



The Alma Dea Morani Renaissance Women in Medicine Oral History Project

JoAnn E. Manson, MD, MPH, DrPH, MACP

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Dr. JoAnn Manson is a physician, epidemiologist, and endocrinologist recognized as one of the most highly-cited medical researchers in the world. She serves as Professor of Medicine and the Michael and Lee Bell Professor of Women's Health at Harvard Medical School, Professor of Epidemiology at the Harvard T.H. Chan School of Public Health, and Chief of the Division of Preventive Medicine at Brigham and Women's Hospital. A leading authority on women's health, Dr. Manson has led landmark randomized trials and other studies on the effects of nutrition, lifestyle, and hormonal factors on heart disease, cancer, and diabetes. She is also committed to public education, authoring books and popular magazine columns that translate complex research into practical guidance. In 2022, she received the Alma Dea Morani Renaissance Woman in Medicine Award for her exceptional contributions.

This four-and-a-half-hour oral history interview was conducted in four virtual sessions in August 2024. A native of Cleveland Heights, Ohio, Dr. Manson credits her female high school chemistry teacher and her parents—who valued education and perseverance—with inspiring her confidence and curiosity. Her mother's death from ovarian cancer during Dr. Manson's early medical training shaped her lifelong commitment to women's health and highlighted how little was known about female-specific and sex-based differences in medicine.

Dr. Manson graduated from Harvard-Radcliffe in 1975, when the male-to-female student ratio was roughly four to one. She returned to Ohio to attend Case Western

Reserve University School of Medicine, earning her M.D. in 1979. Although women were generally treated fairly, the curriculum—even at an innovative medical school—was based on a male model of anatomy and disease, often referred to as “the 70-kilogram male” paradigm. She noted that while awareness of sex differences in medicine has advanced considerably, much more research and education on topics such as menopause and women’s heart health are still needed.

After completing her internship and residency in internal medicine at Beth Israel Deaconess Medical Center in 1982 and a fellowship in endocrinology at Boston Medical Center/University Hospital in 1984, Dr. Manson became increasingly convinced that chronic diseases such as type 2 diabetes, heart disease, and cancer were far more preventable than previously thought. Her early commitment to prevention—and a desire to strengthen her research skills—led her to earn both a Master of Public Health (1984) and a Doctor of Public Health (1987) from the Harvard T.H. Chan School of Public Health.

With this training, Dr. Manson emerged as a leader in some of the most important studies of women’s health over the past four decades, including the Nurses’ Health Study and the Women’s Health Initiative. She described the excitement of conducting large-scale randomized clinical trials and the insights gained into hormone therapy decision-making and lifestyle recommendations. Her work has shown the profound impact of physical activity, heart-healthy diets, sleep, stress management, and other behavioral factors on reducing chronic disease risk. At the same time, she acknowledged the broader social and environmental barriers—such as limited access to affordable healthy food and walkable communities—that affect individual choices.

Balancing research, clinical work, and family life (including three children), Dr. Manson highlighted the ongoing need for better work-life balance and childcare support. She believes that much more must be done in this area to retain women physician-scientists, help them advance to leadership roles, and prevent burnout. She credited her supportive partner, Christopher, and reliable childcare as essential, and though the juggling was demanding, she viewed advancing women’s health as her life’s mission.

In 1999, Dr. Manson became a full professor at Harvard Medical School and Chief of the Division of Preventive Medicine at Brigham and Women’s Hospital, positions she continues to hold. She has won numerous professional awards and is an elected member of the National Academy of Medicine. She now focuses on research leadership, administration, and mentoring, describing mentorship as “tremendously important” and “very rewarding and gratifying.” Through her books and her long-running health columns, other writings, and videos for the popular press, she has educated the public on preventive health and empowered individuals to take charge of their well-being.

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JoAnn E. Manson, MD, MPH, DrPH, MACP

Interview Session 1: August 7, 2024

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[00:00:09]

A. Macdonald

My name is Arlene Macdonald, and I am here interviewing Dr. JoAnn Manson, and I am delighted to be with her. She is the 2022 winner of the Alma Dea Morani Renaissance Women in Medicine Award, which is given by the Women in Medicine Legacy Foundation every year to an outstanding woman in medicine. As part of that award, we do an oral history series with our award winners. So it is a terrific honor to be spending time with JoAnn Manson and hearing a little bit about her life in medicine. Our interview today is taking place on August 7th, late in the afternoon. Dr. Manson is in Boston in her office.

JoAnn Manson

It is wonderful to talk with you, Arlene.

A. Macdonald

Thank you very much. Dr. Manson is a physician, epidemiologist, endocrinologist and one of the most cited women researchers in science. She has been a prolific contributor to our knowledge of women's health, a co-PI or a PI in many of the landmark studies in women's health. She has a strong commitment to preventive health care and has led large randomized clinical prevention trials of nutritional, lifestyle, and hormonal factors related to heart disease, cancer, and diabetes.

Even beyond research, she is really a population health leader who's written scores of popular books and advice columns in magazines, translating scientific findings on preventive health to a general population. She has a very high profile in many worlds, and those are the worlds we are going to explore with her over the next series of interviews.

Just to give her formal titles, which I should really do, she is currently the Michael and Lee Bell Professor of Women's Health at Harvard Medical School. She is also a professor in the Department of Epidemiology at the Harvard T.H. Chan School of Public Health. And she is the Chief of the Division of Preventive Medicine at the Brigham and Women's Hospital. So that is quite an introduction because this is a life of great achievements, and I would love to start exploring how you came to be the person you are today.



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Chapter 1

Early Aspirations and Inspirations

[00:02:33]

A. Macdonald

Normally in these interviews, we like to start with your beginnings—where you were born, how you grew up, where your interest in medicine was fostered, things like that. So I'll just let you take it from here; tell us a little bit about those beginnings.

JoAnn Manson

Well, I grew up in the Midwest. I'm originally from Cleveland Heights, Ohio. I came from a middle income, middle class kind of household in Cleveland Heights, went to a large public elementary school, middle school, high school. We have a large family—five children in my family, I was actually the fourth. It was actually very lovely growing up in that area. There were a lot of opportunities to go to art museums, to take art classes. I was really interested in art for a long time, art and sculpture. So I went to art museums and spent a lot of time taking art classes, taking some dance (modern dance, ballet). There were a lot of opportunities for culture.

My family, my siblings and I, were very close. My father was an aeronautical engineer at NASA, National Aeronautics and Space Administration, and my mother was originally a social worker. But after the children came, she stopped working in social work and was a stay-at-home mom. My parents really valued education. That was like one of the most important things to them. They often told us that they were making sure that there would be enough savings for college for all the children. So I always placed a really high priority on being serious about school, trying as much as I could in school, and looking forward to an opportunity to go to college and have higher education.

A. Macdonald

Were all your siblings that dedicated to education?

JoAnn Manson

My siblings were all good students. It definitely would have been hard for me not to have been serious about school, though there were times when I got a little rebellious—you know, questioning does everyone in the family have to follow this very academic route? Anyway, all my siblings went to good schools. At the time I was applying to college, I had two older siblings who were at Yale, and I had a sibling who had just graduated from the University of Michigan. So I kind of took a different path and went to Harvard Radcliffe. At the time I attended, it was really two somewhat separate schools. Even though the classes were coed, the application was to Radcliffe College. It was a 4 to 1 ratio of males to females.



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A. Macdonald

I didn't know that.

JoAnn Manson

[00:06:44]

Yes. Eventually—we graduated in 1975, so next year will be celebrating the 50th reunion – but the school eventually became gender blind admissions. However, when I was applying, there were only about 300 women and about 1200 men, a 4 to 1 ratio. But over the next few years, there was parity in terms of males and females, and it became gender blind admission. So it really changed quite a bit even while I was there. From the very beginning, the courses were coed, but the living arrangements changed. Women, the first year I was there, lived at Radcliffe in the Radcliffe dormitories and then could move to the Harvard Houses on the main campus near Harvard Square. You said you hadn't been in Boston, so I won't give you too many details about this, but it changed quite a bit over the course of the years. Gradually after I had graduated, it became fully equal in terms of numbers with parity in the numbers of female and male students.

A. Macdonald

Would the girls in high school have been encouraged equally to go to college? What did guidance counselors say? What did teachers say to the female students in your high school? What kind of encouragement (or not) did you get?

JoAnn Manson

I think there was encouragement of both the boys and the girls, to go to college. In fact, a real inspiration for me at the time was a chemistry teacher I had in high school who was really, really supportive of my going into the sciences. She was a chemist and a woman, and teaching chemistry in high school, and she was really encouraging me to stay in the sciences and to even consider either going into one of the basic sciences, going into chemistry, or going to medical school. She talked about that a little. I think there were other major inspirations in my life for going to medical school. But she was one of the people who really inspired me to go into the sciences, and that was important. Having a female high school teacher in the sciences who was very frequently telling me that she had a lot of confidence in my abilities in science and that I was really good at it. That made a difference to me in terms of pursuing it and majoring in a science in college.

A. Macdonald

Yes. Knowing we will get to the arc of what your career has been, how do you think your parents (beyond school and education) instilled in you the kind of qualities that let you overcome challenges and stay determined and have a passion for the things you do? Is that internal to you, or did things in your environment help shape that?



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JoAnn Manson

I think my parents were important influences on my life. With all of the children, they made us believe in ourselves and believe in our capabilities. And also not to give up. They made it really clear to us that there are a lot of hardships in life, but if you get knocked down, you've got to get back up. It can work out really well if you stick to it. Perseverance was something that they really tried to cultivate in us, that you would be able to persevere and not be derailed by criticism or failures or disappointments: to just get back up. And they made us do certain things that seemed really challenging, like taking us to hills for sledding that were quite complicated to navigate and that really, I think, helped to develop self-confidence.

Also, my mother was a very major influence in my life. My mother was the youngest of four children in her family. I think she always really wanted to be a doctor, but she felt that the opportunities really were not available to her, even though she saw that her brothers were able to do exactly what they had expressed an interest in doing with their lives. One was a doctor and one a lawyer, and they were doing what they were interested in doing. And she went into social work, which I think was a great interest of hers, but she often talked about how she had considered going to medical school and maybe would have liked to pursue it. But it really wasn't an opportunity for her. I think that really stuck with me—that I'm going to see if I can make a go of it.

A. Macdonald

[00:13:22]

Yes. It's interesting to think about the women's movement in general. Just being one generation apart, what a difference that made in opportunity and then visions and then possibilities.

JoAnn Manson

There were a lot of changes at that time. Even just my generation, really tremendous changes during that period. The opportunities available to us to pursue sports and do activities that we were interested in even in high school and college, that was all in a state of transition, really rapidly changing.

I do think there were differences between my mother's generation and opportunities for women. Many women did break through those barriers, and there are some really amazing stories of women in that generation who did science and amazing, pioneering breakthrough research and various types of work, won all kinds of awards. But for the most part, there were some limitations put on women in their choices in those days. It did inspire me that my mother wanted to be a doctor.

A. Macdonald

Did she talk a lot about that, about wanting to be a doctor?



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JoAnn Manson

She had talked about how she thought that would have been difficult for her to actually pursue. And then she started having children and talked about how she really didn't think that that would have been feasible, you know, at that time. So she was a big inspiration.

She also was a really big inspiration to me in terms of going into women's health, because my mother was diagnosed with ovarian cancer and she died very early in my medical training.

So very early in my medical training, and this is now 44 years ago, she was diagnosed with advanced ovarian cancer and died before I really had completed my medical training. She never actually had a chance to see any of my successes or any achievements that I had in medicine. However, she has always continued to be an inspiration to me. Even to this day, really throughout the whole process of doing clinical work, doing research, she has been probably the main inspiration to me. One of the reasons (aside from her desire for the opportunity to go into medicine) was when she was diagnosed with ovarian cancer, I realized that there was so little known about how to treat many of these conditions in women and also so few treatment options available.

And this really motivated me to go into the field of women's health and try to help in terms of research. Trying to answer some of the key questions, not only in terms of ovarian cancer; my focus has been more on cardiovascular disease and diabetes and many of the cardiometabolic kinds of health problems although I do some research related to cancer as well. But it just became really clear to me that there were many, many knowledge gaps.

A. Macdonald

That was the first knowledge gap that opened up, the gap around ovarian cancer

JoAnn Manson

[00:18:13]

That was really motivating to me and inspired me to pursue a path in women's health, both clinically and research wise. That was a very important inspiration.

A. Macdonald

Yes, I can see that. Absolutely. And when you came through high school and you had this inspiration from your chemistry teacher, was it in your mind that you were going to be a doctor, you're going to go to Radcliffe? Did you apply to lots of colleges? What was that process like? Did you have a first choice?

JoAnn Manson

I did apply to a large number at that time. You know, seven or eight seemed like a large number. I think now kids apply to a lot more than that. But it was my first choice to go to Harvard Radcliffe. I actually had gotten into some other schools that were also somewhat tempting to me. For example, I was accepted at Princeton, and that would have been the first year that they were



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accepting women. I thought that would be very pioneering and maybe interesting to be in the first class of women at Princeton. But I decided ultimately to go to Harvard Radcliffe.

A. Macdonald

Did you know that the application process for Harvard was going to favor four times as many boys as girls? Were you aware?

JoAnn Manson

I knew that Radcliffe College had at that time only 300 slots for the freshman class. So I knew it was much smaller than the overall Harvard freshman class.

A. Macdonald

Okay. Was it a big transition to leave Cleveland and head for Boston? When I hear you say, "I would have been happy to be one of the first women in a cohort at Princeton," it sounds like you weren't shy or reticent about being a woman in a minority environment. You would have welcomed that.

JoAnn Manson

I would have welcomed that. I mean, it was a time when things were changing in that way. Yale had just started to admit women into the class about two years before that. My sister, as I mentioned, was at Yale, and she was in that first class. There were a lot of changes that were going on right at that time with many of these schools. But there are so many great colleges. It's always a tough decision. But I thought that overall, Harvard Radcliffe was a good choice.

A. Macdonald

And what was the transition like to head off to college? Did it feel daunting? Did it feel easy? Was it mostly exciting?

JoAnn Manson

It was very exciting. I had gone to a summer camp two years before that at Interlochen, Michigan. I had been away from home for the full eight weeks of the summer and had sort of gotten through that process of living on my own, being away from home. I actually found it very challenging. It's very, very difficult doing that for the first time for like eight solid weeks. I felt that had really prepared me for going off to college away from home and being able to deal with it. I didn't find it that difficult to be away at college on my own. And I was glad that I had an opportunity to do that.

A. Macdonald

Did you have roommates there that you were assigned to or how did that work? You were on campus in a dorm with roommates?



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JoAnn Manson

[00:23:06]

We had roommates the first year I lived at Radcliffe; there were assigned roommates. Then after freshman year, I moved to the Harvard houses. I lived in Quincy House. I actually met my husband my sophomore year when I moved to Quincy House (he wasn't my husband then). We lived in separate entryways, where they had all the sophomores living. Eventually the superintendent came and took down the fire door between the two suites where I was living with my roommates and he was living with his roommates. So we got to know the guys across the fire door pretty well. Eventually we started dating. So I've fond memories of living in Quincy House and that experience because I met my future life partner through that dorm.

A. Macdonald

Isn't that amazing? That would certainly change the college years a little bit, too, right?

JoAnn Manson

Yes. I mean, we didn't marry for a long time after that. It was at least seven years after that. We didn't get married during the years in college. But it was interesting to meet him sophomore year.

A. Macdonald

Yes. And did you go in knowing you were going to be in the sciences? Did you dabble in the arts? What did your mind make it up when you went to college about what your future was, or was it still exploring?

JoAnn Manson

I was still exploring, but I was certainly thinking about medicine and being pre-med. As I mentioned, I was really inspired by my mother to pursue that path. I was taking pre-med courses, I was majoring in biology, but I was also taking a lot of courses in literature and social sciences and anthropology. So I was by no means limiting myself to the science or pre-med courses, but I did kind of solidify my interests in going to medical school by early in the college years. And then I pursued that.

A. Macdonald

The award is called the Renaissance Women in Medicine because these are people who have capabilities in the field of medicine and beyond. So you're recognized for that. Do you think having the kind of undergraduate education you had advanced you or helped to shape the ways you are in medicine, in science, and in clinic?

JoAnn Manson

I think that I've always had interests beyond pre-med or medical school and the sciences. I've always had a lot of interest in the arts. As I mentioned, I was taking art classes even in Cleveland in school and earlier than that. Then I went for a summer to Interlochen, which is also known as national music camp. But my main focus there really was on art and sculpture, though I took some music classes—I did play the harp briefly at that camp. But I've had a lot of interest in the



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arts, and I have spent a lot of time over the years visiting museums and going to performances. When I was in college, I took some pottery classes, working with a potter's wheel. And I also wrote some dance reviews, performance reviews, for a school newspaper.

A. Macdonald

I thought I read that somewhere. I was going to ask you about writing on arts for the school.

JoAnn Manson

[00:28:09]

So I've always had an interest in the arts. And when I had an opportunity, I would work summers to help make some money and help pay for college. I had jobs, for instance, at the Cleveland Clinic, working with an American Heart Association stipend. I also had a job working as a waitress, which was really good experience, I'll tell you, in terms of understanding how difficult some jobs can be in terms of how demanding they can be, and a working environment that may not be that terrific. And all of this really motivated me to stick with my plan to be pre-med and to go into medicine! Which is a decision I haven't regretted. I really have not regretted that decision. I also really enjoyed not only clinical practice of medicine, women's health, and the clinical fields that I trained in, in internal medicine and endocrinology, but also the opportunities to do research and particularly randomized clinical trials. This has been really important to me.

A. Macdonald

Yes, it's a broad background. I wonder if some undergraduates would feel like, "oh that's taking away from my grade point average in the sciences, and I can't afford to do that." But it's clearly been important enough for you to be well-rounded, and it feeds you in different ways, I imagine.

JoAnn Manson

Definitely. It really was more important to me to be pursuing some of these additional interests beyond the day-to-day classwork than to have the absolute best possible GPA. It was really more important to me to be pursuing and maintaining some of these outside interests as well as trying to follow this path ultimately toward medical school and a degree in medicine. Being able to do clinical practice was originally my goal. But then my goal became combining clinical practice and research. Then I also added an administrative role as Chief of the Division of Preventive Medicine at Brigham and Women's Hospital.

A. Macdonald

We're going to get there. But in what ways was it important enough for you to do that, you know, not just worrying about the absolute grade point. What did it give you? This world outside of medicine, alongside medicine, the things you did—pottery, the sculpting. In what ways is your artistic life meaningful to you?

JoAnn Manson

So I've always enjoyed making things; I don't know. It's a way to relax. And I've always really enjoyed doing drawings. I used to do pastels and painting and then you can give it to someone. I



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never sold my work, but either make it a gift or, you know, even if it's just within the family. I would very often do a drawing or painting, and I would give it to my mother and she would put it up in one of the rooms in the house. That would be very gratifying, to do something like that. But mostly I really just enjoyed the art and working with my hands and having some product from that work that you could then give to someone or even just enjoy yourself.

A. Macdonald

[00:32:57]

Something tangible and material, not so cerebral. I think that's great.

And then the process of getting ready for medical school and making those applications and the interviewing for medical school and all of that, how was that process for you?

JoAnn Manson

So that process went well. I had been away from home; I had been in Cambridge, Boston, and I thought it might be good to go back home and to go to medical school at Case Western Reserve. I was actually excited about the idea of it because the school was not only back at home (which I thought might be meaningful to my parents, especially my mother), but it also had a really innovative curriculum. The students had early clinical experience; at the very beginning of medical school, you would be assigned to take care of a patient, a woman during her pregnancy. You would follow her during the last several months of the pregnancy, be present at her labor and delivery and help in whatever way possible during that period, and then follow the infant through at least their first year of pediatric clinics. I thought that was terrific because you get that early clinical experience. So from the very beginning of medical school, you're kind of understanding what it's all about, why it matters, and it really motivates you to learn the material, take it even more seriously. I thought that was great.

Another aspect of the medical school curriculum that I was looking forward to was this organ systems curriculum, where you learn about a certain part of the body, for example the heart and the cardiovascular system, and you study the physiology, you study the pathology (looking under a microscope, looking at what the tissue, the muscle tissue looks like). You also do anatomy lab where we would actually be working with cadavers and really trying to understand the anatomy of the heart and how different parts of the body relate to each other. Then there were clinical aspects of it as well, the clinical conditions that involve the heart and how to treat them. It would all be integrated. It wouldn't start with just doing something like physiology, except as part of the organ system.

A. Macdonald

This is different than other medical schools that you had looked at?



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JoAnn Manson

There were several other schools that also had a more integrated organ systems curriculum, but it was one of the earlier schools to have that. So there were several reasons that I thought that would be a good choice. So I was actually happy to do that.

A. Macdonald

Well, we're about 5:10 p.m. and it might make a nice break point for us because we can pick up next session thinking about your years in medical school, what they were like and how it was to be a woman training in medicine in those years. I'm sure it wasn't 50-50 men and women.

JoAnn Manson

It was 4:1 again.

A. Macdonald

Yes, exactly. I was thinking something like that. I want to hear a little bit about what the process of starting there was like. Your parents were glad to have you back in Cleveland, I'm going to assume.

JoAnn Manson

Yes.

A. Macdonald

So I think it's a lovely sort of break point to know that you're about to head off to medical school and I can turn our recording off. I'll say a couple words to you before we go.

JoAnn Manson

Okay. Sounds good Arlene.



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JoAnn E. Manson, MD, MPH, DrPH, MACP

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[00:00:10]

A. Macdonald

So let me just once again welcome JoAnn Manson to the oral history Alma Dea Morani Renaissance Women in Medicine Project run by the Women in Medicine Legacy Foundation. And I'm delighted to be picking up where we left off yesterday.

JoAnn Manson

Great to see you again.



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Chapter 2

Women Welcomed: Diving into Medical School

[00:00:27]

A. Macdonald

I know when we left off, you were just telling us about entering into medical school and why you chose Case Western Reserve with the integrated organ system training and also clinical experience in the early first year of medical school. That appealed to you. So I wanted to ask you what it was like to leave the undergraduate college world and enter into this professional training program. Did they have white coat ceremonies back then? Was it a big threshold? Were you excited? How did you feel about this new commitment, really to a professional path? Undergraduate college leaves us free to go in multiple directions, but this is really a commitment. So how did you feel about all that?

JoAnn Manson

I was very excited to be going to medical school and I was glad to be going back home after four years in Cambridge and Boston. So it was good to go back home. And I was excited about the Case Western Reserve curriculum, as I've mentioned, having early exposure to patients. Often the way they do it is to have you working with a patient during her pregnancy and following her through the obstetrics clinic visits and then through labor and delivery. Then when the baby's born, to follow the baby through pediatric clinic. I thought it was really a great opportunity to have that early clinical exposure and have that context for learning medicine to really see how it's applied to the patient. So I was looking forward to that. Also, as I mentioned, the integrated curriculum just seemed like a really sensible approach to maintain interest, keeping it as clinically relevant as possible throughout the early years of medical school into the more clinically based years when you're actually fully in the clinic and spending all of your time with patient care. I thought that those were really great strengths to the program that I was looking forward to.

And I enjoyed medical school a lot. I thought the teaching was terrific. The professors and lecturers seemed so committed to teaching and sharing their knowledge. I was very impressed by the amount of time that was spent. So many of the teachers and the other students, for the most part, were fantastic. I had a lot of colleagues and close friendships that I developed during those years.

So overall, I would say it was very positive. Of course, it's hard work, and the hours were long. Especially once the clinical years began; in terms of being full time at the hospitals, it was demanding. But I always enjoyed it and I always felt like it was a privilege to be able to talk with patients, to learn about them. And that they would trust a medical student. In those days, I mean, they were aware that many of us they were seeing in the hospital or in the clinic setting were students in training. So often they would be really, really generous and kind about wanting to



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help with training, to talk with you, to entrust their care to you, even though they knew that. Of course, it wasn't just the medical student working with them, but I did always feel it was a privilege to have that opportunity. All of that was very positive. And for a long time I was thinking that I would do full time clinical practice. I really was thinking mostly in terms of going into clinical medicine, not so much into research specifically or administration. So that was my focus: learning clinical medicine and being as good a clinician as I could become.

Overall, I think the training was really good, and I was particularly inspired by some of the teaching in the fields of diabetes and endocrinology. I became really interested in that field because I could see that especially with type 2 diabetes, or what was then often called adult-onset diabetes, there were many opportunities for prevention. That seemed really to be a great focus to be working with patients to try to reduce their risk. You know, talk about what information is available about things that they can do, lifestyle, behavior, or other factors. That controlling those factors and taking charge of their health could make a big difference. That part was very exciting to me.

A. Macdonald

[00:06:44]

Was that unusual, do you think? Because I spent ten years in medical education and often the focus of the education is curative; how can we cure? I think today there's more emphasis on preventive medicine, certainly from researchers like you who have helped push the needle. But in your own education—were you one of few who got excited about preventive medicine? Because sometimes I think medical training tends to emphasize what we can do to cure and treat as opposed to what we can do to prevent.

JoAnn Manson

Absolutely.

A. Macdonald

Was there a mentor, someone who educated about this idea of prevention, or was it just something that grabbed you? Were you an anomaly? Because I think in some settings, in some medical schools, you might have been. So I don't know if you were where you were, but just curious to know.

JoAnn Manson

Yes, I think it may have been more atypical to be interested in prevention. I was also really interested in treatment and what modalities of treatment were available, but I really began to understand that it's called a health care system, yet in the United States, it is really a disease care system; there is very little focus on prevention and health promotion or maintaining health. So in some ways it's a misnomer to be calling it health care. It is very much disease care oriented. I would like to see that changed to be more health care or prevention of chronic disease, prevention of disease, focus.



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But I think I had several teachers who did put a focus on preventability of some of these conditions. So that really helped to inspire me. I think this is one of the reasons why after doing my training in internal medicine, I pursued endocrinology as a subspecialty because that includes diabetes as a major focus as well as other conditions that are considered endocrine disorders. And I think with diabetes in particular, there are so many opportunities for prevention.

A. Macdonald

Yes. I'm curious too—when you mentioned this is a school where clinical care started in the first year, often following pregnant women and then their early childhood years—did all the men also have the same obstetrics, gynecology, pregnancy patients? That's an interesting focus for both genders to be interested in women's reproductive health and childbearing.

JoAnn Manson

So with all of the students, it was this early clinical care that usually would involve pregnancy: a woman during her pregnancy, labor delivery, and then pediatric clinic. In some cases, a pregnancy was already fairly far along, so it may not be a full nine months of obstetrics clinics. After that, much of the focus was on pediatric care, following the baby during that first year of life. So it was very similar for the men and the women.

A. Macdonald

Interesting. And because there was an imbalance of men and women, what did the faculty look like? The students looked 4:1. What did your faculty look like? Was it easy to be a minority in that group of students? Did you feel included, accepted equal, or were there challenges to being a woman? I would think that women physicians were becoming more common, but certainly not to the point we would acknowledge today.

JoAnn Manson

[00:11:00]

The years I was there it was, again, a 4:1 ratio. So this was very familiar to me. It didn't seem at all unusual in that I had just gone through four years of college where there was this 4:1 ratio and now it was again 4:1. But I never really felt that there was any discrimination against the female students. I know that some medical students have talked about experiencing that. I think it can be very individual in light of what the experiences are. There may have been a few cases where I thought there was some unequal treatment, maybe on the wards in the hospitals with certain attending physicians or residents, the physicians in training.

But for the most part, I thought it was extremely equitable. And that there was an interest [in equality] on the part of the attending physicians and the residents and junior residents and interns (because we're talking about the medical student years, so there are all these house officers, interns, and residents and attendings, also working with the medical students). I thought that overall, there wasn't discrimination against the female students there. There was a real respect for



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the fact that these are going to be female physicians soon when they finish medical school. And that there's also a tremendous need for women physicians, because many women—especially in certain areas such as obstetrics, gynecology, some women when they're seeking the pediatrician for the child—will seek out a woman physician. So I think there was a recognition that this is really serving a role for patients as well as just having a fairer society and being more equitable. So I didn't believe that there was much discrimination against the women students. I was not seeing much evidence for that.

A. Macdonald

That's good to hear. I do hear different stories, but I think you point out wisely—the institution you're in and the personalities that are there, these things can all make a difference in how you experience being a minority in a given situation. And this social recognition, as you said, that we do need for patient care reasons to graduate some female physicians, I think that's important too. I hadn't thought about what the conversations might have been at the time about the need for this.

JoAnn Manson

One area I will mention is that occasionally with some of the male interns, residents, you would feel that they were maybe interested in you romantically and that could be—you know, that kind of thing. But it usually could be managed. And because Chris and I were already together (we were already involved from college on), I didn't feel that that was a specific problem for me in terms of handling being asked out, that type of thing.

A. Macdonald

Right.

JoAnn Manson

But I could see how for some of the female students that could become a problem. So I think it's very individual based on their own personal experiences and a lot of different personal factors, individual factors.

A. Macdonald

I think even today, many workplaces struggle for professional environments for women and men.

JoAnn Manson

It is by no means unique to the health care system or to the hospital environment.

A. Macdonald

Right. Exactly. That's really interesting.

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Chapter 3

The Paradigm of the 70kg Male

[00:15:42]

A. Macdonald

Somewhere in an interview you gave, you mentioned that the curriculum in medical school at that time was still very much the male model, the emphasis on male understanding of cardiovascular disease or others. I'm sure you can elaborate more than I can—

JoAnn Manson

That is something that we can talk about. I think that is somewhat separate from whether we felt that the female students were being slighted, were treated differently or discriminated against. But without question, in the curriculum—even at a school that had a very innovative curriculum and really tried very hard to be on the vanguard of change in medical education—I think it was just so steeped in the tradition of medicine to teach this male model of physiology and anatomy and disease. So often the paradigm would be what they would call “the 70-kilogram male” that would require this much medication or would have typically this blood pressure, this—you know, these various metrics and numbers. There was very much a focus on that paradigm without question. Very rarely would you see specifically a woman except in the OB-GYN classes or when talking about female specific conditions. Even in talking about conditions that were much more prevalent in women, very often the paradigm was the male patient. The diagrams and images were of male patients, and it would be rare to have the lecturers and professors actually talking about sex differences: differences in symptoms presentation, treatment, reactions to medications, different dosing of medications.

Much of this information was actually not available at that time, because this male paradigm was also affecting the research and there wasn't a strong interest in understanding sex-specific conditions, sex differences in diagnosis and treatment. So a lot of that research was limited, given short shrift, and the information was not even available to teach in medical schools.

I think there's a slow but progressive change in that. There's more integration of sex differences in conditions predominant in women. For example, they are maybe incorporated into autoimmune diseases, all of the differences in terms of the immune system of men and women and the many conditions like lupus and rheumatoid arthritis that are so much more common in women. Even in terms of heart disease. We know so much more now about differences in presentations, symptoms, diagnostic tests, different types of heart disease that may be more common, like a type of heart failure with preserved ejection fraction and atrial fibrillation in women being more likely to lead to stroke. So there is a greater appreciation of the sex differences and even some dosing of medication differences.



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But it's still—I mean, we're talking in August of 2024, it is still limited. There is a need for so much more research on these questions of sex differences, what we often call sex and gender-informed care of the patient. The research is really very limited.

A. Macdonald

[00:20:32]

So the research I know has grown. The integration of it into training and education perhaps has lagged? Or are there needs on both sides, both research and education?

JoAnn Manson

There are absolutely needs on both sides: the research as well as the teaching and curriculum development. But even when there is some research that would suggest there should be some focus on sex-specific differences, sex and gender-informed medicine, it is not necessarily incorporated into the curriculum. Here's an example, and we'll probably go back to this later. There is very little training of medical students or clinicians on menopause. The menopause transition, perimenopause, the available treatments for symptoms like hot flashes, night sweats and all that. The amount of training really decreased after the Women's Health Initiative results suggested that hormone therapy may not have a favorable benefit ratio for prevention of chronic disease. That led to a major decline in hormone therapy use and less teaching about menopause.

But menopause now is currently one third to even 40% of the average woman's life, and it is a field that is so neglected in medical school, in the clinical training years, and well past internship and residency years. Many, many clinicians do not have adequate training in that area.

A. Macdonald

So if we can't treat it as a piece of treating chronic disease, it's not important enough on its own. Even though it's 40% of women's life spent in menopausal years, it doesn't get the same kind of attention just because?

JoAnn Manson

That's part of it. If it can't be put into that particular category – “this is exactly how you treat it,” everyone agrees that this is the approach. Yet even just having that discussion with the patient and asking certain questions becomes very challenging for the clinician when they don't have this training and patients ask questions they can't answer.

A. Macdonald

They don't know what to suggest if they haven't been trained.

JoAnn Manson

Right. They're not even comfortable often in asking the patient questions about their symptoms. And patients are often uncomfortable bringing up these topics. This is really an area where shared decision making between the patient and the clinician is so important; it really needs to be



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a conversation, discussion of options, and then the patient really sharing and making decisions about what route to take.

A. Macdonald

The best course, yes. This lack of attention to sex differences and gender-informed care, is this something you noticed as a medical student or was this looking back?

JoAnn Manson

Oh yes, I noticed. We would talk, among many of the women students in class, that we were always hearing about the 70-kilogram male. In some ways, we would be amazed that this was so often the image that was presented and so often the reference point for what we were learning. But, you know, after a while, it seemed just to be the way it was. And we were so busy trying to learn everything and doing the training, that you couldn't really at that point focus as much on activism and trying—

A. Macdonald

Being a critical voice as a medical student is probably not—

JoAnn Manson

[00:25:03]

Right. I think the changes really needed to come from people after they completed medical school, although some changes I think can be instigated by the students themselves. I think that students are increasingly vocal and active in asking for certain types of training, teaching, and topics in the curriculum. So there are some very positive changes that got implemented.

A. Macdonald

Ground up sorts of movements. I think as we put more diversity in medical schools, we'll see what we've thought of as the norm get disrupted. So when you put women in.

JoAnn Manson

Right.

A. Macdonald

So when you put women in, you see things; when you put ethnic minorities in, you see things.

JoAnn Manson

Exactly, yes. As we were discussing when the medical school classes were only one-quarter women, it may have been more difficult. Now the medical school classes are really at parity for quite a while; 50% women there and many more of the professors and teachers are women. I think there's going to be even more change over time.



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A. Macdonald

Yes, I think so.



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Chapter 4

A Tumultuous Time and an Emerging Focus: Internship and Residency

[00:26:29]

A. Macdonald

One of the things I wanted to ask: is there a point in those four years, as you're moving into clinical experiences and as you're absorbing things, is there a point you started to feel like a doctor? Or did that come later as you moved into your residencies? Is there a point at which you felt, "Yes, I am a doctor, I know myself to be a physician"?

JoAnn Manson

I think it's a gradual process, in terms of your identity as a physician. I felt that once I was in the clinic and actually being given responsibility for some decision making and working closely with patients and making diagnoses, that I began to feel more of that identity. However, I personally felt it really came after receiving the M.D. degree and during the internship residency years. But it's a very gradual process. Again, this is why, in many ways, it is so surprising that patients can entrust their care to students and trainees.

A. Macdonald

Who don't even feel themselves to be a physician!

JoAnn Manson

Yes! And very often there would be specific patients who would want so badly to call you doctor, even though you keep reminding them that you're a medical student and their doctor is named so-and-so. There were many cases where they would just totally accept you as the doctor and even ask for you, as the doctor to be the one, to talk with.

A. Macdonald

Yes! I'm also thinking I'd like to hear a little more about your residency, but I believe as you come to the end of your M.D., it's also the time when you lose your mother. You get married. Maybe we'll take a moment and think about those personal transitions that were happening? You told us last time that the loss of your mother to ovarian cancer was a real motivator for thinking about what we don't know about women's health, why we need to know more. But this comes right at a moment of celebration for most people, receiving your M.D. is a big moment for many students. So, I wondered if you could comment on that.

JoAnn Manson

Right. So it was a tumultuous time, a lot happening. I had already made a commitment to be in an internship and residency program in Boston. So I was already leaving home again. And Chris and I got married right at that time, very shortly after I graduated from medical school. He



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graduated from law school because he was together with me in Cleveland at Case Western Reserve Law School.

A. Macdonald

Okay, so you had both moved to Cleveland and did the next professional phase.

JoAnn Manson

[00:29:58]

Yes, we were both in Cleveland together and then moved back to Boston. So it was a very, very difficult internship year for me. My mother had very advanced cancer when it was diagnosed. There were maybe a few months of her condition improving when she was actually able to do things, but it was already very advanced at the time it was diagnosed. In fact, as so often happens with ovarian cancer, the cancer is diagnosed at a very advanced stage. And the symptoms can be what's called nonspecific. But I think it also reflects that in the medical field, especially at that time, there wasn't as much focus on conditions that were female-specific diseases or female-specific cancers. Over the years, breast cancer has gotten much more attention, very fortunately, and ovarian cancer has gotten more attention. But it's still really understudied, and there still isn't a terrific treatment.

So the cancer was very advanced. And I am doing my internship and night call and working really hard. And any chance I ever had to take a break and go, take time off, I would go home to see her. It was just a very tough time. I took no true vacation time during that period when I was doing a lot of night call doing the internship. So I would just say it was a very difficult time.

That really underscored for me how little is known about women's health and conditions specific to women, specifically for ovarian cancers. So little was known that it's a cancer so often diagnosed at very late stages. And this really motivated me, as I was thinking about what field do I want to pursue, to be more involved with women's health related conditions. At that time I wasn't thinking that I would necessarily focus on cancer because it actually seemed painful to have that focus.

A. Macdonald

Right. I can imagine.

JoAnn Manson

But I became really interested in the field of women's health. I knew that whether it was clinical practice or some combination of clinical practice and research, a large percentage of my patients would be women, and I would be focusing a lot on sex differences and conditions that were specific to women or more common in women. So I did pursue that.

In my junior residency year after internship, my mother had died. I began applying to endocrine fellowships, and I decided that I would do the endocrine fellowship route. Then, as I was doing



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my endocrine fellowship, I saw so much chronic disease that seemed highly preventable. Really for me that just underscored that prevention, and research on prevention, was what I wanted to focus on most because I was seeing a lot of patients with type 2 diabetes.

A. Macdonald

Diabetes is considered an endocrine disease?

JoAnn Manson

[00:34:50]

Yes, it is considered part of endocrinology. During my training and during the clinics I was doing during my endocrine fellowship, I was seeing a lot of patients with very advanced complications of diabetes. In those days—we're talking about before a lot of these newer treatments were available to reduce risks of complications—there were many patients who had longer duration of diabetes and not only what's called small vessel disease (like vision loss, kidney disease, nerve damage) but also heart disease, stroke, a greater risk of many of the cardiovascular complications. Cardiovascular disease was, and is still, the leading cause of death among people with diabetes.

I became really interested in the topic of what can be done to reduce the risk of type 2 diabetes, which was increasingly prevalent and was almost in those years becoming epidemic. I mean, now it is at an even higher level; very, very high levels that are tracking with some of the other trends in terms of changes in the prevalence of obesity and other risk factors. But I really did want to do research on understanding better, how to prevent type 2 diabetes and cardiovascular disease and cancer. So these were the areas I really wanted to focus on.

And we've done certain estimates in our research of the percentage of these conditions that are preventable or modifiable. The numbers for these estimates are actually just staggering because for type 2 diabetes, we and others have estimated that close to 90% of type 2

A. Macdonald

Oh! I had no idea.

JoAnn Manson

Yes. Type 2 diabetes could be preventable with various lifestyle and behavioral changes. Of course, it's not just as simple as telling people to change their lifestyle. There are many people who don't have access to healthy foods and affordable, healthy diet and safe places to walk and be physically active. So in many ways it's a complex societal issue as well. But if you look at risk factors such as diet—or let's look at the positive side, the healthy part. If you have a healthy diet, you have regular physical activity, you don't smoke, you maintain a healthy weight, and you do not have excessive alcohol intake: even just those factors alone are related to having a 90% lower risk of developing type 2 diabetes.



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Now with heart disease, with heart attacks and coronary heart disease, these estimates are 80% reduction, achievable through factors such as healthy diet, regular physical activity, maintaining healthy weight, avoiding excessive alcohol intake, also controlling blood pressure (which is a preventable, treatable condition), and treating high cholesterol. With stroke, the estimates are close to 70%. And with cancer, it's close to 40 or 50%. A major paper was just published suggesting that dementia, which is often considered an inevitable consequence of aging and also having a strong genetic component, is highly preventable. The most recent estimates were these from the UK, but the most recent estimates were 50% preventable. If 50% of cases worldwide of dementia may be preventable by various modifiable risk factors, I think that there's so much potential for prevention. Really, in terms of population health, prevention is very powerful.

And I became interested in this area, and also interested in doing randomized clinical trials. Because I think that observational research is really important in generating hypotheses to be tested in randomized trials. When the associations are just extremely strong, such as with smoking and the risk of lung cancer or even cardiovascular disease, you don't need randomized trials. You can just move forward with public health campaigns, various ways of intervening and reducing smoking. But experimental evidence goes so far in actually leading to clinical practice change and leading to public health measures.

A. Macdonald

[00:41:28]

When you announced those kind of figures that so much of what we consider to be inescapable or genetically based or deterministic to be actually preventable at those kind of rates, I'm astonished. When did you sort of stumble around and think, this is astonishing? You've already said the curative model, the disease model of medicine needs to be adjusted to a health care model. But was there a point in your evolution as a physician where this became "this is a commitment I want to make." Would you say that was during your residency?

JoAnn Manson

I think some of it started in medical school, just seeing how much of the chronic disease did seem to be related, not only to behavioral factors, but also to social determinants of health: where you live, you know, the zip code being more important than the genetic code.

A. Macdonald

Was that being introduced back then?

JoAnn Manson

That was starting back then. Even then, there was an awareness—not to the point where you would be writing papers saying it very forcefully. But where I really became impressed by this, I would say as I worked more and more in the field of type 2 diabetes. So some of that was during internship, during internship and residency. But a lot of it was also my endocrine fellowship. That's when I decided that I did want to train in public health and go back to school in terms of



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learning research methodology, study design, biostatistics. Doing that type of training so that I could do research in these areas.

A. Macdonald

Okay. That helps me place this as a late arrival or an early arrival. I'm watching our time a little bit to be mindful of your stop time, so rather than get into your MPH and the world of research, we'll leave that for next time. And I just want to say an internship in the shadow of your mother's disease and death, I can't even imagine. Because everyone I speak to tells me how intensive those internships are. I don't know how you managed that. It must have been a struggle.

But you told me during your medical school years, there was encouragement of women; there was no out and out discrimination. Did that environment continue when you moved back to Boston? You're at Harvard medical school doing your internships and residency. Did you still feel equal as a woman in endocrine research and clinical training? Did you face the same kind of "this is not problematic," or were there different challenges in those years as a woman?

JoAnn Manson

I think in general, I didn't feel that there was direct discrimination by my supervisors and our professors or attendings. There were certainly some individual examples in individual cases where I thought that the females on the wards in the hospital were not being given as much credibility and as much attention in the training, as many opportunities to do procedures and to get specific training. I felt that with a few of the supervisors and attendings and mentors. But for the most part, I didn't feel that the women or I specifically was facing discrimination

A. Macdonald

Not systemic. Yes. Okay.

JoAnn Manson

[00:46:04]

Yes, I did not feel it was systemic. I thought it was more on an individual basis. There were some of the attendings who paid more attention to the male interns, residents and trainees and gave them more opportunities.

A. Macdonald

Did you feel that was something you needed to address in some way to make sure you got the training you needed, or did you think it was something to just step around and keep going? How did you fathom what to do in those cases when that did happen?

JoAnn Manson

I think I learned to become more assertive. I would specifically ask for certain opportunities. I remember for a while I even considered pursuing surgery. I did a summer program at a hospital where I worked with a vascular surgeon and spent eight weeks just getting a lot of experience



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being in the operating room and assisting with procedures. But I felt that I really needed to seek out those opportunities specifically or I would not get [them].

A. Macdonald

But you didn't stick with the idea of being a surgeon?

JoAnn Manson

No, no. I definitely decided against it. I mean, it's a great field. There are lots of great surgical fields to go into. But I was really much more interested in internal medicine and endocrinology. I was interested in these continuous, longer term relationships with patients and working with them long term, including ways that they can be empowered to take charge of their health. That seemed more achievable in internal medicine, endocrinology, than in a surgical field. I think that there are other advantages of other specialties, but that was my choice.

A. Macdonald

Yes, I don't see surgery taking up a sort of mantle of prevention in population health in quite the same ways!

JoAnn Manson

I think there are some differences in that regard, yes.

A. Macdonald

That's really interesting and I thank you for that. I think that'll leave us at a nice sort of junction to take up next week, adding the science and research piece in such a deliberate and dedicated way—going off and learning the tools of research. And I will be curious to hear, as a woman now in science, what is the environment there, and how did that go for you? I won't get there today because I know we have to be a little mindful of time and those are rich questions. So I'll turn off the recording and say a proper farewell to you offline.



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JoAnn E. Manson, MD, MPH, DrPH, MACP

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[00:00:09]

A. Macdonald

Okay. I'm delighted to be back again with Dr. JoAnn Manson. This is our third meeting, and we're going to be picking up on those years past residency and fellowship where she is now stepping out into the beginnings of her professional career and her commitments to science. I thank you once again for joining us for this Alma Dea Morani Renaissance Woman Oral History Project. It's really important to be recording these trailblazers in the fields of women's health and in the lives of women professionals.

JoAnn Manson

Thank you, Arlene. It's great to talk with you again.



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Chapter 5

Returning to School: The Launch of a Research Career

[00:00:49]

A. Macdonald

So last time we left off, you were explaining to me why your commitments to preventive medicine and research into preventive measures were taking hold of you even in those early stages of your career, working as a Fellow in endocrinology witnessing late-stage development in diabetes (such as cardiovascular disease) and the things that might be done to modulate or prevent the worst kinds of outcomes of those endocrine diseases. We stopped just as I was going to ask you about the big decision to start to gain the tools of research through a master's in public health and then the doctorate in public health.

This is really kind of exciting. I know lots of researchers who don't do that kind of formal training, but you're combining your early years in clinical practice with obtaining this formal education in research. What prompted that decision? What made it an easy or a hard decision? How did you come to decide that was the right path for you?

JoAnn Manson

Yes, I was seeing a lot of patients with chronic diseases, and late stages of chronic diseases, and I just became increasingly interested in prevention of chronic disease and doing actual research on that topic. It's interesting that in medical school you tend to learn very little about research methodology, epidemiology, biostatistics: how to actually do this research. I thought that if I was going to be actively involved in this kind of research, I wanted to have additional tools and skill sets in order to be able to get grant funding and actually have leadership roles on grants. And I thought it would be very difficult to do that without getting additional training.

[*Laughing.*] Many of my colleagues were literally shocked that I was going back to school because it had already been so many years in school: you have college, medical school, training in internal medicine and endocrinology. And I had originally planned that I would be a clinician almost entirely, that I would hang out a shingle or get some clinically oriented position and would not necessarily be going on to research. But I did feel that this was an area that was understudied and that more could be done. I found it exciting to think about being in research discovery, actually having the tools and the skills to be able to do the research. So it became clear to me that I'd have to go back to the classroom for that.

I started with a master of public health program; many physicians do actually feel that they have enough training, adding the Master's. It's a great program. I went to the Harvard School of Public Health and really enjoyed the MPH program. But when I got to the end of it, I felt that I still wanted to have more experience with research and learn even more about research methods. So I applied to the Harvard School of Public Health Doctor of Public Health Program. Overall it was



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an additional four years to get the MPH plus the Doctor of Public Health, which is somewhat fast, I guess, compared to what it is sometimes. But it certainly seemed like a long time, given that I'd already been in school for such an extended period. But I did feel by the end of the MPH and the DrPH that I was in a position where I really could begin to be actively involved in research and that it wouldn't be too long before I could be an independent investigator putting in my own grants and getting funding to lead grants. So that's what was motivating me.

Also, as I previously mentioned, I was really motivated to pursue women's health because I thought this is such an understudied field. There are so many knowledge gaps and combining prevention research together with women's health research would be very meaningful to me. I wasn't thinking I would focus entirely on women's health, but that it would be a key focus, a key goal, to work on some of the really pressing clinical and public health issues related to women's health.

A. Macdonald

[00:06:48]

Okay. So couple questions for you. The focus on women's health—I've read that you were involved in the Nurses' Health Study, a landmark of women's health observational studies. Did that happen during your training in health research, or was that later? When did you take up that role in that important research?

JoAnn Manson

I was actually very fortunate to become involved with a research team working in the Nurses' Health Study and the epidemiologic research there, while I was doing my doctorate in public health. I began to collaborate with other investigators in the Nurses' Health Study and my dissertation projects were related to research in the Nurses' Health study.

I started out being most interested in prevention of type 2 diabetes. The relationship between diabetes (as well as obesity, high body mass index) in terms of chronic disease outcomes, particularly cardiovascular disease, coronary heart disease, stroke. I was interested in those relationships and how to prevent type 2 diabetes and cardiovascular disease. This became a really major interest of mine. I was fortunate to be able to do some of the earliest work on physical activity as a means to prevent type 2 diabetes. It was surprising there hadn't been more research on that topic. A lot was known about the relationship between high body mass index and weight gain and risk of type 2 diabetes, but it really was not well understood how physical activity—regular moderate or vigorous physical activity or dietary factors and dietary patterns—could affect the risk of type 2 diabetes. So I became very much interested in those topics. I was also very much influenced by one of my mentors, Walter Willett at the Harvard School of Public Health. I collaborated with Walter on several projects in the Nurses' Health Study, particularly related to type 2 diabetes and cardiovascular disease.



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So those were my really early interests. But I became increasingly interested in randomized clinical trials related to prevention because it seemed that many of the associations that we were seeing in observational studies could actually be tested conclusively and rigorously in randomized clinical trials. I was tremendously interested in that subject while I was doing my training in public health and doing the doctorate in public health at the Division of Preventive Medicine at Brigham and Women's Hospital (where I later did become the division chief), and there was randomized clinical trial research going on in that Division. So I had an opportunity to experience firsthand some of the needs for recruitment, retention. I was able to actually play a role in some of the research studies and the clinical trials. Really understand what randomized trials involved in terms of the execution, the conduct of these trials, and the challenges, the needs, the methodological issues involved.

One of the trials that was going on was an aspirin trial, the US Physicians' Health Study randomized trial of aspirin. And we were also talking about trying to launch a new aspirin trial that would be limited to women that would really help answer questions for both men and women about the role of aspirin in the prevention of cardiovascular disease.

[00:12:17]

I became increasingly interested in doing these large-scale randomized placebo-controlled trials where it's very rigorous. That's often considered the gold standard of research, and it can actually convince clinicians to make changes in clinical practice. So I was involved in these two aspirin trials as well as doing some research in the Nurses' Health Study on these questions.

So I was doing research in the Nurses' Health Study and looking at the relationship between aspirin and cardiovascular disease in women. I was looking at some dietary factors, particularly dietary supplements, you know, taking supplements of vitamin E, vitamin C, vitamin D, beta carotene. I became really interested in doing randomized clinical trials of these nutritional supplements where you can actually have a control group, a placebo control group. One of the first randomized trials that I led was a study of a population of high risk women who already had some risk factors for cardiovascular disease or had a history of cardiovascular disease. I was interested in testing whether giving supplements of vitamin E, vitamin C, beta carotene (and later we added folic acid, B6, B12—the B vitamins) compared to placebo would lower risk of subsequent cardiovascular events for women who already had some risk factors for cardiovascular disease.

It's possible to actually test each of these supplements separately, not just in a combined pill. Then, in the end, you can't tell—what was the active factor? You wouldn't be able to tell; is it the vitamin E, the vitamin C, the beta carotene? We were actually doing the type of trial that is called the two by two by two by two factorial design. So each of the interventions was individually randomized compared to placebo. It's a long story, but I became really interested in



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doing that kind of randomized trial research. Then when the Women's Health Initiative came along as an opportunity and let me—

A. Macdonald

Just let me get the dates for some of this. I know you're in your MPH and DrPH 1984 to 1987. So you're getting your chops as a health researcher in these different modes, particularly randomized controlled trials. When does the Women's Health Initiative, which was a large, randomized control trial if I understand correctly, launch?

JoAnn Manson

[00:16:03]

So I'm already doing research in the Nurses' Health Study by the mid-1980s, late 1980s into the early 1990s. And I'm starting to do some randomized clinical trials, working on the aspirin trial. Also, in the late 1980s planning with my colleagues in the Division of Preventive Medicine this new randomized trial of aspirin in women. And around that time also planning this new randomized trial in high-risk women of vitamin E, vitamin C, and the antioxidant dietary supplements. Then, right in 1992, there was what's called a "Request for Proposals" from the National Institutes of Health for this new large scale randomized trial of menopausal hormone therapy, the WHI [*Women's Health Initiative*].

I applied to be one of the principal investigators of a clinical site. We weren't notified until 1993, but the application process began in 1992. Our site in Boston at Brigham and Women's Hospital was selected as one of the initial sites, one of the 16 Vanguard sites. So I became involved in the WHI in 1993, 1994, we were doing recruitment by then. The recruitment actually lasted several years. It was really interesting to me to become involved in the WHI for so many reasons. One was that it was addressing some of the most pressing questions in women's health, which was ultimately a major goal of mine to be contributing in the area of women's health. Also, because I was increasingly interested in randomized clinical trials, this was an opportunity to be involved in this large national trial. Ultimately, there were 40 clinical sites around the country.

A. Macdonald

Wow.

JoAnn Manson

This large national randomized trial of women's health was testing not only menopausal hormone therapy compared to placebo, but was also testing calcium, vitamin D supplementation, and a low-fat dietary pattern (increased fruits and vegetables and grains and lower intake of fat) to see if these interventions could lower risk of some of the most pressing and most common chronic diseases for women: cardiovascular disease, cancer, osteoporosis, hip fracture outcomes. You know, these major health outcomes. So I was really interested in doing that.



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But it was it was a very major time commitment. I never regretted it, but my life was so busy at that time because I was doing clinical practice in internal medicine and endocrinology. So I already had a fairly busy clinical practice. I was doing research with some of these other studies that I mentioned. And at that time I had two young children. I now have three children. But at that time when I started the WHI, my daughter was six, my son was four.

A. Macdonald

Oh, they were very young.

JoAnn Manson

[00:20:50]

You know, it was a lot of fun taking care of them and spending time with them. But my life just seemed so totally hectic at the time. It really became a juggling act. Fortunately, or unfortunately, we were about to try to have a third child. But because of some health issues I developed, I was advised to wait a while before a third child. So we ended up waiting quite a while.

Both of us wanted—my husband and I came from large families and we were kind of wanting three kids, so we waited quite a while. The third child, my son Joshua, wasn't born until 2003. So there's like a 14 and 16 year age difference between his sister and his brother. You know, they're much older. For a long time he couldn't really figure out who they were. Initially, he thought they must be like friends of the family or something. He couldn't imagine that he had a sister and a brother that much older. *[laughing]* But anyway, it was a very busy time.

But I have to admit it was extremely rewarding. It was very exciting working on these randomized trials and especially working on the Women's Health Initiative. One thing I didn't mention was that when I was working with the Nurses' Health Study, I was doing some research on hormone therapy, menopausal hormone therapy. I was looking at the relationship between estrogen therapy and development of type 2 diabetes. I was collaborating on some projects looking at hormone therapy and cardiovascular disease outcomes.

I kind of have the distinction of being the only WHI principal investigator who was also working on hormone therapy in this large-scale observational study [*Nurses' Health Study*]. It ended up that the two types of studies had very different results. Initially, the results seemed highly discrepant between the Nurses' Health Study, which showed that hormone therapy was associated with much lower risk of heart disease in women. The women who were taking hormone therapy had lower rates of heart disease than women not taking hormone therapy. In the WHI randomized trial, that was not found—there was no reduction. Initially, there did not seem to be any benefit, and there was even some concern about risk.

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Chapter 6

The Nuances of Prevention Health Research

[00:24:21]

A. Macdonald

Yes, there was something I recall – was there some point when they stopped administering the menopause estrogen as part of the study for fear of heart disease?

JoAnn Manson

The trial was stopped early. There were two separate hormone therapy trials, one in estrogen plus progestin in women who had an intact uterus because the progestin is added to protect the uterus from endometrial cancer. And then there was a separate trial in women with hysterectomy; that trial was testing estrogen alone. The trial of estrogen plus progestin was stopped three years early, before it was intended to stop, because it appeared that the risks outweighed the benefits.

The goal was to look at chronic disease outcomes and the benefits and risks when hormone therapy was used for the express purpose of preventing chronic diseases. The second trial, the estrogen alone trial, was stopped one year early as the results were initially quite discrepant [*with earlier observational studies such as the Nurses' Health Study*]. However, over time, we were able to delve very deeply into the results of the WHI hormone therapy trials by a woman's age and time since menopause. And then we were able to have a much better reconciliation of the findings from the Nurses' Health Study and from the large randomized trial of hormone therapy in the WHI. It appeared that when you look at the women who were younger, who were in their fifties, they actually had a more favorable benefit/risk ratio on hormone therapy than the women who were being randomized to hormone therapy in their seventies or even late sixties.

A. Macdonald

So it depends on the woman who gets the therapy. It's not a one-size-fits-all answer.

JoAnn Manson

Exactly. It seems like a case of precision prevention. You know, there were some women who were doing better. And the Nurses' Health Study population was largely women starting hormone therapy in their fifties or well below the average age of the women in the Women's Health Initiative, many of whom were in their sixties and seventies. So after further study there did seem to be more concordance or convergence of the findings.

That was actually really exciting. It was particularly seen in the estrogen-alone trial where the younger women seemed to be doing quite well on hormone therapy. Also, it became much clearer to readers, and to clinicians, that hormone therapy was still very appropriate for treatment of bothersome or moderate-to-severe hot flashes, night sweats, especially in early menopause.



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The WHI trial was addressing a question of whether it should be started and used for an extended period for the express purpose of preventing heart disease, stroke, dementia, or cognitive decline.

I think many of these questions were answered and well addressed by the WHI, but some of the initial findings may have been very confusing to clinicians and to women at large. But over time, the messages have become much clearer. It's really been a swinging pendulum with hormone therapy. In the early years, like the 1980s, 1990s before the WHI results were available, hormone therapy was perceived as appropriate for all women. Good for all women, very favorable. It had, and not.

A. Macdonald

Not only just for menopause, but possibly for other prevention of other diseases?

JoAnn Manson

[00:28:56]

Right. Among menopausal women, but for not just for menopausal symptoms, for prevention of many chronic diseases. That was the perception prior to the WHI and then when the WHI results were reported (this was in 2002) and the pendulum swung to the very opposite extreme of hormone therapy is not appropriate for anyone, it shouldn't be used. Many women were tossing their pills and patches, and many clinicians stopped prescribing it. Now the pendulum has come to rest in a more appropriate place: that hormone therapy is appropriate for some, but not all women. It still has a clinical role in management of moderate to severe hot flashes, night sweats, especially in early menopause.

Decisions need to be more individualized. It's not one-size-fits-all, and women themselves really need to share in the decision making about whether or not they're treated with hormone therapy, whether they receive non-hormonal treatments, or whether they need any treatment at all because some women will have milder symptoms. So it's been a saga. Over time, over the many, many years, the messages have become much clearer, they're more nuanced. We've really been able to delve deeply into differences in results by a woman's age, time since menopause, her underlying health status, other risk factors that she may have. And there's a clearer understanding of who's an appropriate candidate for hormone therapy and who isn't.

A. Macdonald

Is that a challenge to epidemiological research at large—that everybody would like a population health size answer? But the reality is, as you're doing this research, that it has to be delved down into the details before it can be useful advice? Does population health drive for the big answers and then have to pull back and find the moderate answers for different populations? Is this a constant issue?

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JoAnn Manson

I think there is tension. I think there continues to be a bit of a debate if an intervention is not found to be of statistically significant benefit in the overall study population. Should you believe it is of benefit in certain subgroups of the population? There continues to be a lot of debate and tension on that very point, I think that we are increasingly understanding that many decisions do need to be personalized and that interventions may be of greater benefit in some groups than others. We're seeing this for our trials of vitamin D supplementation and our trials of omega-3 fatty acid supplementation, that some people benefit and others don't.

Some of this, as with the omega 3s, may depend on whether you start out already having adequate nutrient status. The people who are already at a certain level—I mean, it seems almost straightforward and obvious that there is a threshold effect, and you don't really get additional benefit from taking more and more of something. That's usually the case. We often say in epidemiology, in this field, that more is not necessarily better and it can be worse – such as with mega dosing. There's an optimal range of intake, especially for nutrients and certainly for hormones. This is something that's really clear in endocrinology. There are negative feedback loops to turn off production once you get to certain levels, so more is not necessarily better. If a person is already getting adequate intake of various nutrients or already has adequate hormone levels, they may not benefit from an intervention that is geared to increase their levels.

But we are seeing that some people benefit more than others. It's complicated because sometimes you can see subgroups benefiting by chance, and you can't really be sure it's real unless you replicate the results in a separate trial. Sometimes a really intriguing finding, like a hypothesis generated from one study or one randomized trial, then needs to be tested with that specific hypothesis in a separate trial. You know, maybe a hypothesis that people who start out with a low blood level or intake nutrient intake will benefit and those who already have high levels will not. That could then be tested in a second trial and replicated. Then, usually, it will be believable by virtually everyone.

A. Macdonald

[00:35:33]

I see. I think my, and many people's, common understanding is that population health means us all. But in fact, population health means a lot of subgroups and a lot of variation in our population.

JoAnn Manson

There is variation. But you raise a very good point. There are certain lifestyle factors and behavioral factors that will benefit the population very widely. This is one of the reasons I am so interested in the topic. If you look at some of the lifestyle or behavioral factors, being physically active, having a heart healthy diet, maintaining a healthy weight, avoiding excessive alcohol intake, getting adequate sleep, managing stress, being socially engaged—these are of benefit virtually to the entire population. There are so many research studies now showing that the major



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chronic diseases in the United States and even worldwide—cardiovascular disease, cancer, type 2 diabetes (that can all cause mortality)—are really very substantially reduced by having these healthy lifestyle factors. In many cases, such as type 2 diabetes, it's 80 to 90% reduction in cases.

A. Macdonald

If these risk factors are kept to a healthy parameters.

JoAnn Manson

Right. So there are many factors that really population wide there would be benefit. There are other factors that are more nuanced; precision medicine, precision prevention, comes into play. Some people benefit, others don't. It can become very complex. But I still do think there are some very general recommendations for population health that can reduce risks of various chronic diseases.

A. Macdonald

All across the board almost.

JoAnn Manson

That apply widely, very widely, to the population.

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Chapter 7

Juggling It All: Challenges, Practicalities, and Passions

[00:38:03]

A. Macdonald

Can I return you to a couple of things the story of your arc through this research is raising for me? You mentioned you had young children at a time of ferocious engagement in major studies and becoming a PI on these studies. In a practical sense, how did you [*manage it*]; I know you're still doing work in the clinic as well.

JoAnn Manson

Well, I'm really now focusing on the research and administration and mentoring. But back then, yes.

A. Macdonald

What did a day look like? How did you organize your calendar? How did you yourself get enough sleep, avoid stress, eat properly? Because I think for many people in the population, it's when life becomes too busy, too many demands, that we all let go of some aspect of what we might optimally want to do for our health. So it seems it's a population health question in a way to ask someone like you: how do you do all that when life is making demands from many directions?

JoAnn Manson

I won't deny that my schedule was crazy. It was extremely hectic. My days were very long, and I probably was not getting enough sleep. I would often experiment with just how little sleep can I get away with. I was probably doing [*small laugh*] a lot of things that weren't really optimal for my health. Let me say that it was a challenge to juggle all these different things.

But I was fortunate to have a good partner. I think this makes a huge difference. My husband was very devoted to the family and helped a lot. We shared the child rearing and worked really well together in that way. I think it's even more difficult when you don't have a really good partner in it. Also, child care is so important. Getting some help, having a person you really trust. We had some experiences that you might say were not so favorable, but others that really were. We were very lucky to have someone we very much trusted to help out in taking care of the kids. So, there are a lot of things that you have to seek out. And some of it is chance.

A. Macdonald

Or resources.



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JoAnn Manson

Yes. So some of these forces are a little bit beyond our control. But I'm not necessarily recommending to everyone that they try to juggle all these things at the same time. I mean, I had people really wondering why in the world [*laughs*] was I trying to juggle so, so many different things. You know, I think people make their own choices about this. It was just really important to me, for some of the reasons we've talked about, I really wanted to do research. And I loved my clinical practice; I loved taking care of patients and interacting with patients. I didn't want to give that up for quite a while. And it was really important to me to help to be part of the answer. It's one of the slogans we use in the Women's Health Initiative, be part of the answer. It was really important to me to be part of getting the answer to questions about women's health, a lot because of my mother's illness and what we talked about. So I was very committed. It became almost like a mission to me to do these many, many different things.

I also wasn't quite ready to make a decision not to have a family, not to have kids. So I just kind of grit my teeth and said, "Okay, this is going to be really tough period. I'm going to be working really hard. My days are going to be really long and I'm not going to get a lot of sleep, but it will eventually get better." Though, I have to admit it hasn't gotten that much better! [*Both laugh.*] It has really been a hectic schedule for decades.

A. Macdonald

All the way through.

JoAnn Manson

[00:43:30]

Yes. People kept telling me, and I kept telling myself, "Oh, it's going to get better. There won't be as many demands on you." Yet it kind of stays that way. But I really do think, it may sound cliché, but if you find the work gratifying and you really are able to enjoy it despite the very hectic pace and the long hours—I didn't really find it arduous and onerous. I just found it like, "Wow, it is really busy. I haven't even eaten lunch." You know, all of these decades. Yes, I'm not getting enough sleep, but I could still keep going. And eventually get things more under control in my schedule.

A. Macdonald

Right. It's interesting to think about the role that passion plays in giving us adrenaline and the ability to keep going and not feel burdened and deflated. I can see when you say you want to be part of the answers, but the excitement that comes when the answers start coming is a kind of a fuel of its own, I would imagine.

JoAnn Manson

Exactly. It seemed exciting enough that it was worth making sacrifices for. I never really felt I was being totally forced into it. I think when it's really, really tough is when you feel you have absolutely no control over your schedule. You've no control over any of the decision making



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that's going on. I felt that there were options that I could give up X, Y or Z if I really had to, but I tried to stay the course to do clinical and research and family. At some point, I realized that it really was too much to continue doing all of those things.

A. Macdonald

And clinical is sort of what dropped out of the picture?

JoAnn Manson

Yes. In more recent years, I'm focusing on doing the research; the research, the administrative role as a division chief, and mentoring, education. This is an area where I now feel very motivated, kind of passing the torch to the next generation.

A. Macdonald

We'll speak more about that in tomorrow's interview as we get to more advanced stages of your career as you step into all those leadership and mentorship roles. I'm realizing we're coming up to 2:00 p.m. If you had time, I would ask you one or two short questions to finish us off. But if you need to go, I understand.

JoAnn Manson

I can take a few more questions.



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Chapter 8

A Woman in Science: Being Open to Opportunities

[00:46:53]

A. Macdonald

Okay. Just so we can understand this early part of your career, one of the things that struck me as you're talking about this dive into the research world, it sure seemed to me like your progress was fast and furious. Did you feel that yourself? Like, "Boy, I'm getting my MPH and a doctor of public health and here I am. I'm PI on studies. I'm being sought out for the Women's Health Initiative." It does sound like it all came very quickly. Maybe you were feeling like you were positioning yourself for this. So was it a career that you plotted out and you were not surprised that you hit these things, or was it a career that you were like, "I can't believe another door is opening, I can't believe I have another opportunity"? Was it more serendipitous?

JoAnn Manson

Yes. I would say it was more serendipity than really fully planned out. I wouldn't really have known, for example, that the opportunity to lead clinical trials necessarily would have presented itself. It was fortuitous that I was working in a Division that was doing these very large scale randomized trials and that I had done a few randomized trials during my endocrine fellowship and found that really interesting.

So maybe I was choosing to go to a Division that was doing clinical trials to get more training, but to find a Division like that I consider fortuitous. Then the timing of the WHI opportunity in the early 1990s when I was so interested in the question of estrogen therapy and health, the benefits and risks of menopausal hormone therapy. I had begun to do some research in that area in the Nurses' Health Study, an observational study, not a randomized trial. And we often say with observational research that correlation doesn't prove causation. The observational studies are so important, though, in so many ways. I mean, some associations are so strong, such as cigarette smoking and lung cancer, even smoking and heart disease, that of course you'd never do a randomized trial of cigarette smoking. You don't even need the randomized trials of smoking cessation because it [*the harm*] is so obvious. So observational studies have given a lot of really important answers, especially in public health. And they also generate the hypotheses that are tested in randomized clinical trials. So it's really important to have both, as well as basic science, the bench research. These are all really critical elements of the research foundation.

So it was just really interesting to me as an endocrinologist. I was trained in it, really interested in the health effects of hormones in the field of endocrinology. Then I started doing some work on this topic in observational studies, and then an opportunity came along for the first really large-scale randomized trial of hormone therapy in women. The opportunity to become involved in that with the focus looking at prevention of chronic disease. Does it prevent chronic disease?



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What's the benefit/risk ratio in prevention of chronic diseases? That was a great interest of mine, and it was kind of serendipity that it happened quite that way.

But I've stayed very actively involved in that field for decades. Observational as well as the randomized trial, and also looking at a lot of biomarkers, looking at different biochemical predictors; how does hormone therapy change, for example, biological aging? Really interested in effects on lipids and inflammation and a wide range of other biomarkers as well.

So I would say a lot of it is serendipity, and I think that is the way it often happens for people in research. But I did have like a general plan, or hope, that I would be able to do public health kind of research, population kind of research, that would answer some of the more pressing questions and especially fill knowledge gaps in women's health. Because I do think the WHI, in a randomized trial setting, was addressing some of the key knowledge gaps in women's health.

A. Macdonald

[00:52:40]

Yes. You know, I work with undergraduates; they all think they have to map their careers out. But everyone I talk to [*in medicine*] seems to acknowledge, "I set a direction. I knew what I hoped to do, but it was a lot of things coming together in certain ways that allowed me to move forward."

JoAnn Manson

I think you have to be open because if you map it out too specifically and precisely, you're going to let opportunities go by. I mean, I definitely would have let some of those opportunities go by if I had already planned, "Okay, I have to submit this grant by October of this year, so I don't have time to get involved in that new project that's just out." So I think you need to be open to these opportunities.

A. Macdonald

To what is coming to you as well. Yes, that makes great sense.

Our last couple talks we've talked about what it is like to be a 4:1 ratio of women to men in medical school, and what it is like in your clinical settings to be a minority in terms of gender. So I'm curious what the science world was like for women at the time working in an area of women's health research, which I've heard from other people was sometimes not "mainstream." There was a little bit of pushback against gender specific research. So what was that like for you moving into this science world and establishing this identity as a woman researcher? I think women in science may have been even less plentiful at that point than women in clinical positions. I don't know that for a fact, so I'll let you answer. I'm just curious about being a minority in this world of science.



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JoAnn Manson

Yes. In science as well, I always felt like I was in a minority, that there were more men in the room than women. I found myself in many rooms where I was the only woman or one of only two, maybe three women. And there were, you know, 15, 20 people in the room. So that was common. However, over time, I was seeing progress in this area. Definitely the numbers were balancing out quite a bit. In some of the environments I was in, such as the Nurses' Health Study Research Group, our Division of Preventive Medicine at the Brigham, and the Women's Health Initiative, in all of these different research settings there were at least as many women as men. And even in terms of principal investigators of the WHI nationwide, there were many, many women. So it was balancing out. And I had a lot of camaraderie with other women in science. It was not really like the earliest years where it was 4:1 ratio in college and in med school. As I said, Harvard, Radcliffe became almost equal, really equal numbers. In fact, medical schools for a while now will periodically have more women than men graduating. So it has really equaled out for training in medicine.

There's still a lower ratio unfortunately; fewer women than men who are full professors, who are chairs of departments or chiefs of division in various leadership roles. There is still a gap and a lot more progress needs to be made in those areas. But the numbers are definitely equaling out in terms of going into medicine and some of these other fields; even some of the specialties are equal numbers or even more women than men.

A. Macdonald

Would you say the same for health research? Would you say, "I was a minority, now it's evening out. Leadership is still in the hands of men." How would you describe the research world?

JoAnn Manson

[00:57:44]

I would say that in the research world, the numbers in epidemiology, in clinical research, in public health research, the numbers are similar. It's very reasonable, the ratios are very reasonable. There is still a problem at leadership levels, and it is still a low ratio of women to men in top leadership positions. If you're talking about chairs of academic departments, even research labs are more commonly men, and division chiefs—these leadership roles. It's definitely improved, but it's not parity. It's not really equal.

A. Macdonald

So you came through that ladder through your career, which feels more like an escalator because it seemed it was going up very quickly, did mentorship matter to you and who were some of the people who helped you gain the skills you need, gain the opportunities you need, the introductions you need? They were mostly men, I'm assuming. Did that matter? Tell me a little bit about the stories of your mentorship through your early career.



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JoAnn Manson

Well, I had a number of mentors within the Brigham and Women's Hospital and Harvard Medical School, Harvard School of Public Health. But I also sought out a lot of mentorship in professional societies. I became really interested in finding mentors at other institutions. For example, at some of the meetings I was attending. Some of these meetings of the American Heart Association, the Menopause Society (which used to be called in the North American Menopause Society), I would interact with a lot of women researchers and clinical leaders in the field. And I would often seek out their guidance. I mean, there really too many people to name, internal and external to my institution.

A. Macdonald

You'll feel like you're leaving someone out.

JoAnn Manson

I had many mentors. However, I became a division chief at age 46. So I was a full professor and a division chief at age 46. I probably would have sought out even more mentorship if it had been later than that.

A. Macdonald

It was an escalator; it was moving fast. I thought it was.

JoAnn Manson

Well, it didn't honestly seem that fast [*chuckles*]. It was still many, many years of really, really long days and hectic schedule. But I guess, compared to my current age, it certainly seems like a young age. But at that point, my identity became much more that of wanting to mentor others, to be a mentor and a resource for other trainees and for faculty rather than specifically seeking out mentorship for myself.

A. Macdonald

I think that's a wonderful stopping point because tomorrow when we meet, that's the aspect of your career that I'd like to explore. In my interview guide, I think we call it the mature stage of your career, where you move into administrative roles and leadership roles and mentorship roles. Those early stages of putting it all together and becoming the professional are not done with, but in the rearview mirror a little bit more. I'm looking at the time and I hear you coughing, so maybe that's a lovely point to stop and pick up next time. I'll just turn our recording off, and I'll just take a minute with you before we go.

JoAnn Manson

Absolutely.



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[00:00:09]

A. Macdonald

All right. I'm delighted to be back for our fourth interview with Dr. JoAnn Manson. We've been covering a lot of ground. And today we're going to move to more recent years in Dr. Manson's career.



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Chapter 9

Chief of the Division of Preventive Medicine: Key Directions and Achievements

[00:00:43]

A. Macdonald

You have been an assistant professor as early as 1991 at the Harvard Medical School and co-director of the Women's Health and a Director of Endocrinology in the Division of Preventive Medicine at Brigham and Women's Hospital. We were discussing those things last time. But within six short years, you are a full professor of medicine at Harvard Medical School, and you are the Chief of the Division of Preventive Medicine at Brigham and Women's Hospital.

JoAnn Manson

It was 1999. 25 years ago, I became Chief. I became a full professor of medicine at Harvard Medical School and Chief of the Division of Preventive Medicine. So I think it was a little more than six years.

A. Macdonald

Oh no, six years between where we stopped last time and these leadership roles. No, I know it wasn't six years ago. [*Laughter.*] That was back in 1999. But it really was in some ways a tremendous accelerated pace of your career to go from assistant to full and onto the Chief of the Division. Maybe you would start us off by telling us the story of how the position of Chief of the Division of Preventive Medicine came to you? Were you seeking it? Did someone knock on your door? How did you feel about stepping into that kind of role—prepared, unprepared?

JoAnn Manson

First, I was just clarifying it was eight years, not six years, between being assistant and full professor of medicine (1991 and 1999). Also, let me just mention that my roles in the Division of Preventive Medicine were as co-director of Women's Health. I was not Chief of the Endocrine Division.

A. Macdonald

OK, Sorry, I misspoke.

JoAnn Manson

I just wanted to make that clear as my role in the division. And then I became one of the principal investigators of the Women's Health Initiative and several other studies, randomized trials related to different dietary nutritional interventions and some other randomized trials that I was involved with. The position of Division Chief in the Division of Preventive Medicine did become open and available, and there was a search that was undertaken for that position. So I did apply for the position and I was offered the position that was in 1999. So it is 20, 25 years.



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I also want to mention that I've been involved with the Brigham's Connors Center for Women's Health and Gender Biology; this is one of the few women's health centers around the country that's focused on research and gender medicine issues. Originally, I had the role of being co-director of the Connors Center. Then, very briefly, I became the interim executive director of the Connors Center 2016 to 2017. That's when the executive director at that time took on a different position, so I went into the interim role. But I actually wanted to just continue to be the Chief of the Division of Preventive Medicine and really didn't seek out the long term role. Then they did, in 2017, find a permanent executive director of the Connors Center. I am now serving as a scientific advisor to the Connors Center and continue to be involved with the work of that program.

A. Macdonald

Okay, that's good to know. I had noted you were involved with the Connors Center, but I didn't quite understand all the connections from the one-line thing on the CV. So when you took on the role of Chief of the Division of Preventive Medicine, which you've been in some time now, what were your hopes? What was the direction or the achievements that you wanted to take the division in? Of course, you've been there a long while! But back when you began.

JoAnn Manson

[00:05:35]

I really envisioned the Division having a major role in conducting randomized clinical trials, population based clinical trials that had a prevention focus. Some of the trials did focus on treatment of people with cardiovascular disease or other health conditions, but it was primarily a population health prevention focus. So that was my major vision, what I saw as sort of a unique niche of the Division in that we were conducting very large, cost efficient, pragmatic trials. Many of these trials had more than 20,000 participants nationwide.

A. Macdonald

Wow!

JoAnn Manson

Some of them had nearly 40,000 participants nationwide and tested a large number of interventions across longer term duration. So that was a major focus. But over time, we also have become very actively involved in testing biomarkers, biochemical markers and multiomic biomarkers for chronic disease, including cardiovascular disease, cancer, diabetes, and other chronic diseases. So there are many investigators in our Division who focus on, for instance, genomics, metabolomics and epigenetics, a key area, and proteomics. We're doing more and more with that area. And what is driving some of those.

A. Macdonald

What is prote...? You have to say it again for me! Proteomics.



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JoAnn Manson

It's the proteins in the blood or looking at the proteins' profile and signature. There are actually many conditions that have relatively different proteomic profiles. The different profiles can predict, for example, increased risk of heart disease, type 2 diabetes, certain forms of cancer. So looking at the proteins, you know, in the blood. We also are interested in the effects of some of the interventions we're testing in randomized trials on changes in the omics. We've looked at metabolomic change, changes in small molecules in the metabolome, changes in the protein signatures. We also have a strong interest in looking at effects on biological aging, such as through epigenetic markers, telomere length. So our division has a very large bio specimen repository, and we have many faculty members focusing on looking at biomarkers for chronic disease and changes in biomarkers with different interventions. So that's another major focus of the division. But there are many programs around the country and internationally that do work in biomarkers and multiomic predictors of chronic disease.

I think what may be less common in terms of other research programs is these very large-scale population based prevention trials where we can cost efficiently test different medications or nutritional supplements. We've tested aspirin in both men and women in the prevention of cardiovascular disease in these large scale trials. Also the Women's Health Initiative actually fits in really well with this focus on randomized trials because that included not only the hormone therapy trials, but also calcium vitamin D supplementation and the low fat dietary intervention. But that is a nationwide collaboration. There are centers all around the country; I'm not suggesting that our Division was the only overall director of the Women's Health Initiative, but we were one of the clinical centers.

A. Macdonald

And one of the first ones, I think.

JoAnn Manson

[00:10:36]

Right. One of the original sixteen Vanguard centers.

A. Macdonald

So as you began, you had this focus on randomized controlled trials of preventive measures and interventions, which I am gathering was not the history of the division? That was new?

JoAnn Manson

It started with aspirin trials for prevention of cardiovascular disease. That was early in the history of the division. But it wasn't doing as many different trials and as broad subject matter in terms of clinical trials.



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A. Macdonald

Okay. When I picture those different kinds of studies, I think about the biomarkers and the cellular biological picture of preventive health. I imagine this is two kinds of scientists, one much more bench and blood and one more public health and data. And you would have had to gear up the right kinds of skills and the right kind of people to be able to do both? Was that a big part of what it meant to keep the division moving with the science on prevention?

JoAnn Manson

We do have faculty with a broad array of skill sets. We have several bio statisticians in the Division. I think most of our researchers are epidemiologists and population health researchers as well as clinical researchers. We don't in our Division specifically have bench research wet labs, though we do have the bio repository where we store blood samples, millions of samples from all of these studies. There we have a lot of participant samples across the different studies that have been done. We can send them out to different labs across the country, across the world, to measure the biomarkers.

A. Macdonald

Okay. I'm picturing wet labs and these kind of things. When you said the repository, that helps my visual image.

JoAnn Manson

It's really more of a freezer repository. We have all of these blood samples and some urine samples that are stored within liquid nitrogen freezers, a very large resource where we have all of that.

A. Macdonald

I would imagine, because the size of your trials are large, these would be huge.

JoAnn Manson

It's a lot of space storing the bio specimens. But we also really encourage collaborations with researchers across the country and even internationally to, for example, leverage some of these resources to measure biomarkers that are of interest to them.

A. Macdonald

I see. And their research has advanced understanding the large scale epidemiological side.

JoAnn Manson

Very often their research is focused on major chronic diseases like cardiovascular disease, cancer, type 2 diabetes. We're increasingly interested in the subject of cognition and prevention of memory loss, cognitive decline. So we've done more and more research in that area, also collaborating with many groups studying dementia, ways to prevent dementia, and to predict dementia. So that's another area we maybe can come back to later; we actually are really



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interested in exploring a particular intervention that has shown some promising results for slowing age-related memory loss and cognitive decline.

A. Macdonald

Okay, that sounds wonderful. Over the years that you've been there, are there accomplishments during your tenure as Chief that stand out for you, things you are particularly proud of or glad that you were able to achieve? What would you say some of those have been?

JoAnn Manson

[00:14:58]

Yes. First, the Women's Health Initiative. In terms of participating as one of the principal investigators, I feel very good about the information provided from that study just in advancing women's health. It was an increasingly common practice to start hormone therapy in women, often in their seventies, even eighties, for prevention of cardiovascular disease, for heart disease prevention and stroke prevention, trying to reduce risk of dementia. I think we showed that at least in the older age groups, that practice was not optimal but that hormone therapy still remained a very appropriate option for management of bothersome hot flashes and night sweats and menopausal symptoms in early menopause. As we talked about last time, we've recently tried to synthesize what the clinical messages are for health care providers, as well as women at large in the population.

Another study that I've been very actively involved with, a principal investigator of, is the vitamin D and omega 3 trial. This is a large scale study, more than 25,000 men and women in the US nationwide. And it is a very diverse study population. We actually made it a priority to enroll at least 5,000 African-American or Black participants because we were really interested in whether vitamin D may be of special benefit in that population and could reduce some health disparities. So we made that a point. We have a diverse study population in VITAL,¹ and I think that has been a really strong advantage to be able to look at many factors across educational level, race and ethnicity, across socio-economic status, regional or geographic areas, health insurance coverage issues. So we've been able to look at a lot of questions. We tested 2,000 IUs of vitamin D a day. And by the way, we mailed out calendar packs; they're like blister packs that contain the study pills and make it very easy for the participants. I mean, not that easy, but easier than with a bottle to remember to take them. They also can report to us more easily if they missed some of the study pills.

So in this large scale trial, which lasted an average of 5.3 years, we found that vitamin D supplementation did reduce the risk of advanced cancer, metastatic or fatal cancer, a reduction of about 17%. We also saw that there was a significant reduction, at least in the initial analysis, in autoimmune diseases such as lupus, rheumatoid arthritis, psoriasis, conditions like that we've continued to explore.

¹ VITamin D and OmegA-3 Trial (VITAL)

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We also found some interesting effect, what we call effect modification. When we looked at the analysis stratified by certain factors, such as looking at people of different body mass index or different body weights, we saw that there was a modifying effect of body weight and adiposity. In some ways, higher body mass index was counteracting some of the benefits of vitamin D and those at lower body mass index had greater benefits. We want to delve much more deeply into these findings because they may provide insights into how to make vitamin D a benefit to all, across all body mass index groups. We think we have some clues and some insights at this point that that may be helpful. But we need to continue to look at these questions.

But the main benefits were for advanced cancers, cancer death, and also autoimmune diseases and this modifying effect, for some of the other outcomes as well, by body mass index. There are other randomized trials of vitamin D that have suggested that vitamin D is of particular benefit in preventing cancer death. We've done what we call a "meta analysis," looking at these different trials in combination, and we've seen significant reductions in cancer death when these different trials are combined.

So I think this finding in the VITAL trial of the reduction in advanced cancer or metastatic or fatal cancer is borne out by some other randomized trials. We need to delve more deeply into mechanisms to really try to understand those findings. Then, some of our other findings from VITAL—

A. Macdonald

[00:21:14]

Just let me ask one question about the cancer one before you go on. Is this clinical practice yet? Are you doing the messaging so that vitamin D in cancer patients is now clinically taken up? Or is it not ready for that kind of messaging yet? What are your thoughts?

JoAnn Manson

It's really prior to a diagnosis of clinical cancer. So what's interesting—it remains controversial whether vitamin D supplementation, once cancer is already present and diagnosed, whether you can get a substantial benefit from taking vitamin D supplementation. There are many research groups looking at that very question. What our study was looking at was starting vitamin D supplementation in those without a diagnosed cancer or cardiovascular disease and then seeing if vitamin D or the marine omega 3 fatty acids (EPA, DHA, as in fish) could prevent development of cardiovascular disease or cancer.

So with the vitamin D, we saw that if you start it before diagnosis of cancer, it seemed to be reducing the risk of developing an advanced cancer. It may be because vitamin D has an effect in preventing the deep invasion of cancer cells into the tissue, and this makes it less likely to become metastatic once it's present. But if the cancer is already metastatic or already advanced, then you may not have the same benefit.

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A. Macdonald

Are GP's and family doctors telling people to take vitamin D? Has that moved out there?

JoAnn Manson

There are not yet clinical guidelines for use. In fact, I would say that the recent randomized trials have somewhat tamped *down* the enthusiasm about widespread supplementation with vitamin D. Because there had been tremendous enthusiasm, even very widespread screening for vitamin D deficiency, and a lot of the clinicians were screening and starting vitamin D supplementation. Then some of these randomized trials got started, like the VITAL trial and DO-HEALTH and several other vitamin D trials. And the randomized trials are not showing widespread benefits. It's not like a cure all, a panacea for every chronic disease; it is really a more limited benefit. And we still think that people require only small to moderate amounts of vitamin D; many people get that amount just from diet plus incidental time outdoors, the sun exposure and synthesis in the skin. But particularly older adults tend to need more vitamin D, and they have decreased absorption, decreased synthesis of vitamin D in the skin. So I think, again, it may come down to this precision nutrition. It's not a one-size-fits-all.

A. Macdonald

Just like the menopause and the hormone therapy.

JoAnn Manson

Exactly.

A. Macdonald

It needs targeted messaging.

JoAnn Manson

[00:24:57]

So we think that VITAL has helped to answer some of the questions about vitamin D. Then in terms of the marine omega 3s, we are seeing that there is a reduction in heart attack, there's a reduction in coronary heart disease-related events, but there's no reduction in stroke and no significant reduction in the combination of heart and stroke events, which is often called major cardiovascular events.

Again, even for the omega 3s, we tested a moderate dose of one gram a day. We saw that it was not a benefit to everyone, it was not of benefit for everything. It was seen to be a benefit overall for reducing heart attacks. We found that in those who started out with lower fish consumption, if their nutrient status for fish and omega 3s was lower at baseline, they tended to benefit more, and they actually did have a significant reduction in the primary end point of major cardiovascular events. It was somewhat complicated.



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This was another intervention where African-American and Black participants in our study tended to benefit more from the omega 3 supplements than the other groups. They also seemed to benefit more for certain outcomes from the vitamin D. So that's exciting to us because we did really try very hard to have enough statistical power to look at those questions in VITAL and see if that group benefited. So we want to pursue the findings that we have in VITAL with additional research.

A. Macdonald

Yes. It's a health equity question, if you can solve some of the disparity that exists.

JoAnn Manson

Right. We do think that it may have a role in at least narrowing some of these health disparities in cardiovascular disease, some of the chronic disease outcomes. So, we're excited to do additional research in that area. We have another large scale trial. VITAL was funded by the National Institutes of Health, and we had multiple ancillary studies.

You know, this is another thing that I feel good about in terms of the large randomized trials. Because it was such a large trial and we were able to continue the treatment for more than five years, we were able to look at many health outcomes beyond what we initially planned. So the primary outcomes were cancer and cardiovascular disease, but then we were able to provide opportunities for other researchers, both within the Brigham and Mass General, Harvard Medical School, as well as other outside institutions to collaborate and pursue their own interests and look at outcomes such as type 2 diabetes, depression, change in mood, change in cognition, autoimmune diseases, osteoporotic fractures, many other outcomes. This, we think, was helpful not only in advancing the science and in what could be learned from this resource, but also very helpful to the careers of faculty members who were able to take the lead and become principal investigator of an NIH R01 grant related to this topic. And a lot of them became even more interested in randomized clinical trials, which was exciting, and thinking about future collaborations. So we had opportunities for quite a few researchers in the Division as well as outside of the Division in the Brigham and Women's Hospital, Mass General and Harvard Medical School, the Boston area, as well as outside institutions.

A. Macdonald

It sounds like part of the thrill of large randomized controlled trials is the life that research can take on beyond what you had envisioned when you began the trial.

JoAnn Manson

Absolutely.

A. Macdonald

That would be thrilling. It has its own organic life.



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JoAnn Manson

[00:30:05]

Absolutely, but not all trials are large enough. We were able to develop a lot of resources in the trial, you know, collect blood, as well as most of the participants had clinic visits where we did very detailed in-depth phenotyping, testing, cognition, evaluating mood, body composition, doing oral glucose tolerance tests to evaluate glucose tolerance and diabetes risk. So we were able to do a lot of different evaluations and assessments on the participants. This has provided, together with the questionnaire information that participants provide on a regular basis, a lot of opportunities for researchers around the country.

But I just want to make the point that we are tremendously grateful to the volunteers who participate in these research studies. It is really such a gift to the population and to science that the study participants give, these 25,000 participants around the country.

A. Macdonald

And it isn't simple. When you outline the clinical work that goes with it and the monitoring over five years, this is not a small ask. It isn't, "I took a pill for a week and I'm done."

JoAnn Manson

Exactly. It's not a small ask, and they are just so generous with their time. And they really are very often just interested in helping to answer these questions, even if they don't directly benefit. You know, they're willing to take a study pill for five years. They don't know if it's an active; they don't know if it's vitamin D or placebo. They don't know if it's omega 3s or placebo. It is just incredibly generous. So I really do want to acknowledge that. I always try to acknowledge the volunteers in the study whenever I give a talk about the research, because this research cannot be done without the study participants. And very often volunteers, if they do get some compensation for something that they do, like giving a blood collection or coming in for clinic, it's a very small compensation relative to the actual contribution that they're making and the gift that they're giving in helping to answer these questions.

A. Macdonald

It's phenomenal when you think about it—learning about prevention is a whole science that involves a whole public. You really can't learn without these large public contributions from ordinary people, most of whom are not even sick yet. So as you say, this is not for their own benefit. You make me realize 25,000 people over five years is a tremendous contribution to science.

JoAnn Manson

It is extremely altruistic because they're not looking to have a specific health outcome treated that they already have. Or get access to a specific treatment that they might not have elsewhere, which is also very generous of people to participate in treatment trials and take the chance of getting a placebo. But here, generally healthy people who don't have these conditions, they're just

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trying to help get answers to the scientific questions of whether these interventions can prevent first development of cardiovascular disease, cancer, type 2 diabetes, many, many other outcomes.

A. Macdonald

You couldn't know the answers to your own scientific questions without them.

JoAnn Manson

[00:34:34]

Not without doing the study, yes. It's many, many years. You have to be patient doing research like this; the answers don't come overnight. Even when the intervention ends, there's a long period of continuing to collect medical records to confirm the endpoints. Getting consent for medical record review from the participants, doing data analysis, writing papers, getting papers published. It's a very long extended process. You have to be extremely patient.

You were also asking about other trials and other studies. We did a large-scale trial called COSMOS,² which is a cocoa supplement and multivitamin outcomes study, looking mostly at cocoa extract in terms of cardiovascular disease and multivitamins mostly in terms of cancer. Multivitamins had previously shown, even in our own Physicians' Health Study 2 trial had shown some promise for reducing risk of cancer that may be related to vitamin D and other micronutrients in the multivitamins. So we did this trial; it was a shorter trial, lasted 3.6 years.

But we found some interesting findings for the cocoa extract in terms of cardiovascular death being reduced and also very promising signals for overall cardiovascular disease. We want to follow up with a second trial to see if the cardiovascular outcomes are reduced. We also saw a suggestion of some benefits of the cocoa extract for cognition and slowing age-related memory loss. With the multivitamins the study ended up being really too short a duration, the 3.6 years was probably too short to look at cancer and cancer death.

But we had some very exciting findings from COSMOS showing that multivitamins slowed age-related memory loss and cognitive decline in three separate placebo-controlled studies within COSMOS. Then we did a meta analysis combining these three separate ancillary studies. And in these ancillary studies, cognition was being measured using different methodologies. It was being done by telephone assessments, by web-based online assessments as well as more of a gold standard in person, very detailed cognitive assessment. All of these methods were showing a signal for multivitamins slowing age-related memory loss and having some cognitive benefits. So in the meta analysis we found very strong, highly statistically significant benefits for age-related memory loss as well as global cognition. We want to follow up on those findings with additional studies of multivitamins.

² The COcoa Supplement and Multivitamin Outcomes Study (COSMOS)



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We know nutrition is so important for optimal brain health, and it would be very exciting if multivitamins can be of help, especially in older adults. All of our participants were age 60 and older. I certainly want to highlight that dietary supplements will never be a substitute for healthy diet or a healthy lifestyle, but it may be a complementary approach. And these findings suggest that the multivitamins did have a role in slowing some of the age-related memory loss and cognitive aging among people 60 and older. So we want to look even at some younger age groups and see if there are benefits there, and also see if these findings can be replicated in a separate study.

A. Macdonald

I can see your excitement for now looking at dementia, which hadn't historically been what you and the Division were most focused on. But when people talk about a tsunami of aging and age-related dementias and Alzheimer's, I can imagine the public health impact of some of these studies.

JoAnn Manson

And we're collaborating with other investigators who really focus their careers on dementia and cognition. So it's a really good synergy and collaboration because we can provide the randomized trials and the cognitive outcomes.



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Chapter 10

Chief of the Division of Preventive Medicine: Key Challenges

[00:40:06]

A. Macdonald

So I've been hearing about these things you're particularly excited or proud of over your tenure as Chief of the Division of Preventive Medicine. I'm curious to know what were the difficulties, the challenges, the things that kept you up at night scratching your head as you've tried to move these projects forward?

JoAnn Manson

Well, it's always a challenge getting funding for these studies. These are very expensive studies compared to your more typical grant, which would be maybe one quarter, one fifth, the cost per year. Very often it is challenging making a case to review committees that this is an important trial to do that is worth this larger budget. Even though we do extremely cost efficient trials and our trials are even 1/5 to 1/10 the cost of some of the other trials that are often done by industry or some of the treatment trials. Still, it's expensive in comparison to your more typical cost of a typical budget for a grant.

I would have to say that I sometimes lose sleep over getting grants funded and keeping the Division running because the infrastructure of the Division is heavily dependent on having sources of funding being able to support staff. We never want to have layoff of staff. So to keep funding for them going, we need to get new infusions of funding and new studies going. Long term follow up sometimes after an intervention has ended, it can be challenging to get the long term follow up funded after the trial. Because there are some findings that emerge longer term. We had some really interesting findings recently with the low fat dietary pattern in the Women's Health Initiative. With longer term follow up, like 20 years, there was a reduction in breast cancer death. Sometimes the very long follow up will provide additional results of interest. So maintaining funding is always a challenge.

Promoting faculty—you know, we are very happy our Division has a good track record of getting faculty promoted. We have a very large percentage of our faculty who are full professors or associate—higher rates than many, many other divisions. That's good. It's helpful, these resources that we have. Mentorship also helps to advance the careers of faculty. That's a major mission; that and the educational mission of the Division are really important. But you worry about some of the early career faculty. Are they going to be able to stay funded, or will they end up wanting to leave an institution where it's mostly soft money? You know, they need to get grant funding, plus there are opportunities in industry, a lot of opportunities in the Boston/Cambridge area.



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A. Macdonald

So retention, and the ability to keep people moving on their career paths.

JoAnn Manson

Right. Helping, especially the early career faculty, advance their careers. Providing the mentorship to help them with that by helping them to get grant funding so that their careers will advance.

These are all challenges and actually everything has gotten more difficult over time. I would have to say that in the last 5 to 10 years, there's less funding available for some of this research. It's more of a challenge to get trials, especially large randomized prevention trials, funded. Some of our collaborations are private-public-academic collaborations, some of those are more challenging. So these are the kinds of things that are difficult.

A. Macdonald

[00:45:11]

I was going to ask you about that. As you were describing things I was going to say, has the funding climate changed? And yes, I'm hearing that it has. But has it changed especially for preventive health research, or has it changed for every kind of health research? Or are you seeing different elevations in the landscape of who gets funded and who has less funding available, in terms of the kinds of things you research?

JoAnn Manson

Yes. I think it's a good question. I've seen the funding be a challenge for many, many departments and divisions. So I would have to say more broadly, there are challenges. But I think when you have a division based largely on very large randomized clinical trials that require a lot of resources and support, there may be some additional challenges with that. So it's difficult. I certainly have lost some sleep over it at times, but I'm staying really optimistic. We have several new ideas for randomized trials. We're excited about the ideas and are pursuing funding for them. If even half of these ideas were to end up being funded, that would be good, although we're hoping for an even larger percentage than that.

A. Macdonald

But that would not be bad. Half would be a stellar record, I would think?

JoAnn Manson

It would not be bad at all.

A. Macdonald

Okay. We've talked about each stage of your career, what it was like to be a woman and a minority as a woman. Now you're in leadership roles like the one you're describing and making these decisions. I know you were the first woman Chief of the Division.



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JoAnn Manson

Yes. But the division isn't that old.

A. Macdonald

Yes, right. But I would imagine you were one of few women chiefs of a division. In general, in terms of being a leader in health research and, and health education, academic medicine, women are not at par in those leadership roles the way they are becoming parity in medicine. What was that like? Do you feel there were unique challenges you faced as a woman leader? We've talked about in your past career, how you often felt this is individual, it's not a structural sort of thing. But I'm wondering, as a woman leader, how you envision the special challenges to women, whether or not this is a bad egg here and there, or if this is something that needs more systemic attention to help women achieve parity?

JoAnn Manson

I think it does need some systemic attention. I think that the burnout rates among health care professionals, any of these physician scientists and researchers, tends to be very high. The burnout rate among clinicians, those who focus on clinical practice, tends to be quite high also and higher among women than men. That has been seen in a number of studies. So I think we do need more attention to the challenges of juggling, work-life balance. Also, women continue to have the majority of the child care responsibilities in most of the cases. So this is a real concern. For women to be able to juggle all of the responsibilities of an academic career, certainly a physician scientist where you're trying to blend clinical work and research, and any leadership role, it is very, very difficult. I mean, the hours are really long, and there isn't the kind of support system that you really would want to see in place. I think that our institution tries very hard to help with this, and they do provide a lot of resources. Yet child care remains a very, very great challenge pretty much throughout the country and certainly in the area where I am.

I think that we do need more attention to this issue, but I feel it is really gaining some attention. It is clear that there are fewer women progressing to associate professor, especially full professor academic ranks, than would be expected based on the number of decades since there's been relative parity in number of medical school graduates who are female versus male. You would think that leadership positions –

A. Macdonald

The pipeline would have delivered by now.

JoAnn Manson

[00:51:19]

The percent who are full professors, it would have delivered by now. And the numbers are much lower in women especially when you get to positions such as chair of a full department, a



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Department of Medicine, a Department of Surgery. There's a very big difference in the percentage who are women versus men. So I think a lot more work needs to be done in this area. I think some of it really does need to be institution specific. I don't know that mandates coming externally will help that much.

But a big issue also has been even something as simple as salary parity and equity. When it has been looked at really carefully, just as in the general workforce, there are these salary gaps where women are so disadvantaged in terms of wealth and their average salaries and accumulation of wealth over time. I think this is not something that medicine and research and science is completely immune to. I think that there are some salary equity issues that also go on within that field. So it needs more attention, needs more awareness.

I think especially the concerns about burnout rates and many women going to part-time because they are so burned out by the work.

A. Macdonald

They can't imagine a life that makes sense.

JoAnn Manson

Yes, trying to juggle so, so many responsibilities. I do think it's really important for partners to be supportive and to step up to the plate and really share in child care and make work-life balance more feasible for women.

A. Macdonald

And for you yourself. JoAnn, when you were sitting as a leader in these positions, did you have to argue for salary parity? Did you have to fight some of these battles? Did you feel, "if I don't advocate for me, these things will not happen"? Or did they just unfold?

JoAnn Manson

I didn't feel like I was really actively battling against the system. I think our institution does try very hard to have parity and equity. They worked very hard on that. There also has been an initiative on salary equity issues that is more recent, but we really try to pay attention to that in our division. Pretty much throughout the Brigham and Department of Medicine, there was a lot of attention, and maybe even throughout the Mass General Brigham system more widely, there's a lot of attention to that issue.

I don't want to make it seem like it was a breeze. Everything wasn't just falling into my lap; I felt I had to work extremely hard for everything that came my way.

A. Macdonald

Right.



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JoAnn Manson

But I also couldn't point to that many examples where I was really being treated unfairly. We do try very hard to be equitable regarding a lot of the decisions that are being made about leadership opportunities and salary in the division. But I think individual leaders really have to make it a priority.

A. Macdonald

[00:56:15]

That was my next question. As a woman leader and one of the first as Chief of the Division, have you yourself been giving special attention to these questions of gender parity, inclusivity, work-life balance? How have you been an advocate for the things you recognize as being sort of systemic, now that you're in a position where you have some authority to move some of that agenda forward?

JoAnn Manson

I feel I have actually really prioritized that, but I don't want to do it to the detriment of male faculty. I've been concerned about them as well. I will say that we have a really, really high rate in our division of women faculty being promoted to associate and full professors. I've made that a real priority that we don't delay. Once they've reached a critical mass of accomplishments and publications and research, I try not to delay at all and just move people forward to promotions. So we do have a really, really good record in terms of the percentage of women faculty in our division who are associate or full professors.

But I don't think it's been at the expense of the males because I'm also paying attention to putting them up for promotion when appropriate. But I think what can sometimes happen in some programs—I'm not saying it happens at the Brigham or Mass General; in fact, it may be less likely to happen here and maybe more likely to happen in some other programs—women faculty can feel they've been overlooked for promotion. They feel they really have that critical mass of research achievements and publications and someone who's more junior than them with fewer accomplishments, who's a male, just got promoted to associate.

And because the division chief and department chair play a very big role in putting people up for promotion, it is important to constantly be keeping that in mind that you don't in any way disadvantage one group compared to another. I really make it a priority that in my regular meetings with faculty to go through their CV and look at the various accomplishments, grants, and publication record to see if they're ready for promotion to the next stage. That is something that is really important to me, and I think we're doing a good job in that regard.

A. Macdonald

I don't doubt it. But I just wondered, has being a woman Chief helped avoid some of the overlooking, some of the dismissive kinds of positions?



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JoAnn Manson

I think yes for promotion and salary equity issues; I really keep an eye on that to be sure there aren't the disparities. We have pretty good evidence that there aren't inequities by sex in our division.



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Chapter 11

The Honor of Mentoring; The Evolution of Medical Education

[01:00:06]

A. Macdonald

I realize we're just a little over 3:00 p.m. Do you have a little time for me to ask some questions about mentoring? In your last answer, I get a sense of how important mentoring the careers of others has been for you. I'd love to hear you elaborate a little bit on that. What has the world of mentoring meant to you as you've achieved the ability to be in the position to be a mentor?

JoAnn Manson

I feel when you become a more senior investigator or faculty member and are in a leadership position, it is just *tremendously* important to prioritize mentoring and helping the early career faculty, early career trainees to advance in their careers. I actually consider it a tremendous honor to be able to have that kind of role in the lives of many of the faculty in the division. I can really advocate for them, I can work with them to see how I can help advance their careers, help them with grants, get funded, help provide opportunities to speak at meetings, to become members of a professional society, win awards, sponsor them for awards, and just really help in whatever way I can to advance their careers. In some ways, it has an analogy with what I was saying earlier about the way I feel about clinical practice, that it's such an honor that patients will entrust a doctor with their care. I feel it's such an honor that they're entrusting me with their care and that they're confiding so much in me. It's somewhat similar with mentees that it's an honor; it's really a privilege to be able to play an important role in their lives, in their careers, to help them develop into as successful a researcher, investigator, clinician as they can be.

So I feel that, and I'm very committed to mentorship. It can be a substantial time commitment, I won't deny that. It's very rewarding and gratifying to do it, but it can require large amounts of time, which I'm more than willing to do. But what ends up happening is that your schedule does not get lighter, you know?

A. Macdonald

Right.

JoAnn Manson

Some of the things that you were previously doing and focusing on, you may be able to do a little less of those things. But it gets replaced by attending meetings, serving on search committees, promotions committees, and doing a lot of mentoring and teaching. I do some teaching, particularly some lectures at the Harvard School of Public Health. I was one of the directors of a course at Harvard Medical School on sex and gender-informed medicine that we got started about three years ago. It was very exciting to develop the curriculum along with my colleagues for that course. Of course, third and fourth year medical students are a big time commitment, but



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it was very rewarding. So I do some teaching, especially lecturing in different courses and then co-directing that course. But most of my work with trainees and early career faculty is in the mentorship role as opposed to a tremendous amount of in-class teaching.

A. Macdonald

[01:05:08]

I'm just thinking about the course you developed on sex and gender medicine; it's almost full circle, isn't it? Because I remember you telling me about being a medical school student and recognizing the gaps in the curriculum that just didn't address the female body as an entity. It was defined instead by the male model. And there you are later in your career actually making curriculum.

JoAnn Manson

Exactly.

A. Macdonald

It really is a wonderful, kind of arc to think about you as a student and now you as someone setting curriculum for students.

JoAnn Manson

I did think about that a lot. Often, with the co-directors of the course, we would we would talk about, "Boy, we wish there had been a course like this for us when we were in medical school. Let's develop a course that we would have wanted to have when we were in medical school." Because it was not like that, there wasn't teaching of that nature. Our course was focused not only on women's health and sex differences in medicine. It also had a focus on LGBTQ health and that area. So it was providing education in an area that most medical schools do not provide.

A. Macdonald

Yes, it's fabulous to think about the arc and then think about you changing things for a new generation of learners and practitioners and researchers. I think that's brilliant. I am cognizant we are running over. Do we want to leave a set of questions for next week, or we can keep going?

JoAnn Manson

How much time do you think we would need for discussing the other questions?

A. Macdonald

Yeah, I would say 20 minutes to half an hour because I have some questions about your involvement with professional organizations. I'd love to hear more about that, about your overall contributions to our knowledge of cardiac cardiovascular disease, and then sort of some reflective questions about looking back and looking forward.



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JoAnn Manson

How do you feel about continuing to go for that period of time?

A. Macdonald

I'm game if you are.

JoAnn Manson

I will need to make a quick phone call to find out if someone needs me for something, but I will be right back.

A. Macdonald

That sounds like a good plan. I'll pause the recording, and you do what you need. Wonderful.



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Chapter 12

A Pioneer in Women's Cardiovascular Disease

[01:08:03]

A. Macdonald

We were just speaking about the different roles you've played in teaching and mentoring. One of the questions I wanted to ask was about your involvement with different professional organizations. The American Menopause Society, for example, you were the president in 2011 - 2012. And I know you've done a lot of work with the American Heart Association because I read in one of their statements that "Much of what we know today about women's and cardiovascular disease is a result of Dr. Manson's pioneering efforts."

JoAnn Manson

Well, that's very kind of them. Very. I wouldn't necessarily agree with going that far, but—

A. Macdonald

Well, they certainly felt that! I wanted to know if you might want to reflect for a minute about women's health and cardiovascular disease today. What do we know that we didn't used to do? What are the key findings you've contributed to and what remains to be explored? So I'm interested in cardiovascular disease. Given that wonderful statement from the American Heart Association, I gather they have been a partner for some of your research for some time.

JoAnn Manson

Well, cardiovascular disease is still understudied and underappreciated in women in terms of women's health. It is very surprising that the leading cause of death in women would be so understudied, and that women themselves would often not be aware that cardiovascular disease is their greatest health threat. Many of these surveys show that when women are asked about their greatest health threat, many times they will say breast cancer, even though six times as many women die from heart disease each year as from breast cancer. So the awareness level is low.

Women tend to have delays in seeking medical care. They tend to have more advanced cardiovascular disease by the time of diagnosis. And very concerningly, they're less likely to receive guideline-directed care: to get statins for lowering cholesterol levels, to get good control of blood pressure. They have a higher rate of dying after a heart attack; younger women especially have higher case fatality from heart attacks and coronary heart disease. So there are a lot of concerns in that area. I think that the underappreciation is not just among women; it's also among clinicians who are often not thinking heart disease is also a woman's disease. There's even some evidence they're less likely to be taken to an emergency room for chest pain, you know, with the ambulance siren going, lights flashing.



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A. Macdonald

That it's not a crisis moment in the same way.

JoAnn Manson

[01:11:22]

Right. It's less likely to be believed to be due to a heart attack with these symptoms going on, and often there's delay in getting medical care. Those issues are really concerning. We know that women have some differences in symptoms. I mean, chest pain is still the most common symptom in both men and women. But women are more likely to have some of the atypical symptoms, pain in different areas, including jaw, neck, also nausea, shortness of breath. Some of those atypical symptoms may be more common, symptoms may be a little different. There needs to be a better recognition of that among women and the clinicians that may be caring for them.

There are many other differences. Diagnostic tests have different reliability in women versus men. Women have certain differences in terms of risks. Women are more likely to have small vessel, what's called microvascular, disease. They're more susceptible to stress cardiomyopathy, which is believed related to surges of stress hormones such as adrenaline. They're more likely to have a type of heart failure called "heart failure with preserved ejection fraction" for which there's less known about ways to treat it and to improve outcomes. Women are more susceptible to that type of heart failure. Women are more likely to have strokes when they have the condition called atrial fibrillation where there's already an increased risk of stroke. But it's particularly high in women compared to men. They're more likely to have death from cardiovascular disease in the setting of atrial fibrillation. So there are a number of these differences and very little research.

And this is just a small sampling; there are many other differences. But very little research has really focused on understanding sex differences in cardiovascular disease and understanding ways to improve care for women in the prevention, diagnosis, treatment—ensuring that some of these conditions, such as heart failure, preserved ejection fraction, atrial fibrillation, stroke risk, are directly addressed in terms of ways to improve outcomes. Very little known about microvascular disease. How do you actually treat that and help to improve the prognosis of women?

Another issue that is really important is that there are certain stages of life that provide windows into a woman's cardiovascular risk, and generally very little is done to take advantage of this. For example, we know that complications of pregnancy, such as pre-eclampsia, hypertension in pregnancy and gestational diabetes, are major risk factors for cardiovascular disease or type 2 diabetes. Very often women with that history in pregnancy aren't even fully aware that they have that history. It's not often asked about by the doctors taking care of them after the pregnancies. This should be at least a marker of increased risk, these complications of pregnancy should be understood to be a marker of increased risk, if not directly contributing. There needs to be even more vigilance about modifying lifestyle behaviors, controlling blood pressure, for women who had preeclampsia. She's at very high risk of developing persistent hypertension afterwards and



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having an increased risk of cardiovascular disease, heart failure. So it's really important to control risk factors, control blood pressure, control cholesterol, control blood sugar. If diabetes develops, monitor these women more closely for preventing cardiovascular disease. These are just a few of the areas where I think so much more research is needed.

But we already know there are these differences. And the research is still so limited on how to provide sex and gender-informed care for women with these conditions that are really either specific to them or predominant in them.

A. Macdonald

[01:17:03]

Yes, I listen to you talk and I think, "Well, I knew symptoms for heart attack were different in men and women." But the range of things you describe as different I certainly wasn't aware of! When you talked earlier about the funding challenges for research, what is the climate for women's health research today? Early in your career and around the Women's Health Initiative, there was a bit of a political movement to put women's health on the agenda at the federal level, at the NIH.

JoAnn Manson

Right.

A. Macdonald

Where does that sit today? Is that part of the reason we know all these differences, but we don't know what to do about them or how to mitigate them?

JoAnn Manson

Well, there has been some funding specifically allocated to women's health in the current administration and some requests for funding. Those requests will have to be approved by Congress and go through the whole political process. The overall amount of funding is quite limited. When these different studies have looked at how much funding is allocated to research for conditions specifically in women or predominantly in women compared to how much funding is allocated to conditions specific to men or predominant in men, there is a big difference there. Definitely there is less funding for the women specific or women predominant conditions. I think that there's a lot of advocacy and activism towards changing that. But we'll have to see. Time will tell how much of that will translate into actual major funding initiatives and changes in the health care system, which right now has a lot of issues.

I think that very often women may feel that their questions and concerns aren't being addressed. We talked about menopause. We talked about how rarely women will be asked questions during their visit or really be given an opportunity to discuss some of those concerns that they may have and how many women are having difficulty finding a clinician who is really fully informed or reasonably informed about menopause and options, hormone therapy, other options for



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treatment. Not so much to prescribe hormone therapy for everyone, but to have a conversation and to help in the shared decision making process. I think when women can't get these answers, they feel that, you know, they may be missing out on really important opportunities to, improve their quality of life, improve overall health. So it is so important to bring all of this into the conversation.

A. Macdonald

Yes, thank you for that.



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Chapter 13

The Doctor is In: Empowering the Public to Improve their Health

[01:20:30]

A. Macdonald

The record of publications in your CV is exceptional. Everybody comments, “one of the most cited researchers and among the very top cited women researchers.” But you've had a very active voice as a population health leader, publishing popular books, publishing regular columns, trying to educate the end user of our health care system, as well as the clinicians and the scientists. What made you take on that role of advocating in public for what we know and what people should be aware of around exercise, supplements, menopause, etc. Your publishing record just on the public side, it's extensive. I'm not going to even touch the scientific side; we'd be here for two days! But not every scientist, and not every leader of scientific research, spends as much time, energy and effort in educating the public as I know you've done. I'm very curious to know when you started to see yourself in that role, why it matters to you? What is this story?

JoAnn Manson

I'd have to say that it started early because I've long believed that knowledge is power if it's implemented, if there's something done with that information. I think it would be so unfortunate for the general population and the public not to have information about ways that they can take charge of their health, things that can be done even on an individual basis.

This certainly doesn't suggest that there aren't a lot of structural barriers to making lifestyle changes because this is something else we talk about a lot. That, in fact, it's not totally equitable in terms of who has access to physical activity, safe parks, safe neighborhoods to walk in, access to nutritious foods, affordable foods.

A. Macdonald

If you're working three jobs at a time, if your income is dependent on that.

JoAnn Manson

There are social determinants of health that are tremendously important. We actually have recently written an article on this very subject. On the importance of behavioral factors, but also social determinants of health, how much they're contributing. But having the knowledge, for many people, will help them to make better choices about their own health. That can go such a long way because if you look at the percentages—we talked earlier, the percentage of these chronic diseases that are preventable, it's really astounding. We're talking for type 2 diabetes 80 to 90%; for heart disease close to 80%; stroke close to 70%; cancer close to 40, 50%; dementia close to 40% or 50%. These are really highly preventable conditions. Some of it is genetic, and some of it is actually not going to be that changeable, but a lot of it is.



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I think if people have the knowledge and they have the information....Even if it's as simple as we saw in the study, that walking 30 minutes per day was associated with a 40% lower risk of heart attack, coronary heart disease. Many people do find that walking is accessible and very inexpensive, just a pair of walking shoes. Having that information, which I would often discuss with my own patients—I would write prescriptions for physical activity, and I would very often try to tailor it to what I thought was the right level for them or good level for them. It was generally 30 minutes per day. But if they had some underlying health conditions, it might start out more as 10 minutes and gradually build up to 15, 20. With some of them who are really interested in being more active, it would be for more vigorous exercise and a longer duration. I actually think writing a prescription for physical activity and exercise can be one of the most important prescriptions that a doctor writes all day. There's so much that is within our control, even if everything isn't, even if there are some examples we can all come up with where it's just, you know, a lot of disparities and inequities. There are certain things that with the knowledge, certain choices can help to improve health.

A. Macdonald

[01:26:17]

And knowledge disparities are as real as any other kind. So I think, yes, you are addressing social determinants of health when you impart knowledge.

JoAnn Manson

Yes. This information that I have prioritized over the decades to talk about when I get called by a reporter instead of saying, "My schedule's kind of busy, I don't think I can do it"—I will very often try to find the time because I feel that these media outlets do generally a good job of getting information out to the public. Many people will use that information, and it could improve their lives and their health outcomes and their quality of life. So I've been very open to it.

I would have to say that from my earliest years in research, I was being contacted a lot by the media and a lot by women's magazines as well. I actually was asked to do a column, a health column, for Glamour magazine for many years, which probably is surprising to you.

A. Macdonald

I saw that and I thought, "Wow, did you have to have a special photoshoot for that?" How did that go?

JoAnn Manson

Oh, hold on. My phone is ringing. Hold on.

Tape paused.



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JoAnn Manson

It was called *The Doctor Is In*. I would give advice on a lot of issues across age groups. Some of it was for very young people, even adolescents, related to alcohol and diet, and different health problems that they might be concerned about. I did that for many, many years.

A. Macdonald

The readers asked you questions?

JoAnn Manson

The readers would write in questions. The question would be there, and I would provide an answer to the question. It was a magazine that came out monthly, and it was kind of fun because my kids at the time were teenagers and they would read it. I would bring home a copy or they would sometimes find it in a drugstore and they would say, "I was looking for the last issue to see your column." It was kind of fun. [Laughs.]

A. Macdonald

Something accessible even with your own family, right?

JoAnn Manson

Even if I didn't bring it home. So I thought that being able to provide health-related information to people, across age groups, even very young people who had concerns about different topics, I thought I might be able to contribute something. I was happy to do it. Of course, these are all things that take some time.

But, yes, some of the research would be of interest to magazines; women's magazines were interested in some of the lifestyle factors and things that could be done for improving health or reducing health risks. I decided early on that I was going to be receptive to doing interviews of that nature because I just thought it was important to get information out there. It was almost a responsibility. If it's information that's usable and could actually be of help to people, they would be able to take charge and actually make a change that could improve their health.

I just thought this is a way to get the information out there because so often that information isn't out there. So over the years, I have done a lot of interviews. In the last 12 years or so, I've been doing videos for Medscape. A lot of topics. It's usually on a more recent publication or article where I think that there's some important clinical message and I'll do a video on that topic.

I've done videos for some other organizations, and I give a lot of grand rounds and presentations. Now it's more virtual than it used to be, but I give a lot of seminars and talks at conferences. I have been very open to that. Although eventually I am going to have to really reduce the amount that I'm doing as I try to reduce my schedule a little. Not be eliminated completely, but just, you know, kind of dial down a little.



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A. Macdonald

[01:31:59]

Right. Did it take the development of a different skill set to speak to these different audiences? Do you mentor your younger, more junior colleagues, in this particular role and obligation of scientists? Do you feel that important to pass on in some ways?

JoAnn Manson

In some ways, it's just serving as a role model. They're seeing me do that, and I hope that they'll pick it up as well. They're often offered opportunities because many of the faculty in our division are doing public health related research and they're independently getting called by media outlets to discuss their work. They've been, from what I've seen, quite open to doing interviews and spreading the word about the findings, especially if it's ready for prime time and it's something that relates to a modifiable factor, behavioral factor.



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Chapter 14

Looking Back and Looking Forward: Final Reflections

[01:33:15]

A. Macdonald

I think we've covered a tremendous arc of a very rich career. I know we could talk for three more hours, but when I listen to what all you're carrying and doing, I think that that's not a great idea. [Laughter.] I'd like to ask a bit of a reflexive kind of questions about the overarching scope of where you've been. When I look at your awards—as I'm doing some background research, it's three and five pages of awards, and I haven't even scratched the surface! I won't ask you about all of them, but is there a recognition or award that was particularly significant to you?

JoAnn Manson

I think first, I'm tremendously honored when I do receive these awards. I always feel really humbled by being thought of for these awards. I'm often very surprised when I'm told I'm getting this award. I think the ones that have meant a tremendous amount to me... they all mean something to me. So I don't know.

A. Macdonald

When I asked you to reflect like that, I'm putting you in a position. But it's just for brevity. It's not because you don't think other ones are important.

JoAnn Manson

Right. I think that some of the recognitions I've gotten from the American Heart Association have been very meaningful to me. I think it's a wonderful organization that does so much. This mission of trying to prevent cardiovascular disease obviously puts a lot of emphasis on prevention and getting the word out about prevention. So being honored by the American Heart Association means a lot to me. And I've been very fortunate to have received a number of awards from the AHA, including Distinguished Scientist Award, Population Health and more recently, Research Achievement Award. So those mean a lot to me.

This Renaissance Woman award from the Women in Medicine Legacy Foundation, this is also extremely meaningful to me. Over the years, I've seen many recipients of this award. I've gone to their presentations and have had very deep admiration for them and for the importance of the award. You know, so this is personally very impactful and meaningful to me.

I think having been elected to the National Academy of Medicine, Institute of Medicine, was very important to me in terms of I'm really honored by it. It's an organization that does wonderful work, and I've served on many committees and really tried to contribute to the National Academy. It's a recognition, but it involved service. That's really what it's about, it's not just



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honorific. So that's been very meaningful to me. I gave a talk at the National Academy of Medicine's conference last year which focused on women's health.

I don't know how many to say; I was recently named a master of the American College of Physicians. That is meaningful to me because of, you know, the tremendously important role the ACP plays in physician education, especially internal medicine education.

I will mention one other thing, which is a recent award that I'm going to be receiving, the Outstanding Clinical Investigator Award from the Endocrine Society. That means a lot to me because that is my specialty, endocrinology, and to be recognized for clinical investigation by the Endocrine Society is very meaningful to me.

Maybe a last thing I'll mention. The Bernadine Healy Award for Visionary Leadership in Women's Health was also very personally meaningful to me because I knew Bernadine Healy quite well. She was the director of the NIH who got the funding for the Women's Health Initiative and the first woman director of NIH. And she was a wonderful person. So impactful herself and to get an award in her name was very meaningful to me. So I don't know if I'll mention too many more.

A. Macdonald

[01:39:08]

No, that's a wonderful picture. It helps paint what has been your career and the culmination of your career, recognition of that. To be included in that echelon of people in Bernadine Healy's memory or honor is a great testament to what you've done to move the needle on women's health. So I can see that that's meaningful.

Okay. When we talk about achievements, and this has been a career of achievements, I always like to ask people: is there anything you would have done differently? Were there moments of failure that were instructive in some way? If you look back, would you have done anything differently? Were there points where you questioned what you were doing? Just asking you to think back over your career in those kinds of ways.

JoAnn Manson

It's a very tough question. I think that there are many times when I maybe would have somewhat changed the focus of different grants to maybe make them more fundable. I've had generally very good luck with getting grants funded, but there are always a few areas where you have some challenges. Maybe I could have changed direction a little more quickly.

Maybe I'll say something about the Women's Health Initiative and the Nurses' Health study, because I would have wished that some of the research delving more deeply into the differences by age and time since menopause; some of these factors could have been done really early in the process. Though I'm not sure exactly how that would have been done logistically, just because of



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how complicated everything was at the time, with a trial being stopped early and information needing to get out to the public. But I know that there were certain messages that maybe if they could have been delivered even earlier, it would have been better, but there are some natural delays in doing the research, doing all the analysis and getting everything out there. So that might be another example.

You know, it's really a tough question there. I can think of a few faculty members I wish I could have provided them with some additional bridge support. That's always complicated, and very often the funding is just not available to do that. But there are some faculty members I've worked with over the years where I've wondered—you know, they may have gone to industry or to a different institution, and maybe I could have kept them or provided them with that bridge to help them even more. Generally, I have felt really good about how things have gone with our faculty and helping to support them in their careers. But I think when you're working so many faculty members over decades, there will be a few examples where you wish you could have done more.

A. Macdonald

Yes. Those are some of the professional decisions you wonder about. On a personal level, would you have done anything differently, the work-life balance that we've talked about, the kinds of things that we've addressed over the course of our interview. Would you have any advice for someone else about things they might want to think about that you gleaned from having done it?

JoAnn Manson

[01:44:08]

I would say that if I could go back, I would have taken more vacation time with my family and with my kids when they were young, even though we did always take some vacation time. You kind of think back to all the stresses at the time and how, you know, maybe an additional week off. Of course, we tried to work it out according to their school schedule. So, maybe taking even more time off, having more of those memories of family together or leisure time, taking it easy. I don't have as many memories of that as I might have wanted.

I have to say I've never heard the kids complain about it; they talk about some of the great vacations, some of the times they really enjoyed being together and going various places. So it probably was okay, it's not like anyone was harmed by it. But a little more time off probably would have been good.

And last thing might be email. I really regret how much time I've spent on email. I have a pretty good system of dealing with email, but I actually get 550 to 600 emails a day.

A. Macdonald

Oh, I can't even imagine.



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JoAnn Manson

So it's always such a challenge. There are certain things, I do have different ways of dealing with it. I try to have certain goals for the day that I get to before email.

A. Macdonald

Before you even open that.

JoAnn Manson

Unless something that might be urgent, that I was expecting. But then there are hundreds of emails left to later in the day, and it can become very challenging.

A. Macdonald

Oh I can imagine! Early in your career, before email was a thing was it...

JoAnn Manson

This is something since the late 1990s early 2000s, so certainly the really early years of my career there weren't emails. But there were other communication challenges, other things to take your time. I was getting a lot of voice mail.

A. Macdonald

Right, of course. That would have been the thing.

JoAnn Manson

[*laughing*] Which in some ways those were...

A. Macdonald

More onerous than an email which you get to later, yes.

JoAnn Manson

Or so and so needs you to call them back and then you have this period during the day for me to leave open for a lot of return phone calls. So I don't know that email has made it that much worse, but I think just the ease of other people reaching you and sending you questions at any time. I get a lot of questions from the general public. So I have various strategies and approaches to deal with this. But, you know, it's always...

A. Macdonald

Tough! You should give a talk just on that because many, many administrators probably struggle with the same problem.

JoAnn Manson

Yes, in some ways I'd like to go to a talk given by someone else who's figured out how to handle this [*Arlene laughs loudly*]. But it can be very challenging [*both laughing*].



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A. Macdonald

I can imagine. Okay. Well, let me ask you a final question, and then we will wrap up our time together. We've talked a little bit about what you thought the significant challenges were today to research, so I won't ask you that again. But given the vast amounts of mentoring you've done, what are your hopes and your fears for people coming into the fields of health and preventive health research today? What do you worry about for an upcoming generation; what do you hope for them, and what do you fear for them?

JoAnn Manson

[01:49:18]

I hope for a more favorable funding climate so that they're not dealing with the struggles that many of us overall are dealing with, especially in recent years. I also hope that there will be additional approaches, especially for early career faculty, to make their career advancement a little easier. There are training grants, but then once the training grant is over, moving into being fully supported by R01s and these larger grants is very, very challenging. So I hope that there will be more options and a better funding environment for them.

And I think that burnout is a very real concern. I have seen, especially among clinicians, so many people struggling with this. So I really hope that the environment will improve in that regard, where burnout is less of an issue. There are a number of strategies in place to help, but, especially with electronic health records, things have gotten tougher for clinicians. I think there are several strategies, approaches being tried out to make things better in that regard. But for the physician scientist, it is a real struggle and a real challenge to be juggling clinical work and research. It's not an easy row to hoe. More help with that, better mentorship in general and also more resources to help people get through, especially the early training periods.

We talked about funding, but if there could be more public-private partnerships, really good ways to increase the amount of support available for research and for advancing science. Having investigators more easily navigate that system, because so often it's an either/ or. You go the industry route or everything is the NIH route. There are some public-private partnerships. But I think more in that regard would be very helpful.

A. Macdonald

Wonderful. Well, I can't thank you enough for a grand tour of a very interesting and intricate career that's worn so many hats and achieved so many things. And to read over and over, as I'm preparing for these interviews, that you have been moving the needle on women's health, preventive health in so many different disease categories. And to hear you talk about what's yet to come as you continue to be Chief of the Division and to lead these initiatives. It's really been a pleasure for me, just a delight to be able to talk to you about what a life in science and in medicine and in research has really been about. It's been lovely. Thank you so much.



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JoAnn Manson

It's been a pleasure for me, too, Arlene. I really enjoyed it. It's really been a trip down memory lane in many ways. It's been interesting and enjoyable. Thank you for taking the time.

A. Macdonald

Thank you. And I'm thanking you from the Women in Medicine Legacy Foundation. They will be delighted to be working with your oral history, as well as the Countway Library. So I will pause our recording for the last time to say a quick goodbye.