Performance Status in Cancer: Not Broken, But Time for an Upgrade?

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BACKGROUND

Considerable advances in early detection and combination therapy during the past 70 years[1] have contributed to significant cancer-specific survival gains, with an estimated 17 million individuals currently living with a history of cancer in the United States, a number expected to reach 26 million by the year 2040.[2] The financial investment to achieve such progress, of course, has been enormous.[3,4] Intriguingly, despite the increasing sophistication and cost of contemporary cancer care,[5,6] evaluation of patient performance status (PS)—an integral aspect of treatment selection, toxicity monitoring, and clinical trial eligibility—has remained essentially unchanged since 1948.[7] In this commentary, we provide a historical overview and critical evaluation of PS assessment in oncology. We also discuss alternative approaches to PS assessment that may improve prognostication and risk stratification in research and clinical practice.

PS SCALES: 72 YEARS AND COUNTING

In 1948, Karnofsky and colleagues[7] used three criteria to evaluate nitrogen mustard efficacy in lung cancer: objective improvement (eg, decrease in lesion size), subjective improvement (eg, patient-reported symptoms), and PS (ie, patients' ability to participate in activities of daily life). Evaluation of PS was standardized using a physician-rated scale, now known as Karnofsky Performance Status (KPS), ranging from 0 (dead) to 100 (well functioning) with 10-point increments.[7] The simpler 6-point Eastern Cooperative Oncology Group (ECOG) PS scale (0 [fully active] to 5 [dead]) was introduced by Zubrod and colleagues[8] in 1960 as one of 15 standardized assessments for all ECOG multicenter clinical trials. The intended purpose of the ECOG PS scale was to evaluate patient reaction to chemotherapy, along with patient-reported pain, nausea, and appetite.[8] Both clinician-administered scales were used primarily to evaluate therapeutic efficacy until 1973, when Zelen concluded that failure to consider PS in clinical trial eligibility "will introduce so much variability and bias into the trial that real differences between therapies are likely to be missed altogether."[9(p34)] As a result, subsequent use of PS scales in clinical trials transitioned from the assessment of therapeutic efficacy to eligibility (ie, KPS ≤ 60 or ECOG ≥ 2 ineligible)[10-13] and stratification (ie, more homogenous subgroups).[14-16] Both the KPS and ECOG scales are strong independent predictors of clinical outcome in numerous oncology populations.[17-19] They are also inexpensive and feasible to implement in all oncology clinical settings. Consequently, the KPS and ECOG scales, and therefore the assessment of PS, remain integral tools in contemporary practice incorporated into virtually every clinical visit across the entire cancer care continuum.

KPS AND ECOG: ROOM FOR IMPROVEMENT

The demonstrated clinical value of KPS and ECOG directly contradicts why one would advocate for their replacement. Nevertheless, closer inspection of the KPS and ECOG scales reveal significant limitations. First, these scales are clinician based and therefore subjective, with poor reliability and validity.[20] In a meta-analysis of 15 studies representing 2,808 patients, agreement between clinicians on KPS/ECOG scores was deemed moderate (Pearson correlation coefficients, 0.71 to 0.78).[21] In addition, patient and clinician PS scores have low agreement,[22] with up to 50% of patient-reported functional limitations missed by clinicians[23] and adverse PS change (ie, KPS < 60) reported approximately 15 months earlier by patients than clinicians.[24] Misclassification of PS has obvious implications for clinical trial eligibility as well as planned best practice therapy, with some patients classified as having sufficient PS to tolerate therapy but having nascent impairment, and conversely, another proportion classified as having insufficient PS yet with considerable reserve capacity and able to tolerate therapy.[25-27] Second, poor KPS and ECOG scores are strong predictors of prognosis,[17-19] which is not surprising when impairment is obvious; however, the prognostic value in patients with good PS is limited. A meta-analysis of 66 phase II and III randomized controlled trials (n = 44,511 patients with ECOG 0-2)[18] found no differences in clinical outcomes between patients with either ECOG scores of 0, 1, or 2, suggesting that ECOG provides essentially no additional prognostic information for patients with no obvious physical impairments. Third, KPS/ECOG may have

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on May 22, 2020 and published at ascopubs.org/journal/jco on June 25, 2020: DOI https://doi.org/10.1200/JCO.20.00721

limited use for toxicity risk stratification in the era of contemporary practice. Use of PS scales for toxicity risk prediction is based on work in the 1980s that showed a higher incidence of chemotherapy toxicity in patients classified with poor PS (ie, KPS $\leq$ 60; ECOG $\geq$ 2).[11,26,28] The safety profile of current treatment regimens, however, has evolved considerably, in part because of the use of supportive polytherapy care, the safety profile of modern scheduling approaches/lower-dose combinations, and the use of molecularly targeted agents.[29] Indeed, a retrospective study of 16,233 patients with solid tumors receiving contemporary chemotherapy regimens found negligible differences in relative dose intensity between patients with ECOG PS of 0 versus 1-3.[30] Finally, KPS/ECOG scales are only administered during in-person clinic visits, often weeks, if not months, apart; therefore, a snapshot of PS is captured, which limits the ability to detect more subtle real-time changes of potential clinical importance.

Overall, given the highlighted limitations, it is somewhat remarkable that PS scales exhibit any clinical value. We posit that the reason KPS/ECOG have widespread applicability is because they provide insight into PS, a metric with substantial importance in clinical populations. PS measurement, albeit using a variety of different assessment tools, is of central importance in virtually every area of clinical disease management.[31] We further suggest that more objective, discriminatory, and dynamic tools may actually augment the value of PS assessment in the oncology setting beyond that currently possible with KPS and ECOG scales.

ALTERNATIVE PS MEASURES

Alternative tools with which to assess PS or aspects of PS have been explored in the oncology setting (Table 1). For instance, the geriatric assessment[32] (patients age $>$ 65 years) and the hematopoietic cell transplantation–specific comorbidity index[33] (hematologic malignancies) are multiparametric tools that evaluate different PS domains (eg, activities-of-daily-living questionnaire) and/or comorbidity indices (eg, cardiac disease). Preliminary data suggest that both tools improve toxicity and survival prediction beyond PS,[32,33] leading to widespread clinical uptake, at least in certain oncology settings. Both tools are limited, however, as they are population specific and typically assessed at one time point.[34] Therefore, pan-cancer assessment tools that provide an objective and dynamic PS evaluation must be identified.

Numerous standardized tests that include counting repetitions or timing an activity have been developed to evaluate PS in noncancer clinical populations. The Sit-to-Stand Test,[35] Timed-Up-and-Go test (TUG)[36] and Short Physical Performance Battery[37] were developed to assess lower-extremity strength, balance, and mobility in frail elderly individuals. In patients with cancer age $\geq$ 70 years, both poor TUG test[38] and Short Physical Performance Battery[39] have been associated with an approximately two-fold increased risk of mortality. The 6-minute walk test, originally developed for chronic obstructive pulmonary disease,[31,40] is a robust predictor of mortality in respiratory and cardiac diseases,[31,41] whereas preliminary data in patients with cancer indicate a 6-minute walk test result of $<$ 350 meters predicts mortality risk, even after adjustment for KPS.[42,43] However, these tools fail to discriminate between patients who are classified with good PS[44] and will likely not detect or identify therapy-related toxicity.[41,45]

Cardiorespiratory fitness (CRF), first quantified by Hill and Lupton in 1923,[46] provides an objective assessment of the integrative capacity of the cardiovascular, pulmonary, hematopoietic, and musculoskeletal systems to transport and use oxygen.[31] The gold standard assessment of CRF is a cardiopulmonary exercise test coupled with automated gas exchange assessment, which provides direct quantification of submaximal and peak oxygen consumption (VO_2peak).[31] Prediction equations that are based on achieved exercise workload can also estimate VO_2peak. In chronic lung and cardiac conditions, CRF is considered a clinical vital sign, with assessment recommended across all phases of clinical decision making.[31,47,48] In cancer, Reichel[49] first reported in 1972 that presurgical estimated CRF was a stronger predictor of postoperative complications compared with standard clinical metrics (eg, age and pulmonary function) in lung cancer, concluding that CRF "should be used routinely in the evaluation of the candidate for pneumonectomy."[49(p576)] Subsequently, the tolerability (ie, more than 80% of patients achieve peak criteria) and safety (ie, no exercise-related deaths and an approximate 15% nonserious adverse event rate) of CRF was established in a systematic review of 90 studies representing approximately 5,200 patients.[45] Work in lung,[50,51] GI,[52] hepatobiliary and pancreatic,[53] and hematologic malignancies[54] show that CRF is an independent predictor of postoperative complications and mortality.[55-59] Presurgical CRF stratification values are defined for lung[47] and colorectal cancer,[58] with less than 15 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$ associated with an elevated risk of complications, whereas less than 10 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$ is considered to be associated with a high risk of complications.[47] Poor CRF is also associated with a higher prevalence of acute and chronic treatment-related late effects[55-59] and all-cause, cardiovascular, and cancer mortality.[60] Despite major advantages, CRF requires specialized equipment and trained personnel, likely limiting its widespread clinical application.[48,61]

In summary, despite promising findings, none of the aforementioned tools is currently incorporated into routine clinical practice. In addition to the dearth of evidence that supports the clinical use of such tools, a fundamental weakness of all tools is the stark discrepancy in practicality compared with the KPS/ECOG scales. There is a critical need for tools that can dynamically and

TABLE 1. Exemplar Performance Status Assessment Tools

Tool	Target Population	Assessment Description	Outcome Description	Objective	Dynamic	Widespread Feasibility
KPS[7]	Pan-cancer	Evaluation of patient physical functioning related to activities of daily living	Linear score from 0 (dead) to 100 (well functioning)	No	Possible	Yes
ECOG[8]	Pan-cancer	Evaluation of patient physical functioning related to activities of daily living	Linear score from 0 (fully active) to 5 (dead)	No	Possible	Yes
GA[32]	Age ≥ 65 years	Evaluation of multiple domains (eg, functional status, falls, comorbid conditions, cognitive status, psychological state, nutrition)	Linear or dichotomous scores, depending on domain	No	Possible	No
HCT-CI[33]	Patients undergoing HCT	Evaluation of 17 categories of comorbidities (eg, cardiac, pulmonary, psychiatric)	Weighted score from 0 (low risk) to 29 (high risk)	Yes	Possible	No
Sit-to-Stand[35]	Pan-cancer	Measurement of the No. of times sitting to full standing can be completed in 30 seconds	Linear metric from < 4 (poor) to approximately 20 (excellent)	Yes	Possible	No
TUG[36]	Pan-cancer	Measurement of time taken to rise from a chair, walk 3 meters, turn, walk back, and sit down	Linear metric from < 12 seconds (poor) to approximately 85 seconds (excellent)	Yes	Possible	No
SPPB[37]	Pan-cancer	Evaluation of multiple domains (eg, balance, sit to stand, walking speed)	Linear score in each domain from 0 (poor) to 4 (excellent)	Yes	Possible	No
6MWT[31]	Pan-cancer	Measurement of distance covered during 6MWT in a 100-foot hallway	Linear metric from < 100 meters (poor) to approximately 700 meters (excellent)	Yes	Possible	No
Incremental exercise test/ CPET[31]	Pan-cancer	Estimation or direct measurement of VO_2peak during an 8- to 12-minute exercise test on a bike or treadmill where the load or speed is progressively increased	Linear metric from < 15 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$ (poor) to > 85 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$ (endurance trained)	Yes	Possible	No
Digital phenotyping[71]	Pan-cancer	Measurement of PRO, mobility, and/or physiologic data using digital devices	Metrics of mobility (eg, light, moderate, vigorous activity, minutes/day) and physiologic (eg, sleep duration, [minutes]; heart rate, [beats/ minutes])	Yes	Yes	Possible

Abbreviations: 6MWT, 6-minute walk test; CPET, cardiopulmonary exercise test; ECOG, Eastern Cooperative Oncology Group; GA, Geriatric Assessment; HCT-CI, Hematopoietic Cell Transplantation–Specific Comorbidity Index; KPS, Karnofsky Performance Score; PRO, patient-reported outcome; SPPB, Short Physical Performance Battery; TUG, Timed-Up-and-Go test; VO_2peak, peak oxygen consumption.

objectively assess PS with the widespread feasibility of the KPS/ECOG scales.

THE DIGITAL FRONTIER

Advances in health technology may provide unprecedented opportunities to improve PS assessment in cancer. Most previous and ongoing studies leveraging technology focus on monitoring objective mobility via wearable devices. For instance, accelerometers are small, wireless, digital devices providing objective mobility measurement (eg, steps per day and/or minutes per day of light, moderate, and vigorous activity).[62,63] Saint-Maurice et al[64] found that, compared with less than 4,000 steps per day, more than 8,000 steps per day was associated with a lower risk of all-cause and cancer-specific mortality in 4,840 apparently healthy individuals. Preliminary findings from two studies in patients with advanced disease[65] and those undergoing surgical tumor resection[66] indicate that lower steps per day and total activity per day are associated with increased risk of death and postsurgical complications, respectively. Few studies are performing deep, dynamic phenotyping using multiparametric platforms; however, the rapid expansion of consumer-grade digital mobile devices—for example, Fitbit, Apple iWatch, smartphones—with integrated multisensory systems may offer a unique opportunity for digital phenotyping. Such devices dynamically generate an abundance of unlabeled sensor data points per day, including mobility and physiologic data, such as heart rate and sleep.[67-70] The feasibility of digital phenotyping was recently demonstrated in work showing that 250,000 daily measurements in 43 individuals over 11 months were used to first develop personalized,

activity-based baseline normative data, and abnormal physiologic signals from longitudinal data were subsequently used to identify early signs of disease.[71] An ongoing prospective cohort study in 2,500 patients with heart failure (ClinicalTrials.gov identifier: NCT03810638) will create a digital registry that combines patient-reported outcomes (PROs), mobility, and electronic health record data to monitor changes in quality of life and other clinical outcomes. These are examples of the type of digital phenotyping studies needed in oncology. We posit that the integration of digital technologies assessing physiologic (eg, heart rate), mobility (eg, steps per day), and PRO (eg, PRO-Common Terminology Criteria for Adverse Events),[72] as well as electronic health record data, may be of significant value for treatment selection, clinical trial eligibility, and toxicity monitoring in the oncology setting.

Several challenges remain to realize the potential of digital phenotyping in the oncology setting. Policies governing the privacy and security of patient data captured from digital mobile devices will need to be defined. Research efforts will require development and validation data sets and robust statistical tools, such as discrimination, calibration, and reclassification, to discern whether digital phenotyping–related data provide incremental value beyond the KPS/ECOG scales. Subsequent randomized trials that assess whether baseline/change in digital biomarkers improve current patient stratification approaches for informing clinical decision making are needed. Data repositories that allow for the simultaneous integration, query, and visualization of large amounts of heath data with artificial intelligence tools[73,74] are needed to seamlessly integrate digital phenotyping data into clinical workflows.[75] Overcoming such challenges is a US Food and Drug Administration priority, with efforts underway to advance the standardization of PS data in oncology.[76]

In conclusion, the prognostic utility and widespread applicability of the KPS/ECOG scales reflect the central importance of PS in patients with cancer. Nevertheless, the complex and heterogeneous nature of cancer management has accentuated the need for the development and validation of objective and dynamic measures of PS that can accurately discriminate between patients across the continuum of cancer care in all settings. The clinical impact of such measures would be considerable.

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SUPPORT

Supported by research grants from the National Cancer Institute (J.M.S. and L.W.J.), AKTIV Against Cancer and the Kavli Trust (J.M.S., G.S., E.E., and L.W.J.), and Memorial Sloan Kettering Cancer Center Support Grant/Core Grant No. P30-CA008748 (J.M.S. and L.W.J.).

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI https://doi.org/10.1200/JCO.20.00721.

AUTHOR CONTRIBUTIONS

Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

REFERENCES

1. DeVita VT Jr, Chu E: A history of cancer chemotherapy. Cancer Res 68:8643-8653, 2008
2. Jemal A, Ward EM, Johnson CJ, et al: Annual report to the nation on the status of cancer, 1975-2014, featuring survival. J Natl Cancer Inst 109:djx030, 2017
3. Mariotto AB, Yabroff KR, Shao Y, et al: Projections of the cost of cancer care in the United States: 2010-2020. J Natl Cancer Inst 103:117-128, 2011
4. Wouters OJ, McKee M, Luyten J: Estimated research and development investment needed to bring a new medicine to market, 2009-2018. JAMA 323:844-853, 2020
5. Baumgardner JR, Shahabi A, Linthicum MT, et al: Share of oncology versus nononcology spending in episodes defined by the Centers for Medicare & Medicaid Services oncology care model. J Oncol Pract 14:e699-e710, 2018
6. Manz CR, Porter DL, Bekelman JE: Innovation and access at the mercy of payment policy: The future of chimeric antigen receptor therapies. J Clin Oncol 38: 384-387, 2020
7. Karnofsky DA, Abelmann WH, Craver LF, et al: The use of the nitrogen mustards in the palliative treatment of carcinoma. With particular reference to bronchogenic carcinoma. Cancer 1:634-656, 1948
8. Zubrod CG, Schneiderman MA, Frei E III, et al: Appraisal of methods for the study of chemotherapy of cancer in man: Comparative therapeutic trial of nitrogen mustard and triethylene thiophosphoramide. J Chronic Dis 11:7-33, 1960
9. Zelen M: Keynote address on biostatistics and data retrieval. Cancer Chemother Rep 3 4:31-42, 1973
10. Selawry OS: Initial therapeutic trial of new drugs in lung cancer. Cancer Chemother Rep 3 4:215-225, 1973
11. Stanley KE: Prognostic factors for survival in patients with inoperable lung cancer. J Natl Cancer Inst 65:25-32, 1980
12. Vincent RG, Pickren JW, Fergen TB, et al: Evaluation of methotrexate in the treatment of bronchogenic carcinoma. Cancer 36:873-880, 1975

13. Baker LH, Vaitkevicius VK, Gehan E: Randomized prospective trial comparing 5-fluorouracil (NSC-19893) to 5-fluorouracil and methyl-CCNU (NSC-95441) in advanced gastrointestinal cancer. Cancer Treat Rep 60:733-737, 1976
14. Wolf J: Nitrosoureas as single agents in the treatment of pulmonary cancer. Cancer Treat Rep 60:753-756, 1976
15. Ahmann DL, Bisel HF, Hahn RG, et al: An analysis of a multiple-drug program in the treatment of patients with advanced breast cancer utilizing 5-fluorouracil, cyclophosphamide, and prednisone with or without vincristine. Cancer 36:1925-1935, 1975
16. Ramalingam SS, Vansteenkiste J, Planchard D, et al: Overall survival with osimertinib in untreated, *EGFR*-mutated advanced NSCLC. N Engl J Med 382:41-50, 2020
17. West HJ, Jin JO: Performance status in patients with cancer. JAMA Oncol 1:998, 2015
18. Cheng S, Qureshi M, Pullenayegum E, et al: Do patients with reduced or excellent performance status derive the same clinical benefit from novel systemic cancer therapies? A systematic review and meta-analysis. ESMO Open 2:e000225, 2017
19. Renfro LA, Goldberg RM, Grothey A, et al: Clinical calculator for early mortality in metastatic colorectal cancer: An analysis of patients from 28 clinical trials in the Aide et Recherche en Cancérologie Digestive Database. J Clin Oncol 35:1929-1937, 2017
20. Sørensen JB, Klee M, Palshof T, et al: Performance status assessment in cancer patients. An inter-observer variability study. Br J Cancer 67:773-775, 1993
21. Chow R, Bruera E, Temel JS, et al: Inter-rater reliability in performance status assessment among healthcare professionals: An updated systematic review and meta-analysis. Support Care Cancer 28:2071-2078, 2020
22. Basch E, Wood WA, Schrag D, et al: Feasibility and clinical impact of sharing patient-reported symptom toxicities and performance status with clinical investigators during a phase 2 cancer treatment trial. Clin Trials 13:331-337, 2016
23. Fromme EK, Eilers KM, Mori M, et al: How accurate is clinician reporting of chemotherapy adverse effects? A comparison with patient-reported symptoms from the Quality-of-Life Questionnaire C30. J Clin Oncol 22:3485-3490, 2004
24. Basch E, Jia X, Heller G, et al: Adverse symptom event reporting by patients vs clinicians: Relationships with clinical outcomes. J Natl Cancer Inst 101: 1624-1632, 2009
25. Roman MA, Koelwyn GJ, Eves ND, et al: Comparison of performance status with peak oxygen consumption in operable patients with non-small-cell lung cancer. Respirology 19:105-108, 2014
26. Schnipper LE, Smith TJ, Raghavan D, et al: American Society of Clinical Oncology identifies five key opportunities to improve care and reduce costs: The top five list for oncology. J Clin Oncol 30:1715-1724, 2012
27. West HJ: Patients with advanced non-small-cell lung cancer and marginal performance status: Walking the tight rope towards improved survival. J Clin Oncol 31:2841-2843, 2013
28. Pater JL, Loeb M: Nonanatomic prognostic factors in carcinoma of the lung: A multivariate analysis. Cancer 50:326-331, 1982
29. Meijers WC, Moslehi JJ: Need for multidisciplinary research and data-driven guidelines for the cardiovascular care of patients with cancer. JAMA 322: 1775-1776, 2019
30. Denduluri N, Patt DA, Wang Y, et al: Dose delays, dose reductions, and relative dose intensity in patients with cancer who received adjuvant or neoadjuvant chemotherapy in community oncology practices. J Natl Compr Canc Netw 13:1383-1393, 2015
31. Ross R, Blair SN, Arena R, et al: Importance of assessing cardiorespiratory fitness in clinical practice: A case for fitness as a clinical vital sign—A scientific statement from the American Heart Association. Circulation 134:e653-e699, 2016
32. Mohile SG, Dale W, Somerfield MR, et al: Practical assessment and management of vulnerabilities in older patients receiving chemotherapy: ASCO Guideline for Geriatric Oncology. J Clin Oncol 36:2326-2347, 2018
33. Sorror ML, Maris MB, Storb R, et al: Hematopoietic cell transplantation (HCT)-specific comorbidity index: A new tool for risk assessment before allogeneic HCT. Blood 106:2912-2919, 2005
34. Caillet P, Canoui-Poitrine F, Vouriot J, et al: Comprehensive geriatric assessment in the decision-making process in elderly patients with cancer: ELCAPA study. J Clin Oncol 29:3636-3642, 2011
35. Csuka M, McCarty DJ: Simple method for measurement of lower extremity muscle strength. Am J Med 78:77-81, 1985
36. Podsiadlo D, Richardson S: The timed "Up & Go": A test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 39:142-148, 1991
37. Guralnik JM, Simonsick EM, Ferrucci L, et al: A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 49:M85-M94, 1994
38. Soubeyran P, Fonck M, Blanc-Bisson C, et al: Predictors of early death risk in older patients treated with first-line chemotherapy for cancer. J Clin Oncol 30: 1829-1834, 2012
39. Cesari M, Cerullo F, Zamboni V, et al: Functional status and mortality in older women with gynecological cancer. J Gerontol A Biol Sci Med Sci 68:1129-1133, 2013
40. Butland RJ, Pang J, Gross ER, et al: Two-, six-, and 12-minute walking tests in respiratory disease. Br Med J (Clin Res Ed) 284:1607-1608, 1982
41. Holland AE, Spruit MA, Troosters T, et al: An official European Respiratory Society/American Thoracic Society technical standard: Field walking tests in chronic respiratory disease. Eur Respir J 44:1428-1446, 2014
42. Kasymjanova G, Correa JA, Kreisman H, et al: Prognostic value of the six-minute walk in advanced non-small cell lung cancer. J Thorac Oncol 4:602-607, 2009
43. Jones LW, Hornsby WE, Goetzinger A, et al: Prognostic significance of functional capacity and exercise behavior in patients with metastatic non-small cell lung cancer. Lung Cancer 76:248-252, 2012
44. Granger CL, Denehy L, Parry SM, et al: Which field walking test should be used to assess functional exercise capacity in lung cancer? An observational study. BMC Pulm Med 15:89, 2015
45. Jones LW, Eves ND, Haykowsky M, et al: Cardiorespiratory exercise testing in clinical oncology research: Systematic review and practice recommendations. Lancet Oncol 9:757-765, 2008
46. Hill AV, Lupton H: Muscular exercise, lactic acid, and the supply and utilization of oxygen. QJM 16:135-171, 1923
47. American Thoracic Society; American College of Chest Physicians: ATS/ACCP statement on cardiopulmonary exercise testing. Am J Respir Crit Care Med 167: 211-277, 2003
48. Myers J, Forman DE, Balady GJ, et al: Supervision of exercise testing by nonphysicians: A scientific statement from the American Heart Association. Circulation 130:1014-1027, 2014
49. Reichel J: Assessment of operative risk of pneumonectomy. Chest 62:570-576, 1972
50. Roman MA, Koelwyn GJ, Eves ND, et al: Comparison of performance status with peak oxygen consumption in operable patients with non-small-cell lung cancer. Respirology 19:105-108, 2014

51. Jones LW, Watson D, Herndon JE II, et al: Peak oxygen consumption and long-term all-cause mortality in nonsmall cell lung cancer. Cancer 116:4825-4832, 2010
52. Marshall CH, Al-Mallah MH, Dardari Z, et al: Cardiorespiratory fitness and incident lung and colorectal cancer in men and women: Results from the Henry Ford Exercise Testing (FIT) cohort. Cancer 125:2594-2601, 2019
53. Kumar R, Garcea G: Cardiopulmonary exercise testing in hepato-biliary & pancreas cancer surgery: A systematic review—Are we any further than walking up a flight of stairs? Int J Surg 52:201-207, 2018
54. Kelsey CR, Scott JM, Lane A, et al: Cardiopulmonary exercise testing prior to myeloablative allo-SCT: A feasibility study. Bone Marrow Transplant 49:1330-1336, 2014
55. Jones LW, Haykowsky M, Pituskin EN, et al: Cardiovascular reserve and risk profile of postmenopausal women after chemoendocrine therapy for hormone receptor: Positive operable breast cancer. Oncologist 12:1156-1164, 2007
56. West MA, Parry MG, Lythgoe D, et al: Cardiopulmonary exercise testing for the prediction of morbidity risk after rectal cancer surgery. Br J Surg 101:1166-1172, 2014
57. West MA, Lythgoe D, Barben CP, et al: Cardiopulmonary exercise variables are associated with postoperative morbidity after major colonic surgery: A prospective blinded observational study. Br J Anaesth 112:665-671, 2014
58. West MA, Asher R, Browning M, et al: Validation of preoperative cardiopulmonary exercise testing-derived variables to predict in-hospital morbidity after major colorectal surgery. Br J Surg 103:744-752, 2016
59. Adams MJ, Lipsitz SR, Colan SD, et al: Cardiovascular status in long-term survivors of Hodgkin's disease treated with chest radiotherapy. J Clin Oncol 22: 3139-3148, 2004
60. Groarke JD, Payne DL, Claggett B, et al: Association of post-diagnosis cardiorespiratory fitness with cause-specific mortality in cancer. Eur Heart J Qual Care Clin Outcomes [epub ahead of print on March 13, 2020]
61. Brunelli A, Charloux A, Bolliger CT, et al: ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy). Eur Respir J 34:17-41, 2009
62. Peddle-McIntyre CJ, Cavalheri V, Boyle T, et al: A review of accelerometer-based activity monitoring in cancer survivorship research. Med Sci Sports Exerc 50: 1790-1801, 2018
63. Lee IM, Shiroma EJ, Evenson KR, et al: Accelerometer-measured physical activity and sedentary behavior in relation to all-cause mortality: The Women's Health Study. Circulation 137:203-205, 2018
64. Saint-Maurice PF, Troiano RP, Bassett DR Jr, et al: Association of daily step count and step intensity with mortality among US adults. JAMA 323:1151-1160, 2020
65. Gresham G, Hendifar AE, Spiegel B, et al: Wearable activity monitors to assess performance status and predict clinical outcomes in advanced cancer patients. NPJ Digit Med 1:27, 2018
66. Panda N, Solsky I, Huang EJ, et al: Using smartphones to capture novel recovery metrics after cancer surgery. JAMA Surg 155:1-7, 2019
67. Evangelista L, Steinhubl SR, Topol EJ: Digital health care for older adults. Lancet 393:1493, 2019
68. Veerabhadrappa P, Moran MD, Renninger MD, et al: Tracking steps on Apple Watch at different walking speeds. J Gen Intern Med 33:795-796, 2018
69. Torkamani A, Andersen KG, Steinhubl SR, et al: High-definition medicine. Cell 170:828-843, 2017
70. Pew Research Center: Demographics of mobile device ownership and adoption in the United States: Mobile fact sheet. http://www.pewinternet.org/fact-sheets/mobile-technology-fact-sheet/
71. Li X, Dunn J, Salins D, et al: Digital health: Tracking physiomes and activity using wearable biosensors reveals useful health-related information. PLoS Biol 15: e2001402, 2017
72. Basch E, Dueck AC, Rogak LJ, et al: Feasibility of implementing the patient-reported outcomes version of the Common Terminology Criteria for Adverse Events in a multicenter trial: NCCTG N1048. J Clin Oncol 36:3120-3125, 2018
73. Scott JM, Dolan LB, Norton L, et al: Multisystem toxicity in cancer: Lessons from NASA's Countermeasures Program. Cell 179:1003-1009, 2019
74. Haendel MA, Chute CG, Robinson PN: Classification, ontology, and precision medicine. N Engl J Med 379:1452-1462, 2018
75. Genes N, Violante S, Cetrangol C, et al: From smartphone to EHR: A case report on integrating patient-generated health data. NPJ Digit Med 1:23, 2018
76. US Food and Drug Administration: FDA-ASCO public workshop: 2019 clinical outcome assessments in cancer clinical trials—Fourth annual workshop. https://www.fda.gov/drugs/news-events-human-drugs/fda-asco-public-workshop-2019-clinical-outcome-assessments-cancer-clinical-trials

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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No other potential conflicts of interest were reported.