clude the following: eliminate mandates for direct physician note entry; provide alternatives, such as dictation, document scanning,[9] and/or scribes[10] for EMR note capture; make the EMR inbox smarter about when, and how, to present messages to PCPs; and train clinic support personnel to manage the same proportion of inbox messages they handled with paper systems and to think whether a message is important or just noise before pushing the so-convenient "Forward-to-PCP" button. If changes are not made to reduce or eliminate these time penalties on PCPs, there will be no PCPs left to penalize.

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Financial Disclosure: None reported.
Funding/Support: This work was supported in part by the Intramural Research Program of the National Institutes of Health, National Library of Medicine.
Disclaimer: The findings and conclusions in this Invited Commentary are those of the authors and do not necessarily represent the official positions of National Library of Medicine, the National Institutes of Health, the Department of Health and Human Services, or the University of Wisconsin School of Medicine.
Additional Information: Parties interested in obtaining the full survey instrument should contact the corresponding author.
Additional Contributions: Matthew Hoffman, an MD and PhD student at the University of Wisconsin School of Medicine, organized the institutional review board exemption request at the University of Wisconsin and provided suggestions for improving the manuscript.

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RESEARCH LETTERS
ONLINE FIRST

Young-Onset Colorectal Cancer: Is It Time to Pay Attention?

The 2010 *Annual Report to the Nation on Cancer* celebrated a steady decline in the incidence of colorectal cancer (CRC).[1] This progress has been largely attributed to CRC screening, recommended for adults 50 years or older since 1996.[2] In sharp contrast to overall trends, the incidence of CRC appears to be increasing among adults younger than 50 years,[1,3] a group for whom average-risk screening is not routine. Particularly concerning is a trend toward advanced-stage CRCs,[1,3] suggesting a potential role for increased clinical vigilance and more prompt evaluation of symptomatic patients. To raise clinical awareness and facilitate recognition, we undertook a cohort study to (1) examine incidence trends; (2) define the distinct clinicopathologic manifestations of young-onset CRC; and (3) identify risk factors for advanced-stage disease.

Methods. We used the National Cancer Database (NCDB), a hospital-based cancer registry sponsored by the American College of Surgeons and American Cancer society that captures 70% of all incident cancers annually.[4] We identified patients diagnosed as having invasive adenocarcinoma (behavior code 3 [malignant]; histology codes 8010, 8020-8022, 8140-8144, 8210-8211, 8260-8263, 8470-8473, 8480-8481, and 8490) of the colon and the rectum between January 1998 and December 2007, the most recent decade after the US Preventive Services Task Force (USPSTF) recommended CRC screening. Eligible patients (n=588 869) were stratified by tumor site (colon [site codes C180, 182-189, and 199] vs rectum [site code C209]) and by age at diagnosis (young onset [before age 50 years] vs later onset [at age 50 years or older]). Age-adjusted incidence rates (per 100 000 individuals) were calculated using the 2000 US standard population (SEER*Stat software, version 7.0.4; National Cancer Institute). The temporal trend in the annual percentage change (APC) was identified (Joinpoint Regression Program, version 3.5.1; National Cancer Institute). For a subgroup (n=34 781) of young-onset CRCs diagnosed between 2003 and 2007—the following years after the USPSTF strengthened its screening recommendation in 2002[5]—independent predictors of advanced-stage disease (stages III and IV, nodal and distant metastatic disease) were identified by multiple logistic regression. This study was granted exemption status by The University of Texas MD Anderson Cancer Center institutional review board.

Results. We identified 64 068 young-onset (10.9%) and 524 801 later-onset (89.1%) CRCs. Age-adjusted incidence declined for later-onset CRCs after 2001 (APC, −2.5%; 95% CI, −3.0% to −2.0%) but has consistently increased since 2001 for young-onset disease (APC, 2.1%; 95% CI, 1.1% to 3.1%). The increase was greater for

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young-onset rectal (APC, 3.9%; 95% CI, 3.1% to 4.7%) than colon (APC, 2.7%; 95% CI, 2.0% to 3.3%) cancers. The median age for young-onset CRCs was 44 years, with most (75.2%) occurring between ages 40 and 49 years. Compared with later-onset disease, young-onset CRCs were more prevalent among patients with nonwhite race/ethnicity (29.5% vs 17.6%; $P<.001$), who were not insured or insured by Medicaid (16.5% vs 4.7%; $P<.001$) and who lived in the southern and western parts of the United States (56.2% vs 50.3%; $P<.001$). Young-onset CRC more commonly arose from colon distal to the splenic flexure or the rectum (69.0% vs 57.7%; $P<.001$). Mucinous and signet-ring histologic subtype (12.6% vs 10.8%; $P<.001$) and poor or no differentiation (20.4% vs 18%; $P<.001$) were also more frequently exhibited. Advanced-stage disease was diagnosed significantly more commonly in young patients (Table). Independent risk factors for advanced-stage disease included younger age (age 30-39 years: hazard ratio [HR], 1.21; 95% CI, 1.1 to 1.4; age 18-29 years: HR, 1.4; 95% CI, 1.2 to 1.6; vs age 40-49 years); African American race (HR, 1.2; 95% CI, 1.1 to 1.3; vs white race) and lack of insurance or Medicaid insurance (uninsured: HR, 1.2; 95% CI, 1.1 to 1.3; Medicaid: HR, 1.6; 95% CI, 1.5 to 1.8; vs insured).

Comment. This cohort study of young-onset CRC, the largest to date, highlights an alarming rise in incidence since 2001. Most worrisome is the high proportion of stage III/IV disease (**Figure**), consistent with a prior smaller population-based report.[6] In the absence of routine screening, contributing factors to these trends may include (1) a reluctance on the part of young adults to seek medical care[7]; (2) the large percentage of young adults without insurance or ready access to care (18.3%-29.2% for adults aged 18-44 years vs 1.3%-13.6% for adults older than 45 years[8]); and (3) an underappreciation of the increasing risk for young-onset CRC, leading clinicians to overlook or dismiss symptoms that are nonspecific but may be consistent with CRC (ie, rectal bleeding, abdominal pain or cramping, change in bowel pattern). Finally, the predilection of young-onset CRCs for the distal colon and rectum identify these as high-yield anatomic regions for endoscopic evaluation in symptomatic patients and as potentially cost-effective targets for screening programs in presymptomatic young adults.

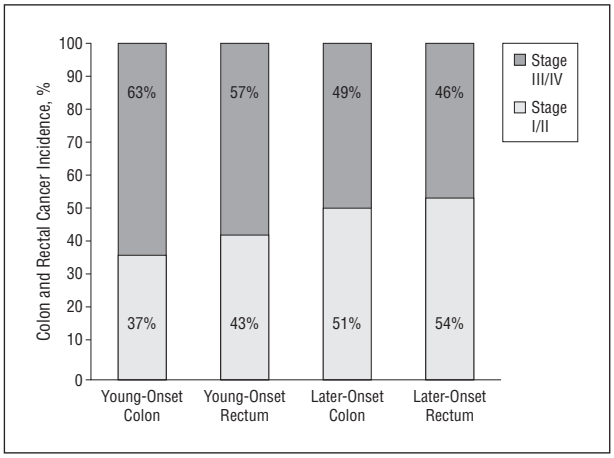

Figure. Distribution of cancer stage at diagnosis for young-onset vs later-onset colon and rectal cancers.

This study could not establish the mechanisms underlying observed sociodemographic disparities, nor did it explore the molecular basis of young-onset CRC (familial adenomatous polyposis was excluded). Notwithstanding, these data argue for heightened awareness of these concerning trends in young-onset CRC. Symptomatic young patients should undergo timely sigmoidoscopy at a minimum, if not a full colonoscopy. Identifying high-risk cohorts for targeted screening should be a priority.

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Published Online: December 12, 2011. doi:10.1001/archinternmed.2011.602. This article was corrected for an error in the Figure key on December 13, 2011.
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Financial Disclosure: Dr Feig served on the speakers bureau for and received honorarium from Genomic Health.
Funding/Support: This study was supported by the University of Texas MD Anderson Cancer Center Institutional Research Grant (Dr You) and The University of Texas MD Anderson Cancer Center's Institute for Cancer Care Excellence.
Previous Presentation: This study was presented in part at the Sixth Annual Academic Surgical Congress, Association for Academic Surgery; February 4, 2011; Orange County, California.
Additional Contributions: Miguel A. Rodriguez-Bigas, MD, and John M. Skibber, MD, assisted with critical revision of the manuscript, and Yan K. Ling, MPH, assisted with data analysis.

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Online First

Supplemental Oxygen Therapy in Medical Emergencies: More Harm Than Benefit?

In medical emergencies, such as acute coronary syndrome, cardiopulmonary resuscitation (CPR), stroke, and exacerbations of chronic obstructive pulmonary disease (COPD), supplemental oxygen is often routinely administered. Most physicians believe this intervention is potentially lifesaving, and many guidelines support the routine use of high-dose supplemental oxygen.

Over the decades, however, potential detrimental effects of supplemental oxygen appear to have been ignored. Many clinicians are unaware of the variety of preclinical studies that have been executed, showing that hyperoxia causes both coronary and systemic vasoconstriction, resulting in deterioration of several important (hemodynamic) parameters (**Table**). The prime candidate mechanism for these unintended effects is believed to be the formation of reactive oxygen species. In this Research Letter, we draw attention to the collective clinical evidence, which argues against the routine use of high-dose oxygen. Awaiting more thorough studies, we strongly recommend a policy of careful, titrated oxygen supplementation.

Methods. We conducted a search of the literature in MEDLINE and EMBASE to identify articles addressing the effect of oxygen therapy in acute coronary syndrome, cardiopulmonary resuscitation, stroke, and exacerbations of chronic obstructive pulmonary disease.

Results. Large (randomized) clinical studies addressing oxygen supplementation are scarce. In 1976, a double-blind randomized trial was performed in 200 patients with suspected acute myocardial infarction. In the supplemental oxygen group, 9 of 80 patients (11%) died, as opposed to 3 of 77 (3.9%) in patients breathing compressed air (relative risk [RR] of mortality, 2.9; 95% CI, 0.8-10.3). A recent Cochrane review combined this trial with a smaller similar one, which generated a composite RR of mortality of 3.03 (95% CI, 0.93-9.83).[1] In acute decompensated heart failure, no clinical studies are available, despite the rather abundant evidence from preclinical studies, suggesting that such patients may experience the adverse effects caused by coronary and systemic vasoconstriction (Table).

In accordance with existing guidelines, supplemental oxygen is often administered during CPR. In the postresuscitation phase, evidence exists that 30% oxygen is more brain protective than pure oxygen.[2] Recently, an observational study in 6326 patients showed that supplemental oxygen induced postresuscitation hyperoxia was independently associated with increased mortality (odds ratio [OR], 1.8; 95% CI, 1.5-2.2). A subsequent analysis of the same cohort indicated that each 25–mm Hg increase in PaO_2 was associated with a sta-

Table. Effects of Supplemental Oxygen in Different Clinical Conditions

Clinical Condition	Effect Parameter	Effect	Reference
Exercise testing	ECG alterations	Prolonged	*JAMA*. 1950;144:373-375
Post myocardial infarction	Heart rate	Decreased	*Lancet*. 1964;2(7364):825-832
	Stroke volume	Decreased	*Br Heart J*. 1965;27:401-407
	Cardiac output	Decreased	*Br Med J*. 1968;4(5627):360-364
	Systemic vascular resistance	Increased	
	Mean arterial pressure	Increased	
Acute myocardial infarction	Vascular resistance of LAD	Increased	*J Appl Physiol*. 2007;102(5):2040-2045
Cardiac catheterization	Coronary vascular resistance	Increased	*Am J Physiol*. 2005;288(3):H1057-H1062
	Coronary blood flow	Decreased	
Congestive heart failure	Stroke volume	Decreased	*J Am Coll Cardiol*. 1996;27(2):353-357
	Heart rate	Decreased	*Am J Physiol Heart Circ Physiol*. 2002;282(6):H2414-2421
	Cardiac output	Decreased	*Chest*. 2001;120(2):467-473
	Systemic vascular resistance	Increased	*Heart*. 2010;96(7):533-538
	LV end diastolic pressure	Increased	
	Isovolumetric relaxation time	Increased	
COPD	Hypercapnia	Increased	*Clin Med*. 2002;2(5):449-451
	Mortality	Increased	*BMJ*. 2010;341:c5462
Stroke	Stroke severity score	Increased	*Stroke*. 2003;34(2):571-574
	Mortality	Increased	*Stroke*. 1999;30(10):2033 – 2037 NCT00414726[a]
Cardiopulmonary resuscitation	Neuron-specific enolase	Elevated	*Resuscitation*. 2006:69(2);199-206
	Mortality	Increased	*JAMA*. 2010;303(21):2165-2171 *Circulation*. 2011;123(23):2717-2722 *Critical Care*. 2011;15(2):R90

Abbreviations: COPD, chronic obstructive pulmonary disease; ECG, electrocardiogram; LAD, left anterior descending coronary artery; LV, left ventricular.
[a]Trial was terminated (Clinical Trial of Normobaric Oxygen Therapy in Acute Ischemic Stroke, not published, clinicaltrials.gov Identifier: NCT00414726).

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