COMMENTARY

# Toward Global Integration of Exercise in Lung Cancer Care: The IREX-Lung Initiative

Jordan Curry, PhD,[a,b,c] Alice Avancini, PhD,[d,e] Thomas Budolfsen, PT,[f] Ana Cardeña-Gutiérrez, MD,[g] Vinicius Cavalheri, PhD,[h,i,j] David Collado Martínez, MD,[k] Narjust Florez, MD,[l] Cecilia Pompili, MD, PhD,[m] Vanesa Rodríguez Sales, PT, PhD,[n] Raquel Sebio-Garcia, PT, PhD,[o,p] Teresa-Soria Comes, MD, PhD,[k] Morten Quist, PT, PhD,[f,q] Sara Pilotto, MD, PhD[e,*]

## From Evidence to Opportunity: Exercise in Lung Cancer Care

People living with and beyond lung cancer often present with low baseline physical activity and fitness, high symptom burden (notably, dyspnea and fatigue), and frequent cardiopulmonary comorbidities. These factors increase vulnerability to treatment-related deconditioning, functional decline, and loss of independence and also create a compelling rationale for exercise as a supportive care strategy. Observational studies consistently report that higher levels of physical activity and fitness are associated with better survival among lung cancer populations, although confounders and reverse causation limit causal inference in this literature.[1] Interventional evidence is strong for outcomes that matter to patients, caregivers, and clinicians, such as functional capacity, symptoms, and health-related quality of life (HRQoL), across multiple points on the care continuum. In the perioperative setting, evidence supports prehabilitation and rehabilitation across the surgical continuum in lung resection. Across systematic reviews and meta-analyses, short-duration preoperative programs (often 1–4 weeks) that include aerobic training can improve cardiorespiratory fitness and walking capacity (commonly assessed using $VO_2$-peak and 6-minute walk distance).[2] Several syntheses report reduced postoperative pulmonary complications and shorter hospital stay compared with usual care, though interventions and outcomes vary, and subgroup data are limited.[2] Postoperatively, structured rehabilitation approaches that incorporate aerobic and strengthening components, sometimes integrated with breathing training, appear to support recovery of functional capacity and daily activities; nevertheless, the optimal timing, dose, and delivery model remain uncertain.[3] During active treatment (chemotherapy and radiotherapy), trials and evidence syntheses indicate that supervised aerobic or combined aerobic-resistance exercise is generally feasible and safe when appropriately screened and tailored, with consistent benefits for

*Corresponding author.

Dr. Curry and Dr. Avancini are listed as co-first authors. Prof. Quist and Prof. Pilotto are listed as co-last authors.

[a]Department of Health and Exercise Science, Colorado State University, Fort Collins, Colorado, [b]Hull York Medical School, University of Hull, Hull, United Kingdom, [c]Faculty of Health, Human Performance Research Centre, INSIGHT Research Institute, University of Technology Sydney, Sydney, Australia, [d]Department of Neurosciences, Biomedicine and Movement Science, University of Verona, Verona, Italy, [e]Section of Innovation Biomedicine - Oncology Area, Department of Engineering for Innovation Medicine, University of Verona, and University and Hospital Trust of Verona, Italy, [f]UCSF-Centre for Health Research, Copenhagen University Hospital-Rigshospitalet, Copenhagen, Denmark, [g]Department of Medical Oncology, Hospital Universitario Nuestra Señora de Cancelaria, Santa Cruz de Tenerife, Spain, [h]National School of Health Sciences, The University of Notre Dame Australia, Perth, Australia, [i]Curtin School of Allied Health, Faculty of Health Sciences, Curtin University, Perth, Australia, [j]Allied Health, South Metropolitan Health Service, Perth, Australia, [k]Department of Medical Oncology, Hospital Universitario Doctor Peset, Valencia, Spain, [l]Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts, [m]The Institute for Clinical and Applied Health Research, University of Hull, Hull, United Kingdom, [n]The Ricky Rubio Foundation, Badalona, Spain, [o]Department of Physical Medicine and Rehabilitation. Hospital Clinic de Barcelona. Barcelona, Spain, [p]Fundació Recerca Clínic Barcelona - Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain, and [q]University of Copenhagen Faculty of Health and Medical Sciences, Copenhagen, Denmark

Address for correspondence: Dr. Sara Pilotto, MD, PhD, Section of Innovation Biomedicine - Oncology Area, Department of Engineering for Innovation Medicine, University of Verona, P.le L.A. Scuro 10, 37134, Verona, Italy. E-mail: sara.pilotto@univr.it

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fatigue, dyspnea, muscle strength, cardiorespiratory fitness, and HRQoL.[4] Smaller studies also suggest potential improvements in psychological outcomes (e.g., anxiety and depression) when exercise is paired with behavior-change support or mind-body components, though these findings require confirmation in larger, adequately powered trials.[5] Moreover, a randomized controlled trial in patients with advanced inoperable lung cancer undergoing chemotherapy (n = 208) found significant improvements in anxiety and depression as secondary outcomes, after 12-weeks of structured exercise.[6] As new programs evolve, there is growing interest in how exercise may influence treatment tolerability (e.g., preserving dose intensity and reducing symptom-driven interruptions) and toxicity profiles, but evidence remains inconsistent and methodologically limited.[7] In survivorship, emerging work supports both center-based and home- or hybrid-delivery models. Some studies show meaningful gains in activity, fitness, and symptom management through remote monitoring, digital support, and individualized exercise prescription, offering promising avenues to extend access beyond specialist centers. Nevertheless, effects on primary endpoints are mixed across trials, reflecting heterogeneity in populations, disease setting, intervention dose, and outcome selection.[8] Evidence is also growing in advanced and metastatic lung cancer, where symptom burden and functional impairment are often substantial. Trials and meta-analyses in advanced lung cancer suggest that well-tailored exercise can be feasible and safe and may help maintain or improve physical function and fatigue, with potential benefits for HRQoL.[9] Nonetheless, the evidence base remains smaller and more heterogeneous than in perioperative settings, with limited data for patients with poorer performance status, younger patients (<50-year-old), and other high-risk populations.

## Closing the Gaps: Research Priorities and Implementation Challenges

Over the past decade, the evidence base supporting exercise interventions in lung cancer has grown substantially. Randomized trials and systematic reviews have reported benefits for physical fitness, functional capacity, symptom burden (including fatigue and dyspnea), and HRQoL across multiple stages of lung cancer care and treatment settings.[8,10] As a result, the central challenge is increasingly not whether exercise is beneficial, but how best to translate this growing body of knowledge into clearer, individualized exercise prescriptions and implementable care pathways in routine clinical practice.

Exercise prescriptions for patients with lung cancer should increasingly account for disease heterogeneity and also remain scalable in routine practice. Priorities differ across stages, from prehabilitation and recovery in resectable disease to symptom control, treatment tolerance, and functional maintenance in advanced disease. Nevertheless, lung cancer-specific guidance remains limited: most recommendations continue to be extrapolated from broader oncology exercise guidelines, leaving uncertainty about optimal modalities, intensity targets, contraindications, and monitoring strategies for common lung cancer phenotypes (e.g., dyspnea, chronic obstructive pulmonary disease burden, cachexia risk, frailty, and older age).[11] Future models should combine standardized assessment pathways with flexible exercise prescription algorithms that can be adapted according to disease stage, treatment modality, comorbidities, symptom burden, baseline physical and psychological status, patient preferences, and available resources.

In parallel, greater methodological harmonization across studies, including consensus on core outcomes, standardized reporting of exercise dose and adherence, and the incorporation of objective measures of fitness and body composition, would strengthen evidence synthesis, long-term follow-up data, and accelerate the development of more precise clinical guidance.

A further priority is coordinating research to address heterogeneity and improve interpretability. Exercise interventions studied to date vary widely in modality (aerobic, resistance, inspiratory muscle training, and multimodal), timing along the continuum (prehabilitation, postsurgery, during treatment, and survivorship), duration, intensity, supervision, and behavior-change support. Although this diversity reflects the adaptability of exercise, it also complicates comparisons. It limits our ability to define dose-response relationships and identify the components most effective for specific clinical goals (e.g., reducing postoperative complications or improving fatigue and treatment tolerance during systemic therapy).[8,10]

Evidence gaps are also increasingly concentrated in specific contexts: data remain limited for certain clinical subgroups, particularly SCLC and oncogene-driven NSCLC, and in the era of contemporary systemic therapies, including targeted therapies and immunotherapy. This is particularly relevant in resectable disease, in which increasingly complex perioperative pathways are expanding opportunities for prehabilitation and perioperative exercise intervention.[12] Interest is also growing in how exercise may interact with contemporary systemic therapies, but key questions remain regarding evolving toxicity profiles, treatment tolerance, completion, and response.[8,13] Mechanistic work remains relatively sparse, with few trials integrating biomarkers, objective activity monitoring, imaging-based body

composition, or immune-inflammatory profiling to clarify the pathways through which exercise may influence symptom trajectories, cardiopulmonary reserve, metabolic health, and treatment tolerance. Likewise, long-term follow-up and hard endpoints (progression-free survival and overall survival) are infrequently evaluated. In parallel, greater integration of patient-reported and patient-centered outcomes is needed to better capture patient experience and priorities. Finally, the largest gap may be implementation. Despite supportive evidence, most patients with lung cancer remain insufficiently active.[14] Sustainable models for referral pathways, reimbursement, workforce development, and integration with pulmonary or cardiac rehabilitation services remain inconsistently evaluated, particularly in low-resource and rural settings.[3] Workforce barriers span training, research, and funding: oncology teams often receive limited formal training in exercise counseling and referral, exercise professionals may lack lung cancer-specific competencies for managing complex symptoms, comorbidities, and treatment toxicities, and insufficient implementation research, reimbursement, and dedicated funding restrict the development of sustainable exercise oncology services. Embedding exercise across the continuum, from screening and prehabilitation to active treatment, survivorship, and advanced disease, will require coordinated collaboration across research, clinical practice, and health policy, alongside education and engagement of patients, caregivers, and clinicians. At the same time, persistent global inequities in access to exercise programs must be addressed, particularly among underserved and socioeconomically disadvantaged populations facing structural barriers (e.g., limited services, transportation, and cost) that restrict participation and contribute to disparities in supportive care access.[13,15] In this sense, implementation strategies will also need to be tailored globally and in economic settings: high-resource settings may support supervised multidisciplinary programs embedded within oncology services, whereas lower-resource settings may require community-based, home-based, hybrid, or digitally supported models that preserve core evidence-based principles and also allow local adaptation.

## A Global Response: The International Research Exercise in Lung Cancer Initiative

Taken together, exercise oncology in lung cancer is at a pivotal moment. Evidence supporting the benefits of exercise for physical fitness, symptom burden, and quality of life has grown substantially; however, research efforts remain fragmented, implementation uneven, and key scientific and clinical questions unresolved. Addressing these challenges now requires coordinated international action (Fig. 1). To address this need, the International Research Exercise in Lung




**Figure 1.** The IREX-Lung Initiative: advancing global integration of exercise in lung cancer care. IREX-Lung, International Research Exercise in Lung Cancer.

Cancer (IREX-Lung) initiative was established by the International Association for the Study of Lung Cancer. IREX-Lung brings together a global, multidisciplinary network of clinicians, rehabilitation specialists, and patient advocates with the shared goal of advancing both the science and implementation of exercise in lung cancer care. The initiative aims to foster international collaboration, strengthen the workforce involved in exercise oncology, and support the development of scalable exercise programs tailored to the needs of people living with lung cancer. The committee is organized into working groups focused on evidence synthesis, guideline development, implementation research, education, and stakeholder engagement. Over the next 2 to 3 years, IREX-Lung aims to deliver an international healthcare professional survey, Delphi-based consensus recommendations for lung cancer-specific exercise assessment and prescription, educational resources for clinicians and patients, collaborative research projects addressing priority evidence gaps, and initiatives to facilitate international research collaborations, grant development, and capacity building across the exercise oncology community. Success will be measured through scientific outputs, international participation, integration of exercise referral pathways into clinical practice, and improved access to exercise services for people living with lung cancer. Through these coordinated efforts, the initiative seeks to move the field beyond isolated research toward sustainable, globally accessible models of exercise oncology care. In summary, the evidence supporting exercise in lung cancer has grown substantially, with consistent data demonstrating benefits across functional, symptomatic, and quality-of-life outcomes. Nevertheless, translating this evidence into routine clinical care will require coordinated global action to address persistent knowledge gaps, optimize intervention design across diverse clinical contexts, and overcome implementation barriers at patient, provider, and system levels. The IREX-Lung initiative represents a strategic and timely step toward this goal, offering a collaborative international platform to harmonize research efforts, generate high-quality evidence, advance implementation strategies, and ultimately support the sustainable integration of exercise into standard lung cancer care worldwide.

## CRediT Authorship Contribution Statement

**Jordan Curry:** Conceptualization, Investigation, Writing - original draft, Visualization, Supervision, Project administration, Writing - review & editing.

**Alice Avancini:** Conceptualization, Investigation, Writing - original draft, Visualization, Supervision, Project administration, Writing - review & editing.

**Thomas Budolfsen:** Conceptualization, Visualization, Writing - review & editing.

**Ana Cardeña-Gutiérrez:** Conceptualization, Visualization, Writing - review & editing.

**Vinicius Cavalheri:** Conceptualization, Visualization, Writing - review & editing.

**David Collado Martínez:** Conceptualization, Visualization, Writing - review & editing.

**Narjust Florez**: Conceptualization, Visualization, Writing - review & editing.

**Cecilia Pompili:** Conceptualization, Visualization, Writing - review & editing.

**Vanesa Rodríguez Sales:** Conceptualization, Visualization, Writing - review & editing.

**Raquel Sebio-Garcia:** Conceptualization, Visualization, Writing - review & editing.

**Teresa-Soria Comes:** Conceptualization, Visualization, Writing - review & editing.

**Morten Quist:** Conceptualization, Investigation, Writing - original draft, Visualization, Supervision, Project administration, Writing - review & editing.

**Sara Pilotto:** Conceptualization, Investigation, Writing - original draft, Visualization, Supervision, Project administration, Writing - review & editing.

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The authors declare no conflict of interest.

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