etiology.[100, 103] Given the broad variety of potential physiologic variables that may be of interest for cancer survivors across the cancer experience, nine studies is too few to enable a summary or to draw any conclusions beyond the general statement that the majority of the reviewed studies reported changes in the hypothesized direction. This area of research has just begun to develop.

Important Early Studies in the Area of Physical Activity Interventions in Cancer Survivors

The inclusion criteria for this report included a requirement that each study must have a concurrent comparison group. This resulted in the exclusion of important early research in this area. In acknowledgement of the importance of these excluded studies, a brief overview of the studies and results of the 14 studies excluded as a result of no-concurrent comparison group[5, 214-226] is given below. Followed by a brief comparison of results from these excluded studies to the results from the 24 studies reviewed more completely for this report.

Of the 14 studies excluded as a result of no-concurrent comparison group, ten included breast cancer survivors, seven focused exclusively on breast cancer survivors. Other diagnoses were mixed, similar to the included studies. All of these studies were pre-post examinations in convenience samples of survivors with sample sizes ranging from five to 78 participants, with a mean of 27. The length of the interventions ranged from 28 days to seven months. Twelve of the 14 studies had intervention lengths between six and 16 weeks. Six of the 14 studies focused exclusively on survivors during treatment, five included survivors during as well as post treatment, and three focused exclusively on post-treatment survivors. Twelve of the 14 studies were exercise only interventions; one included a dietary component and another included an educational component regarding cancer survivorship issues. All of the excluded studies included aerobic activity, two included strength training as well. The exercise intensity ranged from 40 to 85 percent of maximal heart rate, which can be considered a range of moderate to vigorous. Exercise frequency ranged from two to seven times weekly, with exercise sessions lasting from 15 to 60 minutes. There were five studies in which all exercise took place in an exercise facility or hospital, all of these included or focused on survivors undergoing treatment. The ten studies that asked people to exercise at home or on their own (or in combination with visits to an exercise facility) included seven studies with survivors undergoing treatment.

The outcomes examined in these studies included fitness (ten studies); quality of life (six studies), fatigue (five studies each); symptoms/side effects, body size (body weight or fat), and depression (three studies each); vigor, functional ability, strength, and anxiety (two studies each); and sleep, pain, blood pressure, hormones, and immune function were each assessed in one study each. A summary of these findings is provided in Table 22. Notable findings include that the only study that did not report fitness improvements was conducted on bone marrow transplant recipients with acute leukemia.[219] Further, one study[215] performed a mediation analysis that indicated that changes in fatigue mediated the exercise induced QOL improvements. Four of the studies on QOL and fatigue were performed by one researcher.[215-218]

The 14 excluded studies can also be placed into the PEACE framework suggested by Courneya and Friedenreich[13] and described in the introduction of this report. Eight of the 14 excluded studies focused on coping during treatment,[215-219, 221, 223, 224] seven focused on rehabilitation after cancer treatment,[5, 220-224, 226] two focused on health promotion in survivors at least one year post-treatment,[214, 221] and one focused on palliation of fatigue in advanced cancer patients.[225] Three studies focused on cancer survivors in multiple PEACE framework categories.[221, 223, 224]

A comparison of Table 18 and Table 22 suggests that few changes in conclusions for each of the outcome categories would result from inclusion versus exclusion of studies with no comparison group. Exceptions are largely for outcomes examined in few studies of any design, such as sleep. With regard to the timing of exercise within the cancer survivor experience, the balance was similar across included and excluded studies with the vast majority of studies focusing on the coping and rehabilitation periods of cancer survivor experience. There were two notable exceptions. First, there was only one study on buffering prior to cancer treatment,[213] which is included as a study with a concurrent comparison group. Finally, there was only one study on palliation of symptoms in advanced cancer patients, which was not included, as it did not have a control group.[225]

Is Physical Activity Safe in Cancer Survivors?

For physical activity to be recommended for cancer survivors, it is important to first understand the potential for adverse outcomes. The results of the reviewed studies generally indicate that it is safe for cancer survivors to be physically active, even during bone marrow transplant procedures and high dose chemotherapy. Given the small number of studies reviewed, several questions regarding the safety of physical activity across the cancer survivor experience remain, including the potential for bias in self-reported worsening of symptoms or side effects, risk for the development of lymphedema, and worsening of some immune parameters.

Self-report of worsening of symptoms or side effects in cancer survivors can result in bias if physical activity results in such worsening of symptoms that study participants drop out or fail to complete data collection. Therefore, though no studies reported worsening of symptoms due to physical activity, future studies should explore other means for collecting the same data, potentially including medical chart review or proxy interviews with next of kin.

One reviewed study reported onset of lymphedema (swelling of the arm or torso due to lymph system insufficiency) in breast cancer survivors at greater rate in the exercise than comparison group.[90] This finding was confounded by between group differences in risk factors for lymphedema (e.g., radiation of the axilla). The same research group conducted a pilot study

to examine the effect of upper body aerobic and resistance training on women with lymphedema and reported no adverse effects on arm volume.[107] Other controlled and uncontrolled studies have also reported no adverse effects of upper body exercise on breast cancer survivors at risk for lymphedema.[227, 228] Current clinical guidelines from multiple sources (The National Cancer Institute, the National Lymphedema Network, the Susan G. Komen Foundation, and the American Cancer Society) include recommendations to breast cancer survivors to avoid lifting anything heavier than five to 15 pounds for the balance of life. This recommendation has negative health promotion and quality of life implications. There is too little research on this topic thus far to appropriately and safely prescribe physical activity for breast cancer survivors at risk for (or with a diagnosis of) lymphedema. Lymphedema is one of the most common late effects of breast cancer treatment, with close to 50 percent of breast cancer survivors reporting at least one lymphedema symptom in the 20 years following treatment.[229, 230] Further research on this topic is needed to guide the more than two million breast cancer survivors alive in the United States today.[231] Future studies should be specific as to timing of physical activity across the cancer survivor experience, as well as physical activity mode, frequency, intensity, and duration.

The studies that examined the impact of physical activity on immune parameters in cancer survivors reported a mixed set of results. Some parameters worsened, particularly among survivors who had completed treatment (effect sizes ranged from –0.799 to 1.047). Given the animal data that high intensity, high volume exercise can exacerbate the spread of cancer throughout the body,[109-111] it is important to understand further the effects of physical activity on immune parameters. In generally healthy adults, moderate intensity physical activity is associated with improvement in immune parameters, while high intensity, high volume physical activity is associated with a temporary worsening of immune function.[12] Additional studies are needed to clarify the effects on specific immune parameters with specificity as to timing across the cancer experience as well as physical activity mode, frequency, intensity, and duration.

Future Direction

The process of conducting this review has revealed numerous potential areas for future research on the efficacy of physical activity to positively alter physiologic and psychosocial outcomes in cancer survivors across the cancer experience. The small number of studies for each outcome category underscores the need for an expansion of research on a broad spectrum of cancer control outcomes. Therefore, rather than focus the need for further research on specific outcomes, below is a presentation of broader themes and methodologic issues to be addressed as well as recommendations for efficient forward progress toward greater understanding of the effects of physical activity in cancer survivors.

The PEACE framework outlined by Courneya and Friedenreich[13] provides an overview into the specific potential for the use of physical activity to benefit cancer control outcomes across the cancer experience. Using this framework, the current review indicates that the majority of completed studies have focused on coping during active cancer therapy or rehabilitation immediately following cancer treatment. There are many unanswered questions regarding these time frames and additional studies are needed to explicate the mode, frequency, intensity, and duration of physical activity prescriptions needed for particular populations, treatment modalities, and cancer control outcomes. That said, there are many fewer physical activity interventions that focus on buffering cancer survivors prior to treatment, palliation of symptoms at the end of life, or health promotion or survival. The results from these time periods are too

scant to draw any conclusions as yet. Therefore, additional research on the effect of physical activity on cancer control outcomes prior to treatment, as well as for health promotion, survival, and palliation is needed. A convening of researchers interested in this field to develop consensus regarding priority areas with regard to specific outcomes and timing would result in greater efficiency in moving the field forward.

For each outcome assessed in the literature on physical activity interventions in cancer survivors, the methods used differed across multiple studies. This increases the difficulty of comparing results beyond the challenge of comparisons across cancer diagnoses, severity of disease, and timing of intervention across the cancer experience. The methods for reporting these results also differed. For comparison across studies, means and standard deviations at each measurement time point within each group would need to be reported, as well as within person correlations between the measures across time. In particular, measurement of physical activity that includes mode, intensity, frequency, and duration of activity sessions would allow for greater comparison across studies than is currently possible. Standardization of methods for measuring and reporting cancer control outcomes of greatest interest would also assist the field in reaching consensus more efficiently. A conference of researchers interested in this topic to discuss and reach consensus regarding recommended measures for specific constructs would assist toward this goal.

Of the reviewed studies, the average sample size per group was 22 to 23. This indicates small studies that may not be adequately powered to assess the outcomes of interest. The large effect sizes in some studies, despite small sample sizes and statistically insignificant results, indicate the potential for powerful effects of physical activity on some cancer control outcomes. Increased funding for studies adequately powered to assess the impact of physical activity on cancer control outcomes across the cancer survivor experience is needed.

Subject recruitment for physical activity intervention studies, particularly during active cancer therapy, is challenging at best. Recruitment through registries is most desirable to obtain a generalizable sample. Development of cancer registries requires infrastructure. Infrastructure requires funding and organization of researchers to develop useful registries from which cancer survivors can be recruited for many types of studies, including physical activity interventions. Until such registries become common, and for those with limited resources, it is likely that many researchers will continue to use convenience samples to recruit cancer survivors post treatment. Further, for those with advanced cancer, becoming more physically active may not be a high priority. For these and other reasons, convenience sampling may be the only feasible way to conduct research during active treatment. Whether samples are from registries or result from convenience sampling, greater detail in reporting how the subjects were recruited and who they are (sociodemographics, age, gender, race/ethnicity, and cancer diagnosis and treatment course) would assist in evaluation of generalizability of results.