## Praise for The Rabbit Effect

"A beautifully written, inspiring book! *The Rabbit Effect* is truly eye-opening and a joy to read. It illuminates vital public health research showing kindness in our day-to-day lives can make the world a healthier, happier place. I recommend this book highly for anyone who wants to live more healthfully."

-Christy Turlington Burns, humanitarian and founder of Every Mother Counts

"A wonderful demonstration of how our physical health is affected by the kindness we receive—and the kindness we give. Beautifully written and based on really hard science."

-Lord Richard Layard, professor and director of the Wellbeing Program, Center for Economic Performance, The London School of Economics and Political Science, and coauthor of The World Happiness Report

"[V]ery persuasive. This book provides welcome relief from the over-used and endlessly repeated prescription of diet, sleep, exercise, etc. In a voice that is warm, open, inquisitive, and optimistic, Dr. Harding weaves together compelling clinical vignettes with fascinating medical evidence. This comprehensive, holistic view of health is critical, much needed, and absolutely convincing."

-Arthur J. Barsky, MD, professor of psychiatry at Harvard Medical School

"The Rabbit Effect is a blockbuster book that will help all of us have a new view of how we create health. It succeeds at putting relationships where they belong: at the center of life, health, and medicine. Dr. Harding shows us that, by being compassionate, giving, and kind human beings, we can win the great rewards of vitality and longevity for ourselves and the whole world. Read this book! It will change your life."

-Mindy Thompson Fullilove, MD, LFAPA, HonAIA, author of *Urban Alchemy: Restoring Joy* in America's Sorted-Out Cities

Live Longer, Happier, and
Healthier with the Groundbreaking
Science of Kindness

Kelli Harding, MD, MPH

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## Contents

| INTRODUCTION  | What Are We Missing in Medicine?        | xvii       |
|---------------|---|------------|
|               | THE HIDDEN FACTORS                      |            |
| CHAPTER ONE   | The Hidden Factors of Health            | 3          |
| CHAPTER TWO   | One-on-One: Your Intimate Relationships | 15         |
| CHAPTER THREE | Social Ties: Your Community             | 34         |
| CHAPTER FOUR  | Work: What You Do                       | <u>52</u>  |
| CHAPTER FIVE  | Education: Learning Your Purpose        | <u>69</u>  |
| CHAPTER SIX   | Neighborhood: Live and Play             | 83         |
| CHAPTER SEVEN | Fairness: Living by the Golden Rule     | 102        |
| CHAPTER EIGHT | Environmental Influences: The Power     |            |
|               | of Compassion                           | 126        |
|               | ESSENTIALS OF HEALTH                    |            |
| CHAPTER NINE  | The Mind-Body Link: Individual Health   | 149        |
| CHAPTER TEN   | All of Us (Trust): Collective Health    | 169        |
| CONCLUSION    | The Ripple Effect: Getting to Kindness  | <u>191</u> |
| AFTERWORD     | The Enduring Mystery                    | 203        |
| ACKNOWLEDGME  | NTS                                     | 209        |
| NOTES         |   | 215        |
| INDEX         |   | 245        |

# What Are We Missing in Medicine?

The path to helping people as a doctor seemed straightforward when I arrived at medical school. On the first day of my first year, I sat anonymously in the auditorium with ninety-nine other classmates at the University of Rochester. Clad in spotless white coats, we prepared to cloister ourselves inside the walls of the Strong Memorial Hospital complex. Everything we needed to know about the inner workings of the human body lay within—or so I thought.

For the next four years, my classmates and I followed the well-worn route to the knowledge of medicine: peering through microscopes, cramming for exams in silent library cubicles, and racing through a maze of fluorescent-lit corridors to see patients. During this time, I caught glimpses of daylight reflected off white linoleum. I rarely felt the sun on my skin, the wet grass of spring, or even the bustling city beyond the brick fortress of the hospital complex. Through these intense and completely immersive years, which extended through residency and fellowship, the world outside the hospital seemed irrelevant to my work as a physician. If it weren't for the white rabbits, I might never have walked out the sliding doors of the medical center in search of a new perspective on health.

xvii

As a medical student on the hospital wards, I noticed odd patterns with patients, observations unmentioned in my medical books. Two patients with the same diagnosis would have two very different courses of illness; one would become gravely ill, while the other carried on an almost normal life. Others I saw had medically unexplained symptoms; I'd search and search, but there was nothing in my texts that supplied a reason for their reported ills. Initially, I felt a vague sense of discomfort with these inconsistencies. I didn't have the narrative or framework to understand them, so I tried to ignore the puzzles they posed. But the nagging feeling that I was missing something in my diagnoses refused to go away. I had accounted for all the usual biomedical explanations. What were the hidden factors in these individuals' health that I wasn't seeing? I was determined to investigate further.

My first suspect was mental health. I wondered if the mysterious interaction of the mind and body could explain why some patients fared better than others. Since no residency-training program addresses the interaction between mental and physical health directly, I self-designed my course of study. First I immersed myself in internal (adult) medicine training at Mount Sinai Hospital in New York City, followed by psychiatry residency training at Columbia University's Irving Medical Center. I remained at Columbia for a National Institute of Mental Health (NIMH) biological psychiatry research fellowship and focused on medically unexplained symptoms. I also became boarded in psychosomatic medicine (consultation-liaison psychiatry). I was a woman on a mission.

Trying to tease apart medical and psychiatric diagnoses is my area of specialty. Clinically, I made the emergency room my home, seeing patients with both acute medical and behavioral concerns. While this means I've seen more than my share of people found naked on New York City streets, it also has provided a front-row seat to both the power and the limits of traditional biomedical knowledge. Despite the fact that I'd trained in a specialty that gave me more insight into people's minds, I still felt I was missing something. Connections between medical symptoms and mental states seemed clear, but why did some people fare so much worse than others when, medically, that shouldn't have been the case? I

people died unexpectedly.<sup>2</sup> That's as if the entire population of St. Louis, Missouri, just disappeared.

It's not just life expectancy. America has consistently poor performance on numerous global health measures. For instance, despite spending more than any other country for hospital-based maternity care the US is ranked forty-sixth in the world for maternal health.<sup>3</sup> It also has the worst rate of maternal deaths in the developed world with a rising maternal mortality rate (from 17 deaths per 100,000 births in 2000 to 26.4 deaths per 100,000 in 2015).<sup>4</sup> Compounding the heartache, American children are less likely to reach the age of five than children in other developed countries like Japan. Starting at birth, Americans fall far below other wealthy nations on many standardized health indicators, such as infant mortality, car crashes, mental illness, teen pregnancies, heart disease, imprisonment, homicides, substance use, obesity, and premature death.<sup>5</sup>

America has one of the worst gaps between the health outcomes of rich and poor people, which serves as a key marker of a nation's well-being. Out of the thirty-two wealthiest countries in the world, the US ranked thirty-second on the wealth-health gap.<sup>6</sup> The US is such an outlier of extreme income and health inequality, we are practically not even on the same graph.<sup>7</sup> The same unfortunately holds true for childhood emotional well-being.<sup>8</sup> Even the rich don't live as well as they could. Our comparatively worse health cuts across lines of privilege and race. Wealthy, educated white Americans can expect to die several years younger than equally well-off individuals around the world.<sup>9</sup>

And despite, or perhaps because of, America's status as a global leader in biomedicine, it is also by far the world's most expensive place to get sick. Maybe you or a family member has put off a test or a follow-up visit to save money like one in five Americans. <sup>10</sup> I know I have, even as a doctor working in a hospital. And when we do get sick, the price is outrageous. When my mom died, the cost for her two-week hospital stay totaled well over \$100,000. Even with a medical degree, I could barely decipher the bills. Thankfully, she had great insurance and secondary insurance. Through my grief, I understood that we were lucky to be able to pay the remainder; the exorbitant cost of medical care causes half of US

bankruptcies annually. One in five of us—including many families with young children—such as those with preemies who require prolonged stays in intensive care units, struggle to pay medical bills.<sup>11</sup>

In the US, the typical solution to health problems, both on an individual and population level, is to double-down on medical care. Problem is, usually, the vast sums of money we spend goes to care *after* we're already sick. It's like towing your car into the shop *after* the brakes have already failed and you've run into a ditch. The cost becomes a vicious circle. Because of the expense, Americans routinely forgo preventive care and don't seek help until it's a five-alarm emergency. Our cost-induced aversion to preventive care, however, only increases the cost of fixing what's wrong when we do seek help. As Dr. Darrell Kirch, president and CEO of the Association of American Medical Colleges, the organization that represents all the accredited US medical schools and major teaching hospitals, said to me, "Good medical care doesn't guarantee good health. There are other factors at work." <sup>12</sup>

Meanwhile, the majority of the \$3.5 trillion health-directed resources in the US—more than 95 percent—are spent on clinical care–related services. <sup>13</sup> This includes doctor's office visits, hospital stays, medications, imaging studies, laboratory testing, and procedures (i.e., biopsies, surgeries, etc.), nursing care facilities, and related administrative costs. What's

It's like we've walked into a supermarket where the cashier charges us double for the same apples as everyone else, and ours are rotten. strange is our government spends absurd amounts of money on these services compared to every other developed country in the world, and still one in ten Americans does not have health coverage.<sup>14</sup> America

dedicates nearly twice as much of its economy to health care as the UK (17.9 percent US GDP versus 9 percent UK GDP), yet, unlike the British, we don't provide basic free medical care for all.<sup>15</sup> It's like we've walked into a supermarket where the cashier charges us double for the same apples as everyone else, and ours are rotten.

For me as doctor, there's one more point that's truly shocking. Data

shows that clinical care, as we currently provide it, isn't actually making us much healthier. In fact, studies estimate that what happens at the doctor's office and hospital accounts for only 10 to 20 percent of a person's overall health status; it doesn't significantly contribute to overall population health and well-being. Additionally, evidence shows spending more

on medical care access and quality only improves preventable deaths by a slim 10 to 15 percent. Despite our massive investment in health care, numerous well-

Our nation spends a fortune on health care, yet we remain remarkably unwell.

done studies paint the same picture over and over: the contribution of medical measures to the decline in mortality is questionable.<sup>17</sup>

These surprising findings are at the heart of this book. Our nation spends a fortune on health care, yet we remain remarkably unwell.

So if biomedical advances and expensive medical care aren't making the difference to our health, what is? What would actually make us healthier? Which brings us to the rabbits.

New Zealand white male rabbits develop heart disease much like humans if fed a high-fat diet. Today most people know that eating fried food and steaks daily is asking for trouble. But back in 1978, researchers were still trying to establish the relationship between high blood cholesterol and heart health. Dr. Robert Nerem and his team designed a straightforward experiment using what he calls "the standard rabbit model" to show the link. Over several months, he fed a group of rabbits the same high-fat diet. At the end of the study, he measured the animals' cholesterol, heart rates, and blood pressure. As expected, the cholesterol values were all high and virtually identical to one another. The rabbits had similar genes and ate the same diet. Now they all seemed destined for a heart attack or stroke.

As the last step, Dr. Nerem needed to examine the rabbits' tiny blood vessels. Looking through the microscope, he expected all the rabbits to show similar fatty deposits on the inside of their arteries. Instead, Dr. Nerem had a shock. As it turned out, there was a huge variation in the fatty deposits between the animals. One group of rabbits had 60 percent

fewer deposits than the other. It made no sense. He recalls wondering, "What in the world could this be?" There was no clear biological explanation for these findings. He was staring down his microscope at a medical mystery.

Dr. Nerem and his team searched for clues. They looked again at the research design. Nothing unusual. But Dr. Nerem knew to keep looking. He said, "Sometimes there are things involved in a protocol that we don't take into account." So the research team looked at themselves.

A Canadian postdoc named Murina Levesque had recently joined the lab. Dr. Nerem remembers, "She was an unusually kind and caring individual." When it became apparent that all the animals with fewer fatty deposits were under Murina's care, the team dug deeper. They noticed that Murina handled the animals differently. When she fed her rabbits, she talked to them, cuddled and petted them. She didn't just pass out rabbit kibble—she gave them love. As Dr. Nerem explains, "She couldn't help it. It's just how she was."

Now a professor emeritus of bioengineering at Georgia Tech, Dr. Nerem says, "We were not social behavioral scientists," but the team decided they could not ignore the findings of the social environment's effect on physiology. The research group repeated the experiment, this time with tightly controlled conditions. They compared the arteries of one group of rabbits cared for by the new postdoc to the arteries of another group of rabbits cared for in the standard way. They found the same effect again and published these findings in the prestigious journal *Science*. <sup>19</sup> Take a rabbit with an unhealthy lifestyle. Talk to it. Hold it. Give it affection. And many adverse effects of diet disappear. The relationship made a difference. *But how?* 

Medical training teaches doctors to break the body down into disparate parts: organs, tissues, cells, and molecules. Physicians divide by specialty in this same way. There are doctors for every bit: heart, kidney, gut, bone, brain, and so on. This fragmented view stems from the underlying theoretical premise that disease arises from internal biological processes gone haywire. It is an exciting inner-world journey that has dominated medical thinking for the last century, and it is what I—and countless other medical doctors—spent all those years painstakingly studying.

xxiv

But then there were the rabbits. These studies indicate something is missing in the traditional biomedical model. It wasn't diet or genetics that made a difference in which rabbits got sick and which stayed healthy; it was kindness.

It turns out the rabbits were just the introduction to a much larger story. I call it the Rabbit Effect.

When it comes to our health, we've been missing some crucial pieces: hidden factors behind what really makes us healthy. Factors like love, friendship, and dignity. The designs of our neighborhoods, schools, and workplaces. There's a social dimension to health we've completely overlooked in our scramble to find the best and most cutting-edge personalized medical care. Even having something that motivates us to get up and out of bed in the morning makes a difference to our physical well-being.

Because, as it turns out, being and staying healthy isn't something that can be addressed through biomedical advances alone. Or by more and more spending on health care. Even the usual self-help directives—"Eat better! Work out! Get more sleep!"—will only get us so far. All these approaches overlook the critical social dimensions to ensuring sound minds and bodies. Ultimately, what affects our health in the most meaningful ways has as much to do with how we treat one another, how we live, and how we think about what it means to be human than with anything that happens in the doctor's office.

This book will empower you to change your health. But not in the usual ways. I won't give you a ten-step fitness plan or a two-week diet.

That's not what you need. That's not going to make you healthier in the long run. Instead, I'll take you with me through the halls of the hospital, invite you into the room with my patients to discover why they are sick and what might make them well. Together, we'll

This book will empower you to change your health.
But not in the usual ways.

investigate clinical puzzles that defy expectations, unearthing the hidden factors that determine who is sick and who is well, who will live and who will thrive. We'll discuss stories from communities renowned for their

### The Hidden Factors of Health

You are my other me. If I do harm to you, I do harm to myself.

If I love and respect you, I love and respect myself.

—Luis Valdez

Let's begin with a story. It's a tale of two patients, Bella and Daisy, which illustrates how the best of health and the worst of health are not always what they seem.

Looking at Bella's medical record, it was clear she was gravely ill. At seventy, she was diagnosed with pancreatic cancer, a particularly aggressive disease that often results in weight loss and jaundice. At the time of her diagnosis, Bella was surprised to learn that she was so sick. Though she traveled a long road through surgery, chemotherapy, and radiation, three years later, at seventy-three, she looked radiant and seemed surprisingly youthful. Bella showed up to her doctor's visits wearing sporty sneakers. She often spent her Saturdays out in the yard tending her marigolds, going to art classes, or taking a stroll with her son, who lived down the street. She was glad when the chemotherapy ended so she could invite her neighbor and the woman's two young daughters over for freshly baked chocolate chip oatmeal cookies, or "cowgirl cookies," as she called them, her specialty. Her main complaint was that one of her medicines made her more susceptible to sunburn.

Unlike Bella, Daisy had a squeaky-clean bill of health on paper. All

her bloodwork, imaging, and cardiac tests came back normal. Though she was almost half Bella's age, at forty-three, Daisy looked withered and acted much older. Her face held traces of beauty faded by forces unknown. She moved slowly and sighed when she sat down. At each clinic visit, she said she felt "foggy" and exhausted all the time. She lacked the energy to leave her house or travel to see her favorite cousin, Viola, who had recently moved to Pennsylvania. She had a variety of unaccounted for aches and pains and had missed so many days in her job as a paralegal that she had no more vacation or sick time left. Bella would ask despondently, "I just don't feel right. Do you think we've missed something?"

In Western medicine, sick and well are often viewed in black and white, or as mutually exclusive buckets. In the biomedical model—medicine's dominant twentieth-century view that physical factors alone explain human health—a doctor tells Bella, a woman who feels fine but has a suspicious lab finding, that she is sick and needs medical treatment. Meanwhile, Daisy, who feels sick yet has no concerning findings, is assured all is well, perhaps told that what she is experiencing is only in her head, and sent home. Both patients leave the clinic confused.

During my research fellowship exploring medically unexplained symptoms, I saw patients who were ostensibly well, but felt lousy—or who worried they were ill to the point that they couldn't function in life. Many patients had gone from doctor to doctor or ER to ER looking for an answer. The mismatch between how a person feels and their doctor's findings is perplexing. This was the odd pattern I'd discussed with Arthur Barsky during our phone calls that had led me to the rabbits. How can someone be medically ill and feel well? Or be well and feel ill? Is there a way to think about health that accounts for both situations?

Dr. George Engel, an internist at the University of Rochester School of Medicine, posed a daring answer. On April 8, 1977, *Science* published an article in which Dr. Engel questioned the widely held belief in American medicine that biology alone explains human illness. Dr. Engel saw medicine marching along on a narrowly focused quest for physical markers of disease divorced from the broader context of human life. He warned that the ideology of the entrenched biomedical model was the "crippling flaw"

#### The Hidden Factors of Health

of the field and not enough to explain human health.<sup>1</sup> An incomplete truth adopted as a dangerous dogma.

As a physician, Dr. Engel was puzzled by the gray zone between sick and well. He felt the explanation of the gray zone might come from more closely examining "the patient and his attributes as a person, as a human being." In short, Dr. Engel thought the difference between patients like Bella and Daisy might involve examining their lives with a much wider lens than any instrument you'd find in a doctor's office.

Influenced by Dr. Adolf Meyer at Johns Hopkins University, general systems theory, and fields outside of medicine, Dr. Engel proposed a broader, more inclusive concept of health that took a patient's whole life into account. It unified biomedicine and behavioral health into a complete package. Dr. Engel called his new theory the biopsychosocial model. While the name is a mouthful, the concept is simple. The idea is that a person's health occurs in a social context that can't be ignored.

The biopsychosocial model (see figure 1) systematically organizes the layers of health. Nothing exists in isolation: each layer is both simultaneously a whole and a part. A shift in one part affects change elsewhere. The innermost parts contain the molecules, organelles, cells, tissues, organs, and nervous system that comprise a person. This is where the biomedical model and health-care system stop. Dr. Engel saw that, though the vast majority of medical practice is focused on the inner layers alone, health extends far beyond the body.

Looking at individual biology in isolation provides an incomplete picture that makes the cases of Bella and Daisy perplexing. Why is "sick" Bella doing so great and "well" Daisy doing so poorly? If you expand out through the rings, the cases of Bella and Daisy make more sense. When we take the factors in Dr. Engel's outer rings, the rings beyond the "person level," into account, we start to see the grave differences in Bella's and Daisy's situations and thus their health. It reminds me of the stretchy portraits on the walls of the Haunted Mansion at Disneyland, where initially, you see just a painting of a lovely young woman with a bucolic smile holding a parasol. But then the picture frame stretches out to reveal her standing on a tightrope over the open jaws of a crocodile.

Keeping with the idea that health extends far beyond the body alone,

# DR. ENGEL'S BIOPSYCHOSOCIAL MODEL CONTINUUM OF NATURAL SYSTEMS

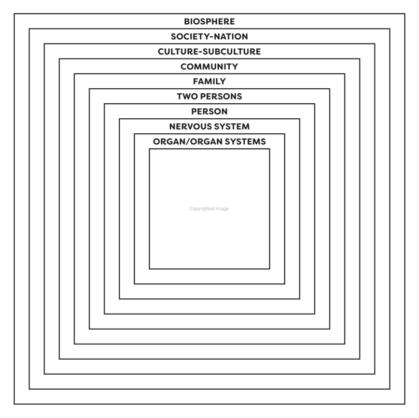


Figure 1

G. L. Engel, "The Clinical Application of the Biopsychosocial Model," American Journal of Psychiatry 137, no. 5 (May 1980): 535–44.

Dr. Engel's model stretches outward from the individual to include a two-person relationship, family, community, culture, society-nation, and biosphere. The outer layers contain the psychological and social factors that I, along with most of my physician colleagues, considered irrelevant or intrusive while hiding out in the medical center with my patients. With a complete picture, we start to see how "sick" Bella's well-being connects to her strolls with her son, sense of community, and favorite

#### The Hidden Factors of Health

could not reach the wound site to work. Treatment A could not bind at Receptor B. If the antibiotic couldn't reach Randy's leg, there would be no improvement of Disease C. He would die from the infection.

Randy sat in his hospital bed. Sherri sat at his side reading a celebrity magazine. Coop was blunt. "Are you still smoking?"

Randy chuckled. "Is Mick Jagger still with the Stones?"

Coop did not crack a smile. Randy's fingers were yellow with tobacco stains. "You understand, smoking prevents the tissues from properly healing after a surgery." Nicotine both weakens the body's fighter immune cells and is a vasoconstrictor, preventing the cells from getting to the site of trauma. It's like drugging soldiers and then putting them in a tank on a blocked road. Randy explained that even if he didn't smoke, everyone else at his job did. Coop continued, "We'll do several tests this afternoon to check the blood flow to your foot and then talk about our options. I have to be frank. From the look of that leg, I'm not optimistic."

Randy had other questions on his mind. "Hey, Doc, is there anything we can do about this?" and he pointed to his pelvic area. He leaned over to us and in a loud whisper said, "The diabetes is really killin' my love life." Sherri sheepishly nodded. Coop put a hand on his shoulder and said, "One thing at a time, sir." The reality was, that was not our area.

After we exited the room, Coop shook his head. He summed up the situation: "If a fem-pop flops, then it's a chop-chop." He made a chopping motion with his arm on his own thigh. "And there, it don't stop," moving up his leg. By evening, the tests confirmed the obvious. The femoral bypass had failed. We shared the news with Randy. It wasn't safe for him to leave the hospital with his left leg intact. Because of the extent of the infection, we'd put him on the schedule for an above-the-knee amputation first thing the next morning. Randy looked at his hands as he took in the news and nodded. We all sat quietly. Sherri cried. Eventually he asked, "Can someone wheel me outside for a smoke?"

I've asked myself many times how Randy might have avoided losing that leg and what else we could have done to prevent further catastrophe. Most clinicians know in their gut that treating a person's leg or body with medical or surgical care alone isn't enough to ensure health. Dr. Engel had encouraged us to look at our patients' lives. But lives are messy, and

asking something off-script feels like cracking open the lid on Pandora's box in a fifteen-minute visit. Our current system says stick to the leg, so that's what we do. And yet when I looked at Randy—at his bad diet, his smoking, his inability to take the medicines prescribed, why a small injury led to a festering sore—it was hard not to feel like the answer lay in his life. And not just his life, but in a more systematic examination of the currents that had shaped his health upstream.

To better understand those upstream forces, I crossed the street from the medical center and enrolled in classes at Columbia University's Mailman School of Public Health. Sitting in seminars with people from all different backgrounds, not just physicians, I felt I'd entered a parallel universe where everyone was talking about health but in a radically different way. Medicine and public health are strangely two separate worlds that look at health from two very different perspectives. Like Alice, I'd passed through the looking glass. On the clinical side, Dr. Engel's model said a patient's life matters to her health, and on the public health side, I saw that the field had a far more in-depth understanding of the specific conditions that shape our lives, and thus a person's behavior and biology. But the two halves needed unification with a common language.

From my new perspective, I saw clearly that the field of public health illuminated what Dr. Engel started. Since Dr. Engel's landmark paper, more than forty years of medical, public health, and scientific research on the social dimensions of disease show that he was right: the vast majority, 80 to 90 percent, of people's health depends on factors outside clinical

Where a person is born, works, lives, plays, and grows older shape a person's behavior and biology in profound ways. care.<sup>2</sup> While genes do play a role (more on that later) the biggest contributor to health outcomes by far are powerful social, political, and environmental conditions. It turns out that where a person is born, works, lives, plays, and grows older—what the field of public

health calls the *social determinants of health*—shape a person's behavior and biology in profound ways. The social determinants, or hidden factors, of health are the "risks of risks," or the conditions under which

#### The Hidden Factors of Health

disease strengthens or withers.<sup>3</sup> It is not the language that Dr. Engel used, but it defines what he described.

By marrying Dr. Engel's elegant biopsychosocial model with the commonsense language of the social determinants, I moved closer to solving the puzzle of not just Randy, but Bella and Daisy and so many others. The key to understanding why they—and we—aren't healthier lay in a new framework, a framework I call the "hidden factors." It unifies not only the fields of medicine and mental health, but makes a substantial leap to include the vast world of public health too. And it also involves you. The hidden factors model brings us back to that first day of medical school and Dr. Hundert's sage, yet unheeded, advice from orientation that considering the broader human condition is critical for health.

In the rings of the hidden factors (see figure 2), at the center is the individual: you. Radiating outward from you is the social and environmental matrix in which you participate every moment of every day. This framework incorporates everything in our lives: family, friends, coworkers, money, vacations, schools, hobbies, homes, sidewalks, streetlights, grocery stores, coffee shops, hairdressers, parks, playgrounds, community centers, places of worship, transportation, times of reflection, and how we navigate one another. It's all the activities of our daily lives.

In the chapters that follow, we'll explore the rings of the hidden factors model together. The first ring, closest to oneself, looks at our one-on-one relationships, or our most intimate bonds. Then we'll look at the vital role of broader social ties in our health and communities. Where and how we work is also critical to our health and well-being, and it dovetails with our education, or learning, and our greater sense of life purpose. Next, we'll travel to our neighborhood, and examine where we live and play. How we treat each other, or living by the "Golden Rule," is essential to creating a culture where we can all thrive with fairness. As we get to the outer edges, we take a look at broader factors, like our environmental influences and specifically childhood exposures that impact the mind and body. And last, we'll delve into how emotional well-being, trust, and conflict resolution skills help all of us live in healthier and more peaceful societies. It's an eye-opening journey with pressing implications for our daily choices.

# THE SOCIAL DIMENSIONS OF HEALTH: THE HIDDEN FACTORS



Figure 2

All these hidden factors were present in Randy's life. In fact, they help explain how Randy got as sick as he did, and why a tiny cut turned into a festering sore. What if his doctors had been trained to treat these factors when Randy first sought care? What if our medical systems considered addressing hidden factors early as part of routine visits and got patients the support they needed? Prevention in medicine reminds me of time travel movies, like *Back to the Future*, where tiny changes to early events lead to shifts in destiny. As it was, Randy was lucky to only lose the leg. In a different version where hidden factors were addressed early, maybe Randy wasn't stuck in a hospital bed awaiting surgery.

#### The Hidden Factors of Health

Here are some of the ways Randy's story could have gone differently. Starting with his closest relationships, he was lucky. He had a huge social support in Sherri. But Sherri needed support, too, and she could have helped us help Randy. A high priority should have been to help Randy stop smoking, or at least cut back. After all, each additional cigarette reduces a person's life by 11 minutes. But beyond an appointment at a smoking cessation clinic, it also would have helped to know that Randy's passion was electric guitar repair. Understanding that was important to him and connecting him to classes may have ultimately provided a better work environment and a healthier sleep schedule. Work and learning are only two hidden factors we'll discuss that could have changed the course of Randy's health.

And here's the thing: Randy isn't the exception. He's the rule. Take Carl. Carl may on the surface need a straightforward "hernia repair." But he's also an older man living alone, with uncontrolled hypertension, a flight of stairs he can't navigate, and unreliable transportation to his doctors' appointments. Or Sandra has a "bowel obstruction." But she's also a single mother of three, living in a one-bedroom apartment, who prioritizes her kids' needs over her own pricey medications. Meanwhile, Sean has a bulging "cervical herniated disc," but also feels trapped in a stressful public relations job with a boss who's a major pain in the neck. Gloria needs a "cholecystectomy" (her gallbladder removed), but she also needs to get out of her abusive marriage.

Illuminating the hidden factors helps us see where to focus our efforts to improve our health. They explain why the same course of treatment or medications for a disease can lead to very different outcomes. Clinically, it's common to see two patients with the same condition, such as recovering after a heart attack, have two very different courses based on seemingly irrelevant factors, such as their family relationships or their education level. In my practice, the sickest people I see often share similar backgrounds: loneliness, abuse, poverty, or discrimination. For them, the medical model isn't enough. It's like fixing up an airplane engine and ignoring that the pilot is on his third drink at the bar and a massive storm is overhead.

The narrow focus of our current medical model may enable doctors

Jamie began moving in short bursts. The midwife explained this was a reflex of the dying. Then his eyes suddenly opened, possibly another reflex. Kate thought Jamie looked around. The staff reminded the family that they needed to let him go. As Kate and David continued to hold and talk to him, Jamie seemed to be breathing. Then, he reached out a hand and grasped David's finger. They excitedly called out for the doctor, who didn't return.

Over the next hour, Jamie continued to grow stronger. As Kate recounted on a *Today* show interview, her husband eventually said, "Go tell [the doctor] we've come to terms with the baby's death, can he just come and explain it?" She added, "That made him come back."<sup>2</sup> Five years later, news reports show Jamie as a happy child with sandy blond hair and a broad smile. He likes to run on the beach near his family's home in Sydney, Australia, play games, make silly faces, and bake cookies with his sister.<sup>3</sup>

What happened that day with Jamie was an extraordinary situation, and we may never know exactly what occurred. But we do know a baby pronounced dead showed glimmers of life as he lay snuggled against his mother's and father's skin. His parents' loving touch somehow changed everything. Or so it seemed. The doctors focused only on Jamie's tiny body. But larger hidden factors, including parental love, were at play.

How could a mother's love change a child's destiny? As a young man studying philosophy in college, Dr. Moshe Szyf wondered about "very, very old questions." Is behavior shaped by experience (such as love) or biology (such as genetics)? As time passed, Dr. Szyf studied genetics at Harvard and eventually became a professor of pharmacology and therapeutics at McGill University, working on cancer research. He never imagined how, years later, his early interest in philosophy would reemerge in a bar in Madrid. That Spanish night in 1992, drinking a couple of pints after a conference with a university colleague, Dr. Michael Meaney, the conversation turned to rats.

Working in his lab, Dr. Meaney had noticed some rats made more loving mothers than others. The more nurturing rat moms lick their babies a lot during the first week postpartum, while the more emotionally distant spend little time grooming their offspring. Dr. Meaney observed

#### One-on-One: Your Intimate Relationships

that "high lickers" raise more relaxed pups that are docile, whereas "low lickers" produce more anxious pups that are hard to handle and may even bite. Anyone in the lab could easily pick out the rat mother's parenting style based on the pup's behavior. Additionally, the mother's style seemed to dictate the pup's behavior for life. Dr. Szyf was intrigued. He told me, "As a scientist, I'm looking for things that seem strange and different." Now he wondered about one of the oldest questions on earth: How does nurture shape our nature? If genetics are fixed, why was love changing personality?

Dr. Szyf, Dr. Meaney, and their colleagues designed an ingenious experiment to find out if a mother's nurturing behavior made the difference to the rat baby even if the baby and the mom had different ge-

netic makeups. Since rats are happy to foster other mothers' babies, the researchers swapped the pups. Then the team tediously counted rat licks. What they found was as strong an argument for nurture over nature as

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any: if the daughter of a low-licker anxious rat was raised by a high-licker relaxed mom, she became a relaxed rat. Eventually, she would go on to be a high-licker mom, too, raising relaxed pups. The opposite held true as well.<sup>5</sup>

Was it possible that with each additional lick, the mother was reshaping the baby's genetic script? This idea rocked Dr. Szyf's understanding of genetics. The answer would reveal the amazing flexibility of life, and he grew determined to figure out how that worked.

Strangely enough, a Nazi-induced famine in the Netherlands during World War II may hold some of the answers. In October 1944, only months after the Gestapo discovered Anne Frank and sent her to Auschwitz, Nazi forces abruptly cut off food supplies to over four million Dutch citizens, including women and children, living in the western Netherlands. There was not enough bread or milk to feed everyone, and over twenty thousand people died of starvation. Those who survived the "hunger winter" did so mostly thanks to airdropped food programs, such as Operation Chowhound and Operation Manna, by neighboring Allied

countries. But 400 to 800 calories a day is insufficient nutrition, especially for expectant mothers.

After the Nazi forces in Norway surrendered on May 5, 1945, food supplies rapidly returned to normal levels. But the catastrophic famine left a hidden mark. Researchers who wished to understand the impact of a mother's diet during pregnancy on her baby's health discovered it. In the Netherlands, citizens' collective health is tracked over time in a database known as a public health registry. A registry provides valuable data on the health of a population. (In the US, with our fragmented medical system and millions of medical records that don't communicate with one another, we do not have anything as extensive.) Thanks to the countrywide registry, the birth records of babies conceived or in utero during the famine provided valuable clues to health investigators.

What the investigators found may not sound so dramatic in and of itself: mothers most affected by the famine had smaller-than-average babies. But what's surprising is that the babies' small size was only the beginning. Researchers tracked these low-weight babies into adulthood. As they grew older, the Dutch Famine cohort went on to develop more health problems, such as increased risk of heart disease, obesity, diabetes, and mental illness. They died years younger than those born before or after the famine. Some studies showed even the following generation—the famine babies' babies—had low weights, suggesting the effects of a grandmother's starvation were passed down through multiple generations. The environment was having a long-term impact. Not getting enough food one winter echoed at least two generations down the line. A subsequent study published in *Cell* replicated these findings in rats and found eating habits in pregnancy did pass down three generations.

But how exactly does it work? Famine doesn't change a fixed DNA sequence. How could an environmental trauma rewrite the genetic script and pass it on?

Before the rat licking studies, Dr. Szyf serendipitously studied DNA methylation, a process he'd seen in tumor cells. Like a period added to a sentence, methylation attaches a methyl group (CH<sub>3</sub>) to the DNA strand and signals pauses during transcription, or the process of gene expression. DNA methylation is known as an *epigenetic* process, meaning it's

#### One-on-One: Your Intimate Relationships

in addition to the genes.9 The methyl group is separate from the DNA strand itself.

Methylation alters the cell's narrative without changing the genetic code. Instead, it twists and turns the DNA story into a new, sometimes better or sometimes worse plot line. With cancer cells, it can transform a lighthearted romantic comedy into a tearjerker. Whereas, with positive lifestyle changes, even if someone has a sinister plot line written into his DNA, alterations in methylation can slow down the progression of the story for the better. This means a person may live healthier longer before symptoms of a disease, such as with neurodegenerative illnesses (including Alzheimer's, Parkinson's, and Huntington's diseases), begin to emerge. 10 It turns out our DNA is far more flexible than we thought.

Dr. Szyf had never imagined that the social environment could influence methylation. Then, in a fortuitous twist, Dr. Szyf and his team's laboratory analysis saw DNA methylation and de-methylation occur with the rat mother's neglect or love of her child. Exposure to love or neglect embedded in the baby's body on a microscopic level, and it seemed to pass on. In other words, as Dr. Szyf explained with delight, he had found, "Experience embedded in the genome!"

Through the flexible epigenetic process, environmental exposures flip genes on and off to adapt to life's unfolding drama. For example, when a baby grows in his mother's womb, stress hormones, such as cortisol, cross the placenta. The stress doesn't change the fixed DNA code itself, but through methylation passes a vital message to the developing life on how to arrange DNA for immediate survival: "It's a rough world out there, kid, get ready!" It seems epigenetics is like fashion. A bikini or a winter coat transforms the person, and if it's summer in Miami or winter in Montreal, it could mean life or death.

The Dutch Famine cohort and Dr. Szyf's rat pups aren't the only babies studied whose genes were affected by their experiences. An unexpected Canadian snowstorm offers even more insight into how exactly the epigenetic process works.

For residents of Quebec and Eastern Ontario with a heavy winter coat, snow is no big deal. Life stays in motion: schools are open, work is business as usual, and traffic hums along. During January 1998, however,

five small winter storms ganged up to create one humongous disaster. In the Great Canadian Ice Storm of 1998, trees toppled onto cars and houses, live power lines snapped, and transmission towers collapsed. Thirty-five people died. Bridges and tunnels closed, leaving millions of people stranded without electricity for up to six weeks.<sup>11</sup> Montreal became paralyzed.

An ice storm is not quite rain and not quite snow. It freezes on impact, creating a magical and dangerous thick glaze on the earth's surface. Just getting around is risky. When I was in medical school in upstate New York, a minor ice storm knocked out our power for several days. The novelty of living by candlelight and on canned food quickly faded. When the lights turned back on in my apartment complex, I emerged a frazzled cavewoman. My white 1980s Ford Escort had transformed into a swan ice sculpture. To live under those conditions for six weeks, while pregnant or with children, is unimaginable.

Since it is unethical—and downright mean—to stress out a pregnant woman to test the physiological effects on her baby, cataclysmic events provide researchers with rare insight into the impact of prenatal maternal stress. As Dr. Szyf joked in a TED Talk, "God does experiments with humans called natural disasters." Epidemiologists at McGill University in Quebec, led by Suzanne King, acted quickly to identify pregnant women exposed to the Great Canadian Ice Storm of 1998, or those who'd conceived around that time. As is typical with major storms, area hospitals reported a baby boom nine months later.

The McGill researchers identified 178 willing study participants. They collected blood and saliva samples to see if the disaster had imprinted itself on the women's bodies. The researchers checked the mothers' physiologic responses to stress, including cortisol levels, a hormone the body pumps out during stressful circumstances. They also collected data about the mothers' objective stress—such as the number of days without power. When the babies arrived, the research team followed the children's physical and behavioral development through age thirteen.

The researchers found that the ice storm babies born to the moms with the highest amount of objective stress had more behavioral, health,

#### One-on-One: Your Intimate Relationships

star student and colleague, psychologist Mary Ainsworth, developed a test of attachment called the "strange situation." She studied what happened to children twelve to eighteen months old when a child was playing with her mom, and then a stranger entered the room. She also looked at what happened if the child's mother stepped out, and then how the child responded when she returned.<sup>16</sup>

A child under two with a secure attachment is friendly to the stranger when the mom is present, gets upset when Mom leaves, and is wary of the stranger when alone. She seems happy to see her mom on her return. Children with nonsecure attachments either show no distress when Mom leaves, seem okay with the stranger, and register little emotion when Mom returns (*avoidant attachment*); or show prolonged distress when Mom leaves, act fearful of the stranger, and become upset with the mom on her return, sometimes even pushing her away (*insecure attachment*). An extensive review of two thousand "strange situations" done in eight different countries shows insecure attachment present across cultures for about one out of every two kids.<sup>17</sup>

Decades of research since Bowlby and Ainsworth published their data shows that without intervention, insecure attachment as a kid translates into trouble expressing and regulating feelings as an adult. A person with a history of nonsecure attachment as a child may experience an intense fear of abandonment as a grown-up, and either avoid getting emotionally close to others or glom on to less-than-perfect partners and fall to pieces when things don't work out. Insecure attachment also leads to increased cortisol levels, lower hippocampal volume (an area of the brain involved in memory and learning), and greater risk of physical and mental illness.<sup>18</sup>

We know, in part, that children with secure attachments or relationships fare differently in life because of one of the longest-running studies in history. Starting at the end of the Great Depression in 1938, the Grant Study tracked a cohort of Harvard undergraduates, including the future president John F. Kennedy, into adulthood. Over time the research expanded to participants' wives, children, and a comparison group of people from less affluent Boston neighborhoods. During the eight decades of research, principal investigator Dr. George Vaillant and his team

consistently found one key predictor of a successful, healthy, happy life: good relationships.<sup>20</sup>

So if you're a parent, you know, no pressure.

Just thinking about attachment makes me want to run and hug my kids. From epigenetic research, we know a parent's love creates a cascade of positive health effects in her child. And even if we didn't grow up with a loving environment, we have an opportunity to foster one for ourselves and our children. This reminds me of a Steve Martin joke, "I gave my cat a bath the other day . . . they love it. He sat there, he enjoyed it, it was fun for me. The fur would stick to my tongue, but other than that . . ." So while we don't lick and groom our loved ones like a mama rat, there are ways our loving touch changes destiny.

For newborns, direct skin-on-skin contact is particularly critical. In those crucial moments following Jamie's birth, Kate Ogg instinctually placed her son on her bare skin, a practice known as "kangaroo care." When kangaroo babies are first born, they look like wiggly pink gummy bears. With no hair, they need the warmth of their mom's pouch to grow strong.

In 1978 neonatologist Dr. Edgar Rey Sanabria got a radical idea after reading an article about kangaroo babies' survival. He worked in Bogotá, Colombia, where three out of every four preterm infants receiving standard medical care in the hospital died. Out of desperation and overcrowded conditions, he asked new mothers to use their body heat as an incubator instead.<sup>21</sup> Given the number of babies dying, they had little to lose. The mother placed the child, in only a diaper, on her chest, making sure its nose and mouth were visible and unobstructed. Immediately Dr. Rey Sanabria noticed more babies survived.<sup>22</sup> Thousands of studies since have shown kangaroo care normalizes the baby's heart rate, breathing, and oxygen saturation. Down the road, these babies are calmer, sleep better, and have higher IQs. Around the world, often in countries with few resources, this practice reduces preterm infant mortality by over 30 percent.<sup>23</sup>

While the benefits of kangaroo care include physical warmth and the comforting sound of the parent's heartbeat, the neuropeptide oxytocin also plays a key role. Oxytocin is known as the "love hormone" because

#### One-on-One: Your Intimate Relationships

it's involved in bonding, empathy, and trust. It is released at childbirth and during breastfeeding, as well as when we hug, kiss, and snuggle. Oxytocin helps us remember faces and build connection, and it increases steadily during the first six months of parenting for both moms and dads.

Could love make us weak in the knees? While the hormone is produced in the brain and released via the pituitary gland into the bloodstream, receptors all over the body explain its widespread effects. Oxytocin helps us feel calm, appreciated, and even sing more. In one study of sixty-eight men, those who received a nasal oxytocin spray were 80 percent more generous sharing cash with a stranger than those who did not.<sup>24</sup> Babies are notoriously rude houseguests, so oxytocin helps. There's evidence that the hormone's released not just from kangaroo care and loving touch, but also with physical play, "raspberries" to the belly, peekaboo, surprise tickles, impersonating stuffed animals, and general silliness.

Kate Ogg's story of the seemingly miraculous recovery of her stillborn baby dramatically illustrates the healing power of physical warmth with our children. Yet touch is vital for every living creature throughout life. When we think about physical intimacy for adults, sex often comes to mind. And while sex plays a role, so too does casual physical touch in our everyday relationships. There is a biological reason that a friend's supportive hand on our shoulder or a pat on the back comforts us. Similar to the animal kingdom, social grooming is a part of social bonding. This might be why some women love their weekly salon blowouts and why we tend to stick with the same hairdresser over years. In medicine, the comforting touch of your doctor, such as when using a stethoscope to listen to your heart and lungs, also might be part of why we stay loyal to the same physician over time. In the same physician over time.

The sense of connection from touch is more than emotional attachment. There's also a physiological factor. Holding hands lowers blood pressure, heart rate, and cortisol.<sup>27</sup> Even twins in utero do it. One tender sonogram revealed one twin, who was healthy, and the other, who was gravely ill, holding hands in the womb.<sup>28</sup> Interlocking hands makes us feel brave. In the "lend a hand study," women who thought they were about to get an electric shock showed less threat activation on

functional neuroimaging brain scans when they held the hand of their spouse or a stranger compared to not holding anyone's hand. (Holding a spouse's hand created the strongest response, but only if the marriage was healthy.)<sup>29</sup>

Studies show that when a person holds the hand of a loved one in distress, the breath and heartbeat of the pair sync up. Their bodies harmonize. Most amazing is that their brainwaves harmonize as well, which is known as entrainment. One study looked at twenty-two couples wearing brain wave monitors, or electroencephalography (EEG) caps, where one partner had heat placed on her arm for two minutes. Researchers found that the more empathetic her partner felt to her pain, the more in sync their brain waves. Additionally, the more synchronized the brain waves, the less pain she reported. Even being in the same room together but not touching, there was some "brain-to-brain" synchronization.30 Similar to fireflies flashing in concert on a summer night.31 A study in Nature's Scientific Reports shows when two people are talking and listening to each other, their brain oscillations synchronize beyond auditory processing alone.<sup>32</sup> They actually get on the same wavelength. Humans are emotionally and biologically connected in ways we don't fully understand, and touch is a key part of this.

Touch is also critical for health throughout the life span. Increasingly studies show the potential benefits of massage for preterm infants, children with autism, women with breast cancer, individuals with autoimmune disorders (including asthma and multiple sclerosis), and seniors with dementia.<sup>33</sup> A study of older adults showed that older patients who had a social visit and a brief massage have more cognitive and emotional benefits than those who just have a social visit alone.<sup>34</sup> In addition, it appears that the benefits of massage may extend not only to the receiver but to the giver as well.<sup>35</sup>

Hugs play a role in physical intimacy and health too. Researchers at Carnegie Mellon University examined the interplay between exposure to illness, social support, and daily hugs. In the name of science (and possibly a hundred bucks), 404 healthy adults agreed to inhale nasal drops that exposed them to the common cold. First, the researchers drew blood samples to confirm that the volunteers were not immune. Then they