Article published online: 2022-02-18

BJO
Brazilian Journal of Oncology

LETTERS TO EDITOR CLINICAL ONCOLOGY

Physical activity recommendations for cancer prevention and control: a Brazilian consortium

Recomendações de atividade física para prevenção e controle do câncer: um consórcio brasileiro

Rafael Deminice[1,*], Leandro F M Rezende[2], Daniela Dornelles Rosa[3,4], Renata Cangussu[3], Leandro Martin Totaro Garcia[5], Rachel Riera[6], Fabio Fotunato Brasil Carvalho[7], Ronaldo Côrrea Ferreira Silva[7], Patrícia Chakur Brum[8]

ABSTRACT

Objective: This article describes the development process and summarizes the results of the Brazilian physical activity recommendations for cancer prevention and control, which was prepared to support health-care professionals. **Material and Methods:** These recommendations were elaborated considering: (i) the effect of physical activity on cancer prevention in the general healthy population; and (ii) on all-cause and cancer-specific mortality in cancer survivors. The process of preparing the recommendations was systematized, transparent and reproducible, following the recommendations of the appraisal of guidelines for research and evaluation (AGREE-II). We appraised the certainty of evidence for breast, prostate, colorectal and lung cancers, which are among the most frequent in Brazil, using the grading of recommendations, assessment, development and evaluations (GRADE) approach. **Results:** Regarding the risk of cancer, we found high certainty of evidence supporting the association between moderate-to-vigorous physical activity and lower risk of breast and colon cancer, moderate certainty of evidence for lung cancer and low certainty of evidence for prostate and rectal cancer. We found moderate certainty of evidence supporting the association between moderate-to-vigorous physical activity and reduction of all-cause and cancer-specific mortality from breast, colon and rectal cancer, and cancer-specific mortality from prostate cancer, when physical activity was performed after the disease diagnosis. We found low certainty of evidence for the association between physical activity and lung cancer mortality. Based on our findings, physical activity recommendations were proposed, including a step-by-step guide to support health-care professionals when recommending physical activity for all adults (including elderly people), with or without a diagnosis of cancer. **Conclusion:** Our recommentations may be useful to support health-care professionals counselling for physical activity, which contribute to reductions in physical inactivity in the general population and in the growing population of cancer survivors.

Headings: Prevention and control; Exercise; Mortality; Practice guideline; Consensus.

1. Universidade Estadual de Londrina, Departamento de Educação Física - Londrina - Paraná - Brasil.
2. Universidade Federal de São Paulo, Departamento de Medicina Preventiva - São Paulo - São Paulo - Brasil.
3. Sociedade Brasileira de Oncologia Clínica, Pesquisa Clínica - São Paulo - São Paulo - Brasil.
4. Hospital Moinhos de Vento, Centro de Oncologia - Porto Alegre - Rio Grande do Sul - Brasil.
5. Queen's University Belfast, Centre for Public Health - Belfast - Belfast - United Kingdom.
6. Universidade Federal de São Paulo, Discipline of Evidence-based Medicine e Hospital Sírio-libanês - Sao Paulo - Sao Paulo - Brasil.
7. Instituto Nacional do Câncer, Pesquisa Clínica - Rio de Janeiro - Rio de Janeiro - Brasil.
8. Universidade de São Paulo, Escola de Educação Física e Esporte - São Paulo - São Paulo - Brasil.

Financial support: none to declare.
Conflicts of interest: The authors declare no conflict of interest relevant to this manuscript.
Correspondence author: Rafael Deminice.
E-mail: rdeminice@uel.br

Received on: Nov 01, 2021 | **Accepted on:** Nov 14, 2021 | **Published on:** Feb 23, 2022
DOI: https://doi.org/10.5935/2526-8732.20220311

RESUMO

Objetivo: Este artigo descreve o processo de desenvolvimento e resume os resultados das recomendações brasileiras de atividade física para prevenção e controle do câncer, elaboradas para apoiar os profissionais de saúde que atuam na promoção da atividade física. **Material e Métodos:** Estas recomendações foram elaboradas considerando: (i) o efeito da atividade física na prevenção do câncer na população geral saudável; e (ii) sobre todas as causas e mortalidade específica por câncer em sobreviventes de câncer. O processo de elaboração das recomendações foi sistematizado, transparente e reprodutível, seguindo *Appraisal of Guidelines for Research and Evaluation* (AGREE-II). Avaliamos a certeza da evidência para câncer de mama, próstata, colorretal e pulmão, os que estão entre os tipos de câncer mais frequentes no Brasil, resultados usando a abordagem de gradação de *The Grading of Recommendations*, *Assessment*, *Development and Evaluations* GRADE. **Resultados:** Em relação ao risco de câncer, encontramos alta certeza de evidência que apoia a associação entre atividade física moderada a vigorosa e o menor risco de câncer de mama e cólon, certeza moderada de evidência para câncer de pulmão e baixa certeza de evidência para câncer de próstata e reto. Encontramos certeza moderada de evidências que apoiam a associação entre atividade física moderada a vigorosa e redução de mortalidade por todas as causas e específica por câncer de mama, cólon e reto, e mortalidade específica por câncer de próstata, quando a atividade física foi realizada após o diagnóstico da doença. Encontramos baixa certeza de evidência para a associação entre atividade física e mortalidade por câncer de pulmão. Com base em nossos achados, foram propostas recomendações de atividade física, incluindo um guia passo a passo para apoiar os profissionais de saúde na recomendação de atividade física para todos os adultos (incluindo idosos), com ou sem diagnóstico de câncer. **Conclusão:** Esperamos que essas recomendações sejam úteis para profissionais de saúde os profissionais de saúde na recomendação de atividade física, o que contribui para a redução da inatividade física na população em geral e na crescente população de sobreviventes de câncer.

Descritores: Prevenção e controle; Exercício; Mortalidade; Orientação prática; Consenso.

INTRODUCTION

Compelling scientific evidence suggests that physical activity reduces the risk of some types of cancer, mitigates symptoms and adverse events directly related to cancer and its treatment, and reduces mortality in cancer survivors.[1-6] In fact, studies and scientific organization positions produced over the last decade have disputed the idea that cancer survivors should "rest and avoid physical exertion". Nowadays, there is a scientific consensus that every cancer survivor should be encouraged to remain physically active during their treatment and thereafter.[2,6]

Despite the scientific progress and the increased access to high quality information, the exercise oncology field in Brazil has not developed as in other countries. Several lines of evidence support this interpretation, including (i) the limited number of Brazilian studies determining the level of physical activity in cancer survivors or data on the knowledge and attitudes of health professionals involved in this area; (ii) the absence of Brazilian epidemiological studies in published systematic reviews and scientific positions around the world; (iii) the absence of guidelines and position stand articles from Brazilian scientific organizations and societies in oncology and physical activity areas; (iv) the low number of courses and training programs for health care in physical activity/exercise oncology; and (v) the limited number of physical activity and exercise programs for cancer survivors in Brazil.

This is particularly relevant given that cancer is the second leading cause of death in Brazil, a disease with increasing incidence that represents an important limiting factor for increasing life expectancy.[7] Indeed, the relative increase of cancer incidence in the next few decades is likely to be greater in Brazil, since developing countries are experiencing increases in the prevalence of risk factors, such as physical inactivity, sedentary behavior, unhealthy diet and obesity, as well as the shifting from incidence of poverty- or infection-related cancers (e.g., cervix, liver, stomach) to cancers more frequently seen in developed countries (e.g., breast, colorectal, prostate). Of note, approximately 27% (114,497 cases) of all cancer cases and 34% (63,371 deaths) of all cancer deaths could be avoided in Brazil by promoting a healthy lifestyle, with smoking avoidance, reducing alcohol intake, maintaining a healthy body weight, eating healthy and performing physical activity.[8]

This paper aims to describe the development process and the results of the Brazilian physical activity recommendation for cancer prevention and control, an initiative of Brazilian researchers supported by scientific and health-care professional societies.

The target audience of these recommendations is health professionals, particularly those involved in the promotion of physical activity for cancer prevention and control.

MATERIAL AND METHODS

The document 'Brazilian physical activity recommendations for cancer prevention and control' was developed as part of an initiative of some Brazilian researchers and the Brazilian Society of Clinical Oncology (SBOC), with the support of the Brazilian Society of Physical Activity and Health (SBAFS) and the Brazilian National Cancer Institute (INCA). A working group was formed in August 2020, composed by nine researchers with experience in oncology, epidemiology, physical activity and evidence-based medicine. The work was completed in September 2021 when a draft version of the recommendation was presented for the societies and institutions representatives, who had the opportunity to provide feedback. The final document was approved through an informal consensus between the working group and the organization's representatives.

Development process

Three *a priori* decisions were made by consensus by the working group. First, the recommendations should focus on: 1) cancer prevention in the general population and 2) reduction of all-cause and cancer-specific mortality in cancer survivors. Second, the recommendations should use evidence-based approaches and tools. Third, it was agreed that the recommendations should be based on breast, prostate, colorectal and lung cancer. This decision was made considering that those are the most frequent types of cancer in Brazil,[7] with high coverage in the physical activity/exercise oncology literature.

These recommendations have two main research questions:

What is the effect of physical activity (compared to non-exercise, physical inactivity or insufficient physical activity conditions) on the prevention of breast, prostate, colorectal and lung cancer in the general healthy population?

What is the effect of physical activity (compared to non-exercise, physical inactivity or insufficient physical activity conditions) on all-cause and cancer-specific mortality in breast, prostate, colorectal and lung cancer survivors?

For each PI/ECO (population, intervention/exposure, comparison and outcome) question, intensity, volume, frequency, dose-response relationship and physical activity domain were considered as important information.

A systematized, transparent and reproducible method was developed, following the recommendations of 'appraisal of guidelines for research & evaluation' (AGREE-II).[9] First, PI/ECO research questions were defined considering the most relevant aspects to inform the recommendations. Later, guidelines and position stands papers referring to the effect of physical activity on cancer prevention and/or reduction of all-cause and cancer-specific mortality in cancer survivors were identified. The guidelines were then graded using the AGREE-II instrument.[9] For each PI/ECO question, the document with the highest scores was selected. When the selected document answered the PI/ECO research question with high certainty of evidence ("strong evidence"), its recommendation was adopted. When the selected document answered the PI/ECO question with moderate, low or very-low evidence certainty (or similar degree, such as limited) or no document answered the PI/ECO question, we searched for recently published systematic reviews to update the certainty of evidence. When more than one systematic review was found for the same PI/ECO research question, the one with the highest methodological quality, according to the critical appraisal tool for systematic review (AMSTAR-2),[10] was used. When two or more systematic reviews achieved the same methodological quality according to the AMSTAR-2 tool, the systematic review with the most recent literature search date was selected. Finally, the 'Grading of Recommendations, Assessment, Development and Evaluations (GRADE). approach[11] was used to assess the certainty of evidence and the strength of the recommendations in the selected systematic reviews. When no systematic reviews were identified, the guideline with the best score in the AGREE-II instrument[9] was adopted, even if the evidence provided was considered to be of moderate, low or very-low certainty of evidence. The search for primary/original studies was not performed.

Guidelines search and selection

Guidelines and position stands papers were searched on Medical Literature Analysis and Retrieval System Online (MEDLINE, via PubMed), Embase and Latin American and Caribbean Health Sciences Literature (LILACS, via *Biblioteca Virtual em Saúde*) in November 2020, without publication date limit and language. Reference lists of related articles were also read for additional guidelines search. Two independent reviewers selected the guidelines.

Guidelines and position stands papers were included if they: 1) were commissioned and published by an organization whose work relates to cancer prevention or control and/or to physical activity promotion; and 2) included the effects of physical activity and/or exercise on the risk of incidence of breast, prostate, colorectal and/or lung cancer, or all-cause or cancer-specific mortality in cancer survivors as one of the primary outcomes. Guidelines and position stands papers were excluded if they: 1) used physical activity as secondary exposure or if the guideline mentioned physical activity as part of the treatment against cancer-specific complication (e.g., cancer-related fatigue); 2) focused only on pediatric population; 3) considered the effects of physical activity on cancer-related symptoms only (e.g., cancer-related fatigue, anxiety, health- related quality of life); or 4) were opinion papers, letters, or editorials.

Systematic reviews search and selection

Systematic reviews were searched on MEDLINE (via PubMed), Embase and LILACS (via BVS) from January 1st, 2016 to November 30th, 2020, using standardized search terms for cancer, physical activity and exercise (Appendix 1). The restriction in the search date was defined considering the absence of studies published since 2016 in the recent guidelines and position stands papers with the best classification in the AGREE II instrument.[4,12] Two independent reviewers selected systematic reviews; a third reviewer resolved disagreements.

Only systematic reviews that aimed to synthesize studies on the effects of physical activity on cancer prevention (in the general population) or reduction of all-cause and cause-specific mortality in breast, prostate, colorectal and lung cancer survivors as one of the primary outcomes were selected. Systematic reviews using physical activity as secondary exposure, or focused only on the pediatric population, or considered the effects of physical activity on cancer-related symptoms only (e.g., cancer-related fatigue, anxiety, health-related quality of life) were excluded.

Synthesis and certainty of the evidence

A pre-established form was used to synthesize the evidence for each type of cancer (breast, prostate, colorectal, lung) and purpose (prevention or survival). Whenever available, observational studies from systematic reviews were also used to present information on the associations between volume, intensity and frequency of physical activity for prevention in the general population and survival in cancer survivors. In addition, the form contained fields to express scientific gaps and specific comments regarding each type of cancer studied, as well as adaptations to the Brazilian context. Based on the information from these forms, a general recommendation on the volume and intensity of physical activity was provided for prevention in the general population and for survival in cancer survivors.

The certainty of evidence was defined considering the following criteria: risk of bias; inconsistency; indirectness; imprecision; publication bias; for observational studies, magnitude of effect, dose-response gradient, and influence of confounding factors were also evaluated.

STRENGTH OF THE RECOMMENDATION

The final step was the definition of the guideline recommendations. A general recommendation on physical activity duration and intensity was provided for cancer prevention and reduction of all-cause and cancer-specific mortality in cancer survivors. To assess the strength of recommendation, the GRADE approach was used, which assesses the strength of health recommendations as high, moderate, low and very low (Appendix 2). The classification expresses the emphasis on adopting or rejecting a certain conduct, considering if the health problem is a priority, balance between harms and benefits, values and preferences, resources, equity, acceptability and feasibility.[11]

RESULTS

Guidelines and systematic reviews selection, quality appraisal and classification.

A total of 15 guidelines and position stands papers were found, but eight were excluded. The seven guidelines included,[1,3-5,12-14], generated five analysis regarding the effects of physical activity on cancer prevention[1,3-5,14] and five analysis regarding the effects of physical activity on all-cause and cancer-specific mortality in cancer survivors.[3-5,12-13]

The physical activity guidelines advisory committee scientific reports that supported the physical activity recommendations from the United States[4] and the diet, nutrition and physical activity report for breast cancer survivors from World Cancer Research Fund and the American Institute of Cancer Research[12] achieved the highest scores, and were selected to answer the PI/ECO research questions regarding cancer prevention and reduction of all-cause and cause- specific mortality in cancer survivors. Guideline quality appraisal and classification using AGREE-II are presented in Appendix 3. Despite having achieved a high score, the pan-Canadian guideline[13] was not included because it was published seven years earlier than the WCRF/AICR Breast[12] and PAGAC.[4] The selected documents did not answer the PI/ECO question or answered with low or moderate certainty of evidence (or similar degree, such as limited) for the preventive effect of physical activity on rectal, prostate and lung cancers, and the effect of physical activity on all-cause and cancers-specific mortality from breast, colon, rectal, prostate and lung cancer in cancer survivors. Then, a search for systematic reviews was performed to answer these PI/ECO research questions. The methodological quality of selected systematic reviews were assessed using AMSTAR-2, and results are presented in Appendix 4.

The search returned 1,009 articles (332 on the effects of physical activity on cancer prevention and 677 on the effects of physical activity on all-cause and cancer-specific mortality). After the exclusion of duplicates and of articles that have not met the inclusion criteria (after title and abstract screening), 44 reviews were selected for full-text screening (19 on the effects of physical activity on cancer prevention and 25 on the effects of physical activity on all-cause and cancer-specific mortality in cancer survivors). Systematic reviews with the most up-to-date search strategy were listed for evaluation using the AMSTAR-2[10] tool. We finally included 12 systematic reviews,[15-26], eight on the effects of physical activity on cancer prevention[16-20,23-25] and four on the effects of physical activity on all-cause and cancer-specific mortality in cancer survivors.[15,21,22,26] The systematic reviews selection flowchart is presented in Figure 1.

Evidence and recommendations

Certainty of evidence was evaluated considering two main purposes: 1) cancer prevention, and 2) reduction of all-cause and cancer-specific mortality in cancer survivors. The certainty of evidence is summarized in Table 1.

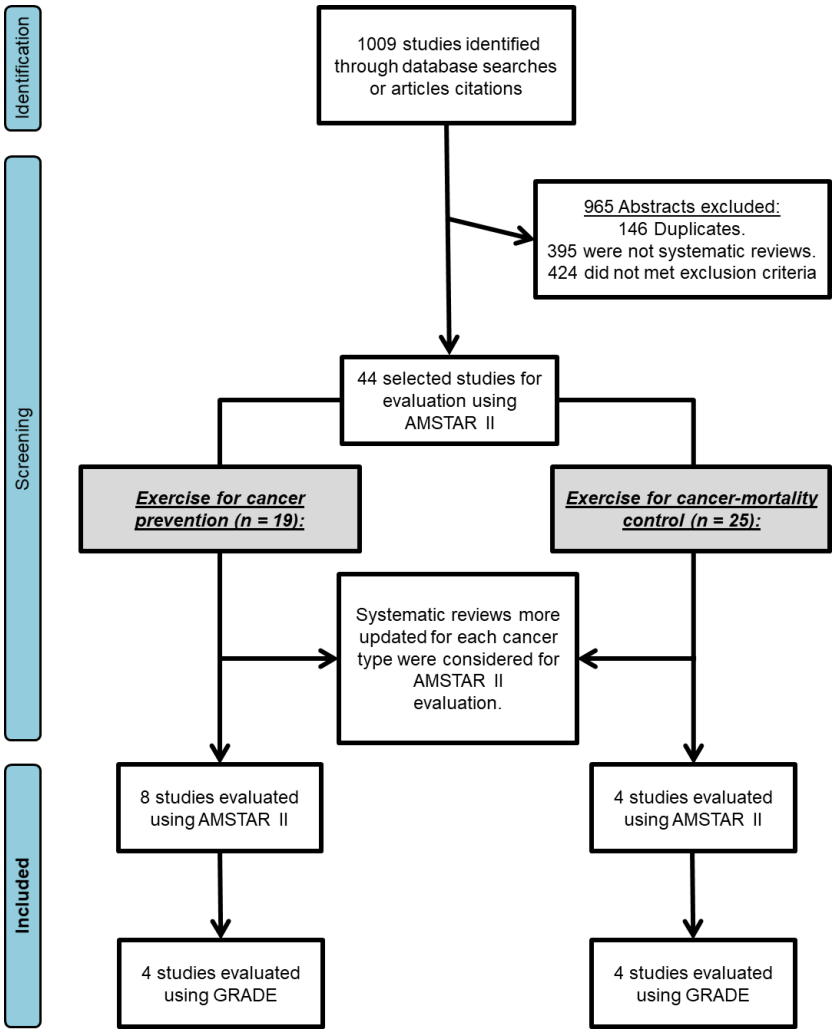

Figure 1. PRISMA flowchart for elected systematic reviews.

Table 1. Summary of evidence for the effects of physical activity on cancer prevention and reduction of all-cause and cancer-specific mortality in breast, prostate, colon, rectal and lung cancer survivors.

Does moderate-to-vigorous physical activity reduce the risk of cancer in the general population (adults and older adults) and reduce all-cause and cancer-specific in cancer survivors?			
	Certainty of evidence		
Cancer type	Risk of cancer	Risk of cancer-specific Mortality	Risk of all-cause Mortality
Breast	high[a,b]	moderate[a,b]	moderate[a,b]
Prostate	low[a]	moderate[a]	low[a]
Colon	high[a,d]	moderate[a,c]	moderate[a,c]
Rectal	low[a]	moderate[a]	moderate[a]
Lung	moderate[a]	NSR	NSR
Is greater, compared to low amounts of physical activity associated with a reduced risk of cancer in the general population (adults and older adults) and reduce all-cause and cancer- specific mortality in breast, prostate, colon, rectal and lung cancer survivors?			
	Certainty of evidence		
Cancer type	Risk of cancer	Risk of cancer-specific Mortality	Risk of all-cause Mortality
Breast	high[a,b]	moderate[a,b]	moderate[a,b]
Prostate	low[c]	low[a]	low[a]
Colon	high[a]	moderate[a,e]	moderate[a,e]
Rectal	very low[e]	moderate[a,e]	moderate[a,e]
Lung	moderate[a]	NSR	NSR

[a]Level of evidence was based on PAGAC et al. (2018)[4]; [b]Level of evidence was based on WCRF/AICR Breast (2018)[1]; [c]Level of evidence was based on Benke et al. (2018)[20]; [d]Level of evidence was based on WCRF/AICR (2011)[12]; [e]Level of evidence was based on Wu et al. (2016)[15]; NSR: There is no systematic review available to determine the level of evidence.

Although the evidence of benefits for the prevention and control of certain types of cancers are low or very low, it does not mean that the practice of physical activity in these cases is contraindicated or harmful. The strength of recommendation for all cancer types studied is strong. Thus, general recommendations of physical activity for cancer prevention and control were formulated and presented for health-care professionals as a four-step guide and one golden rule format, as follows:

Four steps

As a health-care professional, always encourage people at your work with or without a diagnosis of cancer to practice physical activity regularly. Engaging people in at least 150 minutes a week of moderate-intensity physical activity, or at least 75 minutes a week of vigorous-intensity physical activity, or an equivalent combination of moderate and vigorous activity, reduces the risk of developing cancer and mortality.

Every movement counts. Even when people do not reach the recommended levels of physical activity, regular physical activity reduces the risk of developing cancer and reduces cancer mortality, in addition to other health benefits.

Overall, physical activity for cancer patients is tolerable and safe, even when practiced during cancer treatment (chemotherapy, radiotherapy, hormonal therapy or others). Consider particularities of each cancer type, contraindications and possible adverse effects caused by the treatment when recommending physical activity.

When recommending physical activity, consider preferences, time availability and appropriate place to practice. The possibilities are many, from the ones we do on a daily basis such as walking, cycling, dancing, taking a walk with the pet and playing sports recreationally, to more systematic ones, such as gym classes and weight training.

The golden rule: promoting physical activity as a habit, to be incorporated into people's routine, is essential to prevent and control cancer and to overall health promotion.

DISCUSSION

There is scientific evidence that physical activity reduces the incidence and mortality of several types of cancer, as well as promotes positive effects on a broad variety of important health outcomes in individuals living with and beyond cancer. Furthermore, there is a growing need to translate scientific evidence into practice. Indeed, multiple international organizations have published recommendations for physical activity and exercise for cancer prevention for both patients living with cancer and for those who survived, including the American College of Sports Medicine (ACSM),[5,6] the American Cancer Society (ACS),[14] the Exercise and Sports Science Australia,[2] Cancer Care Ontario,[27] and Spanish Society of Medical Oncology.[3] In addition, some initiatives around the globe such as *Moving Through Cancer* (https://www.exerciseismedicine.org/eim-in-action/moving-through-cancer/) and *OnkoActiv* (https://netzwerk-onkoaktiv.de/) have also contributed to make physical activity and exercise standards in oncology practice. Notably, the vast majority of these documents and initiatives are based in high-income countries. Physical activity and exercise standards in oncology practice do not exist in low-and-middle-income countries, such as Brazil.

In response to that, we developed the Brazilian physical activity recommendations for cancer prevention and control, a document that updated and translated the most recent international scientific evidence on the exercise oncology field to support the work of Brazilian health-care professionals when recommending physical activity for cancer prevention and control. To the best of our knowledge, this is the first structured and evidence-based physical activity recommendation for cancer prevention and control published in the Global South. Thus, we consider it the first step to include Brazil into the international scenario to include physical activity and exercise standards in the oncology practice.

Cancer is the second leading cause of death in Brazil, the country with the second largest population in the Americas, among the top six worldwide.[28] As in most of the low-and-middle-income countries, cancer incidence in Brazil is still increasing.[7] Estimates demonstrated that an increase in cancer incidence trends continue for the major cancer types worldwide, but faster in low-and-middle-income countries, compared to high-income ones.[29] Therefore, the health, social and economic burden of cancer will likely increase in Brazil in the next decades. On the other hand, approximately one-third of all cancer cases and deaths in Brazil could be avoided by promoting a healthy lifestyle, such as performing physical activity.[8] Therefore, we urge for initiatives that may prevent and control cancer incidence and mortality in Brazil.

The Brazilian physical activity recommendations for cancer prevention and control was primarily derived from the recent clinical evidence and relevant guidelines on the topic, considering local clinical practice. Using an evidence-based approach, we updated the international evidence and recommendation for the most frequent cancers in the Brazilian population with the aim to reach the highest number of patients living with and beyond cancer. Thus, although considered local specificities, it is also an important international scientific contribution because it contemplates the most recent findings of the exercise oncology field.

Our results demonstrated PAGAC[4] and WCRF/AICR Breast,[12] presented the highest AGREE-II scores. Importantly, although we detect most recent published guidelines such as Patel et al. (2019),[5] Pollán et al. (2020)[3] and Rock et al. (2020),[14] those did not receive the recommendation quality according to AGREE-II (see Appendix 3).

The selected guidelines demonstrated high certainty of evidence supporting the association between moderate-to-vigorous physical activity and lower risk of breast and colon cancer, evidence that was adopted for the Brazilian recommendations development. The selected guidelines did not answer the PI/ECO question or answered with low or moderate certainty of evidence for the preventive effect of physical activity on prostate, rectal and lung cancers; and the effect of physical activity on all-cause and cancers-specific mortality from breast, colon, rectal, prostate and lung cancer in cancer survivors. Then, a search for recent systematic reviews considering the effects of physical activity on cancer prevention and mortality returned 12 studies, all of them with critically low quality according to AMSTAR-2. In addition, the GRADE demonstrated low evidence for the four most recent systematic reviews. Indeed, the low quality of the systematic reviews has enabled us to make significant progress on the recommendations made by PAGAC[4] and WCRF/AICR Breast.[12] Thus, we may affirm that much progress is still needed in the exercise oncology science, especially on the effects of physical activity on survival of different types of cancer.

Although the formulation of a set of statements based on the current scientific evidence was an important component of this proposal, our primary focus was to facilitate appropriate preventive and treatment counseling among Brazilian health-care professionals. Despite the cancer diagnosis may represent an important trigger to make survivors more receptive to include health behavior in their lives,[30] including being more active, the health-care professionals play a central role in behavior change. Thus, the Brazilian recommendations of physical activity for cancer prevention and control were formulated with statements with clear and practical advice for local health-care professionals managing patients with cancer and working with the general population. We expected that these recommendations for the prevention and control of cancer become inductors of health and educational policies, programs and actions to expand safe and pleasant opportunities for physical activity practice, especially for cancer survivors.[14] It is noteworthy that both the expansion of physical activity and the reduction of cancer mortality are within Brazilian government goals until 2030.[31] This document can strengthen ongoing and future initiatives, such as programs to promote physical activity in the healthcare system, and in the sport and leisure sectors, among others.[32]

The effects of physical activity on symptom control in individuals with cancer undergoing treatment and after treatment are another critical dimension in cancer control and should be the object of review and elaboration of recommendations shortly. New scientific publications are expected in the coming years, and we hope that some methodological aspects will be improved so that the quality of evidence is even better. We also expect that Brazilian researchers take ownership of the topic and produce evidence considering the local context, which may vary according to different regions of Brazil.

CONCLUSION

In conclusion, the Brazilian physical activity recommendations for cancer prevention and control may be considered the first step to include Brazil into the international agenda to make physical activity and exercise standards in oncology practice. Of note, it is the first initiative like this among the Global South countries. We expect the recommendations will support health-care professionals recommending physical activity, which may contribute to a reduction in physical inactivity in the general population and cancer survivors in Brazil.

ACKNOWLEDGMENTS

We appreciate the support of the *Sociedade Brasileira de Oncologia Clínica, Sociedade Brasileira de Atividade Física* and *Saúde and the Instituto Nacional do Câncer* and its respective presidents, Clarissa Mathias, Paulo Henrique de Araújo Guerra, Maria Eduarda Leão Diogenes Melo, Liz Almeida and Ana Cristina Pinho Mendes Pereira.

Conflict of interests

Daniela Dornelles Rosa (last 5 years): consulting for: Roche, Novartis, AstraZeneca, Lilly, Libbs, Pfizer, Dr Reddy's, Teva, United Medical, MSD, Daiichi Sankyo. Fabio F. B. de Carvalho, Leandro Fórnias Machado de Rezende, Leandro Martin Totaro Garcia, Patricia Chakur Brum, Rachel Riera, Rafael Deminice, Renata Cangussú and Ronaldo Corrêa Ferreira da Silva declare that they have no conflict of interest.

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APPAPPENDIX 1 - SYSTEMATIC REVIEWS SEARCH STRATEGY

Systematic reviews evaluating the effects of physical activity on cancer prevention

Key question	What is the effect of physical activity on cancer prevention?
population	Healthy adults without a diagnosis of cancer
Intervention	Activity or exercise
Study design	Systematic Review
comparison	Inactive (or less active)
Outcome	Incidence of cancer

Base	Date	Strategy
Medline/Pubmed	**November, 2020**	(((Exercise[mh] OR Exercise*[tiab] OR Physical Activit*[tiab] OR Health Activit*[tiab] OR Training[tiab] OR Physical[tiab] OR Walking[mh] OR Walking[tiab] OR Cycling[tiab] OR Aerobic[tiab] OR Sports[mh] OR Sport*[tiab] OR Active Commuting[tiab] OR Physical Endurance[mh] OR Athletes[mh] OR Athlete*[tiab] OR Active Transport[tiab] OR Cardiorespiratory Fitness[mh] OR Cardiorespiratory Fitness[tiab] OR Cardiovascular Fitness[tiab] OR Tai Ji[mh] OR Tai Ji[tiab] OR Tai Chi[tiab] OR Tai Ji Quan[tiab] OR Taijiquan[tiab] OR Tai Chi Chuan[tiab] OR Yoga[mh] OR Yoga[tiab] OR Resistance Training[mh] OR Muscle Stretching Exercises[mh] OR Stretching[tiab] OR Muscle Strength[mh] OR Arthrogenic Muscle Inhibition[tiab]) AND ((Prevention and Control[sh] OR Primary Prevention[mh] OR Primary Prevention[tiab] OR Disease Prevention[tiab] OR Prevention[tiab]) AND (Radiation Oncology[mh] OR Medical Oncology[mh] OR Surgical Oncology[mh] OR Oncology[tiab] OR Neoplasms[mh] OR Neoplas*[tiab] OR Cancer*[tiab] OR Carcinoma[mh] OR Carcinoma[tiab] OR Epithelioma*[tiab] OR Adenocarcinoma[mh] OR Adenocarcinoma[tiab] OR Sarcoma[mh] OR Sarcoma[tiab] OR Tumor*[tiab] OR Tumour*[tiab] OR Malignan*[tiab] OR Therapeutic Radiology[tiab] OR Drug Therapy[mh] OR Drug Therap*[tiab] OR Chemotherap*[tiab] OR Radiotherapy[mh] OR Radiotherapy, Adjuvant[mh] OR Radiotherapy, Conformal[mh] OR Radiotherap*[tiab]))) AND Systematic[sb]) AND ("2016/01/01"[PDat] : "2020/09/16"[PDat]) NOT (Child*[tw] OR Infant[tw] OR Pediatric*[tw] OR Paediatric*[tw])
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Lilacs	**November, 2020**	(tw:(Exercise* OR "Physical Activity" OR "Physical Activities" OR "Health Activity" OR "Health Activities" OR Training OR Physical OR Walking OR Cycling OR Aerobic OR Sport* OR "Active Commuting" OR "Physical Endurance" OR Athlete* OR "Active Transport" OR "Cardiorespiratory Fitness" OR "Cardiovascular Fitness" OR "Tai Ji" OR "Tai Ji" OR "Tai Chi" OR "Tai Ji Quan" OR Taijiquan OR "Tai Chi Chuan" OR Yoga OR "Resistance Training" OR "Muscle Stretching Exercises" OR Stretching OR "Muscle Strength" OR "Arthrogenic Muscle Inhibition" OR Exercicio* OR "Atividade física" OR "Atividades fisicas" OR "Atividade de saude" OR Treinamento OR Fisico OR Caminhada OR Ciclismo OR Aerobico OR Esporte* OR "Deslocamento ativo" OR "Resistencia fisica" OR Atleta* OR "Transporte ativo" OR "Aptidao cardiorrespiratoria" OR "Aptidao cardiovascular" OR Ioga OR "Treinamento de resistencia" OR "Exercicios de alongamento muscular" OR alongamento OR "Forca muscular" OR "Inibicao muscular artrogenica" OR Ejercicio* OR "Actividad física" OR "Actividades físicas" OR "Actividad de salud" OR Entrenamiento OR Caminar OR "Andar en bicicleta" OR Deporte* OR "Desplazamientos activos" OR "Resistencia fisica" OR "Transporte activo" OR "Aptitud cardiorrespiratoria" OR "Aptitud cardiovascular" OR "Entrenamiento de resistencia" OR "Ejercicios de estiramiento muscular" OR estiramiento OR "Fuerza muscular" OR "Inhibicion de los musculos artrogenicos")) AND (tw:("Radiation Oncology" OR "Medical Oncology" OR "Surgical Oncology" OR Oncology OR Neoplasms OR Neoplas* OR Cancer* OR Carcinoma OR Epithelioma* OR Adenocarcinoma OR Sarcoma OR Tumor* OR Tumour* OR Malignan* OR "Therapeutic Radiology" OR "Drug Therapy" OR "Drug Therapies" OR Chemotherap* OR Radiotherap* OR "Oncologia de radiacao" OR "oncologia radiologica" OR "Oncologia medica" OR "oncologia cirurgica" OR epitelioma* OR "radiologia terapeutica" OR "terapia por drogas" OR quimioterapia* OR radioterapia* OR "Oncologia radioterapica" OR "Oncologia quirurgica" OR "Terapia con medicamentos" OR oncologia)) AND (tw:("Prevention and Control" OR "Primary Prevention" OR "Disease Prevention" OR Prevention OR "Prevencao e Controle" OR "Prevencao Primaria" OR "Prevencao de doencas" OR Prevencao OR "Prevencion y control" OR "prevencion primaria" OR "prevencion de enfermedades" OR prevencion)) AND (db:("LILACS")) AND (year_cluster:[2016 TO 2020]) AND (type_of_study:("systematic_reviews"))

Systematic reviews evaluating the effects of physical activity on cancer survival

Key question	What is the effect of physical activity on cancer survival?
population	Adults diagnosed with cancer (any cancer)
Intervention	Activity or exercise
Study design	Systematic review
comparison	Inactive (or less active)
Outcome	Incidence of cancer

Base	Date	Strategy
Medline/Pubmed	**November, 2020**	((((Exercise[mj] OR Exercise*[tiab] OR Physical Activit*[tiab] OR Health Activit*[tiab] OR Training[tiab] OR Physical[tiab] OR Walking[mj] OR Walking[tiab] OR Cycling[tiab] OR Aerobic[tiab] OR Sports[mh] OR Sport*[tiab] OR Active Commuting[tiab] OR Physical Endurance[mj] OR Athletes[mj] OR Athlete*[tiab] OR Active Transport[tiab] OR Cardiorespiratory Fitness[mj] OR Cardiorespiratory Fitness[tiab] OR Cardiovascular Fitness[tiab] OR Tai Ji[mj] OR Tai Ji[tiab] OR Tai Chi[tiab] OR Tai Ji Quan[tiab] OR Taijiquan[tiab] OR Tai Chi Chuan[tiab] OR Yoga[mj] OR Yoga[tiab] OR Resistance Training[mj] OR Muscle Stretching Exercises[mj] OR Stretching[tiab] OR Muscle Strength[mj] OR Arthrogenic Muscle Inhibition[tiab]) AND (Radiation Oncology[mj] OR Medical Oncology[mj] OR Surgical Oncology[mj] OR Oncology[tiab] OR Neoplasms[mj] OR Neoplas*[tiab] OR Cancer*[tiab] OR Carcinoma[mj] OR Carcinoma[tiab] OR Epithelioma*[tiab] OR Adenocarcinoma[mj] OR Adenocarcinoma[tiab] OR Sarcoma[mj] OR Sarcoma[tiab] OR Tumor*[tiab] OR Tumour*[tiab] OR Malignan*[tiab] OR Therapeutic Radiology[tiab] OR Drug Therapy[mj] OR Drug Therap*[tiab] OR Chemotherap*[tiab] OR Radiotherapy[mj] OR Radiotherapy, Adjuvant[mj] OR Radiotherapy, Conformal[mj] OR Radiotherap*[tiab])) AND (Survival[mj] OR Survivors[mj] OR Survival Analysis[mj] OR Survival Rate[mj] OR Survival[tiab] OR Survivor*[tiab] OR Mortality[mj] OR Mortalit*[tiab] OR Case Fatality Rate*[tiab] OR Death[mj] OR Death[tiab])) AND (Clinical Trial[sb] OR Meta-Analysis[sb] OR Observational Study[sb] OR Randomized Controlled Trial[sb] OR Systematic Review[sb])) AND (English[lang] OR Portuguese[lang] OR Spanish[lang]) AND ("2018/01/01"[PDat] : "2020/09/16"[PDat]) NOT (Child*[tw] OR Infant[tw] OR Pediatric*[tw] OR Paediatric*[tw])

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Embase	**November, 2020**	'roentgen therapy':ti,ab OR 'roentgen treatment':ti,ab OR 'rontgen therapy':ti,ab OR 'therapeutic radiology':ti,ab OR 'therapy, irradiation':ti,ab OR 'therapy, radiation':ti,ab OR 'therapy, roentgen':ti,ab OR 'treatment, irradiation':ti,ab OR 'treatment, radiation':ti,ab OR 'treatment, roentgen':ti,ab OR 'x radiotherapy':ti,ab OR 'x ray therapy':ti,ab OR 'x ray treatment':ti,ab OR 'x-ray therapy':ti,ab OR 'drug therapy'/mj OR 'drug therapy':ti,ab OR 'drug treatment':ti,ab OR 'medicament therapy':ti,ab OR 'medicament treatment':ti,ab OR 'medication':ti,ab OR 'medicinal therapy':ti,ab OR 'medicinal treatment':ti,ab OR 'pharmaceutical therapy':ti,ab OR 'pharmaceutical treatment':ti,ab OR 'pharmaco-therapy':ti,ab OR 'pharmaco-treatment':ti,ab OR 'pharmacological therapy':ti,ab OR 'pharmacological treatment':ti,ab OR 'pharmacotherapy':ti,ab OR 'pharmacotreatment':ti,ab OR 'therapeutic uses':ti,ab OR 'therapy, drug':ti,ab OR 'therapy, pharmacological':ti,ab OR 'treatment, drug':ti,ab OR 'treatment, pharmacological':ti,ab OR 'chemotherapy'/mj OR 'chemotherapeutics':ti,ab OR 'chemotherapy':ti,ab OR 'adjuvant radiotherapy'/mj OR 'adjuvant radiotherapy':ti,ab OR 'radiotherapy, adjuvant':ti,ab OR 'conformal radiotherapy'/mj OR '3-dimensional conformal radiation therapy':ti,ab OR '3-dimensional conformal radiotherapy':ti,ab OR '3d conformal radiation therapy':ti,ab OR '3d conformal radiotherapy':ti,ab OR 'conformal radiation therapy':ti,ab OR 'conformal radiotherapy':ti,ab OR 'radiotherapy, conformal':ti,ab OR 'three-dimensional conformal radiation therapy':ti,ab OR 'three-dimensional conformal radiotherapy':ti,ab) AND ('survival'/mj OR 'survival':ti,ab OR 'survivor'/mj OR 'survivor':ti,ab OR 'survivors':ti,ab OR 'survivorship'/mj OR 'survivorship':ti,ab OR 'survival analysis'/mj OR 'survival analysis':ti,ab OR 'survival rate'/mj OR 'rate, survival':ti,ab OR 'survival curve':ti,ab OR 'survival probability':ti,ab OR 'survival rate':ti,ab OR 'mortality'/mj OR 'excess mortality':ti,ab OR 'mortality':ti,ab OR 'mortality model':ti,ab OR 'cancer mortality'/mj OR 'cancer death':ti,ab OR 'cancer mortality':ti,ab OR 'mortality, cancer':ti,ab OR 'case fatality rate'/mj OR 'case fatalities':ti,ab OR 'case fatality':ti,ab OR 'case fatality rate':ti,ab OR 'case fatality ratio':ti,ab OR 'case fatality risk':ti,ab OR 'death'/mj OR 'death':ti,ab OR 'mors':ti,ab OR 'mortality rate'/mj OR 'death rate':ti,ab OR 'death rate model':ti,ab OR 'fatal outcome rate':ti,ab OR 'fatality rate':ti,ab OR 'lethal outcome rate':ti,ab OR 'mortality rate':ti,ab OR 'rate, mortality':ti,ab) AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) AND ([english]/lim OR [portuguese]/lim OR [spanish]/lim) AND [2018-2020]/py AND ([cochrane review]/lim OR [systematic review]/lim OR [meta analysis]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim) AND [humans]/lim AND [humans]/lim AND ([adult]/lim OR [young adult]/lim OR [middle aged]/lim OR [aged]/lim OR [very elderly]/lim)
Lilacs	**November, 2020**	(tw:(Exercise* OR "Physical Activity" OR "Physical Activities" OR "Health Activity" OR "Health Activities" OR Training OR Physical OR Walking OR Cycling OR Aerobic OR Sport* OR "Active Commuting" OR "Physical Endurance" OR Athlete* OR "Active Transport" OR "Cardiorespiratory Fitness" OR "Cardiovascular Fitness" OR "Tai Ji" OR "Tai Ji" OR "Tai Chi" OR "Tai Ji Quan" OR Taijiquan OR "Tai Chi Chuan" OR Yoga OR "Resistance Training" OR "Muscle Stretching Exercises" OR Stretching OR "Muscle Strength" OR "Arthrogenic Muscle Inhibition" OR Exercicio* OR "Atividade física" OR "Atividades fisicas" OR "Atividade de saude" OR Treinamento OR Fisico OR Caminhada OR Ciclismo OR Aerobico OR Esporte* OR "Deslocamento ativo" OR "Resistencia fisica" OR Atleta* OR "Transporte ativo" OR "Aptidao cardiorrespiratoria" OR "Aptidao cardiovascular" OR Ioga OR "Treinamento de resistencia" OR "Exercicios de alongamento muscular" OR alongamento OR "Forca muscular" OR "Inibicao muscular artrogenica" OR Ejercicio* OR "Actividad física" OR "Actividades físicas" OR "Actividad de salud" OR Entrenamiento OR Caminar OR "Andar en bicicleta" OR Deporte* OR "Desplazamientos activos" OR "Resistencia fisica" OR "Transporte activo" OR "Aptitud cardiorrespiratoria" OR "Aptitud cardiovascular" OR "Entrenamiento de resistencia" OR "Ejercicios de estiramiento muscular" OR estiramiento OR "Fuerza muscular" OR "Inhibicion de los musculos artrogenicos")) AND (tw:("Radiation Oncology" OR "Medical Oncology" OR "Surgical Oncology" OR Oncology OR Neoplasms OR Neoplas* OR Cancer* OR Carcinoma OR Epithelioma* OR Adenocarcinoma OR Sarcoma OR Tumor* OR Tumour* OR Malignan* OR "Therapeutic Radiology" OR "Drug Therapy" OR "Drug Therapies" OR Chemotherap* OR Radiotherap* OR "Oncologia de radiacao" OR "oncologia radiologica" OR "Oncologia medica" OR "oncologia cirurgica" OR epitelioma* OR "radiologia terapeutica" OR "terapia por drogas" OR quimioterapia* OR radioterapia* OR "Oncologia radioterapica" OR "Oncologia quirurgica" OR "Terapia con medicamentos" OR oncologia)) AND (tw:(Survival OR Survivor* OR "Survival Analysis" OR "Survival Rate" OR Mortality OR "Case Fatality Rate" OR Death OR Sobrevivencia OR Sobrevivente* OR "Analise de Sobrevivencia" OR "Taxa de Sobrevivencia" OR Mortalidade OR "Taxa de Fatalidade" OR Morte OR Supervivencia OR Superviviente* OR "Analisis de supervivencia" OR "Tasa de supervivencia" OR Mortalidad OR "Tasa de mortalidad" OR Muerte)) AND (db:("LILACS")) AND (year_cluster:[2018 TO 2020]) AND (type_of_study:("screening_studies" OR "prevalence_studies" OR "prognostic_studies" OR "risk_factors_studies" OR "systematic_reviews" OR "clinical_trials" OR "observational_studies" OR "incidence_studies"))

APPENDIX 2- GRADE RECOMMENDATION EVALUATION

Wu W et al. Pre- and post-diagnosis physical activity is associated with survival benefits of colorectal cancer patients: a systematic review and meta-analysis. Oncotarget. 2016;7(32):52095-52103.

PHYSICAL ACTIVITY VERSUS NO PHYSICAL ACTIVITY FOR PEOPLE WITH COLORECTAL CANCER

Patient or population: colorectal cancer
Context: -
Intervention: with physical activity
Comparison: no physical activity

Outcomes	Potential absolute effects* (IC 95%)		Relative Risk (IC 95%)	Number of participants (studies)	Certain of evidence (GRADE)	Comments
	Risk without physical activity	Risk with physical activity				
Mortality from all causes Follow-up: 4.9 to 11.9 years	-	-	RR 0.71 (0,63-0,81)	9,251 (7 observational studies)	⊕○○○ VERY LOW [a,b]	-
Mortality from colorectal cancer Follow-up: 3.8 to 11.9 years	-	-	RR 0.77 (0,63-0,94)	8,419 (6 observational studies)	⊕○○○ VERY LOW [c,d]	-

Subtitle
* The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk of the comparator group and the relative effect of the intervention (and its 95% CI). CI: Confidence Interval; RR: relative risk.

Explanations for reducing the certainty of evidence

A. Methodological limitations. Only 1 of the 7 studies had the highest score in the quality assessment by the New Castle-Ottawa tool and the others had a score of 7 or 8. Reduced by one level (-1).

B. Inconsistency. I2 = 53.3%. Reduced one level (-1).

C. Methodological limitations. All studies scored in the New Castle-Ottawa tool 7 or 8 (maximum value = 9). Reduced one level (-1).

D. Inconsistency. I2 = 60.3%. Reduced one level (-1).

There was no reduction in certainty due to imprecision, indirect evidence and publication bias.
There was no increase in certainty by effect size, confounding factor control or dose-response gradient.

Classification of certainty of evidence according to GRADE Working Group

High: we are very confident that the true effect is close to the estimated effect

Moderate: We are moderately confident in the effect estimate: the true effect is likely to be close to the effect estimate, but there is a possibility that it will be substantially different.

Low: Our confidence in the effect estimate is limited: The actual effect may be substantially different from the effect estimate.

Very low: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the effect estimate.

HIGH PHYSICAL ACTIVITY VERSUS LOW PHYSICAL ACTIVITY FOR PEOPLE WITH COLORECTAL CANCER

Patient or population: colorectal cancer
Context: -
Intervention: high physical activity
Comparison: low physical activity

Outcomes	Potential absolute effects* (IC 95%)		Relative Risk (IC 95%)	Number of participants (studies)	Certain of evidence (GRADE)	Comments
	Risk without physical activity	Risk with physical activity				
Mortality from all causes Follow-up: 3.8 to 11.9 years	-	-	RR 0.58 (0,49-0,68)	7,426 (6 observational studies)	⊕○○○ VERY LOW [a]	-

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Mortality from colorectal cancer Follow-up: 6.8 to 11.9 years	-	-	RR 0.56 (0,38-0,83)	6,594 (5 observational studies)	⊕○○○ VERY LOW [b]	-

Subtitle

* The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk of the comparator group and the relative effect of the intervention (and its 95% CI). CI: Confidence Interval; RR: relative risk.

Explanations for reducing the certainty of evidence

A. Methodological limitations. Only 1 of the 7 studies had the highest score in the quality assessment by the New Castle-Ottawa tool and the others had a score of 7 or 8. Reduced by one level (-1).

B. Methodological limitations. All studies scored in the New Castle-Ottawa tool 7 or 8 (maximum value = 9). Reduced one level (-1).

There was no reduction in certainty due to inconsistency, imprecision, indirect evidence and publication bias. There was no increase in certainty by effect size, confounding factor control or dose-response gradient.

Classification of certainty of evidence according to GRADE Working Group

High: we are very confident that the true effect is close to the estimated effect

Moderate: We are moderately confident in the effect estimate: the true effect is likely to be close to the effect estimate, but there is a possibility that it will be substantially different.

Low: Our confidence in the effect estimate is limited: The actual effect may be substantially different from the effect estimate.

Very low: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the effect estimate.

Spei ME, Samoli E, Bravi F, La Vecchia C, Bamia C, Benetou V. Physical activity in breast cancer survivors: A systematic review and meta-analysis on overall and breast cancer survival. Breast. 2019;44:144-152.

RECREATIONAL PHYSICAL ACTIVITY VERSUS NO ACTIVITY FOR PEOPLE WITH BREAST CANCER

Patient or population: breast cancer

Context: -

Intervention: recreational physical activity

Comparison: no recreational physical activity

Outcomes	Potential absolute effects* (IC 95%)		Relative Risk (IC 95%)	Number of participants (studies)	Certain of evidence (GRADE)	Comments
	Risk without physical activity	Risk with physical activity				
Mortality from all causes Follow-up: 3.5 to 12.7 years	-	-	HR 0.58 (0,45-0,75)	19,443 (8 observational studies)	⊕○○○ VERY LOW [a,b]	-
Breast cancer mortality Follow-up: 3.5 to 12.7 years	-	-	HR 0.60 (0,36-0,99)	8,330 (5 observational studies)	⊕○○○ VERY LOW [a,b]	-

Subtitle

* The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk of the comparator group and the relative effect of the intervention (and its 95% CI). CI: Confidence Interval; RR: relative risk.

Explanations for reducing the certainty of evidence

A. Methodological limitations. Half of the studies had moderate methodological quality and the other half had high (NewCastle-Ottawa). Reduced one level (-1).

B. Inconsistency. I2 = 70.4. Reduced two levels (-2)

There was no reduction in certainty due to imprecision, indirect evidence and publication bias. There was no increase in certainty by effect size, confounding factor control or dose-response gradient.

Classification of certainty of evidence according to GRADE Working Group

High: we are very confident that the true effect is close to the estimated effect

Moderate: We are moderately confident in the effect estimate: the true effect is likely to be close to the effect estimate, but there is a possibility that it will be substantially different.

Low: Our confidence in the effect estimate is limited: The actual effect may be substantially different from the effect estimate.

Very low: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the effect estimate.

MODERATE TO STRONG PHYSICAL ACTIVITY VERSUS NO PHYSICAL ACTIVITY FOR PEOPLE WITH BREAST CANCER

Patient or population: breast cancer
Context: -
Intervention: moderate to vigorous physical activity
Comparison: no physical activity (or low)

Outcomes	Potential absolute effects* (IC 95%) Risk without physical activity	Risk with physical activity	Relative Risk (IC 95%)	Number of participants (studies)	Certain of evidence (GRADE)	Comments
Mortality from all causes Follow-up: 3.5 to 12.7 years	-	-	HR 0.50 (0,36-0,68)	5,271 (2 observational studies)	⊕○○○ VERY LOW [a]	-
Breast cancer mortality Follow-up: 3.5 to 12.7 years	-	-	HR 0.61 (0,36-1,03)	2,910 (1 observational study)	⊕○○○ VERY LOW [b,c]	-

Subtitle
* The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk of the comparator group and the relative effect of the intervention (and its 95% CI). CI: Confidence Interval; RR: relative risk.

Explanations for reducing the certainty of evidence

A. Methodological limitations. The included studies (Irwin 2011; Bertram 2011) presented a critical risk of bias by the ROBINS-I tool. Reduced two levels (-2).

B. Methodological limitations. The included study (Irwin 2011) presented a critical risk of bias by the ROBINS-I tool. Reduced two levels (-2).

There was no reduction in certainty due to imprecision, indirect evidence and publication bias. There was no increase in certainty by effect size, confounding factor control or dose-response gradient

Classification of certainty of evidence according to GRADE Working Group

High: we are very confident that the true effect is close to the estimated effect
Moderate: We are moderately confident in the effect estimate: the true effect is likely to be close to the effect estimate, but there is a possibility that it will be substantially different.
Low: Our confidence in the effect estimate is limited: The actual effect may be substantially different from the effect estimate.
Very low: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the effect estimate.

MODERATE PHYSICAL LEISURE ACTIVITY VERSUS NO PHYSICAL ACTIVITY FOR PEOPLE WITH BREAST CANCER

Patient or population: breast cancer
Context: -
Intervention: moderate leisure physical activity
Comparison: no physical activity

Outcomes	Potential absolute effects* (IC 95%) Risk without physical activity	Risk with physical activity	Relative Risk (IC 95%)	Number of participants (studies)	Certain of evidence (GRADE)	Comments
Mortality from all causes Follow-up: 3.5 to 12.7 years	-	-	HR 0.52 (0,39-0,69)	7,392 (2 observational studies)	⊕○○○ VERY LOW [a]	-
Breast cancer mortality Follow-up: 3.5 to 12.7 years	-	-	HR 0.55 (0,36-0,84)	7,392 (2 observational studies)	⊕○○○ VERY LOW [a]	-

Subtitle
* The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk of the comparator group and the relative effect of the intervention (and its 95% CI). CI: Confidence Interval; RR: relative risk.

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Explanations for reducing the certainty of evidence

A. Methodological limitations. The included studies (Irwin 2011; Holick 2008 showed critical risk of bias by the ROBINS-I tool. Reduced by two levels (-2).

There was no reduction in certainty due to imprecision, indirect evidence and publication bias. There was no increase in certainty by effect size, confounding factor control or dose-response gradient.

Classification of certainty of evidence according to GRADE Working Group

High: we are very confident that the true effect is close to the estimated effect

Moderate: We are moderately confident in the effect estimate: the true effect is likely to be close to the effect estimate, but there is a possibility that it will be substantially different.

Low: Our confidence in the effect estimate is limited: The actual effect may be substantially different from the effect estimate.

Very low: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the effect estimate.

GENERAL PHYSICAL ACTIVITY VERSUS NO PHYSICAL ACTIVITY FOR PEOPLE WITH BREAST CANCER

Patient or population: breast cancer

Context: -

Intervention: general physical activity

Comparison: no physical activity

Outcomes	Potential absolute effects* (IC 95%)		Relative Risk (IC 95%)	Number of participants (studies)	Certain of evidence (GRADE)	Comments
	Risk without physical activity	Risk with physical activity				
Mortality from all causes Follow-up: 3.5 to 12.7 years	-	-	HR 0.53 (0,24-1,20)	2,658 (2 observational studies)	⊕○○○ VERY LOW [a,b]	-
Breast cancer mortality Follow-up: 3.5 to 12.7 years	-	-	HR 0.81 (0,48-1,36)	2,658 (2 observational studies)	⊕○○○ VERY LOW [a,b]	-

Subtitle

* The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk of the comparator group and the relative effect of the intervention (and its 95% CI). CI: Confidence Interval; RR: relative risk.

Explanations for reducing the certainty of evidence

A. Methodological limitations. The included studies (Irwin 2011; Sternfeld 2009) presented a critical risk of bias by the ROBINS-I tool. Reduced two levels (-2).

B. Inaccuracy: 95% CI estimates compatible with significant risk reduction, no effect on risk or significant increase in risk of death)

There was no reduction in certainty due to indirect evidence and publication bias. There was no increase in certainty by effect size, confounding factor control or dose-response gradient.

Classification of certainty of evidence according to GRADE Working Group

High: we are very confident that the true effect is close to the estimated effect

Moderate: We are moderately confident in the effect estimate: the true effect is likely to be close to the effect estimate, but there is a possibility that it will be substantially different.

Low: Our confidence in the effect estimate is limited: The actual effect may be substantially different from the effect estimate.

Very low: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the effect estimate.

Mahmood S, MacInnis RJ, English DR, Karahalios A, Lynch BM. Domain-specific physical activity and sedentary behaviour in relation to colon and rectal cancer risk: a systematic review and meta-analysis. Int J Epidemiol. 2017;46(6):1797-1813.

PHYSICAL ACTIVITY VERSUS NO ACTIVITY FOR RECTAL CANCER PREVENTION

Patient or population: adults without rectal cancer

Context: -

Intervention: physical activity (highest level)

Comparison: no physical activity (lowest level)

Outcomes	Potential absolute effects* (IC 95%)		Relative Risk (IC 95%)	Number of participants (studies)	Certain of evidence (GRADE)	Comments
	Risk without physical activity	Risk with physical activity				
rectal cancer incidence **Tracking:** Information unavailable	-	-	HR 0.87 (0,75-1,01)	1,227.158 (12 observational studies)	NOT EVALUATED	The authors do not present the assessment of the methodological quality of each study

Subtitle

* The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk of the comparator group and the relative effect of the intervention (and its 95% CI). CI: Confidence Interval; RR: relative risk.

Explanations for reducing the certainty of evidence

Classification of certainty of evidence according to GRADE Working Group

High: we are very confident that the true effect is close to the estimated effect

Moderate: We are moderately confident in the effect estimate: the true effect is likely to be close to the effect estimate, but there is a possibility that it will be substantially different.

Low: Our confidence in the effect estimate is limited: The actual effect may be substantially different from the effect estimate.

Very low: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the effect estimate.

Benke IN, Leitzmann MF, Behrens G, Schmid D. Physical activity in relation to risk of prostate cancer: a systematic review and meta-analysis. Annals of Oncology. 2018;29:1154-1179

PHYSICAL ACTIVITY VERSUS LOWER LEVEL OF PHYSICAL ACTIVITY FOR PROSTATE CANCER PREVENTION

Patient or population: men without prostate cancer

Context: -

Intervention: physical activity (highest level)

Comparison: physical activity (lowest level)

Outcomes	Potential absolute effects* (IC 95%)		Relative Risk (IC 95%)	Number of participants (studies)	Certain of evidence (GRADE)	Comments
	Risk without physical activity	Risk with physical activity				
Incidence of Prostate Cancer **Tracking:** Information unavailable	-	-	RR 0.99 (0,75-1,01)	2,454.147 (31 observational studies)	⊕○○○ VERY LOW [a,b]	-

Subtitle

* The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk of the comparator group and the relative effect of the intervention (and its 95% CI). CI: Confidence Interval; RR: relative risk.

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Explanations for reducing the certainty of evidence

A. Methodological limitations. An important part of the studies included in the meta-analysis had methodological limitations according to the NewCastle-Ottawa tool (only 4 studies scored 8 or 9, out of a total of 9 points). Reduced two levels (-2).

B. Inconsistency. I2 = 68%. Reduced one level (-1)

There was no reduction in certainty due to indirect evidence and publication bias. There was no increase in certainty by effect size, confounding factor control or dose-response gradient.

Classification of certainty of evidence according to GRADE Working Group

High: we are very confident that the true effect is close to the estimated effect

Moderate: We are moderately confident in the effect estimate: the true effect is likely to be close to the effect estimate, but there is a possibility that it will be substantially different.

Low: Our confidence in the effect estimate is limited: The actual effect may be substantially different from the effect estimate.

Very low: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the effect estimate.

APPENDIX 3- GUIDELINE QUALITY APPRAISAL AND CLASSIFICATION USING *AGREE II*

Four independent reviewers rated each selected Guideline using the AGREE-II tool consisting of 23 key items organized in six domains: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, editorial independence, and two overall evaluation items (AGREE). Each item was graded using a scale of 7 points: from 1, meaning "Strongly disagree," to 7, meaning "Strongly agree." The total was presented as a percentage of the maximum possible score for that domain (from 0 to 100%). We also categorized each Guideline according to the extent to which they successfully addressed AGREE-II: Strongly recommended (++), Guidelines whose standardized score exceeds 60% in ≥ 4 AGREE-II domains; the scores of the remaining domains must be ≥ 30% and > 60% for the domain rigor of development. Recommended (+), Guidelines whose standardized score ranges from 30 to 60% in ≥ 4 AGREE-II domains; the rigor of development score must be between 30 and 60%. Not recommended (–), Guidelines whose standardized score is < 30% in ≥ 4 AGREE-II domains or if rigor of development score is less than 30%. In all cases, discrepancies were resolved by a consensus of the whole team.

Chart 1. AGREE-II domain scores (AGREE II, 2009) expressed as a percentage applied to the guidelines and guides that contain the effects of physical activities in cancer prevention.

Guide - year of publication	AGREE-II domain scores (From 0 to 100%)						Guideline Quality 1=lowest, 7= highest	Recom-mended (++, +, -)
	Scope & Purpose	Stakeholders involvement	Rigor in the elaboration	Clarity of presentation	Appli-cability	Editorial independence		
PAGAC et al. 2018	97	79	82	90	58	16	5	++
WCRF/AICR 2018	86	63	86	91	41	16	5	+
Patel et al. 2019	64	8	12	41	12	69	2	-
Pollan et al. 2020	40	19	22	36	20	27	2	-
Rock et al. 2020	54	36	42	80	44	52	3	-
Median	64	39	42	80	41	27	3	
Mean (SD)	68 (23)	47 (23)	55 (40)	67 (27)	35 (18)	36 (23)	3 (1)	

++: Strongly recommended, +: Recommended, -: Not recommended; SD: Standard Deviation;

Chart 2. AGREE-II domain scores (AGREE II, 2009) expressed as a percentage applied to guidelines and guides that contain the effects of physical activity on cancer-specific and all-cause mortality.

Guide - year of publication	AGREE-II domain scores (From 0 to 100%)						Guideline Quality 1=lowest, 7= highest	Recom-mended (++, +, -)
	Scope & Purpose	Stakeholders involvement	Rigor in the elaboration	Clarity of presentation	Appli-cability	Editorial independence		
Howell et al. 2011	94	72	64	55	27	97	5	+
PAGAC et al. 2018	97	79	82	90	58	16	5	++
WCRF/AICR Breast 2018	84	52	78	75	26	33	4	++
Patel et al. 2019	64	8	12	41	12	69	2	-
Pollan et al. 2020	40	19	22	36	20	27	2	-
Median	84	52	64	55	26	33	4	
Mean (SD)	76 (23)	46 (31)	51 (32)	59 (22)	29 (17)	48 (33)	3 (1)	

++: Strongly recommended, +: Recommended, -: Not recommended; SD: Standard Deviation;

APPENDIX 4 – SYSTEMATIC REVIEWS QUALITY ASSESSMENT USING AMSTAR 2

Items following items were judged of critical importance: Comprehensiveness of the literature search (item 4); Included studies described in adequate detail (item 8); Adequacy of Risk of bias assessment of primary studies (item 9); Appropriateness of meta-analytical methods (item 11); Consideration of risk of bias when interpreting the results of the review (item 13). According to the responses to critical items, a final overall judgment of the whole review can be: High quality: No or one non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest. Moderate quality: More than one non-critical weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review. Low quality: one critical flaw with or without non-critical weaknesses: the review may not provide an accurate and comprehensive summary of the available studies that address the question of interest Critically low quality: More than one critical flaw with or without non-critical weaknesses: the review should not be relied on to provide an accurate and comprehensive summary of the available studies. (Shea et al. 2017).

Chart 3. Amstar II critical items scores and quality assessment applied to systematic reviews evaluating the effects of physical activities to prevent cancer.

Systematic reviews	Amstar II critical items							Quality assessment
	Item 2	Item 4	Item 7	Item 9	Item 11	Item 13	Item 15	
Kruk et al. 2016	No	P Yes	No	No	No	Yes	No	Critically low quality
Neil-Sztramko et al. 2017	No	No	No	Yes	Yes	Yes	No	Critically low quality
Neilson et al. 2017	Yes	Yes	No	Yes	Yes	No	Yes	Critically low quality
Mahmood et al. 2017	Yes	P Yes	No	No	Yes	No	Yes	Critically low quality
Benke et al. 2018	No	No	No	Yes	Yes	Yes	Yes	Critically low quality
Brookman-May et al. 2019	No	No	No	No	No MA	No	No	Critically low quality
Dinu et al. 2019	Yes	Yes	No	Yes	Yes	Yes	No	Critically low quality
Chen et al. 2019	No	P Yes	No	Yes	Yes	Yes	Yes	Critically low quality
% Yes	43	29	0	57	71	57	43	
% Partial Yes	-	43	0	0	-	-	-	
% No	57	29	100	43	29	43	57	

P Yes, partial yes; No MA, meta-analysis not performed.

Chart 4. Amstar II critical items scores and quality assessment applied to systematic reviews evaluating the effects of physical activities on cancer-specific and all-cause mortality.

Systematic reviews	Amstar II critical items							Quality assessment
	Item 2	Item 4	Item 7	Item 9	Item 11	Item 13	Item 15	
Wu et al. 2016	No	P Yes	No	Yes	Yes	No	Yes	Critically low quality
Lee et al. 2018	No	P Yes	No	No	No	No	Yes	Critically low quality
Abdin et al. 2019	Yes	No	No	Yes	No MA	Yes	No MA	Critically low quality
Spei et al. 2019	P Yes	No	No	Yes	Yes	Yes	Yes	Critically low quality
% Yes	25	0	0	75	50	50	75	
% Partial Yes	25	50	0	0	-	-	-	
% No	50	50	100	25	50	50	25	

P Yes, partial yes; No MA, meta-analysis not performed.