Age-appropriate cancer screening: A cohort study of adults with psoriasis prescribed biologics, adults in the general population, and adults with hypertension

John S. Barbieri, MD, MBA,[a] Shiyu Wang, MS,[a] Alexis R. Ogdie, MD, MSCE,[b,c] Daniel B. Shin, PhD,[a] and Junko Takeshita, MD, PhD, MSCE[a,c]
Philadelphia, Pennsylvania

Background: Psoriasis is associated with increased risk of developing and dying from cancer.

Objective: To evaluate whether psoriasis patients who are prescribed biologics receive the recommended screening for cervical, breast, and colon cancer.

Methods: We conducted a retrospective cohort study using the Optum deidentified Electronic Health Record data set. Incidence rates for cervical, breast, and colon cancer screening were compared between psoriasis patients who were prescribed biologics and 2 matched comparator cohorts: general patient population and patients being managed for hypertension. Multivariable Cox proportional hazards regression was performed to assess for differences in the rates of cancer screening.

Results: Compared with those in the general population without psoriasis, psoriasis patients who were prescribed biologics had higher screening rates for cervical cancer (adjusted hazard ratio [aHR] 1.09; 95% confidence interval [CI] 1.02-1.16) and colon cancer (aHR 1.10; 95% CI 1.02-1.18). Compared with those with hypertension, patients with psoriasis who were prescribed biologics had lower screening rates for breast cancer (aHR 0.88; 95% CI 0.83-0.94) and colon cancer (aHR 0.89; 95% CI 0.83-0.95).

Conclusions and Relevance: Patients with psoriasis who are prescribed biologic therapies may not be receiving adequate age-appropriate cancer screening, especially for breast and colon cancer. (J Am Acad Dermatol 2021;84:1602-9.)

From the Department of Dermatology,[a] Division of Rheumatology,[b] and Center for Clinical Epidemiology and Biostatistics, Department of Biostatistics, Epidemiology and Informatics,[c] University of Pennsylvania Perelman School of Medicine, Philadelphia.

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Correspondence to: Junko Takeshita, MD, PhD, MSCE, 3400 Civic Center Blvd, Perelman Center for Advanced Medicine, 7th Floor, S Tower, Office 728, Philadelphia, PA 19104. E-mail: junko.takeshita@pennmedicine.upenn.edu.

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INTRODUCTION

Psoriasis may be associated with an increased risk of developing and dying from cancer, which, at least theoretically, could be compounded by immunosuppressive biologic therapy.[1,2] In fact, all tumor necrosis factor inhibitors have black box warnings about potential malignancy risk, and ustekinumab lists possible malignancy risk as a warning and precaution in the prescribing information.[3-7] As a result, the joint American Academy of Dermatology—National Psoriasis Foundation guidelines for the management and treatment of psoriasis recommend that patients with psoriasis, particularly those with severe disease, many of whom are treated with biologics, receive age-appropriate cancer screening.[8] The US Preventive Services Task Force recommends screening for breast cancer with mammography every 2 years for women aged 50 to 74 years, with consideration for beginning screening as early as aged 40 years among those with above-average risk; screening for cervical cancer with cytology (Papanicolaou smear) every 3 years for women aged 21 to 65 years, or with a combination of cytology and human papillomavirus testing every 5 years for women aged 30 to 65 years; and screening for colon cancer with colonoscopy every 10 years, computed tomographic colonography or flexible sigmoidoscopy every 5 years, fecal occult blood or fecal immunochemical testing yearly, or a combination of flexible sigmoidoscopy every 10 years and fecal immunochemical testing yearly for all adults aged 50 to 75 years.[9-11]

Although routine age-appropriate malignancy screening is recommended, studies examining patients with other chronic inflammatory diseases such as rheumatoid arthritis have found that these patients may not receive optimal malignancy screening or other recommended preventive health services.[12,13] Among patients with psoriasis, German data suggest that those with moderate to severe disease have generally low influenza vaccination rates compared with the general population.[14] Additionally, a study in the United States found that patients with psoriasis were less likely to be vaccinated for influenza than those with rheumatoid arthritis.[15] Together, these findings raise the question of whether patients with psoriasis, particularly those with more severe disease, are receiving recommended age-appropriate cancer screenings. Therefore, we aimed to evaluate whether patients with psoriasis who are prescribed biologics, and presumably have more severe disease and greater malignancy risk, receive the recommended screening for cervical, breast, and colon cancer.

CAPSULE SUMMARY

- Patients with psoriasis who are prescribed biologic therapies have lower rates of screening for breast cancer and colon cancer compared with those with hypertension.
- Patients with psoriasis who are prescribed biologic therapies may not be receiving adequate age-appropriate cancer screening, especially for breast and colon cancer.

METHODS

Study design and data source

We performed a retrospective cohort study using the Optum (Eden Prairie, MN) deidentified Electronic Health Record data set between January 1, 2007, and June 30, 2017. It is the largest electronic health record source in the United States and includes deidentified patient-level data for 81 million individuals and their associated health care encounters within a diverse set of health care networks in 38 states.[16-18] Approximately 70% of individuals included in this data set are cared for by integrated delivery networks, meaning that most of a subject's health care encounters are likely to occur within this network and will be captured in the database.[17] The data captured in the database include diagnoses, procedures, prescriptions written, and patient demographic information. This study was performed with a sample of all patients with psoriasis in the database and a 10% random sample of the complete database available to the investigators to identify comparator patients without psoriasis. Because these data are deidentified, this study was deemed exempt by the institutional review board of the University of Pennsylvania.

Study population and time of observation

Our study included patients with psoriasis who met the following inclusion criteria: (1) at least 1 visit with an *International Classification of Diseases, Ninth Revision (ICD-9)* or *ICD-10* code for psoriasis[19]; (2) at least 1 prescription for a tumor necrosis factor inhibitor (adalimumab, certolizumab, etanercept, golimumab, or infliximab), ustekinumab, or an interleukin 17 inhibitor (brodalumab, ixekizumab, or

Abbreviations used:

CI: confidence interval
ICD-9: International Classification of Diseases, Ninth Revision

secukinumab) on or after the date of the first diagnosis of psoriasis, with the date of the first prescription defined as the index date; (3) at least 6 months of continuous enrollment without any prescriptions for biologics before the index date; (4) and at least 1 year of continuous enrollment after the index date. Patients with a diagnosis of inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis, or hidradenitis suppurativa during the 6 months before the index date were excluded.

Two comparator cohorts without psoriasis were created: patients from the general population and patients being managed for hypertension. Up to 4 comparator patients from each group were matched to each psoriasis patient according to age (within 6 months), sex, and index date (within 6 months). The first comparator cohort consisted of patients from the general population without psoriasis. Their index date was 6 months after becoming active in the database, and they were required to have at least 1 year of continuous enrollment after the index date. The second comparator cohort consisted of patients being managed for hypertension to account for the increased contact with the health system that can occur with the management of chronic disease. This hypertension cohort included patients with at least 2 visits with an *ICD-9* or *-10* code for hypertension, with the index date defined as the date of the first visit for hypertension. Patients in the hypertension cohort were also required to have at least 6 months of continuous enrollment before the index date and at least 1 year of continuous enrollment afterward. Patients with a diagnosis of HIV were excluded from all cohorts. Patients included in the study were followed until the first of any of the following censoring events: development of the study outcome, death, or end of the study period.

Outcomes and covariate definitions

The study outcomes were encounters for cervical, breast, and colon cancer screening as identified by their associated *ICD* and Current Procedural Terminology codes (Supplemental Table I available via Mendeley at https://doi.org/10.17632/8r57ypwdj6.1). The cervical and breast cancer screening outcomes were evaluated among women only who were aged 21 to 65 years and 40 to 74 years, respectively. The colon cancer screening outcome was evaluated among all patients aged 50 to 75 years. Covariates assessed as potential confounders included age, sex (colon cancer screening only), race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, Hispanic, and other/unknown), average household income, education level, and the Charlson Comorbidity Index score.[20] History of psoriatic arthritis and the Charlson Comorbidity Index score were determined during the 6-month preindex period. All other covariates were identified on the index date. Household income was provided as an average based on the first 3 digits of the patient's zip code. Similarly, education level was provided as an overall percentage of individuals who had received a college education in the geographic area corresponding to the first 3 digits of their zip code. Insurance type was defined as the most recent recorded insurance status before the index date.

Statistical analysis

Incidence rates for cervical, breast, and colon cancer screening among each cohort were reported descriptively. Multivariable Cox proportional hazards regression was performed to assess for differences in the rate of each cancer screening between the psoriasis and comparison cohorts, controlling for age, sex (colon cancer screening only), race/ethnicity, average household income, percentage college education, insurance type, and Charlson Comorbidity Index score. For the regression analyses, average household income was log transformed to reduce skew. Sensitivity analyses were performed to evaluate the effect of excluding individuals (and their associated controls) with either a history of psoriatic arthritis or a history of any malignancy. Statistical analyses were performed with Stata (version 15, StataCorp, College Station, TX).

RESULTS

Study cohort characteristics

There were 8663 subjects who met the inclusion criteria for the psoriasis biologic cohort (Table I). These psoriasis patients were matched with 31,269 patients with hypertension and 31,857 patients from the general population. The mean age was 49.2 years (SD 12.8 years), 50.8 years (SD 11.9 years), and 48.1 years (SD 13.1 years) for the psoriasis biologic, hypertension, and general population cohorts, respectively. The mean percentage college education was 25.1% (SD 7.7%), 24.0% (SD 7.3%), and 24.7% (SD 7.6%) for the psoriasis biologic, hypertension, and general population

Table I. Subject demographics

Characteristic	Psoriasis biologic cohort	Hypertension cohort	General population cohort
Cohort size	8,663	31,269	31,857
Mean age (SD), y	49.2 (12.8)	50.8 (11.9)	48.1 (13.1)
Women, no. (%)	3914 (45.2)	13,985 (44.7)	14,717 (46.2)
Race/ethnicity, no. (%)			
Non-Hispanic White	7203 (81.1)	22,105 (70.7)	21,807 (68.5)
Hispanic	446 (5.0)	1501 (4.8)	1637 (5.1)
Non-Hispanic Black	236 (2.7)	4105 (13.1)	2776 (8.7)
Non-Hispanic Asian	160 (1.8)	418 (1.3)	557 (1.8)
Unknown	837 (9.4)	3140 (10.0)	5080 (16.0)
Mean household income (SD), $	44,610 (11,242)	42,659 (9863)	43,396 (10,203)
Percentage college education, mean (SD)	25.1 (7.7)	24.0 (7.3)	24.7 (7.6)
History psoriatic arthritis, no. (%)	4396 (50.7)	0	0
Charlson Comorbidity Index score, mean (SD)	0.43 (0.98)	0.57 (1.22)	0.38 (1.07)
Insurance type			
Commercial	5550 (64.1)	17,390 (55.6)	14,805 (46.5)
Medicaid	706 (8.1)	2667 (8.5)	1583 (5.0)
Medicare	392 (4.5)	2808 (9.0)	1575 (4.9)
Other	196 (2.3)	601 (1.9)	694 (2.2)
Uninsured	183 (2.1)	1593 (5.1)	1586 (5.0)
Unknown	1636 (18.9)	6210 (19.9)	11,614 (36.5)
Mean follow-up after index date (SD), d	1267 (689)	1254 (673)	1243 (687)

SD, Standard deviation.

cohorts, respectively. The psoriasis biologic cohort had more non-Hispanic White patients (81.1%) than the hypertension cohort (70.7%) and general population cohort (68.5%). The psoriasis biologic cohort had fewer non-Hispanic Black patients (2.7%) than the hypertension cohort (13.1%) and general population cohort (8.7%) (Table I).

Cervical cancer screening

Among individuals meeting the US Preventive Services Task Force age criteria for cervical cancer screening, the crude rate of screening per person-year of follow-up was 0.23 (95% confidence interval [CI] 0.22-0.25), 0.22 (95% CI 0.21-0.23), and 0.21 (95% CI 0.20-0.22) for the psoriasis, hypertension, and general population cohorts, respectively (Table II). Compared with patients with hypertension, those with psoriasis who were prescribed biologics had similar rates of screening for cervical cancer (adjusted hazard ratio 0.97; 95% CI 0.91-1.04; $P = .41$) (Table III). Compared with patients in the general population without psoriasis, those with psoriasis who were prescribed biologics had a 9% higher screening rate for cervical cancer (adjusted hazard ratio 1.09; 95% CI 1.02-1.16; $P = .01$) (Table IV).

Breast cancer screening

Among individuals meeting the US Preventive Services Task Force age criteria for breast cancer screening, the crude rate of screening per person-year of follow-up was 0.55 (95% CI 0.52-0.61), 0.60 (95% CI 0.58-0.61), and 0.52 (95% CI 0.51-0.54) for the psoriasis, hypertension, and general population cohorts, respectively (Table II). Compared with individuals with hypertension, those with psoriasis who were prescribed biologics had a 12% lower screening rate for breast cancer (adjusted hazard ratio 0.88; 95% CI 0.83-0.94; $P < .001$) (Table III). Compared with individuals in the general population without psoriasis, those with psoriasis who were prescribed biologics had a similar rate of breast cancer screening (adjusted hazard ratio 1.02; 95% CI 0.96-1.08; $P = .58$) (Table IV).

Colon cancer screening

Among individuals meeting the US Preventive Services Task Force age criteria for colon cancer screening, the crude rate of screening per person-year of follow-up was 0.16 (95% CI 0.14-0.17), 0.18 (95% CI 0.17-0.18), and 0.14 (95% CI 0.13-0.14) for the psoriasis, hypertension, and general population cohorts, respectively (Table II). Compared with individuals with hypertension, those with psoriasis

Table II. Incidence rates per patient-year of follow-up for cervical, breast, and colon cancer screening among the psoriasis biologic, hypertension, and general population cohorts

	Rate of screening per person-year of follow-up									
	Cervical cancer			Breast cancer			Colon cancer			
	Psoriasis biologic	HTN	GP	Psoriasis biologic	HTN	GP	Psoriasis biologic	HTN	GP
Cohort size*	N = 3,448	N = 12,264	N = 12,996	N = 2,739	N = 10,638	N = 9,952	N = 4,060	N = 16,059	N = 14,609
Overall*	0.23 (0.22-0.25)	0.22 (0.21-0.23)	0.21 (0.20-0.22)	0.55 (0.52-0.58)	0.60 (0.58-0.61)	0.52 (0.51-0.54)	0.16 (0.14-0.17)	0.18 (0.17-0.18)	0.14 (0.13-0.14)
Age, y									
20-29	0.30 (0.26-0.35)	0.25 (0.22-0.28)	0.24 (0.22-0.26)	—	—	—	—	—	—
30-39	0.28 (0.25-0.31)	0.25 (0.24-0.27)	0.23 (0.22-0.25)	0.14 (0.12-0.17)	0.16 (0.15-0.18)	0.13 (0.11-0.14)	—	—	—
40-49	0.26 (0.23-0.28)	0.24 (0.23-0.25)	0.23 (0.22-0.25)	0.53 (0.49-0.57)	0.53 (0.51-0.56)	0.48 (0.45-0.50)	0.07 (0.06-0.08)	0.09 (0.08-0.09)	0.07 (0.06-0.08)
50-59	0.19 (0.17-0.22)	0.20 (0.19-0.22)	0.19 (0.18-0.20)	0.59 (0.55-0.63)	0.61 (0.59-0.64)	0.54 (0.52-0.57)	0.16 (0.15-0.18)	0.19 (0.18-0.19)	0.14 (0.13-0.15)
60-69	0.15 (0.12-0.18)	0.15 (0.14-0.16)	0.13 (0.11-0.14)	0.54 (0.48-0.60)	0.66 (0.62-0.69)	0.56 (0.52-0.59)	0.16 (0.14-0.18)	0.17 (0.16-0.19)	0.14 (0.13-0.15)

Parenthetical ranges represent 95% CI.
—, Not applicable; *GP*, general population cohort; *HTN*, hypertension cohort.
*Among individuals meeting US Preventive Services Task Force age criteria for routine surveillance. Incidence rates are per patient-year of follow-up.

who were prescribed biologics had an 11% lower screening rate for colon cancer (adjusted hazard ratio 0.89; 95% CI 0.83-0.95; P = .001) (Table III). Compared with individuals in the general population without psoriasis, those with psoriasis who were prescribed biologics had a 10% higher screening rate for colon cancer (adjusted hazard ratio 1.10; 95% CI 1.02-1.18; P = .010) (Table IV).

Sensitivity analyses

Our primary results were robust to sensitivity analyses that excluded patients with a history of psoriatic arthritis and excluded those with a history of malignancy (Supplemental Table II).

DISCUSSION

Our study demonstrated that patients with psoriasis who were prescribed biologics had approximately 10% lower screening rates for breast and colon cancer than those with hypertension and had higher screening rates for cervical and colon cancer than the general population. To our knowledge, this is the first study to evaluate cancer screening rates among patients with psoriasis. Our findings highlight that despite being subject to at least a theoretically increased risk of malignancy, patients with psoriasis who are prescribed biologics are screened less frequently than those with other chronic diseases, such as hypertension, who are regularly interacting with the health care system.

The reasons for the differences in breast and colon cancer screening rates between patients with psoriasis who are prescribed biologics and those with hypertension are unclear. Higher education and income levels have been associated with increased use of cancer screening tests and thus may be important confounding factors. However, the differences in screening rates persisted after controlling for these factors, and our psoriasis biologics cohort was slightly more educated and had slightly higher income yet had lower breast and colon cancer screening rates than the hypertension comparator group.[21] Another possibility is that patients with psoriasis are less likely to be screened owing to cost.[22,23] Because biologic therapies can be associated with significant out-of-pocket expenses, patients who are prescribed them may be more price sensitive to the cost of screening compared with those with hypertension.

It is also possible that patients with psoriasis who are prescribed biologics are not receiving cancer screening recommendations as frequently as their hypertensive counterparts. This could be due to several reasons, including different health care use patterns whereby patients with psoriasis may be less

Table III. Cox proportional hazard models for cervical, breast, and colon cancer screening comparing those who were prescribed biologics for psoriasis versus those with hypertension

	Cervical cancer (women 21-65 years), HR (95% CI)	Breast cancer (women 40-74 years), HR (95% CI)	Colon cancer (50-75 years), HR (95% CI)
Cohort			
Hypertension	Reference	Reference	Reference
Psoriasis biologic	0.97 (0.91-1.04)	0.88 (0.83-0.94)	0.89 (0.83-0.95)
Age	0.99 (0.98-0.99)	1.00 (1.00-1.01)	0.99 (0.98-0.99)
Sex			
Men	—	—	Reference
Women	—	—	1.04 (0.99-1.10)
Mean household income, ln($)	2.23 (1.89-2.63)	1.95 (1.68-2.25)	1.45 (1.23-1.70)
Percentage college education	0.99 (0.98-0.99)	0.98 (0.98-0.99)	0.99 (0.99-1.00)
Charlson Comorbidity Index score (updated)	0.93 (0.90-0.95)	0.99 (0.97-1.01)	0.96 (0.94-0.98)
Race/ethnicity			
Non-Hispanic White	Reference	Reference	Reference
Hispanic	0.97 (0.85-1.09)	0.97 (0.87-1.08)	0.88 (0.76-1.02)
Non-Hispanic Asian	1.36 (1.12-1.66)	1.10 (0.90-1.33)	1.11 (0.88-1.40)
Non-Hispanic Black	0.99 (0.91-1.07)	0.95 (0.88-1.02)	1.02 (0.93-1.13)
Non-Hispanic unknown	0.89 (0.80-0.98)	0.78 (0.72-0.86)	0.80 (0.72-0.89)
Insurance			
Commercial	Reference	Reference	Reference
Medicaid	0.63 (0.56-0.70)	0.69 (0.62-0.76)	0.75 (0.66-0.85)
Medicare	0.61 (0.52-0.70)	0.75 (0.68-0.82)	0.84 (0.76-0.93)
Other	0.93 (0.78-1.12)	1.20 (1.02-1.41)	0.95 (0.78-1.14)
Uninsured	0.65 (0.56-0.75)	0.81 (0.72-0.92)	0.91 (0.78-1.07)
Unknown	1.03 (0.97-1.10)	0.92 (0.86-0.97)	0.98 (0.92-1.05)

CI, Confidence interval; *HR*, hazard ratio.

likely than those with hypertension to consult primary care providers, who are often relied on to recommend and facilitate preventive health measures. This may be compounded by dermatologists not routinely recommending age-appropriate cancer screening to their patients with psoriasis. Additional research is needed to better understand what factors may explain the differences in screening rates between patients with psoriasis who are prescribed biologics and those with other chronic medical conditions.

There is strong evidence that screening for cervical, breast, and colon cancer reduces mortality of those who are screened.[9-11,24] As a result, the potential underuse of age-appropriate cancer screening among patients with psoriasis who are prescribed biologic therapies may result in increased morbidity and mortality. Some psoriasis patients may consult their dermatologist more frequently than their primary care provider, or they may not even have a primary care provider. As a result, it is important for dermatologists to inquire about age-appropriate cancer screening in this population and make appropriate referrals for patients who are not up to date with screening recommendations. In addition, there may be opportunities to leverage existing electronic health record infrastructure to identify patients who may not be up to date with screening recommendations and remind these patients and their clinicians about the need for screening.[25]

The results of this study should be interpreted in light of its limitations. We were not able to evaluate whether screening differences were directly associated with differences in cancer-related outcomes. In addition, there were baseline differences in the racial/ethnic distributions of patients in the psoriasis and comparator cohorts whereby there were fewer Black patients in the psoriasis biologic cohort than in each comparator cohort. Prior studies have suggested a racial disparity in cancer screening whereby Black individuals are less likely to receive cancer screening;[26,27] therefore, it is possible that our findings in comparison to those of the hypertensive cohort are an underestimation despite adjusting for race/ethnicity in our multivariable regression models. Because we matched on age and sex, we were unable to assess for an association between these covariates and our cancer screening outcomes. Household income and education level were assessed at the level of zip code rather than on an

Table IV. Cox proportional hazard models for cervical, breast, and colon cancer screening comparing those who were prescribed biologics for psoriasis versus those in the general population

	Cervical cancer (women 21-65 years), HR (95% CI)	Breast cancer (women 40-74 years), HR (95% CI)	Colon cancer (50-75 years), HR (95% CI)
Group			
General population	Reference	Reference	Reference
Psoriasis biologic	1.09 (1.02-1.16)	1.02 (0.96-1.08)	1.10 (1.02-1.18)
Age	0.98 (0.98-0.99)	1 (1-1.01)	0.99 (0.98-0.99)
Sex			
Men	—	—	Reference
Women	—	—	0.92 (0.87-0.98)
Mean household income, ln($)	2.29 (1.95-2.69)	2.04 (1.75-2.38)	1.31 (1.09-1.57)
Percentage college education	0.99 (0.99-1.00)	0.99 (0.98-0.99)	1.00 (0.99-1.00)
Charlson Comorbidity Index score (updated)	1.01 (0.98-1.04)	1.04 (1.02-1.07)	1.03 (1.01-1.06)
Race/ethnicity			
Non-Hispanic White	Reference	Reference	Reference
Hispanic	0.88 (0.78-1.00)	0.96 (0.86-1.09)	0.90 (0.76-1.07)
Non-Hispanic Asian	1.42 (1.19-1.68)	1.2 (0.99-1.44)	1.26 (1.01-1.59)
Non-Hispanic Black	0.84 (0.76-0.94)	0.89 (0.8-0.98)	0.93 (0.81-1.06)
Non-Hispanic unknown	0.67 (0.61-0.73)	0.63 (0.57-0.68)	0.56 (0.50-0.63)
Insurance			
Commercial	Reference	Reference	Reference
Medicaid	0.58 (0.50-0.67)	0.63 (0.56-0.72)	0.75 (0.64-0.87)
Medicare	0.57 (0.48-0.69)	0.78 (0.70-0.88)	0.92 (0.81-1.05)
Other	0.87 (0.73-1.03)	1.01 (0.85-1.19)	0.89 (0.72-1.09)
Uninsured	0.65 (0.55-0.76)	0.75 (0.65-0.87)	0.84 (0.70-1.02)
Unknown	0.77 (0.72-0.82)	0.64 (0.60-0.68)	0.72 (0.67-0.78)

CI, Confidence interval; *HR*, hazard ratio.

individual level. Finally, because this study is based on administrative data, we were unable to determine the appropriateness of screening tests that were performed.

CONCLUSIONS

Our study findings suggest that patients with psoriasis who are prescribed biologic therapies may not be receiving adequate age-appropriate cancer screening, especially for breast and colon cancer. Additional research is needed to understand why these differences exist in order to develop interventions to optimize cancer screening among this patient group that has been suggested to be at increased risk of developing and dying from cancer. In addition, increasing education about the importance of age-appropriate cancer screening in this population may represent an opportunity to improve outcomes with respect to cancer-related morbidity and mortality.

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