Beyond the clinic, this analysis touches on the role of supportive and symptomatic care in persons who have cancer and the use of cost-effectiveness criteria in determining coverage of supportive care agents. Given the median age of diagnosis noted by Lathia et al. (1), about 50% of persons with lymphoma will qualify for Medicare at diagnosis; thus how insurers make use of cost-effectiveness information has important implications for national health policy (12). Furthermore, incremental costs per QALY (or other measure of time) are challenging to estimate and use in clinical practice and policy making, particularly estimates of survival benefits and longer term benefits as well as inclusion of nonclinical outcomes such as hospital avoidance. Additionally, situations like the one modeled here, in which the time horizon is very short, complicate the use of outcomes like the QALY. Despite this understanding, the optimal choice of an outcome to model in persons with cancer remains incompletely understood (13). Last, the importance of patient-reported outcomes is rising. In the current case, the potential to avoid hospitalizations is likely to be important from the patient’s perspective. Although this trend does not change the conclusions Lathia et al. make regarding prophylactic use of filgrastim and pegfilgrastim, patient satisfaction, ability to function, and time preferences are likely to play an increasing role in future coverage and clinical use decisions.

References

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Cancer Incidence Among Specific Asian and Pacific Islander Populations in the United States

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To identify disease etiology and its consequences, epidemiologists compare disease rates in different populations, geographic areas, and time periods. These statistical comparisons become difficult when diseases are relatively rare (eg, most cancers), and this problem is often resolved by broadening the definition of the groups (eg, all Asians or Pacific Islanders), geographic areas (eg, many
Asian or Pacific Island countries), or time of observation (eg, 1990–2010). Populations may also be grouped when specific groups are difficult to identify (eg, Chinese vs Vietnamese of Chinese descent) or when individuals are classified from nonpatient sources such as medical records, resulting in very general categories such as “Asian” or “Unknown” race or ethnicity. Yet, disease rates may be different among consolidated groups of people, geographic areas, or time periods. The companion articles in this issue of the Journal by Gomez et al. and Liu et al. (1,2) address many of these difficulties in calculating cancer incidence rates in specific Asian and Pacific Islander populations in the United States and, in overcoming many of these, provide new insights into the roles of immigrant populations in cancer etiology and help elucidate environmental aspects potentially involved in the induction of cancer. These studies are the first to publish cancer incidence rates with improved classification methods. They mainly discuss implications of the data for cancer control, but to more completely understand the patterns reported, it is useful to examine immigration patterns among these populations.

Almost 50 years ago, studies of cancer mortality among Japanese immigrants to Hawaii and the US mainland reported remarkable reductions in stomach cancer deaths with concomitant increases in breast and colorectal cancer mortality (3,4). Since then, numerous studies (5) of immigrants to the United States have reported the common phenomenon of decreasing incidence rates of cancers of infectious origin, such as liver (linked to hepatitis B virus), stomach (associated with Helicobacter pylori infection), and cervix (caused by human papilloma virus), common in the countries of origin, whereas incidence rates of breast, colon, prostate, and lung cancer have increased despite remaining relatively low in the host nation. Those patterns are confirmed in the articles by Gomez et al. and Liu et al. (1,2). Factors related to changing incidence rates of cancers not related to infections are not well understood but include age at immigration, place of immigration (such as rural areas), time in the United States, and socioeconomic status of the immigrants (6).

People immigrate for many reasons (eg, famine, war, education, employment, family unification, and health), and immigrants usually are not representative of the population of their native country in terms of age, sex, education, occupation, and urban or rural residence. Ability to immigrate is not the same for all populations and is influenced by multiple factors. One factor is previous relationships with the United States. For example, Guamanians are US citizens, American Samoans are US nationals, and Western Samoans are neither. Immigration is easier for citizens (7,8). A second factor is changing immigration policy. For example, in 1882 the Chinese Exclusion Act halted immigration of the Chinese until the 1943 Magnuson Act again permitted immigration, and in 1965 separate quotas were maintained for mainland China, Taiwan, and Hong Kong (9). Japanese citizens began immigrating to Hawaii and the US west coast after the 1868 Meiji Restoration; in 1907 an agreement between Japan and the United States ended immigration of unskilled laborers, and the Immigration Act of 1924 banned immigration of almost all Japanese (10). A third factor is wars. Examples include immigration of mostly laborers from Korea in the 1950s after the Korean War and of Vietnamese, Laotians, and Cambodians in the 1970s after the Vietnamese war (9). A fourth factor is US economic needs. For example, immigration of highly educated people from India to work in high technology industries has increased in recent years (9).

The cancer incidence rates reported by Gomez et al. may be explained by these immigration policies. The recent immigrants to the United States during the last 30 years, from Southeast Asia, display the continued and increasing high incidence rates of liver cancer, whereas the more established immigrant groups, the Japanese and Chinese, have higher incidence rates of prostate and lung cancer than found in Japan or China.

As seen in the Gomez paper, liver cancer incidence rates are increasing in recent immigrants, including Filipinos, Laotians, Vietnamese, and Kampuchean (1). The continuing role of infections such as perinatal transmission of hepatitis B virus is still of concern in contributing to the increasing incidence rates of liver cancer and because two-thirds of Asian Americans are born abroad. These trends take on urgency because, as noted by Gomez et al., Asian Americans constitute a rapidly growing segment of the US population, currently accounting for 5.6% of the population and projected to increase to 9.2% by 2050 (40.6 million) (11). Liver cancer is associated with hepatitis B infection, and in 2008, Asian American/Pacific islanders aged 19 to 24 years had an acute hepatitis B incidence of 3.1 per 100,000 population, which was 1.6 times greater than the incidence in non-Hispanic whites of the same age (12).

Early published studies of gastric and colorectal cancer mortality in Japanese immigrants to Hawaii and the mainland United States were based upon death certificate review in limited geographic areas (13). The studies by Gomez et al. and Liu et al. have used the resources of the Surveillance Epidemiology and End Results (SEER) program of the National Cancer Institute, which allows calculation of population-based incidence rates rather than relying upon mortality rates. However, the studies have some limitations. Gomez et al. studied a number of ethnic groups that are essentially based on the California experience, which may or may not reflect Asian immigrant experiences to other areas of the United States, such as New York, Chicago, and Houston. The specific groups evaluated by the authors are quite heterogeneous, both genetically and culturally. For example, among the Indian/Pakistani population, there is a great degree of genetic and cultural heterogeneity, which includes admixture of non-Asian blood in that the Indo/Aryan population of India (in contrast with the Dravidian population) is essentially derived from a white population. This might explain the relatively high incidence of ovarian cancer in the Indian/Pakistani populations. Even within the Indian/Pakistani populations, there is great heterogeneity in the time since immigration and duration of US residence variables, with the Sikh population in California originating from the rural Punjab area arriving in California nearly 100 years ago (primarily as farmers and merchants) whereas more recent immigrants from India are more highly educated professionals originating from urban areas.

In summary, the articles by Gomez et al. and Liu et al. have carefully classified subgroups among Asian and Pacific Islander populations in the United States and present cancer incidence rates from 1990 to 2008 for these groups. This information is important for control efforts for somewhat preventable cancers such as cervical and liver cancer and for cancers that can be
detected early through screening such as breast and colon cancers. In these papers by Gomez and Liu, the authors’ discussions of cancer etiology are limited and can be more completely understood as the immigration patterns of these populations are investigated.

References

Notes
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BRAF Mutation and Microsatellite Instability Status in Colonic and Rectal Carcinoma: Context Really Does Matter

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The molecular characteristics of colorectal cancer (CRC) have been studied extensively since the 1980s, but translation of the remarkable increase in genomic knowledge into clinically used biomarkers has been distressingly slow. The Cancer Genome Atlas for CRC was published in mid-2012 (1), and molecular and pathologic findings including genetic and epigenetic abnormalities have now been incorporated into classification systems that have been reported to have implications for the clinical management of patients (2–4). Numerous individual molecular biomarkers with potential applications have been published, but few have achieved levels and breadth of evidence to become standard of care. Difficulty in convincing payers of the value of biomarkers and fiscal constraints have impeded adequate reimbursement for testing and disinvested their clinical use.

In this issue of the Journal, Lochhead and colleagues (5) provide important additional evidence supporting the routine clinical use in CRC patients of two extensively investigated molecular alterations: microsatellite instability and BRAF mutation. Both of these characteristics of CRC are in use as biomarkers (6), but they have been uncommonly addressed together in the four microsatellite instability (MSI)/BRAF subgroups for clinical usage in prognostication.

High levels of MSI (MSI-H) occur in about 15% of CRC, and the presence of this feature is a hallmark of Lynch syndrome (hereditary nonpolyposis colorectal cancer syndrome). Although most MSI-H CRC are sporadic because of acquired hypermethylation of the MLH1 mismatch repair gene promoter region, germline mutation in one of several mismatch repair genes, most frequently MLH1 or MSH2, results in MSI-H tumors in Lynch syndrome patients. At least three professional organizations (7–9) have issued recommendations for routine testing for MSI status in CRC to identify tumors in patients who should be evaluated further for Lynch syndrome because of the implications for family members as well as the affected patient with an MSI-H tumor. In addition, abundant evidence supports MSI-H as a favorable biomarker for improved stage-specific survival, and testing for MSI status has therefore demonstrated value as a prognostic marker, also contributing to its frequent routine evaluation in CRC.