What happy physicians have in common: A qualitative study of workplace perceptions of physicians with low burnout scores

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Abstract

Introduction: Burnout is a phenomenon in the medical field that adversely affects patient care, physician retention, and physician well-being. The preponderance of burnout research has primarily focused on exploring what parts of medical practice and individual characteristics contribute to burnout. Our research aims to add to the growing body of evidence exploring what physicians who love their work have in common.

Methods: Physician participants in this qualitative study were recruited through their local medical society from those who indicated a willingness to share tips for joy in practice. Potential participants were then screened for low probability of burnout using a validated single-item burnout inventory. Nine primarily mid- to late-career physicians engaged in semistructured interviews and thematic analysis was used to analyze data. Of the interviewed physicians, five were practicing in the primary care specialties of family or internal medicine and four in specialties outside of primary care.

Results: Six major themes arose from the nine interviews and included variety in work, a sense of empowerment, connection with patients, visible impact of one's work, feelings of community with coworkers and colleagues, and experiencing a sense of calling.

Conclusion: While further research is needed to demonstrate the transferability of the themes from these interviews, an asset-rooted approach to physician wellness is a direction for research and intervention that deserves further attention. Focusing only on alleviating the factors that contribute to burnout is a worthy goal, but ignores the necessity of designing training systems and workplaces that are built to foster the elements of medicine that bring joy and fulfillment to practice.

Keywords

Burnout, physician resiliency, healthcare training

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Introduction

Burnout is a phenomenon characterized by the constellation of depersonalization, emotional exhaustion, and feelings of diminished personal accomplishment.¹ High burnout rates have plagued service professions for decades, but recent reports show that the incidence of burnout in the medical field is rising at an alarming rate, with reported prevalence of greater than 50% in physicians.² In comparison, the average burnout rate for general full-time professionals is 23%.^{3,4}

The high prevalence of burnout among healthcare providers is concerning for a number of reasons. Burnout severity is a significant predictive factor for individuals leaving the healthcare profession and is correlated with depression.^{5,6} A 2016 cross-sectional study of 422 family physicians and general internists found that those who reported burnout had 4.94 times the odds of expressing intent to leave the practice compared with those who did not report burnout (95% confidence interval (CI) = 3.10-7.85).⁷ The increased odds of

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intent to leave practice may pose a problem, especially in rural and underserved regions where primary care shortages are already a concern.

While there are overlaps in characteristics of burnout and depression, the relationship between the two is a topic that continues to be explored. Some have argued that the correlations and overlapping symptoms between the two are mere coincidences and do not have a causal relationship.⁸ Others have discussed that illnesses such as depression are consequences of physician burnout (along with increased odds of alcohol abuse, suicide, and motor vehicle crashes).^{6,9–11} Burnout has been argued to be better conceptualized as a depressive condition.^{12,13} Interestingly, a recent cross-sectional study of 1354 physicians found that depression but not burnout is associated with suicidal ideation.¹⁴ Despite this finding, more work is needed to examine the relationship between burnout, depression, and a physician suicide rate that remains well above the general population.^{15,16}

Another area that has gained attention over the years is the concern that physician burnout negatively affects quality of care and patient satisfaction. While numerous studies have found that provider burnout results in poorer quality of care, more recent research, including a large meta-analysis, have been less conclusive in this correlation.^{17–20} The first conference on burnout occurred decades ago in Krakow, Poland in 1990.²¹ Despite this turning point for academic research in burnout, three decades later, there are still significant gaps in our understanding of the burnout phenomenon and in developing effective approaches for remediating or preventing it. With the majority of modern burnout literature focusing on the negative aspects of physician work life, comparatively few studies have explored the positive factors that sustain resiliency.

Perhaps the largest work to date with physician joy as the focus has been the Institute for Healthcare Improvement (IHI) white paper on creating joy in the healthcare workplace. These authors proposed nine critical components for experiencing joy in work, with the onus for a systems improvement approach squarely placed on the shoulders of clinical leadership.²² Other work has suggested that physician joy may be analogous to the pinnacle of self-actualization in Maslow's hierarchy of needs—positing that mental health, physical safety, and operational efficiencies are prerequisites to finding joy and connection in work.²³ Our hope is to add to this growing body of research by further discovering and naming what joyful and fulfilled physicians have in common.

Methods

Study design

In 2015, the increasing rate of burnout arose as a major concern for members of the Western Carolina Medical Society (WCMS) when they were surveyed to help shape the organization's strategic plan. A follow-up survey asked members whether they would be willing to share experience and ideas for how to maintain joy in practice. Using purposive sampling with permission of the WCMS and Institutional Review Board approval through the University of North Carolina, we contacted those physicians who had indicated an interest in sharing their experiences. Through email, these individuals were asked whether they would be willing to participate in a qualitative study investigating what gives physicians joy and meaning in their practice. Twelve physicians expressed a desire to participate in our study and were asked to complete a single-item burnout tool validated against the lengthier Maslach Burnout Inventory.²⁴ Of the 12 physicians who completed the survey, nine met the inclusion criteria of a low likelihood of suffering from burnout. A low likelihood of burnout was defined as a response of "a few times a month" or less on the single-item question, "I feel burned out from my work"-correlating with a 36% or less pooled risk of burnout in the validation study by West et al. While specific support was not available through our research team for those with higher levels of burnout, our interviews did coincide with the creation of the "Healthy Healer Program" by WCMS through which all physician-members were invited to participate in free therapy, professional coaching, and other wellness programs.

The undergraduate researcher (T.C.), who had no prior relationship with study participants, then conducted hourlong in-person interviews with each of the eight practicing and one retired physicians in which she used a semi-structured interview script previously piloted with three local physicians. Research participants had the option of completing interviews in their office at work or in a reserved room at the institutional library of the research team. Interviews began with open-ended questions asking participants to describe what factors bring them joy and meaning in their work. These factors were further explored by asking for examples of "peak experiences" or "aha moments" in their work as well as for factors that carry them through "day in and day out." Interviews concluded with a presentation of themes that the authors had found in their prestudy literature review whereby participants were given the opportunity to comment on any factors not previously discussed. Additional participants were recruited by snowball method with all interviews completed over the course of 10 months in 2017.

Data analysis

The audio of each interview was recorded and subsequently transcribed, at which time identifying information was removed from the transcripts. The authors performed a thematic analysis of the interview transcripts to organize and code qualitative data.²⁵ Two members (R.W. and T.C.) of the research team reviewed half of the interview transcripts independently. At the time, R.W. was a medical student and T.C. was an undergraduate premedical student. Common

recurring factors identified by the coders were cut by hand from paper transcriptions and grouped into subthemes and, subsequently, major themes. The team (R.W. and T.C.) then met to discuss themes identified independently and to reconcile discrepancies. Themes not previously noted in the prestudy literature review were added to the final section of the interview script for subsequent interviews. The coders then met periodically during the remainder of interviews to reconcile new themes until saturation of themes was achieved. Final nomenclature of major themes and the identification of exemplifying quotes were completed in summer 2018.

Results

Ten physicians reported low scores on the single-item burnout measure used to identify physicians at low risk of burnout.²⁴ Of these 10, one was unable to be reached for an interview. As described in Table 1, of the nine physicians interviewed, five were practicing in the primary care specialties of family medicine or internal medicine (of whom one was a hospitalist) and four were practicing in other specialties. All nine physicians were located in western North Carolina with an average age of 55 and an average of 24 years in practice.

Six major themes emerged from the interview and coding process. These themes were visible impact, connection, calling and spirituality, sense of empowerment, variety, and community.

Visible impact

Many of the physicians interviewed described the reward and satisfaction inherent in seeing the impact that they have on individual patients or in their community. In our current medical system, a physician's likelihood of seeing the longor even short-term outcomes of their work is highly variable. We found that instances where our participants were able to see their own impact were frequently cited as experiences that sustain fulfillment in their work:

And then there's the more intensive things. Like I've had people that have lost children. This one woman comes to mind who lost her son two years ago in a motor vehicle accident and I really didn't actually know her, I'd only seen her once before, but you know like helping her through that trauma and to where I saw her back just this last week and she's now on the other side of that. It's still difficult for her but she said to me, you know you really helped me through that and I don't know what I would have done without you and that kind of thing so that is very rewarding. It's kind of draining when you're going through it, but when you come out the other side, you know that makes it worthwhile. (Physician 6)

Examples of visible impacts ranged from positive treatment outcomes, to patients expressing their gratitude, to moving the meter on public health statistics within the community. A notable subtheme within this larger theme was the importance for many of fulfilling an unmet need. Multiple
 Table I. Participant demographic characteristics.

| Variable | Value 55 (SD 11.9) | | |
|----------------------------------|-----------------------|--|--|
| Average age (years) | | | |
| Average time in practice (years) | 24 | | |
| Sex (n) | | | |
| Male | 3 | | |
| Female | 6 | | |
| Specialty (n) | | | |
| Primary care ^a | 5 | | |
| Specialists | 4 | | |
| Practice location (n) | | | |
| Outpatient only | 5 I | | |
| Inpatient only | | | |
| Inpatient and outpatient | 3 | | |
| Practice setting (n) | | | |
| Employed | 5 | | |
| Private group practice | 4 | | |
| Solo practice | 0 | | |

SD: standard deviation.

^aComprised of family medicine and internal medicine.

physicians described that they found significant satisfaction in leveraging their skills to address an unmet need or underserved population within their communities:

I find just those interactions with both patients and their family members extremely rewarding. Some of it is, as I said, filling a need that doesn't get met elsewhere in our medical system. That sense of being very useful. (Physician 2)

Connection

An overwhelming theme that arose within our interviews was the importance of connection. The majority of examples that participants provided in feeling this sense of connection related to patients and their families:

Again, because people are so different, I mean, even if I saw the same types of families all the time, that to me is where I am intrigued by human nature and I find ways to connect with people, and that's meaningful to me. That gives me joy. (Physician 4)

This theme of human connection was present across specialties and ages interviewed. One physician described these connections as peak experiences:

And when you connect with patients. I feel like that is when I'm like 'this is what I'm meant to do.' I think I went into medicine because I knew that I had an ability to connect with people in a way that would be healing. (Physician 8)

The subtheme of empathy was present and, in many cases, overlapping with participants' descriptions of connection. The ability and desire to be moved by the lived experience of their patients was touched on repeatedly as an energy-giving phenomenon.

Calling and spirituality

A sense of calling as well as feeling that their work was tied to a greater spiritual meaning was another theme that participants described. For many, this was described as an anchoring factor, the element that sustains them and keeps them going even on the toughest days:

It's stressful no matter what you do. If you don't feel like it's a calling, you're going to burn out. You're going to get tired, you're going to get pissed off at the bureaucracy and the paperwork, and you're going to leave. (Physician 9)

Sense of empowerment

Multiple conversations arose across our interviews that dealt with the sense of empowerment that our participants felt in their workplace. Many of these experiences described autonomy in practice, both among employed physicians and independent physicians:

I think it's autonomy, you know we don't work for a hospital and so I think that's important. We feel like we can do what we [want to] do when we [want to] do it, whatever the patient needs. (Physician 6)

However, another employed physician also experienced a similar sense of empowerment in knowing that his voice was heard:

I feel heard. I think having a sense of autonomy and having things presented in a way that is respectful of me is important, and for the most part happens. On the rare occasions it doesn't, I speak up and am heard mostly. That gives a sense of joy and meaning. (Physician 4)

A sense of empowerment was also portrayed in participants' descriptions of the trade-offs that they make in their work and the ability to choose:

Large group, less autonomy but there's more cushion, if you will. Smaller group, more autonomy but probably more financial stress, at least on the individual provider, so I'm okay with where I am right now. (Physician 1)

A sense of empowerment was the major theme with the largest number of assigned subthemes in our final coding framework (Table 2). One of these subthemes contained a sense of perspective gained over time, another spoke specifically to autonomy as described above, and another included participants' description of emotional regulation in their work. Given the broad nature of this theme, further exploration of its subthemes and, more importantly, their cultivation may lead to additional insights.

Variety

Variety arose as a common theme among many whom we interviewed and was present across specialties. This included variety in clinical cases and patient populations, but also included variety in professional roles both in and outside of clinic:

I have the ability to stretch myself and squeeze all this stuff in. And I like squeezing it in because all of it gives me energy. I would probably be a heck of a lot more frustrated, down, bummed out by the system if I was just doing my . . . practice. (Physician 7)

A subtheme included within the theme of variety was the element of curiosity that many participants described. Curiosity was described by participants as a driver of continued learning and appreciation of growth.

Community

While somewhat intuitive, professional community arose as a prominent theme among those interviewed. The community that was described included both that within their practice sites and as the larger medical community. For many, this was described as an "in it together" phenomenon through which they were pursuing a shared mission with colleagues:

We're here to do the right thing for folks. I would say being surrounding by people that think as I do, and having the blessing of time to do what we're called to do is amazingly helpful. (Physician 4)

Another physician described this phenomenon in terms of emotional connection:

I think you need to surround yourself with people where you both trust their judgement and their skill, but you also can connect with them emotionally. (Physician 6)

Anchoring and peak factors

We also observed a distinction between themes described as *peak factors* and those that we chose to name *anchoring factors*. In the semi-structured interview, participants were asked to share about the last time that they thought to themselves, "this is what I'm meant to be doing." They were then asked to differentiate this experience from factors in their workplace that help to sustain them day in and day out.

As illustrated in Figure 1, the themes of connection, visible impact, and sense of calling comprise the majority of what participants described as peak experiences. Interestingly, connecting with a patient, seeing the impact of care, and being in touch with the calling in one's work could be considered times in which participants are most in touch with what brought them to medicine in the first place. A separate

| Table 2. The identified six major themes, their subthemes, and examples of coded quotes that embodied each subtheme. | |
|--|--|
|--|--|

| Theme | Sub themes | Example of quotes for subthemes |
|--------------------------------|---------------------------------------|--|
| I. Community | Shared mission | We're here to do the right thing for folks. I would say being surrounding by people that think as I do, and having the blessing of time to do what we're called to do is amazingly helpful |
| | Coworkers | I have nice friendships with the nurses. I know about the nurses, I know about their families, most of them have brothers and sisters that work at the hospital. I connect with the nurses and that keeps me going |
| | Medical community | I never need to be in a place where I am too prideful or embarrassed to ask for help and to ask for a second opinion I think that also leads to satisfaction or joy in what we do because I never have to think that I am absolutely the last one |
| 2. Visible impact | Fulfilling unmet needs | I find just those interactions with both patients and their family members extremely rewarding. Some of it is, as I said, filling a need that doesn't get met elsewhere in our medical system. That sense of being very useful |
| | Gratefulness | But then there's also those times when people will actually verbally tell you you've made such a big difference in my life, I don't know what I would have done without you. Or you know of course those are when you are better than just regular routine, positive interactions. |
| 3. Connection | Empathy | I really try to work hard to find something that I can connect, in some way to connect with every patient. It might be we have kids the same age, it might be we both have parents with dementia, it might not be something social at all, it might be oh where did you use to live? Or what's your hobby? It could be just about anything. And that little window will let you in for some of the hard things that we have to do in this world |
| | Patient interactions | I think that probably a third piece that makes the job meaningful or worthwhile or helps me deal with the stresses are just being in relationship with people. There are a few jobs, there are a few vocations where there's instant and expected trust and confidentiality where people come and tell you their stuff, clergy and attorney and a doctor. Those are the three relationships in our society that are legally protected. I count it a privilege to meet people who don't they have no other reason to trust me than the initials behind my name, who will come in and tell me things that are very vulnerable or very important to them, I think with that trust comes great responsibility of how to delicately handle that information. They're trusting you because they need help. They're vulnerable. Those relationships and that trust fuels me as well |
| 4. Variety | Curiosity | The teaching is, it's a blast and it keeps you on your toes. I mean it keeps you reading and learning, trying to stay ahead of these whippersnappers who are learning all the latest creatives. We're old guys with old brains. |
| 5. Calling and Spirituality | No subthemes | It means that I am not only practicing medicine, but fed by what I do. Emotionally and spiritually fed by what I do. |
| 6. Sense of empowerment | Perspective | I believe I'm a cup half full kind of person. I do think that makes a difference. I try to find meaning even amidst suffering or loss or heartache. As a psychiatrist in prior years, when I did psychotherapy with folks I helped people learn how to navigate loss. I think that's a huge part in avoiding burnout, just being able to reframe things |
| | Emotional regulation Career Stages | That is really frustrating but I can't do anything about it so I just have to let it go. I always enjoyed my work, but it's got a different meaning as I get older than it did when I was younger. I think just aging in general softens the rough edges, like sandpaper almost. |
| | Autonomy | I feel heard. I think having a sense of autonomy and having things presented in a way that is respectful of me is important, and for the most part happens. On the rare occasions it doesn't, I speak up and am heard mostly. That give sense of joy and meaning. |
| | Attitude | I think if you have the right attitude toward the patients and you have the average amount of training and skills in medicine and you're not overly concerned with making a lot of money and you have family obligations that require you to keep your practice within a scope of time that you can actually have family time, I think you can manufacture a situation where you can maintain |
| | Trade-offs | your happiness and joy and not burn out Large group, less autonomy but there's more cushion, if you will. Smaller group, more autonomy but probably more financial stress, at least on the individual provider, so I'm okay with where I am right now. |

The six themes were identified from the interviews: community, visible impact, connection, variety, calling and spirituality, and sense of empowerment.

grouping applied to the themes of community, sense of empowerment, and variety in the day to day. Rather than the transient but powerful peak experiences, these other themes are reliably present or absent during each workday. These anchoring factors make work bearable even on the most difficult days.

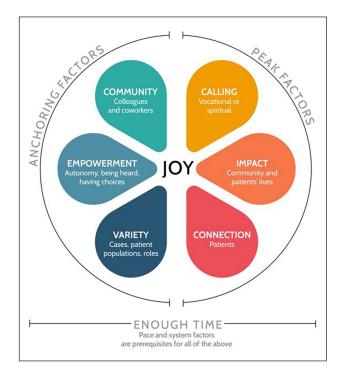


Figure 1. Six themes arranged by peak and anchoring factors.

The role of pace and system structure

Interestingly, while many physicians talked about the importance of pace and the structure of the system in which they work, these concepts were consistently described differently from the other core themes. Rather than being an independent factor that sustained joy and meaning, pace seemed to arise as a prerequisite for many of the other themes described above. For example, having enough time allowed for meaningful connections with patients. Having a manageable pace at work allowed for the cultivation of strong bonds with coworkers and the fostering of a sense of community.

Discussion

The results of our interviews with physicians who love their work and have low burnout scores point toward common themes that may foster resilience and combat burnout. Variety in work, a sense of empowerment, connection with patients, visible impact of one's work, feelings of community with coworkers and colleagues, and experiencing a sense of calling all emerged as important themes. As illustrated in Figure 1, three of these themes arose when participants were describing "peak experiences," and the other three arose as "anchoring factors" that sustain physicians day in and day out. In addition, the pace of the work environment plays an important prerequisite role in having enough time to engage with these drivers of joy in practice.

Much of the existing literature has centered around what factors are identified among providers with high burnout scores.^{3,7,25,26} In many ways, such methods are modeled on the disease-centric approach that is the mainstay of diagnosis and treatment in modern medicine. If research focuses on what is deficient in the work and lives of burnt out providers, it stands to reason that interventions will be designed to address these deficiencies. In a *Lancet* systematic review of programs to prevent and reduce physician burnout, only 4 of 52 studies included funding to take time during the workday for the implementation of interventions.²⁷ There exists growing recognition that both individual and organizational interventions are important in burnout reduction efforts.²⁸ However, significant work and further research is needed to move us beyond the important but inadequate organizational wellness models of lunch-hour yoga and after-work mindfulness training.

Calls have increasingly been made to consider physician health and wellness as one of the critical indicators that health systems must attend to, and the quadruple aim has largely superseded its threefold predecessor in our discussions around organizational health.^{29–31} Our interviews with physicians who love their work is one piece in the larger puzzle that needs to be solved in order for us to shift from solely treating deficiencies to an asset-based approach that fosters individual and organizational resilience.

The predominant system of reimbursement in our healthcare system is driven by real value units (RVUs) which incentivizes high-volume and/or procedures rather than time with patients. This lack of time in clinic schedules works directly against the attainment of the themes described by the physicians in this study. While organizational wellness initiatives squeezed into off hours are not likely to be the solution, our healthcare institutions do have a significant role to play. Some have suggested that at least 20% of full-time equivalents (FTEs) should be set aside for physicians to engage in meaningful work that increases overlap between their core values and organizational imperatives.³² This type of organizational structure aligns well with our findings. If time is available for structured and intentional engagement in activities that build community, increase variety in tasks, and reconnect physicians with their sense of calling in medicine, both providers and patients benefit. The nature of such work to align individual and professional values will, by definition, vary greatly from one individual to another. Examples could range from working with local shelters to coordinate clinical care for individuals experiencing homelessness to creating online check-in processes that save staff and patients time otherwise spent on paper forms and data entry. Currently, organizations may go so far as to give their physicians scores for levels of "organizational engagement," but rarely do these evaluations carve out dedicated time for the physician, nor do they typically evaluate contributions beyond quality metrics. Activities pursued during time dedicated to individual "meaningful

work" will differ from one physician to another and must be led by the individual.

Further study will be necessary across larger and more diverse groups of physicians to demonstrate the transferability of the themes described above. While some of the themes identified can be positively impacted through existing interventions, others will need further study to understand how best to foster them on the individual and organizational level. We suggest that based on our findings, adequate protected time is a critical prerequisite to beginning to cultivate and reconnect with the themes that will foster joy and meaning in the practice of medicine.

Reflexivity statement

Background

Both members of the research team who participated in the coding process (T.C. and R.W.) aspired to enter the medical field. At the time of the study, T.C. was an undergraduate premedical student with limited firsthand clinical experience. She is a female and immigrated with her family from Taiwan at the age of 8. R.W. was a 26-year-old medical student during the study and is a Caucasian male who grew up in the region where participants were practicing.

Medical hierarchy

As in many professions, how we speak to a colleague at a similar stage of training may defer from how we speak with a trainee or a mentor. Knowing that the interviewer (T.C.) was a premed student, it is conceivable that the participants may have adjusted their language or attitudes to assume habitual roles when speaking with a trainee. Whether such an adaptation is a less accurate portrayal is unclear since we may be more apt to complain to peers than trainees. In addition, because T.C. did not have clinical experiences from which to draw, it is conceivable that she was able to respond to participants' stories with less internal biases. Furthermore, it is conceivable that she also experienced greater hesitation in asking probing follow-up questions because of her desire for future acceptance within the "in-group" of the participants she was interviewing.

Space

While sharing what brings you joy may not be as vulnerable of an experience as sharing what brings sadness, participants did share openly about experiences that had touched them. We wanted to balance the comfort of participants with the need for convenience. Participants were given the option to conduct interviews in their office or in a reserved library room. It is conceivable that comfort levels may have deferred between interview's within the clinics and those held in the library space.

Training experience

During the study, R.W. was a medical student and, subsequently, a resident intern. As a new entrant in the medical field, R.W.'s motivations for participating in this research related very closely to his desire to not become burned out in his own career. Because of this, it was difficult for him to separate his role as a researcher from his role as an earlycareer physician. This provided opportunity for in-group interpretation of the transcribed interviews, but also introduced the bias of his own experiences from training within a rigorous academic institution. In addition, as an intern during the coding process, 80 h work weeks led to a delay in the coding process which caused the completion of coding to be extended over a greater duration.

Limitations

Our sample was limited geographically to western North Carolina and the physicians interviewed had a mean age of 55 years. It is quite possible that sustaining factors for a midcareer physician are different from those for early-career or late-career physicians; therefore, future research would do well to include all age groups. Our initial email invitation to participants included a request for interviews with those willing to share tips on finding "joy and meaning in medicine." While we can assume that those who responded felt some level of joy and meaning in their work that fueled their desire to participate in our study, our screening tool only allowed us to select for individuals with low burnout scores. Therefore, while our subset had low burnout scores, we cannot say quantitatively that they have "high" joy and meaning in their work. In addition, we specifically asked participants to share elements of their work life that contribute to their joy and fulfillment. It is possible that the balance of work with home life and arrangements in one's personal life are also important co-requisites to finding joy in medicine; however, we chose to focus specifically on themes within the workplace.

Conclusion

While limited in scope, the findings above can contribute to our understanding of what factors bring physicians joy and meaning in their practice of medicine. Much of the literature surrounding burnout focuses on asking the most burnt out physicians one question: "What makes you unhappy?" Although such questions are important in the effort to reduce burnout among physicians, the solutions derived in this way can only ever hope to shine light on the negative and burdensome parts of work. If we only understand the burdens of medicine, then all we can hope to achieve is a lessening of their impact. By interviewing physicians who love their work, we aim to enrich understanding of the positive elements at play in these individuals. The themes culled from our interviews point toward distinct interpersonal, intrapersonal, and structural factors that might be cultivated in order to truly sustain joy and meaning in medicine. Our hope is that further research will begin to point the way for healthcare organizations, medical education, and individual providers to begin the process of reclaiming and restructuring medicine to be what we dreamed it would be on our medical school essays—a profession full of joy, sorrow, hard work, meaning, and fulfillment.

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Declaration of conflicting interests

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Ethical approval

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Informed consent

Written informed consent was obtained from all subjects before the study.

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Supplemental material

Supplemental material for this article is available online.

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