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Residents and Fellows Edition



October 10, 2024

Dear Physician:

As a resident nearing 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 2024 *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 for the Virtual Physician-Job Interview

The interview has become a new world, for now, with the pandemic, and both prospective employers and physician candidates are adjusting

By Bonnie Darves, a Seattle-based freelance health care writer

Physicians and other health care professionals know well that functioning — and practicing medicine — in a pandemic is a very different and much altered experience from a year ago. Even though physicians and residents are often providing care in fraught and challenging environments, when it comes to looking for a new practice opportunity, they're not likely to find themselves at the point of care but rather in their living rooms. Interviews have gone virtual in a big way as the risks and logistics of the traditional site interview have prompted employers and even candidates to forgo site visits.

What this means is that both parties are having to adjust. Employers are increasingly vetting candidates without ever shaking hands or watching physicians interact in live group settings. Physicians are trying to figure out how to put their best face forward over video platforms such as Zoom, Skype, GoToMeeting, or Cisco Webex, to name a few, and how to make the most of what can be an awkward exchange.

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The good news for physicians is that this is a new and evolving experience for all involved. As such, it's important to keep in mind that many people, including employers and senior physicians on the call, might find the virtual-video interview challenging. It's not a technology-proficiency test, after all. However, on the technology front, physicians who find themselves in job-search mode during the coronavirus pandemic should do their best to prepare themselves, their environment, and their computers or devices for a successful meeting. The means "attending" the session as professionally as possible and ensuring that extraneous factors or technology don't get in the way of a productive conversation.

Some of the prerequisites for virtual interviews are no different than they would be for a formal site-visit interview. First and foremost, look the part and dress professionally. It might feel awkward to don a suit or, for women, other formal business attire, but that's a must. Physicians should be well dressed, well groomed, and reasonably refreshed when going to a video interview. In other words, treat the experience as if it were a formal site interview that you traveled to and prepared for in advance. Leave the casual demeanor behind, or at least in the other room.

It's key to know exactly who will be on the video call and what their roles are, so that candidates can read bios and prepare accordingly. It's also appropriate to ask about the length of the interview and to request an agenda, if one will be prepared.

Following are some of the most important considerations in preparing for a video interview:

Prepare and "professionalize" the immediate environment. For starters, the room should be well and brightly lit and the background clean and free of clutter. That means ensuring that there isn't an unsightly stove or a television or even a stack of books or laundered T-shirts in view. As a background, a blank wall, an unembellished window, or a background cabinet with a non-distracting tasteful décor item all work well. Alternatively, many video platforms enable use of green-screen effects, which replace the actual background with a digital or virtual background. A word of caution is in order here: Candidates whose home environments are unsuitable and who want to use a background should opt for something clean and simple, not a potentially distracting image of a tropical beach, an old-growth forest, or a fake wine cellar. Finally, make sure that the lighting in the room is unobtrusive and doesn't interfere or produce visible glare.

Do a trial run and then take the time to record a hypothetical session with a friend or family member. In advance of a virtual interview, candidates should receive specific instructions on the technology that will be used, as well as a link for getting into the session. For those who haven't used the technology that will host the meeting, it's important to get a trial subscription and ensure they're familiar with the way it works and any features that might be used. Many physicians in primary care and internal medicine subspecialties have already had their trial by fire conducting patient virtual visits, but for others, video-meeting platforms might be new turf.

Get rid of noise and potential distractions. The interview setting should be quiet and calm. That means ensuring that background noises, including pets and family members, aren't a factor. Ideally, opt for a completely quiet room — and house or apartment — if possible, and close windows to minimize street noise. Even minor background sounds, such as someone starting a washing machine two rooms away, can be bothersome enough to be overheard or, worse, distract the interviewee. Of course, it goes without saying that cell phones should be silenced and that all computer notifications that might chime during the session are turned off.

Ensure optimal body and face positioning. Even virtual-meeting veterans have likely found out the hard way that having the face positioned too far up or down and the computer screen below eye level can affect the experience. The interviewee's head should be looking straight ahead, not down toward a keyboard, which could be very distracting to the interviewer(s). If a candidate is hunched over, for example, that will be visible to interviewers.

Having the computer or device properly elevated before the interview begins is key, so that the physician doesn't need to make adjustments during the session. And once the session is underway, it's important to maintain focus by not moving the head too much or looking off to the side. Even if that feels somewhat stiff, it won't come across that way to the interviewer. It's OK to use some body language, when appropriate, but that should be kept to a minimum because there's not a large room to "absorb" it. Finally, physicians who aren't sure how best to position their devices should ask for help from someone with virtual-meeting experience before the interview. In any event, the interviewee and the equipment should be positioned to enable natural-seeming eye contact between all parties.

Get the technology in order. First and foremost, ensure that the Internet connection is solid and that the computer or device is fully charged

and updated, so that it's not likely to interject with an "update-needed" message. It's also a good idea to close out any applications and websites that might be running in the background, not only because of potential distraction but also to ensure that the call loads efficiently.

Second, although computers and devices have built-in speakers and some have microphones, the quality of that audio experience can vary considerably. Physicians who expect to attend multiple video interviews over a period of a few months should consider purchasing and installing high-quality USB audio technology. One of the frequent complaints that business people make these days about video meetings that involve potentially multiple attendees is that poor-quality audio from an attendee's computer is distracting.

The same goes for the video quality. Most laptops have an integrated web camera, but some might not, and older desktop computers likely don't have one. If the video quality on the computer is poor, it might be worthwhile to purchase a good-quality web camera. Then, ensure that it's optimally positioned — ideally above the screen — and look at the camera, not the screen, while speaking.

Finally, if the physician candidate might be asked to share a document or other item onscreen, preparing in advance is crucially important. Spending a fretful minute or two trying to get the requested item in view can be nerve-racking for the physician and possibly annoying for the interviewer.

Some aspects of interviews haven't changed


After physicians have prepared their environments and equipment to support a successful interview, they should remember that even with the pandemic, the expectation is that the proceedings will be business focused. Just because there's not a conference room in the mix, it doesn't mean that casual behavior is okay. It isn't. The session likely will be conducted formally and highly professionally. As such, interviewees should avoid chitchat or lengthy discussion about the pandemic unless the interviewer raises the topic and seeks their perspective.

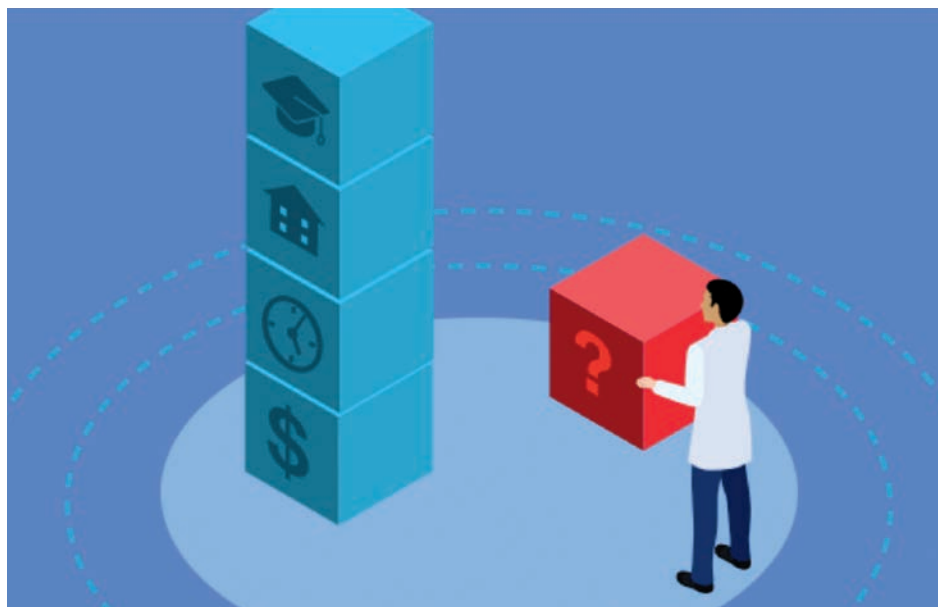
One thing to watch for in the video interview is that people sometimes talk over each other more than they might in a room, when they're anxious to make a point. That's never okay in a face-to-face meeting, and it's potentially more distracting (and apparent) within the confines of a video session. Because there is sometimes a brief lag after someone speaks, depending

on the technology in use, it's advisable to wait an extra second or two before speaking.

As with any interview, candidates should ask questions at the end of the interview — about culture, team makeup, and roles and responsibilities — and during proceedings if it's appropriate. Those questions should be prepared ahead of time. The candidate should also spend extra time researching the organization and reviewing any information that's available online about both the practice and the community. Without the benefit of a facility walkthrough, the physician candidate might need to elicit important information about the actual working environment, available equipment, and other factors that would affect daily practice. It also helps to keep the names of interview participants handy in any virtual roundtable interview involving more than three participants.

As with any type of interview, timely follow-up is important. Candidates should send an email thank-you note to key interviewers and any recruiter or staff member(s) who arranged the session, ideally within 24 hours. If the candidate is highly interested in the position, it's appropriate to express that in the thank-you note and to inquire about possible next steps.

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Unusual Parts of Compensation Packages

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

In speaking to so many about their job offers, I've realized that we're often myopic in terms of what we think can be negotiated when discussing a contract. There are the traditional things everyone asks about — salary, bonus structure, call responsibilities, vacation schedule, and signing bonuses, to name a few. However, when talking to people about what their ideal job looks like, there's often more random things on a wish list. What we fail to realize is that those are all things that can be asked for, but that nobody else would even think to offer them to sweeten the deal.

Some examples of these?

- An early start and end to the day
- Dedicated academic or administrative time
- Unique FTEs such as 0.7 or unique structuring of their FTEs, such as alternating four- and two-day weeks
- Bonuses for creation of alternative revenue streams for the practice

- Changes in the amount of allotted CME money or money for office furnishings or technology
- The ability to work from home a certain number of days a week (for example, doing telehealth)
- A specified patient population according to their area of academic interest/desired practice panel
- An increased number of support staff, such as scribes or medical assistants
- The speaker system that you will have in your operating room

Some of these may sound silly to you to ask for, but I know of physicians who have asked for and received these things as part of their contract negotiations. Remember, what brings happiness in your day-to-day life as a physician is very individualized, and therefore, asking for those things that will enhance your satisfaction (e.g., career longevity) at that job is not unreasonable.

Of course, asking for these things can be an art form. Understand that every institution has different flexibility or bandwidth for accommodating individual requests. You may want to look at what other accommodations have been made for other physicians on staff as precedent for what may be realistic prior to compiling your list of asks. Also, be careful about how many of these additional things you ask for. If you have 10 unusual requests, even if they are relatively minor, the message to the employer could be that this is a pattern of behavior where you will always be asking for exceptions to normal operating procedures.

Figure out which ones mean the most to you. Also figure out which ones are going to be harder to negotiate later, as your negotiating power is always greatest before you sign a contract. Be prepared to justify the asks so they understand why they would make accommodations. For example, if you are able to clearly articulate why something will lead to increased efficiency, lead to better patient outcomes, or contribute to your career longevity and prevent burnout, this would help your case. It would also help them to explain to others who question why these special accommodations were granted.

As demographics in medicine change, unusual asks will become more frequent. The sustainability of our health care workforce requires out-of-the-box solutions, and for some of you, these may be part of them! If you don't ask, you won't get it.

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CLINICAL PRACTICE

Patrick G. O'Malley, M.D., M.P.H., *Editor*

Sexual Dysfunction in Women

Susan R. Davis, M.B., B.S., Ph.D.

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.

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A 54-year-old woman presents with low libido, diminished arousal, and anorgasmia. She had undergone a hysterectomy and bilateral salpingo-oophorectomy at 49 years of age owing to menorrhagia and a family history of ovarian cancer. She has been using transdermal estradiol patches and topical vaginal estradiol and has no menopausal symptoms or dyspareunia. She is in a loving relationship with no major life stressors, does not have depression, and takes no other medication. All other clinical characteristics, including her weight and blood pressure, are normal. She has recently become aware that there may be treatment options for low libido and would like to discuss these with you. How would you respond?

THE CLINICAL PROBLEM

BECAUSE THERE IS NO UNIVERSAL DEFINITION OF NORMAL SEXUAL FUNCTION, what constitutes sexual difficulty is determined by a person's subjective definition of unsatisfactory sexual well-being. The condition is usually described as unsatisfactory interest, arousal, orgasm, or other aspects of sexuality (e.g., sexual self-image), and the symptoms often coexist. The term "sexual dysfunction" is used when at least one of the symptoms is of substantial concern to the affected person.¹ Sexual dysfunction negatively affects mental health, vitality, and social functioning and has an overall effect on quality of life that is of similar magnitude to that associated with chronic back pain or diabetes.²

CLASSIFICATION OF SEXUAL DYSFUNCTION IN WOMEN

The classification of sexual dysfunction in women continues to evolve, with the *International Classification of Diseases and Related Health Problems*, 11th revision (ICD-11), providing substantive changes to the classification, and hence the diagnosis, of sexual dysfunctions.³ The ICD-11 recognizes that sexual response is influenced by a complex interplay of biologic, psychological, and social factors (Table 1). Hence, sexual dysfunction is no longer defined as either related to or caused by a disease or medication (organic) or independent of an identifiable cause (nonorganic).³ This change is clinically important because it allows for associated factors to be recognized and, when possible, managed but does not prevent persons with associated factors from receiving treatment for sexual dysfunction.

Another modification is that the ICD-11 no longer categorizes all sexual dysfunctions according to male or female sex, because most determinants of sexual response are not sex-specific. Only arousal disorder in women and erectile dysfunction in men remain categorized as sex-specific sexual dysfunctions.³ Unlike the *Diag-*

KEY POINTS

SEXUAL DYSFUNCTION IN WOMEN

- Sexual dysfunction in women is common and is associated with impaired well-being and quality of life.
- Many women with sexual dysfunction will not seek care unless prompted by their health care provider. However, there are no evidence-based screening recommendations for sexual dysfunction as part of routine care.
- Sexual well-being is determined by a complex interplay of biologic, psychological, and sociocultural factors. Therefore, an assessment of sexual dysfunction involves a comprehensive review of the patient's general health and psychosocial circumstances and a history of the patient's use of prescription and nonprescription medications and other drugs.
- Management pathways for sexual dysfunction include lifestyle modification, counseling and psychosexual therapies, physical therapy, and pharmacologic therapy.

nostic and Statistical Manual of Mental Disorders, fifth edition,⁴ the ICD-11 has retained hypoactive sexual desire dysfunction and arousal dysfunction as separate conditions because they have differing etiologic characteristics and risk factors and, in most cases, are associated with different psychological and biologic interventions.¹ Table 1 provides descriptions of sexual dysfunctions.

Although sexual pain disorders may contribute to other sexual dysfunctions,⁵ both sexual pain disorders and persistent genital arousal disorder are classified separately in the ICD-11³ and are not discussed in detail here. However, vaginal symptoms that cause dyspareunia are common, and treatment options are described below.

PREVALENCE OF SEXUAL DYSFUNCTION IN WOMEN

Contemporary data regarding the prevalence of sexual dysfunction across the adult female life span are limited, in part because several epidemiologic studies have excluded women who were either sexually inactive or unpartnered or did not include assessments of the degree to which the sexual concern caused distress, which is a necessary criterion for the identification of sexual dysfunction. In addition, findings from some studies are difficult to reconcile owing to the use of different questionnaires for sexual function and sexual distress. For example, in a population-based German study involving 2059 women, 19.4% of the younger participants (18 to 24 years of age) and 31.5% of the older participants (46 to 55 years of age) had low desire; hypoactive sexual desire dysfunction with severe distress in the previous 12 months was reported in 6.2% of participants in the younger age group and 7.3% of participants in the older age group.⁶ In contrast, a contemporaneous population-based Australian study involv-

ing 10,554 women who answered validated questionnaires showed that 27.4% and 58.9% of women 18 to 24 years of age and 45 to 49 years of age, respectively, had low desire, and 12.2% and 31.6%, respectively, had hypoactive sexual desire dysfunction.⁷ The discrepancies between the studies reflect different wordings of the questions used, combined with the severity of distress required to classify a participant as having a dysfunction. Nonetheless, both show that low desire progressively increases with age, and sexually-associated distress concurrently declines, so that the peak in hypoactive sexual desire dysfunction in women emerges during midlife (Fig. 1).⁷

The prevalence of arousal dysfunction and orgasm dysfunction is also unclear. The percentages of women with unspecified arousal dysfunction that have been reported in population-based studies are 3 to 9% among women 18 to 44 years of age,^{6,8,9} 5 to 7.5% among women 45 to 64 years of age,^{6,8} and 3 to 6% among women 65 years of age or older.^{6,8} Anorgasmia with distress has been reported to affect 7 to 8% of women younger than 40 years of age, approximately 5 to 7% of women 40 to 64 years of age, and 3 to 6% of women 65 years of age or older in studies conducted in Europe, the United States, and Australia.^{6,8,9}

The most common sexual difficulty with associated distress in women younger than 40 years of age is poor sexual self-image, a characteristic that was observed in 13.4% of women of this age group in a large Australian study.¹⁰ Risk factors for low sexual self-image dysfunction included breast-feeding, overweight and obesity, and having a partner.¹⁰ A disturbing finding was that 30% of the participants scored above the threshold for sexually related personal distress but did not

Table 1. Summary of ICD-11 Classification of Sexual Dysfunction in Women.*

Dysfunction Category	Manifestation or Description
Hypoactive sexual desire dysfunction†	Absence or marked reduction in desire or motivation to engage in sexual activity as manifested by any of the following: reduced or absent spontaneous desire, reduced or absent responsive desire to erotic cues and stimulation, or inability to sustain desire or interest in sexual activity once initiated
Sexual arousal dysfunction†	Despite the desire for sexual activity and adequate sexual stimulation, absence or marked reduction in any of the following: genital response (vulvovaginal lubrication, genital engorgement, or genital sensitivity), nongenital responses (hardening of nipples, flushing of skin, or increased heart rate, blood pressure, or respiration rate), or feelings of sexual arousal (sexual excitement and sexual pleasure)
Orgasmic dysfunction	Absence or marked infrequency of the orgasm experience or markedly diminished intensity of orgasmic sensations, including marked delay in orgasm, despite desire for sexual activity and orgasm and adequate sexual stimulation
Other or unspecified sexual dysfunction	Not specified

* For classification purposes, symptoms should have been episodic or persistent over a period at least several months and associated with clinically significant distress. Etiologic considerations include associations with any of the following: a medical condition, injury, or the effects of surgery or radiation treatment; psychological or behavioral factors, including mental disorders; use of psychoactive substance or medication; lack of knowledge or experience; associated with relationship factors; cultural factors; and other specified etiologic considerations (e.g., gender incongruence, changes in anatomy, pregnancy, postpartum status). ICD-11 denotes the *International Classification of Diseases and Related Health Problems*, 11th revision.

† Subcategories include lifelong, acquired, generalized, situational, and unspecified.

have a specific sexual difficulty.¹⁰ Although several factors were independently associated with nonspecific sexual distress (receiving current treatment for infertility, taking psychotropic medication, smoking, alcohol consumption, and being in paid employment) other potential determinants, such as relationship issues and abuse, were not captured.

COMMON CONTRIBUTING HEALTH CONDITIONS

Estrogen insufficiency is a hallmark of menopause, hypothalamic amenorrhea, hyperprolactinemia, hypopituitarism, and antiestrogen therapy (aromatase inhibitors or selective estrogen-receptor modulators). Low sexual desire may be related to estrogen-insufficiency symptoms such as hot flashes and night sweats, mood change, sleep disturbance, or vulvovaginal dryness.¹¹ Low testosterone levels have not been consistently associated with low orgasm satisfaction; however, in one analysis, when sociodemographic factors were taken into consideration, low testosterone was independently associated with low orgasm satisfaction in premenopausal women.¹⁰ Serum testosterone levels have not been consistently associated with sexual function in postmenopausal women,^{12,13} but representative studies that use a more pre-

cise measurement of testosterone are still needed. Other endocrine disorders associated with a greater likelihood of sexual dysfunction include adrenal insufficiency (including adrenal suppression by systemic glucocorticoids),¹⁴ diabetes,¹⁵ and polycystic ovary syndrome.¹⁶

Chronic disease, particularly conditions that reduce mobility or cause chronic pain, mental health conditions, pelvic-organ prolapse, and cancer therapy may all contribute to sexual dysfunction.¹ An array of psychosocial factors may underlie sexual dysfunction, including relationship difficulties, poor self-image, past or current abuse, stressors, and sociocultural beliefs and expectations.^{1,17} Both depressive symptoms and psychotropic medications are independently and bidirectionally associated with sexual dysfunction.¹⁸

Findings from a randomized, controlled trial suggest that the use of combined oral contraceptives may cause low sexual desire.¹⁹ However, simply switching contraceptive pills can provide substantial improvement in sexual function, irrespective of the androgenicity of the progestin in the new preparation.²⁰ Other common medications can cause sexual dysfunction — notably cardiac and antihypertensive medications.^{1,17}

Figure 1. Prevalence of Sexual Dysfunction in a Representative Sample of 10,554 Women in a Community-Based Australian Study.⁷

Women 18 to 39 years of age completed the Profile of Female Sexual Function (PFSF), and all others completed the Female Sexual Function Index (FSFI). Responses of “never” or “seldom” to the question “How often in the past 30 days did the following statement apply to you? ‘I felt sexual desire’” on the PFSF indicated low desire, and responses of “almost never or never” or “a few times” to the question “How often did you feel sexual desire and interest?” on the FSFI indicated low desire (Panel A). Sexually associated distress was assessed among women in all age groups with the use of the Female Sexual Distress Scale–Revised (Panel B). Hypoactive sexual desire dysfunction was defined as the presence of both low desire and sexually associated distress (Panel C). Percentages shown are absolute percentages, with I bars indicating 95% confidence intervals.

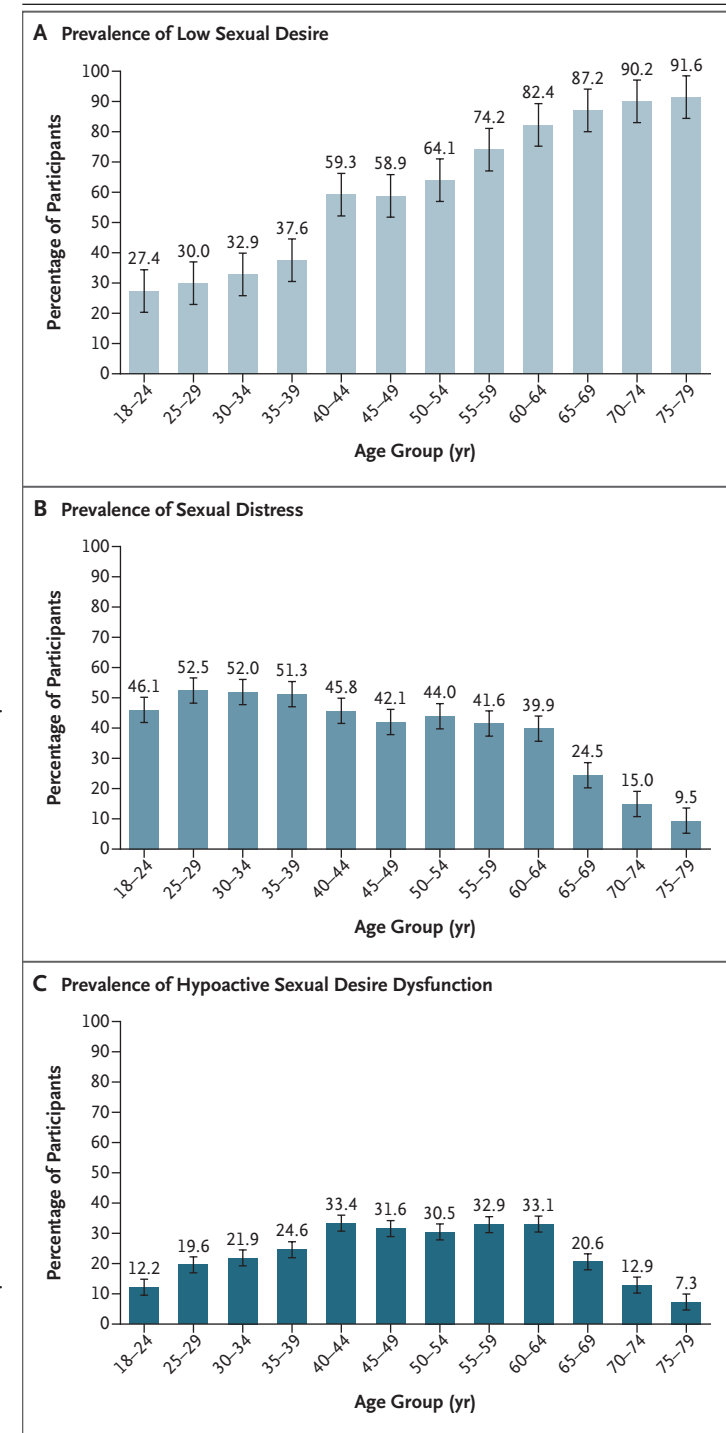
STRATEGIES AND EVIDENCE

ASSESSMENT

Available data suggest that less than 50% of persons with sexual difficulties that cause them distress seek help.²¹ Persons younger than 35 years of age are most likely to seek support from the Internet, whereas older persons are more likely to consult a doctor.²¹ This difference highlights the potential importance of incorporating screening for sexual difficulties in routine clinical care, although there are no available screening trials evaluating this strategy.

It is crucial to recognize that women who are unpartnered or sexually inactive may have sexual dysfunction¹⁸ and that sexual dysfunction does not have an age limit. One strategy to ascertain information regarding a patient’s sexual function is to pose an open-ended question as to whether the patient has any sexual concerns.^{1,22} It is helpful to normalize the conversation by reassuring the patient that sexual concerns are common. If a concern is identified, a simple framework can be applied that comprises eliciting the patient’s story; providing a name to or, if more appropriate, reframing the concern in a meaningful way for the patient; acknowledgment of the issues and challenges being met by the patient; and either making time for further assessment or, if preferred by the patient, referring the patient for care.^{1,22} This approach informs treatment options that are described below.

Full assessment will guide the management



and referral pathways (Table 2). Establishing the recency of onset and whether the problem is generalized, situational, or partner-specific is important. For example, life-long sexual dysfunction is addressed by means of psychosocial care, whereas dysfunction that arises after bilateral oophorec-

Table 2. Checklist of Factors to Be Considered in the Assessment of Sexual Dysfunction in Women.**Biologic and hormonal factors**

Sex-hormone insufficiency

Depression

Illness

Fatigue

Urinary incontinence

Prescription and nonprescription medication

Alcohol or other drug use

Intrapersonal development history

Trauma (sexual, physical, emotional, or medical)

Negative emotions (anxiety, fear, shame, or guilt)

Poor body image

Gender-identity concerns

Level of education

Expectation of negative outcomes

Past disappointing or painful sex

Interpersonal issues

Lack of a partner

Relationship discord

Absence of emotional intimacy

Contextual factors

Lack of privacy

Safety concerns

Emotional rapport

Cultural norms and religious beliefs

Lack of appropriate stimuli

Lack of knowledge regarding sexual stimulation

Partner's ill health or sexual dysfunction

sexual function, so their use should be ascertained.

Physical examination should be guided by the medical history, such as breast examination for galactorrhea if hyperprolactinemia is suspected. Similarly, biochemical assessments and imaging should be performed on the basis of the medical history and examination findings. Hormone measurement and other biochemical testing should be performed only to identify a clinically suspected endocrinopathy or to monitor a known condition. Measurement of testosterone levels offers no diagnostic usefulness because there is no serum testosterone level below which a female patient can be classified as being testosterone-deficient.²³ Serum testosterone should only be measured to provide a baseline value if testosterone therapy is to be initiated.²³

MANAGEMENT

The management of sexual dysfunction should be guided by the patient's concerns and wishes, as well as by their physical and psychological health and social circumstances, and may involve a partner. Treatment options are summarized in Table 3.

Attention should be given to potentially modifiable factors. When possible, medications known to be associated with sexual dysfunction, most commonly antidepressant therapy, should be modified or changed. Lifestyle interventions may reduce sexual difficulties.⁴⁰ For example, a post hoc analysis involving women with diabetes and obesity showed that lifestyle intervention might reduce generalized sexual dysfunction, with 28% of persons included in the analysis no longer meeting the diagnostic criteria for sexual dysfunction after lifestyle interventions, as compared with 11% of those who received supportive care.⁴¹

Psychosocial interventions are frequently effective in treating sexual dysfunction.²⁴ These interventions may be in the form of sexual counseling, body awareness counseling, cognitive therapy, couples counseling, or referral to a psychologist (if a mood disorder is identified). Targeted sexual therapy may involve pelvic-floor relaxation training, vaginal dilator therapy (in women with vaginismus),⁴² and clitoral devices that may improve clitoral sensation and orgasm in women with an arousal disorder.⁴³ The efficacy of each of these interventions is difficult to quantitate be-

cause studies have included small, heterogeneous samples across different age ranges and with different outcomes.^{24,25,42,43}

PHARMACOTHERAPY

Although estrogen therapy is not a treatment for generalized sexual dysfunction, hormone therapy should be considered for menopausal symptoms that are troubling to the patient, because symptom relief may reduce sexual symptoms. Dyspareunia due to estrogen insufficiency can be treated with a local topical vaginal estrogen cream, pessary, or ring; prasterone (a form of dehydroepiandrosterone for vaginal use); oral ospemifene; or vaginal moisturizers.⁴⁴ Vaginal erbium and carbon-dioxide laser therapy have been promoted for relief of dyspareunia. However, in 2018 the Food and Drug Administration warned against the use of these therapies owing to insufficient evidence to support their efficacy and safety for the treatment of dyspareunia.⁴⁵

Flibanserin and bremelanotide are approved in the United States for treatment in premenopausal women with generalized, acquired hypoactive sexual desire dysfunction. Flibanserin is thought to disinhibit pathways involved in sexual desire. Studies involving both premenopausal and postmenopausal women with hypoactive sexual desire dysfunction showed sufficient efficacy for the approval of flibanserin for premenopausal women in the United States.³¹ The efficacy of flibanserin is modest.³¹ In a meta-analysis of eight trials including 5914 participants, flibanserin was shown to have increased the number of satisfying sexual experiences per month by 0.5 but with considerable side effects (e.g., dizziness, somnolence, nausea, and fatigue). Bremelanotide is a melanocortin receptor agonist that is thought to increase dopamine release and thus increase excitation in brain regions that are associated with sexual desire.⁴⁶ A combined analysis of two trials involving 1267 participants showed a modest improvement in sexual desire and decrease in distress related to low sexual desire with bremelanotide but more nausea, flushing, and headache side effects than with placebo.³²

There are no therapies approved in North America for postmenopausal women with hypoactive sexual desire dysfunction, but testosterone has been prescribed off-label for hypoactive sexual desire dysfunction since the 1940s.⁴⁷ A trans-

dermal testosterone patch was approved in Europe for surgically postmenopausal women having hypoactive sexual desire dysfunction despite adequate estrogen therapy,³⁵ but the patch was removed from the market by the manufacturer when the approval was not extended to naturally menopausal women, despite clinical trial data showing efficacy of the patch in those women that was similar to that seen in surgically postmenopausal women.⁴⁸ A transdermal 1% testosterone cream⁴⁹ has been approved in Australia for the treatment of postmenopausal women with hypoactive sexual desire dysfunction.

An international task force evaluated the available clinical trial data and concluded that transdermal testosterone therapy, which restores serum testosterone levels to approximately those seen in premenopausal women, is moderately effective for the treatment of postmenopausal hypoactive sexual desire dysfunction. Table 3 provides a summary of the trial evidence.²³ The task force recommended against the use of oral testosterone therapy owing to potential adverse effects related to lipoprotein levels and inconsistent absorption.²³ Clinical trial data have shown that transdermal testosterone, when administered at the recommended doses, may cause a small but significant increase in the likelihood of acne, growth of facial or body hair, and weight gain, and long-term safety data are lacking.³⁴

Nonetheless, it has been estimated that more than 2 million prescriptions of testosterone are written each year for women in the United States, many of which are probably for compounded preparations.⁵⁰ Compounded formulations are not subject to requirements for pharmacokinetic profiling, and their uncertain absorption may cause overdose and harm.²³ The international task force recommendation that if an approved female-specific testosterone formulation is unavailable and testosterone therapy is considered indicated for treatment of postmenopausal hypoactive sexual desire dysfunction, the preferred option is a fractionated dose of a regulator-approved male formulation.²³ When transdermal testosterone is prescribed, regular monitoring of serum testosterone concentrations and clinical assessment for signs of androgen excess are recommended.²³

Systemic dehydroepiandrosterone therapy has not been shown to improve sexual dysfunction in randomized, double-blind clinical trials involving women with intact adrenals⁵¹ or with adrenal

tomy may be effectively treated with hormone replacement. A full history will provide information about menstrual irregularity in premenopausal women (possibly due to stress or to hormonal disorders such as hyperprolactinemia or polycystic ovary syndrome), vulvovaginal atrophy symptoms that occur after menopause (e.g., vaginal dryness or irritation [dyspareunia]), pelvic floor disorders (urinary incontinence, fecal incontinence, or prolapse, which may contribute to loss of desire), gynecologic surgery (residual discomfort or concerns about sex), dyspareunia, and vaginismus. Both prescription and nonprescription medications, as well as alcohol consumption and the use of other drugs, may affect

Table 3. Recognized Treatment Options.*

Category and Treatment	Strength of Evidence	Potential Adverse Events
Nonpharmacotherapy		
Psychosocial therapy — sexual education and counseling, body awareness, cognitive therapy, couples therapy, social interventions	Varies; primarily from small trials in differing populations ^{24,25}	Not applicable
Physical therapy — pelvic floor physiotherapy; FDA-approved clitoral vacuum device may improve sensation, lubrication, orgasm with or without arousal disorder	Varies according to patient population ²⁶	Not applicable
Pharmacotherapy†		
Vaginal dryness causing dyspareunia	Constituents vary; some may cause irritation, impair sperm motility, or contain parabens ²⁷	
Lubricants for vaginal dryness associated with sexual activity ^{27,28}	Moderate evidence for reduced dyspareunia ^{27,28}	
Vaginal moisturizers for dryness, itch, and soreness ²⁷	Strong evidence for reduced dyspareunia ^{27,28}	
Vaginal dryness in postmenopausal women		
Estradiol vaginal tablet (FDA-approved at a dose of 0.01 mg nightly for 2 wk, then 2 or 3 times per wk); estradiol ovule (0.5 mg nightly for 2 wk, then 2 or 3 times per wk); estradiol cream (0.5 mg nightly for 3 wk, then 2 times per wk); estradiol gel (0.05 g nightly for 3 wk, then 2 times per wk); estradiol 0.01% cream (FDA-approved at a dose of 2 to 4 g daily for 1 to 2 wk, then 1 g applied 1 or 2 times per wk); estradiol 2-mg ring (FDA-approved at a dose of 0.0075 mg per day, replaced every 90 days; and conjugated estrogen cream 0.625 mg per gram (FDA-approved for cyclic use of 0.5 to 2 g intravaginally once daily for 21 days, then off for 7 days)	Moderate efficacy shown for vaginal dryness and dyspareunia, with similar efficacy in all formulations ²⁹	Vaginal discharge, vulvovaginal candidiasis, vaginal bleeding, and breast pain; dose and formulation dependent ³⁰
Prasterone insert (6.5 mg nightly)‡	Strong evidence of reducing dyspareunia ²⁸	Vaginal discharge ³⁰
Ospemifene tablet (60 mg taken orally once daily)‡	Moderate evidence of improvement in sexual function ²⁸	Vasomotor symptoms, vaginal discharge and candidiasis, may increase endometrial thickness ²⁸
Hypoactive sexual desire dysfunction in premenopausal women		
Flibanserin (100 mg taken orally once daily at bedtime)‡§	Evidence of modest effect (approximately 0.5 to 0.65 additional satisfactory sexual events per month) ³¹	Somnolence, sedation, or fatigue (28%) ³¹ ; owing to potential hypotension and syncope, caution regarding alcohol consumed within 2 hr before or after taking flibanserin; contraindicated with concurrent strong CYP3A4 inhibitor medication or liver impairment ³¹
Bremelanotide (1.75 mg administered subcutaneously 45 min before sexual activity)‡	Evidence of modest effect on sexual desire vs. placebo (0.35-point difference out of a possible total score of 5); no evidence for increased satisfactory sexual events ³²	Nausea (40% of patients; may resolve with use), facial flushing (in 20%), headache (in 11%) ³²

Hypoactive sexual desire dysfunction in postmenopausal women		
Transdermal testosterone 1% cream (0.5 to 1 ml applied topically once daily); off-label in most countries; female-specific 1% transdermal testosterone cream approved in Australia and South Africa	Low-quality clinical trial evidence for this formulation ³³ ; strong evidence for transdermal testosterone overall ³⁴ ; increase in 1–1.4 satisfactory sexual events per month ^{35,36}	Acne, increased hair growth, and weight gain. ³⁴
Genital arousal dysfunction in premenopausal and postmenopausal women		
Sildenafil for spinal cord injury–associated arousal dysfunction (50 mg taken before sexual encounter) ³⁸	Improved subjective arousal in small double-blind trial ³⁸	Headache, flushing, and dyspepsia. ³⁷
Sildenafil for antidepressant-associated arousal dysfunction (50 mg taken before sexual encounter) ³⁷	Low-quality evidence from small open-label trial ³⁷	
Tadalafil for type 1 diabetes-associated arousal dysfunction (5 mg daily) ³⁹	Low-quality evidence from small open-label trial ³⁹	

* Specialized interventions for sexual pain disorders or hyperactive sexual desire dysfunction are not included. FDA denotes Food and Drug Administration.

† The availability of hormonal and nonhormonal treatments and indications for use from regulatory bodies vary among countries.

‡ This use is FDA-approved.

§ This use is approved in Canada for persons up to 60 years of age.

GUIDELINES

The International Society for the Study of Women’s Sexual Health has published processes of care for the identification of sexual concerns and problems in women¹ and for the assessment of hypoactive sexual desire dysfunction.¹⁷ The processes of care are valuable resources for enhancing the skills and capabilities of both primary health care providers and medical specialists. The Global Consensus Position Statement on Testosterone for Women, developed and endorsed by leading women’s health groups worldwide and available in 14 languages, provides comprehensive guidance regarding the use of testosterone therapy in women.²³ The recommendations in this article align with these guidelines.

AREAS OF UNCERTAINTY

Clarification of the prevalence of sexual dysfunction relies on an investment in quality epidemiologic studies that are inclusive of all women, irrespective of gender identity, sexual preference, and partner status. Furthermore, the understanding of the physiology of female sexuality has been constrained by the necessary reliance on animal models, anatomical and functional studies involving humans, and imaging. The uncertainty of the biologic features of the brain in sexual function and in turn the development of pharmacotherapies. Clinical trials to further evaluate available psychosocial interventions and pharmacotherapies are still needed. Consequently, treat-

insufficiency.⁵² Bupropion and buspirone are psychotropic medications that have been used off-label in patients with sexual dysfunction, but efficacy and safety data are insufficient, and currently neither therapy can be recommended.¹⁷

Effective pharmacotherapies for arousal and orgasm dysfunction are lacking. Small studies suggest potential benefits of phosphodiesterase-5 (PDE5) inhibitors for arousal difficulties in women with spinal cord injury³⁸ and antidepressant-associated arousal dysfunction.³⁷ PDE5 inhibitors have also shown promise for the treatment of genital arousal dysfunction in women with type 1 diabetes.³⁹ There is no evidence of benefit of PDE5 inhibitor therapy in healthy women with arousal dysfunction.⁵³

ment algorithms, particularly regarding arousal and orgasm dysfunction, remain inadequate because they are limited to modification of contributing factors, counseling, and physical therapies.

CONCLUSIONS AND RECOMMENDATIONS

With regard to the patient described in the vignette, I would seek to identify relationship issues, major psychosocial contributors, or modifiable factors and to determine whether the loss of libido was of meaningful concern to the patient. If the

diagnosis of hypoactive sexual desire dysfunction was established, I would address any psychosocial issues as appropriate, and I would discuss treatment options. In most countries, the approach would involve off-label pharmacotherapy, with the most evidence-based option currently being the administration of transdermal testosterone at a dose appropriate for a female patient. Unfortunately, this case highlights the ongoing inadequacy of treatment options for women with sexual dysfunction.

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

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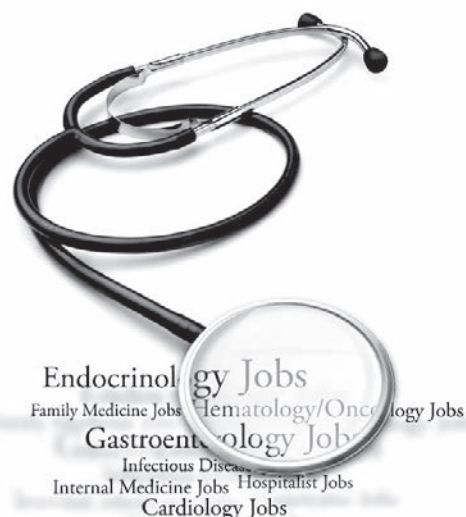
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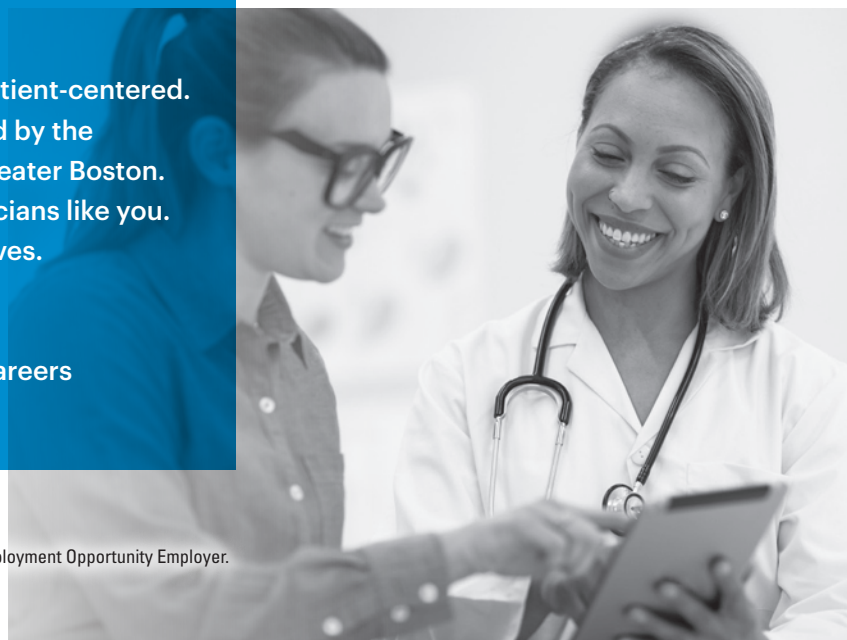
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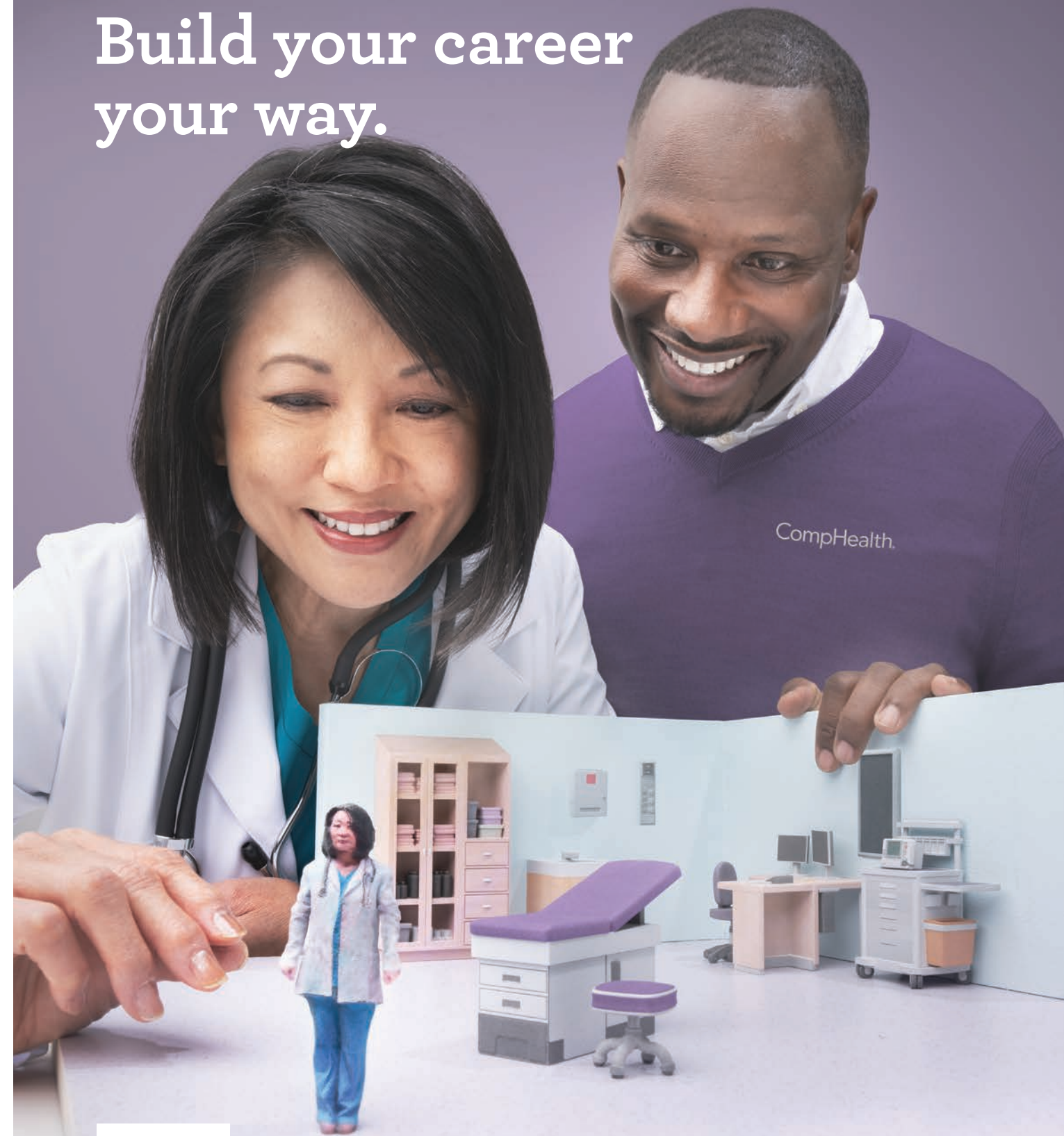
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Joseph Li, MD - Chief of Hospital Medicine
JLi2@bidmc.harvard.edu

and

Rusty Phillips, MD - Director of Recruitment
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Non-Invasive Cardiologist

North Suffolk Cardiology (NSC), an affiliate of Stony Brook University Hospital, is a full-service, outpatient, cardiology physician practice, offering a wide range of expertise in cardiovascular health and wellness. North Suffolk Cardiology has four office locations that span the north Suffolk region of Long Island, and fourteen highly specialized, well-trained physicians and 11 advanced practice providers who see over 40,000 patient visits per year - making NSC the largest cardiology physician practice on the north shore.

NSC provides comprehensive cardiovascular care by using state-of-the-art technology in PET/CT, SPECT, echo/vascular ultrasound services, as well as education in nutrition and lifestyle management to promote proper cardiovascular health. NSC offers interventional procedures to treat coronary artery disease, heart valve disorders, and other heart conditions, and also houses a device clinic that offers holter and event monitoring for patients with heart rhythm disorders. Intensive cardiac rehab services are also offered on-site for patients who are rehabilitating after an experiencing significant cardiac event and procedure.

North Suffolk Cardiology is seeking a non-invasive cardiologist to join their rapidly growing practice. The ideal candidate is BE/BC in cardiology, nuclear cardiology, and echocardiography. Excellent compensation package.

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Department of Medicine Division of Hospital Medicine

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dhmrecruitment@wustl.edu

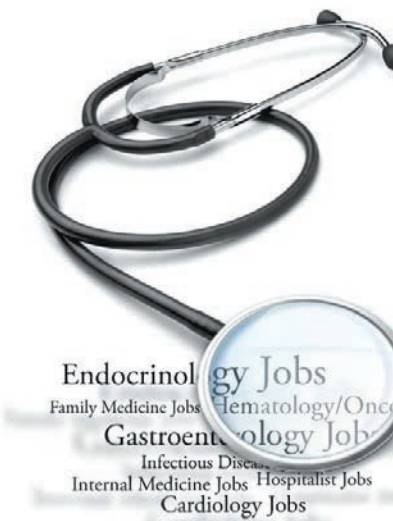
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Electrophysiologist

North Suffolk Cardiology (NSC), an affiliate of Stony Brook University Hospital, is a full-service, outpatient, cardiology physician practice, offering a wide range of expertise in cardiovascular health and wellness. North Suffolk Cardiology has four office locations that span the north Suffolk region of Long Island, and fourteen highly specialized, well-trained physicians and 11 advanced practice providers who see over 40,000 patient visits per year - making NSC the largest cardiology physician practice on the north shore.

NSC provides comprehensive cardiovascular care by using state-of-the-art technology in PET/CT, SPECT, echo/vascular ultrasound services, as well as education in nutrition and lifestyle management to promote proper cardiovascular health. NSC offers interventional procedures to treat coronary artery disease, heart valve disorders, and other heart conditions, and also houses a device clinic that offers holter and event monitoring for patients with heart rhythm disorders. Intensive cardiac rehab services are also offered on-site for patients who are rehabilitating after an experiencing significant cardiac event and procedure.

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LI CHEN Ph.D.

Founder, Executive Director, CEO

Dr. Li Chen, Executive Director and Chief Executive Officer, founded and leads Hua Medicine to discover and develop clinically differentiated medicine in China for Global. Under his leadership, Hua Medicine has successfully brought a disease modifying first-in-class glucokinase activator (GKA) HuaTangNing (华堂宁®) (dorzagliatin tablets, HMS552) into the China market. Dorzagliatin is approved by the National Medical Products Administration (NMPA) of China for type 2 diabetes with its unique mechanism of action in restoring the impaired glucose homeostasis.

Q: What motivates you to develop new medicines for diabetes?

Dr. Chen: In 2010, Professor Wenyang Yang, a leading Chinese expert in diabetes, published an epidemiological study on diabetes prevalence in China. In this study, Professor Yang's team used the oral glucose tolerance test to diagnose diabetes and prediabetes. The results showed that the prevalence of diabetes and prediabetes in China had already reached 9.7% and 15.5%, respectively, making China the country with the highest number of diabetes cases globally. It was this paper that inspired me to focus on the field of diabetes and metabolic disorders. I selected glucokinase (GK) as a therapeutic target for diabetes due to my involvement in the development of glucokinase activators (GKAs) at Roche during that time. GK is a glucose sensor, regulating the secretion of key hormones such as insulin, glucagon, and glucagon-like peptide-1 (GLP-1) in response to fluctuations in blood glucose levels, thereby maintaining glucose homeostasis. Recognizing the critical role of GK in glucose metabolism, we developed dorzagliatin, a GKA designed to restore proper glucose regulation.

Q: What led to your success in the development of GKA?

Dr. Chen: First, the mechanism of action of dorzagliatin is unique. It functions as an ectopic allosteric GK full activator, with minimal impact on GK's Hill coefficient, thereby preserving the kinetic cooperativity between GK and glucose. This ensures that GK is activated in response to changes in blood glucose levels. Furthermore, dorzagliatin acts on

GK targets in three key organs involved in blood glucose regulation—the pancreas, liver, and intestines—activating GK within these organs to restore physiological glucose homeostasis. Secondly, Hua Medicine has consistently employed a steady and methodical approach, focusing on generating robust data to support the regulatory approval and clinical application of dorzagliatin. In 2017, we launched a multicenter phase 3 clinical trial involving 110 hospitals across China. At the time, conducting such a large-scale, randomized controlled trial for a first-in-class drug in China was rare. However, the broad geographic distribution of research centers allowed more medical professionals to gain firsthand experience with this novel GKA and ensured that our patient population was more representative. Finally, dorzagliatin has garnered strong support and trust from both the government and the clinical community. These factors, combined with the strength of scientific research, have served as both internal and external drivers of our success.

Q: What are your visions for the future of diabetes treatment?

Dr. Chen: First, I believe that GKAs hold significant therapeutic potential for diseases currently considered complications of diabetes, such as diabetes-related cognitive impairment, which are driven by dysregulation of glucose homeostasis. Secondly, since GK is upstream of both glucose and lipid metabolism pathways, it may play a key role in weight management, promoting muscle mass while reducing body fat. This presents novel strategies

for managing diabetes and related metabolic disorders. Thirdly, our team is investigating the excessive secretion of insulin, GLP-1, and other hormones caused by hyperactive glucokinase. We are developing allosteric modulators or inhibitors to downregulate glucokinase activity in order to address this challenge. Additionally, we are investigating the potential of combining GKAs with existing diabetes treatments, aiming to provide physicians with a broader range of therapeutic options. In summary, as a glucose sensor, GK presents important scientific questions and offers promising clinical applications not only for the treatment of diabetes and its complications but also for potentially broader medical fields.

Hua Medicine

Hua Medicine is an innovative drug development and commercialization company based in Shanghai, China, with companies in the United States and Hong Kong, China. Hua Medicine focuses on developing novel therapies for patients with unmet medical needs worldwide. Based on global resources, Hua Medicine teams up with global high-calibre people to develop breakthrough technologies and products, which contribute to innovation in diabetes care. Hua Medicine's cornerstone product HuaTangNing (华堂宁®) (dorzagliatin tablets), targets the glucose sensor glucokinase, restores glucose sensitivity in patients with type 2 diabetes, and stabilizes imbalances in blood glucose levels in patients.

Section Chief in Gastroenterology/Hepatology

8/12/2024 position # 20001220

**Augusta University's Medical College of Georgia,
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