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Residents and Fellows Edition

Featured Employer Profile



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October 9, 2025

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As you near the completion of your training, I'm sure that finding the right employment opportunity for you is a top priority. The *New England Journal of Medicine* (NEJM) is the leading source of information about job openings, especially practice opportunities, in the country. To assist you in this important search, we've enclosed a complimentary copy of the 2025 *Career Guide: Residents and Fellows* booklet containing current physician job openings across the country and a couple of recent selections from our Career Resources section of NEJMCareerCenter.org.

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On behalf of the entire *New England Journal of Medicine* staff, please accept my wishes for a rewarding career.

Sincerely,

Eric J. Rubin, MD, PhD



Preparing Physician CVs and Resumes for Consumption in the Digital Age

Customization and confidentiality are key considerations in the current recruiting marketplace

By Bonnie Darves

A physician's curriculum vitae (CV) has long functioned as a passport of sorts into the realm of potential practice opportunities, which is why physicians must make sure that the all-important document does well what it's intended to do: provide a comprehensive but succinct and completely accurate overview of your medical training, work, and accomplishments, in a format that's easy to read and digest. Today, however, when everything moves at, well, cyberspeed, physicians should be prepared to respond in near real time when a desirable opportunity comes up — by not only submitting a polished document but by also ensuring that the CV is tailored to the position, according to Peter Angood, MD, chief executive officer of the American Association for Physician Leadership.

“It's important for physicians to customize their CV each time they submit it, to ensure they're including the appropriate keywords,” Dr. Angood said, to match qualifications the organization is seeking in a candidate. “Remember that you're trying to get through the initial screening, so the CV keywords should ideally match those in the job position.”

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That screening, these days, often includes computer technology that ingests, “scrapes,” and dissects the document via machine learning, artificial intelligence, and other mechanisms to identify specific experience or specialization. Because this process typically occurs before the document is routed for human review, the CV should include keywords included in the job description, Dr. Angood said. The idea is to make sure that the physician’s qualifications “pop out” readily during both electronic and human screening. “Even in that human screening, keep in mind that the HR professional or a recruiter might only spend 30 seconds to a minute initially reviewing the CV — that’s why it should be customized,” he added.

Getting the CV through the first electronic screening hurdle is, to some extent, a numbers game, according to John Lastinger, manager of candidate experience for the national recruiting firm Merritt Hawkins. Because computer programs that match candidates with practice opportunities are primarily keyword-based, Mr. Lastinger said, the facility seeking a physician prioritizes the skill set and experience it desires and then the system scans inbound CVs for matches to those keywords. “The more matches within the text of the CV, the higher the match rate and score, and the higher the probability the physician will be interviewed,” he said.

That’s where the specificity comes in. “Physicians should highlight all key skills and experience that fit the opportunity. For example, radiologists who are certified to read mammography should include that on their CV, as should a cardiologist who performs peripheral interventions,” Mr. Lastinger said. At the same time, he added, physicians should choose keywords judiciously and place them strategically, to avoid disseminating a document that’s obviously (and intentionally) overfilled with keywords. “We advise physicians to keep focused and be purposeful about their keyword usage,” he said. Physicians who are very particular about where they want to practice — whether that’s a specific metro area or state, or a particular region — should also ensure they communicate that information in their CV or in an accompanying cover note.

Brenda Reed, a senior recruitment and retention consultant at Atrius Health in Boston, said that even though computer CV screening is ubiquitous these days, physicians shouldn’t be unduly concerned that their CV will be overlooked if it doesn’t pass the computer screen. “Do organizations get so many CVs that they sort them only by bot and not by people? I’d be truly surprised if there’s an institution that only uses bots,” Ms. Reed said. “There’s a recognition in the industry, I think, that CV parsing isn’t that advanced yet, and I’m not aware of any applicant tracking systems that

do it very well.” Applicant tracking systems are software programs that organizations use to help them facilitate recruitment and hiring, by helping HR personnel and recruiters organize and navigate potentially large numbers of applicants.

Assemble a CV “package,” including a resume, in advance

Creating a polished, effective CV is the most important task for physicians seeking a practice opportunity, but that’s only the first step. All sources interviewed for this article agreed that physicians should have a complete, customizable package prepared before they start actively identifying and applying for open positions. That package, ideally, includes a CV, resume, and draft cover letter or note that can be readily adjusted to fit the opportunity, according to Dr. Angood. “I think it’s critically important to create a set of documents and then tailor them,” he said. “There’s an ongoing need, in my experience, for physicians to appreciate the intent and purpose of these materials,” he said.

The physician resume is a short version of the CV that quickly highlights skills and qualifications for a particular position, and, more importantly, provides an opportunity to briefly explain why the candidate is a good fit for the prospective position. For example, if a physician is seeking an opportunity that includes a mix of clinical and administration or leadership roles, a resume might focus on the physician’s direct experience in the latter two areas. A well-structured resume that includes any business experience or credentials is a must for physicians who want to transition from clinical practice to nonclinical roles, Dr. Angood noted, and the document should also include both specific achievements — even specifics such as increasing patient volumes over time through efficiency — and a forward-looking focus or statement.

“Organizations today are looking for physicians who can demonstrate not just their experience but also how their work made an impact and how their accomplishments have prepared them to contribute to the organization they join,” Dr. Angood said, given the changing priorities of and increasing demands on hospitals and health systems today. For example, physicians who have either experience or interest in such areas as patient-centered care models, shared decision-making, or value-based care should include those details in a resume. “Hiring organizations are very interested

in knowing the opportunities and results physicians accomplished in their position,” said Dr. Angood.

Young or early-career physicians likely won’t need a resume, Ms. Reed said, unless they have obtained specific skills or experience in business, technology, or organization-wide initiatives. “Sometimes a physician applying for a patient-care opportunity might be a good candidate for an innovation position that includes some nonclinical work, so that extra experience is worth noting,” she said, in either the CV or a resume.

Be selective — and careful — when using job boards to upload your CV

While physicians can likely expect a personal review of their CV when they send it directly to a hiring organization, that’s not necessarily the case when it comes to job boards. Scott Edwards, chief executive officer of Metropolis, a marketplace for health care jobs, advises physicians to be very selective when using job boards and to exercise due diligence before creating an account and uploading their information and documents into a database.

“It’s important to check out the job board’s reputation and to ensure that you have some control over how your documents are handled. In some cases, you might upload your documents thinking that you’re applying for a particular position, when in fact you’ve simply placed your CV and personal information into a repository that all can see and that’s searchable,” said Mr. Edwards. When that happens, physicians may quickly be overwhelmed with inquiries regarding positions they’re not interested in or opportunities in unsuitable geographic areas — or possibly run the risk that their current colleagues might come across their information.

“Physicians should understand that many job boards aren’t private,” said Mr. Edwards, whose company uses a private and confidential “match” model that only connects applicants with prospective employers that have subscribed to the service and agreed to be connected if a match is found. He recommends that physicians avoid job boards that don’t allow for confidentiality or aren’t nimble enough to enable narrowing the search parameters — in terms of practice type, subspecialty, and geographic location — to only those desired.

“Physicians really should understand, before submitting their CV to a job board or repository, exactly how their materials are ingested, dissected, and disseminated once they upload it to a database,” said Ms. Reed. In

short, in the persisting highly competitive, high-demand market for physician services, CVs are such hot commodities that there are technologies and software programs waiting in the wings to “snatch” the document from the internet and route it to unknown recipients.

Tips for making your CV stand out — in the right way

Be careful about how you label your CV document. Keep the recipient in mind when you create a filename, so that recruiters or others who might be reviewing candidates’ CVs can readily identify you, advises Brenda Reed, a senior recruitment and retention consultant at Massachusetts-based Atrius Health. The ideal filename would be ordered like this: Last name, first name, discipline, and specialty. “That way, reviewers can quickly figure out whose CV it is. I’ve received CVs with document names like ‘JoesCV.’ That makes it hard for recipients to figure out whose document it is,” Ms. Reed said. The same filename structure should also be used for the cover letter, she added.

Don’t “over-stuff” the CV. Sometimes, physicians think that because they’re trying to cover a lot of ground in a few pages, it makes sense to fill every available inch. That’s not helpful to the readers who have to make their way through a densely packed document, according to John Lastinger, manager of candidate experience for Merritt Hawkins. “White space is your friend. Make sure to leave plenty of white space,” he said, which makes it easier on readers’ eyes when they’re navigating the document. He also stresses the importance of including a name header and page number on every page of the CV, so that the document is readily identifiable. “Formatting is very important when it comes to having a document scanned, which it likely will be,” he said.

Create and submit your CV in a .pdf format rather than a .doc or other word-processing program format — and protect your personal information. The benefit of using a .pdf format is that the document can’t be readily altered by someone in the receiving chain, noted Scott Edwards, chief executive officer of Metropolis. “That might be unlikely, but it can happen if someone who is unscrupulous gains access to your CV, so it’s better to be safe,” he said. On another note, physicians who plan to submit their CVs and other materials to numerous entities and are engaging in a broad search should consider purchasing a dedicated email address specifically for their search activities. “It’s also a good idea to consider getting a dedi-

cated cellphone number for the job search, to avoid being contacted on their personal cellphones while they're at work," Mr. Edwards said.

When physicians "launch" their CV, they should be prepared to respond to the flurry of inquiries that will ensue. Putting the CV out into the universe of potential job opportunities is a serious undertaking, and physicians should be ready to adjust their schedules accordingly to accommodate the responsiveness and professionalism required to manage a search, according to Peter Angood, MD, chief executive officer of the American Association for Physician Leadership. "I often tell physicians that it's close to a two-and-a-half-time job when they're trying to get a new full-time job, because so many of the activities happen after hours," he said.

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How to Prepare for Your Physician Job Interview

Customization and confidentiality are key considerations in the current recruiting marketplace

By Nisha Mehta, MD, a physician leader whose work focuses on physician empowerment, community building, and career longevity in medicine

Finally! You've done countless interviews at this point, but for many of you, this is the first one where you are interviewing for a "real job." Some of the same rules apply, but others are very different.

To start, the dynamic in this interview is much different than others. You are likely interviewing with people who will be your colleagues, and your impression of them counts just as much as their impression of you. Depending on the job market in your field, there's a distinct possibility that they may even need you more than you need them.

Additionally, in an ideal scenario, you are picking a job that will last longer than a set time period of training. You are designing what potentially decades of life could look like for you and your family. Since this isn't just a stepping-stone to the next thing, your approach will need to be more all-inclusive. Also, unlike residencies and fellowships, where a similar core set of responsibilities and expectations are already outlined, there is a lot of variability between jobs, even within the same city and specialty. It's

important you are able to leave the interview with a 360-degree view of the position and the life you will build around it.

Keeping all of that in mind, here are some of my core tips for preparing for an interview:

- 1. Do your research about a job ahead of time.** Not doing this is one of the biggest mistakes I see applicants making. Showing up to a job and asking basic questions whose answers can easily be found online will cause interviewers to question why you're at the interview and how serious you are about the job. You want to come in knowing how the group is structured from a management perspective, what its patient population looks like, who the referral base may be, and what areas within your field the group specializes in, as well as some areas or topics where you may be able to add value. Look at the group's website and the members and see if there are any connections that you might have where you might be able to find common ground. Call the people you know who may be familiar with the group and ask them for insights. Find out if people have left the group recently, as it may raise some red flags. This will all lead to more sophisticated questions that you can ask and more valuable information to consider when you are making your decision. It will also tell group members you are serious about the opportunity, which will help your chances as they decide whether to extend a job offer. Time and resources are precious in this process, and many won't want to waste their time if they feel they are 1 of 100 possibilities.
- 2. Try and allot time to get to know the city you are interviewing in.** For those of you who are trying to return to a known place, this may be less of an issue, but nonetheless, training somewhere or growing up somewhere is different from living there as an adult and potentially raising a family in that location. Make sure the place offers outlets to foster your interests outside of work, as it will play into your happiness and burnout. Tour neighborhoods you may want to live in, and if you have educational preferences for your children, take some time to explore your options. If applicable, bring your significant other with you so that you're on the same page about pros and cons of living there.
- 3. When interviewing with potential future colleagues, don't be afraid to be yourself.** It's important that the fit feels natural and that there is a mutual desire to work together. As the saying goes, you can't choose your family, but you can choose your friends. Similarly, you can choose colleagues that you are confident will contribute to your happiness at the

job, whether it be via friendships, accommodating emergencies when they arise, splitting work in a way that feels equitable, and being respected. You should see yourself fitting into the culture of the group's members and in line with the standards, ethics, and practice patterns that they embrace.

- 4. In a similar vein, take note of how colleagues are interacting with each other.** As the landscape of healthcare delivery gets more challenging and complicated, it's important that you feel that the group is cohesive and supports each other. If there are obvious tensions within the group, it may be a sign that there is more beneath the surface that's resulting in conflict, whether it's RVU (relative value unit) structures, partnership issues, different beliefs about the direction the company is taking, etc.
- 5. Talk about money and opportunities for growth.** After all, this is a job. Put some effort into figuring out how revenue is generated, when you get to share in those profits, and what the plans of the group are in terms of expansion. If the compensation structure is complicated, ask for details. You don't have to take up your entire interview time talking about it, but get a basic sense and then ask the interviewer to send you a summary with details later. Understand the benefits. If the group's members do something a lot different from other groups you've interviewed with or your colleagues are interviewing with, ask them why they chose to structure things in that way.
- 6. If possible, spend some time shadowing someone whose job is similar to the one you're interviewing for.** Make sure you can see yourself happy in his or her shoes, and if there are obvious pain points or dealbreakers, take note of them. You may not be able to do this on the day of the interview, but if you have doubts about whether you'd enjoy the particular setting ahead of time, see if an interviewer can incorporate this on a later date. Again, it's in everybody's best interest to ensure a job is a good fit for you.

I could go on, but your goal on your interview day is to confirm the job is one you can see yourself enjoying for years to come. You're really picking more than a job — you're picking a lifestyle and a vision for your future, and you want to make sure you are keeping a keen eye out for pros, cons, and red flags.

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CLINICAL PRACTICE

Cancer of Unknown Primary Site

Kanwal Raghav, M.D.¹

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

A previously healthy 47-year-old woman presented with abdominal bloating and discomfort that had worsened over the previous 3 months. Her examination was notable for abdominal distention with bulging flanks and shifting dullness consistent with ascites. Further workup revealed a normocytic anemia (hemoglobin level, 10.4 g per deciliter; reference range, 12.0 to 14.0), elevated serum cancer antigen 125 level (168 U per milliliter; reference value, <38), and elevated carcinoembryonic antigen level (14.7 ng per milliliter; reference value, <3.8). A computed tomographic (CT) scan of her chest, abdomen, and pelvis with the use of contrast material showed liver, lymph node, and peritoneal tumors with ascites. She was referred to an oncologist because of suspicion of cancer, and an omental biopsy revealed poorly differentiated carcinoma with immunohistochemical assays positive for CK20, CDX2, and SATB2 (lower gastrointestinal tract immunostains) and negative for multiple other immunostains. A subsequent fluorodeoxyglucose (FDG) positron-emission tomographic (PET) scan showed FDG-avid liver, lymph node, and peritoneal metastases. Further testing with mammography, colonoscopy, and upper endoscopy failed to identify any primary site. Molecular profiling to find the tissue of origin and identify targetable genomic alterations was deemed indeterminate. How would you further evaluate and treat this patient?

THE CLINICAL PROBLEM

CANCER OF UNKNOWN PRIMARY SITE IS AN EVER-EVOLVING DISEASE ENTITY and one of the most challenging diagnoses to manage in oncology.¹⁻³ The term “cancer of unknown primary site” encompasses a diverse group of histologically confirmed cancers that have metastasized by the time of presentation, with the primary site of origin eluding detection despite a standard diagnostic workup.⁴⁻⁶ Patients with cancer of unknown primary site use more health care resources, including more investigations, emergency visits, and hospitalizations, than patients with known primary sites.^{7,8}

Cancer of unknown primary site is an uncommon diagnosis that accounts for 2 to 4% of all cancers.⁹ The American Cancer Society estimates that approximately 37,370 new cases of cancer of unknown primary site will be diagnosed in the United States in 2025.¹⁰ Worldwide, incidence rates have been declining and range between 2 and 15 cases per 100,000 person-years.⁹ Factors that have possibly contributed to this decreasing trend include enhanced diagnostic methods together with the expanded use of molecular profiling that can more accurately identify the primary site, improved quality of reporting, and better identification of key differential diagnostic elements, such as recurrence of antecedent cancers and cholangiocarcinoma.¹¹⁻¹⁴ As with all cancers, smoking, alcohol consumption, diabetes, and family

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CME



KEY POINTS

CANCER OF UNKNOWN PRIMARY SITE

- Cancer of unknown primary site is a heterogeneous group of histologically confirmed metastatic cancers, with the primary anatomical site of origin remaining unidentified after a standard diagnostic workup.
- Baseline evaluation involves a detailed history; physical, laboratory, and imaging assessments (ideally, a contrast-enhanced computed tomographic scan of the chest, abdomen, and pelvis); and a thorough pathological workup of adequate tumor tissue.
- Although immunophenotyping is the mainstay of diagnosis, recent advances have led to the integration of molecular profiling in predicting the tissue of origin and identifying targetable alterations in the management of cancer of unknown primary site.
- Both site-specific therapy (treatment of a putative primary site) and empirical chemotherapy (with a platinum-based cytotoxic regimen) are acceptable options for treatment.
- The overall prognosis for patients with cancer of unknown primary site remains poor. Participation in clinical trials should be encouraged.

history have been implicated as risk factors for cancer of unknown primary site.¹⁵ Typically, patients present with incidental findings or clinical signs and symptoms of multiorgan metastases. Imaging and pathological examination reveal diverse histologic findings (adenocarcinoma in 59% of cases, poorly differentiated or undifferentiated carcinoma or neoplasm in 31%, and squamous carcinoma in 9%) with varied metastatic patterns (multiple sites in 33% of cases, liver in 25%, and lymph nodes in 7%, among others).^{16,17}

Although cancer of unknown primary site has been classified into “favorable” and “unfavorable” subsets, these labels are evolving in the current era of molecular diagnostics and tailored therapies. Favorable cancer of unknown primary site refers to distinct clinicopathological manifestations in which the pattern of metastatic disease is typical of certain known cancers, such as breast cancer occurring with axillary lymphadenopathy (Table 1).⁴⁻⁶ The favorable subset comprises 20% of cases of cancer of unknown primary site and is associated with a better prognosis than unfavorable disease.¹⁸ The larger unfavorable subset of cancer of unknown primary site is associated with poor survival, although modest improvement has been noted in the past several years.¹⁷⁻²² Survival outcomes in patients with cancer of unknown primary site appear to be worse than those in patients with metastatic cancers of known primary site, which suggests a more aggressive behavior of the former.²² Male sex, poor performance status, histologic findings indicating adenocarcinoma, a high number of metastases, the presence of liver or peritoneal metastases, a high neutrophil-lymphocyte ratio, and molecular alterations (KRAS or

NRAS mutation and CDKN2A deletion) have been implicated as adverse prognostic factors.²³⁻²⁵

Although the pathophysiologic mechanisms underlying cancer of unknown primary site remain unclear, a broad postulate has emerged, fostered by our understanding of the biologic underpinnings of metastases from known primary sites (Fig. 1).^{26,27} One hypothesis is that cancer of unknown primary site is a metastatic syndrome with early and rapid dissemination from a primary tumor that either is very small or has regressed and is below the threshold of detection by contemporary diagnostic methods. This remarkably divergent behavior suggests a core programming distinct from cancers of known primary site that is driven by a prometastatic phenotype and ecosystem.^{28,29} Evidence of heterogeneity and of biologic subtypes that are associated with distinct metastatic patterns, immunophenotypic and molecular profiles, and survival among persons with diverse cancers of known primary site furthers this hypothesis.³⁰⁻³³

STRATEGIES AND EVIDENCE

CLINICAL EVALUATION

The diagnosis of cancer of unknown primary site relies on a comprehensive workup aimed at evaluating for the presence of any primary lesion (Figs. 2 and 3).⁴⁻⁶ However, the extent of diagnostic testing may be restricted by resource constraints, coexisting medical conditions, and the therapeutic window (the urgency of treatment dictated by the extent and pace of disease and the symptom burden). The clinical evaluation begins with obtaining a careful history, including

Table 1. Key Subsets within Cancer of Unknown Primary Site and the Therapeutic Implications.*

Manifestation	Analogous Known Primary Site	Therapeutic Strategy
Clinicopathological		
Blastic bone metastases with elevated prostate-specific antigen level (in men)	Prostate cancer	Combination androgen-deprivation therapy
Carcinoma (serous) with peritoneal carcinomatosis (in women)	Ovarian cancer	Chemotherapy (paclitaxel and carboplatin with or without bevacizumab)
Carcinoma with isolated axillary lymphadenopathy (in women)	Breast cancer	Chemotherapy, surgery, and radiation therapy (according to breast cancer guidelines)
Solitary or oligometastatic disease	Any tissue of origin	Chemotherapy with or without radiation therapy or chemoradiation with or without surgery
Squamous-cell carcinoma with cervical lymphadenopathy	Head and neck squamous-cell cancer	Surgery with or without radiation therapy or chemoradiation with or without chemotherapy (according to head and neck squamous-cell cancer guidelines)
Immunohistochemical		
CK20+ and CDX2+	Lower gastrointestinal or colorectal cancer	FOLFOX, XELOX, FOLFIRI, or FOLFOXIRI
Molecular		
BRAF V600E mutation	Any tissue of origin	Dabrafenib with trametinib
Fusions		
NTRK	Any tissue of origin	Entrectinib, larotrectinib, or repotrectinib
RET	Any tissue of origin	Selpercatinib
HER2 amplification or overexpression†	Any tissue of origin	Trastuzumab deruxtecan
Immunotherapy eligible		
Mismatch repair–deficient and microsatellite instability–high	Any tissue of origin	PD-1 and PD-L1 monoclonal antibodies
High tumor mutational burden‡	Any tissue of origin	Pembrolizumab

* FOLFIRI denotes folinic acid, fluorouracil, and irinotecan; FOLFOX fluorouracil, leucovorin, and oxaliplatin; FOLFOXIRI fluorouracil, leucovorin, oxaliplatin, and irinotecan; HER2 human epidermal growth factor receptor 2; PD-1 programmed cell death protein 1; PD-L1 programmed death ligand 1; and XELOX capecitabine and oxaliplatin.

† HER2 amplification or overexpression was defined as an immunohistochemical score of 3+.

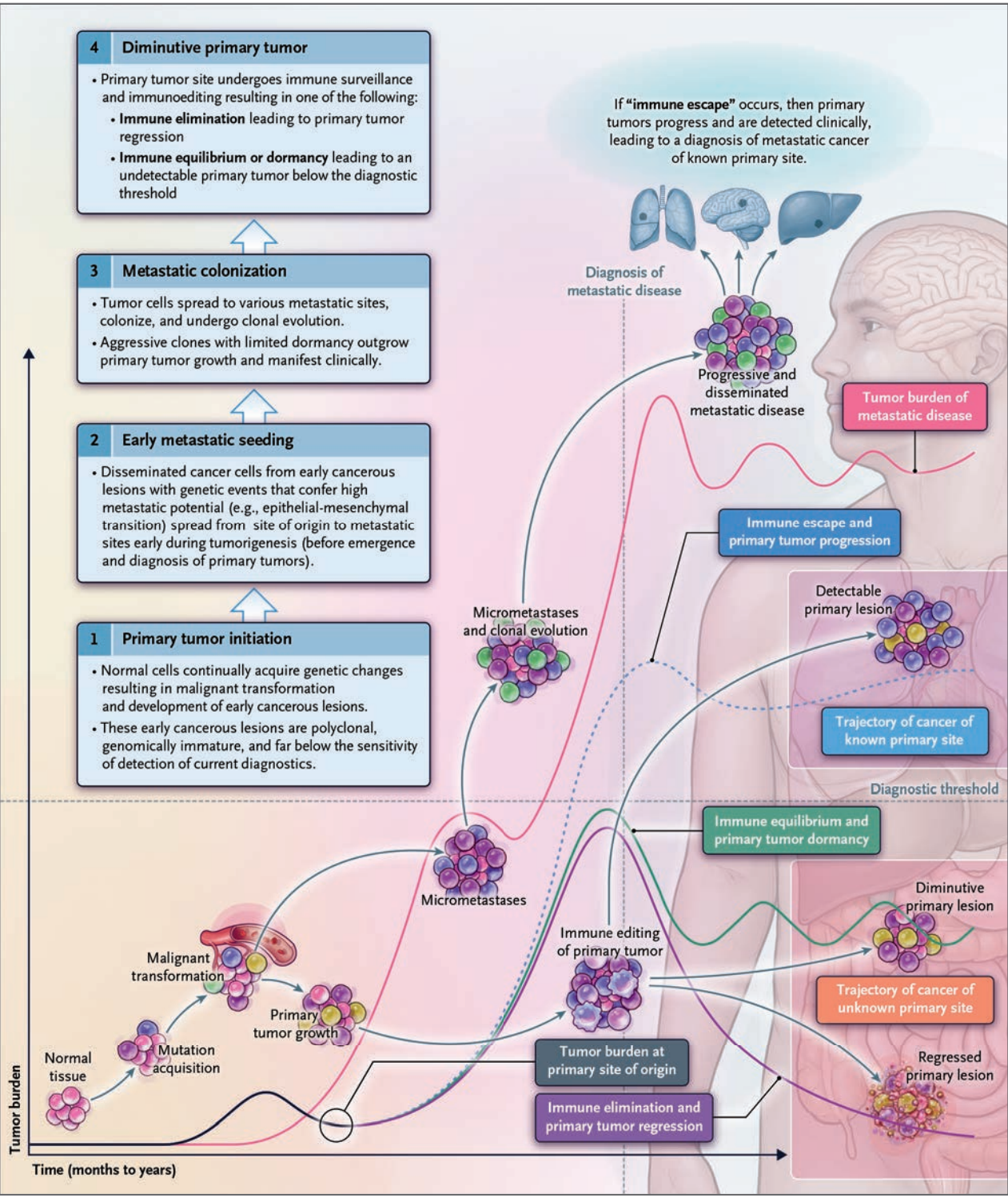
‡ A high tumor mutational burden was defined as at least 10 mutations per megabase.

a review of family and personal history of previous cancers. A physical examination and baseline laboratory evaluation can help direct further workup. All patients should undergo imaging (ideally a CT scan with the use of contrast material) of the chest, abdomen, and pelvis. The use of adjunct diagnostic methods, such as PET scan, magnetic resonance imaging, mammography, testicular ultrasonography (in young men with midline lymphadenopathy), or invasive procedures (upper endoscopy, colonoscopy, bronchoscopy, laryngoscopy, or cystoscopy), should be guided by symptoms, imaging, or pathological findings indicative of a primary origin.¹ The diagnostic usefulness of any one test is limited, especially in the face of atypical biologic characteristics and patterns; therefore, the development of a man-

agement plan on the basis of the overall manifestation of the disease and the expertise of the multidisciplinary team is warranted (Figs. 2 and 3).

Immunophenotyping

Light microscopic examination of tumor tissue with immunophenotyping remains the mainstay in the diagnosis of cancer of unknown primary site. The accuracy of immunohistochemical testing for diagnosing tissue type is high, especially if adequate tumor tissue is assessed.^{34,35} When possible, a core-needle biopsy is preferred to preserve features of tissue architecture that assist with diagnosis. During this process, close communication with a pathologist as a part of a multidisciplinary team can enable directed and judicious use of tissue for the immunohistochemical assay



since sufficient tumor tissue is also required for molecular profiling. Pathologists use an average of 8.8 immunostains (range, 0 to 20) in evaluating metastatic tumors, and nearly two thirds of patients with cancer of unknown primary site will have insufficient tissue left for molecular profiling during the course of their clinical care.^{35,36} Despite this heavy reliance on immunohistochem-

Figure 1 (facing page). Development of Cancer of Unknown Primary Site.

The hallmark of cancer of unknown primary site is the presence of detectable metastatic disease without an identifiable primary lesion. The biologic features of cancer of unknown primary site, as opposed to cancer of known primary site, favor an aggressive phenotype with a propensity for early metastases and metastatic tumor outgrowth. While the metastatic disease grows, the primary tumor undergoes extensive immunoediting that is orchestrated by diverse anti- and protumorigenic immune cells and cytokines. Unlike cancer of known primary site, in which the primary tumor will progress by evading the immune system, cancer of unknown primary site involves a process that results in either immune elimination with regression of the primary tumor or an immune equilibrium (a state of dormancy) that leads to a subclinical primary lesion below the limits of diagnostic sensitivity. The graph shows tumor-burden growth over time in both metastatic and primary disease. Biologic features of the disease leading to differences between the primary tumor and the metastatic disease with respect to growth trajectory and diagnostic sensitivity result in the entities known as cancer of known primary site and cancer of unknown primary site.

ical testing, its accuracy in identifying a primary organ is limited, especially in cases of poorly differentiated tumors.³⁵ Because no one immunostain is pathognomonic of the tissue of origin, a panel of tests performed in a stepwise fashion may be warranted.³⁷ The use of deep-learning methods for determining the tissue of origin may be the next frontier in the pathology of cancer of unknown primary site.³⁸

Molecular Profiling for the Prediction of Tissue of Origin

Molecular profiling in cancer of unknown primary site has been used to predict a putative primary site (tissue-of-origin profiling) and to identify targetable genomic alterations (genomic profiling) amenable to targeted therapies.^{1,2} Several tissue-of-origin assays have been developed on the premise that cancer of unknown primary site and metastases from known primary sites are alike. Therefore, a biomarker set can be generated on the basis of commonalities in genomic, transcriptomic, and epigenetic profiles with the use of a discovery cohort of known primary sites to predict the probability of a match between the signature of cancer of unknown primary site and that of cancer of known primary site.^{1,2} Various strategies that use RNA, microRNA, DNA, and

methylation coupled with machine learning have been developed, with accuracy in predicting the tissue of origin ranging from 65 to 99%.³⁹ Among these strategies, only gene-expression profiling has been evaluated in randomized trials, with mixed results (see below).^{21,39-42}

PRINCIPLES OF TREATMENT

The goal of treatment in most patients with cancer of unknown primary site is largely palliative owing to the disseminated nature of the disease, except for a small subpopulation of patients who present with single-site or limited metastatic disease. In these patients, a multidisciplinary approach incorporating radiation therapy or surgery can be potentially curative (Fig. 4).

Site-Specific Therapy and the Potential Role of Molecular Profiling for Tissue of Origin

Patients with cancer of unknown primary site who present with a characteristic, recognizable, clinicopathological pattern that is analogous to specific known primary cancers can be treated according to guidelines pertaining to those specific tumors, a treatment approach that simply emulates a site-specific approach to therapy for cancer of unknown primary site (Table 1). However, most patients with cancer of unknown primary site do not have a typical presentation. In these cases, clinicopathological clues can be used to discern a putative primary site, despite the clear absence of a primary lesion. Tissue-of-origin profiling for discerning primary sites may also be helpful. For cancer of unknown primary site with a discernible primary site, preference should be given to first-line site-specific therapy, which mirrors the standard care for the corresponding metastatic cancer of known primary site. For instance, a patient with adenocarcinoma and mediastinal lymphadenopathy positive for thyroid transcription factor 1 and with liver metastases without a lung lesion who is a long-term smoker may be treated for putative primary lung cancer, although high-quality evidence to support this strategy is lacking.

Several retrospective studies and prospective trials have investigated the benefit of site-specific therapy over empirical chemotherapy with conflicting results (Table 2). Two multicenter trials, the Next Generation Sequencing for Patients with Cancer of Unknown Primary Site (CUP-NGS) trial (involving 130 patients) and the Groupe d'Etude

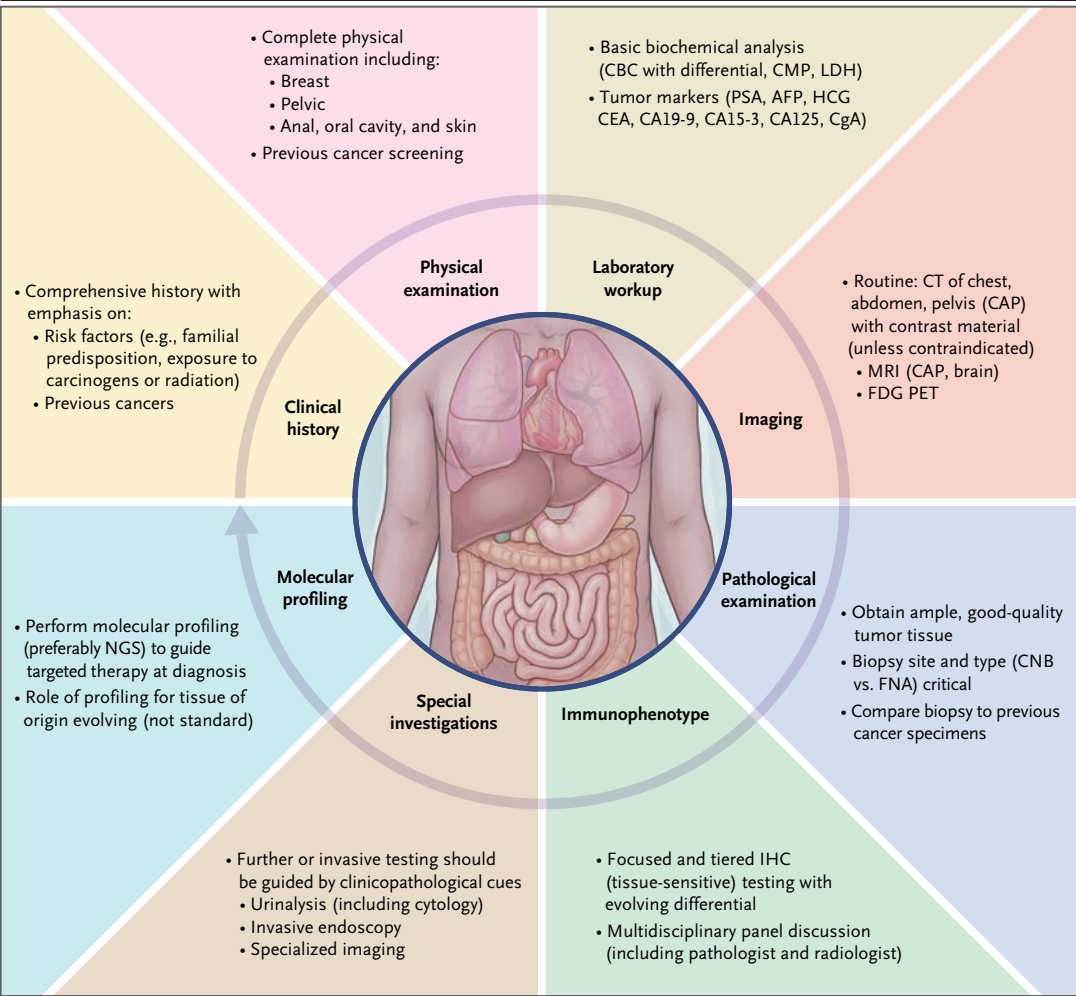


Figure 2. Diagnostic Workup for Patients with Cancer of Unknown Primary Site.

Cancer of unknown primary site is a diagnosis of exclusion, with workup designed to rule out any known primary site. Investigations should follow a tiered format with emphasis on tailoring the workup with each subsequent test. The critical decision is centered on striking the appropriate balance between the intensity of and time required for testing and the indication for and ability to start treatment guided by the patient's clinical status, disease trajectory, and goals of care. Immunophenotyping takes center stage in the diagnosis, but no one stain is sensitive or specific enough; therefore, a modular approach is necessary. With respect to imaging, magnetic resonance imaging (MRI), positron emission tomography (PET), or both can be performed in patients with contraindication to CT with the use of intravenous contrast material. The multidisciplinary team includes a medical oncologist, pathologist (with or without a molecular pathologist), radiologist, and in certain cases a surgical oncologist, radiation oncologist, and interventional radiologist. Special investigations include urinalysis, invasive endoscopy (involving colonoscopy and esophagogastroduodenoscopy [if clinical history or symptoms or immunohistochemical findings suggest a gastrointestinal primary cancer], cystoscopy, or panendoscopy with biopsies and tonsillectomy [for cases in which head and neck carcinoma is suspected]), and specialized imaging (such as breast imaging [mammography or breast MRI] and ¹⁸F-fluorodeoxyglucose [FDG] PET), among others. Molecular profiling to determine the tissue of origin is useful as an adjunct to standard workup and preferably in a research context. The value of molecular profiling over the diagnostic methods currently used is yet to be established. AFP denotes α -fetoprotein, CA cancer antigen, CA19-9 carbohydrate antigen 19-9, CBC complete blood count, CEA carcinoembryonic antigen, CgA chromogranin A, CMP complete metabolic profile, CNB core needle biopsy, FNA fine-needle aspiration, HCG β -human chorionic gonadotropin, LDH lactate dehydrogenase, IHC immunohistochemical, NGS next-generation sequencing, and PSA prostate-specific antigen.

Français des Carcinomes de site Primitif Inconnu-04 (GEFCAPI-04) trial (involving 243 patients), randomly assigned patients with newly diagnosed cancer of unknown primary site to site-specific therapy (on the basis of gene-expression profiling to predict the primary site) or to empirical chemotherapy (carboplatin plus paclitaxel in the CUP-NGS trial and gemcitabine plus cisplatin in the GEFCAPI-04 trial).^{21,41} Neither trial showed superiority of site-specific therapy over empirical chemotherapy.^{21,41} Overall survival at 1 year was 44.0% in the site-specific therapy group and 54.9% in the empirical therapy group ($P=0.26$) in the CUP-NGS trial and was 41.3% and 40.7%, respectively ($P=0.71$), in the GEFCAPI-04 trial.^{21,41} The corresponding median progression-free survival was 5.1 months and 4.8 months ($P=0.55$) in the CUP-NGS trial and 4.6 months and 5.3 months ($P=0.71$) in the GEFCAPI-04 trial.^{21,41}

Contrary to these trials, the single-center, randomized Fudan CUP-001 trial (involving 182 patients) showed superiority of site-specific therapy guided by gene-expression profiling over platinum-based empirical chemotherapy (plus a taxane or gemcitabine).⁴⁰ The median progression-free survival was 9.6 months with site-specific therapy and 6.6 months with empirical chemotherapy ($P=0.017$).⁴⁰ Heterogeneity of the population and improved systemic therapies, specifically the incorporation of targeted therapies and immunotherapy (in nearly 45% of patients) in the experimental group, may have affected this advantage with respect to progression-free survival.

Empirical Chemotherapy

A meta-analysis of five studies (three observational studies and two randomized trials; the Fudan CUP-001 trial was excluded from the analysis) investigating the role of site-specific therapy and empirical chemotherapy in cancer of unknown primary site showed that site-specific therapy was not significantly associated with an improvement in either progression-free survival or overall survival, indicating that empirical chemotherapy remains the standard against which newer strategies should be compared.⁴² The most common empirical chemotherapy used in practice is a combination of a platinum agent (carboplatin or cisplatin) with either paclitaxel or gemcitabine. Other regimens comprising gemcitabine plus



Figure 3. Immunophenotyping in Cancer of Unknown Primary Site.

Shown are key positive immunostains that are indicative of specific tumor types during phenotyping. Detailed descriptions of the immunostains are provided in Table S3.

docetaxel and a fluorouracil-based therapy are also used. A meta-analysis of 32 studies (including 7 randomized trials) evaluating 42 regimens did not show clear superiority of any one regimen.⁵⁰

Molecularly Guided Targeted Therapy

Biomarker-driven therapies, specifically those with proven efficacy regardless of the specific tissue or organ where the cancer originated (sometimes termed tissue-agnostic therapy), are endorsed by guidelines for cancer of unknown primary site (Table 1).^{4,6} Genomic aberrations are common in cancer of unknown primary site, and response

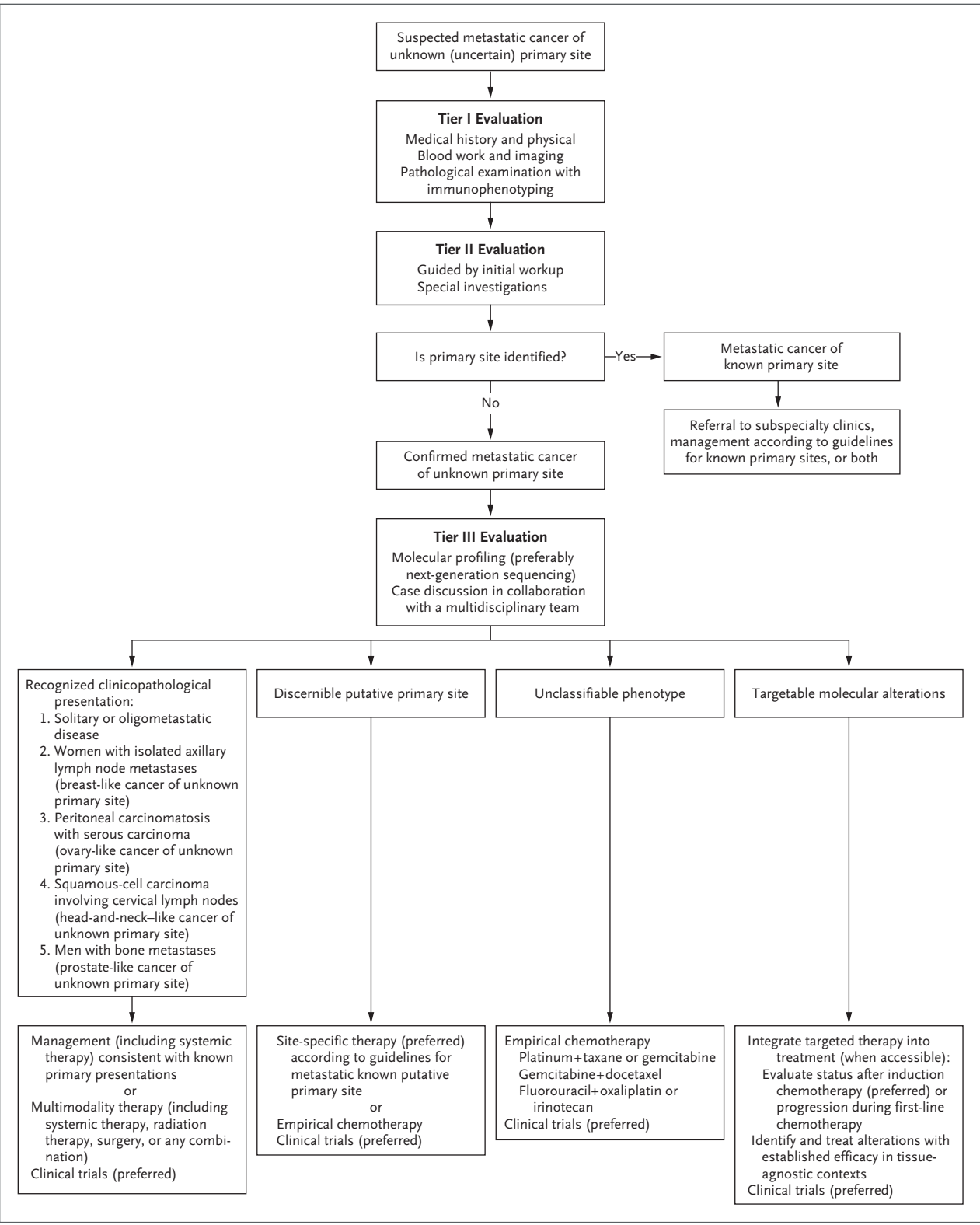


Figure 4 (facing page). Treatment Algorithm for Management of Cancer of Unknown Primary Site.

Confirmation and classification of cancer of unknown primary site for therapeutic purposes involve a tiered workup, which leads to the categorization of the disease into one of four discrete subgroups. These subgroups differ in their treatments and prognosis. Systemic cytotoxic chemotherapy with palliative intent is the mainstay of therapy for most patients with cancer of unknown primary site. In select cases, incorporation of targeted or biomarker-guided therapy, immunotherapy, or multimodality therapy (or a combination of these) with curative intent is appropriate. Despite these options, the prognosis is poor, and early referral and participation in clinical trials should be encouraged whenever possible. Multimodality therapy involving systemic therapy, radiation therapy, surgery, or a combination of these therapies is often used in patients presenting with solitary or oligometastatic disease. Empirical chemotherapy regimens include but are not restricted to platinum-based doublet therapies (cisplatin or carboplatin) combined with either a taxane (paclitaxel or docetaxel) or gemcitabine. Gemcitabine plus docetaxel and fluorouracil-based regimens are other options used empirically in the treatment of cancer of unknown primary site. Some overlap can occur within these subgroups of cancer of unknown primary site; therefore, molecular targets can manifest within any subgroup, and all attempts should be made to incorporate targeted therapies into the treatment plan. Biomarker-guided therapy is established for advanced solid tumors that harbor a *BRAF* V600E mutation, human epidermal growth factor receptor 2 overexpression (immunohistochemical score of 3+), *NTRK* fusion, *RET* fusion, high tumor mutational burden (≥ 10 mutations per megabase), and those that are mismatch repair-deficient and microsatellite instability-high.

to targeted therapies has been documented in case series and nonrandomized studies.^{36,51-53} The CUPISCO trial (involving 436 patients) evaluated the clinical benefit of incorporating molecular profiling to identify targetable genomic alterations; the trial used tumor tissue, blood-based assay, or both to inform systemic therapy in cancer of unknown primary site.⁵⁴ In this trial, patients with cancer of unknown primary site who had disease control after three cycles of standard first-line platinum-based chemotherapy and were randomly assigned to receive therapy guided by molecular profiling had progression-free survival that was 6 weeks longer than those who were assigned to continued chemotherapy (median, 6.1 vs. 4.4 months; $P=0.008$), even though less than one third of the patients assigned to molecular profiling-guided therapy had an actionable target.⁵⁴

AREAS OF UNCERTAINTY

The rarity of cancer of unknown primary site and the paucity of research amplify the uncertainty in the treatment of patients with this morbid orphan disease. Although the debate on effective therapy for cancer of unknown primary site is shifting toward site-specific and molecularly guided therapies, high-level evidence regarding improvement in outcomes with these therapies over treatment guided by standard clinicopathological assessment is lacking.³⁹

We know very little about the biologic differences between cancer of unknown primary site with a putative primary site and corresponding metastatic cancers of known primary site. For instance, should *BRAF* V600E-mutated cancer of unknown primary site be treated with *BRAF*-MEK inhibition (as for melanoma) or with *BRAF*-epidermal growth factor receptor (EGFR) inhibition (as for colorectal cancer), and how do we incorporate the tissue-of-origin context in this case?⁵⁵ Also crucial is understanding the molecular subsets that cancer of unknown primary site represents within the framework of known primary cancers and the response to standard therapies. For example, do cancers of unknown primary site with a colon profile behave as cancers on the right or left side of the colon or as consensus molecular subtype 4 tumors when treated with anti-EGFR-based chemotherapy?³¹ Immunotherapy has also been investigated in cancer of unknown primary site, with responses in approximately 20% of patients (Table S2). However, in the absence of any validated biomarkers, a broad approach is not recommended in clinical guidelines, and immunotherapy is appropriate only for tumors that have high microsatellite instability or DNA mismatch repair deficiency (dMMR) or that have a high mutational burden or as part of site-specific therapy. More research on the efficacy and safety of immunotherapy in cancer of unknown primary site is needed.^{4-6,56}

GUIDELINES

The National Comprehensive Cancer Network (NCCN), the National Institute for Health and Care Excellence (NICE), and the European Society for Medical Oncology (ESMO) publish and regularly update guidelines focused on the evaluation

Table 2. Summary of Studies Evaluating the Role of Site-Specific Therapy as Compared with Empirical Therapy in Cancer of Unknown Primary Site.*

Study†	Study Type and Primary End Point	Tissue-of-Origin Profiling	Sample Size (Site-Specific vs. Empirical Therapy)	Empirical Therapy Regimen	Sites of Common Predicted Tumors	Outcomes‡
Fudan CUP-001 ⁴⁰	RCT, PFS	Canhelp-Origin, a 90-gene expression assay (archived FFPE)	182 (91 vs. 91)	Platinum and paclitaxel or gemcitabine	Stomach or esophagus, lung, ovary, cervix, breast	Median PFS, 9.6 vs. 6.6 mo (HR, 0.68; 95% CI, 0.49–0.93; P=0.017) Median OS, 28.2 vs. 19.0 mo (HR, 0.74; 95% CI, 0.52–1.06; P=0.09) Objective response, 49% vs. 46% (P=0.76)§
New South Wales ⁴³	Retrospective	Clinicopathological (tissue-based)	57 (26 vs. 31)	Platinum and gemcitabine or carboplatin and paclitaxel	Head and neck, colon or rectum, pancreas, lung, stomach or esophagus	Median PFS, 9.8 vs. 7.3 mo (HR, 0.70; 95% CI, 0.40–1.30; P=0.29) Median OS, 25.9 vs. 13.2 mo (P=0.30)
Japan-8 CUP ⁴⁴	Retrospective	Clinicopathological (tissue-based)	144 (60 vs. 84)	Various	Lung, stomach or esophagus, pancreas, colon or rectum, ovary	Median OS, 10.0 vs. 10.1 mo (HR, 1.01; 95% CI, 0.70–1.45; P=0.95)
CUP-NGS ²¹	RCT, OS	Microarray-based gene expression analysis (fresh frozen)	101 (50 vs. 51)¶	Carboplatin and paclitaxel	Pancreas, stomach or esophagus, lymphatic system, bladder, cervix	Median PFS, 5.1 vs. 4.8 mo (HR, 0.88; 95% CI, 0.59–1.33; P=0.55) Median OS, 9.8 vs. 12.5 mo (HR, 1.03; 95% CI, 0.68–1.56; P=0.89) Overall response, 34.7% vs. 41.2% (P=0.50)§
GEFCAPI-04 ⁴¹	RCT, PFS	92-Gene RT-PCR (tissue-based)	243 (123 vs. 120)	Gemcitabine and cisplatin	Pancreas, gallbladder, or bile duct; squamous-cell carcinoma; kidney, lung, intestines	Median PFS, 4.6 vs. 5.3 mo (HR, 0.95; 95% CI, 0.72–1.25; P=0.71) Median OS, 10.7 vs. 9.9 mo (HR, 0.92; 95% CI, 0.69–1.23; P=0.72)
Aichi CUP ⁴⁵	Retrospective	Clinicopathological (tissue-based)	122 (90 vs. 32)	Platinum-based therapy	Colon or rectum, gynecologic system, lung, pancreas, neuroendocrine system	Median PFS, 5.1 vs. 4.2 mo (P=0.02) Median OS, 15.7 vs. 10.7 mo (P=0.07)
EPICUP ⁴⁶	Retrospective	Microarray DNA methylation signatures (tissue-based)	92 (31 vs. 61)	Various	Lung, head and neck, breast, colon or rectum, liver	Median OS, 13.6 vs. 6.0 mo (P=0.008)
Sarah Cannon ⁴⁷	Prospective, OS	92-Gene RT-PCR (tissue-based)	223 (194 vs. 29)	Various	Biliary tract, bladder, colon or rectum, lung, pancreas	Median OS, 12.5 vs. 9.1 mo (historical control)
Lower GI CUP ⁴⁸	Retrospective	Immunohistochemical test (tissue-based)	68 (53 vs. 15)	Gemcitabine- or taxane-based therapy	Lower gastrointestinal tract	OS (HR, 0.52; 95% CI, 0.22–1.22; P=0.13)
CancerTYPE ID-GI ⁴⁹	Retrospective	92-Gene RT-PCR (tissue-based)	42 (24 vs. 18)	Various	Colon or rectum	Median PFS, 8.5 vs. 6 mo (P=0.11)

* No primary end points were specified for the retrospective studies listed. CI denotes confidence interval; FFPE formalin-fixed, paraffin embedded; NS not specified; RCT randomized, control trial; and RT-PCR reverse-transcriptase polymerase chain reaction.
† Study titles and references are provided in Table S1 in the Supplementary Appendix (available with the full text of this article at NEJM.org).
‡ Values are site-specific therapy as compared with empirical therapy. Hazard ratios (HRs) for analyses of overall survival (OS) indicate the risk of death, and hazard ratios for the analyses of progression-free survival (PFS) indicate the risk of disease progression or death.
§ Response was according to Response Evaluation Criteria in Solid Tumors, version 1.1.
¶ The numbers shown are the number of patients who received treatment.

and treatment of patients with cancer of unknown primary site.^{4,6} The recommendations in the present article are largely concordant with these key professional guidelines. Barring selected favorable subsets of cancer of unknown primary site, the guidelines mentioned here do not explicitly support the use of site-specific therapy over empirical chemotherapy. Adenocarcinoma with a colorectal immunophenotype (CK7-negative, CK20-positive, and CDX2-positive) or molecular profile (colon-like cancer of unknown primary site) is now classified by ESMO in the favorable subset of cancer of unknown primary site, and treatment analogous to that for metastatic colorectal cancer is generally recommended. Similarly, NCCN recommends fluorouracil-based regimens as one of the preferred treatment options for occult primary adenocarcinoma, primarily for disease with a presumed gastrointestinal primary site. Because of limited data supporting improved outcomes with the use of molecular profiling to guide site-specific therapy over conventional diagnostic approaches, clinical practice guidelines recommend against the routine use of molecular profiling to identify the tissue of origin in cancer of unknown primary site.^{4,6} Given this limited availability of high-level clinical evidence, all guidelines encourage the participation of patients with cancer of unknown primary site in clinical trials.

CONCLUSIONS AND RECOMMENDATIONS

Regarding the patient in the vignette with cancer of unknown primary site, I would manage her care according to the most likely putative cancer of known primary site given the phenotype and genotype. She had an immunophenotype suggestive of a gastrointestinal primary cancer (colon-

like cancer of unknown primary site) on the basis of assays positive for CK20, CDX2, and SATB2, which are immunostains used for samples from the lower gastrointestinal tract. I would start by obtaining a repeat biopsy and sending tissue for genomic profiling to identify targetable alterations. Alternatively, genomic profiling with blood-based assays can also be used to detect potential actionable genetic alterations (e.g., dMMR, BRAF V600E, human epidermal growth factor receptor 2 amplification).

I would then recommend palliative systemic chemotherapy that corresponded to the best treatments known for the presumed primary cancer. In this case, I would use fluorouracil (plus leucovorin), oxaliplatin, and irinotecan (FOLFOXIRI), drawing from evidence supporting the role of triplet cytotoxic chemotherapy in metastatic colorectal cancer. The use of doublet fluorouracil-based therapy with oxaliplatin (FOLFOX) or irinotecan (FOLFIRI) is also defensible, but a 47-year-old patient should be able to receive the more aggressive and more effective FOLFOXIRI therapy.⁵⁷ The results of molecular profiling can enable the integration of molecularly guided therapy in a treatment continuum that is based on response to therapy, the level of evidence that supports targeting the alteration, and the availability of molecularly guided therapies, preferably within the context of clinical trials. I would also seek early referral to a center with a multidisciplinary program focused on cancer of unknown primary site and enroll the patient in a clinical trial, if she were willing.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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*physicians
currently work
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2023*



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Classified Advertising Section

Sequence of Classifications

Addiction Medicine	Neonatal-Perinatal Medicine	Preventive Medicine	Urology
Allergy & Clinical Immunology	Nephrology	Primary Care	Chiefs/Directors/ Department Heads
Ambulatory Medicine	Neurology	Psychiatry	Faculty/Research
Anesthesiology	Nuclear Medicine	Public Health	Graduate Training/Fellowships/ Residency Programs
Cardiology	Obstetrics & Gynecology	Pulmonary Disease	Courses, Symposia, Seminars
Critical Care	Occupational Medicine	Radiation Oncology	For Sale/For Rent/Wanted
Dermatology	Ophthalmology	Radiology	Locum Tenens
Emergency Medicine	Osteopathic Medicine	Rheumatology	Miscellaneous
Endocrinology	Otolaryngology	Surgery, General	Multiple Specialties/ Group Practice
Family Medicine	Pathology	Surgery, Cardiovascular/ Thoracic	Part-Time Positions/Other
Gastroenterology	Pediatrics, General	Surgery, Neurological	Physician Assistant
General Practice	Pediatric Gastroenterology	Surgery, Orthopedic	Physician Services
Geriatrics	Pediatric Intensivist/ Critical Care	Surgery, Pediatric	Positions Sought
Hematology-Oncology	Pediatric Neurology	Surgery, Plastic	Practices for Sale
Hospitalist	Pediatric Otolaryngology	Surgery, Transplant	
Infectious Disease	Pediatric Pulmonology	Surgery, Vascular	
Internal Medicine	Physical Medicine & Rehabilitation	Urgent Care	
Internal Medicine/Pediatrics			
Medical Genetics			

Classified Advertising Rates

We charge \$11.20 per word per insertion. A 2- to 4-time frequency discount rate of \$8.35 per word per insertion is available. A 5-time frequency discount rate of \$7.95 per word per insertion is also available. In order to earn the 2- to 4-time or 5-time discounted word rate, the request for an ad to run in multiple issues must be made upon initial placement. The issues do not need to be consecutive. **Web fee:** Classified line advertisers may choose to have their ads placed on NEJM CareerCenter for a fee of \$140.00 per issue per advertisement. The web fee must be purchased for all dates of the print schedule. The choice to place your ad online must be made at the same time the print ad is scheduled. **Note:** The minimum charge for all types of line advertising is equivalent to 30 words per ad. Purchase orders will be accepted subject to credit approval. For orders requiring prepayment, we accept payment via Visa, MasterCard, and American Express for your convenience, or a check. All classified line ads are subject to the consistency guidelines of NEJM.

How to Advertise

All orders, cancellations, and changes must be received in writing. E-mail your advertisement to us at ads@nejmcareercenter.org, or fax it to 1-781-895-1045 or 1-781-893-5003. We will contact you to confirm your order. Our closing date is typically the Friday 20 days prior to publication date; however, please consult the rate card online at nejmcareercenter.org or contact the Classified Advertising Department at 1-800-635-6991. Be sure to tell us the classifica-

tion heading you would like your ad to appear under (see listings above). If no classification is offered, we will determine the most appropriate classification. Cancellations must be made 20 days prior to publication date. Send all advertisements to the address listed below.

Contact Information

Classified Advertising
The New England Journal of Medicine
860 Winter Street, Waltham, MA 02451-1412
E-mail: ads@nejmcareercenter.org
Fax: 1-781-895-1045
Fax: 1-781-893-5003
Phone: 1-800-635-6991
Phone: 1-781-893-3800
Website: nejmcareercenter.org

How to Calculate the Cost of Your Ad

We define a word as one or more letters bound by spaces. Following are some typical examples:

Bradley S. Smith III, MD..... = 5 words
Send CV = 2 words
December 10, 2007 = 3 words
617-555-1234 = 1 word
Obstetrician/Gynecologist ... = 1 word
A = 1 word
Dalton, MD 01622 = 3 words

As a further example, here is a typical ad and how the pricing for each insertion is calculated:

MEDICAL DIRECTOR — A dynamic, growth-oriented home health care company is looking for a full-time Medical Director in greater New York. Ideal candidate should be board certified in internal

medicine with subspecialties in oncology or gastroenterology. Willing to visit patients at home. Good verbal and written skills required. Attractive salary and benefits. Send CV to: E-mail address.

This advertisement is 56 words. At \$11.20 per word, it equals \$627.20. This ad would be placed under the Chiefs/Directors/ Department Heads classification.

Classified Ads Online

Advertisers may choose to have their classified line and display advertisements placed on NEJM CareerCenter for a fee. The web fee for line ads is \$140.00 per issue per advertisement and \$240.00 per issue per advertisement for display ads. The ads will run online two weeks prior to their appearance in print and one week after. For online-only recruitment advertising, please visit nejmcareercenter.org for more information, or call 1-800-635-6991.

Policy on Recruitment Ads

All advertisements for employment must be non-discriminatory and comply with all applicable laws and regulations. Ads that discriminate against applicants based on sex, age, race, religion, marital status or physical handicap will not be accepted. Although the *New England Journal of Medicine* believes the classified advertisements published within these pages to be from reputable sources, NEJM does not investigate the offers made and assumes no responsibility concerning them. NEJM strives for complete accuracy when entering classified advertisements; however, NEJM cannot accept responsibility for typographical errors should they occur.

Classified Ad Deadlines

Issue	Closing Date
November 13	October 24
November 20	October 31
November 27	November 7
December 4	November 14

Help employers find you!

Create a physician profile today on NEJMCareerCenter.org.



Hematology-Oncology

WE CURRENTLY HAVE AN EXCEPTIONAL OPPORTUNITY — For a Medical Oncologist/Hematologist to join an 8-person Oncology Hematology private practice located at a rapidly growing cancer center in Fairfield County, CT. Active in clinical research, and have faculty appointment with a major medical school. Strong affiliation with a world-renowned tertiary cancer center. Excellent compensation and benefits package including health and liability insurance, vacation, and pension plan. Excellent support staff with nurse practitioners, research nurses, data managers, RNs, and pharmacists. EMR transitioning to EPIC. Rotating call schedule to be 1 in 9. 4-Clinic days per week. First year employment leading to partnership opportunity. Need to be board certified or eligible in both hematology and oncology. Expectation to subspecialize. Anticipated start 2026. Please send CV to: Lina Adams Hematology Oncology, P.C. E: ladams@stamhealth.org

PHYSICIAN RECRUITER

The physician you're seeking is one of our readers. Advertise in the next issue of the *New England Journal of Medicine* and reach physicians in all specialties nationwide. For more information, contact us at ads@nejmcareercenter.org.

Hiring is a numbers game — place your ad in 3 issues and get the 4th FREE.

NEJM CareerCenter

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